

# **Weight management in young women**

A thesis submitted by

**Siew S Lim**

For the degree of Doctor of Philosophy

in the Discipline of Physiology

School of Molecular and Biomedical Science

University of Adelaide

February 2009

# Table of contents

<i>Declaration of originality</i>	4
<i>Acknowledgements</i>	6
<i>List of figures</i>	7
<i>List of tables</i>	9
<i>Abbreviations</i>	10
<i>Abstract</i>	12
<b>Chapter 1 Introduction</b>	14
1.1 <i>Young women and weight gain</i>	15
1.1.1 <i>Prevalence of weight gain</i>	15
1.1.2 <i>Long term consequences of excess weight or weight gain in young women</i>	16
1.1.3 <i>Short term consequences of excess weight or weight gain in young women</i>	20
1.1.4 <i>Why do young women gain weight?</i>	26
1.2 <i>Young Women and Weight loss</i>	40
1.2.1 <i>Prevalence of weight loss attempts</i>	40
1.2.2 <i>Lifestyle interventions and weight loss in young women</i>	42
1.2.3 <i>Quantitative or qualitative lifestyle advice</i>	51
1.2.4 <i>Internet as a medium to provide long term weight management support</i>	52
1.2.5 <i>Metformin and weight loss in young women</i>	53
1.3 <i>Summary and gaps in knowledge</i>	61
1.4 <i>Objective</i>	62
1.5 <i>Aims</i>	63
1.6 <i>Hypotheses</i>	64
<b>Chapter 2 Hyperandrogenemia, psychosocial distress, and food cravings in overweight and obese young women</b>	65
2.1 <i>Abstract</i>	68
2.2 <i>Introduction</i>	69
2.3 <i>Methods</i>	70
2.4 <i>Results</i>	74
2.5 <i>Discussion</i>	75
2.6 <i>Figures and tables</i>	80
<b>Chapter 3 The effect of comprehensive lifestyle intervention or metformin on obesity in young women</b>	82
3.1 <i>Abstract</i>	85
3.2 <i>Introduction</i>	86
3.3 <i>Methods and procedure</i>	87

3.4	<i>Results</i>	91
3.5	<i>Discussion</i>	95
3.6	<i>Figures and tables</i>	98
<b>Chapter 4</b> <i>The psychological effects of prescriptive vs general lifestyle advice for weight loss in young women</i>		102
4.1	<i>Abstract</i>	105
4.2	<i>Introduction</i>	106
4.3	<i>Methods</i>	107
4.4	<i>Results and discussion</i>	110
4.5	<i>Conclusions</i>	114
4.6	<i>Figures and tables</i>	115
<b>Chapter 5</b> <i>Long term weight management through internet program in young women</i>		117
5.1	<i>Abstract</i>	118
5.2	<i>Introduction</i>	120
5.3	<i>Methods</i>	121
5.4	<i>Results</i>	125
5.5	<i>Discussion</i>	127
5.6	<i>Figures and tables</i>	132
<b>Chapter 6</b> <i>Discussion and conclusion</i>		136
6.1	<i>Drug or diet</i>	136
6.2	<i>Restraint or freedom</i>	137
6.3	<i>Stress, hyperandrogenemia and food cravings</i>	138
6.4	<i>Internet-based weight management program</i>	140
6.5	<i>Young women and weight management</i>	140
6.6	<i>Limitations</i>	142
6.7	<i>Conclusion</i>	143
<b>Appendix 1. Questionnaires on socio-demographic characteristics, psychological distress (GHQ), self-esteem (RSE-B), food cravings inventory (FCI) and internet usage</b>		146
<b>Appendix 2. Post intervention questionnaire</b>		156
<b>Appendix 3. Exit interview (conducted by psychologist)</b>		160
<b>Bibliography</b>		171

## Declaration of originality

NAME: SIEW SEEN LIM

PROGRAM: PhD in Physiology

This work 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 made available for loan and photocopying, subject to the provisions of the Copyright Act 1968.

I acknowledge that copyright of published works contained within this thesis (as listed below\*) resides with the copyright holder(s) of those works. I also give permission for the digital version of my thesis to be made available on the web, via the University's digital research repository, the Library catalogue, the Australasian Digital Theses Program (ADTP) and also through web search engines, unless permission has been granted by the University to restrict access for a period of time.

