28th August 2023

Dear Parliament of Australia,

I am an Accredited Practising Dietitian with a Doctor of Philosophy in Medicine and Health and a Master of Nutrition and Dietetics, both awarded by the University of Sydney in 2022 and 2017 respectively. I have been working with Australian adults on a one-to-one basis in clinical practice for the last six years, and I have been formally evaluating and contributing to the scientific literature on dietary interventions for diabetes management as part of my PhD thesis for the last 4 years. I am writing this submission to offer a summary of the evidence and to provide justification for why the Standards of Care for Diabetes Management need to change. Specifically, the consistent promotion of low-fat high-carbohydrate diets for all individuals with diabetes must be reconsidered, and professionally supported low-carbohydrate diets should be offered as a therapeutic option for diabetes management.

The information contained within this submission has been taken from my published thesis available from the University of Sydney Library. The primary aim of my thesis was to explore the use of low-carbohydrate (LC) diets for the management of diabetes, including the practicalities and effect(s) of developing and implementing a LC diet specifically for adults with T1D.

Please do not hesitate to contact me if you have any questions or would like further clarification on the topics discussed within this submission.

Warmest regards,

Dr Jessica Turton | PhD, Dietitian & Nutritionist

1. Diabetes in Australia: Overview

Diabetes mellitus was defined by Osler and McCrae in 1921 as a 'disease of metabolism in general with especial disturbance of carbohydrate metabolism in which the normal utilisation of carbohydrate is impaired with an increase in the sugar content of the blood, and consequent glycosuria'.(1) This 'disturbance of carbohydrate metabolism' develops as a result of insulin resistance and/or insulin deficiency given the primary role of insulin is to restore normal blood glucose levels after they have risen. If glucose levels rise in the context of insulin resistance and/or insulin deficiency, excess glucose remains circulating in the blood, and cells that should otherwise be taking up glucose (such as brain, liver, and muscle cells) become energy depleted. In Australia, diabetes affects one in 20 people, meaning that over one million Australians have a known diagnosis of diabetes,(2) and it was ranked seventh in the leading causes of death in 2021.(3)

1.1 Type 1 diabetes

Type 1 diabetes (T1D) is caused by an autoimmune process that destroys the islet cells in the pancreas that produce insulin, resulting in insulin deficiency.(4) . Without insulin treatment, T1D leads to life-threatening ketoacidosis (a state where both glucose and ketone production is excessive and uncontrolled due to insulin deficiency). Currently, there is no cure for this condition and people living with T1D face the incredible challenge of manually regulating blood glucose levels for their lifetime.

Every day in Australia an estimated eight people are diagnosed with T1D, and over 50,000 new cases were recorded between 2000 and 2020.(5, 6) Although T1D was previously referred to as 'early-onset' diabetes, 35% of new cases in 2020 were among adults >29 years old, with data suggesting that Australia has the eighth highest rate of

adult-onset T1D.(5-8). In 2018, T1D accounted for around 17,000 disability-adjusted life years (DALY) in Australia, with 8,100 years of life lost due to fatal burden and 8,800 years of life lost due to non-fatal burden.(5, 9) The average annual cost of T1D is \$22,000 per person, with the majority of this attributed to the high prevalence of diabetes-related complications.(10) An estimated 40% of people with T1D in Australia have one or more complication, including cardiovascular disease (CVD), kidney disease, neuropathy, limb amputation, and blindness, with costs being at least five-fold higher compared to those without complications.(10)

1.2 Hyperglycaemia

The primary management target for diabetes is to maintain healthy glycaemic control, as measured by glycated haemoglobin (HbA1c \leq 7.0%).(11-13) Maintenance of HbA1c within this target range over five years has been associated with reduced risk of CVD, neuropathy, nephropathy, and peripheral vascular disease in individuals with type 2 diabetes (T2D) (n=3,067).(14) In individuals with T1D, the Diabetes Control and Complications Trial (DCCT) demonstrated that achieving a median HbA1c level of 7.0% reduced all cardiovascular and microvascular complications of diabetes.(15, 16) Sadly, the average HbA1c of people with T1D living in Australia is 8.4%,(12) and data from 324,501 individuals from 19 countries worldwide reported that only 16% achieved an HbA1c <7.0%, suggesting the majority of people living with T1D are unable to control their blood glucose levels within safe target ranges.(17)

