Cardiac, Vascular and Metabolic Characteristics in Young Women with Abdominal Obesity: Comparison and Intervention

By

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Bianca Louise Share

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"Go confidently in the directions of your dreams… and live the life you've imagined"

Henry David Thoreau

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Manuscripts currently under construction

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Conference Presentations During Candidature

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Melbourne, Australia. 25th November, 2010.

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Student award: Runners-up ($500)

Author/presenter: B L. Share

2011 **Heart Foundation Conference.**

Melbourne, Australia. 17-19 March, 2011.

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Australian Catholic University *3 Minute Thesis* Competition.

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Oral presentation: Cardiovascular Health in Young Women.

Student award: Best presentation ($1,000)

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Perth, Australia. 29th September, 2011.

Oral Presentation: Cardiovascular Health in Young Women.

Student award: Recognition of outstanding performance

Author/presenter: B L. Share

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Sydney, Australia. 1-3 November, 2012.

Oral Presentation: Lifestyle Intervention Improves Cardiovascular Disease Risk Factors in Young Overweight Women.

Authors: B L. Share (presenter), G. Naughton, P. Obert, E. Aumand, J. Peat, & J. Kemp

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Melbourne, Australia. May 2012

Oral presentation: Cardiovascular Disease in Young Women: The Young Women's Heart Health Study

Author/presenter: B L. Share

2014 **World Congress of Cardiology**

Melbourne, Australia. 4-7 May, 2014.

Poster presentation: Assessment of Left Ventricular Mechanics Using Speckle Tracking Imaging Echocardiography in Young Women with Abdominal Obesity.

Authors: B L. Share (presenter), G. Naughton, A. La Gerche, P. Obert, E. Crendal, & J. Kemp

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Thesis Abstract

Cardiovascular disease (CVD) is the leading cause of death in women worldwide. Despite this, CVD in women is under-researched. Overweight/obesity, particularly abdominal obesity, together other established risk factors, increases the chance of developing CVD. Previous research has also shown that young women with overweight/obesity have cardiac dysfunction that may predispose them to future CVD events, suggesting that early detection and prevention of underlying CVD risk factors may be the best public health approach. Lifestyle interventions incorporating exercise, diet and behavioural therapy are currently recommended as the cornerstone to reduce CVD risk factors in individuals with overweight/obesity.

Part 1. Cross-sectional studies

CVD risk factors were investigated in a cross-section of young women aged 18-30 years with abdominal obesity [waist circumference (WC) ≥ 80 cm, n=39] and compared with a non-obese [WC < 80 cm, n=33] aged-matched control group. Metabolic risk factors, including anthropometric, blood-borne (biochemical), fitness and dietary measures (Chapter 5), together with cardiac and vascular characteristics (Chapter 6), were assessed. Cardiac morphology and function, myocardial deformation and mechanics, and carotid intima-media thickness (c-IMT), were measured via ultrasonography. Results showed that women with abdominal obesity had elevated markers of insulin resistance, low-grade systemic inflammation (high-sensitivity C-reactive protein) and systolic blood pressure, and poorer fitness, compared to women without abdominal obesity. Furthermore, the unadjusted odds ratio of being classified with overweight/obesity [defined by WC or body mass index] was high for elevated homeostatic model assessment of insulin resistance (HOMA-IR) and low physical activity. Cardiac morphology was similar between groups, with the exception of dilated left atrium in women with abdominal obesity. Cardiac function measures demonstrated impaired left ventricular diastolic parameters and reduced systolic tissue velocity in women with abdominal obesity. Longitudinal strain and diastolic strain rate were also reduced in women with abdominal obesity but circumferential deformation indices,

myocardial mechanics and c-IMT did not differ between groups. Therefore, a young, otherwise-healthy group of adult women with abdominal obesity displayed elevated markers of insulin resistance and low-grade systemic inflammation and subclinical cardiac dysfunction compared with non-obese women.

Part 2. Intervention study

A systematic review (Chapter 3) found that multi-disciplinary lifestyle interventions incorporating exercise, diet and/or behavioural therapy improved CVD risk factors in premenopausal women with overweight/obesity. However, the systematic review highlighted a need for more rigorous studies involving younger (< 30 years of age) women, a deeper understanding of mechanisms that accompany intervention-induced changes in CVD risk, and long-term follow-up evaluating program sustainability.

Women identified with abdominal obesity (from Part 1) participated in a randomised wait-list control trial (RCT) involving a 12-week multi-disciplinary lifestyle intervention. The intervention design incorporated physical activity, nutrition education and cognitive behavioural therapy. Participants underwent screening for anthropometric, blood-borne, fitness and dietary risk factors for CVD (Chapter 7), as well as cardiac and vascular characteristics measured via ultrasonography (Chapter 8), at baseline, post-intervention, and at 12 weeks after post-intervention. A subsample of participants (n=7) was assessed again at 52 weeks post-intervention (Chapter 9). Results from a linear mixed model analysis comparing changes in CVD risk factors and lifestyle behaviours of women completing the intervention (n=19) and the overweight/obese control group (n=11) showed no notable *between-group* differences for any metabolic risk factors or markers derived from cardiac and vascular ultrasonography. However, *within-group* improvements were observed in the intervention group for anthropometric markers, blood pressure, aerobic fitness, physical activity engagement, dietary energy intake and left ventricular mass indexed, with some of these changes maintained 12 weeks after intervention completion. Similarly, women in the control group displayed significant *within-group* improvements in anthropometric markers and changes in left ventricular mass indexed, suggesting that a traditional RCT design may not be appropriate for this population. At one-year post-intervention, further improvements in

anthropometric measures were evident, along with improved lifestyle behaviours for physical activity and dietary intake. Therefore, despite complex compliance issues with the control group, a multi-disciplinary lifestyle intervention improved some metabolic and cardiac risk factors in women with abdominal obesity compared with controls, with evidence of long-term sustainability of behaviour modification.

In summary, this thesis provides new knowledge on the cardiac, vascular and metabolic profiles of young (premenopausal) adult women with abdominal obesity, and a better understanding of the effects on CVD risk factors, and their sustainability, of a multi-disciplinary lifestyle intervention in this under-research population.

Abbreviations

ABS	Australian Bureau of Statistics
AIHW	Australian Institute of Health and Welfare
A_m	Late-diastolic mitral annulus tissue velocity
ANZCTR	Australian New Zealand Clinical Trials Registry
AUC	Area under the curve
AusDiab	Australian Diabetes, Obesity and Lifestyle Study
A WAVE	Late-diastolic transmitral blood velocity
BMI	Body mass index
CBT	Cognitive behavioural therapy
CHO	Carbohydrates
CI	confidence interval
c-IMT	Carotid intima-media thickness
CV	Coefficient of variation
CVD	Cardiovascular disease
DBP	Diastolic blood pressure
DEXA	Dual-energy x-ray absorptiomety
DT	Deceleration time
ECG	Electrocardiogram
E_m	Early-diastolic mitral annulus tissue velocity
E WAVE	Early-diastolic transmitral blood velocity
FM	Fat mass
GE	General Electric
HDL	High density lipoprotein
HOMAR-IR	Homeostasis model of assessment – insulin resistance

HR	Heart rate
hs-CRP	High sensitivity C-reactive protein
Hz	Hertz
ICC	Intraclass correlation coefficient
IDF	International Diabetes Federation
IR	Insulin resistance
IVRT	isovolumetric relaxation time
IVS	Inter-ventricular septum
LA	Left atrium
LDL	Low density lipoprotein
LM	Lean mass
LMM	Linear mixed model
LOA	Limits of agreement
LV	Left ventricle/ left ventricular
LVED	Left ventricular end-diastolic
LVES	Left ventricular end-systolic
ME	Measurement error
NHMRC	National Health and Medical Research Council
RCT	Randomised controlled trial
ROC	Receiver operating characteristic
RPE	Rating of perceived exertion
SBP	Systolic blood pressure
SD	Standard deviation
SDT	Self-determination theory
S_m	Systolic mitral annulus tissue velocity
SPSS	Statistical package for the social sciences

SR	Strain rate
STE	Speckle tracking echocardiography
T2DM	Type 2 diabetes mellitus
TDI	Tissue Doppler imaging
WHO	World Health Organisation
WHF	World Heart Foundation
WHR	Waist-to-hip-ratio
WHtR	Waist-to-height ratio
WC	Waist circumference
1RM	One repetition maximum
2D	Two-dimensional

Chapter 1. Introduction and Overview

1.1. Cardiovascular Disease

Cardiovascular disease (CVD) is a non-communicable disease involving the heart and blood vessels (arteries, capillaries, and veins), comprising coronary or ischaemic heart disease, cardiomyopathy, cerebrovascular disease, heart failure, rheumatic heart disease, peripheral arterial disease and hypertension (World Heart Federation, 2013). CVD is the leading cause of death, particularly in industrialised countries, despite improvements in life expectancy. An estimated 17 million people world-wide die from CVD each year, equating to approximately 30% of all deaths, with incidences projected to increase linearly (World Health Organisation, 2011)

In Australia, CVD is the primary cause of mortality in both men and women (Figure 1.1). In 2009, CVD accounted for 33 per cent of all deaths nationally (Australian Bureau of Statistics, 2013). Additionally, CVD contributes to the social, personal and financial burden of disease, costing the Australian economy six billion dollars in health care expenses annually. This cost represents 11 per cent of the total health expenditure (Australian Institute of Health and Welfare, 2012). Cardiovascular health is one of eight Australian National health priority areas, in recognition of its high prevalence, its impact on morbidity and mortality, and its potential for health improvements through prevention and treatment programs (The Department of Health, 2012).

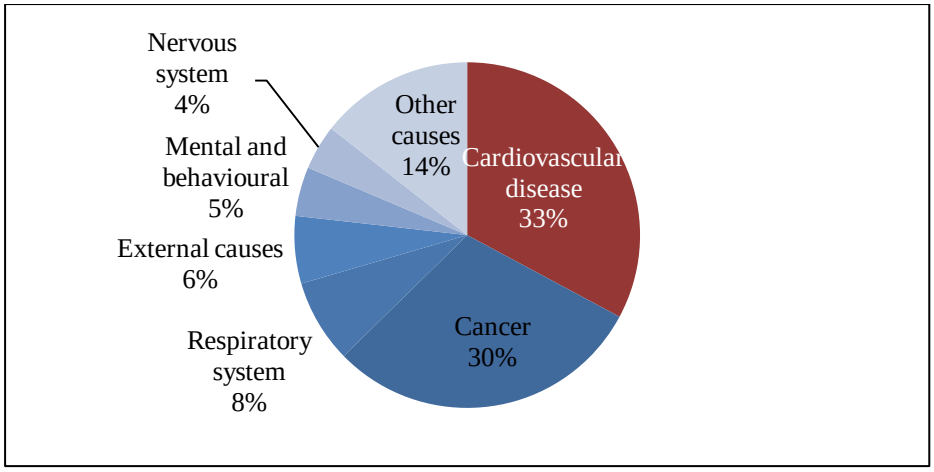

Figure 1.1. Causes of death in Australian men and women, 2009 (Data sourced from: Australian Bureau of Statistics, 2013).

1.2. Obesity and CVD

Excess body fat, particularly obesity, is established as a risk factor for CVD and increased mortality rates (Hubert, Feinleib, McNamara, & Castelli, 1983). The most serious form of obesity is central (i.e. abdominally located) rather than peripheral obesity, as it is associated with higher risks for CVD (Alberti, Zimmet, & Shaw, 2005). Incidences of overweight and obesity continue to rise, already reaching epidemic proportion (Figure 1.2). Worldwide, prevalence of overweight and obesity combined rose by 27% for adults and 47% for children between 1980 and 2013 (Ng et al., 2014). Globally, the proportion of adults who are either overweight or obese is currently 37% in men, and 38% in women (Ng et al., 2014). Furthermore, a large number of studies have demonstrated higher rates of death from obesity and CVD in people who are from a lower socioeconomic status (Houweling, Kunst, & Mackenbach, 2001; Woodward et al., 2015).

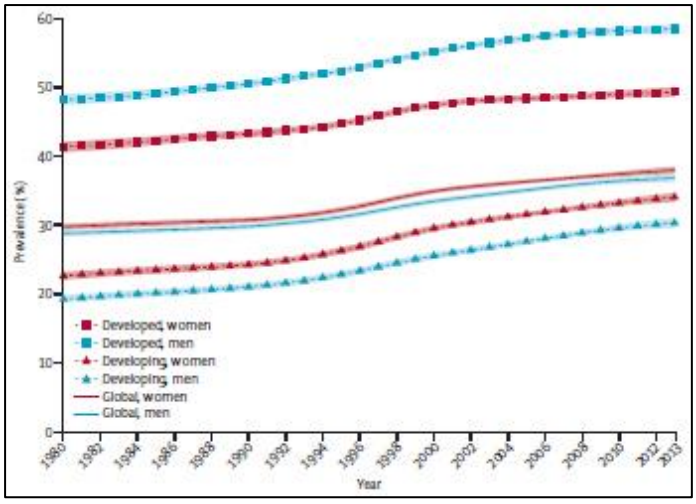

Figure 1.2. Global prevalence of overweight and obesity combined, for women (red) and men (blue), in developed and developing countries between 1980 and 2013 (Image modified from: Ng et al., 2014, p.2)

The prevalence of overweight and obesity among Australians has been steadily increasing for the past 30 years (Australian Bureau of Statistics, 2013). According to the National Health Survey, in 2007-08, based on body mass index, an estimated 62% of Australian adults aged 18 years or older were overweight or obese (Australian Bureau of Statistics, 2013), equating to over 12 million Australian adults (Figure 1.3). It has been projected that by 2025, more than 75% (approximately 17 million) of Australian adults will be overweight or obese (Vic Health, 2014).

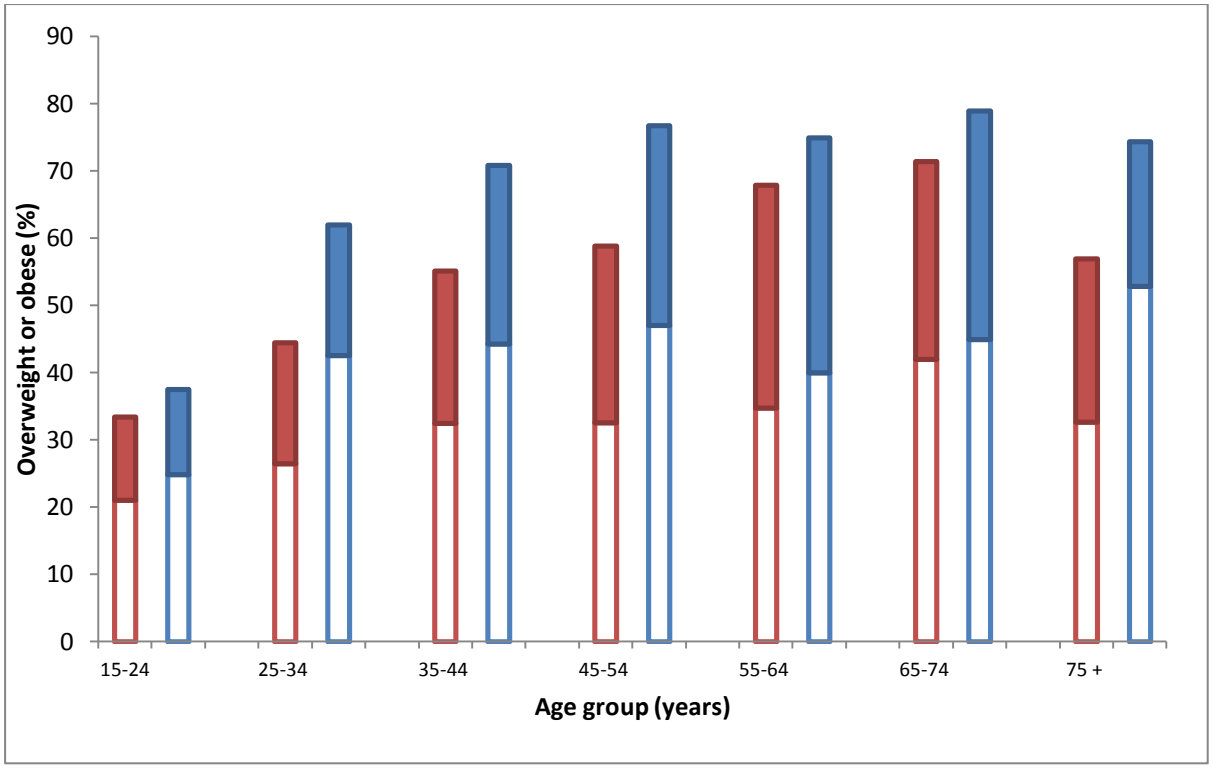

Figure 1.3. Overweight and obesity in Australians aged 15 years and older (data sourced from: (Australian Institute of Health and Welfare, 2012). Unshaded red, women overweight; solid red, women obese; unshaded blue, men overweight; solid blue, men obese.

1.3. Modifiable Risk Factors for CVD

Chronic accumulation of excess body fat can lead to the development of intermediate 'modifiable' CVD risk factors (Bastien, Poirier, Lemieux, & Després, 2014). Risk factors describe any attribute, characteristic or exposure of an individual that increases the likelihood of developing a disease or injury (World Health Organisation, 2011). Modifiable risk factors such as physical inactivity, dyslipidemia, hypertension, insulin resistance, glucose intolerance, systemic inflammation, type 2 diabetes mellitus (T2DM), a prothrombotic state, cardiac remodelling and impaired vascular function (Alberti et al., 2009; Tadic, Ivanovic, Petrovic, Celic, & Neskovic, 2013) are associated with obesity and are linked to the development of CVD (Figure 1.4) (Bastien et al., 2014). Furthermore, as many as six in every ten deaths from CVD are related to modifiable risk factors, and women have a higher prevalence of risk factors for CVD than men (Villablanca, Jayachandran, & Banka, 2010;

World Health Organisation, 2011). This suggests that much of the CVD burden is avoidable, and efforts to decrease modifiable risk factors are urgently needed.

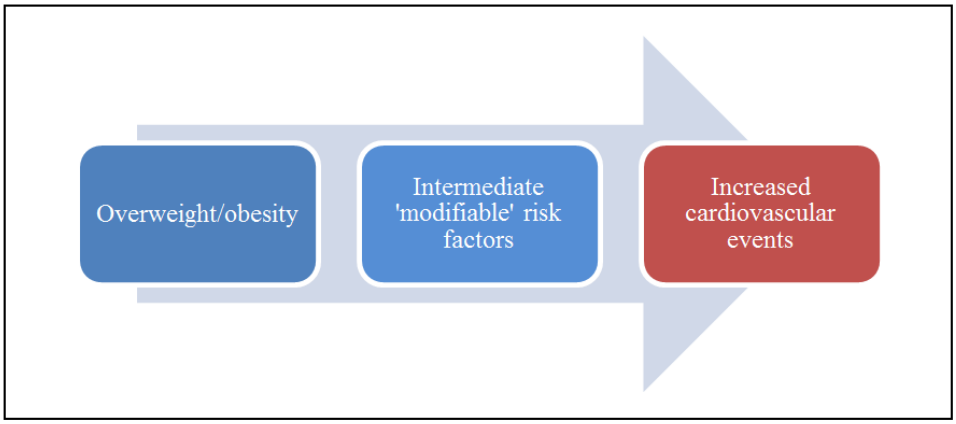

Figure 1.4. Relationship between increased adiposity (overweight/obesity), intermediate 'modifiable risk factors' (e.g. hypertension, insulin resistance, the metabolic syndrome) and increased cardiovascular events in the general population (adapted from Bastien et al., 2014).

1.4. Women's Heart Health

Cardiovascular disease in women is described in the international literature as under-recognised, under treated and under researched (National Heart Foundation of Australia, 2011).

The Framingham Heart Study, initiated in 1948 (Dawber, Moore, & Mann, 1957), identified that overt CVD develops 10 years later in women than men, resulting in CVD being labelled a 'male condition'. As a consequence, women experience poorer prognosis and receive suboptimal preventive care and treatment which, in turn, contributes to inferior outcomes in comparison to men (Worrall-Carter, Edward, & Page, 2012). Similarly, a systematic review investigating the major risk factors for CVD in women (aged > 18 years) in the published literature between 1999 and 2011 highlighted important differences between men and women relating to modifiable risk factors. Specifically, women are more likely to suffer from T2DM,

hypertension, physical inactivity, depression, and stress, which place them at high risk of CVD (Worrall-Carter, Ski, Scruth, Campbell, & Page, 2011). Similarly, others have reported the prevalence of several risk factors, such as hypertension, T2DM, high alcohol intake and low physical activity as being greater in women than men (Norhammar & Schenck-Gustafsson, 2013). Furthermore, hypertension, elevated fasting glucose, abdominal obesity and dyslipidemia may have a greater impact on deleterious left ventricular remodelling in women than men (Tadic et al., 2013). Given that women's health research has traditionally focused primarily on matters of sexual and reproductive health, enormous improvements in women's CVD outcomes through targeted research are possible (Norhammar & Schenck-Gustafsson, 2013).

In Australia alone, more than 26,000 women die each year from CVD, accounting for 41% of all female deaths (Australian Institute of Health and Welfare, 2012). The longitudinal, population-based Australian Diabetes, Obesity and Lifestyle (AusDiab) Study found that young (premenopausal) women gained more weight and waist circumference over a 12-year period than men and older (post-menopausal) women (Stewart, Tikellis, Carrington, Walker, & O'Dea, 2008). Specifically, an average weight gain of 6 to 12 kg was observed in women between the ages of 20 to 30 years (Adamson et al., 2007; Lucke et al., 2007). Currently, in Australia, the prevalence of overweight and obesity is 35% for women aged 18-24 years, and 42% for women aged 25-34 years (Australian Bureau of Statistics, 2013). Similarly, 51% of non-hispanic white American women aged 20-39 years are either overweight or obese (Flegal, Carroll, Kit, & Ogden, 2012), while the prevalence among women of a similar age (25-34 years) in the United Kingdom is 47% (Health and Social Care Information Centre, 2011). Figure 1.5 shows the global age pattern of overweight and obesity in 2013. For women, it is evident that rapid weight gains occurred between the ages of 20 and 40 years, with prevalence of overweight and obese doubling during this timeframe.

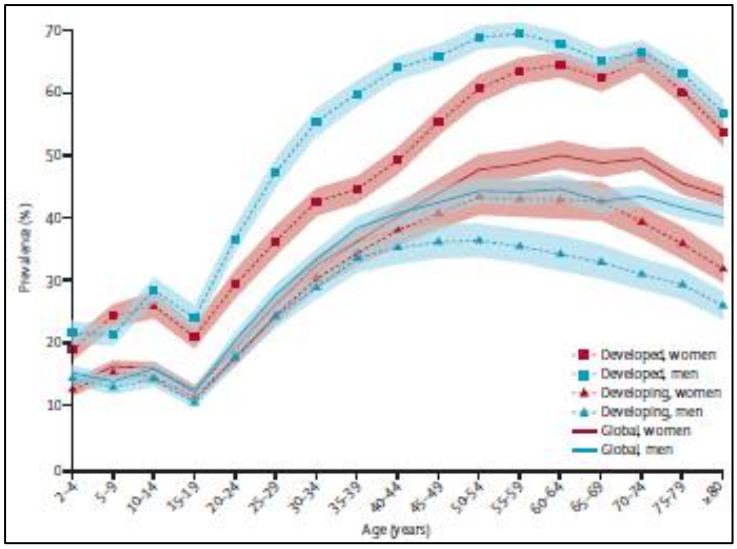

Figure 1.5. Global prevalence of overweight and obesity, by age, for females (red) and males (blue) in developed and developing countries in 2013 (Image modified from: Ng et al., 2014, p. 4).

In addition to the increases in the prevalence of overweight and obesity, young women are also exhibiting low levels of physical activity (Figure 1.6). The greatest prevalence of 'sedentary' behavior exists for women aged 25 to 34 years, with almost 35% of these women performing no structured physical activity (Australian Bureau of Statistics, 2013). Even for women aged 18 to 24 years, 'sedentary' behaviour exceeds 30% for that age group, with another 40% exhibiting low physical activity behaviour.

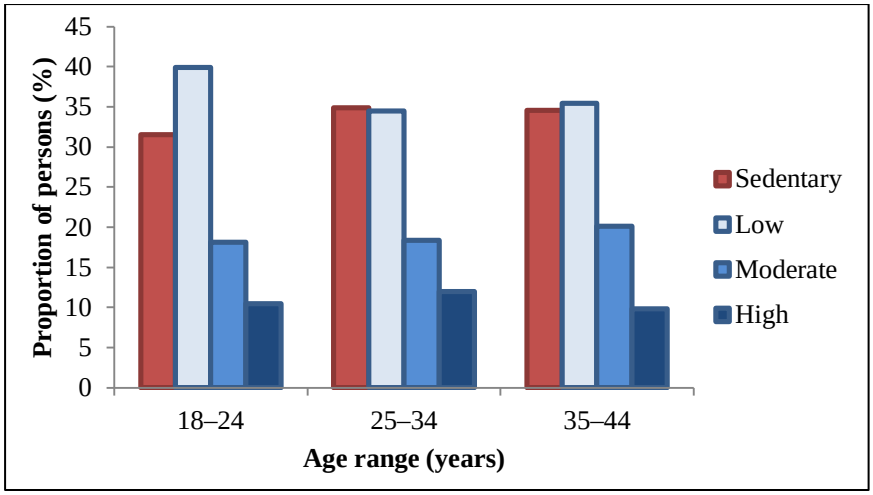

Figure 1.6. Levels of exercise in premenopausal Australian women. Results from the Australian National Health Survey, 2012 (Data sourced from: (Australian Bureau of Statistics, 2013).

Ultimately, carrying excessive weight and exhibiting sedentary exercise behaviours predisposes young adult women to CVD risk and premature death. This suggests that lifestyle modification is critical for halting CVD risk progression in premenopausal women.

1.5. Lifestyle Modification

Lifestyle management and behaviour modification has shown to be effective in the reduction of CVD risk by reducing overweight/obesity and improving the risk factor profile associated with CVD development (Irving et al., 2008). In a review assessing a range of management strategies to address overweight and obesity, multi-disciplinary lifestyle interventions that incorporate diet, exercise and behavioural therapy were most effective for weight loss and reduction of CVD risk factors (A. Lang & Froelicher, 2006) (Wing, 2002). Thus, CVD risk modification through lifestyle intervention is highly recommended (Deaton et al., 2011) (Mosca et al., 2004), with suggestions that a heart healthy lifestyle encouraged from youth and continuing into adulthood is the best approach for the prevention of CVD (Mitrakou, 2006). It is often suggested that women are underrepresented in cardiac research, in particular premenopausal women, because they are ‘protected’ against CVD due to the presence of

oestrogen, but this protective effect may not be the case (Maas et al., 2011). Therefore, the detection, prevention, and treatment of modifiable risk factors are strategically recommended for the reduction of CVD (Galassi, Reynolds, & He, 2006), and female-specific research and clinical programs should aim at a more multi-disciplinary approach to cardiovascular health in women (Worrall-Carter et al., 2011).

1.6. Statement of the Problem

Greater research is required to improve the understanding of CVD in women (Norhammar & Schenck-Gustafsson, 2013). However, most research of overweight/obesity and CVD risk to date has focused on women aged over 40 years, even though earlier detection and prevention of risk factors may be the best public health approach. In the Australian context, CVD accounts for 41% of all female deaths (Australian Institute of Health and Welfare, 2012). In parallel, the prevalence of overweight and obesity is 35% for women aged 18-24 years and 42% for women aged 25-34 years (Australian Bureau of Statistics, 2013). In these age groups, approximately 70% of women are also classified as exhibiting 'sedentary' or 'low activity' exercise behaviors (Australian Bureau of Statistics, 2012). Despite these and similar international figures, enrolment of young adult women in clinical and epidemiological research remains relatively low in studies of populations with chronic disease. Thus, the ability to detect the establishment and progression of CVD in younger populations, and then put in place preventative strategies, is limited. Moreover, while lifestyle modification has been recommended as the cornerstone treatment of obesity and CVD risk factors (Bantle et al., 2008), little is known about its effectiveness for reducing modifiable CVD risk factors in young adult women with overweight/obesity

1.6.1. Significance of the Study

This study addressed the prominent gap in CVD research concerning young adult women with overweight/obesity. In this project, a range of traditional and contemporary initiatives were utilised to examine the CVD risk profile of young women. This research then explored the impact of a lifestyle modification program on these risk factors. Results from this study are expected to provide new insights into the detection and prevention of CVD in young adult women, and encourage health care providers to conduct appropriate and sustainable interventions. Ultimately, the outcome of this thesis aimed to inform new directions for the management of lifestyle factors to prevent CVD and, thus, enhance the long-term health of young women with overweight/obesity. The results of this research are important for policy makers, as the knowledge gained about the health status of young women with abdominal obesity can be utilised to reduce personal and societal burden. This thesis also provides insights to inform the direction of future studies, particularly when targeting a participant cohort of young adult women.

1.6.2. Statement of Purpose

The collective purpose of the studies in this thesis was to investigate cardiovascular health in young adult women and advance the knowledge of early detection and prevention of CVD risk. This was achieved by (i) profiling markers of CVD risk in a cross-section of young women with and without abdominal obesity, and (ii) providing proof of concept in the early detection and prevention of CVD risk in overweight/obese young women through a multi-disciplinary lifestyle intervention, using a randomised controlled trial (RCT) design and a sustainability component.

1.7. Research Question

The research questions for this study were:

1. What (*cardio*)metabolic, cardiac and vascular risk factors for CVD are associated with overweight/obesity, defined by abdominal obesity measured from waist circumference, in premenopausal adult women aged 18-30 years?

2. Does a multi-disciplinary lifestyle intervention comprising exercise, nutrition education and cognitive behavioural therapy (CBT) improve the CVD risk factor profile of young women with abdominal obesity? And if so, are these improvements sustainable beyond the completion of the program?

1.8. Specific Aims

The specific aims of this research were to:

1. Investigate blood-borne metabolic and lifestyle markers of CVD risk in a cross-sectional profile of young adult women with (and without) overweight/obesity, defined by both elevated waist circumference and BMI (Chapter 5).

2. Investigate cardiac and vascular remodelling and myocardial function in a cross-sectional profile of young women with and without overweight/obesity using traditional and advanced techniques of ultrasonography (Chapter 6).

3. Assess the efficacy and sustainability of a 12-week multi-disciplinary (exercise + nutrition education + CBT) lifestyle intervention, using a randomised wait-list control design, for improving the metabolic and lifestyle CVD risk factor profile in young adult women with abdominal obesity (Chapter 7 and 9).

4. Assess the efficacy and sustainability of a multi-disciplinary lifestyle intervention, using a randomised wait-list control design, for improving cardiac and vascular morphology, cardiac function, and myocardial deformation and mechanical indices, in young adult women with abdominal obesity, using traditional and advanced techniques of ultrasonography (Chapter 8 and 9).

1.9. Research Hypotheses

The hypotheses formulated for the research were:

Hypothesis 1

Young adult women with abdominal obesity exhibit metabolic markers of CVD risk and poorer lifestyle behaviours, when compared with age-matched women without abdominal obesity.

Hypothesis 2

Young adult women with abdominal obesity exhibit markers of cardiac and vascular remodelling, and cardiac and myocardial dysfunction, measured from ultrasonography, when compared with age-matched women without abdominal obesity.

Hypothesis 3

Involvement in a 12-week multi-disciplinary lifestyle intervention produces improvements in anthropometric measures, reductions in metabolic risk factors for CVD, and lifestyle modifications supporting weight management, with these changes sustained or improved at follow-up testing, in young adult women with abdominal obesity.

Hypothesis 4

Involvement in a 12-week multi-disciplinary lifestyle intervention produces improvements in cardiac, vascular and myocardial measures, using ultrasonography, with these changes sustained or improved at follow-up testing, in young adult women with abdominal obesity.

Chapter 2. Literature Review

2.1. Obesity and CVD

The dramatic increase in obesity worldwide over the past 20-30 years has resulted in the World Health Organisation labelling it a "global epidemic" (World Health Organisation, 2000). Excess body fat is an established risk factor for CVD (Hubert et al., 1983), but it also increases the development of other intermediate risk factors for CVD(Australian Institute of Health and Welfare, 2012). The understanding of the role that adipose tissue plays in metabolic and homeostatic regulation has advanced in recent years (Berggren, Hulver, & Houmard, 2005; Kershaw & Flier, 2004; Matsuzawa, 2006b). Moreover, it is now established that, when in excess, adipose tissue is a significant contributor to biological dysregulation and disease progression (Kahn, Hull, & Utzschneider, 2006). Therefore, early identification and control of this dysregulation is critical for individual and societal health, especially given that obesity is a modifiable risk factor for many diseases. With respect to this work, adipose tissue and obesity is addressed in the context of CVD risk, development and progression.

2.1.1. Adipose tissue

Once thought to be simply a passive storage reservoir for excess energy in the form of triglycerides, adipose tissue is now considered an active autocrine, paracrine and endocrine organ (Brugger et al., 2014; Kershaw & Flier, 2004; Matsuzawa, 2006b). Adipose tissue plays a prominent role not only in energy metabolism and lipolysis but also contributes to other important metabolic processes such as regulation of inflammation, blood pressure, fibrinolysis and appetite (Mitrakou, 2006; Stears & Byrne, 2001). When adipose tissue has reached its maximum expansion capacity, a "spill over" of lipids from adipocytes occurs, resulting in an increase in circulating free fatty acids (Bastien et al., 2014). Lipids then start to accumulate at various sites in the form of subcutaneous adipose tissue, visceral adipose tissue, intra-hepatic fat, intra-muscular fat, renal sinus fat, epi/pericardial fat, myocardial fat and perivascular fat (Bastien et al., 2014; Montani et al., 2004). It is therefore unsurprising

that the most critical factor in the emergence of metabolic diseases is excess adipose tissue (Kahn et al., 2006).

2.1.2. Obesity assessment

The most commonly used anthropometric tool to classify overweight and obesity is body mass index (BMI). BMI is an index of weight-for-height calculated as kg/m^2 (World Health Organisation, 2000). According to this calculation, individuals with a BMI ranging from 25 to 29.9 kg/m^2 are classified as overweight, whilst obesity is classified as a BMI $\geq$ 30 kg/m^2 (Table 2.1).

Table 2.1. Classification of body weight according to body mass index (BMI) (adapted from: World Helath Organisation, 2000).

Classification	BMI (kg/m^2)
Underweight	< 18.5
Normal range	18.5 – 24.9
Overweight	25.0 – 29.9
Obese:	≥ 30.0
Obese class I	30.0 – 34.9
Obese class II	35.0 – 39.9
Obese class III	≥ 40.0

Although a useful and simple tool to estimate and classify obesity, BMI does not discriminate lean mass from fat mass, nor does it account for variations in body fat distribution (Dalton et al., 2003). Adiposity indices that incorporate a measure of waist circumference, including waist-to-hip ratio (WHR), waist-to-height ratio (WHtR), and waist circumference itself, should therefore be considered by clinicians in risk stratification and to discriminate individuals at higher risk of chronic disease (Bastien et al., 2014; National Health and Medical Research Council, 2003). A cross-sectional survey of anthropometric characteristics

of Australian women (n = 4,487, aged 20-69 y) showed central adiposity measured by waist circumference, WHR, and WHtR to be better predictors of CVD risk than BMI (Goh, Dhaliwal, Welborn, Lee, & Della, 2014). Similarly, results from a meta-analysis of 24 cross-sectional studies in adults showed that WHtR had a stronger ratio of relative risk for cardiometabolic risk than BMI (Savva, Lamnisos, & Kafatos, 2013).