\* List of publications contained within the thesis:

Siew S Lim, Robert J Norman, Peter M Clifton, Manny Noakes.

Hyperandrogenemia, psychosocial distress, and food cravings in overweight and obese young women. *Physiology and Behaviour* (2009), 98: 276-280.

Lim SS, Norman RJ, Clifton PM, Noakes M. The effect of comprehensive lifestyle intervention or metformin on obesity in young women. *Nutrition, Metabolism and Cardiovascular Disease (in press)*.

SS Lim, RJ Norman, PM Clifton, M Noakes. The psychological effects of prescriptive vs general lifestyle advice for weight loss in young women. *Journal of the American Dietetic Association (in press)*.

Signed \_\_\_\_\_ Date \_\_\_\_\_

## Acknowledgements

*My supervisors*—Manny Noakes, Peter Clifton and Robert Norman. Thank you for your patience, encouragement, and guidance in the past 3 years. It is your presence and involvement that made this a wonderful experience.

*The young women volunteers*—Thank you for giving up your time and effort in making this study a reality. You helped us realise how difficult it can be to take up lifestyle modifications at your life-stage. You ought to be applauded for having the courage to sign up for this study.

*The clinic and laboratory staff*—Julia Weaver, Kathryn Bastiaans, Rosemary McArthur, Lindy Lawson, Ruth Pinches, Vanessa Courage, Lesley Donnelly, Xenia Cleanthous, Lynn Field, Candita Sullivan, and Cathryn Seccafien. Thank you for your outstanding support in this study. It has been a great pleasure working with such a competent team like you.

*Friends at CSIRO*—Grant Brinkworth, Jane Bowen, Karma Pearce, and Adam Harrison. Thank you for your friendship and support. Grant and Adam, your contributions to the study in the exercise program and exit interviews are much appreciated.

*Healthy Development Adelaide*—It is because of you that I have stumbled upon this wild and wonderful ride of research in young women. Thank you for opening my eyes to the challenges of this group.

*My Bible Study Group*—Eating, studying, praying and laughing with you every Friday night reminded me of the truly important things in life. Without you I would be a different person today.

*Mom*—Thank you for encouraging me to pursue passion over career stability. It is a great advice, one that allows me to wake up most days feeling grateful for my life.

*My husband*—Thank you for breathing love, affirmation, and stability into my life whenever I am gripped by fear and insecurities. I pray for the wisdom and patience to guide and help you as you take on new challenges in the coming years.

*God*—Thank you for reassuring me that my future is in Your hands. I look forward to live another day to discover Your plans in my life.

## List of figures

<i>Figure 1.1 The 10-year incidence of major weight gain (<math>\geq 5</math> kg/m<sup>2</sup>) among men and women in US. The error bars indicate 95% confidence intervals. The numbers above the bars show relative risks for major weight gain in women compared to men, with 95% confidence intervals in parentheses. (Taken from Williamson et al, 1990, p669 [7]).....</i>	<i>14</i>
<i>Figure 1.2 Mean BMI by birth cohort for women in Australia in 1990 to 2000 with projections to 2010. (Taken from Allman-Farinelli et al, 2006, p6 [1]).....</i>	<i>16</i>
<i>Figure 1.3 The effect of adiposity signals such as leptin on the homeostatic (ie satiety) and non homeostatic (ie food reward) pathways in the regulation of food intake. ARC, arcuate nucleus (highlighted in blue); DMN, dorsomedial nucleus; FX, fornix; ME, median eminence; PFA, perifornical area; VMN, ventromedial nucleus. (Taken from Morton et al, 2006, p290 [81]).....</i>	<i>27</i>
<i>Figure 1.4 Causes of weight gain in young women.....</i>	<i>39</i>
<i>Figure 1.5 Mean expenditure on weight management strategies by young women (age 18 to 32, n=445) in Australia. (Taken from Ball et al, 2003, p586 [130]).....</i>	<i>40</i>
<i>Figure 1.6 Effect of metformin on BMI in non diabetic persons, percentage change. (Taken from Salpeter et al, 2008, p151 [75]).....</i>	<i>56</i>
<i>Figure 2.1 Food cravings score (means <math>\pm</math> SE, n=198) in young women with or without hyperandrogenemia (defined as Free Androgen Index &gt; 4.97). * P&lt;0.05 between groups after correcting for age, BMI and PCOS status. ....</i>	<i>80</i>
<i>Figure 2.2 Food cravings score (means + SE, n=198) in young women with or without menstrual disturbances (MD). * P&lt;0.05 between groups after correcting for age, BMI and PCOS status. ....</i>	<i>80</i>
<i>Figure 3.1. Flow diagram of participants' recruitment, randomization and completion of the interventions.....</i>	<i>98</i>