1.3 Hypoglycaemia

Hypoglycaemia is a term used to describe low blood glucose levels and is commonly defined as blood glucose <4.0 mmol/L.(13, 18-20) Severe hypoglycaemia is generally

defined by the requirement of some form of assistance from another person for recovery, and is considered a medical emergency which can progress to brain damage, seizures, coma, and death if not effectively treated.(13, 18, 21) A recent systematic review found that the incidence rate of hypoglycaemia experienced by individuals with T1D ranged from 14.5 to 42,890 episodes per 1,000 person-years.(22) A 2021 study reported that in a cohort of individuals with T1D patients (n=88), 40% experienced at least one episode of severe hypoglycaemia in the previous six months, and 11% had a loss of consciousness related to hypoglycaemia in the previous 12 months.(21)

1.4 'Double diabetes'

The metabolic syndrome (previously referred to as 'insulin resistance syndrome') refers to a cluster of symptoms associated with insulin resistance, such as visceral obesity, poor glucose tolerance, dyslipidaemia, and high blood pressure.(23-25) The metabolic syndrome is a major risk factor for the development of T2D and CVD.(26, 27) Contrastingly, T1D is characterised by insulin deficiency due to an autoimmune process and affected individuals are traditionally considered to be lean. However, modern T1D management may involve an excessive reliance on high doses of insulin to control blood glucose levels, with insulin therapy being the cornerstone of T1D management.(11, 15) Chronic exposure to high levels of insulin (hyperinsulinemia) and insulin resistance has been demonstrated to lead to the development of the metabolic syndrome.(24, 28, 29) Data from the DCCT demonstrated that individuals with T1D who underwent intensive insulin therapy and were in the top quartile of excess weight gain experienced sustained increases in central adiposity, insulin resistance, dyslipidaemia and blood pressure.(30) A recent systematic review examining the global prevalence of metabolic syndrome in individuals with T1D also showed that almost a quarter of 45,811 patients with T1D were

affected by the metabolic syndrome, and other research demonstrates that Australia has the highest rates worldwide (27.3%).(31, 32) Given the increasing prevalence of metabolic-related issues in people living with T1D, experts are describing an epidemic of 'double diabetes' wherein the characteristics of the metabolic syndrome and T2D are displayed in individuals with T1D.(33) This highlights the imperative need for modern interventions for T1D management to improve glycaemic control whilst concurrently reducing metabolic risk factors associated with insulin resistance and the metabolic syndrome.

2.0 The Role of Diet in Diabetes Management

The Principles and Practice of Medicine published in 1921 reported the dietary requirements for a patient with 'severe diabetes'.(1) To avoid hyperglycaemia and its related complications, dietary carbohydrates comprised only 2% of total energy intake while dietary fats made up 75%.(1) Foods without carbohydrates, including meat, poultry, game, fish, eggs, butter, and olive oil, comprised the majority of the diet prescription, and limited quantities of low-sugar fruits and non-starchy vegetables were included according to individual 'carbohydrate tolerance'.(1) However, the discovery of glucose lowering medications and self-monitoring technologies have since allowed individuals living with diabetes to employ more flexibility with their dietary intake, and strict low-carbohydrate (LC) diets are no longer routinely recommended.

2.1 Current Dietary Recommendations for T1D

Currently, individuals with T1D are advised to practice 'carbohydrate counting' and follow a high-carbohydrate (HC) diet.(11) Aside from this, national authoritative bodies, including the National Health and Medical Research Council (NHMRC),

recommend that individuals with T1D follow the same dietary principles as people without diabetes.(11) This includes consumption of a HC diet in which 45-65% of total energy intake (TEI) comes from dietary carbohydrates as per the Australian Dietary Guidelines (ADG).(34) To address the lack of information describing current dietary intakes of adults with T1D as well as their adherence to ADG, Chapter 2 of my thesis analysed data from the Australian Health Survey 2011-13 and showed that energy and macronutrient intake profiles of an Australian-based sample of adults living with T1D were consistent with the HC dietary pattern promoted in the ADG.(35)

Despite apparent adherence to current dietary recommendations, the majority of patients with T1D in Australia and globally are not achieving glycaemic control targets.(12, 17) Notably, the ADG have not been designed with considerations for people with chronic diseases, including T1D, and people with T1D were excluded from the studies used to formulate these evidence-based recommendations intended for the general population.(34, 36) Individuals with T1D are physiologically different to individuals without diabetes and experience daily health challenges that have the potential to be life-threatening, of which people without diabetes do not experience. Ultimately, the current ADG may not be appropriate for people living with T1D and the Standards of Care for Diabetes should refer healthcare professionals to robust data from well-controlled clinical trials conducted with T1D participants to guide dietary recommendations for this target population.