2.1.3. Abdominal obesity

The distribution of adipose tissue, in addition to the amount of body fat, is an important determinant of morbidity and mortality (Landin et al., 1990). Evidence indicates that excess intra-abdominal fat (abdominal adiposity) is associated with greater risk of obesity-related morbidity than overall adiposity (Dalton et al., 2003; Zhang, Rexrode, van Dam, Li, & Hu, 2008). Furthermore, abdominal adipose tissue plays a major role in the pathogenesis of atherosclerosis through various metabolic and hormonal pathways (Mitrakou, 2006). Abdominal obesity increases the risk of various health problems that predispose an individual to increased risk of CVD (Australian Institute of Health and Welfare, 2012). As a measure, elevated waist circumference is a reliable anthropometric index of abdominal obesity (Lucke et al., 2007) for the prediction of CVD risk (Goh et al., 2014); (Alberti et al., 2009). Based on expert consensus, the WHO has proposed sex-specific cut-off values for waist circumference that are associated with increased CVD risk (World Health Organisation, 2011). A waist circumference of ≥ 80 cm in women and ≥ 94 cm in men is indicative of increased risk, while a waist circumference of ≥ 88cm in women ≥ 102 cm in men and represents substantially increased risk. Therefore, measuring waist circumference, given its low cost and convenience, represents a valuable tool for health care professionals, in addition to BMI (Balkau et al., 2007).

International Day for Evaluation of Abdominal Obesity, conducted across 63 countries, evaluated waist circumference in 168,000 participants aged 18-80 years who consulted with a primary care provider between May and July 2005 (Balkau et al., 2007). According to the National Cholesterol Education Program – Third Adult Education Panel (NCEP:ATP III)

criteria, 48% of women had abdominal adiposity (i.e. WC > 88 cm), whilst 71% of women had a WC ≥ 80 cm (International Diabetes Federation, 2006) Furthermore, women with an elevated waist circumference had an odds ratio of 1.97 for CVD (Balkau et al., 2007). Additionally, the Australian Diabetes, Obesity and Lifestyle Study (AusDiab), a population-based cross-sectional survey of CVD risk factor prevalence in Australia, investigated waist circumference in adults aged ≥ 25 years (Dunstan et al., 2002). Abdominal obesity for women aged 25-34 years was 20% for WC ≥ 80 cm, and 17% for WC ≥ 88 cm (Cameron et al., 2003).

2.2. Modifiable Risk Factors of CVD

An excess in adipose tissue, or obesity, is associated with increased incidence of cardiovascular and cerebrovascular events in men and women (Landin et al., 1990) Large prospective studies such as the Framingham Heart Study have shown obesity is an independent predictor of CVD. Furthermore, the relationship between obesity, intermediate risk factors, and the development of CVD is evident (Bastien et al., 2014). Results suggest that increased adiposity leads to the development of CVD risk factors, and the burden of these risk factors, not adiposity itself, is critical to the development of CVD (Wilson, 2004) (Figure 1.4). Adipose tissue excess, particularly visceral (intra-abdominal) fat, is associated with insulin resistance, type 2 diabetes mellitus (T2DM), hyperglycemia, dyslipidemia, hypertension, atherosclerotic vascular disease, and prothrombotic and inflammatory states (Kershaw & Flier, 2004; Stears & Byrne, 2001). Furthermore, the International Diabetes Federation (International Diabetes Federation, 2006) has identified the direct role of visceral fat accumulation in the development of multiple risks and CVD. Figure 2.1 describes the abnormalities associated with increased risk of CVD among individuals with excessive adipose tissue.

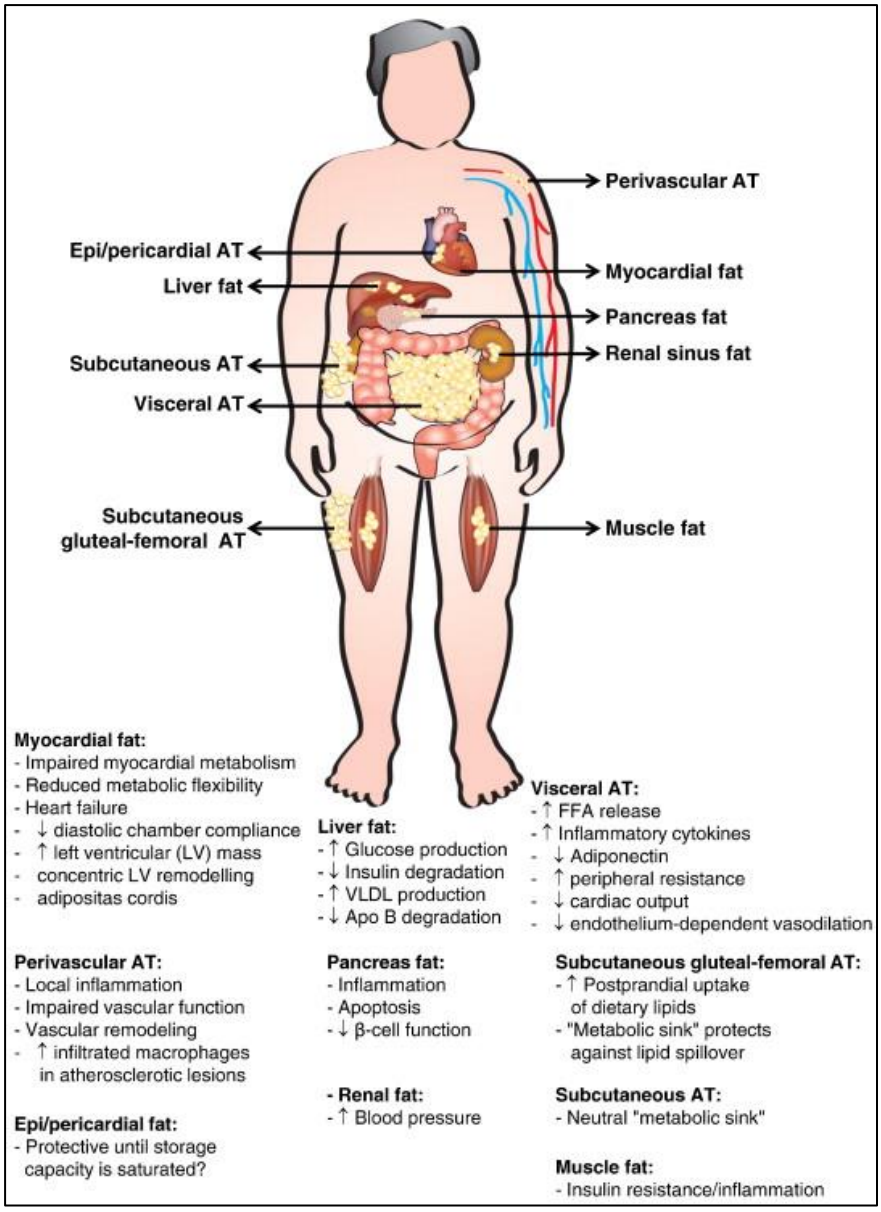

Figure 2.1. Increased risk of CVD among overweight/obese individuals. Abbreviations: Apo, apolipoprotein; FFA, free fatty acids; AT adipose tissue (Sourced from: Bastien et al., 2014, p.373).

The traditional approach to CVD risk assessment involves identifying and quantifying the presence of CVD risk factors. Estimating 10-year risk for CVD may also be performed using the Framingham risk score model (Dawber et al., 1957) for adults (aged ≥ 25 y). However, individuals at intermediate risk may benefit from identification of subclinical risk factors to further refine their CVD risk estimates (Stein et al., 2008).

2.2.1. Inflammatory markers

Systemic inflammation is believed to play a role in the pathogenesis of cardiovascular events, and CVD (Ridker, Hennekens, Buring, & Rifai, 2000). Many inflammatory mediators produced by adipose tissue are altered in the obese state, particularly in individuals with abdominal obesity or increased visceral adipose tissue (Berggren et al., 2005; Matsuzawa, 2006b). Adipose-secreted cytokines (or adipokines) play a role in the regulation of satiety (Kershaw & Flier, 2004), carbohydrate and lipid metabolism (Kondo, Kobayashi, & Murakami, 2006), and insulin sensitivity (Matsuzawa, 2006a). Adipokines can be classified into two main categories: 1) "healthy" adipokines, such as adiponectin, and 2) "unhealthy" adipokines, including markers of low-grade systemic inflammation (e.g. high-sensitivity C-reactive protein, tumor necrosis factor-alpha, interleukin-6), indicators of a thrombotic state (e.g. plasminogen activator inhibitor-1, fibrinogen), and the satiety regulator, leptin (Ridker et al., 2000; You & Nicklas, 2008).

Chronic low-grade systemic inflammation, observed in obese populations, promotes atherogenic profiles, endothelial dysfunction, and insulin resistance and, ultimately, coronary artery disease, T2DM, and heart failure (Steinbaum, 2004). While there is an array of commercially available assays employed in clinical settings for the analysis of inflammatory markers, the Centre for Disease Control and Prevention favours high-sensitivity C-reactive protein (hsCRP) from a clinical chemistry perspective, given its predictive abilities for CVD events (Pearson et al., 2003). Synthesised and secreted by the liver, hsCRP is an acute reactant that reflects low-grade systemic inflammation and plays a pathogenic role by acting on endothelial cells (McWilliam & Riordan, 2010; Mitrakou, 2006). Studies have consistently shown hsCRP as a strong predictor of future coronary events in apparently healthy men and women. Therefore, hsCRP assays are used for risk assessment of CVD, and used in the stratification of patients into high- and low-cardiovascular risk groups (Ridker, 2001). Results from the Women's Health Study showed that hsCRP was a strong predictor of future cardiovascular events even among subgroups of women with no history of hyperlipidemia, hypertension, smoking, diabetes, or family history of coronary heart disease (Ridker, Buring, Shih, Matias, & Hennekens, 1998; Ridker et al., 2000). Thus, hsCRP may play an important role as an adjunct in the comprehensive assessment of risk in the primary prevention of CVD (Ridker, 2001).

2.2.2. The metabolic syndrome

The metabolic syndrome, first described by Reaven as 'syndrome X' in 1988 (G. M. Reaven, 1988), is a combination of atherogenic risk factors that increase the chance of developing CVD and T2DM (Alberti, Zimmet, & Shaw, 2006; Byrne & Wild, 2005). The metabolic syndrome is characterised by a clustering of several risk factors, including abdominal obesity, raised serum triglyceride, reduced high-density lipoprotein (HDL) cholesterol, elevated blood pressure, and elevated fasting plasma glucose concentrations (Kassi, Pervanidou, Kaltsas, & Chrousos, 2011). In many individuals, the metabolic syndrome is associated with obesity and a sedentary lifestyle, and is being diagnosed with increasing frequency worldwide. It is estimated that 20 to 25 % of the world's adult population has the metabolic syndrome (International Diabetes Federation, 2006), with results from the AusDiab Study showing prevalence of the metabolic syndrome to be as high as 29% in Australian adults aged 25 years and over (Cameron, Magliano, Zimmet, Welborn, & Shaw, 2007). Individuals diagnosed with the metabolic syndrome are twice as likely to die from CVD and have a 1.5-fold increase in all-cause mortality (Mottillo et al., 2010). Moreover, the relative risk of CVD associated with the metabolic syndrome is higher in women than men (Galassi et al., 2006). Women with the metabolic syndrome are also at increased risk of complications during pregnancy, and offspring of obese mothers are at an elevated risk of developing the metabolic syndrome later in life (Ramos & Olden, 2008). Thus, the importance of early detection of the metabolic syndrome and its component risk factors is therefore critical in the attenuation of disease progression.

Over the years, a number of international expert groups have developed clinical criteria for the metabolic syndrome, and in particular, the WHO, European Group for the Study of Insulin Resistance (EGIR), National Cholesterol Education Program – Third Adult Education Panel (NCEP:ATP III), the American Heart Association/National Heart, Blood and Lung Institute (AHA/NHBLI), and the International Diabetes Federation (IDF). All groups agreed on the essential components of the metabolic syndrome being abdominal obesity, glucose intolerance, hypertension and dyslipidaemia (Table 2.2); however, each group's definition differed in its numeric criterion for each component. The application of different criteria gave rise to a proliferation of varying data and, thus, highlighted the need for a globally standardised definition (Zimmet, Alberti, & Shaw, 2005). In 2005, the IDF released a definition for the metabolic syndrome that introduced abdominal obesity as the pre-requisite

criterion in its diagnosis (Alberti et al., 2006; International Diabetes Federation, 2006). This definition addressed both clinical and research needs, focusing on abdominal obesity, and allowed for gender- and ethnic-specific values for waist circumference. Those involved in establishing this definition agreed that insulin resistance had largely been over-emphasized in earlier definitions, and that the essential component should be abdominal obesity, with its surrogate measure being waist circumference (Alberti et al., 2005). The IDF with the AHA/NHBLI updated the definition of the metabolic syndrome (Alberti et al., 2009) in an attempt to resolve the remaining differences that still existed between definitions. It was agreed that abdominal obesity should not be a prerequisite for its diagnosis but rather all individual components should be considered as important risk factors. Metabolic syndrome diagnosis now required the presence of any three of the five risk factors.

Table 2.2. Historical overview of the metabolic syndrome criteria for adults (Kassi et al., 2011).

Year	Expert Group	Inclusion Criteria	Risk Factors
1998	World health Organisation (WHO)	Insulin resistance PLUS two other risk factors	abdominal obesity (WHR), ↑triglycerides, ↑BP, microalbuminuria
1999	European Group for the Study of Insulin Resistance (EGIR)	Insulin resistance PLUS two other risk factors	Abdominal obesity (WC), ↑triglycerides, ↑BP, ↑fasting glucose
2001	National Cholesterol Education Program – Third Adult Education Panel (NCEP – ATP III)	Any three or more risk factors	Abdominal obesity (WC), ↑triglycerides, ↓HDL, ↑BP, ↑fasting glucose
2004	American Heart Association/National Heart, Blood and Lung Institute (AHA/NHBLI)	Any three or more risk factors	Abdominal obesity (WC), ↑triglycerides, ↓HDL, ↑BP, ↑fasting glucose
2005	International Diabetes Federation (IDF)	Ethnic-specific abdominal obesity (WC) PLUS two other risk factors	↑triglycerides, ↓HDL, ↑BP, ↑fasting glucose
2009	AHA/NHBLI and IDF joint statement	Any three or more risk factors	Ethnic-specific abdominal obesity (WC), ↑triglycerides, ↓HDL, ↑BP, ↑fasting glucose

Although obesity and insulin resistance remain at the centre of the pathophysiology of the metabolic syndrome, a number of potential mechanistic factors are involved in its pathogenesis. Figure 2.2 presents a flowchart of the interaction of a complex multi-pathway relationship involving behavioural, genetic, and environmental interactions, which may ultimately lead to CVD. Specifically, chronic stress and dysregulation of the hypothalamic-pituitary-adrenal axis and autonomic nervous system, increases in cellular oxidative stress, renin-angiotensin-aldosterone system activity, and intrinsic tissue gluco-corticoid actions each play a part in the pathophysiology of the metabolic syndrome (Kassi et al., 2011). Other conditions such as dysfunction in uric acid metabolism, haemodynamic irregularity, an increased pro-inflammatory state, and hyperinsulinaemia are also associated with the development of the metabolic syndrome (G. Reaven, 2001).

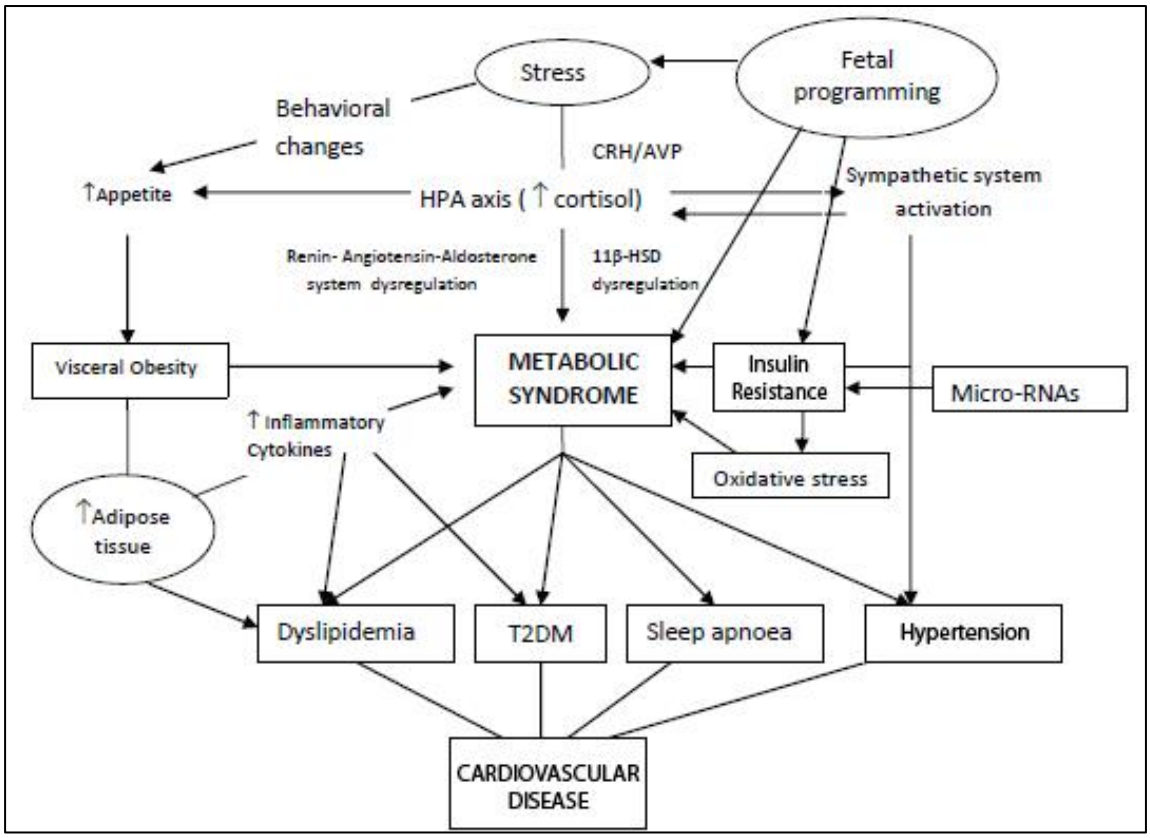

Figure 2.2. Schematic representation of the conditions implicated in the pathophysiology of the metabolic syndrome and their potential interactions. Abbreviations: HPA axis, hypothalamic-pituitary-adrenal axis; T2DM, type 2 diabetes mellitus; CRH, corticotrophin releasing hormone; AVP, arginine vasopressin (Image modified from: Kassi et al. (2011), p.5)

2.2.3. Insulin resistance

In obese individuals, adipose tissue releases increased concentrations of many biomolecules, including non-esterified fatty acids, glycerol, hormones, and pro-inflammatory cytokines, that are involved in the development of insulin resistance (Kahn et al., 2006). Insulin resistance is recognised as an early metabolic abnormality that precedes the development of T2DM and contributes to increased incidences of CVD (Carroll & Dudfield, 2004); (Mitrakou, 2006). Impaired insulin action occurs when target tissues are unable to respond to normal circulating concentrations of insulin. As a compensatory response, pancreatic β-cells secrete increased amounts of insulin. Initially, this increased insulin secretion and hyperinsulinemia are adequate to preserve glucose homeostasis. However, when homeostasis is chronically disrupted, insulin resistance progressively occurs. Insulin resistance is defined as a defect in the ability of insulin to drive glucose into tissue (Hawley & Zierath, 2008). As a consequence, T2DM evolves due to the gradual development of insulin resistance and deterioration of the body's ability to transport glucose from the blood across muscle, liver or other tissue cells. This dysfunction is typically followed by a decline in pancreatic β-cell function, resulting in the inability to secrete insulin in response to changes in blood glucose concentrations, and ultimately, a failure to produce insulin (Hawley & Zierath, 2008). In addition, inflammatory mediators, other adipokines, and proteins related to coagulation affecting glucose and fat metabolism (e.g. PAI-1) also contribute to the development of hepatic insulin resistance, and the progression of CVD (Mitrakou, 2006; Steinbaum, 2004).

Even mild impairments in insulin release may have important effects on metabolic homeostasis (Kahn et al., 2006). Thus, the assessment of insulin sensitivity is a valuable clinical tool (Bonora et al., 2000). Homeostasic model assessment of insulin resistance (HOMA-IR) is a method of assessing β-cell function and insulin resistance from fasting (basal) glucose and insulin concentrations. This technique, first described in 1985 (Matthews et al., 1985), uses a mathematical assessment of the interaction between β-cell function and insulin resistance. The relationship between glucose and insulin in the basal state reflects the balance between hepatic glucose output and insulin secretion. Consequently, a high HOMA-IR score denotes insulin resistance (Wallace, Levy, & Matthews, 2004).

2.2.4. Vascular dysfunction

Atherosclerosis is considered a chronic, inflammatory disease of the vascular system, and a degenerative process that starts in childhood and progresses throughout the lifetime (Epstein & Ross, 1999). Atherosclerosis arises when an artery wall thickens or hardens as a result of fatty substance and cholesterol deposit accumulation, commonly referred to as plaque. Obesity and the associated elevated blood lipids, such as triglycerides and high plasma concentrations of low-density lipoprotein (LDL) cholesterol, are considered principle risk factors for atherosclerosis (American Heart Association [AHA], 2014). Imaging of arteries to identify and quantify the presence of vascular disease has been suggested to refine CVD risk assessment (Stein et al., 2008). Non-invasive assessment of carotid intima-media thickness (c-IMT) is an established and validated surrogate assessment used to gauge the progression and regression of atherosclerosis (Hodis et al., 1998). Measured by ultrasound, c-IMT provides a quantitative evaluation of the morphological changes in the carotid artery. Findings from the Genetic Epidemiology of Metabolic Syndrome (GEMS) Study showed an increased cross-sectional c-IMT was associated with unfavourable levels of established CVD risk factors and atherosclerosis in middle-aged overweight/obese adults (Genoud et al., 2008). Furthermore, increases in the IMT of the common carotid artery and the number of atherosclerotic plaques were significantly greater in participants with an elevated lipid profile than in normolipidemic individuals (Genoud et al., 2008).

Arterial endothelial dysfunction precedes the development of atherosclerosis and is believed to play a central role in its pathophysiology (Juonala et al., 2004; Raitakari & Celermajer, 2000). The endothelium is the monolayer of endothelial cells covering the inner surface of blood vessels and plays a vital role in the regulation of vascular tone and structure, as well as vascular inflammation and thrombosis (Giannotti & Landmesser, 2007). Furthermore, the higher incidences of CVD events in obese populations are proposed to be related to endothelial dysfunction, along with low-grade systemic inflammation and insulin resistance (Bastien et al., 2014). Figure 2.3 describes potential mechanisms for the association of obesity, insulin resistance and endothelial dysfunction. Obesity, particularly abdominal obesity, leads to an imbalance in the production of several metabolic products including hormones (e.g. leptin, resistin) and cytokines (adipokines), which precede the development of insulin resistance and endothelial dysfunction (A. E. Caballero, 2003).

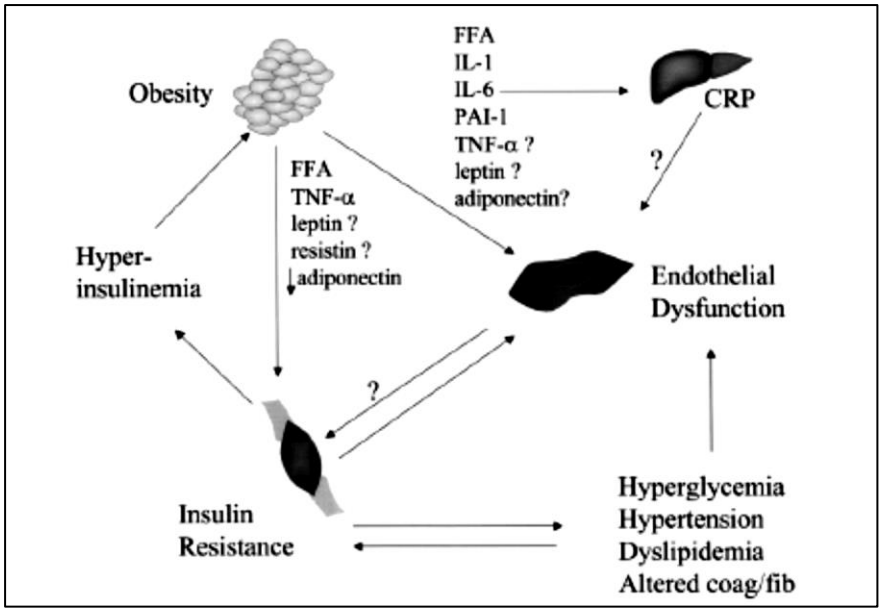

Figure 2.3. Mechanisms through which obesity, insulin resistance, and endothelial dysfunction are closely associated (Sourced from: Caballero (2003), p. 1284). Abbreviations: FFA, free fatty acids; TNF-α, tumor necrosis factor alpha; IL; interleukin; PAI; plasminogen activator inhibitor; CRP; c-reactive protein; coag/fib, coagulation/fibrinogen.

It has been suggested that systemic endothelial dyfunction may modify the association between atherosclerosis and its risk factors. Therefore, the non-invasive ultrasonographic assessment of endothelial function in the peripheral vascular system has been used as a risk marker for CVD (Sibal, Agarwal, & Home, 2011). Briefly, this technique involves assessing the response of the endothelium, usually of the brachial artery, to post-occlusive (transient occlusion of the forearm) reactive hyperaemia, known as flow-mediated dilation (FMD) (Raitakari & Celermajer, 2000). In the Cardiovascular Risk in Young Finns Study, c-IMT together with brachial artery FMD were measured in healthy young adults (n = 2,109; age 24-39 years), with participants grouped into 'impaired' or 'normal' FMD response. The number of CVD risk factors associated with increased cross-sectional c-IMT was highest in participants with evidence of endothelial dysfunction, but not in participants with preserved endothelial function (Juonala et al., 2004). This suggests a crucial link between c-IMT and endothelial dysfunction (Sibal et al., 2011).

2.2.5. Physical inactivity

Physical inactivity is the fourth highest risk factor for reducing Australian productivity, with the cost of physical inactivity to the Australian economy estimated at $13.8 billion per year (Keegan, Keegan, Daley, Ordway, & Edwards, 2013). Furthermore, physical inactivity is associated with an increase in ill-health and death, particularly relating to CVD. When assessed against the National Physical Activity Guidelines, the majority of adult Australians are insufficiently active, with 54% performing less than the national recommendations (< 150 minutes of activity per week) for health-related benefits (Australian Bureau of Statistics, 2013).

The current national guidelines for Australian adults recommend 300 minutes of accumulated moderate exercise, plus muscle strengthening activities on at least two days, each week (Australian Bureau of Statistics, 2013). However, only 20% of females aged 18-44 years participated in levels of physical activity recommended by these national guidelines (Australian Bureau of Statistics, 2013) (Figure 1.6) . Moreover, results from the Australian Longitudinal Study on Women's Health showed that the population predicted risk of heart disease was possibly highest from physical inactivity (Figure 2.4), outweighing that of other risk factors including obesity (BMI $\geq$ 25 kg/m^2), from age 30 (Brown, Pavey, & Bauman, 2014). Smoking is also noted as an immense risk factor for heart disease in young women, especially between the ages of 22 to 30 years.

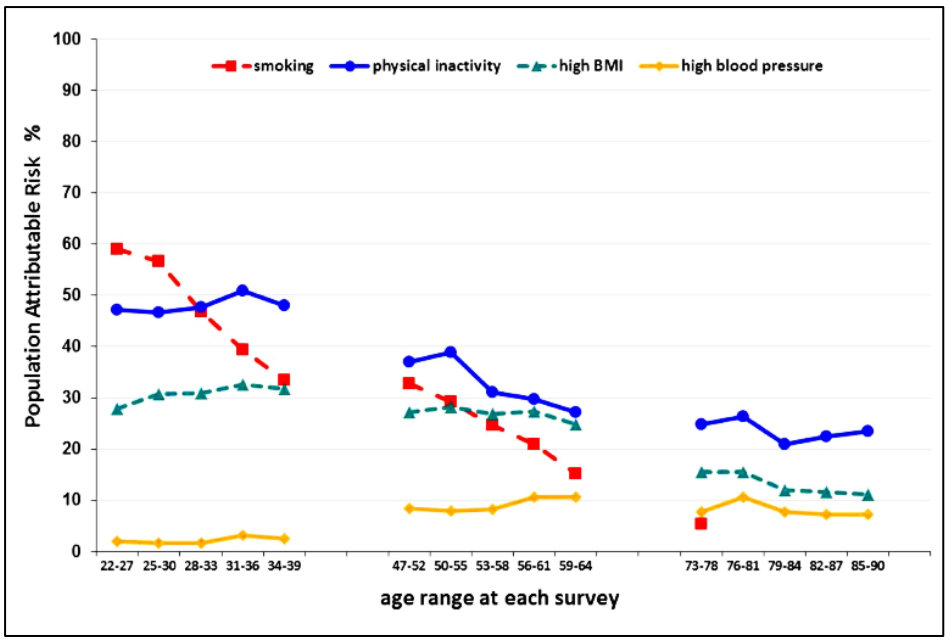

Figure 2.4. Population attributable risk factors for heart disease in women across the adult lifespan (Sourced from: Brown et al., 2014, p. 6).

Despite the clear benefits of exercise, fewer women engage in recommended levels of physical activity than men (Moreno & Johnston, 2014). Researchers have identified gender differences in initiation and maintenance of regular physical activity (Speck & Harrell, 2003), with women experiencing multiple barriers to physical activity that significantly reduce the likelihood of engaging in physical activity long-term. These barriers are different from the experiences of men (Yeats, 2010), with women citing perceived lack of time, caring-giving demands, and self-consciousness about body size as reasons for not being physically active (Moreno & Johnston, 2014).

2.3. Cardiac Dysfunction

Overweight and obesity are an independent risk factor for cardiac dysfunction (Bastien et al., 2014; Wong et al., 2004). In a recent cross-sectional study of older adults, abdominal obesity and other cumulative metabolic risk factors (e.g. inflammation and glucose intolerance) were associated with impaired systolic and diastolic function (Crendal et al., 2013).

2.3.1. Cardiac morphology and function

Excess adipose tissue causes an increase in blood flow and, consequently, blood volume expands to compensate for the increased oxygen demand (Pascual et al., 2003). The subsequent expansion of blood volume results in dilation of the left ventricle (LV) and is accompanied by an eccentric hypertrophy of the myocardium, even in normotensive individuals (Di Bello et al., 2013). Furthermore, both eccentric and concentric patterns of LV hypertrophy have been described in overweight/obese adults (Wong et al., 2005). Additionally, changes in cardiac morphology and function associated with obesity are not isolated to adult populations, with the impact of overweight/obesity on myocardial dysfunction also noted in young adults (Peterson, Waggoner, et al., 2004) and youth (Obert et al., 2012).

Over time, excessive accumulation of body fat causes adaptations of the heart. Specifically, cardiac changes associated with overweight/obesity included atrial remodelling, increased cardiac output (due to augmentation in circulating blood flow), reduced peripheral resistance, LV hypertrophy, ventricular remodelling (e.g. increased LV wall thickness, increased LV mass), increased LV filling pressure, diastolic dysfunction and, eventually, impairment in systolic function (Pascual et al., 2003).

2.3.2. Myocardial characteristics and mechanics

The architectural layout of the heart muscle plays a critical role in the mechanical and electrical function of the ventricles (Sengupta et al., 2006). The myocardium is described as a transmural continuum of two helical fibre organisations, made up of a right-handed helical formation in the inferior aspect of the myocardium (sub-endocardium) which gradually rotates into a left-handed helical formation in the superior aspect of the myocardium (sub-epicardium) (Figure 2.5). Due largely to the architectural characteristics of fibres arranged in two helical orientations, contraction of these fibres causes a twisting or “wringing” motion of the LV around its longitudinal axis (Sengupta et al., 2006).

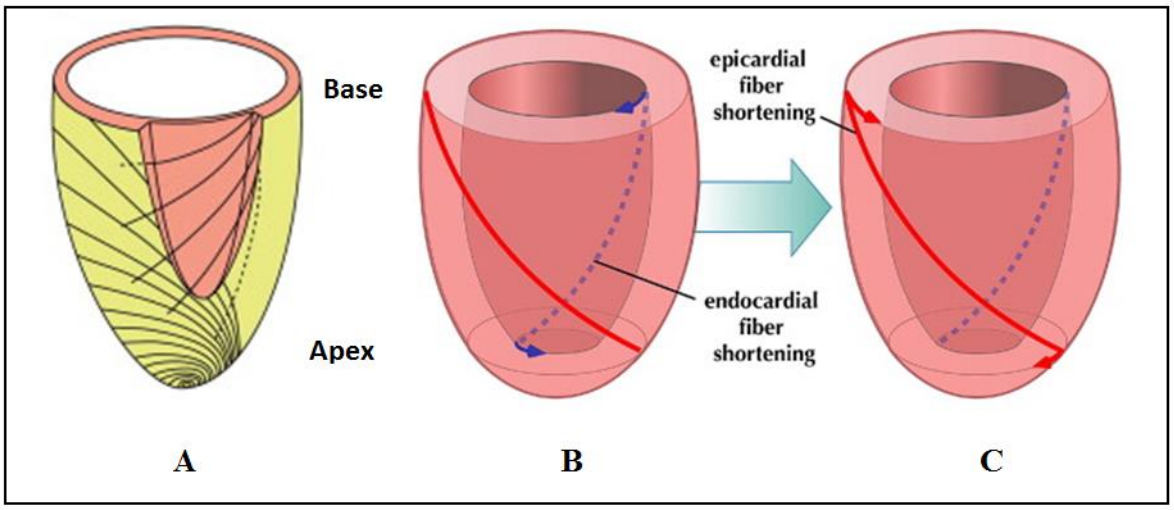

Figure 2.5. Schematic representation of the fibre orientation and mechanics of the LV. **(A)** LV fibre orientation changes from a right-handed helix in the sub-endocardium to a left-handed helix in the sub-epicardium at base and apex of the heart. **(B)** Isovolumetric contraction: endocardial fibres (blue dashed line) wrapped in a right-handed helix. **(C)** Ejection: epicardial fibres (red solid line) wrapped in an opposite, left-handed helix (Image modified from: Ashikaga, van der Spoel, Coppola, and Omens, 2009, p. 209).

During a cardiac cycle, the LV wall shortens, thickens, and then twists along its long axis. Viewed from the apex, a clockwise rotation of the base, and a counter-clockwise rotation of the apex is evident (Figure 2.6). An understanding of the heart's function and mechanical intricacies are important for assessing risk and pathophysiology of CVD (Sengupta et al., 2007).

