

# **DIETARY MANAGEMENT OF POLYCYSTIC OVARY SYNDROME**

**Lisa Jane Moran**

B.Sc (Hons), B.N.D

Research Centre for Reproductive Health  
Faculty of Health Sciences  
School of Paediatrics and Reproductive Health  
Discipline of Obstetrics and Gynaecology  
University of Adelaide  
CSIRO Human Nutrition

**Supervisors:**

Professor Robert Norman  
Associate Professor Manny Noakes  
Professor Peter Clifton

A thesis submitted to the University of Adelaide for the degree of

Doctor of Philosophy in Medical Science

**March 2007**

# TABLE OF CONTENTS

<b>LIST OF FIGURES</b> .....	<b>IV</b>
<b>LIST OF TABLES</b> .....	<b>V</b>
<b>DECLARATION</b> .....	<b>VI</b>
<b>DESCRIPTION OF THESIS</b> .....	<b>VII</b>
<b>ACKNOWLEDGEMENTS</b> .....	<b>VIII</b>
<b>ABSTRACT</b> .....	<b>X</b>
<b>PUBLICATIONS ARISING FROM THIS THESIS</b> .....	<b>XII</b>
<b>PRESENTATIONS ARISING FROM THIS THESIS</b> .....	<b>XV</b>
<b>ABBREVIATIONS</b> .....	<b>XVII</b>
<b>CHAPTER 1: LITERATURE REVIEW</b> .....	<b>1</b>
1.1: INTRODUCTION.....	2
1.2: OVERWEIGHT AND OBESITY.....	3
1.2.1: <i>Overview of overweight and obesity</i> .....	3
1.3: INSULIN RESISTANCE AND HYPERINSULINAEMIA.....	4
1.3.1: <i>Insulin resistance and hyperinsulinaemia</i> .....	4
1.3.1.1: Insulin resistance.....	4
1.3.1.2: Mechanisms of insulin resistance.....	5
1.3.1.3: Obesity and insulin resistance.....	7
1.3.1.4: Measurement of insulin resistance.....	9
1.4: PREVALENCE AND DEFINITION OF PCOS.....	10
1.4.1: <i>Definition and overview of PCOS</i> .....	10
1.4.2: <i>Diagnosis of PCOS</i> .....	12
1.4.3: <i>The relationship of obesity to PCOS</i> .....	15
1.4.3.1: Obesity and reproductive parameters.....	15
1.4.3.2: Obesity and PCOS.....	16
1.5: PATHOPHYSIOLOGY AND AETIOLOGY OF PCOS.....	17
1.5.1: <i>Hypothalamic-pituitary dysfunction in PCOS</i> .....	19
1.5.2: <i>Excessive androgen production and secretion in PCOS</i> .....	19
1.5.3: <i>PCOS, insulin resistance and hyperinsulinaemia</i> .....	22
1.6: OVERVIEW OF THE PATHOPHYSIOLOGY OF PCOS.....	26
1.7: TREATMENT OF PCOS.....	28
1.7.1: <i>Overview of the treatment of PCOS</i> .....	28
1.7.2: <i>Dietary management of PCOS</i> .....	28
1.7.2.1: Overview of dietary management of PCOS.....	28
1.7.2.2: Effects of weight loss on the presentation of PCOS.....	30
1.7.2.3: Degree of weight loss for improving the presentation of PCOS.....	31
1.7.3: <i>Altering dietary composition in the dietary management of PCOS</i> .....	33
1.7.3.1: Altering dietary protein amount.....	35
1.7.3.2: Altering dietary carbohydrate amount.....	36
1.7.3.3: Altering dietary glycemic index or glycemic load.....	38
1.7.3.4: Safety of different dietary compositions.....	40
1.7.3.5: Summary of dietary management of obesity and overweight in PCOS.....	41
1.8: PATHOPHYSIOLOGY RELEVANT TO IMPLEMENTATION OF LIFESTYLE MANAGEMENT IN PCOS.....	42
1.8.1: <i>Overview of pathophysiology relevant to lifestyle management implementation in PCOS</i> .....	42
1.8.2: <i>Modification of energy expenditure and energy intake in PCOS</i> .....	45
1.8.3: <i>Appetite regulation overview</i> .....	46

