LIFESTYLE INTERVENTION STRATEGIES FOR DIABETES MANAGEMENT

A thesis submitted for the Degree of

Doctor of Philosophy

by

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This thesis is dedicated to my grandparents,

Mr Tay Kheng Yong & Mdm Lee Guat Eng,

You instilled in me a love for reading, writing and research,

Mr Tan Tiong Tai & Mdm Pan Ah Yoke,

Diligence, tenacity and resolve are traits that I have learnt from you.

And my parents,

Mr Tay Chor Suay & Mdm Tan Suat Eng

You are my pillars of strength. Thank you for your agápē love.

For the glory of God

Thank you Jesus, the author and perfecter of our faith (Hebrews 12:2)

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ABSTRACT

The inexorable rise of type 2 diabetes (T2D) worldwide is a serious public health problem with significant health and socioeconomic costs. Diabetes- related complications are underpinned by poor glycaemic control that is greatly influenced by diet composition. Sustainable lifestyle modifications in diet and physical activity form the cornerstone of T2D prevention and management. Energy- restricted, high unrefined carbohydrate, low fat (HC) diets have traditionally been recommended for the dietary management of T2D. However, accumulating nutrition research indicate that carbohydrate restriction and higher intakes of protein and unsaturated fats, improve glycaemic control and reduce cardiovascular disease (CVD) risk markers. Based on this evidence, a novel dietary approach incorporating a very low carbohydrate, high unsaturated fat/ low saturated fat (LC) diet was designed. This LC diet was nutritionally adequate, with the potential to improve glycaemic control and mitigate CVD risk to a greater extent than the traditional HC diet. This thesis discusses the findings of a large, well- controlled, randomised, clinical trial that compared the long- term effects of consuming a traditional HC diet with an energy- matched LC diet, on a range of health outcomes including glycaemic control and CVD risk markers. Both diets were delivered as part of a holistic lifestyle intervention that included a structured exercise program. After one year, both diets achieved substantial weight loss, and reduced blood pressure, HbA1c, fasting glucose and LDL-C. However, the LC diet sustained greater reductions in diabetes medication and glycaemic variability, as well as triglycerides (TAG), and greater increases in HDL-C. Both diets had similar changes in renal and cognitive outcomes, suggesting that the LC diet did not adversely affect renal or cognitive function. These results have important implications for the lifestyle management of T2D with direct relevance to achieving better health outcomes and reducing healthcare costs.

DECLARATION

I certify that this work contains no material which has been accepted for the award of any other degree or diploma in my name, in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. In addition, I certify that no part of this work will, in the future, be used in a submission in my name, for any other degree or diploma in any university or other tertiary institution without the prior approval of the University of Adelaide and where applicable, any partner institution responsible for the joint-award of this degree.

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Tay Jiahui (Jeannie Tay)

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GLOSSARY OF ABBREVIATIONS

ACCORD	Action to Control Cardiovascular Risk in Diabetes trial
ACR	Albumin creatinine ratio
ADVANCE	Action in Diabetes and Vascular Disease: Preterax and Diamicron MR Controlled Evaluation trial
CBT	Cognitive behavioural therapy
CGMS	Continuous glucose monitoring systems
CKD-EPI	Chronic Kidney Disease Epidemiology Collaboration equation
CV	Cardiovascular
CVD	Cardiovascular disease
DCCT	Diabetes Control and Complications Trial
DKD	Diabetic kidney disease
DSST	Digit Symbol Substitution Test
eGFR	Estimated glomerular filtration rate
ESRD	End stage renal disease
FBG	Fasting blood glucose
FMD	Flow-mediated dilatation
GL	Glycaemic load
GV	Glycaemic variability