2.2 Low-carbohydrate diets

In response to the ongoing challenges in achieving safe and healthy blood glucose levels experienced by people with diabetes, there has been a re-emerging interest in the use of LC diets. Diets with <45% TEI from carbohydrates are commonly referred to as LC diets because they include carbohydrate intakes below conventional HC dietary recommendations (i.e., 45-65% TEI from carbohydrates). Whilst a global consensus definition of a LC diet is yet to be established, expert consensus groups have defined diets with 26-45% TEI from carbohydrates (or 130-225 g/day) as 'moderate-carbohydrate' or 'false LC diets'; <26% TEI from carbohydrates (or <130 g/day) as 'true LC diets'; and $\leq 10\%$ TEI from carbohydrates (or ≤ 50 g/day) as 'very LC diets'.(37, 38) Beyond the variances in carbohydrate prescription, the primary features of LC diets have previously been poorly described and understood. To address this gap in the literature, a systematic analysis of LC diet intervention studies that demonstrated effectiveness for improving glycaemic control in T2D was conducted in Chapter 4 of my thesis to identify common prescriptions for total energy, carbohydrates, proteins, and dietary fats, as well as the types of foods recommended.(39)

2.2.1 Type 2 diabetes

Over the past decade, a strong body of evidence from prospective interventional studies of T2D patients has demonstrated that LC diets are effective for improving glycaemic control. In 2019, I conducted the largest systematic review to date of LC diets for T2D management and identified 41 interventional studies of which 40/41 were classified as 'effective' for improving glycaemic control.(39) Six other systematic reviews have been previously conducted by independent research teams to compare the effect(s)

of high-carbohydrate (HC) diets with LC diets in adults with T2D.(40-45) The HC diet comparators included conventional approaches such as low-fat diets, low-glycaemic index diets, the Diabetes Prevention Program, and the American Diabetes Association Diet.(40) The collective evidence demonstrates that the LC diets had superior advantages for improving HbA1c levels,(40-45) reducing use of anti-glycaemic medications,(40-42, 44) achieving clinically significant weight loss,(40-45) and improving lipid profiles (decreasing triglycerides and increasing HDL cholesterol).(40-43, 45)

Although the safety and efficacy of LC diets in T2D has been well demonstrated, there may be a lack of translation into clinical practice because healthcare practitioners, including dietitians, are not routinely educated on how to construct well-formulated LC diet interventions in clinical practice. In response to this need, the systematic review that I completed in 2019 includes a content analysis performed on the reported methodologies of effective LC diet studies to identify core design and delivery components used for improving glycaemic control. In addition, I conducted a systematic approach to achieving nutritional adequacy when constructing LC dietary interventions to further support healthcare practitioners wishing to implement this approach in clinical practice.(46) These resources are designed to support the practical implementation of low-carbohydrate diets in clinical practice.

2.2.2 Type 1 diabetes

LC diets may offer an alternative dietary approach for individuals with T1D to improve glycaemic control while reducing the need for large doses of insulin

at mealtimes that potentially improves the predictably of blood glucose levels by reducing large glucose fluctuations.(37, 47, 48) The extensive evidence base in T2D raises the attractive possibility that LC diets may be an effective solution for addressing the 'double diabetes' phenomenon wherein individuals with T1D are becoming increasingly impacted by metabolic-related issues that are usually associated with T2D.(33)

In 2018, I conducted and published the first systematic review investigating lower-carbohydrate dietary approaches for T1D management.(38) All primary studies containing a methods section (excluding cross-sectional studies) published up until March 2017 could be included.(38) Of the nine eligible and included studies, two were randomised controlled trials, four were pre-post intervention studies, two were retrospective case series, and one was a case report.(38) Of the studies examining true and very LC diets (<26% TEI from carbohydrates) that measured changes in HbA1c (excluding case reports), clinically meaningful HbA1c reductions between 0.7-1.3% were achieved.(47, 49, 50) Further, concurrent reductions in total daily insulin doses (11-22 U/day) were reported.(47, 49, 50) Lastly, two studies reported reductions in the frequency of severe hypoglycaemia.(51, 52)