1.8.3.1: Cholecystokinin, peptide YY and ghrelin .....	51
1.8.3.2: Appetite hormones, obesity and diet composition .....	53
1.8.3.3: Appetite regulation and insulin .....	54
1.8.3.4: Appetite regulation and reproductive steroids .....	55
1.8.3.5: Appetite hormones and PCOS .....	57
1.9: THESIS AIMS AND HYPOTHESES .....	59
1.9.1: Thesis aims .....	59
1.9.1.1: Summary of thesis aims .....	59
1.9.1.2: Specific thesis aims .....	59
1.9.2: Specific thesis hypotheses .....	60
<b>CHAPTER 2: WEIGHT LOSS AND WEIGHT MAINTENANCE STRATEGIES IN POLYCYSTIC OVARY SYNDROME .....</b>	<b>62</b>
2.1: ABSTRACT .....	63
2.2: INTRODUCTION .....	63
2.3: METHODS .....	65
2.3.1: Subjects and recruitment .....	65
2.3.2: Study design .....	67
2.3.3: Dietary treatment .....	69
2.3.4: Biochemical measurements .....	70
2.3.5: Statistics .....	72
2.4: RESULTS .....	73
2.4.1: Subjects .....	73
2.4.2: Physical activity, diet and compliance .....	75
2.4.3: Weight loss, body composition, energy expenditure and quality of life .....	79
2.4.4: Fasting blood pressure, lipids, CRP, ghrelin, insulin and glucose homeostasis ...	83
2.4.5: Insulin homeostasis, reproductive hormones and menstrual cyclicality .....	83
2.5: DISCUSSION .....	89
<b>CHAPTER 3: DIFFERENTIAL EFFECT OF WEIGHT LOSS ON CARDIOVASCULAR RISK FACTORS IN OVERWEIGHT WOMEN WITH AND WITHOUT POLYCYSTIC OVARY SYNDROME .....</b>	<b>94</b>
3.1: ABSTRACT .....	95
3.2: INTRODUCTION .....	95
3.3: METHODS .....	98
3.3.1: Subjects and recruitment .....	98
3.3.2: Study design and dietary treatment .....	100
3.3.3: Biochemical measurements .....	102
3.3.4: Statistics .....	102
3.4: RESULTS .....	103
3.4.1: Subjects, physical activity and diet .....	103
3.4.2: Weight loss and body composition .....	105
3.4.3: Fasting lipids, CRP and adiponectin .....	105
3.4.4: Fasting and post-prandial glucose and insulin .....	106
3.4.5: Reproductive hormones and menstrual cyclicality .....	110
3.5: DISCUSSION .....	110
<b>CHAPTER 4: DIET COMPOSITION, GHRELIN AND SATIETY IN OVERWEIGHT WOMEN WITH AND WITHOUT POLYCYSTIC OVARY SYNDROME .....</b>	<b>116</b>
4.1: ABSTRACT .....	117
4.2: INTRODUCTION .....	117
4.3: METHODS .....	119
4.3.1: Subjects .....	119
4.3.2: Dietary intervention .....	120

4.3.3: <i>Study design</i> .....	121
4.3.4: <i>Biochemical measurements</i> .....	122
4.3.5: <i>Statistics</i> .....	122
4.4: RESULTS .....	123
4.4.1: <i>Subjects</i> .....	123
4.4.2: <i>Diet and compliance</i> .....	124
4.4.3: <i>Weight and body composition</i> .....	127
4.4.4: <i>Fasting and post-prandial glucose, insulin and HOMA</i> .....	127
4.4.5: <i>Fasting and post-prandial ghrelin</i> .....	129
4.4.6: <i>Visual analogue scores</i> .....	130
4.4.7: <i>Correlations and multiple regressions</i> .....	135
4.5: DISCUSSION .....	135
<b>CHAPTER 5: APPETITE HORMONES AND <i>AD LIBITUM</i> FOOD CONSUMPTION IN OVERWEIGHT WOMEN WITH AND WITHOUT POLYCYSTIC OVARY SYNDROME .....</b>	<b>140</b>
5.1: ABSTRACT.....	141
5.2: INTRODUCTION .....	141
5.3: METHODS .....	143
5.3.1: <i>Subjects and recruitment</i> .....	143
5.3.2: <i>Study design and dietary treatment</i> .....	143
5.3.3: <i>Biochemical measurements</i> .....	146
5.3.4: <i>Statistics</i> .....	146
5.4: RESULTS .....	147
5.4.1: <i>Subjects, physical activity, diet, weight loss, body composition and reproductive hormones</i> .....	147
5.4.2: <i>Fasting and post-prandial insulin and glucose homeostasis</i> .....	147
5.4.3: <i>Fasting and post-prandial ghrelin, PYY, CCK and visual analogue scores</i> .....	150
5.4.4: <i>Buffet dietary intake</i> .....	151
5.4.5: <i>Weight loss status</i> .....	151
5.5: DISCUSSION .....	155
<b>CHAPTER 6: FINAL DISCUSSION.....</b>	<b>162</b>
6.1: THESIS OVERVIEW .....	163
6.2: WEIGHT MANAGEMENT AND DIETARY COMPOSITION IN PCOS .....	164
6.3: EFFECT OF WEIGHT LOSS ON REPRODUCTIVE AND METABOLIC PARAMETERS IN PCOS .....	170
6.4: APPETITE, APPETITE HORMONES AND FOOD INTAKE.....	172
6.5: STUDY LIMITATIONS AND FUTURE RESEARCH .....	176
6.6: CONCLUSIONS.....	179
<b>CHAPTER 7: REFERENCES.....</b>	<b>181</b>
<b>APPENDIX 1: EFFECT OF DIETARY INTERVENTION IN PCOS ON CLINICAL, ENDOCRINE AND METABOLIC PARAMETERS .....</b>	<b>211</b>
<b>APPENDIX 2: ASSAY METHODOLOGY .....</b>	<b>215</b>
REPRODUCTIVE HORMONES .....	216
LIPIDS, INSULIN, GLUCOSE, C-REACTIVE PROTEIN, ADIPONECTIN, UREA AND CREATININE...	216
LEPTIN, GHRELIN, CHOLECYSTOKININ AND PEPTIDE YY .....	217
<b>APPENDIX 3: PUBLISHED PAPERS.....</b>	<b>219</b>
CHAPTER 2: PUBLISHED PAPER .....	220
CHAPTER 3: PUBLISHED PAPER .....	232