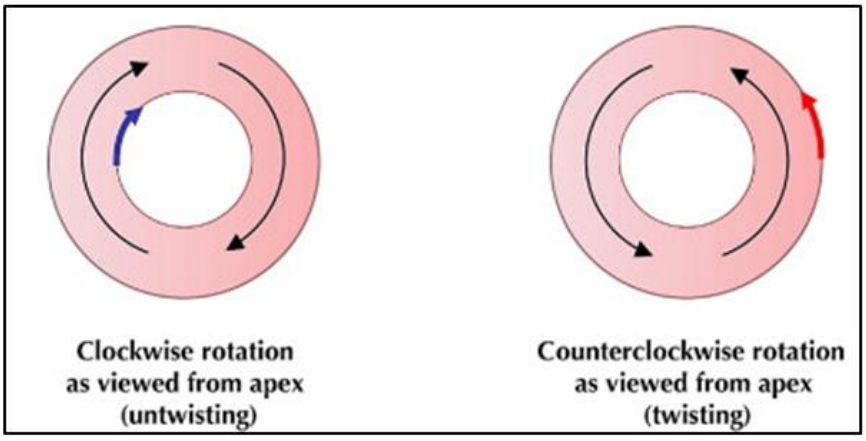

Figure 2.6. Mechanics of LV untwisting/twisting during isovolumetric contraction and ejection, respectively. Circumferential components of force (arrows) are generated by myocardial fibres shortening in opposite directions, causing a resultant "wringing" action. Endocardial fibres rotate clockwise (untwisting, blue arrow) while epicardial fibres rotate counter-clockwise (twisting, red arrow), as viewed from the apex (Image modified from: Ashikaga, van der Spoel, Coppola, and Omens, 2009, p. 209).

2.3.3. Cardiac assessment

The non-invasive imaging technique known as transthoracic echocardiography is used to quantify structural and functional changes of the heart. Echocardiography permits the evaluation of heart morphology, blood dynamics (global function) and, more recently, myocardial mechanics (regional function), with relatively new techniques shown to support conventional ones (Di Bello et al., 2013). Conventional two-dimensional (2D) echocardiography is used in the assessment of adverse arterial and ventricular remodelling via morphological and functional indices (measured with grey-scale M-Mode imaging), and of blood flow impairments (measured with pulsed Doppler). Furthermore, tissue Doppler imaging (TDI) echocardiography is used in the evaluation of global longitudinal tissue motion, specifically enabling measurement of systolic (S_m), early-diastolic (E_m), and late-diastolic (A_m) myocardial velocities. However, the assessment of myocardial tissue from TDI is limited by several factors including: (i) its inability to differentiate actively contracting myocardium from passive myocardial motion; (ii) measurements being susceptible to 'tethering' of neighbouring segments; and (iii) its insonation angle dependence (Anderson, 2007; Leitman et al., 2004). The introduction of 2D speckle tracking echocardiography (STE) in 2004 has overcome these limitations. STE is insonation angle-independent and considered

to be a more sensitive analysis of myocardial function (Leitman et al., 2004). Furthermore, the advantage of STE, compared with conventional echocardiographic and TDI techniques, is in the relative independence from load conditions and, in particular, from heart rotation and translational motion (Di Bello et al., 2013). Additionally, STE may permit earlier diagnosis of systolic and diastolic dysfunction, even when conventional indices of LV function remain within normal range (Obert et al., 2012). STE has shown excellent agreement with gold standard heart-imaging techniques such as Sonomicrometry (Amundsen et al., 2006) and tagged Magnetic-resonance imaging (Helle-Valle et al., 2005). However, STE is not without its limitations and may be influences by loading parameters within the human heart (Burns, La Gerche, D'hooge, MacIsaac, & Prior, 2010).

STE permits the measurement of myocardial velocities and assessment of myocardial contraction and relaxation, known as deformation. STE works by tracking the movement of natural acoustic markers, known as "speckles", throughout the cardiac cycle in ultrasound on 2D grey scale images (Leitman et al., 2004). Deformation is typically referred to as strain, and its *rate* of deformation as strain rate (SR). Deformation occurs in three planes; circumferential, longitudinal, and radial (Figure 2.7). In addition to indices of deformation, STE permits the quantification of myocardial mechanics, including the magnitude, timing, and dynamics of regional LV rotation and twist/untwist.

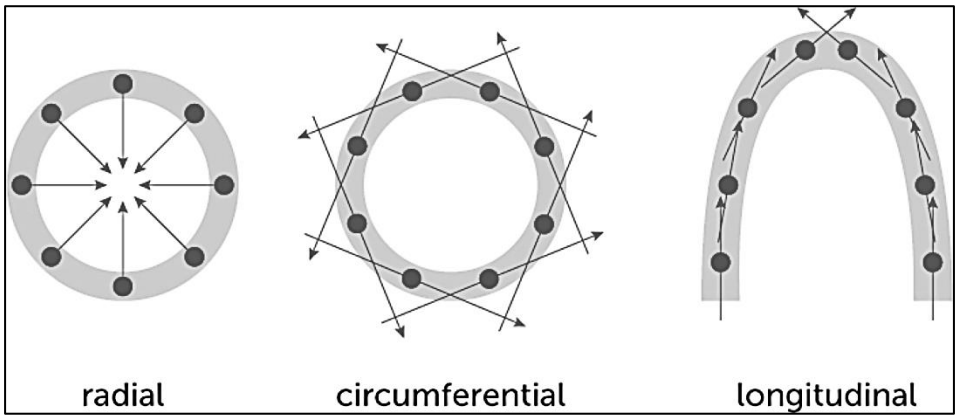

Figure 2.7. During a cardiac cycle, the LV wall shortens, lengthens, and twists along its long axis. This myocardial deformation can be measured using STE in the radial, circumferential and longitudinal planes (Image sourced from: http://123sonography.com/node/855).

The development of STE provides the potential for earlier detection of diastolic and systolic dysfunction and, consequently, earlier identification of subclinical diseases (Geyer et al., 2010). This makes it a popular tool for assessing myocardial dysfunction in populations with subclinical risk factors for CVD, particularly in those who are overweight or obese but who are not yet diagnosed with CVD (Edvardsen, Helle-Valle, & Smiseth, 2006).

2.4. CVD Risk in Premenopausal Women

The risk of CVD increases after menopause, with several CVD risk factors such as abdominal obesity, the metabolic syndrome, insulin resistance, hypertension, and dyslipidemia prevalent in post-menopausal women (Ardern & Janssen, 2007; Paul & Smith, 2005). This has been linked in part to the lower circulating concentrations of estrogen and progesterone after menopause. For example, estrogen exerts positive regulatory effects on the vascular endothelium (Cid, Schnaper, & Kleinman, 2002). Nevertheless, premenopausal women also incur increases in CVD risk. For example, in a sample of US women of "child bearing age" (n = 2,027, 18-4,4 years), 24% of non-Hispanic white women were obese (BMI $\geq$ 30 kg/m^2), 42% had abdominal obesity (WC $\geq$ 88 cm), 25% had the metabolic syndrome, and 37% demonstrated clinical evidence of a pro-inflammatory state as defined by elevated serum hsCRP (i.e. > 3.0 mg/L) (Ramos & Olden, 2008). The pattern of prevalence was the same for Blacks and Hispanics, although the prevalence of each risk factor was higher in these racial/ethnic groups compared with non-Hispanic white women (Ramos & Olden, 2008). Similarly, the Madrid Riesgo Cardiovascular Study assessed the prevalence of CVD risk factors in a cross-section of premenopausal women aged 31-40 years (n=141). The frequency of abdominal obesity was 54% and 24% for an elevated waist circumference $\geq$ 80 cm and $\geq$ 88 cm, respectively, with the metabolic syndrome prevalent in 6% of Spanish women using both the IDF and NCEP:ATP III definitions (Martinez et al., 2008). Similarly, the prevalence of the metabolic syndrome (according to the IDF definition) was reported to be 6% in Australian women aged 25-34 years and 15% in women aged 35-44 years (Cameron et al., 2007). There is also evidence that obesity in young women is associated with concentric LV remodelling and decreased systolic and diastolic function (Peterson, Waggoner, et al., 2004).

These early abnormalities in cardiac morphology and function have implications for future myocardial dysfunction associated with increased cardiovascular morbidity and mortality.

2.5. Prevention of CVD Risk

Despite research-based gains in the treatment of CVD, it remains the leading cause of death in women in most developed areas of the world (World Heart Federation, 2013). Overweight and obesity are major preventable and modifiable risk factors for the disease. To achieve long-term weight loss and maintenance requires a lifelong commitment to behavioural change (Wing, 2002). Therefore, early detection and prevention of CVD risk factors through innovative lifestyle interventions may be the best public health approach in chronic disease management. For example, the Chicago Heart Association Detection Study assessed young women (n = 7302, baseline age = 18 to 39 y) for CVD risk, including overweight/obesity, T2DM, hypertension, elevated serum cholesterol and smoking. Those who possessed greater numbers of risk factors at baseline also experienced a 6-fold increase in CVD mortality risk at 31-year follow-up, compared to women with no risk factors at baseline (Daviglus et al., 2004). Similarly, the Health Hunters study implemented an obesity *prevention* program targeting young women considered 'high-risk' (n = 30, aged 18-28 y), in that they had at least one severely obese parent (BMI $\geq$ 37 kg/m^2). In the 12-month program, participants received customised dietary and physical activity advice, while the control group received standard care (Eiben & Lissner, 2006). At program completion, intervention participants had reduced their weight (group mean: -1.9 kg), while control participants experienced weight gain (+1.4 kg).

Non-pharmacological lifestyle management and behaviour modification have a 'first line of treatment' role in the prevention of CVD risk (Steinbaum, 2004). It has been suggested that the primary treatment of overweight/obesity, through lifestyle interventions, should focus on weight management/reduction, increased physical activity, and a heart-healthy diet, to reduce intermediate risk factors and prevent their progression to CVD (Paul & Smith, 2005). Furthermore, prevention of the development of risk factors through a positive lifestyle approach (lifestyle intervention) may minimise the future need for intensive or alternative treatment, such as drug therapy or surgery (Mosca et al., 2004). Yet for people with whom lifestyle change has had limited success and are considered 'high risk' for CVD, appropriate

pharmacological agents or surgical intervention (Sjöström et al., 2007) may be required (International Diabetes Federation, 2006). Nevertheless, lifestyle modification will continue to be the cornerstone of CVD treatment, irrespective of the availability of new pharmacological therapies (Bantle et al., 2008).

2.5.1. Lifestyle intervention research trends

The majority of research investigating the effects of lifestyle intervention on CVD risk has been conducted in middle-aged and older adults (Dutheil et al., 2013; Kosmala, O'Moore-Sullivan, Plaksej, Przewlocka-Kosmala, & Marwick, 2009; Watkins et al., 2003) or adolescent populations (Obert et al., 2013; Tjonna et al., 2009). Meanwhile, the majority of studies focusing solely on female participants have assessed post-menopausal women (Kuller et al., 2006). This highlights the paucity of CVD-related research addressing the effects of lifestyle interventions on, premenopausal women, with only limited studies available (Cotie, Josse, Phillips, & MacDonald, 2014; Esposito et al., 2003; Thomson et al., 2008). Weight loss programs that use a multi-disciplinary or multi-component (e.g. exercise + diet + behavioural therapy) lifestyle intervention approach have been mostly proven effective for reducing risk factors for CVD. Markers of body composition, insulin resistance, lipid profile and/or systemic inflammation have been reduced with multi-disciplinary lifestyle interventions ranging in duration from 12 weeks to 4.5 years (Esposito et al., 2003; Kuller et al., 2006; Kuller, Simkin-Silverman, Wing, Meilahn, & Ives, 2001; Tjonna et al., 2009; Watkins et al., 2003). Furthermore, multi-disciplinary lifestyle interventions have a positive effect on endothelial function, LV function, myocardial mechanics, and atherosclerosis in programs lasting from 16 weeks to 9 months, albeit in older or youth populations (Cotie et al., 2014; Dutheil et al., 2013; Kosmala et al., 2009; Obert et al., 2013). Moreover, in light of some recent large, longitudinal intervention trials in middle-aged and older adults (Ross et al., 2012; The Look AHEAD Research Group, 2013), it is apparent that multi-disciplinary lifestyle interventions have a strong evidence base for success in reducing CVD risk in a variety of populations. However, lifestyle interventions specifically targeting treatment or management in young women are limited in number and quality and, thus, the needs of this age group are currently unmet (Hutchesson, Hulst, & Collins, 2013).

Chapter 3. The effectiveness of randomised controlled trial lifestyle interventions on cardiovascular disease risk factors in premenopausal women with overweight and obesity: A systematic review

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Publication Statement:

This work has been prepared for submission to the *International Journal of Behavioral Nutrition and Physical Activity*, please see Appendix 1.

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3.1. Abstract

Background and objectives: Cardiovascular disease (CVD) is the leading cause of death in women worldwide, with overweight and/or obesity a principle risk factor. To address overweight and obesity and reduce CVD, lifestyle modification is recommended. Therefore, the aim of this paper was to systematically review the effectiveness of multi-disciplinary lifestyle interventions on CVD risk factors in overweight/obese premenopausal women.

Data sources and study selection: A systematic search was conducted to capture all randomised controlled trials assessing the effect of a lifestyle intervention on CVD risk factors in overweight/obese premenopausal women published from 2004 to 2014. Included studies required the lifestyle intervention to have at least two of the following three components (1) exercise, (2) diet, and/or (3) behavioural therapy. Studies were excluded if the lifestyle intervention was less than eight weeks in duration. Three electronic databases were searched (MEDLINE, CINAHL, and EMBASE) during March 2014, and additional studies were included following manual search of eligible studies and recent reviews.

Results: Five studies met the inclusion criteria. Length of the lifestyle interventions ranged from 10 to 104 weeks, with three studies performing follow-up. All five studies had an exercise component. Specifically, the lifestyle interventions consisted of: (1) exercise + diet + behavioural therapy (n=3), (2) exercise + diet (n=1), and (3) exercise + behavioural therapy (n=1). Independent of the components of the lifestyle intervention, all studies observed changes in some CVD risk factors, with improvements in body composition the most reported, while albeit few in number, blood-borne markers of CVD risk remained unchanged.

Conclusion: Multi-disciplinary lifestyle interventions are modestly effective in reducing CVD risk factors in overweight/obese premenopausal women, with no specific type of lifestyle intervention prevailing as demonstrating greater success than others. There remains a need for more rigorous studies, with long-term follow-up evaluating program sustainability.

Keywords: Overweight, exercise, physical activity, female, nutrition, diet, behavioural therapy, metabolic syndrome, weight loss

3.2. Introduction

In the USA, United Kingdom and Australia, 45-50% of women aged 20-39 years are overweight or obese (Australian Bureau of Statistics, 2013; Flegal et al., 2012; Health and Social Care Information Centre, 2011). Clinical and community studies have demonstrated a relationship between overweight and/or obesity and increased cardiovascular disease (CVD) risk factors in young women (Peterson, Waggoner, et al., 2004; Sokmen et al., 2013). Most modifiable CVD risk factors, including being overweight or obese can be improved through lifestyle interventions (Irving et al., 2008; Kemmler, Von Stengel, Engelke, & Kalender, 2009). With CVD being the leading cause of death in women worldwide (World Health Organisation, 2011), early intervention of CVD risk may lead to more effective attenuation of disease progression.

The therapeutic role of lifestyle interventions in the prevention, treatment and/or, control of CVD risk has been effective in adolescents (Obert et al., 2013), middle-aged women (Meckling & Sherfey, 2007) and older adults (Ross et al., 2012; The Look AHEAD Research Group, 2013). Furthermore, the management of overweight and/or obesity using lifestyle interventions in adults (aged 19 – 74 y) have been reviewed for their effects on long-term weight-loss and maintenance. It was concluded that the most effective lifestyle interventions were those combining diet, exercise and behavioural modification (A. Lang & Froelicher, 2006). More recently, (Aguiar, Morgan, Collins, Plotnikoff, & Callister, 2014) reviewed the effects of multi-component lifestyle interventions involving diet, aerobic exercise and resistance training on body composition and fasting glucose in pre-diabetic middle-aged/older adults (54 ± 7 y). The results showed lifestyle interventions were effective for inducing modest weight loss and eliciting small improvements in glycemic control, together with improvements in aerobic fitness and dietary intake. Despite global strategies for preventive health, research assessing the effectiveness of lifestyle interventions specifically targeting overweight and/or obese premenopausal women is currently limited (Hutchesson; Hulst & Collins, 2013), with longer-term sustainability of multi-component lifestyle interventions unclear.

Therefore, the aim of this work was to systematically review the effects of randomised controlled trial, multi-disciplinary lifestyle interventions that included at least two of

exercise, diet and/or behavioural therapy components in overweight/obese premenopausal women. Specifically, this review assessed the effects of these interventions on CVD (metabolic, cardiac and vascular) risk factors, including anthropometric measures, markers of the metabolic syndrome, blood biochemistry, fitness, nutrition and psychological outcomes.

3.3. Methods

The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement (Moher, Liberati, Tetzlaff, & Altman, 2009) guided the conduct and reporting of this review.

3.3.1. Data sources and searches

A systematic review was performed on the literature published between 2004 and February 2014. The search strategy consisted of three online databases: Medline, EMBASE, and CINAHL. The general search strategy is shown in tables 3.1, 3.2 and 3.3.

Table 3.1. Title, abstract and key words used across all database searches (Medline, CINAHL, EMBASE) in the electronic search strategy.

Population	Intervention components	Study type	Risk factors	"NOT"
Women	**PART A.**	Randomized control*	**METABOLIC**	Pregnan*
Female	Exercise	trial	Cardiovascular disease	Breast feed*
	Exercise therapy	Randomised control*	Metabolic syndrome	Postpartum
	Resistance train*	trial	Cardiometabolic	Polycystic ovar*
	Weight train*	Controlled clinical trial	Abdominal obesity	syndrome
	Fitness	Clinical trial	Waist circumference	Post menopaus*
	Aerobic		Obes*	Elderly
	Physical activity		Sedentary	Older
	PART B.		**CARDIOVASCULAR**	Middle age*
	Diet		Myocardial dysfunction	Child*
	Diet therapy		Myocardial function	Adolescen*
	Nutrition		Global strain	Youth
	Nutrition therapy		Carotid intima-media	Juvenile
	PART C.		thickness	HIV
	Lifestyle		Echocardiogra*	Bariatric surgery
	Life style		Speckle tracking imaging	Supplement*
	Counsel*		echocardiography	Drug*
	Cognitive therapy		Tissue Doppler imaging	Rehabilitation
	Cognitive behaviour*		Left ventric*	Cancer
	therapy			
	Motivational interviewing			

*Footnotes: Part A and Part B, or Part A and Part C, or Part B and Part C, or Part A and Part B and Part C. *truncation of word.*

Table 3.2. MeSH (2014) terms specific to Medline used in the electronic search strategy.

Population	Intervention components	Publication type	Risk factors	"NOT"
Women	**PART A**.	Randomized controlled trial	**METABOLIC**	Pregnant women
Female	Exercise	Clinical trial	Cardiovascular diseases	Breast feeding
	Exercise therapy		Metabolic syndrome X	Postpartum period
	Resistance training		Obesity	Polycystic ovary syndrome
	Physical fitness		Waist circumference	Postmenopause
	PART B.		Abdominal fat	Middle aged
	Diet		Abdominal obesity	Aged
	Diet, Reducing		Sedentary lifestyle	Child
	Diet therapy		**CARDIOVASCULAR**	Adolescent
	Nutrition therapy		Left ventricular function	HIV
	PART C.		Lefty ventricular dysfunction	Bariatric surgery
	Cognitive therapy		Ventricular remodelling	Drug therapy
	Life style		Left ventricular hypertrophy	Dietary supplements
	Counselling		Carotid intima-media thickness	Rehabilitation
	Motivational interviewing		Echocardiography	Cancer
			Doppler echocardiography	
			Pulsed Doppler echocardiography	

Table 3.3. Subject headings specific to CINAHL used in the electronic search strategy.

Population	Intervention components	Publication type	Risk factors	"NOT"
Women	**PART A.**	Randomized controlled trial	**METABOLIC**	Expectant mothers
Female	Exercise	Clinical trials	Cardiovascular risk factors	Breast feeding
	Resistance training		Metabolic syndrome X	Postnatal period
	Group exercise		Obesity	Polycystic ovary syndrome
	Physical fitness		Waist circumference	Middle aged
	Physical activity		Abdominal fat	Aged
	PART B.		Life style, sedentary	Child
	Diet		**CARDIOVASCULAR**	Adolescence
	Diet, reducing		Left ventricular hypertrophy	HIV
	Diet therapy		Ventricular remodelling	Bariatric surgery
	Nutrition		Left ventricular function	Drug therapy
	PART C.		Carotid intima-media thickness	Pharmacological and
	Cognitive therapy		Echocardiography	biological treatments
	Life style changes		Echocardiography, Doppler	Dietary supplementation
	Counselling		Echocardiography, Doppler,	Rehabilitation
	Motivational interviewing		Pulsed	Cancer
			Heart left ventricle	

Individual databases were searched with specific MeSH terms (Medline), subject headings (CINAHL) and/or title, abstract, and keywords (Medline, CINAHL, EMBASE). Select terms were excluded by using the Boolean operator "NOT". Results were limited to 'English language' and publication type 'journal article'. Age was also limited to 19-44 years for Medline and CINAHL, and 18-64 years for EMBASE.

Although medication and the surgical treatment of obesity are important and critical for certain circumstances, this review regarding overweight and/or obesity emphasised non-pharmacological behavioural lifestyle interventions. Thus, all studies incorporating a medical or surgical intervention were excluded.

3.3.2. Study selection

Intervention studies investigating CVD risk factors in overweight/obese pre-menopausal women were included. The search strategy included the use of terms in four broad categories. Each category was individually searched with 'OR', then combined with 'AND' to form the overarching search strategy, including:

(i) Population: only female data were included in the review. If studies incorporated both female and male participants, data were only included if the female data were presented separately. Women had to be overweight and/or obese, pre-menopausal, free from polycystic ovarian syndrome, and not pregnant or lactating. Studies were excluded if the mean age of the sample was > 40 years. Studies including women with a history of bariatric surgery were also excluded.

(*ii) Intervention components*: the lifestyle intervention was required to have at least two of the following three components (or derivations of these terms): (A) exercise, (B) diet, (C) behavioural therapy (Tables 3.1-3.3). For the purpose of this review, exercise was referred to as aerobic and/or resistance training. Diet was referred to as a restriction of calories or nutrition education but excluded drug trials or supplementation. The behavioural therapy component was referred to as counselling or motivational interviewing, either as a group or provided on an individual basis. A minimum duration of 8 weeks was required for the lifestyle intervention.

(*iii) Study type:* The search was limited to randomised controlled trials (RCT).

(iv) Risk factors: The search was limited to key risk factors with the known potential to increase the development of CVD, such as overweight and/or obesity, the metabolic syndrome, and sedentary behaviour (referred to as *metabolic* in Tables 3.1-3.3). Ultrasound techniques used in the detection of cardiac and vascular dysfunction, including echocardiography, intima-media thickness and Doppler, were also searched (referred to as *cardiovascular* in Tables 3.1-3.3).

One author (BS) conducted all electronic searches and collated the abstracts. After duplicate deletion, two authors (BS and GN) screened all articles based on title and abstract for preliminary inclusion, using the eligibility criteria below. If the abstract did not provide a clear indication of eligibility, the full text was obtained and reviewed. After screening titles

and abstracts, full text was retrieved for all potentially relevant articles and assessed according to the selection criteria outlined below. Manual searches were also conducted from the reference lists of the retrieved included articles and recent reviews.

3.3.3. Data extraction and quality assessment

After duplicate deletion, characteristics and results of studies were extracted by one author (BS). A single study with multiple published articles was reported as one study. Quality assessment of all studies included in the review were categorised via the Physiotherapy Evidence Database (PEDro) scale (Table 3.4). The PEDro scale is an 11-item measure of the methodological quality of RCTs (Maher, Sherrington, Herbert, Moseley, & Elkins, 2003). Each item was scored with a '1' for 'yes' or '0' for 'no' (Table 3.5)

Table 3.4. The Physiotherapy Evidence Database **(**PEDro) scale items (Maher et al., 2003).

1. Eligibility criteria
2. Random allocation
3. Concealed allocation
4. Baseline comparability
5. Blind subjects
6. Blind therapists
7. Blind assessors
8. Adequate follow-up
9. Intention-to-treat analysis
10. Between-group comparisons
11. Point estimates and variability

Table 3.5. The Physiotherapy Evidence Database (PEDro) Scale (Maher et al., 2003).

Reference	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**Score (%)**	**Quality**
Carroll et al	1	1	0	1	NA	NA	0	1	1	1	1	7/9 (78)	High
Chang et al	1	1	0	1	NA	NA	1	0	0	1	1	6/9 (67)	High
Kerksick et al	1	1	0	1	NA	NA	0	0	0	1	1	5/9 (55)	High
Schmitz et al	1	1	0	1	NA	NA	1	1	0	1	1	7/9 (78)	High
Silva et al	1	1	0	1	NA	NA	0	1	1	1	1	7/9 (78)	High
Total	**5**	**5**	**0**	**5**	**NA**	**NA**	**2**	**3**	**2**	**5**	**5**	**6.4 (71)**	**High**

NA, not applicable.

3.3.4. Data analysis

The primary outcomes of the review were *between-group* differences in metabolic, cardiac and/or vascular risk factors for CVD following the multi-disciplinary lifestyle intervention. Vast differences were observed in the lifestyle interventions implemented in each study in this review. For example, differences were apparent in exercise mode, length and intensity, and use of nutrition education versus calorie restriction. Therefore a meta-analysis was not conducted. Furthermore, it has been noted previously that meta-analysis is deemed inappropriate for variables where results from fewer than three studies are (Aguiar et al., 2014); which was common in this review (Table 3.6).

Table 3.6. Cardiovascular disease (CVD) risk factors and psychological inventories reported across the studies used in the review.

Variable	# of studies	Reference/s
Anthropometric measures		
Body weight (kg)	5	Silva, Schmitz, Kerksick, Carroll, Chang
BMI (kg/m^2)	4	Silva, Schmitz, Kerksick*, Carroll
Body fat (%)	4	Carroll*, Silva, Schmitz, Kerksick
Fat mass & lean mass (kg)	3	Schmitz, Silva, Kerksick
Waist circumference (cm)	2	Carroll*, Kerksick
Metabolic syndrome markers/ blood biochemistry		
HDL-cholesterol ($mmol \cdot L^{-1}$)	2	Carroll, Kerksick
Triglycerides ($mmol \cdot L^{-1}$)	2	Carroll, Kerksick
Fasting glucose ($mmol \cdot L^{-1}$)	3	Carroll, Chang, Kerksick
Systolic & diastolic blood pressure (mmHg)	2	Carroll, Kerksick*
Total cholesterol ($mmol \cdot L^{-1}$)	2	Carroll*, Kerksick
LDL-cholesterol ($mmol \cdot L^{-1}$)	1	Kerksick
Insulin ($pmol \cdot L^{-1}$)/ HOMA-IR	1	Kerksick
Fitness markers		
VO_2 ($ml \cdot kg^{-1} \cdot min^{-1}$)	2	Carroll, Kerksick
Physical activity#	3	Silva, Chang, Schmitz
Bench-press/ leg-press 1RM (kg)	2	Schmitz, Kerksick
Dietary outcomes		
Caloric intake§	2	Schmitz, Kerksick
Fat intake¥	2	Chang, Kerksick
Carbohydrate & protein intake ($g \cdot kg^{-1} \cdot d^{-1}$)	1	Kerksick
Fruit & vegetable intake ($cups \cdot d^{-1}$)	1	Chang
Psychological characteristics		
Perceived Stress Scale (PSS) Cohen, 1983	2	Carroll, Chang
General Wellbeing (GWB) Dupuy, 1977	1	Carroll
Positive Affect and Negative Affect Scale (PANAS) Watson, 1988	1	Chang
Health Care Climate Questionnaire (HCCQ) Williams et al., 1996	1	Silva
Treatment Self-regulation Questionnaire (TSRQ) Ryan & Connell, 1989	1	Silva
Self-determination Scale (SDS) Sheldon et al., 1996	1	Silva
Locus of Causality for Exercise Scale (LCE) Markland, 1999	1	Silva
Self-regulation Questionnaire (SRQ-E) Ryan & Connell, 1989	1	Silva
Intrinsic Motivation Inventory (IMI) McAuley et al., 1989	1	Silva
Exercise Motives Inventory-2 (EMI-2) Mark;and & Ingledew, 1997	1	Silva

BMI, body mass index; HDL, high-density lipoprotein; LDL, low-density lipoprotein; HOMA-IR, homeostasis model assessment of insulin resistance; 1RM, one repetition max.
**baseline only. # presented as mins/d or MET. § presented as kcal/kg/day or kcal. ¥ presented as % of total calories or g/kg/day.*

3.4. Results

3.4.1. Study selection and study inclusion

Electronic searches returned 100, 200 and 87 results for Medline, CINAHL and EMBASE, respectively (Figure 3.1). From these electronic searches, duplicates were removed and 52 articles were identified as potentially relevant after an initial examination of titles and abstracts. After retrieval of full text, 44 articles were excluded due to the following: data were calculated as the average from male and female results (n = 23); the study design did not include a control group (n = 6); the intervention did not have at least two of the three intervention components (n = 4), the study design was not randomised (n = 4); participants were not classified as overweight/obese (n = 3); participants ingested a supplement as part of the diet component (n = 2); the lifestyle intervention was less than 8 weeks in duration (n=1); or the intervention was investigating an acute response (n = 1). In total, eight papers from the search met the inclusion criteria. Additional manual searches, including a search of reference lists of included articles and recent reviews, returned four additional results, with one meeting the inclusion criteria (Carroll, Borkoles, & Polman, 2007). From these nine papers, five intervention trials were identified (i.e. three cases of multiple papers stemming from a single research study) and these are described in Table 3.7.

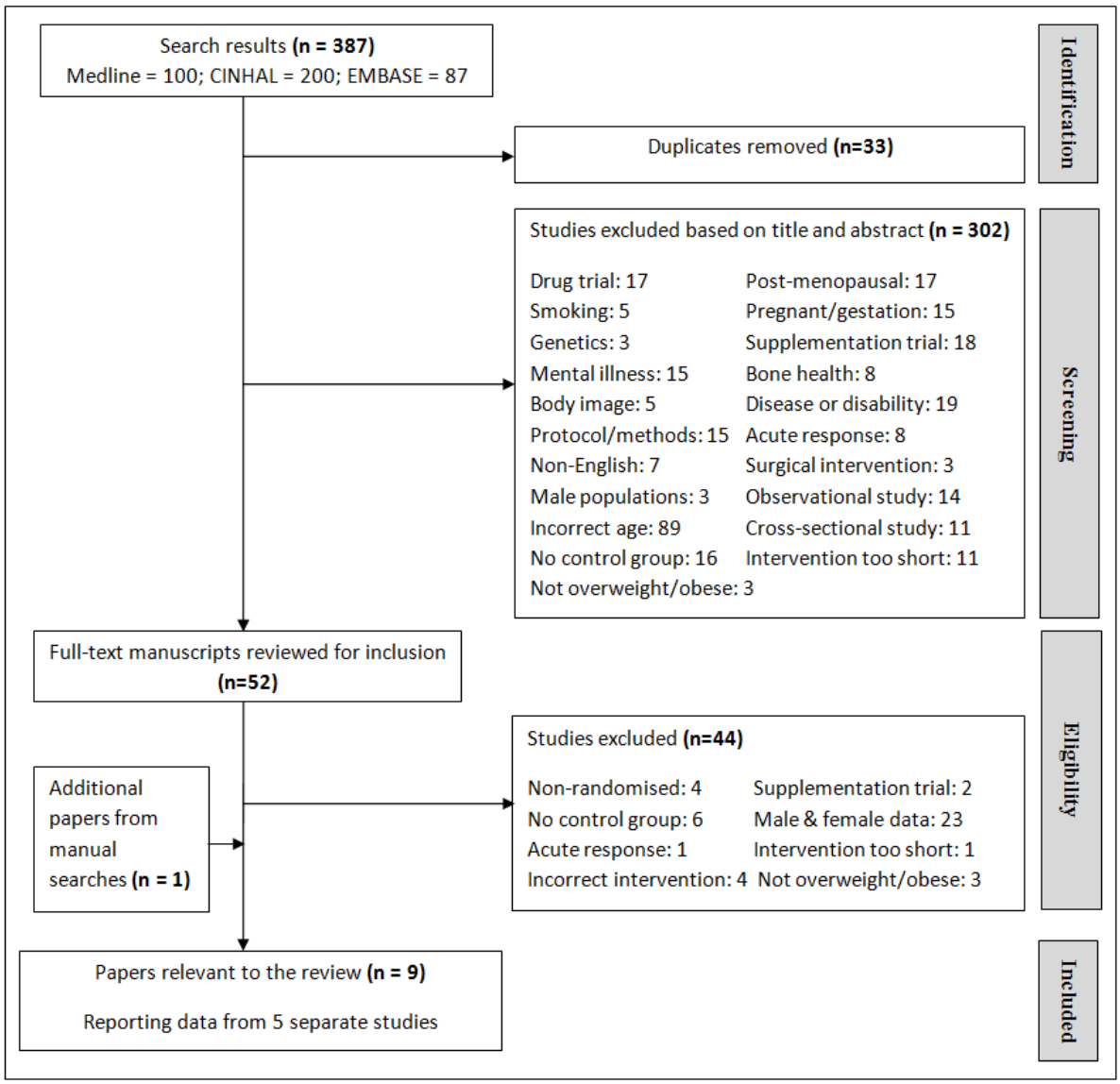

Figure 3.1. Flow diagram of the process of study selection.

Table 3.7. Characteristics of included studies.

Reference	Population characteristics						Lifestyle intervention						Data collection			Results
Authors (Year)	Mean age (y)	Age range (y)	Baseline sample Size (int, control)	Post sample size (int, control) [total retention]	BMI (kg/m^2) inclusion criteria	Baseline BMI (kg/m^2)	Exercise component	Diet component	Behavioural therapy component	Control group/s	Intervention duration	Adherence to intervention	Data time points (wk)	Post follow-up	Outcome measures	Major findings of intervention group
Exercise + Diet + Behavioural therapy																
Carroll et al (2007) Carroll et al (2012)	40 ± 8	24-55	31 (17, 14)	20 (10, 10) [72%]	BMI ≥ 30	38.6 ± 7.6	2 h/wk supervised, structured aerobic + 2 h/wk unsupervised	3 week nutrition education course led by dietician	Weekly SDT-guided lifestyle change sessions	Wait-list design. Maintain usual lifestyle	12 wk	89%	0, 12	9 mo NR	BM, BMI, BP, HDL, trig. FG, VO_2, GWB, PSS	↑ VO_2. ↑ GWB score.
Silva et al (2010) Andrade et al (2010) Mata et al (2009)	38 ± 7	25-50	239 (123, 116)	208 (115, 93) [87%]	BMI 25-40	31.5 ± 4.1	Promotion through theory + dance classes and an activity challenge program	Nutrition advice (embedded in behavioural therapy)	Bi-monthly (30 sessions) face-to-face SDT-guided program (120 mins)	Bi-monthly (29 sessions) face-to-face health info (120 mins)	52 wk	87%	0, 16, 52	2 y NR	BM, BMI, BF%, FM, LM, PA, HCCQ, TSRQ, SDS, LCE, SRQ-E, IMI, EMI-2	↓ BM, BMI, BF%, FM, LM. ↑PA & steps/d. ↑ self-regulation, self-determination, intrinsic motivation & exercise motives
Chang et al (2010) Chang et al (2009)	25 ± 4	18-34	129 (64, 65)	At 8 wk: 70 (28, 42) [49%] At 32 wk: 48 (16, 32) [34%]	BMI 25.0-39.9	NR	Physical activity advice (imbedded in DVD)	Nutrition advice (embedded in DVD)	SCT framework. Theory viewed bi-weekly on a DVD + 5 x 30 min peer-support group teleconference	Usual care	10 wk	66%	0, 8, 32	8 mo	BM, FG, PA, PSS, PANAS, fat intake, fruit & veg. intake	↑ fruit & veg. ↑ PSS score
Exercise + Diet																
Kerksick et al (2010)	39 ± 8	NR	216 (203, 13)	141 (132, 9) [65%]	NR	35.0 ± 6.2	3 x wk, 30 min per session supervised, structured circuit resistance-training + callisthenics	One of four different calorie restriction diets: HC (n=15), VLCHP (n=60), LCMP (n=56) or HCLP (n=65)	None	No diet/ no ex (n=7) or No diet + ex (n=13)	14 wk	NR	0, 1, 10, 14	None	BM, BMI, WC, BF%, FM, LM, BP, VO_2, TC, HDL, LDL, trig, FG, IN, HOMA-IR, BPR, LPR, CI, fat/ CHO/ protein intake, PA	↓ BM, FM LM. ↑ VO_2. ↓ fat intake
Exercise + Behavioural therapy																
Schmitz et al (2007)	36 ± 5	25-44	164 (82, 82)	At 52 wk: 138 (71, 67) [84%] At 104 wk: 133 (70, 63) [81%]	BMI 25-35	29.4 ± 0.4	2 x wk, 45-60 min per session of structured, supervised strength-training (for 16 wk); then unsupervised (with supervised session once per 12 wk)	None	SCT framework + semi-annual social gatherings + website, newsletter	Standard care (AHA brochure)	104 wk	At 52 wk: 76% At 104 wk: 61%	0, 52, 104	None	BM, BMI, BF%, AbF%, FM, LM, PA, BPR, LPR, CI	↓BF%, AbF%. ↑BPR, LPR.