HbA1c	Glycated haemoglobin A1c
HC diet	High carbohydrate, low fat diet
HDL-C	High density lipoprotein cholesterol
IFG	Impaired fasting glucose
IGT	Impaired glucose tolerance
LC diet	Very low carbohydrate diet
LDL-C	Low density lipoprotein cholesterol
MES	Medication effect score
MIND- ACCORD	Memory in Diabetes study of the ACCORD trial
MUFA	Monounsaturated fats
PPG	Postprandial glucose
RDA	Recommended dietary allowance
RCT	Randomised controlled trial
ROS	Reactive oxygen species
SCr	Serum creatinine
SMBG	Self- monitoring of blood glucose
TAG	Triglycerides
T1D	Type 1 diabetes
T2D	Type 2 diabetes

UKPDS	UK Prospective Diabetes Study
VADT	Veterans Affairs Diabetes Trial
VLDL-C	Very low density lipoprotein cholesterol

LIST OF PUBLICATIONS ARISING FROM THESIS

2015 Tay J, Thompson CH, et al. Luscombe-Marsh ND, 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. 2015; 94: e2181

Tay J, Luscombe-Marsh ND, Thompson CH, et al. **Comparison of low- and high-carbohydrate diets for type 2 diabetes management: a randomized trial.** Am J Clin Nutr 2015; 102:780-790

Tay J, Thompson CH and Brinkworth GD. **Glycemic Variability: Assessing Glycemia Differently and the Implications for Dietary Management of Diabetes.** Annu Rev Nutr 2015;35:389-424

2014 Tay J, Luscombe-Marsh ND, Thompson CH, et al**. A Very Low Carbohydrate, Low Saturated Fat Diet for Type 2 Diabetes Management: A Randomized Trial.** Diabetes Care 2014; 37(11):2909-2918.

LIST OF CONFERENCE PRESENTATIONS DURING CANDIDATURE

2015 **International Diabetes Federation (IDF) World Diabetes Congress, 30 November - 4 December 2015, Vancouver, Canada (Poster presentation).**

Tay J, et al. Long-term effects of a very low- and high carbohydrate diet on renal function in individuals with type 2 diabetes [abstract].

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Tay J, et al. Long-term effects of a very low- and high carbohydrate diet on renal function in individuals with type 2 diabetes [abstract].

Tay J, et al. Long term consumption of a very low carbohydrate diet does not adversely affect cognitive performance in individuals with type 2 diabetes [abstract].

Asia Pacific Conference on Clinical Nutrition, 26-29 January 2015, Kuala Lumpur, Malaysia (Oral presentation)

Tay J, et al. Long-term consumption of a low carbohydrate, low saturated fat diet improves glycemic control and reduces diabetes medication use and cardiovascular risk factors in type 2 diabetes [abstract].

2014 **Nutrition Society of Australia (NSA) Annual Scientific Meeting, 26-28 November 2014, Hobart, Australia (Oral presentation)**

Tay J, et al Long-term consumption of a low carbohydrate, low saturated fat diet improves type 2 diabetes management [abstract].

International Diabetes Federation-Western Pacific Region (IDF-WPR) Congress, 21-24 November 2014, Singapore (Oral presentation).

Tay J, et al. Long-term consumption of a low carbohydrate, low saturated fat diet improves type 2 diabetes management [abstract].

Obesity Week- The Obesity Society Annual Scientific Meeting,
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Tay J, et al. Long-term consumption of a low carbohydrate, low saturated fat diet improves glycemic control and reduces diabetes medication use and cardiovascular risk factors in type 2 diabetes [abstract].

Australian Society for Medical Research (ASMR) SA Annual Scientific Meeting, 4 June 2014, Adelaide, Australia (Oral presentation)

Tay J, et al. Very low carbohydrate, low saturated fat diet improves glycemic control and cardiovascular risk factors in type 2 diabetes [abstract].

2013 **International Diabetes Federation (IDF) World Diabetes Congress, 2-6 December 2013, Melbourne, Australia (Oral presentation).**

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2012 National Science Scholarship (PhD), The Agency for Science, Technology and Research (A*STAR), Singapore