# LIST OF FIGURES

Figure 1.1: Insulin receptor signalling.....	6
Figure 1.2: Clinical features associated with Polycystic ovary syndrome .....	11
Figure 1.3: Steroid biosynthetic pathways in the adrenal, ovary and peripheral tissue.....	21
Figure 1.4: Polycystic ovary syndrome, the hypothalamic pituitary axis and insulin .....	27
Figure 1.5: The major causal linkages among genetics, environmental effects, physiology, behaviour and energy balance.....	44
Figure 1.6: Energy homeostasis and peripheral signals.....	49
Figure 2.1: Study flow diagram .....	66
Figure 2.2: Weight loss for data analysed as completers analysis, baseline value carried forward for study drop-outs and last clinic visit carried forward for study drop-outs.....	80
Figure 2.3: Fasting insulin (a) and homeostasis model assessment of insulin sensitivity (b) before and after 8 weeks of energy restriction on one dietary pattern (meal replacements) and 24 weeks of follow-up on either a fat counting (FC) or carbohydrate counting (CC) dietary protocol .....	85
Figure 2.4: Fasting testosterone (a), SHBG (b), free androgen index (c) and free testosterone (d) before and after 8 weeks of energy restriction on one dietary pattern (meal replacements) and 24 weeks of follow-up on either a fat counting (FC) or carbohydrate counting (CC) dietary protocol .....	86
Figure 3.1: Study flow diagram .....	99
Figure 3.2: C-reactive protein before and after 8 weeks of energy restriction on one dietary pattern (meal replacements).....	108
Figure 3.3: Glucose (a) and insulin (b) concentrations at baseline and 15, 30, 45, 60, 90, 120 and 180 min after the ingestion of a test meal at week 0 and week 8.....	109
Figure 4.1: Fasting and post-prandial ghrelin after 12 weeks of energy restriction and 4 weeks of weight maintenance on a standard protein or high protein diet.....	131
Figure 4.2: Subjective measures of hunger, fullness, satiety and desire to eat after a test meal before and after 12 weeks of energy restriction and 4 weeks of weight maintenance on a standard protein or high protein diet.....	133
Figure 5.1: Glucose (a), insulin (b), ghrelin (c), cholecystokinin (d) and peptide YY (e) concentrations at baseline and 15, 30, 45, 60, 90, 120 and 180 min after the ingestion of a test meal at week 0 and 8 before and after 8 weeks of energy restriction on one dietary pattern (meal replacements).....	152