Since the publication of our review in March 2018, additional studies investigating LC diets for T1D have been published. Researchers from Harvard conducted a large survey (n=316) of an international social media group for people with T1D who had been following a very LC diet for two years.(53) Participants reported a mean carbohydrate intake of ~36 g/day and a

mean HbA1c level of 5.7%.(53) Only seven (2%) of respondents reported diabetes-related hospitalisations in the past year, including 1% for ketoacidosis and 1% for hypoglycaemia.(53) More recently, Schmidt et al. published results from a randomised crossover trial comparing a LC diet (~100 g/day) with a HC diet (~250 g/day) over 12 weeks in 10 adults with T1D.(54) Time spent <3.9 mmol/L was less (1.9 vs. 3.6%; P<0.001) and glycaemic variability was lower (33 vs. 38%; P=0.013) during the LC diet, with no events of severe hypoglycaemia were reported.(54) Participants lost 2.0 kg during the LC diet and gained 2.6 kg during the HC diet.(54) The LC diet did not lead to any negative changes in CVD risk factors, including blood lipids and inflammatory markers.(54)

To add to the growing evidence base, I conducted a retrospective case series of Australian adults with T1D self-selecting to follow a LC diet with the support of a registered dietitian and diabetes educator.(55) The LC diet represented a patient-led approach involving adjustments to energy and macronutrient intakes, glucose self-monitoring, and insulin management.(55) Improvements in measures of glycaemic control (HbA1c reduced from 9.0 to 7.0%; estimated A1c: 7.1 to 6.3%) and reductions in total daily insulin use (44 to 31 U/day) were observed with no change(s) in the negative direction for any health outcomes.(55) This research highlights the growing public interest in LC diets for T1D management in Australia and provides preliminary evidence for the real-world use of a LC diet in clinical practice for the management of T1D.(55)

I also led the design and conduct of a single arm within-participant controlled intervention study to prospectively investigate the effects, feasibility, and safety of a healthcare professional supported LC diet in adults with T1D.(56) This was the first LC diet study in Australia offering fully remote, nationwide participation to adults with T1D. This trial demonstrated that, compared to habitual diets higher in dietary carbohydrates, a healthcare professional delivered LC diet prioritising minimally processed foods achieved improved outcomes for T1D management.(56) During the 12-week intervention period, mean HbA1c levels reduced from 7.7% to 7.1% (P=0.003) and time in range (3.5-10 mmol/L) increased from 59% to 74% (P<0.001), with less use of insulin overall (65 to 49 U/day).(56) Significant improvements in diabetesrelated quality of life, glycaemic variability outcomes, fasting blood glucose levels, body weight, and body mass index were also observed during the LC diet intervention, while no increased risk of hypoglycaemia and no severe adverse events were reported.(56) Participants were followed up for another 12 weeks post-intervention and it was shown that HbA1c reductions were largely sustained up to 24 weeks.

2.3 Clinical Practice Case Study ('Double Diabetes')

Neil initially came to see me in 2020 with his wife, Julie. He was desperate for support with weight management after experiencing years of gradual weight gain despite his best dieting efforts. Neil was diagnosed with type 1 diabetes in 1978 and considered himself an expert in type 1 diabetes management given he had lived with it for over 40 years. He was told time after time by his specialists that his diabetes management was exceptional and nothing more could be done to improve it – except lose weight. Since 2001, Neil had developed numerous

comorbidities including morbid obesity, diabetic retinopathy, fatty liver, peripheral vascular disease, sleep apnoea, renal impairment, osteoarthritis, and hypertension. At our initial consultation, he weighed 150 kg and felt at a loss about what to do because he thought he had 'tried everything'.