*Figure 3.2 Estimated weight changes ( $\pm$  standard error) in participants randomised to comprehensive lifestyle program (circles, n=59), metformin plus general lifestyle advice (squares, n=65), or placebo plus general lifestyle advice (triangles, n=79).  $P < 0.05$  between changes in comprehensive lifestyle group compared to metformin and placebo groups. .... 99*

*Figure 3.3 Weight outcomes of participants after 12-weeks on comprehensive lifestyle program (n=59), metformin (n=65), or placebo (n=79).  $P < 0.05$  for chi-square analysis. 99*

*Figure 4.1 Flow diagram of participants' recruitment, participation and completion of the interventions..... 115*

*Figure 5.1 Flow diagram of participants' recruitment, randomization and completion of the interventions..... 132*

*Figure 5.2 Estimated weight changes ( $\pm$ SEM) of the groups receiving quantitative lifestyle advice (QT) or qualitative lifestyle advice (QL) from week 0 to 12 according to mixed model analyses. Both groups received online quantitative lifestyle intervention from week 12 to 48. Time, treatment and time-by-treatment were fixed factors in the linear mixed models.  $P < 0.0005$  for time-by-treatment effect. .... 133*



## List of tables

<i>Table 1.1 The long term consequences of excess weight or weight gain in early adulthood: a summary of results from prospective studies in women .....</i>	<i>20</i>
<i>Table 1.2 The effect of insulin on androgen production.....</i>	<i>22</i>
<i>Table 1.3 The short-term consequences of excess weight or weight gain in early adulthood: a summary of results in young women.....</i>	<i>25</i>
<i>Table 1.4 Behavioural factors associated with weight gain in young women.....</i>	<i>32</i>
<i>Table 1.5 Dietary trials conducted in young women (mean age: 18 to 40 years).....</i>	<i>44</i>
<i>Table 1.6 Exercise trials in young women.....</i>	<i>48</i>
<i>Table 1.7 Randomised-controlled trials on the effect of metformin on body weight in non diabetic individuals.....</i>	<i>57</i>
<i>Table 1.8 Randomised-controlled trials on the effect of metformin on body weight in PCOS women .....</i>	<i>59</i>
<i>Table 2.1 Characteristics of study participants (n=198) .....</i>	<i>81</i>
<i>Table 2.2 Regression coefficients for food cravings<sup>a</sup> in predicting psychological distress<sup>b</sup> (n=198)<sup>c</sup> .....</i>	<i>81</i>
<i>Table 3.1 Estimated means and changes on clinical and metabolic outcomes<sup>a</sup> .....</i>	<i>100</i>
<i>Table 4.1 Estimated means and changes for psychological measures for the prescription lifestyle advice (PLA) group (n=59) and the general lifestyle advice (GLA) group (n=144) .....</i>	<i>116</i>
<i>Table 5.1 Treatment conditions in Phase I (week 0 to 12) and Phase II (week 13 to 48). .....</i>	<i>134</i>
<i>Table 5.2 Baseline characteristics of participants (n=203).....</i>	<i>134</i>
<i>Table 5.3 Body weight, energy intake and physical activity outcomes by treatment condition from baseline to Week 48<sup>a</sup> .....</i>	<i>135</i>
<i>Table 5.4 Attrition by treatment condition over time<sup>a</sup> .....</i>	<i>135</i>

## Abbreviations

AGRP	Agouti-related peptide
AMPK	AMP-activated protein kinase
ATP	Adult Treatment Panel
BMI	Body mass index
C	Carbohydrate
CARDIA	Coronary Artery Risk Development in Young Adults
CHD	Coronary heart disease
DBS	Dieting Belief Scale
DPP	Diabetes Prevention Program
F	Fat
FAI	Free androgen index
FCI	Food Craving Inventory
GHQ	General Health Questionnaire
GLP-1	Glucagon-like peptide-1
HDL	High density lipoprotein
HOMA	Homeostasis model assessment
I	Internet support
IP	Internet plus in-person support
IRS-2	Insulin receptor substrate 2
LCD	Low calorie diet
LDL	Low density lipoprotein
LH	Luteinising hormone
M	Metformin
NA	Not available