## LIST OF TABLES

Table 1.1: Abnormalities associated with insulin resistance and hyperinsulinaemia.....	5
Table 1.2: Factors secreted from the adipocyte .....	9
Table 1.3: 1990 National Institute of Health and 2003 Rotterdam criteria for clinical diagnosis of Polycystic ovary syndrome.....	14
Table 1.4: Phenotypes and estimated prevalence of phenotypes of Polycystic ovary syndrome according to the National Institute of Health 1990 and Rotterdam 2003 Criteria.....	14
Table 1.5: Insulin effects related to ovarian function .....	25
Table 1.6: Changes in the macronutrient composition of various diets.....	34
Table 1.7: Hypothalamic and gut peptides involved in appetite control .....	48
Table 2.1: The food sources that subjects in the fat counting and carbohydrate counting diet groups were required to count grams of fat or carbohydrate from daily .....	71
Table 2.2: Baseline subject characteristics .....	74
Table 2.3: Dietary intake during 8 weeks of energy restriction on one dietary pattern (meal replacements).....	76
Table 2.4: Dietary intake at baseline and during 24 weeks on either a fat counting (FC) or carbohydrate counting (CC) dietary protocol (week 8 to 32).....	77
Table 2.5: Dietary intake (micronutrient) before study commencement (week 0) and during 24 weeks on either a fat counting (FC) or carbohydrate counting (CC) dietary protocol (week 8 to 32).....	78
Table 2.6 Weight, body composition, blood pressure, energy expenditure, lipids, glucose, ghrelin and CRP before and after 8 weeks of energy restriction on one dietary pattern (meal replacements) and 24 weeks of follow-up on either a fat counting (FC) or carbohydrate counting (CC) dietary protocol.....	81
Table 3.1: Subject baseline characteristics .....	104
Table 3.2: Weight, body composition, lipids, HOMA and reproductive hormones before and after 8 weeks of energy restriction on one dietary pattern (meal replacements) .....	107
Table 4.1: Subject baseline characteristics .....	125
Table 4.2: Dietary intake for 12 weeks of energy restriction and 4 weeks of weight maintenance on a standard or high protein diet.....	126
Table 4.3: Combined data for weight, body composition, fasting and post-prandial glucose and insulin and homeostasis model assessment before and after 12 weeks of energy restriction and 4 weeks of weight maintenance on a standard protein or high protein diet.....	128
Table 5.1: Subject baseline characteristics .....	148
Table 5.2: Weight, body composition, lipids, glucose and reproductive hormones before and after 8 weeks of energy restriction on one dietary pattern (meal replacements) .....	149
Table 5.3: Ad libitum energy and macronutrient intake 3 hours after test meal consumption before and after 8 weeks of energy restriction on one dietary pattern (meal replacements) ..	154

# DECLARATION

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

I give consent to this copy of my thesis, when deposited in the University Library, being available for loan and photocopying.

I acknowledge that copyright of published works contained within this thesis (as listed below) resides with the copyright holders/s of these works.

**Moran LJ**, Noakes M, Clifton PM, Wittert GA, Williams G, Norman RJ. 2006, Short term meal replacements followed by dietary macronutrient restriction enhance weight loss in Polycystic Ovary Syndrome. *The American Journal of Clinical Nutrition*; 84(1):77–87.

**Moran LJ**, Noakes M, Clifton PM, Wittert G, Tomlinson L, Galletly C, Luscombe N, Tomlinson L, Norman RJ. 2004, Ghrelin and measures of satiety are altered in polycystic ovary syndrome but not differentially affected by diet composition. *Journal of Clinical Endocrinology and Metabolism*, 89(7):3337–44.

**Moran LJ**, Noakes M, Clifton P, Wittert GA, Norman RJ. 2007, Weight loss, CRP and adiponectin in overweight women with and without Polycystic Ovary Syndrome. *The Journal of Clinical Endocrinology and Metabolism*, in press.

SIGNED.....

DATED.....

## **DESCRIPTION OF THESIS**

Chapters 2–6 were submitted for publication prior to the completion of this thesis. Chapters 2 and 4 have been accepted and published, Chapter 3 has been accepted and is in press and Chapter 5 is currently under review. For this reason, this thesis was prepared in a similar style to a Thesis by Publication. The bulk of the study methodology is included within the relevant chapters conforming to the style of the relevant journal to which the chapters were submitted. Additional methodological information is provided in Appendix 2. Where new information pertinent to the topic of the chapter has been published after the relevant paper, it is discussed in the final conclusion as opposed to the Chapter/Paper discussion being amended. Paper co-authors are acknowledged in the Acknowledgement Section and Appendix 3 contains the published papers.



## ACKNOWLEDGEMENTS

I would firstly like to acknowledge the co-authors for the manuscripts arising from these studies: Professor Robert Norman, Associate Professor Manny Noakes, Professor Peter Clifton, Professor Gary Wittert, Gemma Williams, Lisa Tomlinson, Dr Cherrie Galletly, Dr Natalie Luscombe-Marsh, Dr Carel Le Roux, Dr Mohammed Ghatei and Professor Stephen Bloom. I would also like to acknowledge Unilever and McDonalds Australia for assistance with study supplies and The National Health and Medical Research Council Program Grant (to Robert Norman), The University of Adelaide Faculty of Health Sciences Small Research Grants Scheme and Colin Matthews Research Grants for Clinically Based Research and CSIRO Human Nutrition for funding for that contributed to this research.