Neil's baseline diet comprised of three meals daily and no snacks. He diligently restricted his intake of saturated fats - using cholesterol-lowering margarine and small servings of eggs and red meat. He avoided full-fat dairy products, such as cheese and butter. His diet was predominantly made up of vegetables, legumes, and grain products (e.g., whole grain bread, muesli bar). He rarely ate meals out of the house but sometimes enjoyed a glass of wine with dinner. Neil reported that most healthcare professionals didn't believe him when he told them what he ate because they couldn't explain why he wasn't losing weight on his current diet.

His previous diet education was heavily focussed on carbohydrate counting and the glycaemic index. He had always been told to eat a low-glycaemic index (GI) diet and to limit proteins and fats. However, this advice was not working for Neil as his health was progressively worsening despite exceptional adherence to a low-fat, low-GI, carbohydrate-focussed dietary approach that was consistent with the Australian Dietary Guidelines.

It was very clear to me during our initial assessment that Neil had severe insulin resistance. This was evidenced by the Metabolic Syndrome (fatty liver, hypertension, hyperglycaemia, abdominal obesity) and the fact that Neil reported increasing use of insulin over the years for a given amount of carbohydrate. His total daily insulin use at baseline was 190-210 U/day and his HbA1c was 7.5%.

Given that insulin resistance prevents the safe and effective metabolism of dietary carbohydrates, insulin resistance may be considered a form of carbohydrate intolerance. As such, I provided Neil and his wife with in-depth education on the impact(s) of carbohydrates, proteins, and fats on post-prandial blood glucose levels and insulin requirements. Despite living with type 1 diabetes for over 40 years and being very confident in his insulin management, Neil had never been informed of the impact(s) of proteins and fats on blood glucose levels. Immediately after receiving this information, Neil realised that he needed to decrease his intake of carbohydrate foods and increase his intake of proteins and fats. Together, we developed a nutritionally adequate low-carbohydrate dietary approach that Neil considered to be achievable and sustainable. The diet involved a carbohydrate target of 30 grams per day evenly distributed over three meals. Minimally processed sources of proteins and healthy fats were to be consumed 'to satiety', although minimum portions to meet energy and nutrient requirements were specified.

Neil and I have reviewed with each other regularly, every three months over the last three years, since he commenced a low-carbohydrate dietary approach. I am thrilled to report the following improvements in his health outcomes:

	2020	2023
Body weight (kg)	150	132
HbA1c (%)	7.5	6.5
Total daily insulin (units)	190-210	70
CRP (units)	8.8	6.4

Neil continues to adhere to a low-carbohydrate diet three years on and reports to be enjoying his new lifestyle. However, he is frustrated that he wasn't given this dietary information earlier in his life. Neil describes himself as a 'top student' when it comes to type 1 diabetes – he has attended all his specialist appointments and followed their advice to a tee without excuses or complaints. He now feels that this advice wasn't right for him, and a low-

carbohydrate diet which allows him to use less insulin to safely control his blood glucose levels, is beyond doubt, the most appropriate approach for him to follow as someone with type 1 diabetes and the Metabolic Syndrome.

2.4 References

1. Osler W, McCrae T. The Principles and Practice of Medicine: Designed for the Use of Practitioners and Students of Medicine: D. Appleton; 1921.

2. Australian Bureau of Statistics. Diabetes [Internet]. Canberra: ABS; 2020-21 [cited

2022 December 8]. Available from: https://www.abs.gov.au/statistics/health/health-

conditions-and-risks/diabetes/latest-release.

Australian Bureau of Statistics. Causes of Death, Australia [Internet]. Canberra: ABS;
 2021 [cited 2022 December 8]. Available from:

https://www.abs.gov.au/statistics/health/causes-death/causes-death-australia/latest-release.

4. American Diabetes Association. Standards of Medical Care in Diabetes—2013.

Diabetes Care. 2013;36(Supplement 1):S11.

5. Australian Institute of Health and Welfare. Diabetes: Australian facts [Internet].

AIHW, Australian Government; 2022 [updated 13 Jul 2022; cited 2022 Dec 8]. Available

from: https://www.aihw.gov.au/reports/diabetes/diabetes/contents/summary.

6. Australian Institute of Health and Welfare. National (insulin-treated) Diabetes

Register [Internet]. AIHW, Australian Government; 2022 [updated 9 June 2022; cited 2022

Dec 9]. Available from: https://www.aihw.gov.au/about-our-data/our-data-

collections/national-insulin-treated-diabetes-register.

