

Lifestyle Intervention Strategies for Type 2 Diabetes Management

A thesis submitted to the University of Adelaide
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SUMMARY

In parallel with the world wide increase in obesity there has been a dramatic rise in the prevalence of type 2 diabetes (T2DM) which is associated with a number of micro- and macro-vascular complications and increases the risk of coronary heart disease. Lifestyle intervention incorporating a hypocaloric weight loss diet and exercise training is currently recommended as the cornerstone of diabetes management and has been demonstrated to improve glycemic control and reduce cardiovascular disease (CVD) risk factors in individuals with T2DM.

Previous research suggests that manipulating the dietary macronutrient composition may enhance the weight loss and improve the health status in patients undertaking a hypocaloric, weight-reducing diet. Within a low fat caloric restricted diet replacing a portion of carbohydrate with protein has been demonstrated to provide beneficial effects for weight loss, body composition, and cardiometabolic risk outcomes in overweight and obese individuals including patients with T2DM. Moreover combining a high protein, low fat hypocaloric diet with exercise training may provide additive benefits, however the efficacy of this strategy in patients with T2DM who may achieve the greatest benefits has been largely unexplored.

The first study in this thesis was a randomised-controlled clinical study which investigated the effects of a high protein, low fat hypocaloric diet combined with exercise training compared to an isocaloric high protein, low fat diet without exercise training or an isocaloric standard protein, low fat diet with or without exercise training on weight loss, body composition and cardiometabolic risk markers in overweight and obese patients with T2DM. The results showed that compared to caloric restriction alone participation in

exercise training during caloric restriction produced greater reductions in body weight and total body fat mass (FM) and increases in muscular strength. Additionally, replacement of some carbohydrate with protein further magnified these effects resulting in participants who consumed the high protein diet and participated in resistance exercise training experiencing the greatest reductions in weight, total body FM, abdominal FM and insulin levels. All treatments had similar improvements in glycemic control and CVD risk factors. These results suggest a lifestyle modification program that combines a calorie restricted high protein diet and exercise training appears to be a preferred treatment strategy in overweight/obese patients with T2DM.

A separate line of evidence suggests manipulating the timing of protein intake in relation to exercise training (consuming protein adjacent to exercise training compared to a delayed intake) stimulates greater muscle protein synthesis and hypertrophy. This strategy may therefore promote greater muscle tissue retention and improvements in body composition during calorie-restricted induced weight loss. This hypothesis was tested in the second study in this thesis. However, this study showed in overweight and obese patients with T2DM undertaking a 16 week hypocaloric high protein, low fat diet plus exercise training lifestyle intervention program, that altering the timing of protein ingestion relative to exercise (by consuming a 21g protein supplement immediately before exercise compared to delaying ingestion 2 hours post-exercise) provided no additional benefit to weight loss and changes in body composition or cardiometabolic risk.

The sustainability of the benefits obtained from intensive short-term research-based lifestyle intervention programs which incorporate an energy restricted diet and exercise is often poor, with a rebound frequently occurring following the cessation of the intensive support. The final study in this thesis followed up participants 1-year after the

commencement of a 16-week research-based intensive lifestyle (diet and exercise) intervention program and reported factors identified by those participants as enhancing or impeding post-intervention program sustainability. Participants identified multiple reasons for the discontinuation of program components including; a desire for increased diet variety, a desire for increased portion size, limited access to appropriate exercise programs and facilities, the cost of gym membership and the withdrawal of professionals to motivate them. The main factors identified that would have facilitated continuation included having continued supervision or having to report to someone, having regular recorded weight checks and diet visits and access to affordable and appropriate exercise facilities.

The findings of this thesis provide information that can be used by health professionals and policy makers for the development of evidence based recommendations and programs for the management of T2DM through diet and exercise based lifestyle intervention.

DECLARATION

This work contains no material which has been accepted for the award of any other degree or diploma in any university or 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.

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Wycherley, T.P., Noakes, M., Clifton, P.M., Cleanthous, X., Keogh, J.B., Brinkworth, G.D. A high protein diet with resistance exercise improves weight loss and body composition in overweight and obese patients with type 2 diabetes. Diabetes Care. 2010. May;**33(5)**:969-976

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Wycherley, T.P., Mohr, P, Noakes, M., Clifton, P.M., Brinkworth, G.D. Self-reported facilitators of and impediments to maintenance of healthy lifestyle behaviours following a supervised research-based lifestyle intervention program in patients with type 2 diabetes.

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AUTHOR STATEMENTS

Publication 1:

A high protein diet with resistance exercise training improves weight loss and body composition in overweight and obese patients with type 2 diabetes

Thomas P Wycherley^{1,2} (BSci (Hons)), Manny Noakes¹ (PhD), Peter M Clifton¹ (PhD), Xenia Cleanthous¹ (MND), Jennifer B Keogh¹ (PhD), Grant D Brinkworth¹ (PhD)

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The authors' responsibilities were as follows:

Thomas Wycherley was responsible for the conception and design of the study (including developing the scientific basis for the research, formulating of the ethics proposal; identification of outcome testing methodology; development of the exercise training protocol; establishment of desired macronutrient compositions of the study diets and relative protein quantities; preparation of data record forms, information and results sheets), recruitment and screening of the participants, co-coordinated the study (troubleshoot participant concerns, personal training for exercise groups), performed data collection (strength assessment, blood pressure assessment, DEXA analysis, auto-analyser biochemical analysis), managed the study data files, performed data analyses, interpreted the data and coordinated the writing of the manuscript.