I'd also like to acknowledge the invaluable assistance of a large number of people in the implementation of these studies at CSIRO Human Nutrition and Repromed. I gratefully acknowledge Anne McGuffin, Kathryn Bastiaans, Julia Weaver, Jodie Avery and Vanessa Courage for clinical trial co-ordination; Grant Brinkworth, Emma Farnsworth, Eleni Argyiou, Bronwen Roberts and Gillian Homan for assisting in clinical measurements; Gemma Williams, Jennifer Keogh and Paul Foster for assisting in the dietary interventions; Rosemary McArthur, Ruth Pinches, Sue Evans, Sue Davies, Marcia Parish and Deborah Roffe for their nursing expertise and Alan Gilmore, Anne-Marie Carrera, Michelle Kolo, Mark Mano, Candita Sullivan, Cherie Keatch, Julie Turner, Cathryn Seccafien, Paul Orchard and Michael Mular for assisting with the sample collection and biochemical assays. Thank you also to all the study participants who volunteered their time and made these studies possible.

I'd like to thank my supervisors Robert Norman, Manny Noakes and Peter Clifton. Specifically, Rob who provided me with support, understanding, opportunities and challenges and Manny who kept my enthusiasm for research alive and always provided a critical eye for

my presentations and papers. Thank you to Peter and Gary Wittert for their useful scientific input and assistance in interpreting all my study results. Thank you also to post-docs and students Grant Brinkworth, Natalie Luscombe-Marsh, Jane Bowen, Damien Belobradjic, Leana Coleman, Amanda Aloia, Karma Pearce, Bianca Benassi, Sasja Beetstra, Denise Furness, Phil Thomas, Caroline Bull, Shusuke Toden, Melanie Bagg, Cadence Minge, Theresa Hickey and Rebecca Robker both for scientific input and for all their help in de-stressing and staying sane!

Finally, thank you to my parents Rosemary and Terry for their unconditional assistance and love, to Kevin for proof-reading and editing and to all my friends who provided me with much needed escapism over the years (and who helped me label thousands of tubes). A special thanks to Nick for his love, patience and understanding!

# ABSTRACT

## Background

Polycystic ovary syndrome (PCOS) is a common endocrine condition in women associated with obesity, reproductive and metabolic abnormalities. It improves with weight loss, however currently no specific dietary recommendations exist and there may be abnormalities in appetite regulation in PCOS that contribute to difficulty in weight management.

## Aims

To assess the effect of 1) short and long-term weight loss and weight maintenance strategies on weight loss, reproductive and metabolic parameters in overweight women with PCOS and to 2) assess the relative effect of weight loss on cardiovascular risk factors and 3) post-prandial appetite, appetite hormones (ghrelin, CCK, PYY) and food intake in overweight women with and without PCOS.

## Results

Overweight women with PCOS followed an 8-week weight loss (2 meal replacements/day, 4904.4±127 kJ, n=32) followed by a 6 month carbohydrate (<120 g/day) or fat restricted (<50 g/day) weight maintenance regime (n=23). Reductions in weight (5.6±2.4 kg) and improvements in body composition, insulin, reproductive hormones and menstrual cyclicity occurred and were sustained equivalently for both diet groups. We then assessed the effect of weight loss (4.2±0.7 kg over 8 weeks as described above) in overweight women with (n=15) and without (n=17) PCOS on cardiovascular risk factors. All subjects had similar improvements in body composition, triglycerides, reproductive hormones and fasting and post-prandial insulin. C-reactive protein decreased with weight loss for non-PCOS women (-1.2±0.5 mg/L, P=0.025) but not for PCOS women.

We finally assessed appetite regulation in PCOS. Women with (n=20) and without (n=12) PCOS followed a standard protein (55% carbohydrate, 15% protein) or high protein diet (40% carbohydrate, 30% protein) for 16 weeks (~6000 kJ/day). Non-PCOS subjects were more satiated (P=0.001) and less hungry (P=0.007) after the test meals and had a 70% higher fasting baseline ghrelin (P=0.011), a greater increase in fasting ghrelin (57.5 versus 34.0%, P=0.033), a greater post-prandial ghrelin decrease at week 16 (113.5±46.3 versus 49.3±12.2 pg/mL, P=0.05) and a greater maximal decrease in post-prandial ghrelin (-144.1±58.4 versus -28.9±14.2 pg/mL, P=0.02) following weight loss than subjects with PCOS. Lastly, women with (n=14) and without (n=14) PCOS undertook an 8-week weight loss regime (4.2±0.7 kg as described above). At week 0 and 8, women with PCOS again displayed lower ghrelin levels (P=0.01 and P=0.097 respectively) and a lesser post-prandial ghrelin decrease (P=0.048 and P=0.069 respectively) but similar post-prandial appetite, buffet consumption and fasting or post-prandial peptide YY and cholecystokinin compared to women without PCOS.