Int, intervention. SDT, self-determination theory. SCT, social-cognitive theory. AHA, American Heart Association. BM, body mass. BMI, body mass index. BF, body fat. FM, fat mass. LM, lean mass. AbF, abdominal fat. WC, waist circumference. PA, physical activity, BPR, bench press. LPR, leg press. BP, blood pressure. HDL, high-density lipoprotein. LDL, low-density lipoprotein. TC, total cholesterol. Trig, triglycerides. FG, fasting glucose. CI, caloric intake. IN, insulin. HOMA-IR, homeostasis model assessment of insulin resistance. VO_2, maximal oxygen uptake. PSS, perceived stress scale. GWB, general well-being. HCCQ, health care climate questionnaire. TSRQ, treatment self-regulation questionnaire. SDS, self-determination scale. LCE, locus of causality for exercise scale. SRQ-E, self-regulation questionnaire. IMI, intrinsic motivation inventory. EMI-2, exercise motives inventory-2. PANAS, Positive Affect and Negative Affect Scale. CHO, carbohydrate. Veg, vegetable. HC, high carbohydrate diet. VLCHP, very low carbohydrate, high protein. LCMP, low carbohydrate, moderate protein. HCLP, high carbohydrate, low protein. NS, not reported.

3.4.2. Study characteristics

Of the five included studies, three were conducted in the United States (Chang, Nitzke, & Brown, 2010; Kerksick et al., 2010; Schmitz et al., 2007), one in the United Kingdom (Carroll et al., 2007) and one in Portugal (Silva et al., 2010). Inclusion criteria were similar across all five studies, requiring participants to be overweight and/or obese (based on BMI), premenopausal, sedentary, free from major illness, and not taking medication known to interfere with weight loss (e.g. anti-depressive). All studies stated exclusion criteria for participants not in good health, pregnant, or with a history of cardiovascular disorders or chronic disease.

The collective sample size of the studies at baseline was 779 participants, with a range of 31 to 239. Of these 779 participants, 577 completed post-intervention testing (range: 20 to 208). Participant samples were predominantly Caucasian, with Chang et al. (2010) also including African American participants, and Schmitz et al. (2007) using an ethnically diverse sample (Caucasian, Black, Asian, Native American, and Pacific Islanders). Age ranged from 18-55 years across all studies. However, only Chang et al. (2010) had a mean participant age below 30 years, while the other studies presented a mean age of 36 to 40 years.

The research design components of each study are outlined in detail in Table 6. Of the five studies, three comprised Exercise + Diet + Behavioural therapy (Carroll; Chang; Silva), one comprised Exercise + Diet (Kerksick), and one comprised Exercise + Behavioural therapy (Schmitz). The lifestyle intervention duration ranged from 10 to 104 weeks. Data were collected at baseline and post-intervention time points, with three studies performing data collection at mid-intervention (Kerksick; Schmitz; Silva). Additionally, three studies performed follow-up testing at 6 months (Chang), 9 months (Carroll), and 24 months (Silva) after completion of the intervention, but only Chang et al. (2010) reported these data. Compliance rates were reported in four studies (Carroll; Chang; Schmitz; Silva), with adherence to the lifestyle intervention ranging from 61-89%. One study (Chang) provided monetary incentives to reimburse participants for their time, whilst another study provided free child care (Schmitz) when participants performed their supervised exercise sessions.

The nature of the control group varied across studies. Three studies (Carroll; Chang; Schmitz) provided usual care (maintenance of usual lifestyle behaviour). Of these, one provided control participants with brochures (Schmitz) detailing the current recommendations for

weekly physical activity, and one used a wait-list (delayed start) design, during which participants were scheduled to start the intervention at the completion of the control period. One study (Kerksick) used a two control group design, with a (i) no diet and no exercise control group or (ii) exercise only (no diet) control group. One study (Silva) provided bi-monthly, face-to-face sessions for their control group, lasting 120 minutes, on 'lifestyle themes'.

Exercise component

All studies incorporated exercise as part of their lifestyle intervention. Three studies (Carroll; Kerksick; Schmitz) provided a combination of structured, supervised sessions conducted by a trainer and unsupervised sessions, 2-3 times per week, ranging from 30-120 minutes in duration. The exercise training comprised aerobic activities and/or strength/resistance training, using gym facilities to deliver the exercise component. In comparison, two studies (Chang; Silva) encouraged participation in physical activity and promoted the importance of exercise via a theory-based module designed by exercise physiologists. In both cases, physical activity was unstructured, unsupervised and self-driven. Silva et al. (2010) also offered additional, supervised dance classes and an 'activity challenge'.

Diet component

Four studies provided a dietary component (Carroll; Chang; Kerksick; Silva). One study provided nutrition education delivered by a dietitian (Carroll). Two studies had nutrition 'themes' designed by dieticians that were embedded in the behavioural therapy sessions (Chang; Silva). And one study (Kerksick) provided modest caloric restriction, with women randomised into one of four groups of a specific macronutrient profile, being either (i) high-carbohydrate, (ii) low-carbohydrate with high-protein, (iii) low-carbohydrate with moderate-protein, or (iv) high-carbohydrate with low-protein. In contrast, the other study (Schmitz) requested all participants to maintain their current diet throughout their trial.

Behavioural therapy component

Four studies provided a behavioural therapy component (Carroll; Chang; Schmitz; Silva). Two studies conducted weekly (Carroll) or 120 minute bi-monthly (Silva) small group sessions, using a face-to-face mode as the means of intervention delivery. In both studies, self-determination theory (Deci & Ryan, 1985) guided the 'lifestyle change' program. Two studies (Chang, Schmitz) used social cognitive theory (Bandura, 1991) as a framework for developing support networks amongst intervention participants. One study (Schmitz) conducted semi-annual gatherings and provided a study website and monthly newsletters. One study (Chang) encouraged participants to view health behavioural change themes presented bi-weekly in their homes via DVD, and these participants were asked to complete a weekly worksheet to self-monitor progress and partake in a fortnightly peer-support teleconference lasting 30 minutes with a moderator and 10-15 other participants.

3.4.3. Quality assessment and potential bias

To estimate the quality of methods in each study, the previously validated 11-item PEDro scale with a cut-off at 6 was used (Maher et al., 2003). In this review, the PEDro scale was modified to exclude criteria 5 and 6 (blinding of all subjects to the intervention and blinding of therapists, respectively) which were considered difficult to implement in exercise intervention trials (Sherrington, Moseley, Herbert, Elkins, & Maher, 2009).

All studies specified their eligibility criteria for participation (criterion 1) and randomised participants into either an intervention or control group (criterion 2). No studies reported group-allocation concealment (criterion 3). The analysis of baseline differences was reported in all studies, with no differences found between intervention and control groups (criterion 4), suggesting homogeneity between groups at baseline. Blinding of assessors (criterion 7) was reported in two studies (Chang; Schmitz), in which the measurement staff were blinded to group assignment during data collection and analyses. Three studies (Carroll; Schmitz; Silva) satisfied the criterion of obtaining key outcome measurements in 85% of participants (criterion 8), with a retention rate across the five studies ranging from 49-87% from baseline to post-intervention (see Table 6). Two studies (Carroll; Silva) specified intention-to-treat statistics were used (criterion 9). The determination of sample size with sufficient power was reported in three studies (Kerksick; Schmitz; Silva). All studies performed between-group

statistical comparisons (criterion 10). Both point measures and measures of variability were satisfactorily reported in all studies (criterion 11). Based on the remaining 9-item scale, the average quality of the trials was 71% (range from 55-78%), with a mean point score of 6.4 out of 9. A score of ≥ 5 for the modified scale was indicative of 'high' quality (Sherrington et al., 2009), and was met by all studies (Table 3.5).

3.4.4. Outcome measures of included studies

A summary of the outcome measures is presented in Table 3.7. A description of the effects of the lifestyle interventions on key CVD risk factors for the five studies is presented below. Body composition was the most commonly reported outcome measure across the five studies (Table 3.6). Conversely, none of the studies measured cardiac or vascular outcomes using echocardiographic or ultrasonographic techniques.

Anthropometric measures

All participants in the five studies were classified as overweight or obese defined by BMI (≥ 25 kg/m^2) at baseline. A variety of anthropometric measures were also reported across the studies, with body mass reported in all studies, and BMI and body composition (body fat percentage, fat mass, lean mass) calculated in four studies (Carroll; Kerksick; Schmitz; Silva).

Two of the five studies (Kerksick; Silva) reported greater *between group* reductions in body mass (kg) for their respective interventions. Silva et al. (2010) reported a *time x group* interaction for the intervention group compared with controls in percentage weight change at 4 and 12 months (3% and 6% mean difference, respectively) compared with baseline. Silva et al. (2010) also demonstrated a reduction in BMI (INT -2.3 ± 1.9 vs CON 0.7 ± 1.9 kg/m^2) at the end of the intervention. Similarly, the diet + exercise groups in the study of Kerksick et al. (2010) displayed greater *group x time* anthropometric (body mass) and body composition (fat mass, lean mass) changes, measured using dual-energy x-ray absorptiometry, compared with the control groups. Moreover, the intervention groups, irrespective of macronutrient distribution (with the exception of the high-carbohydrate diet), showed *within-group* differences from baseline for waist circumference, body mass, lean mass, fat mass and

percentage body fat. Overall, the largest weight loss at the conclusion of their 14-week intervention was reported by participants in the very-low carbohydrate, high-protein diet + exercise group (-5.0 ± 4.2 vs CON 0.5 ± 2.9 kg). Conversely, three studies (Carroll; Chang; Schmitz) reported no *between-group* differences in body mass at post-intervention. In addition, participants at post-intervention in the Schmitz et al. (2007) and Carroll et al. (2007) studies reported no differences in BMI compared with controls. Two studies (Silva; Schmitz) reported greater reductions in percentage body fat for the intervention group (Silva: -6.9 ± 7.9% vs CON -2.5 ± 7.5%; Schmitz: -3.7 ± 1.0% vs CON -0.1 ± 1.0%) after one and two years, respectively. Silva et al. (2010) also reported greater reductions in fat mass (-5.6 ± 4.1 vs CON -1.5 ± 4.3 kg) and lean mass (-1.1 ± 1.8 vs CON -0.2 ± 1.6 kg) in their intervention group. Conversely, fat mass, lean mass, and subcutaneous abdominal fat were not different *between groups* at post-intervention in Schmitz et al. (2010), while there were gains in intra-abdominal fat in both groups but these gains were less for the intervention group (7.0 ± 5.1% vs CON 21.4 ± 5.3%).

Markers of the metabolic syndrome and other blood biochemistry

Three studies (Carroll; Chang; Kerksick) examined markers of the metabolic syndrome (Alberti et al., 2009) and, collectively, none of the markers were different *between groups* at post-intervention in all three studies. Specifically, HDL-cholesterol, triglycerides, glucose and blood pressure were unchanged in the intervention group compared with controls at three months, although both intervention and control participants showed favourable *within-group* changes for HDL-cholesterol and diastolic blood pressure at post-intervention (Carroll). Similarly, Kerksick et al. (2010) found no *group x time* differences for metabolic syndrome markers (HDL-cholesterol, triglycerides, and glucose). However, *within-group* analysis showed a reduction in fasting glucose for the high-carbohydrate, low-protein group at post-intervention. Chang et al. (2010) examined fasting glucose exclusively and found 'trends' but no significant differences between intervention and control groups at 2 and 8 months post-intervention.

In addition, two studies (Carroll; Kerksick) investigated other biochemical markers associated with increased CVD risk; specifically cholesterol and indicators of insulin resistance (IDF, 2006). Both studies reported baseline total cholesterol, but only one (Kerksick) reported post-intervention results. Kerksick et al. (2010) reported no differences

between the intervention and control groups for total cholesterol and LDL-cholesterol, or for fasting insulin and the homeostasis model assessment of insulin resistance (HOMA-IR). However, a *within-group* improvement in both insulin and HOMA-IR was observed in the very-low carbohydrate, high protein intervention group.

Fitness markers

A variety of physical activity, aerobic and strength outcome measures were investigated via questionnaires or exercise testing across the five studies. Two studies (Carroll; Kerksick) measured cardiorespiratory capacity (VO_{2max}) using a maximal treadmill walking test to volitational exhaustion, with both studies showing improvements in VO_{2max} ($ml \cdot kg^{-1} \cdot min^{-1}$) following lifestyle intervention compared with controls. One study (Schmitz) used accelerometers to objectively assess physical activity, with no differences over at least a four-day measurement period from the control group at one or two years of intervention. In contrast, self-reported physical activity was used in two studies (Chang; Silva), with participants detailing frequency, intensity and duration of physical activity over a 7 day period. Chang et al. (2010) found no *between* or *within group* differences for physical activity at 2 or 8 months post-intervention, while the intervention group of Silva et al. (2010) showed greater physical activity after the 12-months intervention.

Two studies (Kerksick; Schmitz) measured improvements in muscular strength via a one-repetition maximum (1RM) bench-press and leg-press. For both measures, Schmitz et al. (2007) reported improvements at 1 and 2 years of intervention compared to controls, while Kerksick et al. (2010) did not observe such improvements. However, Kerksick et al. (2010) did report *within group* improvements in 1RM (kg/kg) leg-press for three Exercise + Diet intervention groups, and *within group* improvements for 1RM bench-press for four Exercise + Diet groups.

Dietary outcomes

Diet composition (e.g. calories, macronutrient distribution) was assessed in three (Chang; Kerksick; Schmitz) of the five studies. Kerksick et al. (2010) was the only study to manipulate the dietary intake of participants, reporting within group reductions in caloric intake (kcal/kg/day) compared with baseline at 10 and 14 weeks. However, inadequate

dietary recording by control group participants prevented between group analyses. In contrast, Schmitz et al. (2007) found no between or within group differences at any time point for total energy intake (kcal/day) measured via a food-frequency questionnaire. Chang et al. (2010) reported increases in fruit and vegetable intake behaviour at post-intervention compared with their control group, but this difference was no longer significant at 8-month follow-up.

Psychological characteristics

A variety of psychological approaches were used across three studies (Carroll; Chang; Silva). Carroll et al. (2007) reported improvements from pre- to post-intervention on all variables of the General Well-Being (GWB) schedule compared with controls. However, no *between group* differences were observed for the 9-item Perceived Stress Scale (PSS) score or its two subscales. In contrast, at post-intervention, Chang et al. (2007) reported improvements in the PSS for the intervention group compared with controls. However, no *between-group* differences were reported for the Positive Affect and Negative Affect Scale (PANAS). In the study of Silva et al. (2007), using seven self-determination theory-based instruments to investigate psychological variables, the intervention group reported higher levels of self-determination and autonomous self-regulation after 12 months of intervention. Participants scored higher for exercise-related intrinsic motivation, autonomous self-regulation, and exercise motives.

3.5. Discussion

We aimed to systematically review the evidence in the existing literature (2004-2014) on the effectiveness of multi-disciplinary lifestyle interventions in reducing CVD risk in overweight and/or obese premenopausal women. With respect to the inclusion criteria of this review, there were only five RCT-designed studies, and there was pronounced heterogeneity in their research designs, intervention characteristics, and outcome measures. It was found that lifestyle interventions incorporating exercise, diet and/or behavioural therapy were effective in eliciting improvements in CVD risk in this population, appearing to induce modest weight loss and improve fitness and selected measures of psychological behaviour. However, four

studies had mean age of 36 to 40 years, highlighting the paucity of data for younger women below 30 years of age. Moreover, only one study reported longer term follow-up data, at 8 months after intervention completion. Thus, the effectiveness of multi-disciplinary interventions for sustaining improvements in CVD risk or behavioural change is still unclear in this population.

3.5.1. Lifestyle intervention effect on outcome measures

All interventions in this review produced improvements in at least some markers of CVD risk. The most prominent change was noted in markers of weight loss, with three (Kerksick; Schmitz; Silva) of the five studies reporting improvements in body composition (percentage body mass, fat mass, lean mass) and/or anthropometric measures (body mass, BMI) compared to controls. Similarly, lifestyle interventions had a positive effect on estimates of cardiovascular fitness, represented by increased physical activity, improved aerobic capacity and/or improved muscular strength, reported in four (Carroll; Kerksick; Schmitz; Silva) of the five studies. Moreover, two (Carroll; Chang) studies incorporating a behavioural therapy component within their lifestyle intervention group compared with controls demonstrated improved scores on psychological behaviour inventories. A moderate intervention effect was observed in dietary composition changes, with two (Chang; Kerksick) of three studies showing selective improvements in dietary outcomes. In contrast, lifestyle interventions had no influence on markers of the metabolic syndrome (Alberti et al., 2009; Alberti et al., 2005), including blood lipids, fasting glucose and blood pressure, and on other measures of blood biochemistry (insulin, HOMA-IR, total cholesterol).

3.5.2. Lifestyle intervention program evaluation

No specific type of multi-disciplinary lifestyle intervention included in this review appeared to be more successful program than others, with each displaying improvements in some CVD risk factors. Three studies (Carroll; Silva; Schmitz) had retention rates above 72%, and these studies included regular contact with participants through exercise, nutrition and/or behavioural sessions. In contrast, the lifestyle intervention delivered via the theory-based education program (Chang), reported the poorest retention rates, of 49% at post-intervention and 34% at 8-month follow-up. Chang et al. (2009) speculated that this could be due to

population characteristics and economic hardship. This lifestyle intervention also delivered the fewest improvements for CVD risk factors. For the study of Kerksick et al. (2010), the retention rate was only 65%, and we speculate that this could be due to difficulties in adhering to a dietary intervention involving caloric restriction and macronutrient modification (Wycherley, Mohr, Noakes, Clifton, & Brinkworth, 2012).

The range of body composition measures used made cross study comparisons problematic. Three studies (Kerksick; Schmitz; Silva) measured markers of body composition, including percentage body fat, fat mass and lean mass using pencil-beam scanning (Silva), dual-energy X-ray absorptiometry (Kerksick; Schmitz) and computed tomography scans (Schmitz), respectively. These techniques of body composition measurement are generally more accurate than standard anthropometric (e.g., body mass, WC, BMI) assessment. In the two studies (Carroll; Chang) not using these more sophisticated measures of body composition no changes were observed in anthropometric markers at post-intervention. With standard anthropometric measures weight loss as an outcome by itself can be confounded by the inability to discriminate between loss of fat mass and gains in lean mass, so the results from these two studies must be interpreted with caution.

All studies included the implementation of exercise/physical activity. Exercise programs were well described in two studies (Kerksick; Schmitz) for duration, exercise mode, sets and repetitions prescribed. Conversely, the description of exercise intensity in the other studies (Carrolll; Schmitz; Silva) was poor. Moreover, measures of exercise-related outcomes across the studies ranged from self-reported questionnaires (Chang; Silva) to physical tests for aerobic capacity and muscular strength testing (Carroll; Kerksick; Schmitz). Exercise delivery also appeared to influence the chances of demonstrating improved fitness and physical activity outcomes. Three (Carroll; Kerksick; Schmitz) of the five studies provided regular supervised exercise training, one study (Silva) provided a combination of group exercise classes and promotion of physical activity through theory, and one (Chang) provided education about the importance of exercise only. The latter (Chang) was the only study not to produce improvements in fitness or physical activity at post-intervention, which may imply, that contact with fitness professionals and others during the intervention phase is important for realising improvements in fitness and/or physical activity outcomes.

Four studies implemented a dietary component in their lifestyle intervention. However, Carroll et al. (2007) and Silva et al. (2010) failed to report any dietary outcomes, and Chang et al. (2010) only reported changes in fat, fruit and vegetable intake. And while Kerksick et al. (2010) controlled nutritional intake by prescribing four different dietary regimens, inadequate dietary recording by the control group prevented any between group analyses. Therefore, collectively, the heterogeneity in the dietary components among studies and the inadequate reporting of post-intervention data do not provide additional understanding of dietary behaviour for weight management in premenopausal women.

Four of the five studies incorporated a behavioural therapy component in their lifestyle intervention: two (Carroll; Silva) were guided by self-determination theory, and two (Chang; Schmitz) used the social cognitive theory framework. Only two (Carroll; Chang) of these studies measured the success of their behavioural therapy component through various psychological inventories. Without evaluation of behavioural change, it is difficult to determine if the addition of a behavioural therapy component in multi-disciplinary programs contributes to improvements in CVD risk.

3.5.3. Limitations and future directions

This review has limitations. Meta-analyses were not performed due to the lack of consistency in the reporting of data across studies, as well as the differences in intervention design characteristics. We did not include unpublished data, nor studies that were published in languages other than English, with the review limited to papers dating from 2004 onwards. Therefore, we acknowledge that there might be work that meets our inclusion criteria in the greater literature pool. Nonetheless, findings from this systematic review confirm that multi-disciplinary lifestyle interventions are associated with health benefits for overweight/obese premenopausal women.

It is recommended that future studies involving multi-disciplinary lifestyle interventions provide comprehensive descriptions of their exercise programs, and evaluate fitness and physical activity outcomes with objective testing measures. Furthermore, there is a need to include more comprehensive assessments of cardiac and vascular effects as a result of intervention. The non-invasive use of echocardiography and ultrasonography techniques have shown promise as sensitive early detection markers of CVD, particularly in young adult

women (Peterson, Waggoner, et al., 2004). Moreover, these techniques may provide insight into mechanistic changes that accompany weight loss and increased fitness. Studies that conduct a lifestyle intervention on a mixed-sex population should discriminate their results to enable sex-specific comparisons.

3.5.4. Conclusions

While the evidence is limited to only five studies, the data suggest promising trends for multi-disciplinary lifestyle interventions which incorporate exercise, diet and/or behavioural therapy to improve the CVD risk profile of overweight/obese premenopausal women. However, these data are distinctly lacking with respect to young adult women (< 30 years of age). The internal validity of these and future data would be improved with more explicit and detailed reporting of research designs and outcome measures. Similarly, external validity could be improved with greater homogeneity among study designs and the reporting of data from longer-term follow-up. The inclusion of more advanced techniques of metabolic, cardiac and vascular assessment is also suggested for earlier identification of, or greater sensitivity to change in, CVD risk.

Chapter 4. Extended Methods

The methods used in this thesis are described in full or in part in subsequent experimental chapters. Therefore, this chapter is included to detail methodological procedures not comprehensively described within the experimental chapters. Some methods were germane to all studies. The same researcher (i.e. the author of this thesis) performed all aspects of the methods, here and in the experimental chapters, unless otherwise stated.

4.1. Ethical Approval

The study and its protocols were approved by the Australian Catholic University Human Research Ethics Committee (V2009 91; Appendix 2). Additionally, the study was registered with the Australian New Zealand Clinical Trials Registry [ANZCTR] (Identifier: ACTRN12612001017819; Appendix 3). Written informed consent was obtained from all participants prior to testing (Appendix 4 & 5).

4.2. Research Design

The Young Women's Heart Health Study was an efficacy trial, with all experimental procedures and data collection conducted on campus at the Australian Catholic University, Melbourne, Australia. Two separate components: (i) the cross-sectional studies and (ii) the lifestyle intervention (Figure 4.1), were completed between August 2010 and February 2012.

In the cross-sectional studies, women with abdominal obesity (WC $\geq$ 80cm) were compared with an aged-matched, non-obese (WC < 80cm) control group (Figure 4.2; Chapters 5 and 6). Women participating in the cross-sectional studies who presented with abdominal obesity (WC $\geq$ 80cm) were invited to participate in a 12-week randomised controlled lifestyle intervention trial, which incorporated an experimental intervention group and a wait-list control group. The study design ensured all women had access to the intervention.

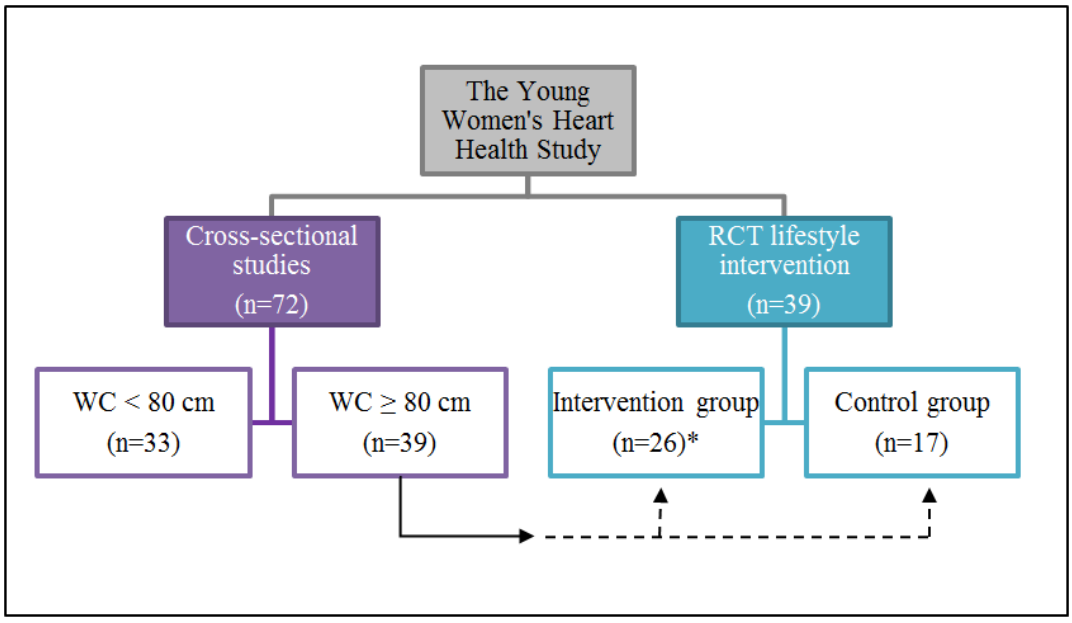

Figure 4.1. Study design for the Young Women's Heart Health Study conducted between August 2010 and February 2012, incorporating a cross-sectional and lifestyle intervention component. *four participants from the wait-list control group continued into the intervention phase.

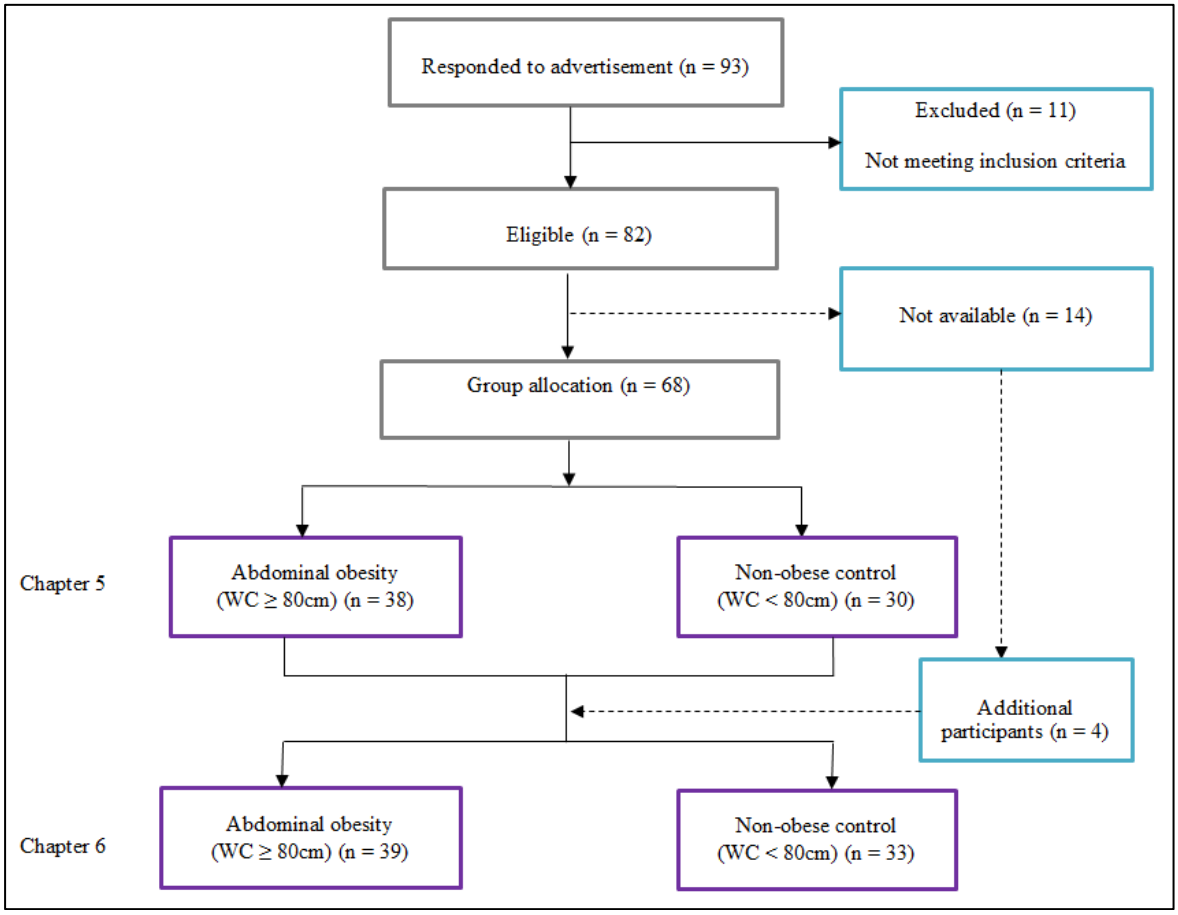

Figure 4.2. Participation of individuals in the cross-sectional studies of the Young Women's Heart Health Study.

4.3. Participants

Women were recruited to participate in the University-based Young Women's Heart Health Study by local advertisement (Appendix 7) and internal email service. The following inclusion and exclusion criteria applied: All participants were Caucasian females, aged between 18 to 30 years, and fluent in spoken and written English. Ethnicity-related differences in cardiovascular risk limited recruitment to Caucasian (Ajjan, Carter, Somani, Kain, & Grant, 2007). Participants were excluded from the study if they were current smokers, pregnant or lactating, taking medication treatment for lipid abnormalities, diagnosed with cardiovascular or respiratory conditions that might limit participation in exercise, had a pre-existing physical or medical condition (liver or kidney disease, heart arrhythmia, insulin dependent diabetes mellitus, gestational diabetes, polycystic ovarian syndrome, or thyroid

abnormalities), or previous bariatric surgery. Women also completed a cardiovascular risk assessment (Appendix 6). Women who responded to the advertisement had their eligibility confirmed by attending a short consultation with the researcher before inclusion was permitted.

4.4. Lifestyle Intervention

4.4.1. Participants

In addition to the previously listed set of inclusion criteria, eligibility for the lifestyle intervention was based on abdominal obesity, defined using the IDF definition [(Alberti et al., 2005); the current definition at the time of initial recruitment] as a raised waist circumference ≥ 80cm, and leading a sedentary lifestyle according to the then guidelines for physical activity (Department of Health and Ageing, 1999). All participants were willing and able to increase daily physical activity. A detailed CONSORT flow diagram of participants in the lifestyle intervention is presented in Chapters 7 and 8.

4.4.2. Sample size power

A power analysis was performed to determine the appropriate sample size. Estimates were based on a moderate within-subject effect size for the primary outcome criterion of waist circumference. With approximately 18 women per group and by offering the control group access to the intervention, this number per group was predicted to provide the appropriate statistical power to detect a large within-subject difference of 1.0 standard deviation in the major variable between baseline and post-intervention (ß = 80%, statistically significant at an alpha level of $P < 0.05$), assuming equal variances within groups. Allowing for 20% attrition (drop-out), it was calculated that 44 women (22 in each group) were required to retain statistical power (Peat, 2001).

4.4.3. Study design

A 12-week multi-disciplinary lifestyle intervention was comprised of three components: (1) moderate-intensity physical activity (Table 4.1); (2) non-dieting nutrition education (i.e. strategies of everyday choices for nutritional balance rather than restrictive eating regimes); and (3) weekly (60 min) small-group cognitive behavioural therapy (CBT) sessions entitled "Mission Possible". In contrast, participants in the wait-list control group were requested to continue existing lifestyle choices, and after 12 (control) weeks were invited to complete the lifestyle intervention. The multi-disciplinary lifestyle intervention is described in detail in Chapters 7 and 8.

Sustainability component

The lifestyle intervention incorporated a sustainability component, in which all participants had outcome measures tested at 12 weeks *after* the conclusion of the lifestyle intervention; that is, 24 weeks from pre-intervention measures. During this phase, participants did not attend structured sessions, and despite minimal contact with the research team, were encouraged to maintain their new lifestyle habits. Each participant received a fortnightly follow-up newsletter from the researcher, via email, until the time of re-testing at 24 weeks. The newsletter contained lifestyle and healthy living tips. Participants were also provided with a booklet containing the activities they had completed during the exercise component of the lifestyle intervention.

Table 4.1. Outline of the training program for the physical activity component of the 12-week multi-disciplinary lifestyle intervention.