Manny Noakes contributed to the conception and design of the study, data interpretation and the writing of the manuscript and designed the experimental diets.

Peter Clifton was responsible for the medical monitoring of the research participants and contributed to the data interpretation and writing of the manuscript.

Xenia Cleanthous designed the experimental diets, coordinated the implementation of the dietary protocols and contributed to the writing of the manuscript.

Jennifer Keogh assisted in the design of the experimental diets, contributed to the conception and design of the study, and contributed to the manuscript.

Grant Brinkworth was responsible for the conception and design of the study, coordinated the study, interpreted the data and coordinated and contributed to the writing of the manuscript.

All authors agreed on the final version of the manuscript. None of the authors had a conflict of interest in relation to this manuscript.

Authors Signatures:

I agree with the author contributions for the manuscript “A high protein diet with resistance exercise training improves weight loss and body composition in overweight and obese patients with type 2 diabetes”, and give permission for the use of this manuscript in the thesis.

Thomas Wycherley

Manny Noakes
Peter Clifton
Xenia Cleanthous
Jennifer Keogh
Grant Brinkworth

Publication 2:

Timing of protein ingestion relative to resistance exercise training does not influence body composition, energy expenditure, glycemic control or cardiometabolic risk factors in a hypocaloric, high protein, low fat diet in patients with type 2 diabetes.

Thomas P Wycherley^{1,2} (BSci (Hons)), Manny Noakes¹ (PhD), Peter M Clifton¹ (PhD), Xenia Cleanthous¹ (MND), Jennifer B Keogh¹ (PhD), Grant D Brinkworth¹ (PhD)

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Xenia Cleanthous designed the experimental diets, coordinated the implementation of the dietary protocols and contributed to the writing of the manuscript.

Jennifer Keogh assisted in the design of the experimental diets and contributed to the writing of the manuscript.

Grant Brinkworth was responsible for the conception and design of the study, coordinated the study, interpreted the data and coordinated and contributed to the writing of the manuscript.

All authors agreed on the final version of the manuscript. None of the authors had a conflict of interest in relation to this manuscript.

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Thomas Wycherley

Manny Noakes
Peter Clifton
Xenia Cleanthous
Jennifer Keogh
Grant Brinkworth

Publication 3:

Self-reported facilitators of and impediments to maintenance of healthy lifestyle behaviours following a supervised research-based lifestyle intervention program in patients with type 2 diabetes.

Thomas P Wycherley^{1,2} (BSci (Hons)), Philip Mohr¹ (PhD), Manny Noakes¹ (PhD), Peter M Clifton¹ (PhD), Grant D Brinkworth¹ (PhD)

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The authors' responsibilities were as follows:

Thomas Wycherley was responsible for the conception and design of the study (including developing the scientific basis for the research, formulating of the ethics proposal; preparation of data record forms, information and results sheets), recruitment of the participants, co-coordinated the study, performed data collection (DEXA analysis), managed the study data files, performed data analyses, interpreted the data and coordinated the writing of the manuscript.

Philip Mohr was responsible for the conception and design of the study, interpreted the data and contributed to the writing of the manuscript

Manny Noakes contributed to the conception and design of the study, data interpretation and the writing of the manuscript and designed the experimental diets.

Peter Clifton was responsible for the medical monitoring of the research participants and contributed to the data interpretation and writing of the manuscript.

Grant Brinkworth was responsible for the conception and design of the study, coordinated the study, interpreted the data and coordinated and contributed to the writing of the manuscript.

All authors agreed on the final version of the manuscript. None of the authors had a conflict of interest in relation to this manuscript.

Authors Signatures:

I agree with the author contributions for the manuscript “Self-reported facilitators of and impediments to maintenance of healthy lifestyle behaviours following a supervised research-based lifestyle intervention program in patients with type 2 diabetes”, and give permission for the use of this manuscript in the thesis.

Thomas Wycherley

Philip Mohr

Manny Noakes

Peter Clifton

Grant Brinkworth

PUBLICATIONS ARISING FROM THESIS

Wycherley, T.P., Mohr, P, Noakes, M., Clifton, P.M., Brinkworth, G.D. Self-reported facilitators of and impediments to maintenance of healthy lifestyle behaviours following a supervised research-based lifestyle intervention program in patients with type 2 diabetes.