## **Conclusion**

Meal replacements and moderate macronutrient restriction are effective strategies for the dietary management of PCOS. Equivalent weight losses improved cardiovascular risk factors similarly for overweight women with and without PCOS with the exception of CRP which did not decrease with weight loss for overweight women with PCOS. PCOS status is associated with altered fasting and post-prandial ghrelin levels but is not consistently associated with other impairments in post-prandial gut peptides or food intake. Further investigation is required to assess if appetite regulation is impaired in PCOS and the optimal strategies and amount of weight loss for improvement of reproductive and metabolic parameters in PCOS.

## **PUBLICATIONS ARISING FROM THIS THESIS**

**Moran LJ**, Noakes M, Brinkworth G, Norman RJ. 2006, Diet, Nutrition and Exercise in Reproduction. *Reproductive BioMedicine Online*, 12(5):569–578

**Moran LJ**, Noakes M, Clifton P, Wittert GA, Le Roux C, Ghatei M, Bloom S, Norman RJ. 2006, Post-prandial ghrelin, cholecystokinin, PYY, appetite and food consumption before and after weight loss in overweight women with and without Polycystic Ovary Syndrome. *The Journal of Clinical Endocrinology and Metabolism*, (Submitted 23<sup>rd</sup> January 2007).

**Moran LJ**, Noakes M, Clifton P, Wittert GA, Norman RJ. 2007, Weight loss, CRP and adiponectin in overweight women with and without Polycystic Ovary Syndrome. *The Journal of Clinical Endocrinology and Metabolism*, in press.

Brinkworth GD, **Moran LJ**, Noakes M, Norman R, Clifton PM. 2006, Flow mediated dilatation in overweight and obese women with polycystic ovary syndrome. *British Journal of Obstetrics and Gynaecology*, 113:1308–1314.

**Moran LJ**, Noakes M, Clifton PM, Wittert GA, Williams G, Norman RJ. 2006, Short term meal replacements followed by dietary macronutrient restriction enhance weight loss in Polycystic Ovary Syndrome. *The American Journal of Clinical Nutrition*, 84(1):77–87.

Norman RJ, **Moran L**. 2005, Lifestyle factors in the aetiology and management of polycystic ovary syndrome. *Polycystic Ovary Syndrome* (2<sup>nd</sup> edition). Cambridge University Press.

Noakes M, Brinkworth G, **Moran L**, Norman RJ. 2005, Weight Reduction and Life-Style Modification in the Treatment of Androgen Excess. *Androgen Excess Disorders*, in press.

Norman RJ, Homan G, **Moran L**, Noakes M. 2005, Lifestyle choices, diet and insulin sensitisers in polycystic ovary syndrome. *Endocrine*, in press.

**Moran LJ**, Noakes M, Clifton PM, Wittert G, Tomlinson L, Galletly C, Luscombe N, Tomlinson L, Norman RJ. 2004, Ghrelin and measures of satiety are altered in polycystic ovary syndrome but not differentially affected by diet composition. *The Journal of Clinical Endocrinology and Metabolism*, 89(7):3337–44.

**Moran L** and Norman RJ. 2004, Understanding and managing disturbances in insulin metabolism and body weight in overweight women with polycystic ovary syndrome. *Best Practice and Research Clinical Obstetrics and Gynaecology*, 18(5):719–36.

Norman RJ, Hickey T, **Moran L**, Boyle J, Wang J, Davies M. 2004, Polycystic ovary syndrome – diagnosis and etiology. *International Congress Series*, 1266; 225–232. Elsevier.

Norman RJ, Noakes M, Wu Ruijin, Davies MJ, **Moran L**, Wang JX. 2004, Improving reproductive performance in overweight/obese women with effective weight management. *Human Reproduction Update*, Vol 10 (3) 267–280.

**Moran LJ**, Norman RJ. 2002, The obese patient with infertility: a practical approach to diagnosis and treatment. *Nutrition in Clinical Care*, 5(6): 290–9.