 Harding JL, Wander PL, Zhang X, Li X, Karuranga S, Chen H, et al. The Incidence of Adult-Onset Type 1 Diabetes: A Systematic Review From 32 Countries and Regions.
 Diabetes Care. 2022;45(4):994-1006.

International Diabetes Federation. IDF Diabetes Atlas: 10th edition [Internet]. IDF;
 2021 [cited 2022 Dec 8]. Available from: <u>https://diabetesatlas.org/idfawp/resource-</u>
 <u>files/2021/07/IDF Atlas 10th Edition 2021.pdf.</u>

 Australian Institute of Health and Welfare. Australian Burden of Disease Study: impact and causes of illness and death in Australia 2018 [Internet]. Canberra: AIHW; 2021 [cited 2022 Nov 1]. Available from: <u>https://www.aihw.gov.au/getmedia/5ef18dc9-414f-4899bb35-08e239417694/aihw-bod-29.pdf.aspx?inline=true</u>.

10. JDRF. Economic cost of type 1 diabetes in Australia [Internet]. Accenture; 2021 [cited 2022 Dec 8]. Available from: <u>https://jdrf.org.au/wp-content/uploads/2021/06/The-</u> economic-cost-of-

<u>T1D.pdf?utm_source=pardot&utm_medium=email&utm_campaign=accenture_report_releas</u> e&utm_content=first_send_wide_audience_cash_header.

 Craig M, Twigg S, Donaghue K, Cheung N, Cameron F, Conn J, et al. National evidence-based clinical care guidelines for type 1 diabetes in children, adolescents and adults Canberra: Australian Government; 2011 [Available from:

https://diabetessociety.com.au/documents/Type1guidelines14Nov2011.pdf.

 Australian National Diabetes Audit – Australian Quality Clinical Audit. Annual Report 2019 [Internet]. Australian Government Department of Health; 2019 [cited 2022 December 8]. Available from: <u>https://nadc.net.au/wp-content/uploads/2020/03/ANDA-AQCA-2019-Annual-Report.pdf</u>.

13. American Diabetes Association Professional Practice Committee. 6. Glycemic
Targets: Standards of Medical Care in Diabetes—2022. Diabetes Care.
2021;45(Supplement_1):S83-S96.

14. Boye KS, Thieu VT, Lage MJ, Miller H, Paczkowski R. The Association Between Sustained HbA1c Control and Long-Term Complications Among Individuals with Type 2 Diabetes: A Retrospective Study. Advances in Therapy. 2022;39(5):2208-21.

15. Nathan DM. The diabetes control and complications trial/epidemiology of diabetes interventions and complications study at 30 years: overview. Diabetes Care. 2014;37(1):9-16.

 The Diabetes Control and Complications Trial Research Group. The Effect of Intensive Treatment of Diabetes on the Development and Progression of Long-Term Complications in Insulin-Dependent Diabetes Mellitus. New England Journal of Medicine. 1993;329(14):977-86.

McKnight JA, Wild SH, Lamb MJ, Cooper MN, Jones TW, Davis EA, et al.
Glycaemic control of Type 1 diabetes in clinical practice early in the 21st century: an
international comparison. Diabetic medicine : a journal of the British Diabetic Association.
2015;32(8):1036-50.

 Sircar M, Bhatia A, Munshi M. Review of Hypoglycemia in the Older Adult: Clinical Implications and Management. Canadian journal of diabetes. 2016;40(1):66-72.

19. Cryer PE. Hypoglycemia in type 1 diabetes mellitus. Endocrinology and metabolism clinics of North America. 2010;39(3):641-54.

20. American Diabetes Association. Defining and reporting hypoglycemia in diabetes: a report from the American Diabetes Association Workgroup on Hypoglycemia. Diabetes Care. 2005;28(5):1245-9.

Pinés Corrales PJ, Arias Lozano C, Jiménez Martínez C, López Jiménez LM, Sirvent Segovia AE, García Blasco L, et al. Prevalence of severe hypoglycemia in a cohort of patients with type 1 diabetes. Endocrinología, Diabetes y Nutrición (English ed).
 2021;68(1):47-52.

22. Alwafi H, Alsharif AA, Wei L, Langan D, Naser AY, Mongkhon P, et al. Incidence and prevalence of hypoglycaemia in type 1 and type 2 diabetes individuals: A systematic review and meta-analysis. Diabetes Research and Clinical Practice. 2020;170.