Week	Circuit Training			Interval training		
	Aerobic activity	**Strength/resistance activity**	**RPE**	**Time (mins)**	**Interval**	**RPE**
1*	Cycling, rowing, step-ups	Bicep curls, squats, chest press, triceps extensions, push-ups, calf-raises, lunges	5-7	30	1 min on: 4 mins off	5
2	Cycling, rowing, step-ups	Squats, triceps dips, lunges, calf-raises, push-ups	5-7	30	1 min on: 4 mins off	5
3	Boxing, skipping, step-ups	Squats, push-ups, lunges, triceps dips, box jumps	5-7	30	1 min on: 4 mins off	5
4*	Boxing, skipping, step-ups	Squats, push-ups, calf-raises, lunges, triceps dips, single-leg (SL) dead lift	6-8	35	2 mins on: 3 mins off	6
5	Cycling, running, step-ups	Triceps pull down, lunges, upright row, squats, bicep curls, push-ups, sprints	6-8	35	2 mins on: 3 mins off	6
6	Cycling, running, step-ups	Squats, push-ups, calf-raises, lunges, triceps dips, SL dead lift	6-8	35	2 mins on: 3 mins off	6
7*	Interval cycling	Squats, push-ups, lunges, triceps dips	7-9	40	3 mins on: 2 mins off	7
8	Interval cycling	Squats, lunges, triceps dips, SL dead lift, box jumps, push-ups, SL hopping	7-9	40	3 mins on: 2 mins off	7
9	Stair climbing	Squats, push-ups, lunges, triceps dips, calf raises, SL dead lift	7-9	40	3 mins on: 2 mins off	7
10*	Stair climbing	Calf-raises, push-ups, squats, triceps dips, lunges, bridging, SL dead lift	8-10	45	4 mins on: 1 min off	8
11	Cycling, boxing, step-ups	Push-ups, bridging, lunges, biceps curls, upright row, triceps pull down, squats	8-10	45	4 mins on: 1 min off	8
12	Cycling, boxing, step-ups	Box jumps, lunges, triceps dips, squats, push-ups, bridging, calf raises, SL dead lift	8-10	45	4 mins on: 1 min off	8

RPE, ratings of perceived exertion (Robertson, 2004).

Footnotes: Format for circuit training included alternating between aerobic (2-8 minutes in duration per activity) and strength activities (1-4 minutes in duration per activity); plus alternating between upper and lower body strength activities. Interval session pace was personal choice of brisk walking, jogging or running. OMNI picture scale was used for RPE (Robertson, 2004; Appendix 18). Sessions were conducted either in a gym or at the local park.*Bruce fitness test (Bruce, Kusumi, & Hosmer, 1973) and 5 repetition maximum (Abadie & Wentworth, 2000) were conducted every 3 weeks (i) as an anchoring procedure for RPE and (ii) to direct progressive exercise prescription. **Warm-up:** Each session began with gentle physical activity (OMNI-scale RPE 4) that elevated body temperature (e.g. walking or jogging): weeks 1-3 (5 min) and weeks 4-12 (10 min). **Core strength**: Each session included three core/abdominal activities (e.g. crunches, plank, oblique) after the completion of the circuit training. **Cool-down:** Each session concluded with 5 min of static stretching of each major muscle group, including hamstrings, quads, hip flexors, adductors, calves, back, shoulders and trunk.

4.4.4. Data collection

For participants allocated to the intervention group, testing was performed at pre-intervention (0 weeks), post-intervention (12 weeks), and again at sustainability (24 weeks post-intervention) (Figures 4.3). For participants allocated to the wait-list control group, testing was performed at pre-control (0 weeks) and at post-control (12 weeks). Participants in this group were then provided the opportunity to continue into the intervention phase of the study. All measurements were taken at the same time of day (±2 hr) and by the same researcher.

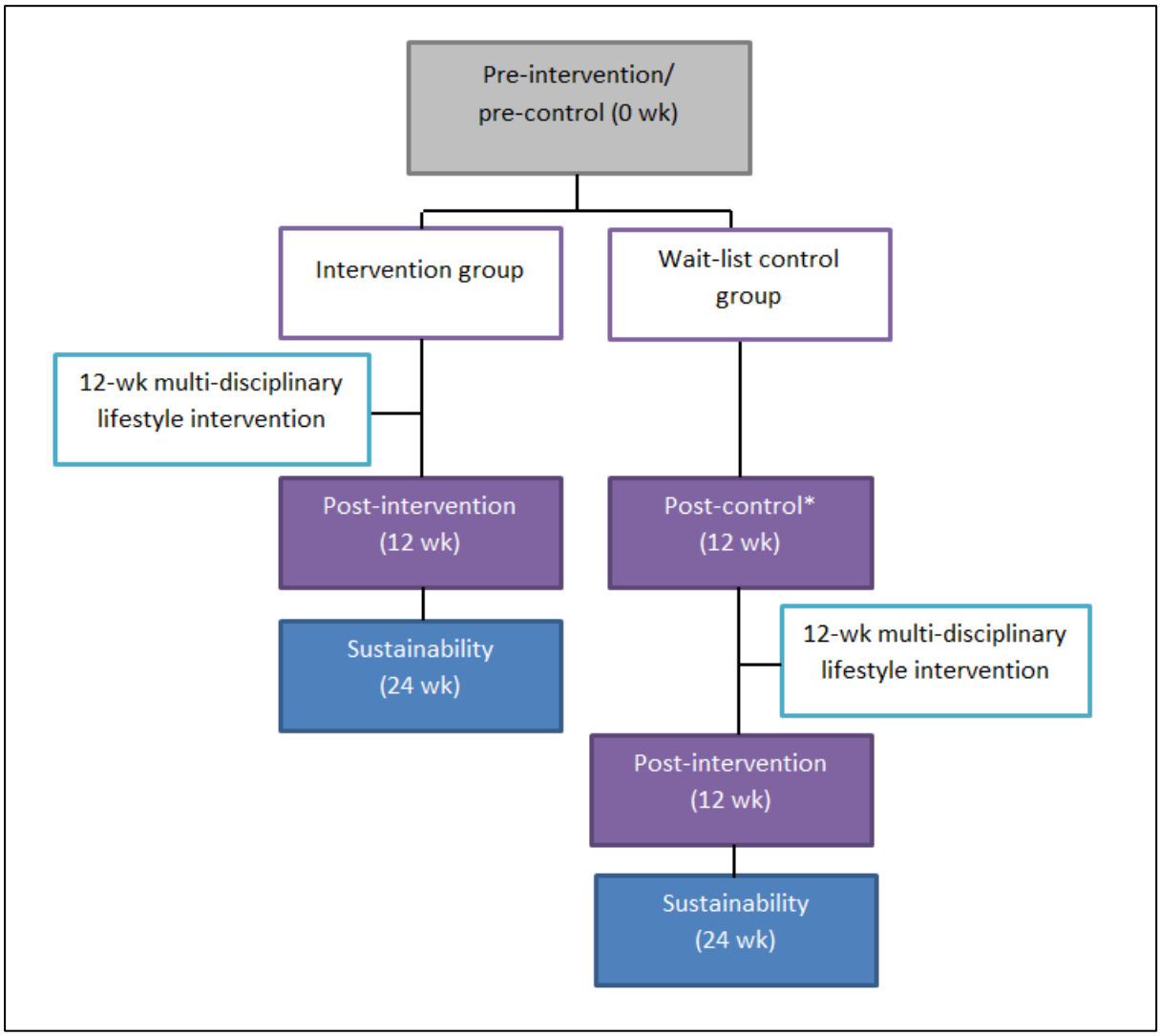

Figure 4.3. Data collection design for intervention and wait-list control groups showing each time point and the 12-week multi-disciplinary lifestyle intervention.
*Also used as pre-intervention data for participants who continued into the intervention phase (n=4).

4.5. Outcome Measures

Each data collection time point for the cross-sectional and intervention studies comprised two laboratory testing sessions, separated by 7 days. On each occasion, participants were requested to refrain from strenuous physical activity in the 24 hours prior to testing. For the first of the two laboratory sessions at each time point, participants were also required to fast from all food and beverages including vitamins, minerals and medications for a minimum period of 12 hours (overnight). This laboratory session lasted 75 min and involved anthropometric, blood, and vascular ultrasound measures. The second laboratory session only required participants to abstain from caffeine and alcohol in the preceding 12 hours and lasted 60 min for fitness, echocardiography and survey measures (Figure 4.4). Menstrual cycle phase was recorded on the initial day of testing to ensure that re-testing occurred during the same phase at subsequent sessions. The same request applied to both the cross-sectional and intervention studies. Environmental conditions within the laboratory were maintained at 20-23°C and 40-60% humidity. Outcome measures collected during each of the two laboratory visits are presented in Table 4.2.

Table 4.2. Outcome measures collected at each data collection time point.

Laboratory session ONE	
Category	**Outcome measure**
Anthropometry measures	Body mass; stature; WC; hip circumference
Metabolic syndrome markers	Fasting glucose; HDL-cholesterol; triglycerides; BP
Additional blood biochemistry	Total cholesterol; insulin; hs-CRP
Vascular ultrasonography	Carotid IMT
Laboratory session TWO	
Fitness assessment	Estimated aerobic capacity
Echocardiography	Morphology, function, deformation, mechanics
Survey documents	Custom survey; psychological inventories; food recall

WC, waist circumference; HDL, high-density lipoprotein; BP, blood pressure; hs-CRP, high sensitivity C-reactive protein; IMT, intima-media thickness

LABORATORY SESSION ONE

PREPARATION	ASSESSMENT					EXPLANATION
	8:00	8:15	8:25	8:35	8:40	9:15
Fasted Consent form	Blood collection (10 ml)	Anthropometric measures (body mass, height, girths)	Seated	Blood pressure Resting HR	Vascular ultrasound	Take-home survey Food recall

LABORATORY SESSION TWO

PREPARATION	ASSESSMENT					EXPLANATION
	8:00	8:05	8:15	8:20	8:40	9:00
No caffeine CV risk form	Anthropometric measures (body mass, waist circumference)	Seated	Blood pressure Resting HR	Echocardiography ultrasound	Fitness evaluation	Training diary

Figure 4.4. Outline of the experimental procedure for laboratory session one and two.

In this study, WC was used to define abdominal obesity (i.e. WC ≥ 80cm) and acted as the primary measure to calculate sample power. WC was measured to the nearest 0.1 cm in the horizontal plane at the level of the midpoint between the iliac crest and lower costal margin (Alberti et al., 2009) using a non-elastic measuring tape, with the average of two measures reported. Consequently, to ensure that the measurement technique for WC assessment was reliable, intra-rater reliability analysis was conducted on a sample of 20 participants (see section 4.5.3 for calculations used for reliability measures). WC was evaluated twice by the same observer (i.e. author of this thesis) and reliability was determined to be: coefficient of variation (CV), 1.3%; intra-class coefficient [ICC (3, 1)], 0.98; limits of agreement (LOA), -4.4 to 3.0; and measurement error (ME), ± 2.6 cm.

Detailed explanations of the data collection procedures for anthropometric measures, metabolic syndrome markers, additional biochemical, and fitness assessments are presented in Chapter 5 and 7. Details of the procedures for vascular ultrasonography and echocardiography are briefly discussed in Chapters 6 and 8, with a comprehensive explanation of these techniques, and of the survey documents, presented below.

4.5.1. Vascular ultrasonography

As an assessment of CVD risk, the carotid artery wall can be examined to identify areas of increased thickness and plaque, and is used as an early marker of atherosclerosis (Bots, 2006; Stein et al., 2008). Specifically, the assessment of carotid arterial intima-media thickness (c-IMT) is used as a non-invasive measure to gauge progression and regression of vascular pathology (Hodis et al., 1998). Examination of the right common carotid artery was performed with B-mode ultrasonography using standard ultrasound equipment (Vivid-i, GE Healthcare, Horten, Norway) in a dark, temperature-controlled room, after participants had rested quietly for 10 minutes in the supine position. All scans were performed according to a pre-determined standardised scanning protocol (Jarvisalo et al., 2002). The right common carotid artery was scanned longitudinally, 2cm proximal to the bulb (carotid bifurcation), using a high-resolution 12 MHz linear-array probe (Figure 4.5). All scans were digitally stored for subsequent off-line analyses (EchoPAC v108.1.5, GE Medical Systems, Horton, Norway). Images were analysed at the end-diastolic frame (captured adjacent to the R-wave on continually recorded echocardiogram), performed on the far (posterior) wall of the right

common carotid artery. Semi-automated, edge-detection, wall-tracking software was used to determine mean c-IMT, which is measured from the leading edge of the lumen-intima interface and the leading edge of the media-adventia interface (Chodakauskas, 2006). All reported measurements were averaged from three frames.

All ultrasound data collection and analyses were performed by the same experienced operator, with intra-rater reliability analysis conducted for mean c-IMT on a sample of 20 participants (see section 4.5.3 for calculations used for reliability measures). A scan of the right common carotid artery was evaluated twice, using off-line software analyses, by the same operator (author of this thesis). Reliability for mean c-IMT was determined to be: CV, 2.3%; ICC (3, 1), 0.81; LOA, -0.03 to 0.03; and ME ± 0.02 mm. This reliability is consistent with previous research, with a CV of 3.9% (n=22) established for mean c-IMT (Järvisalo et al., 2004).

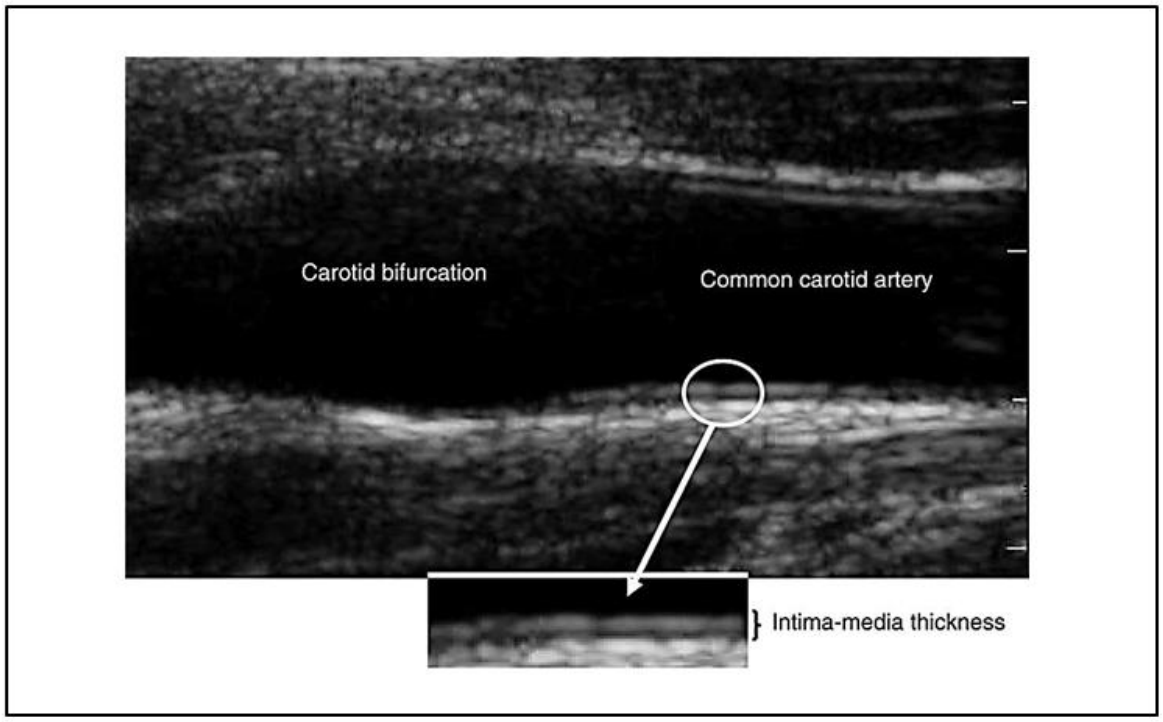

Figure 4.5. Image of the common carotid artery, illustrating the carotid bifurcation and intima-media thickness (c-IMT) of the far wall (Image sourced from: Wald et al., 2009, p.156).

4.5.2. Echocardiography

Echocardiography is a popular, non-invasive technique for obtaining markers of cardiac structure and function, including quantitative measures of cardiac chamber size, wall thickness, blood flow, and wall motion velocities (Sahn, DeMaria, Kisslo, & Weyman, 1978). Standard two-dimentional (2D) transthoracic echocardiographic examinations were conducted in accordance with American Society of Echocardiography standards (R. M. Lang et al., 2005). All image acquisition and subsequent off-line analyses (EchoPAC, GE Medical Systems ; Appendix 22) were performed by the same experienced operator using standard ultrasound equipment (Vivid-i, GE Healthcare, Horten, Norway)

Conventional echocardiography

Motion-mode (M-Mode) measurements were obtained in the parasternal long-axis view (Figure 4.6). Left atrial (LA) and LV dimensions and wall thickness were assessed at both end-diastole and end-systole. LV mass was calculated by the Penn-Cube method (Devereux et al., 1984) and indexed for height (Cornell adjustment). LV ejection fraction was quantified by the Simpson's bi-plane method, with systolic dysfunction diagnosed if the ejection fraction was less than 50% (Nagueh et al., 2009).

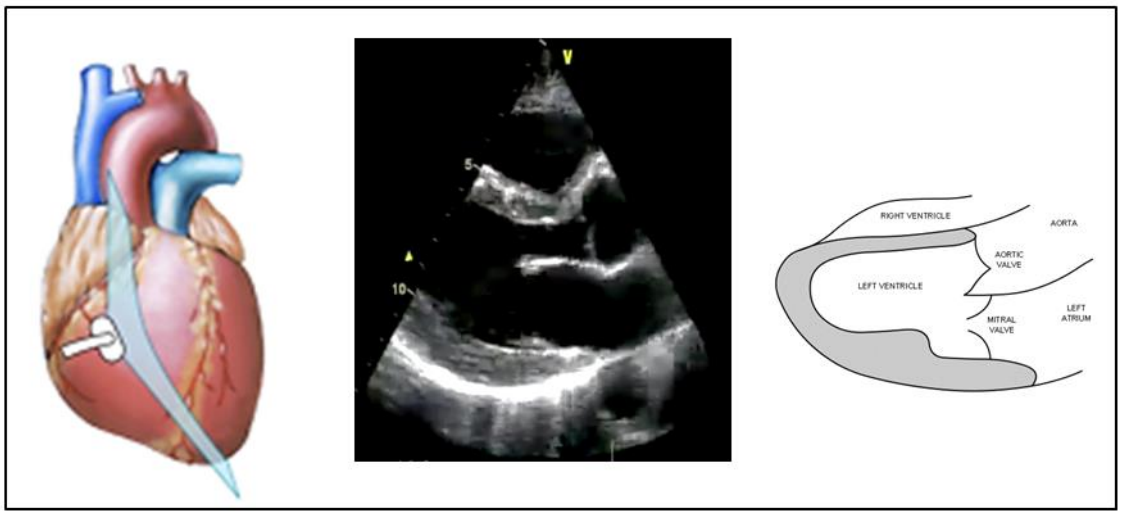

Figure 4.6. Parasternal long-axis view of the heart, showing (i) the probe and scanning view, (ii) 2D ultrasound image, and (iii) schematic representation of the view.
(Image sourced from: http://www.123sonography.com).

Pulsed-Doppler LV transmitral flow velocity for early-diastolic (E) and late-diastolic (A) waves was performed in the apical four-chamber view (Figure 4.7). Isovolumetric relaxation time (IVRT), and aortic ejection velocity were measured by pulsed-Doppler in the apical five-chamber view (Figure 4.8).

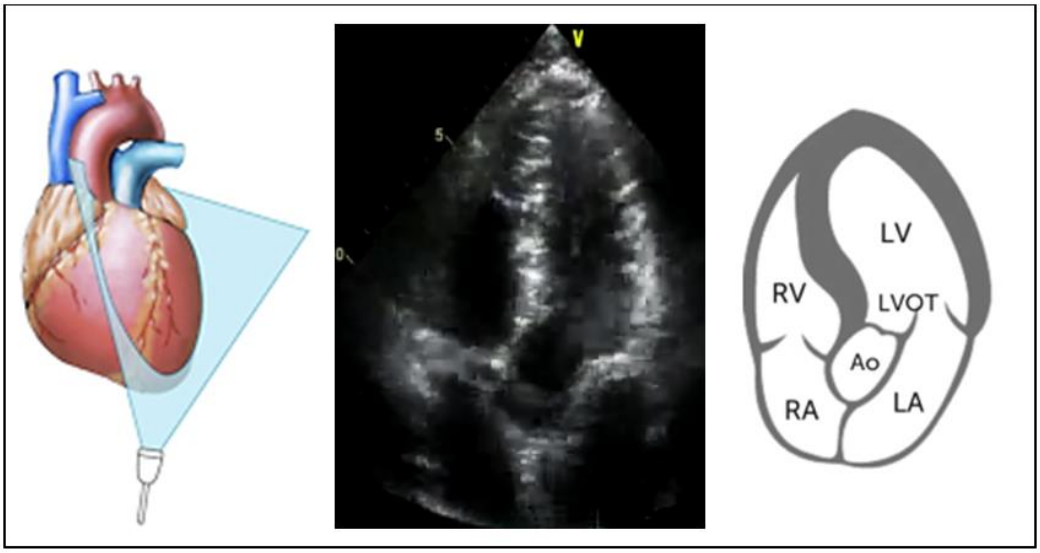

Figure 4.7. Apical four-chamber view of the heart, showing (i) the probe and scanning view, (ii) 2D ultrasound image, and (iii) schematic representation of the view. LA, left atrium; MV, mitral valve; LV, left ventricle; RA, right atrium; TV, tricuspid valve; RV, right ventricle.
(Image sourced from: http://www.123sonography.com).

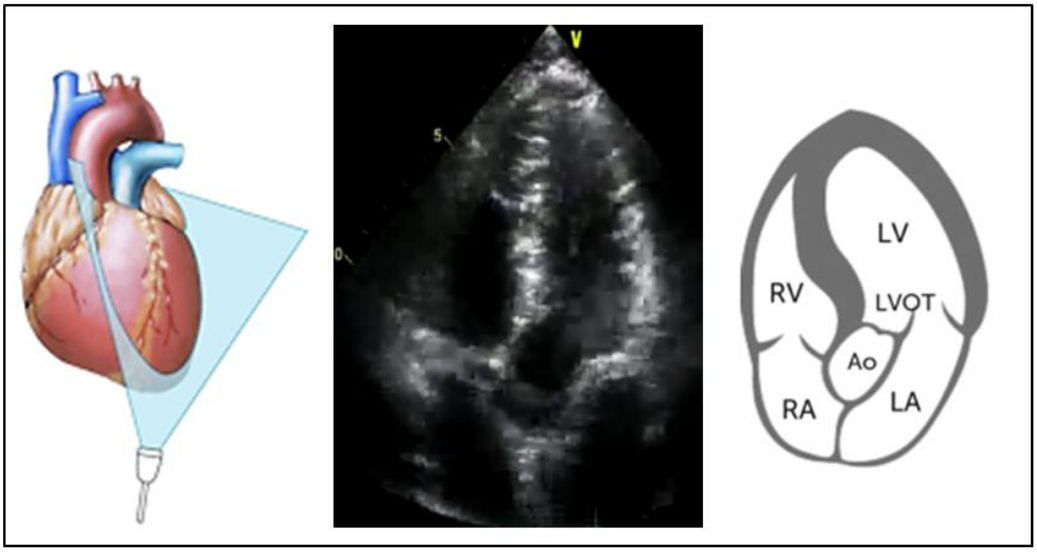

Figure 4.8. Apical five-chamber view of the heart, showing (i) the probe and scanning view, (ii) 2D ultrasound image, and (iii) schematic representation of the view. LA, left atrium; LVOT, left ventricular outflow tract ; LV, left ventricle; AO, aorta; RA, right atrium; RV, right ventricle. (Image sourced from: http://www.123sonography.com).

Pulsed tissue Doppler imaging (TDI)

Pulsed-TDI was used to assess myocardial wall motion velocities at the mitral annulus of the LV, in the apical four-chamber (septal and lateral walls) and apical two-chamber (inferior and anterior walls) views (Figure 4.9). Systolic (S_m), early diastolic (E_m) and late-diastolic (A_m) velocity was calculated at each site.

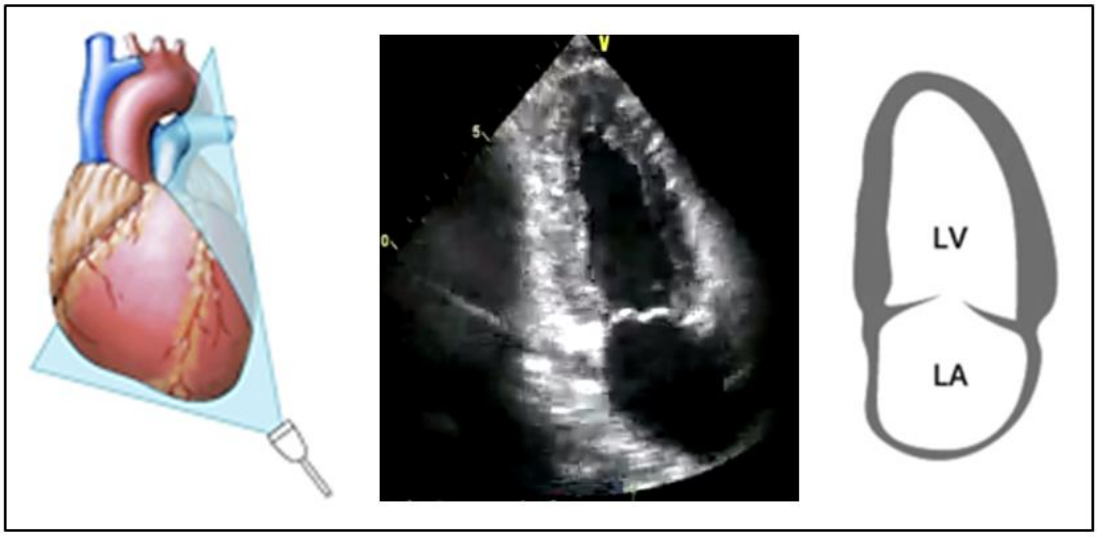

Figure 4.9. Apical two-chamber view of the heart. showing (i) the probe and scanning view, (ii) 2D ultrasound image, and (iii) schematic representation of the view. LA, left atrium; LV, left ventricle. (Image sourced from: http://www.123sonography.com).

Several estimates of diastolic function were subsequently calculated using diastolic velocities from transmitral flow and TDI, and measurements from IVRT. These measurements included: (i) the E/E_m ratio, recorded at the lateral wall of the mitral annulus, used as an index of LV filling pressure: (ii) the *E/A* ratio, indicative of LV diastolic filling efficiency; and (iii) E-wave deceleration time (DT), representative of myocardial relaxation capacity. LV diastolic dysfunction was graded according to well-documented criteria (Nagueh et al., 2009) using indices of diastolic function (Figure 4.10).

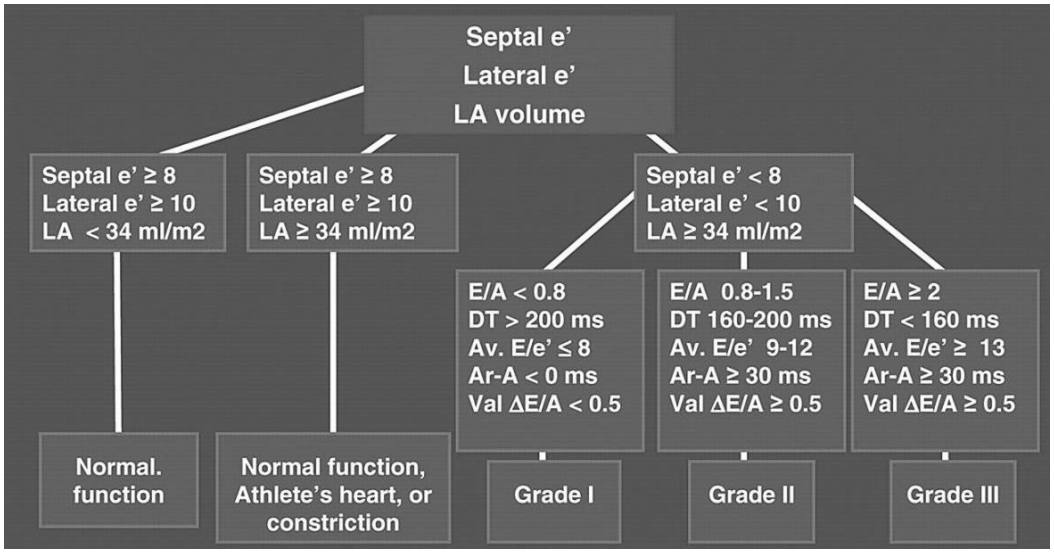

Figure 4.10. Grading scheme for LV diastolic dysfunction. Av, average; LA, left atrium; Val, Valsalva; DT, deceleration time; e`, early diastolic (referred to as Em in this thesis); E, early diastolic; A, late diastolic; Ar, pulmonary venous flow reversal
(Figure sourced from: Nagueh et al., 2009, p. 188).

Speckle tracking echocardiography (STE)

STE was used to quantify myocardial wall motion for the assessment of LV systolic and diastolic function (Leitman et al., 2004). Peak myocardial tissue deformation (or strain) and its rate of deformation (strain rate or SR) were assessed in the longitudinal and circumferential axes of the LV. In addition, myocardial mechanics, including rotation, twist and twist/untwist rate, were analysed. Longitudinal LV strain and SR were obtained from 2D harmonic grey scale images in the apical four-chamber view. Radial and circumferential strain and SR analysis was obtained from the parasternal short-axis view, at apical, mid, and basal levels of the LV (Marwick et al., 2009) (Figure 4.11). Data were recorded for subsequent offline analyses.

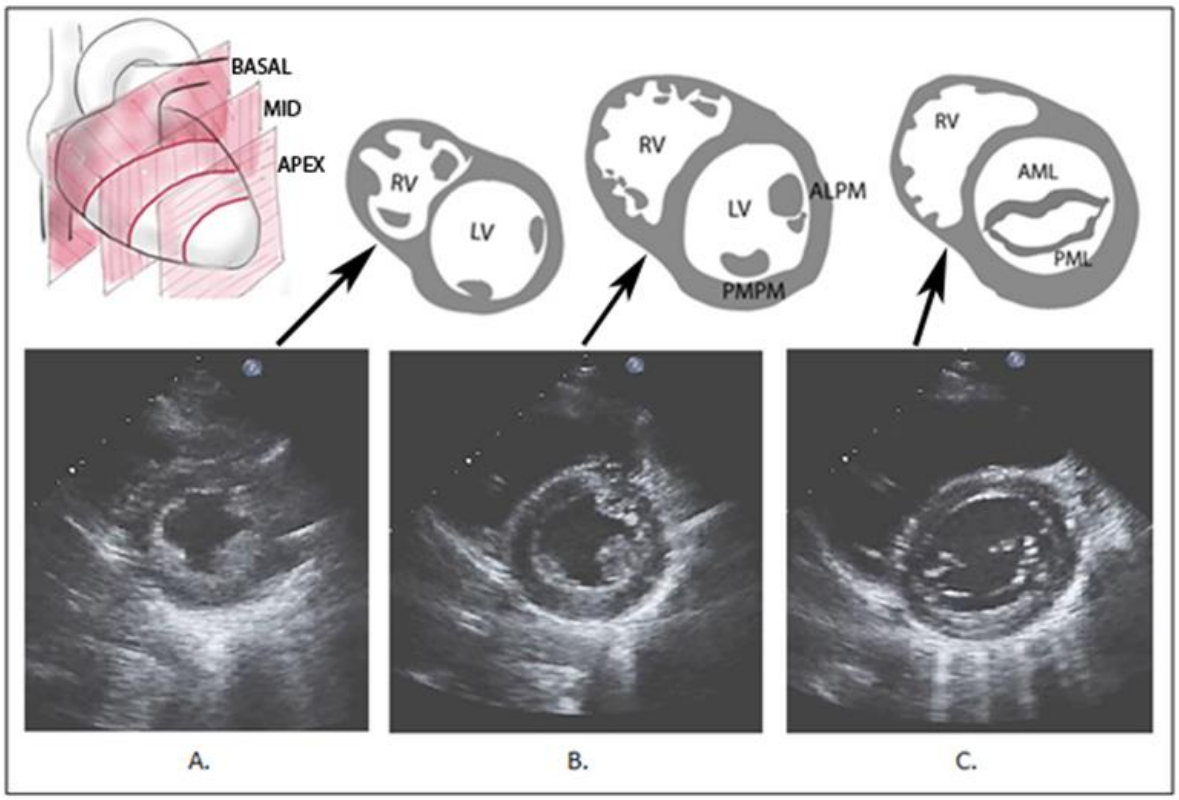

Figure 4.11. Parasternal short-axis view of the heart at the: **A.** apex, **B.** mid (papillary muscle), and **C.** base (mitral valve) level of the LV. RV, right ventricle, LV; left ventricle; PMPM, posteromedial papillary muscle; ALPM, anterolateral papillary muscle; AML, anterior mitral leaflet; PML, posterior mitral leaflet *(Image sourced from: echocardiographer.org/TTE).*

For STE measures, following manual endocardial border tracing (Marwick et al., 2009), proprietary software (EchoPAC v108.1.5, GE Medical Systems, Horton, Norway) automatically tracked myocardial motion (Figure 4.12). Subsequently, LV Lagrangian strain and SR, and their time to peak values, were obtained from six anatomical segments (i.e. anterior, antero-septal, inferior, lateral, posterior, septal). LV rotation was assessed from basal and apical short axis views, with care taken to ensure that the basal short-axis plane contained the mitral valve, and the apical short-axis plane was acquired distally to the papillary muscle. LV twist was calculated as the maximal apical LV rotation, minus the maximal basal LV rotation (Helle-Valle et al., 2005). Only cine-loops with adequate frame rate (≥ 70 Hz), as well as endocardial border definition and good image tracking as determined by the proprietary software, were used (Leitman et al., 2004); Marwick et al., 2009).

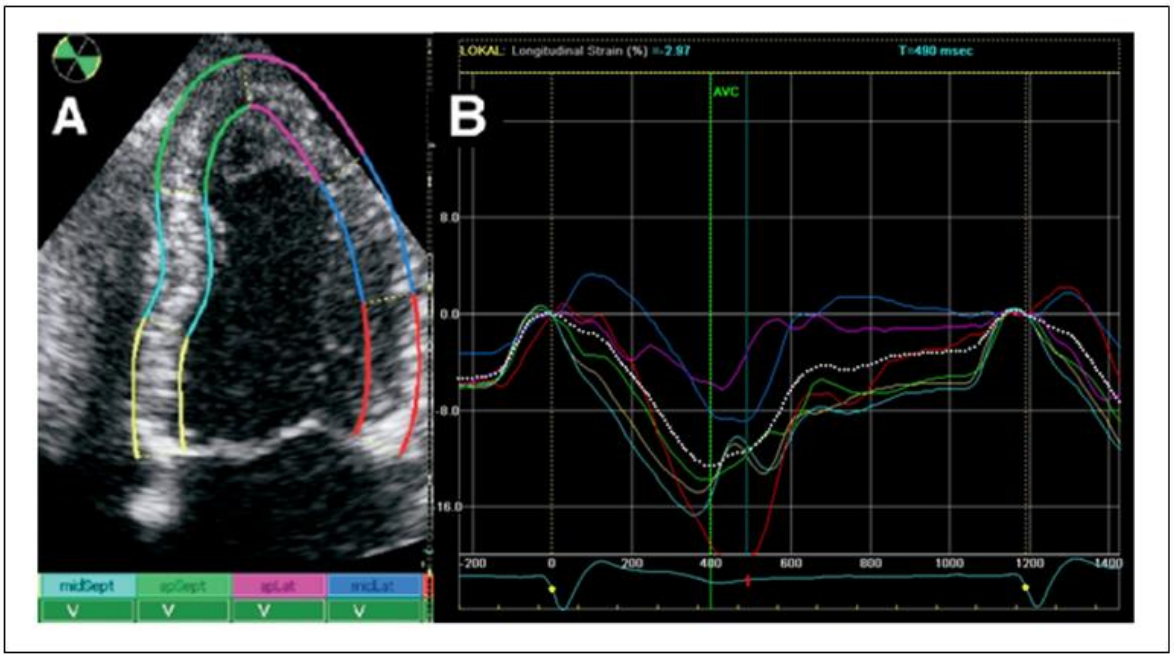

Figure 4.12. Example of the processing and presentation of LV longitudinal strain generated from proprietary software. A. Tracking quality approval screen; segments with adequate tracking are assigned a green V mark. B. Strain profile from the apical four-chamber view.
(Image adapted from: Marwick et al., 2009, p. 82).