Norman RJ, Davies MJ, Lord J, **Moran LJ**. 2002, The role of lifestyle modification in polycystic ovary syndrome. *Trends in Endocrinology and Metabolism*, 13(6): 251–7.

Norman RJ, **Moran L**, Davies MJ. 2001, Nutritional aspects of polycystic ovary syndrome. *Reproductive Medicine Reviews*, 9(2):91–107.

### **Conference proceedings**

**Moran LJ**, Noakes M, Clifton PM, Wittert GA, Williams G, Norman RJ. 2005, Effective weight loss and maintenance strategies in polycystic ovary syndrome. *Asia Pac J Clin Nutr*, 14 Suppl:S94.

**Moran LJ**, Luscombe-Marsh ND, Noakes M, Wittert GA, Keogh JB, Clifton PM. 2005, The satiating effect of dietary protein is unrelated to post-prandial ghrelin secretion. *Asia Pac J Nutr*, 14 Suppl: S64.

**Moran LJ**, Noakes M, Wittert GA, Clifton PM, Norman RJ. 2004, Short term energy restriction (using meal replacements) improves reproductive parameters in polycystic ovary syndrome. *Asia Pac J Clin Nutr*, 13 Suppl:S88.

**Moran LJ**, Noakes M, Clifton PM, Wittert G, Tomlinson L, Galletly C, Luscombe N, Tomlinson L, Norman RJ. 2003, Ghrelin and measures of satiety are altered in polycystic ovary syndrome but not differentially affected by diet composition. *Asia Pac J Clin Nutr*, 12 Suppl:S52.

**This citation not included in the original print copy of thesis**

Published Abstract:

Moran, L.J., Noakes, M., Clifton, P.M., Wittert, G.A., Belobrajdic, D.P. and Norman, R.J. (2007) C-Reactive Protein before and after Weight Loss in Overweight Women with and without Polycystic Ovary Syndrome.

*Journal of Clinical Endocrinology and Metabolism*, v. 92 (8) pp. 2944-51 August 2007



# PRESENTATIONS ARISING FROM THIS THESIS

## Oral presentations

### 2006:

Androgen Excess Society International Meeting, Athens, Greece

‘Obesity and Polycystic Ovary Syndrome’. **Moran LJ** and Norman RJ.

International Congress of Obesity, Sydney, Australia

‘Post-prandial ghrelin, cholecystokinin, PYY, appetite and food consumption before and after weight loss in overweight women with and without Polycystic Ovary Syndrome’, **Moran LJ**, Noakes M, Clifton P, Wittert GA, Le Roux C, Ghatei M, Bloom S, Norman RJ.

### 2005:

Dietetics Association of Australia State Conference, Adelaide, Australia

‘Diet and Polycystic Ovary Syndrome’, **Moran LJ**.

## Poster presentations

### 2006:

International Congress of Obesity, Sydney, Australia

‘Weight loss does not lower CRP in overweight women with Polycystic Ovary Syndrome’, **Moran LJ**, Noakes M, Clifton P, Wittert GA, Norman RJ.

### 2005:

North American Society for the Study of Obesity International Conference,  
Vancouver, Canada

Australasian Society for the Study of Obesity National Conference, Adelaide, South Australia

Nutrition Society of Australia National Conference, Melbourne, Victoria

‘Effective weight loss and maintenance strategies in polycystic ovary syndrome’, **Moran LJ**, Noakes M, Clifton PM, Wittert GA, Williams G, Norman RJ.

**2004:**

Nutrition Society of Australia National Conference, Brisbane, Queensland

Australasian Society for the Study of Obesity, Brisbane, Queensland

‘Short term meal replacements followed by dietary macronutrient restriction enhance weight loss in Polycystic Ovary Syndrome’, **Moran LJ**, Noakes M, Clifton PM, Wittert GA, Williams G, Norman RJ.

**2003:**

Endocrine Society of Australia National Conference, Melbourne, Victoria

Australian Medical Research Council National Conference, Adelaide, South Australia

Nutrition Society of Australia National Conference, Hobart, Tasmania

Dietetics Association of Australia State Conference, Adelaide, South Australia

‘Ghrelin and measures of satiety are altered in polycystic ovary syndrome but not differentially affected by diet composition’, **Moran LJ**, Noakes M, Clifton PM, Wittert G, Tomlinson L, Galletly C, Luscombe N, Tomlinson L, Norman RJ.