23. Roberts CK, Hevener AL, Barnard RJ. Metabolic syndrome and insulin resistance:
underlying causes and modification by exercise training. Comprehensive Physiology.
2013;3(1):1-58.

24. DeFronzo RA, Ferrannini E. Insulin resistance. A multifaceted syndrome responsible for NIDDM, obesity, hypertension, dyslipidemia, and atherosclerotic cardiovascular disease. Diabetes Care. 1991;14(3):173-94.

25. Huang PL. A comprehensive definition for metabolic syndrome. Disease models & mechanisms. 2009;2(5-6):231-7.

26. Gami AS, Witt BJ, Howard DE, Erwin PJ, Gami LA, Somers VK, et al. Metabolic syndrome and risk of incident cardiovascular events and death: a systematic review and metaanalysis of longitudinal studies. Journal of the American College of Cardiology. 2007;49(4):403-14.

27. Galassi A, Reynolds K, He J. Metabolic syndrome and risk of cardiovascular disease: a meta-analysis. The American journal of medicine. 2006;119(10):812-9.

28. Haffner SM, Valdez RA, Hazuda HP, Mitchell BD, Morales PA, Stern MP.
Prospective analysis of the insulin-resistance syndrome (syndrome X). Diabetes.
1992;41(6):715-22.

29. Barnard RJ, Roberts CK, Varon SM, Berger JJ. Diet-induced insulin resistance
precedes other aspects of the metabolic syndrome. Journal of applied physiology (Bethesda,
Md : 1985). 1998;84(4):1311-5.

30. Purnell JQ, Zinman B, Brunzell JD. The effect of excess weight gain with intensive diabetes mellitus treatment on cardiovascular disease risk factors and atherosclerosis in type 1

diabetes mellitus: results from the Diabetes Control and Complications Trial/Epidemiology of Diabetes Interventions and Complications Study (DCCT/EDIC) study. Circulation. 2013;127(2):180-7.

Belete R, Ataro Z, Abdu A, Sheleme M. Global prevalence of metabolic syndrome among patients with type I diabetes mellitus: a systematic review and meta-analysis.Diabetology & Metabolic Syndrome. 2021;13(1):25.

32. Lee AS, Twigg SM, Flack JR. Metabolic syndrome in type 1 diabetes and its association with diabetes complications. Diabet Med. 2021;38(2):e14376.

33. Cleland SJ, Fisher BM, Colhoun HM, Sattar N, Petrie JR. Insulin resistance in type 1 diabetes: what is 'double diabetes' and what are the risks? Diabetologia. 2013;56(7):1462-70.

34. National Health and Medical Research Council. Australian Dietary Guidelines
[Internet]. Canberra: National Health and Medical Research Council; 2013 [cited 2022 Dec
14]. Available from: https://www.eatforhealth.gov.au/sites/default/files/2022-

09/n55_australian_dietary_guidelines.pdf.

35. Turton JL, Struik NA, Riley M, Brinkworth GD. Adults with and without type 1 diabetes have similar energy and macronutrient intakes: an analysis from the Australian Health Survey 2011-2013. Nutrition research (New York, NY). 2020;84:25-32.

36. National Health and Medical Research Council. A Modelling System to Inform the Revision of the Australian Guide to Healthy Eating [Internet]. Commonwealth of Australia;
2011 [cited 2018 Nov 17]. Available from:

https://www.eatforhealth.gov.au/sites/default/files/files/public_consultation/n55a_dietary_gui delines_food_modelling_111216.pdf.

37. Feinman RD, Pogozelski WK, Astrup A, Bernstein RK, Fine EJ, Westman EC, et al. Dietary carbohydrate restriction as the first approach in diabetes management: Critical review and evidence base. Nutrition. 2015;31(1):1-13.

Turton JL, Raab R, Rooney KB. Low-carbohydrate diets for type 1 diabetes mellitus:
 A systematic review. PLOS ONE. 2018;13(3):e0194987.

39. Turton J, Brinkworth GD, Field R, Parker H, Rooney K. An evidence-based approach to developing low-carbohydrate diets for type 2 diabetes management: A systematic review of interventions and methods. Diabetes, Obesity and Metabolism. 2019;21(11):2513-25.