Submitted for Journal Review

Wycherley, T.P., Noakes, M., Clifton, P.M., Cleanthous, X., Keogh, J.B., Brinkworth, G.D. Timing of protein ingestion relative to resistance exercise training does not influence body composition, energy expenditure, glycemic control or cardiometabolic risk factors in a hypocaloric, high protein, low fat diet in patients with type 2 diabetes. *Diabetes Obes Metab.* 2010. Dec;**12(12)**:1097-1105

Wycherley, T.P., Noakes, M., Clifton, P.M., Cleanthous, X., Keogh, J.B., Brinkworth, G.D. A high protein diet with resistance exercise improves weight loss and body composition in overweight and obese patients with type 2 diabetes. *Diabetes Care.* 2010. May;**33(5)**:969-976

OTHER PUBLICATIONS ARISING DURING CANDIDATURE

Sjoberg, N., Brinkworth, G.D., Wycherley, T.P., Noakes, M., Saint, D.A. Heart rate variability increases with weight loss in overweight and obese adults with type 2 diabetes.

Submitted for Journal Review

Wycherley, T.P., Brinkworth, G.D., Noakes, M., Keogh, J.B., Buckley, J.D., Clifton, P.M. Long term effects of weight loss with a very low carbohydrate and high carbohydrate diet on vascular function in obese subjects. J Int Med. 2010. May;**267(5)**:452-461

Wycherley T.P., Brinkworth G.D., Noakes M., Buckley J.D., Clifton P.M. Effect of caloric restriction with and without exercise training on oxidative stress and endothelial function in obese subjects with type 2 diabetes. Diabetes Obes Metab. 2008. Nov;**10(11)**:1062-73

Brinkworth G.D., Wycherley T.P., Noakes M., Clifton P.M. Reductions in blood pressure following energy restriction for weight loss do not rebound after re-establishment of energy balance in overweight and obese subjects. Clin Exp Hypertens. 2008. Jul;**30(5)**:385-96.

CONFERENCE PRESENTATIONS DURING CANDIDATURE

International

2009 The Obesity Society's 2009 Annual Scientific Meeting, Tuesday October 27th 2009, Washington DC, USA.

Poster presentation: Caloric restriction with or without resistance exercise improves emotional distress and quality of life in overweight and obese patients with type 2 diabetes.

2009 International Diabetes Federation, 20th World Diabetes Congress, Tuesday October 20th 2009, Montreal, Canada.

Oral presentation: A high protein diet with resistance exercise improves weight loss and body composition in overweight and obese patients with type 2 diabetes.

National

2010 Nutrition Society of Australia Annual Scientific Meeting, Wednesday December 1st 2010, Perth, Western Australia.

Student award: Best oral presentation (\$500).

Oral presentation: Timing of protein ingestion relative to resistance exercise training does not influence body composition, energy expenditure, glycaemic control or cardiometabolic risk factors in a hypocaloric, high protein, low fat diet in patients with type 2 diabetes.

2009 Nutrition Society of Australia Annual Scientific Meeting, Thursday December 10th 2009, Newcastle, New South Wales.

Oral presentation: A high protein diet with resistance exercise improves weight loss and body composition in overweight and obese patients with type 2 diabetes.

2009 Australian Diabetes Society & Australian Diabetes Educators Association Annual Scientific Meeting, Wednesday August 26th 2009, Adelaide, South Australia

Oral presentation: A high protein diet with resistance exercise improves weight loss and body composition in overweight and obese patients with type 2 diabetes.

2008 Nutrition Society of Australia Annual Scientific Meeting, Monday December 1st 2008, Glenelg, South Australia.

Oral presentation: Long term effects of weight loss from a very-low-carbohydrate diet on endothelial function in subjects with abdominal obesity.

ABBREVIATIONS

Chapter 1 & Chapter 5

Action for Health in Diabetes (AHEAD)

Australian Diabetes, Obesity and Lifestyle Study (AusDiab)

Body mass index (BMI)

Cardiovascular disease (CVD)

Cardiovascular disease (CVD)

Fat mass (FM)

Fat-free mass (FFM)

Glycosolated Hemoglobin (HbA1c)

Resting energy expenditure (REE)

Type 2 diabetes (T2DM)

Chapter 2

Analysis of variance (ANOVA)

Body mass index (BMI)

Cardiovascular disease (CVD)

Commonwealth Scientific and Industrial Research Organisation (CSIRO)

Dual-energy X-ray absorptiometry (DXA)

Fat-free mass (FFM)

Glycosolated Hemoglobin (A1c)

High protein (HP)

One repetition maximum (1RM)

Resistance exercise training (RT)

Standard carbohydrate (CON)

Waist circumference (WC)

Chapter 3

Type 2 diabetes (T2DM)

Glycosolated Hemoglobin (HbA1c)

Resistance exercise training (RT)

High protein (HP)

Fat-free mass (FFM)

Resting energy expenditure (REE)

Commonwealth Scientific and Industrial Research Organisation (CSIRO)

One repetition maximum (1RM)

Fat mass (FM)

Computerised homeostatic model assessment – insulin resistance (HOMA2-IR)

Analysis of variance (ANOVA)

Chapter 4

Type 2 diabetes (T2DM)

Commonwealth Scientific and Industrial Research Organisation (CSIRO)

Research-based supervised lifestyle intervention program (RLP)