NHANES	National Health and Nutrition Examination Survey
NHLBI	National Heart, Lung, and Blood Institute
NPY	Neuropeptide Y
NS	Not significant
OR	Odds ratio
P	Protein
P	Placebo
PCOS	Polycystic ovaries syndrome
PI-3	Phosphoinositide 3
PKC	Protein kinase C
QL	Qualitative lifestyle advice
QT	Quantitative lifestyle advice
RCT	Randomised controlled trial
RR	Relative risk
RSE-B	Bachman's revision of Rosenberg Self-esteem Scale
S	Structured, quantitative lifestyle advice
SEM	Standard error of the mean
SHBG	Sex hormone binding globulin
T	Testosterone
VLCD	Very low calorie diet

# **Abstract**

## **Context**

Young women are at high risk of weight gain but there has been limited knowledge on weight management in this group. Hyperandrogenemia and menstrual abnormalities are common co-morbidities of obesity in young women but their associations with food cravings are not known. Metformin has been shown to reduce body weight and improve metabolic outcomes in older adults but its effects on healthy overweight and obese young women have not been investigated. Quantitative lifestyle advice has been shown to be effective in inducing weight loss but its psychological effects on young women have not been extensively studied. The overall objective of this study was to investigate the effectiveness of metformin, quantitative lifestyle advice and internet-based intervention on weight management in young.

## **Methods**

In the first 12-weeks, 203 overweight and obese young women (BMI  $33.3 \pm 0.3$  kg/m<sup>2</sup>, age  $28 \pm 0.3$  years; age range: 17-37) were randomized to one of three treatment arms to receive metformin (Diabex XR 1500mg a day) plus qualitative lifestyle advice (M-QL), placebo plus qualitative lifestyle advice (P-QL) or a structured lifestyle program (L-QT). L-QT consisted of an energy restricted diet with quantitative lifestyle advice (6000KJ; 40% protein, 40% carbohydrate, 30% fat), structured exercise program, and behavioural therapy. From weeks 13 to 48, all participants were placed on the structured lifestyle program conducted through a website. Outcome measures include body weight, fasting lipids, insulin, glucose, psychological distress, self-esteem, food cravings, energy intake and physical activity. Primary analyses were conducted using linear mixed models.

## Results

At baseline, psychological distress and hyperandrogenemia were associated with increased food cravings ( $P < 0.01$ ). At 12-weeks, L-QT group had greater weight loss ( $-4.2 \pm 0.4$  kg) compared to M-QL ( $-1.0 \pm 0.4$  kg) and P-QL groups ( $-0.2 \pm 0.3$  kg) ( $P < 0.001$ ). Attrition at week 12 was high particularly in L-QT group, ie 48% (28/59) for L-QT group, 34% (22/65) for M-QL group and 29% (23/79) for P-QL group ( $P = 0.08$ ). Baseline psychological distress and food cravings predicted attrition at week 12. At week 12, L-QT group had significantly greater improvements in psychological distress ( $-3.0 \pm 0.9$  vs  $-0.84 \pm 0.52$ ,  $P = 0.013$ ) and self-esteem ( $3.2 \pm 0.8$  vs  $-0.04 \pm 0.4$ ,  $P < 0.001$ ) compared to the M-QL and P-QL groups. At 48 weeks, both QT and QL groups maintained significant weight loss ( $-4.8 \pm 0.1$  kg vs  $-1.3 \pm 0.4$  kg respectively,  $P = 0.0005$ ). Weight changes from week 13 to 48 were similar between the groups ( $P > 0.05$ ). Attrition was similarly high in both groups by week 48 (78%; 159/203) ( $P = 0.003$ ). Being married or having children predicted attrition at week 48.

## Conclusions

A structured lifestyle intervention program was more effective than metformin in achieving weight loss in young women. Quantitative lifestyle advice produced greater improvements in psychological outcomes compared to qualitative lifestyle advice. Internet-based weight loss program was effective in maintaining weight loss in young women independent of initial weight loss. High attrition rates were seen throughout the study, particularly among those who had greater psychological distress or food cravings, and those who were married or had children. Strategies on managing issues relating to psychological distress, food cravings and family responsibilities may allow better tailoring of weight management programs for this group.