40. Sainsbury E, Kizirian NV, Partridge SR, Gill T, Colagiuri S, Gibson AA. Effect of dietary carbohydrate restriction on glycemic control in adults with diabetes: A systematic review and meta-analysis. Diabetes research and clinical practice. 2018;139:239-52.

41. Huntriss R, Campbell M, Bedwell C. The interpretation and effect of a lowcarbohydrate diet in the management of type 2 diabetes: a systematic review and metaanalysis of randomised controlled trials. European journal of clinical nutrition.

2018;72(3):311-25.

42. Goldenberg JZ, Day A, Brinkworth GD, Sato J, Yamada S, Jönsson T, et al. Efficacy and safety of low and very low carbohydrate diets for type 2 diabetes remission: systematic review and meta-analysis of published and unpublished randomized trial data. BMJ. 2021;372:m4743.

43. Meng Y, Bai H, Wang S, Li Z, Wang Q, Chen L. Efficacy of low carbohydrate diet for type 2 diabetes mellitus management: A systematic review and meta-analysis of randomized controlled trials. Diabetes research and clinical practice. 2017;131:124-31.

44. Snorgaard O, Poulsen GM, Andersen HK, Astrup A. Systematic review and metaanalysis of dietary carbohydrate restriction in patients with type 2 diabetes. BMJ open diabetes research & care. 2017;5(1):e000354.

45. Li S, Ding L, Xiao X. 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. International Journal of Endocrinology. 2021;2021:8521756.

46. Turton JL, Field RJ, Parker HM, Rooney K, Struik NA. Formulating Nutritionally Adequate Low- Carbohydrate Diets - An Analysis of the Australian Food Composition Database. Biomedical Journal of Scientific & Technical Research 2022;44:35166-80.

47. Nielsen JV, Gando C, Joensson E, Paulsson C. Low carbohydrate diet in type 1 diabetes, long-term improvement and adherence: A clinical audit. Diabetology & Metabolic Syndrome. 2012;4(1):23.

48. Bernstein RK. Dr. Bernstein's diabetes solution: the complete guide to achieving normal blood sugars: Little, Brown; 2011.

49. Krebs JD, Parry Strong A, Cresswell P, Reynolds AN, Hanna A, Haeusler S. A randomised trial of the feasibility of a low carbohydrate diet vs standard carbohydrate counting in adults with type 1 diabetes taking body weight into account. Asia Pacific journal of clinical nutrition. 2016;25(1):78-84.

50. O'Neill DF, Westman EC, Bernstein RK. The effects of a low-carbohydrate regimen on glycemic control and serum lipids in diabetes mellitus. Metab. 2003;1(4):291-8.

51. Bernstein RK. Virtually continuous euglycemia for 5 yr in a labile juvenile-onset diabetic patient under noninvasive closed-loop control. Diabetes Care. 1980;3(1):140-3.

52. Knight BA, Hickman IJ, Gibbons K, McIntyre HD. Quantitative assessment of dietary intake in adults with Type 1 diabetes following flexible insulin therapy education with an active promotion of dietary freedom. Diabetes research and clinical practice. 2016;116:36-42.

53. Lennerz BS, Barton A, Bernstein RK, Dikeman RD, Diulus C, Hallberg S, et al.
Management of Type 1 Diabetes With a Very Low–Carbohydrate Diet. Pediatrics.
2018;141(6):e20173349.

54. Schmidt S, Christensen MB, Serifovski N, Damm-Frydenberg C, Jensen JB, Floyel T, et al. Low versus high carbohydrate diet in type 1 diabetes: A 12-week randomized openlabel crossover study. Diabetes, obesity & metabolism. 2019;21(7):1680-8.

55. Turton J, Brinkworth G, Parker H, Rush A, Johnson R, Rooney K. Clinical Application of Reduced-Carbohydrate Diets for Type 1 Diabetes Management: A Retrospective Case Series. Curre Res Diabetes & Obes J 2022.

56. Turton JL, Brinkworth GD, Parker HM, Lim D, Lee K, Rush A, et al. Effects of a low-carbohydrate diet in adults with type 1 diabetes management: A single arm non-randomised clinical trial. PLOS ONE. 2023;18(7):e0288440.