## ABBREVIATIONS

- $\alpha$ -MSH:  $\alpha$ -melanocyte stimulating hormone
- ADP: Adenosine diphosphate
- AgRP: Agouti-related peptide
- AI: Adequate intake
- AMH: Anti-mullerian hormone
- Apo A-IV: Apolipoprotein A-IV
- ATP: Adenosine triphosphate
- AUC: Area under the curve
- BIA: Bioelectrical impedance analysis
- BMI: Body mass index
- BNRP: Bombesin/bombesin related peptides
- CART: Cocaine and amphetamine regulated transcript
- CC: Carbohydrate counting
- CCK: Cholecystokinin
- CHO: Carbohydrate
- CIGMA: Continuous infusion of glucose with model assessment
- CRF: Corticotropin-releasing factor
- CRP: C-reactive protein
- CV: Coefficient of variation
- CVD: Cardiovascular disease
- DBP: Diastolic blood pressure
- DEXA: Dual X-ray absorptiometry
- DHEA: Dehydroepiandrosterone
- DHEAS: Dehydroepiandrosteronesulfate
- 5 $\alpha$ -DHT: 5 $\alpha$ - Dihydrotestosterone
- DHT: Dihydrotestosterone

ER: Energy restriction

FAI: Free androgen index

FC: Fat counting

FFA: Free fatty acid

FSH: Follicle-stimulating hormone

FSIVGTT: Frequently sampled intravenous glucose tolerance test

hCG: Human chorionic gonadotrophin

GH: Growth hormone

GHRH: Growth hormone releasing hormone

GHS-R: Growth hormone secretagogue receptor

GI: Glycaemic index

GL: Glycaemic load

GLP-1: Glucagon-like peptide 1

Glucose-6-P: Glucose-6 phosphate

GLUT4: Glucose transporter 4

GnRH: Gonadotrophin releasing hormone

HA: Hyperandrogenism

HDL-C: High density lipoprotein cholesterol

HOMA: Homeostasis model assessment

HP: High protein

3 $\beta$ HSD: 3 $\beta$ -hydroxysteroid dehydrogenase

17 $\beta$ HSD: 17 $\beta$ -hydroxysteroid dehydrogenase

20 $\alpha$ HSD: 20 $\alpha$ -hydroxysteroid dehydrogenase

HSD: Hydroxysteroid dehydrogenase

IGF: Insulin-like growth factor

IGFBP: Insulin-like growth factor binding proteins

IGT: Impaired glucose tolerance

IL: Interleukin

IR: Insulin resistance

IRS: Insulin receptor substrate

IST: Insulin sensitivity test

ITT: Insulin tolerance test

IVF: In vitro fertilization

LDL-C: Low-density lipoprotein cholesterol

LH: Luteinising hormone

LP: Low protein

MAPK: Mitogen activated protein kinase

MCH: Melanin-concentrating hormone

MTT: Meal tolerance test

MUFA: Monounsaturated fatty acid

NIH: National Institute of Health

NPY: Neuropeptide Y

OGTT: Oral glucose tolerance test

OXM: Oxyntomodulin

P450AR: Cytochrome P450 aromatase

P450csc: Cytochrome P450 side chain cleavage

P450c11AS: Cytochrome P45011 aldosterone synthetase

P450c11B: Cytochrome P450 11-hydroxylase

P450c17 $\alpha$ : Cytochrome P450 17  $\alpha$  hydroxylase

P450c17,20: Cytochrome P450 17,20 lyase

P450c21: Cytochrome P450 21-hydroxylase

PAI-1: Plasminogen-activator inhibitor activity

PCO: Polycystic Ovary Syndrome

PCOS: Polycystic Ovary Syndrome

PI3-K: Phosphatidylinositol 3-kinase

POMC: Pro-opiomelanocortin

PP: Pancreatic polypeptide

PPAR: Peroxisome proliferator activator receptor

PUFA: Polyunsaturated fatty acid

PVN: Paraventricular nucleus

PYY: Peptide YY

QUICKI: Quantitative insulin sensitivity check index

RDI: Recommended dietary intake

REE: Resting energy expenditure

RR: Relative risk

RQ: Respiratory quotient

SFA: Saturated fatty acid

SHBG: Sex-hormone binding globulin

SP: Standard protein

StAR: Steroidogenic acute regulatory protein.

T2DM: Type II diabetes mellitus

TFM: Total fat mass

TFFM: Total fat free mass

TNF- $\alpha$ : Tumour necrosis factor  $\alpha$

TSH: Thyroid stimulating hormone

VAS: Visual analogue scores

VLCD: Very low calorie diets

VLDL: Very low density lipoprotein

VO<sub>2max</sub> : Maximal oxygen consumption

WHR: Waist-hip ratio

WM: Weight maintenance