4.5.3. Reliability analyses for echocardiography

For this study, the same experienced operator performed all ultrasonography scans and relevant off-line analyses, using the same equipment and settings for each participant. The relative disadvantage of ultrasonography is that it is difficult to perform, requiring a skilled sonographer and an appropriate training period (Raitakari & Celermajer, 2000). A measure is considered *reliable* if it produces the same result under a number of possible situations (Peat & Barton, 2005). *Intra*-rater reliability describes the agreement between measures performed by the same rater on the same data on different occasions (test-retest), while *inter*-rater reliability is the agreement between measurements performed on the same data by different raters. In order to demonstrate that the off-line echocardiographic analyses were reproducible, intra- and inter-rater reliability testing was conducted for this study. For major conventional and TDI echocardiography variables, 10 participant scans were randomly selected for analysis, and for selected STE variables, 20 participant scans were randomly selected for analysis. Each variable was analysed twice by the same observer separated by at least two

days (O1 and O2), and once by another experienced observer (O3) blinded to previous results. The following data set comparisons were performed: O1 vs. O2, and O1 vs. O3. In this study, O1 and O2 represented the author of this thesis, while O3 represented an operator experienced in all measures listed in Table 4.3. Four measures of reliability were calculated for the echocardiography variables (Table 4.3), and these were:

Coefficient of variation (CV)

The mean ($\bar{x}$) and standard deviation (SD) of two data points were calculated and CVs established (below). A CV less than 10% is generally accepted to represent 'good' reliability (Atkinson & Nevill, 1998). Intra- and inter-observer CVs are shown in Table 3.

$$CV\% = \left(\frac{\mathrm{SD}}{\bar{x}}\right) \times 100$$

Intra-class correlation coefficient (ICC)

To calculate ICCs, a two-way, mixed effect (repeated) model ICC (3, 1) was computed in SPSS. The ICC reflects the degree of correspondence and agreement among ratings, with an ICC of 1.00 indicating perfect agreement and minimal variation within measures of interest. Generally, an ICC ≥ 0.75 is indicative of good reliability, whilst an ICC < 0.75 describes moderate to poor reliability (Portney & Watkins, 2008).

Limits of agreement (LOA)

Upper and lower LOA were calculated from the Bland and Altman method (below), to provide a range in which 95% of the differences lie (Bland & Altman, 1999).

$$LOA = \text{mean difference} \pm (1.96 \times \text{SD})$$

Measurement error (ME)

ME represents the deviation of the outcome of a measurement from the true value. ME was calculated (below) and subsequently converted to an error range (±) by multiplying by the critical value, 1.96 (Peat & Barton, 2005).

$$ME = \left(\frac{\text{SD of difference}}{\sqrt{2}}\right) \times 1.96$$

Table 4.3. Intra- and inter-rater reliability analyses for echocardiographic parameters.

	Intra-rater				Inter-rater			
	CV (%)	**ICC**	**LOA**	**ME**	**CV (%)**	**ICC**	**LOA**	**ME**
Conventional & TDI echocardiography (n=10)								
Morphology								
LV mass	2.66	0.96	-6.75 to 5.98	± 8.04 g	2.12	0.97	-13.2 to 14.1	± 9.67 g
LVED diameter	1.11	0.98	-0.13 to 0.21	± 1.19 mm	1.98	0.93	-0.09 to 0.34	± 5.21 mm
IVS thickness	3.20	0.91	-0.07 to 0.14	± 0.76 mm	4.85	0.46	-0.13 to 0.26	± 1.40 mm
LVPW thickness	2.35	0.85	-0.12 to 0.12	± 0.86 mm	3.55	0.69	-0.05 to 0.15	± 0.72 mm
Function								
E Velocity	1.95	0.96	-0.09 to 0.22	± 4.8 $cm \cdot s^{-1}$	1.60	0.98	-0.04 to 0.06	± 3.5 $cm \cdot s^{-1}$
A velocity	2.53	0.99	-0.040 to 0.05	± 3.0 $cm \cdot s^{-1}$	1.85	0.99	-0.03 to 0.04	± 2.6 $cm \cdot s^{-1}$
E/A Ratio	2.51	0.97	-0.16 to 0.20	± 0.13	1.97	0.98	-0.12 to 0.16	± 0.10
Septal S_m velocity	1.41	0.68	-0.01 to 0.01	± 0.70 $cm \cdot s^{-1}$	2.35	0.74	-0.09 to 0.10	± 0.70 $cm \cdot s^{-1}$
Septal E_m velocity	2.21	0.83	-0.01 to 0.02	± 0.10 $cm \cdot s^{-1}$	4.03	0.56	-0.01 to 0.02	± 1.20 $cm \cdot s^{-1}$
Septal A_m velocity	1.47	0.74	-0.01 to 0.01	± 0.80 $cm \cdot s^{-1}$	4.18	0.68	-0.01 to 0.01	± 0.80 $cm \cdot s^{-1}$
Speckle tracking echocardiography (n=20)								
Myocardial deformation								
LV L strain	5.87	0.86	-2.78 to 3.65	± 2.27 %	5.09	0.90	-2.47 to 5.34	± 1.18 %
LV L diastolic SR	4.33	0.96	-0.21 to 0.16	± 0.13 $S \cdot s^{-1}$	7.83	0.94	-0.02 to 0.36	± 0.11 $S \cdot s^{-1}$
LV L systolic SR	4.10	0.89	-0.09 to 0.14	± 0.08 $S \cdot s^{-1}$	5.48	0.70	-0.09 to 0.26	± 0.08 $S \cdot s^{-1}$
LV C strain	4.67	0.91	-3.42 to 2.97	± 2.26 %	5.51	0.99	-0.56 to 2.02	± 0.55 %
LV C diastolic SR	5.73	0.95	-0.30 to 0.35	± 2.23 $S \cdot s^{-1}$	8.30	0.47	-0.05 to 0.45	± 1.00 $S \cdot s^{-1}$
LV C systolic SR	5.78	0.79	-1.10 to 1.01	± 0.74 $S \cdot s^{-1}$	5.38	0.67	-0.12 to 0.31	± 0.92 $S \cdot s^{-1}$
Myocardial mechanics								
Apical rotation	7.08	0.92	-1.12 to 0.92	± 0.72 º	11.52	0.88	-0.18 to 1.7	± 0.34 º
Basal rotation	6.56	0.97	-1.25 to 0.64	± 0.67 º	9.73	0.95	-0.68 to 2.02	± 0.49 º
LV twist	7.95	0.97	-1.35 to 1.97	± 1.18 º	10.04	0.98	-1.24 to 2.73	± 0.84 º
LV twist/untwist rate	9.20	0.82	-21.72 to 27.19	± 8.82 º·s^{-1}	11.75	0.68	-20.94 to 31.63	± 12.36 º·s^{-1}

CV, coefficient of variation; ICC, intra-class correlation coefficient; LOA, limits of agreement; ME, measurement error; TDI, tissue Doppler imaging; LV, left ventricle; LVED, left ventricular end diastolic; IVS, intra-ventricular septum; LVPW, left ventricular posterior wall; L, longitudinal; SR, strain rate; C, circumferential; S, strain; NA, not available. Circumferential and radial are the average of base and apex. Twist/untwist rate is the average of diastolic and systolic.

In summary, all variables measured using conventional and TDI echocardiography showed good reliability, with CVs < 5% for both intra-rater (range: 1.1 to 3.2%) and inter-rater (range: 1.6 to 4.8%) reliability (Table 4.3). In comparison, CVs of variables measured using STE were moderate to good for intra-rater (range: 4.0 to 9.2%) and moderate to weak for inter-rater (range: 5.1 to 11.7%) reliability.

Additionally, the variables with the strongest CV for both intra- and inter-rater reliability were LV end-diastolic diameter and transmitral *E* velocity, while the weakest CV for both intra- and inter-rater reliability was observed in LV twist measures. For ICC, values ranged between 0.46 to 0.99, with the strongest variable being transmitral *A* velocity, and the weakest ICCs were found in the variables of septal S_m velocity (intra-rater) and inter-ventricular septum (inter-rater). Limits of agreement were similar for intra- and inter-rater reliability, with the exception of LV mass, which was greater for inter-rater reliability. In agreement with previous statistical reliability calculations, measurement error was similar for intra- and inter-rater reliability. However, measurement errors for LV end-diastolic diameter and LV twist were greater for the inter-rater measure. The same rater performed all image acquisition and subsequent data analyses, and all values for intra-rater CV (< 10%) and ICC (< 0.75) were within an acceptable range (Atkinson & Nevill, 1998; Portney & Watkins, 2008).

4.5.4. Survey documents

Self-administered, take-home survey documents were completed by participants; once for the cross-sectional studies, and at the pre-intervention/pre-control, post-intervention/post-control, and sustainability time points for the intervention study. These documents comprised:

Customised survey

All participants completed a written custom survey (Appendix 9). It was difficult to use currently available surveys because they lacked detailed questions, and showed some deficits in age appropriateness, for the population targeted in this study. For this reason, the survey that participants completed was customised and based on a collection of other questionnaires. i.e. (i) Dietary Questionnaire for Epidemiological Studies (The Cancer Council Victoria, 2005); (ii) Barriers to Healthy Eating Scale (Fowles & Feucht, 2004); (iii) 7-day Physical Activity Recall (Sallis, Buono, Roby, Micale, & Nelson, 1993); (iv) The Short Form (36) Health Survey (Ware, 1996); and (v) Women's Health Australia Survey (Women's Health Australia, 2009). The custom survey was subsequently validated using the method of face validation. Face validation describes the extent to which a method (i.e. the custom survey) measures what it is intended to measure. A measure was therefore deemed valid if it

measured the construct that it aimed to measure (Peat & Barton, 2005). Based on subjective judgement, face validation is acknowledged to be the simplest form of validity (Gravetter & Forzano, 2012). To validate the customised survey used in this study, a pilot study with face validation was conducted. A group of young women, representative of the population (n=5) and several experts in the field of qualitative research (n=5), each completed the survey and provided feedback on its design (Appendix 8). Participants were asked if the language and layout of the survey were clear and easy to understand; how long it took to complete; and to provide comments on areas of ambiguity and/or difficult questions (Fink & Koseoff, 1985). Based on this peer-review process, the survey was revised before implementation.

The survey document was divided into three sections: (i) health and lifestyle; (ii) nutrition; and (iii) physical activity. Data were collected on demographic parameters and living conditions, family medical history, health status, medication use, food-frequency, reproductive and body weight history, and frequency, duration, intensity and importance of physical activity. The importance (or value) placed on physical activity was assessed using a single-item question. Participants responding to the question using a Likert-scale (1 = not at all important, 5 = very important). Furthermore, physical activity records were edited for completeness and clarity by the researcher in the presence of the participant. These details provided information about each participant's background and current lifestyle trends, which assisted the researcher with program design during the lifestyle intervention study.

Psychological inventories

Participants completed three self-reported psychological inventories, including:

1) Motives for Physical Activity Measure – Revised (MPAM-R) (Ryan, Frederick, Lepes, Reubio, & Sheldon, 1997). The MPAM-R is a 30-item inventory intended to assess the strength of five general motives for participation in physical activities including: enjoyment (7 items), competence (7 items), appearance (6 items), fitness (5 items), and social (5 items); with each rated on a 5-point Likert scale (1 = not at all true, 5 = very true).

2) Perceived Barriers to Activity (Booth, Bauman, Owen, & Gore, 1997; King et al., 2000). This inventory consists of 18 often-reported personal barriers to physical activity participation. Participants were required to identify the frequency with which barriers occurred, rated on a 5-point Likert scale (1= never, 5 = very often).

3) Stage of Change for Exercise (B. Marcus, Selby, Niaura, & Rossi, 1992). Participants provided details of their stage of exercise behaviour change by selecting the most appropriate response. The model, which provides an indication of readiness to exercise, is modelled on the Transtheoretical Stage of Change Model (Figure 4.13) (Prochaska & Diclemente, 1986), 1983). Participants were classified as: (i) pre-contemplation [do not perform exercise and have no intentions of doing so within the next six months], (ii) contemplation [do not perform exercise, but have the intention of doing so within the next six months], (iii) preparation [I currently exercise, but not regularly], (iv) action [have performed exercise for less than six months], (v) maintenance [have performed exercise for more than six months], and (vi) relapse [performed exercise regularly, but abandoned it recently].

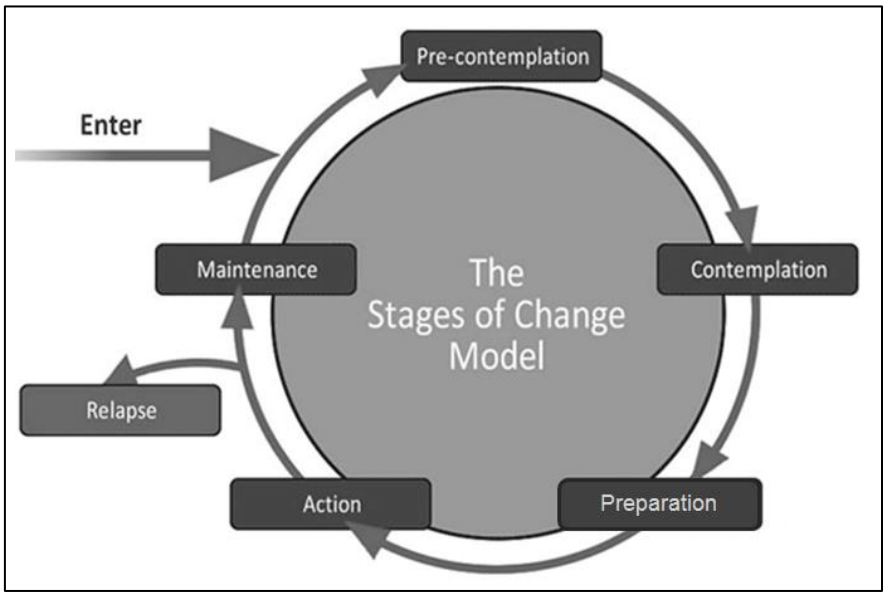

Figure 4.13. The Transtheoretical Model of Behaviour Change, also known as the Stage of Change Model (image adapted from (Prochaska & Diclemente), 1983).

Food recall

Participants completed a 3-day food recall (Appendix 10). This document required each participant to record a detailed account of all food and beverage intake for a 3-day period (two consecutive weekdays and either a Saturday or Sunday), without altering their normal consumption pattern during the recall period. Documenting began upon waking in the morning until going bed that evening. Information was entered into the FoodWorks® 7 Professional (Edition 2006; Xyris Software, Highgate Hill, Queensland, Australia) database software system by a dietitian accredited by the *Dietitians Association of Australia* to calculate daily energy balance, macronutrient (i.e. carbohydrate, fat, protein), and micronutrient (i.e. iron, calcium, magnesium) intake. Information obtained at pre-intervention from the food recall, together with data attained from the Barriers to Healthy Eating Scale (Fowles & Feucht, 2004), and food frequency questions, contained within the custom survey, was used by the dietitian to develop the theoretical material for the nutrition component of the lifestyle intervention.

Training diary

Participants completed a training diary to record structured physical activities performed during the lifestyle intervention. Participants were required to detail the frequency, type, intensity and duration of any extra sessions they performed (in addition to those prescribed by the researcher) during the intervention period (Appendix 11). A training diary of weekly physical activity was also kept during the sustainability phase (Appendix 12).

4.6. Statistical Analysis

This section describes the statistical tests conducted for the cross-sectional and intervention studies. All statistical procedures were performed using SPSS (Statistical Package for Social Sciences) version 21.0, with an alpha level of $P < 0.05$ representing statistical significance.

4.6.1. Normal distribution

All continuous variables were checked for normal distribution according to established standards, with the following critical appraisal criteria applied (Peat & Barton, 2005):

(1) Data are continuous, interval or ratio
(2) Difference between mean and median is < 10%
(3) The mean is greater than twice the SD
(4) Skewness and kurtosis scores do not exceed ± 1.00
(5) The Shapiro-Wilk test ($n<100$) has $P > 0.05$

Variables that did not satisfy the above Gaussian distribution criteria were log-transformed before being evaluated with parametric statistical analyses (Peat & Barton, 2005) (Appendix 21).

4.6.2. Statistical tests

After checks for normal distribution and subsequent log transformation, data were treated with a variety of statistical approaches. Both parametric and non-parametric analyses were performed, where appropriate.

Cross-sectional studies

Differences in descriptive characteristics between women with abdominal obesity (WC ≥ 80cm) and control participants (WC < 80cm) were assessed using an independent-samples *t*-test. Descriptive data were generally presented as mean ± SD, with select non-normally distributed data presented as median ± interquartile range. Effect sizes and power were calculated with Hedge's *g* (uneven groups) described below. Chi-square analyses were used in the comparison of categorical data and for the evaluation of incidences of specific parameters [for example, the percentage of women with abdominal obesity who have elevated insulin resistance (i.e HOMA-IR score ≥ 2.0) compared with control participants who display elevated HOMA-IR]. Unadjusted odds ratios estimated the disease risk between overweight/obesity (classified by WC, BMI and WHtR) and cardiometabolic risk factors, with continuity correction used to establish significance (Peat & Barton, 2005). Furthermore, receiver operating characteristic (ROC) curves were used to establish the cut-off point and positive likelihood ratio in continuously distributed variables (i.e. WC, BMI, WHtR). Pearson's *r* correlation coefficient analyses were used to measure the strength of association between cardiometabolic risk factors and cardiac morphology, function and myocardial measures (Chapter 6).

Lifestyle intervention study

Data were analysed with a linear mixed model (LMM) analysis. LMM is a longitudinal, multi-level model that allows for assessment of both within-subject and between-group differences (Chapters 7, 8 and 9). LMM is similar to a multiple regression, in which a separate regression is created for each individual, then the regression coordinates are combined into a single model (Peat & Barton, 2005). LMM has several advantages compared with a repeated measures analysis of variance (ANOVA), including: (i) all participants are included regardless of missing cells and incomplete data sets; (ii) there is no requirement for cell balance, sphericity or homogeneity of variance across the model; (iii) it is based on regression modelling, therefore allowing for unequal distances between time points; and (iv) interactions are not automatically included (Cnaan, Laird, & Slasor, 1997; Peat & Barton, 2005). Conversely, one disadvantage of LMM is that no estimates of effect size are included in the statistical model. In this study, LMM was used to compare differences in outcome

measures between groups and across time (i.e. pre-intervention, post-intervention and sustainability) for the intervention and control groups.

The statistical analysis included a linear mixed model using "starters" compared with "completers". In addition, a per-protocol comparison was made by which only data of those who completed the entire trial according to protocol were counted towards the final results and removed participants who withdrew from the study. The same strategy applied to the intervention and control groups. No differences were found using both analyses. Furthermore, a sensitivity analysis was performed to compare differences between participants who represented both the wait-list control and intervention participants, with participants from the intervention and control groups who did not change groups. No differences were found using both analyses and the findings were not altered.

4.6.3. Effect size

Effect size was used to calculate the magnitude of the difference for both cross-sectional and intervention study variables. Equal variances were assumed An effect size of >0.2 was considered small, >0.5 moderate, and >0.8 large (Cohen, 1988). The following formula for Cohen's *d* was used, where $\bar{x}1$ and $\bar{x}2$ represent the mean of two populations:

$$d = \frac{\bar{x}\,1 - \bar{x}\,2}{\mathrm{SD}\ pooled}$$

The SD *pooled* was derived from the following formula (Cohen, 1988), where n1 and n2 represents the sample sizes for the two populations, and SD1 and SD2 represents the standard deviation of the mean in the variable compared between each population:

$$SD\ pooled = \sqrt{\frac{(\mathrm{n1}-1)\mathrm{SD1}^2 + (\mathrm{n2}-1)\mathrm{SD2}^2}{\mathrm{n1}+\mathrm{n2}}}$$

Due to uneven group sizes, Hedge's g effect size was subsequently calculated. Therefore, following the calculation of Cohen's *d*, Hedge's g was obtained:

$$g = \frac{d}{\sqrt{\frac{n1 - n2}{n1 - n2 - 2}}}$$

4.6.4. Power analysis

A power analysis was conducted to determine the power achieved for effect size for variables were there was a significant *between-group* difference. Table C.1.2 in Portney and Watkins (2008), p. 845 was used, together with effect size achieved from Hedge's *g,* to calculate 1-ß for a two-tailed t-test (α = 0.05). The following equation was used to determine the *harmonic mean* of the two unequal samples, where n1 and n2 represents the sample sizes for the two populations:

$$n` = \frac{2n1n2}{\mathrm{n1} + \mathrm{n2}}$$

4.7. Evaluation of the lifestyle intervention

At the completion of the intervention phase, a focus group (n = 7) was conducted to gather rich data from participants about their experience during the lifestyle intervention. In addition, a process evaluation survey was completed anonymously by all participants at the completion of the intervention. Similarly, wait-list control participants who withdrew from the study were invited to provide feedback regarding reasons for withdrawal. These procedures are described in more detail in Addendum 7.2.

In summary, this chapter has presented details of methods and procedures not elsewhere included in the thesis. The descriptions here are provided to strengthen the rigour and rationale for all selected physical and statistical tests as well as protocols and procedures used throughout the thesis.

Chapter 5. Cardiometabolic and behavioural risk factors in young overweight women identified with simple anthropometric measures.

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Abstract

Objectives: This study aimed to (1) investigate cardiometabolic risk markers in young women (18-30 years) with overweight/obesity, and (2) establish whether the measures of waist circumference (WC) and body mass index (BMI) possess similar associations of cardiometabolic risk.

Methods: Cross-sectional study design. Cardiometabolic risk factors including, anthropometric, metabolic syndrome markers, biochemical, and other health/fitness indicators were assessed in women when classified as overweight/obese by WC [WC 91.9 ± 10.1 cm, age 22.3 ± 3.5 y, n=38] versus control [n=30, WC 71.4 ± 3.5 cm, age 20.1 ± 0.9 y], and when classified by BMI [n=35, BMI 32.2 ± 5.2 $kg \cdot m^2$, age 22.5 ± 3.6 y] versus control [BMI 21.7 ± 1.9 $kg \cdot m^2$, age 20.1 ± 0.9 y, n=33].

Results: Compared with controls, women with overweight/obesity (classified by WC or BMI) displayed elevated body mass, systolic blood pressure and HOMA-IR, and reduced estimated VO_{2max} and weekly physical activity, with no differences in self-reported energy intake. The unadjusted odds ratio of being classified with overweight/obesity and an elevated HOMA-IR and/or less than recommended physical activity ranged between 5.1 to 10.0. Receiver operator characteristic curves indicated WC, BMI and waist-to-height ratio cut-off points of ≥ 84.2 cm, ≥ 30.6 $kg \cdot m^{-2}$ and ≥ 0.5, respectively, for HOMA-IR, and ≥ 80.6 cm, ≥ 25.2 $kg \cdot m^{-2}$ and ≥ 0.46, respectively, for less than recommended physical activity.

Conclusion: WC and BMI have similar associations with cardiometabolic risk, with greater HOMA-IR and lower physical activity, rather than differences in traditional metabolic syndrome markers, observed in young women with overweight/obesity.

Keywords: Obese, waist circumference, body mass index, waist-to-height ratio, cardiovascular disease, physical activity.

Introduction

In Australia, the prevalence of overweight/obesity is 35% for women aged 18-24 years, and 42% for women aged 25-34 years (Australian Bureau of Statistics, 2012). However, cardiometabolic risk data are more frequently described in adolescents (Wedin, Diaz-Gimenez, & Convit, 2012) and even more so in older people (Fogelholm, 2010), with women in young adulthood under-represented. The gains in weight in young adult women are paralleled by substantial declines in physical activity (Adamson et al., 2007), with the greatest declines occurring between 25 to 34 years of age (Australian Bureau of Statistics, 2012). When assessed against current National Physical Activity Guidelines (Department of Health and Ageing, 2005), 59% of Australian women aged 18-34 years failed to achieve recommended weekly amounts (210 min) of moderate exercise (Cleland, Schmidt, Salmon, Dwyer, & Venn, 2011), while the Australian Longitudinal Study on Women's Health found that 45% of overweight/obese women aged 18-23 years performed none or very low levels of daily physical activity (Lucke et al., 2007). A better understanding of cardiometabolic risk factors in this age group is important for early detection of chronic disease risk, especially given the rise in overweight/obesity and low prevalence of physical activity of young women.

With overweight/obesity being a modifiable risk factor for cardiovascular disease (CVD), Type 2 diabetes mellitus, and the metabolic syndrome (Alberti et al., 2009), simple anthropometric measures of body mass index (BMI) and waist circumference (WC) are in frequent clinical use. BMI is an estimate of total fat mass and has been used as a predictor of health risk (National Health and Medical Research Council, 2003). For adults, a BMI of 25.0 to 29.9 $kg \cdot m^{-2}$ is classified as overweight, and a BMI $\geq$ 30 $kg \cdot m^{-2}$ is classified as obese (World Health Organisation, 2000). Correspondingly, centrally distributed (abdominal) obesity using WC has gender and ethnic-specific criteria available (Alberti et al., 2009). For Caucasian women, abdominal obesity is defined as a WC $\geq$ 80 cm (Alberti et al., 2009). Given the differing criteria for BMI and WC in classifying overweight/obesity in young women, it is important to establish whether these anthropometric measures identify the presence and/or similar relative risk of other markers of cardiometabolic risk.

Therefore, the aims of this study were to: (1) investigate blood-borne and lifestyle markers of cardiometabolic risk in young women (18-30 years) with overweight/obesity classified by clinically useful methods, and (2) establish whether WC and BMI possess similar associations of cardiometabolic disease risk in these women. For comparative purposes, waist-to-height ratio (WHtR) was included in some statistical analyses.

Methods

Ninety-three university-enrolled participants responded to recruitment advertisements and emails. Of these, 11 did not meet the inclusion criteria (below) and a further 14 eligible participants did not continue through testing. Therefore, 68 Caucasian women aged 18 to 30 years completed all testing, between 2010-2012. Participants were divided into two groups: (1) an "elevated" waist circumference ≥ 80 cm [n = 38, abdominal obesity, mean ± standard deviation, WC 91.9 ± 10.1 cm, age 22.3 ± 3.5 y], or (2) a waist circumference < 80 cm control group [n=30, WC 71.4 ± 3.5 cm, age 20.1 ± 0.9 y]. There was no difference between groups in socio-economic status [χ^2 (4, n = 66) = 0.42, p = 0.382], with 51.4% of participants in the elevated WC group and 62.1% of participants in the control group living in metropolitan suburbs of the most advantaged quintile of socio-economic status (Australian Bureau of Statistics, 2011). Exclusion criteria included being pregnant or breastfeeding, liver or kidney disease, heart arrhythmia, insulin dependent diabetes mellitus, gestational diabetes, polycystic ovarian syndrome, thyroid abnormalities and a history of bariatric surgery or liposuction. All participants were non-smokers. For additional analysis, the same 68 participants were divided into two groups according to the classifications of BMI, resulting in participants being classified as either overweight/obesity [n=35, defined as a BMI ≥ 25 kg·m^{-2}, BMI 32.2 ± 5.2 kg·m^{-2}, age 22.5 ± 3.6 y] or normal BMI [n=33, BMI 18.5 - 24.9 kg·m^{-2}, BMI 21.7 ± 1.9 kg·m^{-2}, age 20.1 ± 0.9 y].

Following approval by the University Human Research Ethics Committee (V2009-91), written informed consent was obtained and all participants completed a Cardiovascular Risk Assessment Form prior to testing. Participants arrived at the laboratory following a 12 hour fast. They were also requested to refrain from strenuous physical activity in the 24 h prior to testing.

Waist circumference (WC) was measured (Alberti et al., 2009) to the nearest 0.1 cm using a non-elastic measuring tape, with the average of two measurements reported. The coefficient of variation for WC, assessed from duplicate measures, was 1.26%, with an intra-class correlation (ICC, 2, 1) of 0.986 and measurement error of 1.34%, which equates to an error range of ± 2.6 cm. Body mass was measured to the nearest 0.1 kg using digital scales (Tanita, Tokyo, Japan). Height was measured to the nearest 0.1 cm using a wall-mounted stadiometer (Seca, Germany). Body mass index (BMI) (weight [kg]/height [m^2]), was defined as overweight BMI 25.0 – 29.9 $kg \cdot m^{-2}$ and obese BMI ≥ 30.0 $kg \cdot m^{-2}$ (World Health Organisation, 2000) Participants were dichotomised by waist-to-height ratio (WHtR) using WC divided by height. A ratio of 0.5 was defined as the boundary value (Browning, Hsieh, & Ashwell, 2010).

Metabolic syndrome was defined according to the most recent and unified criteria (Alberti et al., 2009), where three of the following five are met: 1) waist circumference ≥ 80 cm, 2) raised serum triglycerides ≥ 1.7 $mmol \cdot l^{-1}$, 3) reduced HDL-cholesterol < 1.30 $mmol \cdot l^{-1}$, 4) raised systolic blood pressure ≥ 130 mmHg or raised diastolic blood pressure ≥ 85 mmHg, and 5) elevated fasting plasma glucose ≥ 5.6 $mmol \cdot l^{-1}$ or previously diagnosed type 2 diabetes. No participants in this study were taking medication to treat elevated triglycerides or reduced HDL-cholesterol, which is considered an alternative indicator of abnormal levels (Alberti et al., 2009). Additional measurements of insulin resistance, including fasting insulin and HOMA-IR, and the pro-inflammatory marker high sensitivity C-reactive protein (hs-CRP) were also measured in participants.

Intravenous blood sampling provided blood lipid profiles: serum concentrations of triglycerides, total cholesterol and high-density lipoprotein (HDL) cholesterol (Reflotron Plus, Roche, Switzerland). A CV of 3.8% was found between Refloton measurements for total cholesterol and a standardised wet-chemistry method (Statland, 1990). Fasting plasma glucose, insulin and hs-CRP concentrations were analysed by a pathology unit at a leading hospital (reagents Beckman Coulter, assays on Olympus AU2700, Abbott Architect i1000, and Olympus AU640 analyser). Insulin resistance was estimated by the homeostasis model assessment (HOMA-IR), using the equation: HOMA-IR = fasting insulin concentration (µU/mL) x fasting glucose concentration (µU/mL) / 22.5 (Matthews et al., 1985). HOMA-IR was used as a surrogate measure of whole body insulin sensitivity and β-cell functioning and has been shown to correlate well with estimates using the euglycemic clamp method (r =

0.88) (Bonora et al., 2000; Matthews et al., 1985). A HOMA-IR value ≥ 2.0 was considered indicative of insulin resistance (Jensterle et al., 2008). For hs-CRP, a value of > 3.0 $mg \cdot l^{-1}$ was deemed high risk (Pearson et al., 2003). Blood pressure was obtained with an automated digital sphygmomanometer (Dinamap, GE technology, USA).

The YMCA submaximal cycle ergometer test (Golding, Meyers, & Sinning, 1989) (Appendix 19) was used to estimate maximal oxygen uptake (predicted VO_{2max}). After completing a short submaximal warm-up, participants cycled (Monark, Ergomedic 838E, Sweden) for three consecutive 3-min work rates at a constant cadence of 50 rpm, and an initial power output of 25 W, resulting in a total test time of 9 min. Heart rate during the last 15 s of stage one was used to determine subsequent workloads. At the completion of the test, heart rate was extrapolated against work rate (W) using regression analysis to estimate maximal aerobic capacity.

Within the acknowledged limitations of dietary recall (Magarey et al., 2011), participants completed a three-day food diary of food and beverage intake on two weekdays and one weekend day. Macro and micro nutrients, and average daily energy intake were estimated (FoodWorks® 7 Professional) by a research dietician, blinded to grouping.

Participants completed a self-administered lifestyle survey addressing (i) health status and medical conditions, (ii) self-reported physical activity and exercise, (iii) nutrition habits, and (iv) perceived barriers to physical activity (King et al., 2000). Additionally, type, frequency and duration of typical leisure and/or sporting activities were confirmed during an interview with the researcher.

Data were analysed using IBM SPSS Statistics, Version 19 for Windows (SPSS Inc, Chicago IL) and first tested for normal distribution using the Shapiro-Wilk statistic and skewness and kurtosis values (Peat & Barton, 2005). Log transformation was used when data were not normally distributed. All data are presented as mean ± standard deviation, with the exception of medians [interquartile range] for non-normally distributed data, reported prior to log transformed treatment. An alpha level of $p < 0.05$ was used to determine significance. Group comparisons were performed using independent t-tests. Due to uneven group size, Hedge's g calculated effect size. An effect size of ≥ 0.2 was considered small, ≥ 0.5 was considered medium, and ≥ 0.8 was considered large (Vincent, 1995). The mean difference between

overweight/obesity and control participants for each cardiometabolic risk factor included 95% confidence intervals.

Unadjusted odds ratios were used to estimate disease risk given exposure and describe the strength of association between overweight/obesity (classified by WC, BMI and WHtR) and cardiometabolic risk factors. Continuity correction was used to establish significance (Peat & Barton, 2005)

Receiver operating characteristic (ROC) curves were plotted to determine the point that maximises the likelihood ratio and cut-off points for WC, BMI and WHtR. Furthermore, the positive likelihood ratio was computed for each cut-off point. Pearson's Chi-square analysis was used to compare the frequency of scores for barriers to being physically active between the two groups.

Results

Anthropometric and cardiometabolic data are shown in Table 5.1 and Table 5.2 (see also graphs in Appendix 14). Compared with controls, women with abdominal obesity (WC $\geq$ 80 cm) had greater body mass, body mass index, waist circumference and waist-to-height ratio ($p < 0.001$). Similar differences were observed for BMI.

Table 5.1. Cardiometabolic risk factors in participants with and without abdominal obesity, as defined by waist circumference

Variable	Control WC < 80cm (n=30)	Abdominal obesity WC ≥ 80cm (n=38)	*P*-value	Effect size Hedge's *g*	Power (1-ß)	Mean difference (95% CI)
Anthropometric assessment						
Body mass (kg)	60.3 ± 6.7	86.7 ± 18.3	<0.0001*	1.61	1.00	26.4 (19.9, 32.8)
Stature (m)	1.7 ± 0.06	1.7 ± 0.06	0.311	0.15	-	-0.01 (-0.44, 0.01)
Body mass index ($kg \cdot m^{-2}$)	21.6 ± 1.9	31.5 ± 5.5	<0.0001*	2.00	1.00	9.9 (7.9, 11.8)
Waist circumference (cm)	71.4 ± 3.5	91.9 ± 10.1	<0.0001*	2.28	1.00	20.5 (16.9, 24.0)
Waist-to-height ratio (WHtR)	0.43 ± 0.02	0.55 ± 0.06	<0.0001*	2.41	1.00	0.13 (0.11, 0.15)
Metabolic syndrome markers						
Systolic BP (mmHg)	114 ± 8	121 ± 8	0.007*	0.60	0.75	5.7 (1.6, 9.7)
Diastolic BP (mmHg)	67 ± 8	67 ± 7	0.834	0.04	-	-0.4 (-4.0, 3.3)
HDL-cholesterol ($mmol \cdot L^{-1}$)	1.5 ± 0.3	1.6 ± 0.5	0.241	0.26	-	0.13 (-0.08, 0.33)
Triglycerides ($mmol \cdot L^{-1}$)	1.1 ± 0.3	1.2 ± 0.4	0.400	0.17	-	0.07 (-0.10, 0.25)
Fasting glucose ($mmol \cdot L^{-1}$)	4.8 ± 0.4	4.7 ± 0.5	0.152	0.29	-	-0.2 (-0.4, 0.1)
Additional biochemical parameters						
Total cholesterol ($mmol \cdot L^{-1}$)	4.6 ± 1.0	4.4 ± 0.6	0.313	0.26	-	-0.2 (-0.6, 0.2)
Fasting insulin ($mU \cdot L^{-1}$)#	5.0 [2.2]	8.0 [5.0]	<0.0001*	0.84	0.94	3.7 (2.0, 5.4)
HOMA-IR#	1.1 [0.5]	1.7 [1.1]	<0.0001*	0.75	0.87	0.7 (0.3, 1.1)
hs-CRP ($mg \cdot L^{-1}$)#	1.4 [1.4]	1.9 [3.5]	0.024*	0.46	0.42	1.2 (0.2, 2.3)
Health and fitness evaluation						
PredictedVO_{2max} ($mL \cdot kg^{-1} \cdot min^{-1}$)	41.3 ± 8.14	30.4 ± 8.2	<0.0001*	1.61	1.00	11.0 (7.0, 15.0)
Physical activity ($min \cdot wk^{-1}$)#	285 [194]	100 [124]	<0.0001*	1.11	1.00	-193 (-275, -111)
Daily energy intake (KJ)	5797 ± 1421	6263 ± 2478	0.343	0.187	-	-466 (-1443, 511)

*Data presented as mean ± SD or median [IQ range]; # log_{10} transformation; * $p \leq 0.05$; blood pressure (BP); high-density lipoprotein (HDL); high sensitive C-reactive protein (hs-CRP); homeostasis model assessment of insulin resistance (HOMA-IR). An effect size of ≥ 0.2 was considered small, ≥ 0.5 was considered medium, and ≥ 0.8 was considered large (Vincent, 1995).*

Table 5.2. Cardiometabolic risk factors in participants with and without overweight/obesity, as defined by body mass index.

Variable	Control BMI <24.9 kg·m^{-2} (n=33)	Overweight/obesity BMI ≥25.0 kg·m^{-2} (n=35)	*P*-value	Effect size Hedge's *g*	Power (1-ß)	Mean difference (95% CI)
Anthropometric assessment						
Body mass (kg)	60.8 ± 6.6	88.6 ± 18.0	<0.0001*	2.00	1.00	27.7 (21.1, 34.4)
Stature (m)	1.7 ± 0.05	1.6 ± 0.06	0.254	0.36	-	-0.02 (-0.05, 0.01)
Body mass index (kg·m^{-2})	21.7 ± 1.9	32.2 ± 5.2	<0.0001*	2.60	1.00	10.4 (8.5, 12.3)
Waist circumference (cm)	72.5 ± 4.8	92.6 ± 10.3	<0.0001*	2.44	1.00	20.0 (16.1, 24.0)
Waist-height-ratio (WHtR)	0.43 ± 0.03	0.56 ± 0.05	<0.0001*	3.09	1.00	0.12 (0.10, 0.15)
Metabolic syndrome markers						
Systolic BP (mmHg)	115 ± 8	120 ± 9	0.014*	0.60	0.75	5.1 (1.0, 9.2)
Diastolic BP (mmHg)	66.8 ± 7.9	67.3 ± 6.9	0.770	0.07	-	0.5 (-3.0, 4.1)
HDL-cholesterol (mmol·L^{-1})	1.5 ± 0.3	1.7 ± 0.5	0.114	0.38	-	0.17 (-0.04, 0.38)
Triglycerides (mmol·L^{-1})	1.2 ± 0.4	1.2 ± 0.3	0.959	0.01	-	-0.00 (-0.18, 0.17)
Fasting glucose (mmol·L^{-1})	4.7 ± 0.4	4.7 ± 0.5	0.811	0.06	-	-0.03 (-0.25, 0.20)
Additional biochemical parameters						
Total cholesterol (mmol·L^{-1})	4.7 ± 0.9	4.3 ± 0.6	0.128	0.40	-	-0.3 (-0.7, 0.1)
Fasting insulin (mU·L^{-1})#	5.0 [3.0]	8.00 [5.00]	<0.0001*	1.00	0.99	0.2 (0.1, 0.3)
HOMA-IR#	1.1 [0.7]	1.81 [1.08]	<0.0001*	1.00	0.99	0.7 (0.3, 1.1)
hs-CRP (mg·L^{-1})#	1.4 [2.0]	1.98 [2.95]	0.079	0.43	-	1.0 (-0.1, 2.0)
Health and fitness evaluation						
Predicted VO_{2max} (mL·kg^{-1}·min^{-1})	40.9 ± 8.8	30.0 ± 7.7	<0.0001*	1.31	1.00	10.87 (6.89, 14.85)
Physical activity (min·wk^{-1})#	260 [220]	100 [112.50]	<0.0001*	1.13	1.00	-179.00 (103, 257)
Daily energy intake (KJ)	6164 ± 1615	5946 ± 2434	0.671	0.10	-	218.14 (-804, 1241)

*Data presented as mean ± SD or median [IQ range]; # log_{10} transformation; * $p \leq 0.05$; blood pressure (BP); high-density lipoprotein (HDL); high sensitive C-reactive protein (hs-CRP); homeostasis model assessment of insulin resistance (HOMA-IR). An effect size of ≥ 0.2 was considered small, ≥ 0.5 was considered medium, and ≥ 0.8 was considered large (Vincent, 1995).*

None of the women with overweight/obesity were diagnosed with the metabolic syndrome (Alberti et al., 2009). Of the metabolic syndrome markers, only systolic blood pressure was higher than controls in participants with overweight/obesity, regardless of classification. The proportion of women in the intervention and control groups, respectively exhibiting each of the metabolic syndrome markers were: WC (100%, 0%); triglycerides (8%, 6%); HDL-cholesterol (32%, 27%); systolic blood pressure (10%, 3%); diastolic blood pressure (0%, 0%); glucose (3%, 0%).

Again, independent of the classification used, the two predictors of glycaemic risk, fasting insulin and HOMA-IR were more elevated in participants with a raised WC and/or BMI > 25 $kg.m^{-2}$ than controls (Tables 5.1 and 5.2).

The pro-inflammatory marker hs-CRP was significantly (40%) higher in women with elevated WC than controls but did not differ when using BMI thresholds. Additionally, the prevalence of elevated hs-CRP > 3 $mg \cdot l^{-1}$ (Pearson et al., 2003) was 35% for women with overweight/obesity compared with 20% in the control group, for WC [χ^2 (1, n = 67) = 1.20, p = 0.274] and BMI [χ^2 (1, n = 67) = 0.22, p = 0.642].

Aerobic fitness estimated from a submaximal cycling protocol was 26% lower in participants with elevated WC than controls. Similarly, subjective approximations of weekly physical activity were 63% less in women with elevated WC than controls. Estimated daily energy intake did not differ between groups. Similar results were observed using BMI (Tables 5.1 and 5.2).

HOMA-IR, fasting insulin, hs-CRP and physical activity were used as dependent variables and anthropometric measures of WC, BMI and WHtR were the independent variables in calculating unadjusted odds ratios. From this analysis only HOMA-IR and physical activity produced significant unadjusted odds ratios (Table 5.3). Approximately 41% of participants in the exposed group (overweight/obesity – classified by WC, BMI and WHtR) and 6.7 to 11.0% in the non-exposed group (controls) were diagnosed with elevated HOMA-IR. Furthermore, the unadjusted odds ratio for the association between overweight/obesity and elevated HOMA-IR ranged between 5.1 to 10.0. The percentage of less than recommended physical activity levels in the exposed group (approximately 80%) was double that of the non-exposed group (approximately 40%) (Table 5.3).

Table 5.3. Associations between cardiometabolic risk factors and overweight/obesity.

Variable	% diagnosed in exposed group	% diagnosed in non-exposed group	Unadjusted odds ratio (95% CI)	*P*-value
Waist circumference	*WC ≥ 80 cm*	*WC < 80cm*		
HOMA-IR	41.7%	6.7%	10.0 (2.1, 48.6)	0.003
Physical activity (min·wk^{-1})	78.9%	36.7%	6.5 (2.2, 19.0)	0.001
Body mass index	*BMI ≥ 25 kg·m^{-2}*	*BMI ≤ 24.9 kg·m^{-2}*		
HOMA-IR	42.4%	9.1%	7.4 (1.9, 29.1)	0.005
Physical activity (min·wk^{-1})	80.0%	39.4%	6.1 (2.1, 18.2)	0.002
Waist-to-height-ratio	*WHtR ≥ 0.5*	*WHtR < 0.5*		
HOMA-IR	40.6%	11.0%	5.1 (1.4, 18.0)	0.016
Physical activity (min·wk^{-1})	82.0%	38.2%	7.6 (2.4, 23.1)	0.001

A participant with a HOMA-IR score of ≥ 2.0 or physical activity levels of ≤ 210 minutes per week was allocated to the exposed group. Please note, two data sets for HOMA-IR were unavailable due to compromised samples.

ROC curves determined the cut-off point for three anthropometric (WC, BMI, WHtR) measures. The area under the curve (AUC) for elevated HOMA-IR was 0.79 ($p < 0.001$) and a cut-off value of 84.25 cm when calculated for WC. Additionally, the positive likelihood ratio was 2.9. Less than recommended physical activity produced a value of 0.72 for the AUC ($p = 0.002$), with a cut-off value of 80.65 cm and a positive likelihood ratio of 3.3 for WC. For BMI, HOMA-IR produced a value of 0.82 for the AUC ($p < 0.001$), with a BMI cut-off value of 30.61 kg·m^{-2}, and a positive likelihood ratio of 4.9. Moreover, the AUC for less than recommended physical activity levels was 0.73 ($p = 0.002$), with a BMI cut-off of 25.25 kg·m^{-2}, and a positive likelihood ratio of 3.7. For WHtR, HOMA-IR value for AUC was 0.76 ($p < 0.001$), with a WHtR cut-off value of 0.50, and a positive likelihood ratio of 1.2. Additionally, the AUC for less than recommended physical activity levels was 0.71 ($p = 0.003$), with a WHtR cut-off of 0.46, and a positive likelihood ratio of 2.8.

Participants completed a questionnaire, rating their perceived barriers to physical activity. Chi-square frequencies revealed 84% of participants agreed that exercise was important to them. Despite this, 65% of women with elevated WC or BMI >25 kg·m^{-2} shared difficulties in motivation for physical activity (17% in controls), however both groups ranked feeling too

tired as their number one barrier (Table 5.4). Additionally, 56% of participants with elevated WC or BMI >25 $kg \cdot m^{-2}$ reported that being self-conscious about their looks was a major barrier to regular physically active (3% in controls).

Table 5.4. Most prevalent perceived barriers to engaging in physical activity.

Perceived Barrier	**% overweight/obesity (rank)**	**% control (rank)**
Feeling too tired	79 (1)	63 (2)
High cost of classes or venues	68 (2)	47 (4)
Lack of motivation	65 (3)	17 (7)
Poor weather	58 (4)	53 (3)
Lack of time	55 (5)	73 (1)
Self-conscious about physical appearance	55 (5)	3 (9)

Discussion

Data on the prevalence, characteristics and consequences of overweight/obesity in young women are important for providing an indication of the need for early detection, timely treatment, and the adaptation of lifelong interventions (van Emmerik et al., 2012). In this study, classification of overweight/obesity using WC and BMI were associated with similar cardiometabolic risk. Risk markers commonly used in standard health checks did not differentiate between women with overweight/obesity and those in healthy anthropometric ranges, while women with overweight/obesity did display higher markers of insulin resistance (fasting insulin and HOMA-IR) and lower estimates of physical activity (weekly exercise duration and aerobic fitness). This finding suggests that anthropometric measures are useful first-line diagnostic measures of cardiometabolic risk, with insulin resistance and lifestyle factors providing deeper insight into this risk for young adult women than traditional metabolic syndrome markers.

No individual was diagnosed with the metabolic syndrome (Alberti et al., 2009) and, as a group mean, none of the markers (i.e., other than WC) was elevated to that of the current

metabolic syndrome definition. In contrast, data from the Australian Diabetes, Obesity and Lifestyle Study (AusDiab) reported the prevalence of the metabolic syndrome in women aged between 25-34 years to be 6% (Cameron et al., 2007). Given the younger age of our participants (22.3 ± 3.5 years) compared with those in the AusDiab Study (Cameron et al., 2007), these data suggest that traditional metabolic syndrome markers may not be sufficiently sensitive to indicate cardiometabolic risk in young adulthood (< 30 years). Therefore, markers of insulin resistance may be more useful indicators of future cardiometabolic risk in younger women with overweight/obesity than markers currently used in the metabolic syndrome definitions and during standard health checks.

As a marker of insulin dysfunction, elevated HOMA-IR ≥ 2.0 (Jensterle et al., 2008), was present in more than 41% of women with overweight/obesity in the present study, compared with 6.7 - 11.0% of the control group. Moreover, the odds ratio for the association between overweight/obesity and an elevated HOMA-IR score was large, suggesting a strong relationship between these two variables. Raised concentrations of circulating hs-CRP were also present in women with an elevated WC, in agreement with previous reports (Da Costa et al., 2012; Ramos & Olden, 2008). These raised hs-CRP concentrations could have contributed to higher HOMA-IR scores in the overweight/obesity group, given that hs-CRP disrupts insulin signalling and action (Da Costa et al., 2012).

Similar predictors of cardiometabolic risk were found when using WC and BMI as proxy measures of overweight/obesity, suggesting that both are useful markers for potential insulin resistance in young women. This agrees with previous results showing WC and BMI have a similar strength of association with CVD risk in adults, when assessed using individual records from 58 cohorts (Emerging Risk Factors Collaboration [ERFC], 2011). Results from ROC curves showed that the WC cut-off point for determining increased risk of insulin resistance, as measured by both fasting insulin and HOMA-IR, was ≥ 84 cm. This value is higher than current guidelines of ≥ 80 cm for Caucasian females (Alberti et al., 2009). Similar trends were observed for the cut-off point for classifications of BMI, in which a measure of ≥ 30.0 $kg \cdot m^{-2}$, rather than ≥ 25 $kg \cdot m^{-2}$, was identified an increased risk of elevated HOMA-IR. In contrast, the dichotomization cut-off points for cardiometabolic risk associated with low physical activity (≤ 210 min of weekly exercise) in our study were determined to be ≥ 80 cm for WC and ≥ 25.25 $kg \cdot m^{-2}$ for BMI, strongly supporting the probability of risk within the

existing overweight/obesity classification scores (Alberti et al., 2009; World Health Organisation, 2000).

The use of WHtR may also be a suitable and easy to administer anthropometric screening tool for the prediction of cardiometabolic outcomes applicable to a variety of populations (Browning et al., 2010). ROC curves showed that the WHtR margin for determining increased risk of insulin resistance, as measured by HOMA-IR, was ≥ 0.5, strongly supporting the current global boundary value (Browning et al., 2010). Additionally, a cut-off value of ≥ 0.46 was determined for cardiometabolic risk associated with low physical activity (≤ 210 min of weekly exercise), which is lower than the current threshold. Furthermore, the unadjusted odds ratios of WHtR in predicting risk factors are comparable to WC and BMI.

In the present study, 80% of women with overweight/obesity failed to achieve minimum weekly exercise recommendations compared with 35% of the control group, while 3-day dietary recall data showed no differences in daily energy intake between the groups. Although dietary recall has limitations, these data show insufficient energy expenditure from physical activity relative to energy intake appears to be a significant factor in weight gain in the young women in our study. From data reported in a qualitative questionnaire, a prominent barrier to being active for the overweight/obesity women was self-conscious feelings about their own appearance. Therefore, lifestyle interventions for the prevention/reduction of overweight/obesity need to address psychological barriers to physical activity.

The study has several limitations. The cross-sectional design could conceivably be a weakness, but it provided proof of concept prior to larger trials. Future studies using a prospective design could provide predictive data that addresses WC/BMI and the development of cardiometabolic disease. Ideally, central fat distribution would be measured using MRI, but waist circumference still provided a level of sensitivity relevant to most clinical settings (National Health and Medical Research Council, 2003). Additionally, the results are specific to Caucasian women at a tertiary institution and largely from suburbs in the most advantaged quintile of socio-economic status. Given this however, our data raise concerns that key health promotion messages are either poorly sourced or understood, and/or are very difficult to apply. When more educated, advantaged young women have difficulties, it may be assumed that individuals from less advantaged backgrounds may at least share these health issues.

Conclusion

This study supports the use of WC and BMI as first-line diagnostic measures of cardiometabolic risk. However, risk markers beyond the traditional metabolic syndrome blood-borne criteria, such as fasting insulin and HOMA-IR, may be required when screening further for cardiometabolic risk in young women. A higher order of investigation (e.g. blood sampling) may help convince young women of the need to take action. Furthermore, sedentary behaviour in young women with overweight/obesity is a lifestyle risk factor of concern, with a need for addressing identified age- and gender-specific barriers to engagement. The value of additional research into managing cardiometabolic risk in young women cannot be understated.

Practical Implications

- In young adult women, WC and BMI as measures of overweight/obesity have similar associations with other cardiometabolic risk factors.

- Markers of insulin and HOMA-IR may be useful indicators of future cardiometabolic risk in younger women with overweight/obesity.

- The first line of treatment for cardiometabolic risk should be centred on modifiable lifestyle changes, such as those associated with sedentary behaviour through increased physical activity.

- Given the poor engagement in physical activity in our study population, the approach to engagement should be age and gender appropriate, and take into account perceived barriers to physical activity.

Chapter 6. Young women with abdominal obesity have sub-clinical myocardial dysfunction.

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Abstract

Background: Abdominal obesity is an independent risk factor for cardiovascular disease. The impact of abdominal obesity on myocardial function in young obese women remains unknown. Therefore, we aimed to investigate cardiac morphology and function, myocardial deformation and mechanical indices, in young women with and without abdominal obesity.

Methods: Cross-sectional analyses of 39 women with abdominal obesity (waist circumference ≥ 80 cm) and 33 non-obese controls (waist circumference < 80cm) aged 18-30 years underwent conventional echocardiographic measures of cardiac morphology and function together with tissue Doppler, and 2D speckle tracking measures of myocardial deformation and mechanics. Cardiometabolic risk factors including anthropometric, hypertension, biochemistry and fitness were also assessed.

Results: Standard echocardiography results for cardiac morphology and function were similar between women with abdominal obesity and their age and-gender-matched controls, with the exception of larger left atrial dimensions in women with abdominal obesity ($P \leq 0.05$). Compared with controls, women with abdominal obesity also demonstrated reduced systolic (S_m) and diastolic (E_m) mitral annular plane velocities, increased LA pressure surrogates (E/E_m), and prolonged timing measures of diastolic function including isovolumic relaxation time and transmitral deceleration time ($P \leq 0.05$). In addition, longitudinal strain and diastolic strain rate were reduced in women with abdominal obesity ($P \leq 0.05$) but circumferential deformation and myocardial mechanics (twist indices and rotation) were preserved.

Conclusion: A young, otherwise-healthy group of women with abdominal obesity displayed sub-clinical cardiac dysfunction indicated by selected TDI and STE measures.

Keywords: Waist circumference, cardiometabolic, speckle tracking imaging, echocardiography, female, tissue Doppler imaging.

Introduction

Obesity is an established independent risk factor for cardiovascular disease (CVD), with a global, increasing prevalence reaching epidemic proportions (Grundy, 2008; World Health Organisation, 2000). In countries such as Australia, the prevalence of obesity in young women appears to be increasing at an exponential rate (Lucke et al., 2007). Elevated waist circumference, is a reliable anthropometric index of abdominal obesity (Klein et al., 2007), allowing early identification of CVD risk (Share, Naughton, Obert, Peat, & Kemp, 2013). However, the cardiac consequences of risk factors are poorly understood in young women; a population emerging as highly vulnerable to cardiometabolic disorders.

Young women specifically continue to be underrepresented in cardiac research (Rosenfeld, 2006), perhaps due to the misperception that females are 'protected' against CVD via the role of oestrogen in pre-menopausal females (Maas et al., 2011). Additionally, enrolment of women in clinical and epidemiological research remains relatively low in studies of populations with chronic disease (Melloni et al., 2010).

Obesity can unfavourably alter left ventricular (LV) morphology and function with greater LV hypertrophy and cardiac remodelling observed in both adolescent (Obert et al., 2012; Shah et al., 2011) and older females populations (Orhan et al., 2010). Early detection of myocardial abnormalities in obese individuals may represent a critical and cost-effective strategy to attenuate the time-related consequences of CVD (Orhan et al., 2010). Despite this, the understanding of the effects of obesity on CVD risk in women is largely limited to middle-aged and older individuals with scarce attention to young obese females (Di Bello et al., 2013; Peterson, Waggoner, et al., 2004). Therefore, it remains unclear whether or not obesity in young women is associated with cardiac dysfunction. As such, identification of sub-clinical disease such as myocardial dysfunction in young women with obesity would highlight a group in which targeted interventions may be of greatest impact. Furthermore, the recently described "obesity paradox" (Lavie et al., 2013) creates some ambiguity surrounding the effects of obesity on cardiac function and it may be argued this issue is particularly pertinent to young women with obesity in whom targeted interventions may be of greatest value.

Sub-clinical cardiac dysfunction can be detected using non-invasive conventional and tissue Doppler imaging (TDI) echocardiography (Ho & Solomon, 2006; Wong, Leano, & Marwick, 2006). However, speckle tracking echocardiography (STE), a deformation imaging technique, was developed to address potential limitations in the sensitivity of existing measures for detecting subtle myocardial dysfunction. Speckle tracking echocardiography may help overcome the limitations of conventional and TDI echocardiography by permitting angle-independent evaluation of strain and strain rate (SR) in the longitudinal and circumferential planes, as well as rotation and twist mechanics (Esch & Warburton, 2009; K. A. Marcus et al., 2011).

The aim of this study was to investigate cardiac morphology and function, myocardial deformation and mechanical indices, in a cross-sectional profile of young women with and without abdominal obesity using traditional and advanced techniques of echocardiography.

Methods

Participants

Ninety-three university-enrolled women aged 18 to 30 years responded to recruitment advertisements. Participants were a low-risk population, free of CVD risk factors (hypertension, diabetes, and smoking), or endocrine disorders who had not undergone bariatric surgery and were not pregnant. Eleven women did not meet the inclusion criteria and a further ten eligible participants did not complete testing. Therefore, 72 women (all Caucasian) completed testing between August 2010 and February 2012. Participants were divided into two groups; (1) 39 women with abdominal obesity defined by a waist circumference (WC) $\geq$ 80 cm, and (2) 33 women without abdominal obesity (WC $<$ 80 cm). Participants arrived at the laboratory following a 12 hour fast and were requested to refrain from strenuous physical activity in the 24 hours prior to testing.

The study was approved by the Australian Catholic University Human Research Ethics Committee (V2009-91), and participants provided written informed consent.

Cardiometabolic risk factors

A range of clinical characteristics were assessed to profile the population. Body mass was measured to the nearest 0.1 kg (Tanita, Tokyo, Japan). Height was measured to the nearest 0.1 cm (Seca, Germany). Body mass index (BMI) was subsequently calculated as weight [kg]/height [m^2] (World Health Organisation, 2000). Waist circumference and hip circumference were measured (Alberti et al., 2009) to the nearest 0.1 cm, with the average of two measurements reported. Measurements relating to waist circumference including, waist-to-hip ratio (WHR), and waist-to-height ratio (WHtR) were also calculated. Values of ≥ 0.8 for WHR (Dalton et al., 2003; World Health Organisation, 2000) and 0.5 for WHtR (Browning et al., 2010) have been considered indicative of increased CVD risk.

Blood pressure and resting heart rate were obtained with an automated digital sphygmomanometer (Dinamap, GE technology, USA). Fasting venous blood samples were analysed for the following biochemical parameters: triglycerides, total cholesterol, high-density lipoprotein (HDL), plasma glucose, insulin and high sensitivity C-reactive protein (hs-CRP). Insulin resistance (IR) was estimated by the homeostasis model assessment (HOMA-IR) (Matthews et al., 1985), with values > 2.5 considered indicative of IR (Jensterle et al., 2008). For hs-CRP, a value of > 3.0 $mg \cdot l^{-1}$ was considered high CVD risk (Pearson et al., 2003).

A submaximal cycle ergometer test (Golding et al., 1989) was used to predict maximal oxygen uptake (estimated VO_{2max}) by extrapolating heart rate against work rate (W) on a regression analysis to estimate maximal aerobic capacity. Estimated VO_{2max} was indexed for body mass to provide a relative measurement. Participants self-reported habitual weekly physical activity levels.

Echocardiography examination

Participants underwent a standard two-dimensional (2D) transthoracic echocardiography examination for the assessment of both global and regional ventricular function in accordance with the recommendations of the American Society of Echocardiography (R. M. Lang et al., 2005). Image acquisition was performed by the same experienced operator using a commercially available ultrasound (Vivid *i*, GE Healthcare, Horten, Norway) with a 3.5 MHz phased-array transducer. Participants were examined in the left-lateral decubitus position in a

dark room and connected to a 3-lead ECG. A minimum frame rate of 70 Hz was used when acquiring gray-scale cine-loops. Digital data were stored for subsequent off-line analyses with specific software (EchoPAC v108, GE Medical Systems, Horton Norway) by an observer blinded to group assignment. All reported measurements were averaged from three consecutive cardiac cycles.

M-mode measurements were obtained in the parasternal long-axis view for the quantification of cardiac chamber size and ventricular mass, using the Penn-Cube method (Devereux et al., 1984) and indexed for height (Cornell adjustment). LV volumes and ejection fraction were quantified using a Simpson's bi-plane method.

Pulsed-wave Doppler-derived transmitral inflow velocities were obtained from the apical four-chamber view with the sample volume at the tips of the mitral leaflets. Early-diastolic (*E*), *E*-wave deceleration time, late-diastolic (*A*) waves and the *E/A* ratio were calculated. Isovolumetric relaxation time (IVRT) was obtained from pulse-wave Doppler in the apical five-chamber view. Pulsed tissue Doppler Imaging (TDI) was used to measure mitral annular velocities during systole (S_m), early-diastole (E_m) and late-diastole (A_m). The S_m, E_m, and A_m are means of four sites at the mitral annulus from apical 4-chamber (septal, lateral) and 2-chamber views (inferior, anterior). The E/E_m ratio, recorded from the mitral annulus lateral wall, was used as an index of LV diastolic filling pressure.

STE analysis of myocardial wall motion was performed using frame-by-frame tracking of natural acoustic markers known as "speckles" in a region of interest from greyscale images. Using proprietary software (EchoPAC v108, GE Medical Systems, Horton Norway), endocardial borders were manually traced and the region of interest was adjusted to include all of the myocardium. Results were expressed as the average from all segments but strain and SR data was excluded if there were more than two segments in which tracking was inadequate (assessed visually). Both systolic and diastolic strain rate (SRs and SRe, respectively) were calculated in the longitudinal and circumferential axis of the LV. The values from circumferential apical and basal views were averaged. Twist (calculated as the difference between basal and apical rotations), twist rate, untwist rate, and apical and basal rotational mechanics of the LV, were calculated. To allow for inter-participant differences in heart rate, customised software (Scilab 4.1, Avignon University, Avignon, France) was used to normalise time sequence as a percentage of systolic duration.

Statistics

Data were analysed using IBM SPSS Statistics, Version 20 for Windows (SPSS Inc, Chicago IL). Normal distribution of qualitative variables was checked using skewness, kurtosis and the Shapiro-Wilk test (Peat & Barton, 2005). Log transformation was used where appropriate. Variables were analysed as continuous variables, and are presented as mean (standard deviation). Group comparisons were performed using independent t-tests. Additionally, Hedge's *g* was used to calculate magnitudes of differences, with an effect size of ≥ 0.2 considered small, ≥ 0.5 considered medium, and ≥ 0.8 considered large (Cohen, 1988). Pearson's *r* correlation coefficient analysis was used to identify associations between cardiometabolic risk factors and morphological, global function and myocardial measures. An alpha level of $p < 0.05$ was considered statistically significance.

Intra and inter-observer reproducibility were estimated for major cardiac variables in randomly selected participants (conventional echocardiography and TDI, n=10; STE, n=20) in order to demonstrate the reproducibility of off-line analyses. Variables were evaluated twice by the same observer, and once more by another experienced observer, both blinded to participant details.

Results

Cardiometabolic risk factors

Table 6.1 summarises the clinical characteristics of the two groups. No differences were found for height, blood pressure, triglycerides, HDL-cholesterol, or resting heart rate when comparing women with abdominal obesity (WC 92.5 ± 10.6 cm, range 80.5 -123.0 cm, age 22.4 ± 3.5 y) and the control group (WC 72.5 ± 4.8 cm, range 63.6 – 77.8 cm, age 20.0 ± 0.7 y). Independent of obesity status, all participants were eumennorehic. Additionally, the young women with abdominal obesity in this study can be described as non-diabetic, non-insulin resistant and normotensive. When anthropometric measures were compared with controls, women with abdominal obesity had greater body mass, BMI, waist circumference, hip circumference, WHR and WHtR ($P < 0.001$). The average BMI for women with abdominal obesity placed them in the obese category and average WHR and WHtR placed them in an increased CVD risk range. Women with abdominal obesity also had greater elevated fasting

insulin, HOMA-IR, and hs-CRP ($P < 0.05$) than the control group. However, the mean HOMA-IR value remained within normal range. In contrast, the elevated hs-CRP in the women with abdominal obesity was deemed 'high' risk (> 3.0 mg·l^{-1}). Pearson's *r* correlation showed a strong relationship between abdominal obesity and both fasting insulin ($r = 0.521$, $P < 0.01$) and HOMA-IR ($r = 0.455$, $P < 0.01$), without a significant relationship with hs-CRP. Relative to controls, women with abdominal obesity performed 63% less weekly physical activity ($P < 0.001$) and had reduced aerobic capacity (predicted VO_{2max}). Perhaps surprisingly, control participants had slightly higher fasting glucose and total cholesterol ($P < 0.05$) than women with abdominal obesity but notably values remained within normal ranges.

Table 6.1. Cardiometabolic risk factors in participants with and without abdominal obesity.

	Controls WC < 80 cm (n = 33)	Abdominal obesity WC ≥ 80 cm (n = 39)	*P*-value	Hedge's *g* Effect size	Power (1-ß)	Mean difference (95% CI)
Anthropometric assessment						
Body mass (kg)	61.6 ± 7.4	88.2 ± 19.6	<0.001*	1.72	1.0	26.6 (19.7, 33.4)
Stature (cm)	1.7 ± 0.1	1.7 ± 0.1	0.44	0.00	-	0.0 (-0.04, 0.02)
BMI ($kg \cdot m^{-2}$)	22.1 ± 2.5	31.9 ± 6.0	<0.001*	2.05	1.0	9.8 (7.6, 11.9)
Waist circumference (cm)	72.5 ± 4.8	92.5 ± 10.6	<0.001*	2.34	1.0	20.0 (16.2, 23.8)
Hip circumference (cm)	96.9 ± 5.9	115.2 ± 12.5	<0.001*	1.80	1.0	18.3 (13.8, 22.8)
Waist-to-hip ratio	0.75 ± 0.03	0.80 ± 0.04	<0.001*	1.38	1.0	0.05 (0.03, 0.07)
Waist-to-height ratio	0.43 ± 0.03	0.56 ± 0.06	<0.001*	2.64	1.0	0.13 (0.10, 0.14)
Blood Pressure evaluation						
Systolic BP (mmHg)	115.6 ± 8.3	119.5 ± 9.9	0.08	0.42	-	3.9 (-0.5, 8.1)
Diastolic BP (mmHg)	67.8 ± 7.5	65.9 ± 7.2	0.26	0.26	-	-1.9 (-5.4, 1.5)
Blood biochemistry						
Fasting glucose ($mmol \cdot L^{-1}$)	4.9 ± 0.4	4.6 ± 0.5	0.01*	0.65	0.75	0.3 (-0.5, -0.1)
Triglycerides ($mmol \cdot L^{-1}$)	1.1 ± 0.3	1.2 ± 0.4	0.31	0.28	-	0.1 (-0.1, 0.3)
HDL cholesterol ($mmol \cdot L^{-1}$)	1.4 ± 0.3	1.7 ± 0.5	0.13	0.70	-	0.3 (0.1, 0.5)
Total cholesterol ($mmol \cdot L^{-1}$)	4.7 ± 1.0	4.3 ± 0.5	0.01*	0.51	0.60	-0.4 (-0.8, 0.1)
Fasting insulin ($mU \cdot L^{-1}$)#	5.9 ± 2.6	8.9 ± 4.6	0.01*	0.78	0.94	3.0 (1.2, 4.7)
HOMA-IR#	1.3 ± 0.6	1.8 ± 1.0	0.03*	0.59	0.75	0.5 (0.1, 0.9)
hs-CRP ($mg \cdot L^{-1}$)#	1.7 ± 1.6	3.3 ± 2.9	0.01*	0.66	0.75	1.6 (0.5, 2.7)
Fitness variables						
Resting heart rate (bpm)	73.9 ± 12.6	71.9 ± 12.1	0.49	0.16	-	2.0 (-7.9, 3.8)
Estimated VO_{2max} ($mL \cdot kg^{-1} \cdot min^{-1}$)	40.7 ± 7.8	30.1 ± 9.1	<0.001*	1.23	1.0	10.6 (-14.6, -6.5)
Physical activity ($min \cdot wk^{-1}$)#	302 ± 201	110 ± 82	<0.001*	1.28	1.0	192 (-267, -116)

*Data expressed as mean ± SD. WC: waist circumference, BMI: body mass index, BP: blood pressure; HDL: high-density lipoprotein, HOMA-IR: homeostatic model assessment of insulin resistance, hs-CRP: high sensitivity C-reactive protein, CI: confidence interval. #Data are log transformed. * P ≤ 0.05. An effect size of ≥ 0.2 was considered small, ≥ 0.5 was considered medium, and ≥ 0.8 was considered large (Vincent, 1995).*

Cardiac morphology and function

Despite similar LV ejection fractions, women with abdominal obesity displayed greater LA dimensions than controls ($P < 0.05$). A modest correlation was also observed between abdominal obesity and the internal diameter of the LA ($r = 0.437$, $P < 0.01$). In contrast, no differences were found between groups for LV structural parameters such as mass, internal dimensions, or wall thickness (Table 6.2).

Women with abdominal obesity displayed impaired LV diastolic parameters, including greater decreases in transmitral *E*, E_m, and greater increases in E/E_m, IVRT and DT ($P < 0.05$) than controls. Additionally, systolic tissue velocity (S_m) was reduced in women with abdominal obesity ($P < 0.05$) relative to controls. Although these values remained within ranges that would be considered "normal" in clinical settings, statistically significant differences were supported by moderate effect sizes. No differences were found between groups for *E/A* ratio, and parameters of late-diastolic function including transmitral *A*, and A_m.

Table 6.2. Cardiac morphology and function parameters measured from conventional and tissue Doppler imaging echocardiography in participants with and without abdominal obesity.

	Control WC < 80 cm (n = 33)	Abdominal obesity WC ≥ 80 cm (n = 39)	*P*-value	Hedge's *g* Effect size	Power (1-ß)	Mean difference (95% CI)	Reference values/ranges
Cardiac Morphology							
LA diameter (mm)	30.2 ± 4.3	32.7 ± 4.6	0.02*	0.55	0.60	2.5 (0.04, 0.5)	27.0 to 38.0[d]
LV mass (g)	148 ± 31	149 ± 40	0.98	0.03	-	1.0 (-17.8, 18.1)	103.9 ± 28.3[c]
LV mass indexed ($g \cdot m^{-2.7}$)	37.5 ± 7.4	40.5 ± 7.0	0.11	0.41	-	3.0 (-0.7, 6.6)	-
LVED diameter (mm)	44.4 ± 4.5	44.0 ± 3.8	0.71	0.09	-	0.4 (-0.2, 0.2)	43.0 ± 4.1[c]
LVES diameter (mm)	28.8 ± 3.5	29.4 ± 4.4	0.55	0.15	-	0.6 (-0.1, 0.2)	28.8 ± 4.3[c]
LV PW thickness (mm)	9.7 ± 1.4	10.3 ± 1.7	0.12	0.38	-	0.6 (-0.02, 0.1)	8.5 ± 1.5[c]
IVS thickness (mm)	10.0 ± 1.4	10.5 ± 1.7	0.21	0.31	-	0.5 (-0.03, 0.1)	8.2 ± 1.5[c]
LV shortening fraction (%)	34.9 ± 5.7	32.7 ± 6.9	0.17	0.34	-	-2.2 (-5.3, 1.0)	-
Cardiac Function							
LV ejection fraction (%)	64.0 ± 8.1	61.0 ± 10.2	0.09	0.32	-	-3.0 (-0.6, 6.7)	59.2 ± 4.6[a]
Stroke volume (ml)	58.8 ± 16.0	53.7 ± 12.7	0.16	0.35	-	-5.1 (-12.3, 2.0)	-
E velocity ($cm.s^{-1}$)	96.7 ± 13.0	87.0 ± 14.7	0.01*	0.70	0.87	-9.7 (-0.2, -0.03)	72.0 ± 12.0[a]
A velocity ($cm.s^{-1}$)	44.7 ± 12.0	42.4 ± 11.0	0.40	0.20	-	-2.5 (-0.08, 0.03)	40.0 ± 8.0[a]
E/A ratio	2.3 ± 0.7	2.2 ± 0.6	0.44	0.15	-	-0.1 (-0.4, 0.2)	1.85 ± 0.38[a]
Deceleration time (ms)	174.4 ± 34.9	209.0 ± 29.8	<0.001*	1.06	1.00	34.6 (19.2, 50.1)	166.0 ± 14.0[b]
IVRT (ms)	78.4 ± 9.9	85.8 ± 10.7	0.01*	0.71	0.87	7.4 (2.5, 12.4)	77.9 ± 8.8[a]
S_m velocity ($cm.s^{-1}$)	10.4 ± 1.3	9.0 ± 1.4	<0.001*	0.94	0.99	-1.4 (-0.02, -0.01)	-
E_m velocity ($cm.s^{-1}$)	17.2 ± 2.3	14.6 ± 2.7	<0.001*	1.10	1.00	-2.6 (-0.04, -0.01)	14.9 ± 2.0[e]
A_m velocity ($cm.s^{-1}$)	6.9 ± 1.2	6.9 ± 1.1	0.99	0.00	-	0.0 (-0.01, 0.01)	-
E/E_m lateral wall	4.9 ± 0.7	5.4 ± 1.4	0.04*	0.47	0.60	0.5 (0.02, 1.1)	5.5 ± 1.0[e]

*Data expressed as mean ± SD. LA: left atrium, LV: left ventricle, LVED: left ventricular end-diastolic, LVES: left ventricle end-systolic, PW: posterior wall, IVS: inter-ventricular spetum, IVRT: isovolumic relaxation time, CI: confidence interval. S_m, E_m, & A_m are means of four sites at the mitral annulus from apical 4-chamber (septal, lateral) and 2-chamber views (inferior, anterior). #Data are log transformed. * $P \leq 0.05$. An effect size of ≥ 0.2 was considered small, ≥ 0.5 was considered medium, and ≥ 0.8 was considered large (Vincent, 1995). Reference values/ranges: [a]adults 25-32 y (Takahashi et al., 2010); [b]adults 21-40 y(Nagueh et al., 2009); [c]women 20-40 y (Kou et al., 2014); [d]adults 20-60 y (Roberto M Lang et al., 2015); [e]adults 20-40 y (L. Caballero et al., 2015).*

Myocardial deformation and mechanics

Women with abdominal obesity had lower longitudinal strain and diastolic SR ($P < 0.05$) than controls (Table 6.3). Circumferential strain and SR parameters were not different between the groups with and without abdominal obesity. No differences were found between groups in apical and basal rotation, as well as resultant twist. Similarly, twist and untwist rate did not differ between women with abdominal obesity and controls.

Table 6.3. Myocardial deformation and mechanics measured using speckle tracking imaging echocardiography in participants with and without abdominal obesity.

	Control **WC < 80 cm (n = 33)**	**Abdominal obesity** **WC ≥ 80 cm (n = 39)**	***P*-value**	**Hedge's *g* Effect size**	**Power (1-ß)**	**Mean difference (95% CI)**	**Reference values/ranges**
Myocardial Deformation							
L Strain (%)	-17.6 ± 3.0	-16.1 ± 2.1	0.05*	0.55	0.60	-1.5 (-0.01, 3.0)	-18.6 ± 0.1[b]
L Systolic SR (strain.s^{-1})	-0.9 ± 0.2	-0.9 ± 0.1	0.18	0.00	-	0.0 (-0.03, 0.1)	-1.10 ± 0.01[b]
L Diastolic SR (strain.s^{-1})	1.4 ± 0.3	1.1 ± 0.3	0.01*	0.87	0.94	-0.3 (-0.5, -0.1)	1.02 ± 0.01[b]
C Strain (%)	-20.8 ± 2.4	-19.8 ± 2.9	0.15	0.37	-	-1.0 (-0.4, 2.3)	-20.9 to -27.8[c]
C Systolic SR (strain.s^{-1})	-1.3 ± 0.2	-1.3 ± 0.2	0.19	0.00	-	0.0 (-0.03, 0.1)	-
C Diastolic SR (strain.s^{-1})	2.0 ± 0.3	1.8 ± 0.3	0.08	0.66	-	0.2 (-0.3, 0.02)	-
Myocardial Mechanics							
Apical rotation (°)	4.6 ± 1.8	4.7 ± 1.9	0.78	0.05	-	0.1 (-0.8, 1.1)	8.9 ± 3.5[a]
Basal rotation (°)	-5.6 ± 2.3	-5.8 ± 2.3	0.85	0.09	-	0.2 (-1.5, 1.3)	-4.8 ± 2.5[a]
Twist (°)	6.2 ± 2.7	7.2 ± 3.1	0.26	0.34	-	1.0 (-0.8, 2.8)	-
Twist rate (°.s^{-1})	68.8 ± 22.1	70.3 ± 18.8	0.80	0.07	-	1.5 (-10.4, 13.4)	62.5 ± 17.4[a]
Untwist rate (°.s^{-1})[#]	-76.8 ± 39.1	-62.2 ± 18.8	0.11	0.48	-	-14.6 (-2.8, 32.0)	-82.3 ± 32.8[a]

Data expressed as mean ± SD. LV: left ventricle, L: longitudinal, C: circumferential, SR: Strain rate, CI: confidence interval. Circumferential (average of apical and basal views). [#]*Data are log transformed.* [*]*P ≤ 0.05. Nb. four data sets were excluded from STE analysis in the abdominal obesity group (n=35) due to poor image quality. An effect size of ≥ 0.2 was considered small, ≥ 0.5 was considered medium, and ≥ 0.8 was considered large (Vincent, 1995). Reference values/ranges:* [a]*young adults 25-32 y (Takahashi et al., 2010);* [b]*adults 18-80 y, data expressed as mean ± standard error (Marwick et al., 2009);* [c]*adults 47± 11 y (Yingchoncharoen, Agarwal, Popović, & Marwick, 2013).*

Reliability

Intra and inter-observer CVs for selected conventional echocardiographic and TDI indices were: 1.9% and 1.6%, respectively for *E* velocity; 2.5% and 1.8%, respectively for *A* velocity; 2.2% and 4.0%, respectively for Septal E_m; 1.5% and 4.2%, respectively for Septal A_m, and 1.4% and 2.4%, respectively for Septal S_m. Additionally, intra and inter-observer CVs for select STE indices were: 5.9% and 5.1%, respectively for longitudinal strain; 4.3% and 7.8%, respectively for longitudinal diastolic SR; 4.7% and 5.5%, respectively for circumferential strain; 7.0% and 11.5%, respectively for apical rotation; 6.5% and 10.0%, respectively for basal rotation, and 9.2% and 10.0% respectively for LV twist. Previous research reports an intra and inter-observer CV of 7.1% and 8.1%, respectively for global longitudinal strain and, 7.5% and 10.2%, respectively for circumferential strain (K. A. Marcus et al., 2011). A CV of 1.26% in WC measures was also reported in 20 participants.

Discussion

This cross-sectional study used a combination of cardiometabolic risk factors and comprehensive measures of cardiac morphology and function, myocardial deformation and mechanical indices in young women with and without abdominal obesity. We showed that young women with relatively moderate abdominal obesity displayed subtle early myocardial impairment identified by traditional and advanced echocardiography measures compared with controls. The value of using both traditional echocardiography methods (conventional and TDI markers) and more advanced techniques (STE) lies in a comprehensive description of some measures of cardiac morphology and function that may be associated with obesity in young females. This data advances the understanding of CVD risk factors in a population which is currently under-represented in the literature. Specifically, our findings extend existing knowledge by demonstrating that young women with moderate abdominal obesity displayed some markers of (1) sub-clinical cardiac abnormalities that may have been associated with remodelling, and (2) myocardial dysfunction. We can confirm, for the first time in this population, the presence of subtle early myocardial dysfunction in the

longitudinal axis but preserved circumferential deformation and twist mechanics - identified using STE - of young women with abdominal obesity.

Effects of obesity on sub-clinical cardiac abnormalities in cardiac morphology

Women with abdominal obesity had larger LA dimensions than controls but otherwise cardiac morphology were similar. The LA enlarges in response to increases in LV pressure due to impaired LV filling, making it a useful adjunct in the assessment of chronic diastolic dysfunction (Gottdiener et al., 2004). Prior studies have found an association between LA dimensions and obesity in females. Specifically, abnormalities in LA diameter have been linked to obesity in a group of young women (29 ± 10 years, n=48) with isolated obesity (Pascual et al., 2003), in a population of slightly older (32 ± 4 years) obese young adults (Peterson, Waggoner, et al., 2004), and in obese middle-aged adults (Orhan et al., 2010; Wong et al., 2004), with normal EF. In light of this, the findings form our study is potentially of even greater concern in a population of women who were notably younger and had milder obesity than previously reported studies. Mechanisms behind this link may occur as a consequence of the hemodynamic changes associated with obesity (Wong & Marwick, 2007a). LV structure was similar between groups, as were the load -dependent echocardiographic indices of systolic function. Similarly, no between-group differences were observed for LV end-systolic and LV end-diastolic diameters.

Effects of obesity on sub-clinical cardiac abnormalities in cardiac function

Obesity impairs cardiac loading (Wong et al., 2004). In our study, conventional load-dependent parameters of LV diastolic function, including reduced mitral inflow velocity (*E*-wave), and indicators of filling and relaxation, including elevated *E*/$E_{m,}$ and elongated IVRT, and elongated DT (a measure of LV stiffness), were observed more frequently in women with abdominal obesity than controls. These observations are supported by previous literature on diastolic dysfunction, suggesting underlying abnormalities in relaxation and/or myocardial compliance, in obese individuals without hypertension or cardiac hypertrophy (Crendal et al., 2013). However, this is the first study to identify diastolic impairment in such a young group of females in the absence of cardiac ventricular hypertrophy and hypertension.

In the present study, women with abdominal obesity also demonstrated attenuated TDI-derived velocities including significantly lower systolic (S_m) and early-diastolic (E_m) function than the control group. The TDI echocardiography parameters of S_m, E_m and E/E_m have established independent prognostic value in a wide variety of cardiac disorders and are powerful predictors of cardiac mortality (Wang et al., 2003). In the present study, we reported decreased S_m indicating systolic dysfunction in women with abdominal obesity Additionally, low E_m values may be indicative of abnormal LV relaxation, has previously been reported to correlate with IVRT. In our study, IVRT was elongated and E_m reduced, albeit only minimal, which may link to early onset of cardiac dysfunction in this young population. Despite significant differences between groups, women with abdominal obesity displayed normal "within range" LV filling pressure, indicated by the E/E_m ratio being ≤ 8 (Nagueh et al., 2009). Thus, early but not late diastolic dysfunction was associated with obesity among the young women in the present study.

The negative impact of obesity on early diastolic function has been reported but, again, these results were found in older, less healthy adults. Also, in a group of 29 middle-aged adults (49 ± 8 years) with isolated obesity (average BMI of 37.2 ± 2.7 kg/m^2), participants had reduced E_m velocity, and significantly increased IVRT, DT, and E/E_m ratio than 20 aged-matched non-obese controls (Orhan et al., 2010). It is again striking that we identified similar diastolic changes to those observed in this older mixed gender population of more profoundly obese participants who also had greater LV mass. It may be possible that the observed dysfunction is part of a disease progression from subtle myocardial dysfunction and atrial remodelling to also eventually involve structural remodelling of the ventricles. Longitudinal studies are required to investigate this question further. In addition, a focus on weight reduction, including the prevention and early detection of cardiometabolic risk factors in young obese adults, might be advantageous for inducing positive reversible changes in cardiac morphology and function.

Effects of obesity on myocardial dysfunction via deformation

Non-invasive ultrasound techniques such as conventional and TDI echocardiography have a major role in the diagnosis and management of CVD. An inability to accurately differentiate actively contracting myocardium from passive myocardial motion is one of the principle limitations of conventional and TDI echocardiography in the assessment of LV structure and

function (Anderson, 2007). The innovation of STE enables unique acoustic speckles within the myocardium to be tracked thereby permitting analysis of the relative regionals of the myocardium, thus separating deformation from passive motion (Brugger et al., 2014). In some settings, STE has enabled early diagnosis of systolic and diastolic dysfunction, even when conventional and TDI echocardiography parameters of LV function remain within normal range (Di Bello et al., 2013; Nagueh et al., 2009). In our study, we confirmed and extended previous data by demonstrating that *young* women with abdominal obesity displayed impaired longitudinal myocardial dysfunction, but preserved circumferential function, compared with the control group. While the exact mechanisms behind this remain unclear, the finding is consistent with previous studies in older, disease-free populations (Crendal et al., 2013). The reduced longitudinal strain and SR in our women with abdominal obesity highlight early diastolic and systolic dysfunction that could be explained by depressed relaxation and compromised contractile properties of myocardial fibres. Although measures of deformation are *less* load dependent than some traditional parameters, it is clear that strain and SR are still influenced by loading conditions and it is difficult to completely isolate change in contractility from the aforementioned change in load (Burns et al., 2010). It is possible that increases in ventricular and atrial filling pressure are both a cause and consequence of reduced myocardial deformation.

The reduced LV strain observed in our young women with abdominal obesity has been reported previously. A study of obese middle-aged women (n=663, 47.8 ± 13.6 years, waist circumference 88.5 ± 11.7 cm) showed a strong relationship between elevated waist circumference and an undesirable reduction in LV strain (Dalen et al., 2011). Similarly, other research has shown reduced strain indices and reduced *E* velocity in 26 middle-aged women (49 ± 8 years) with isolated obesity (WC 105 ± 7.0 cm), compared with 18 age-matched non-obese controls (Orhan et al., 2010). The identification of these pre-clinical myocardial abnormalities in obese young women provides a marker which could be followed through treatment interventions with the logical hypothesis that weight reduction and increased physical activity may attenuate further decline in myocardial function.

Effects of obesity on myocardial dysfunction via mechanics

Speckle tracking echocardiography can also be used to assess myocardial mechanics such as twist and twist rate which describe the torsional rotation of the heart produced by the helical

structure in which the myocardial fibres are arranged (Sengupta et al., 2007; Wong, Leano, et al., 2006). Twist and the resulting rate of untwist have been promoted as sensitive determinants of cardiac performance, particularly during diastolic relaxation and filling (Beladan, Calin, Rosca, Ginghina, & Popescu, 2014). However, their acceptance in clinical practice has been limited by reproducibility issues (Beladan et al., 2014). Therefore, the improvements in sensitivity provided by deformation and the twist-based mechanical actions of the LV remain unclear.

Nevertheless, the role of LV twist as a major contributor to LV filling has generated much interest (Sengupta, Tajik, Chandrasekaran, & Khandheria, 2008). For example, reductions in diastolic and systolic LV twist as well as basal rotation showed a stronger correlation with waist circumference ($r=-0.24$, $P<0.05$) in obese middle-aged (44 ± 10 years) participants compared with non-obese controls (Wong, Leano, et al., 2006). Similarly, obese adolescents had more pronounced LV twist and greater apical rotation than lean controls, confirming the feasibility of detection in younger populations (Obert et al., 2012). It was postulated that, even in adolescent populations, the greater LV twist in the obese individuals could be viewed as a compensatory phenomenon for their depressed longitudinal function, critical for LV filling and ejection (Obert et al., 2012). However, previous LV myocardial mechanics in rotational indices of twist/untwist rates were not supported by the results from the present study. Variability may have limited accurate conclusions from these results, with the coefficient of variability for intra-and inter-observer differences averaging around 9.6%. Discrepancies in twist mechanics between obese and control could also be related to difficulties in imaging capacities, particularly for apical rotation (Beladan et al., 2014).

Obesity is strongly associated with insulin resistance, impaired glucose tolerance and diabetes. The metabolic changes, as well as activation of the sympathetic nervous system and renin-angiostensin-aldosterone system, provide possible links between obesity and myocardial dysfunction (Wong & Marwick, 2007a). In our study, changes in cardiac and myocardial parameters were accompanied by some but not all biological markers in women with abdominal obesity compared with non-obese controls. However, the correlations between significant markers of TDI and STE with biomarkers of CVD risk were only moderate. We propose that obesity is directly related to a sequence of yet to be clarified early markers of cardiac risk.

Study limitations

The cross-sectional design of this study means that we cannot address the intriguing hypotheses regarding changes in myocardial function over time and the resulting clinical consequences. However, this novel demonstration of significant myocardial dysfunction in a young population provides necessary motivation for longitudinal interventional studies. Moreover, results are specific to Caucasian women at a tertiary institution; however, the selected population could also be interpreted as truly representative of a relatively educated group of young women in Australia. Also, ultrasound acquisition and analyses are dependent on operator skill. Whilst this is a potential explanation of the failure to demonstrate differences in some myocardial mechanical indices, the reliability reported for the current study was similar to previously published work. Additionally, we did not assess right ventricular function or myocardial reserve during exercise studies and it is possible these specialised measures may have corroborated our findings of diminished cardiac performance (La Gerche, Claessen, & Burns, 2013). Finally, central fat distribution in these young women could have been more ideally measured using more precise estimations from devices such as MRI and dual energy x-ray absorptiometry.

Conclusion

Young women with moderate abdominal obesity, measured by waist circumference, displayed larger left atrial dimensions and reduced measures of diastolic and systolic myocardial function, compared with non-obese controls. Low grade systemic inflammation was also present in young women with abdominal obesity. These findings may provide important insights into the links between obesity and the increased incidences of cardiometabolic disease. Furthermore, our data provides additional motivation for prospective studies which assess whether lifestyle interventions may attenuate the increased risk of cardiovascular morbidity.

Chapter 7. Effects of a multi-disciplinary lifestyle intervention on cardiometabolic risk factors in young women with abdominal obesity: A randomised controlled trial.

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Abstract

Background: Young women are under-represented in chronic disease research, with interventions for obesity and other CVD risk factor generally targeting older adults. Therefore, this study aimed to assess the impact of a 12 week multi-disciplinary lifestyle intervention on reducing cardiometabolic risk in sedentary Caucasian women with abdominal obesity.

Methods: Women aged 18-30 y with abdominal obesity [waist circumference (WC) ≥ 80 cm] participated in a 12 week lifestyle intervention. Using a randomised controlled design, an intervention group undertook physical activity, nutrition education and cognitive behavioural therapy (n = 26) alongside a wait-list (delayed-start) control group (n = 17). Both groups completed anthropometric, biochemical, nutrition and fitness testing, at pre-intervention/pre-control (0 week) and post-intervention/post-control (12 week), and with intervention participants only, completing follow-up testing at 24 weeks. Physical activity and dietary behaviour were also documented at each time-point

Results: Results from a linear mixed model showed no between-group differences other than increased physical activity (minutes/week) in the intervention group following the intervention. In the intervention group alone, positive within-group changes were observed in WC, waist-hip-ratio (WHR), waist-height-ratio (WHtR), resting heart rate, blood pressure, predicted VO2max, and total energy intake, with most of these changes maintained at 12 weeks after intervention cessation. Similar within-group improvements in WC, WHR, WHtR, and systolic blood pressure were observed in control participants, but no changes were detected in their self-reported markers of nutrition and physical activity.

Conclusions: CVD risk factors were decreased as a result of a lifestyle intervention in young women with abdominal obesity. It is difficult to describe observations in the control group without a greater understanding of the behaviour of wait-list participants. New thinking for control group designs in studies with Generation Y women is recommended.

Trial registration: Australian New Zealand Clinical Trials Registry (anzctr.org.au) Identifier: ACTRN12612001017819

Key words: Female, waist circumference, abdominal obesity, physical activity, sustainability, cardiovascular disease, control group, multi-disciplinary.

Background

Cardiovascular disease (CVD) represents a major health threat to women worldwide (World Health Organisation, 2006), consequently placing substantial burden on public health systems. Most risk factors for CVD, including overweight/obesity and physical inactivity, can be modified through lifestyle interventions (Irving et al., 2008; Kemmler et al., 2009). The rising prevalence of overweight and obesity is a worldwide concern among young women from developed and developing nations (Stewart et al., 2008). Currently, 51% of non-hispanic white American women aged 20-39 years are either overweight or obese (Flegal et al., 2012), while prevalences among women in the United Kingdom (Health and Social Care Information Centre, 2011), and Australia (Australian Bureau of Statistics, 2013) aged 25-34 years are 47% and 42%, respectively. An average weight gain of 6 to 12 kg between the ages of 20 to 30 years was noted in a large longitudinal study of women's health (Lucke et al., 2007), and this weight gain was more than for any other age group (Adamson et al., 2007; Lucke et al., 2007) . Concurrently, sedentary behaviour is increasing in young women (Cleland et al., 2011), with 85% of women aged 18-35 years reporting inactive lifestyles and decreased physical activity (Adamson et al., 2007). Among women, weight gain is not only a risk factor for CVD but increases the risk of the metabolic syndrome (Alberti et al., 2009), type 2 diabetes mellitus, depression, polycystic ovarian syndrome, infertility and adverse pregnancy outcomes (Emaus et al., 2008).

Despite global strategies for preventive health, there is poor understanding of early risk factors (cardiometabolic risk factors) in young women, and lifestyle interventions can improve health outcomes. Moreover, research assessing the effectiveness of weight management interventions specifically targeting young women is relatively recent (Hutchesson et al., 2013). Effective age-appropriate interventions for improving cardiometabolic risk are required for young adults born between 1977 to 1994 ("Generation Y") who share an urgency for feedback and success (Gokee-LaRose et al., 2009; Martin, 2005). The limited research that has been conducted in young overweight/obese women suggests they are difficult to recruit forweight management trials, with high attrition and limited success in losing weight compared with older populations (Griffin, O'Connor, Rooney, & Steinbeck, 2013).

Therefore, the primary aim of this study was to assess the feasibility of a lifestyle intervention for reducing CVD risk in young women with abdominal obesity, using a randomised controlled trial (RCT) design. Specifically, the RCT involved a 12-week multi-disciplinary program (physical activity, nutrition education, cognitive behavioural therapy) with Caucasian women aged 18 to 30 years, who shared the cardiometabolic risk factor of abdominal obesity [elevated waist circumference (WC) ≥ 80 cm]. A secondary aim was to examine the effectiveness of the intervention through an improved understanding of the sustainability of any changes. It was hypothesised that the lifestyle intervention would be effective (and sustainable) in reducing cardiometabolic risk in young women with abdominal obesity.

Methods

Ethics statement

The study protocol was approved by the Australian Catholic University Human Research Ethics Committee (V2009-91). Written informed consent was obtained, together with a cardiovascular risk assessment, from all participants prior to testing.

Participants

Sixty-two female Caucasian tertiary students at risk of CVD volunteered for this study. Data were collected between August 2010 and February 2012. Advertisements for recruitment specifically sought young women with abdominal obesity (WC ≥ 80 cm), who were also leading a sedentary lifestyle. Prospective participants were contacted and underwent an initial screening to confirm eligibility. Included were women aged 18 to 30 years; with a waist circumference ≥ 80 cm, and who were physically inactive (< 210 minutes per week of organised physical activity in the past six months). Exclusion criteria were being pregnant or breastfeeding; with a history of bariatric surgery; and/or having a diagnosis of liver or kidney disease; heart arrhythmia; insulin dependent diabetes mellitus; polycystic ovarian syndrome; thyroid abnormalities. All participants were non-smokers.

A power analyses estimated that 18 participants per group would provide the appropriate sample size to detect a large within-subject difference of 1.0 standard deviation ($\beta = 80\%$, alpha $P < 0.05$) in waist circumference from pre-intervention to post-intervention. To allow for 20% attrition, there was an attempt to recruit an initial sample size of 44 participants (22 per group). Figure 7.1 shows the participation of individuals in this study. From 62 women who responded to the recruitment strategy, 11 prospective participants were excluded, and a further 12 did not respond to preliminary contact. Therefore, 39 willing participants underwent pre-intervention/pre-control testing, after which group (block) randomisation occurred via a central administrator who allocated participants to either the intervention group or wait-list (delayed-start) control group. Block randomisation involved a block size of four participants thus allowing for six sequences for allocating participants to the two arms of the intervention (Peat & Barton, 2005). Group allocations occurred using identical opaque envelopes. Anecdotally, none of the participants assigned to the control group provided an immediately negative response. A wait-list control design was chosen because the investigators desired an ethically-sound model which provided all participants with access to the lifestyle intervention. Also, a wait-list control group was considered more appropriate than a passive control group given that health risks were comparable in both groups. After allocation to the wait-list control group for 12 weeks, only four participants continued into the lifestyle intervention phase. Participants were not blinded to their group, but where possible assessors were blinded to group allocation.

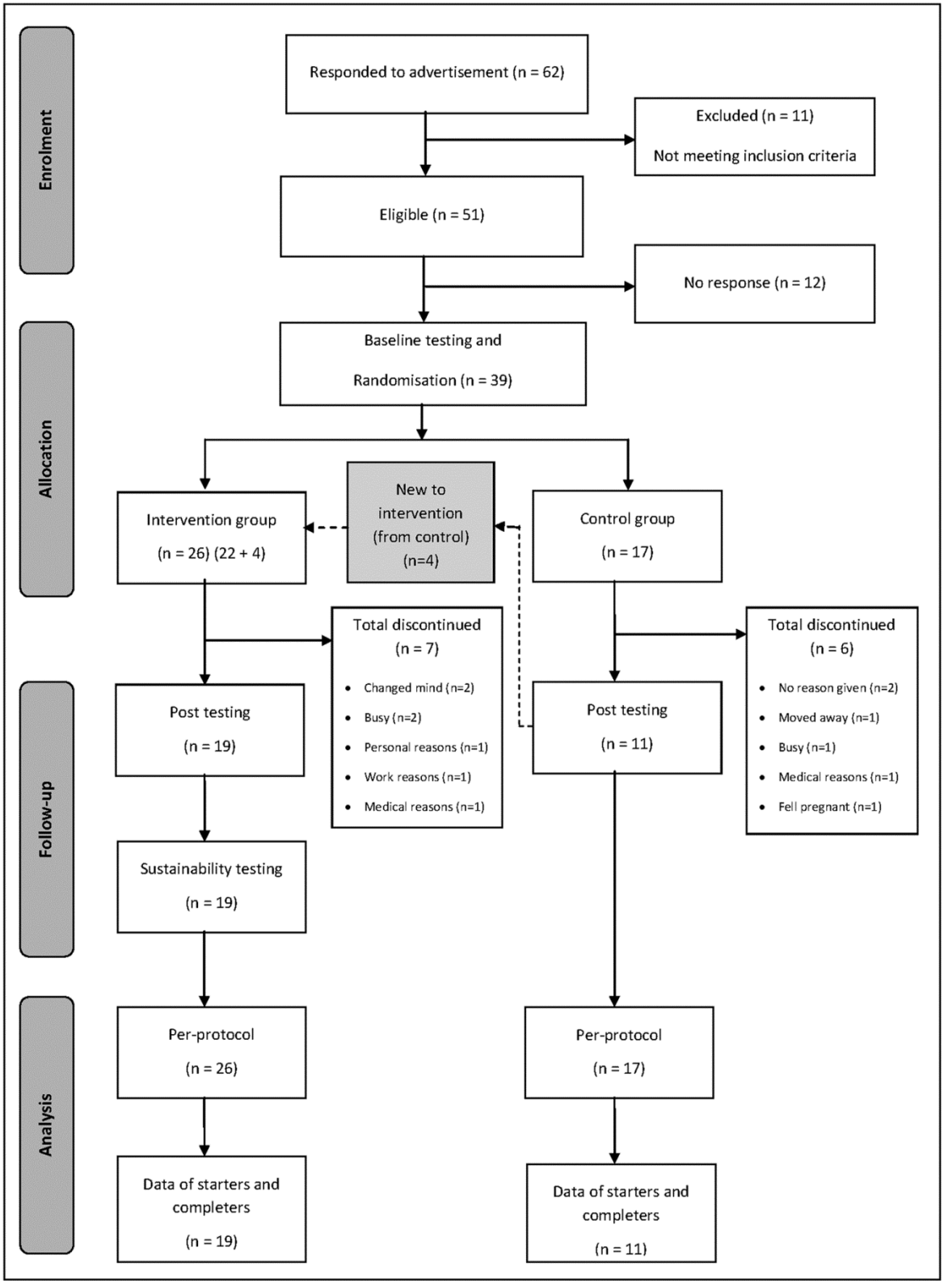


Figure 7.1. CONSORT participant flow-chart of intervention and control participants. (note: four participants from the wait-list control group continued into the intervention phase.

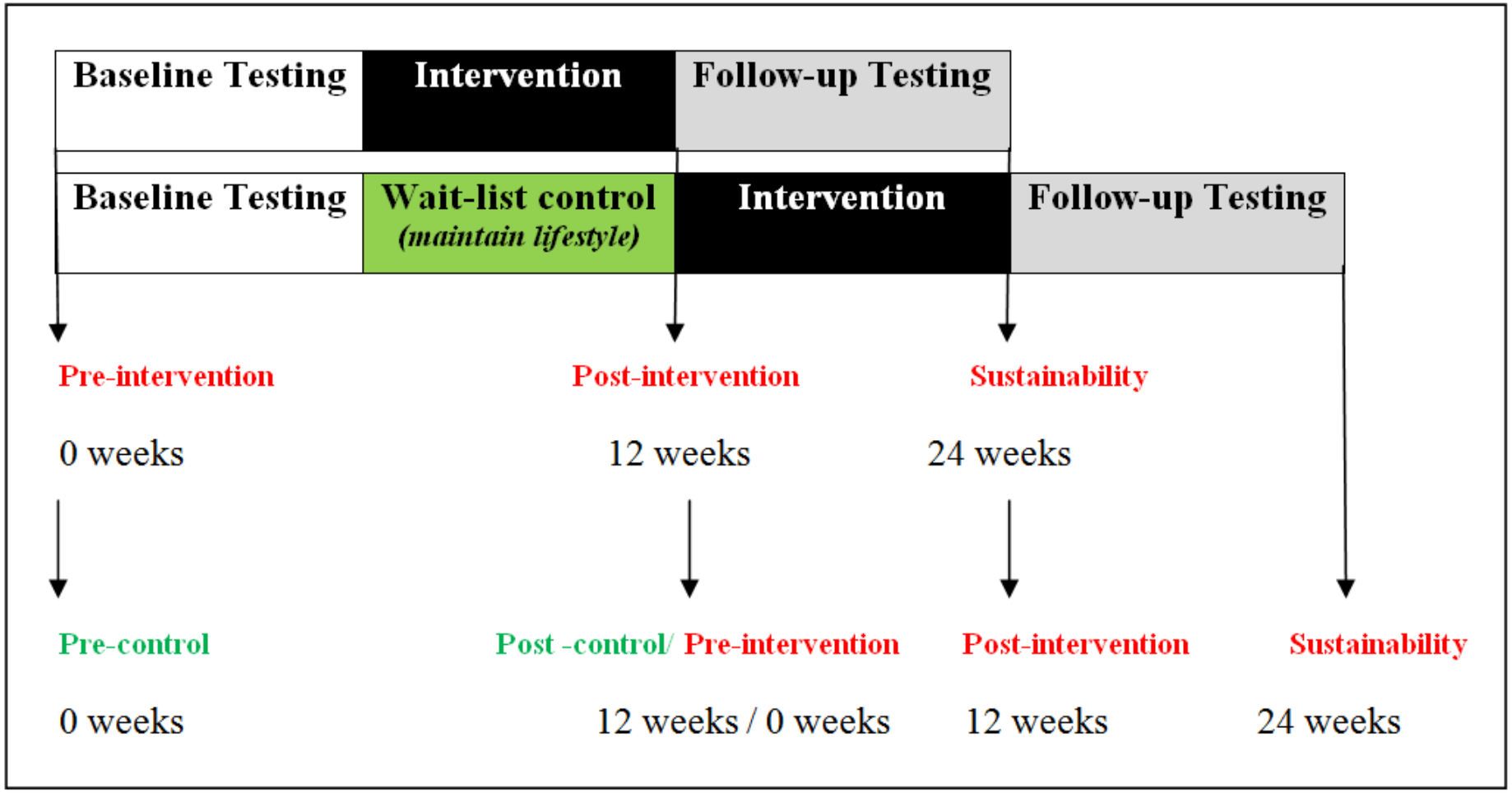
Experimental design

For each testing period (0, 12, 24 weeks), participants attended the laboratory on two occasions. They were requested to refrain from strenuous physical activity in the 24 hours prior to all laboratory sessions. The first visit required the participant to arrive in a fasted state and clinical testing lasted 75 minutes. The second visit of 60 minutes required participants to abstain from caffeine and alcohol for 12 hours. A time course of the experimental procedures in these testing sessions is presented in Figure 4.4.

For the intervention group, testing of cardiometabolic risk factors was performed at pre-intervention (0 weeks), post-intervention (12 weeks) and following a sustainability phase (24 weeks). The control group underwent testing at pre-control and post-control (12 weeks) time periods only (Figure 7.2). For all testing, measurements were taken at the same time of day (±2 hours) and by the same researcher. For participants in the control group, monthly contact was made to remind them of the control criteria. For the sustainability phase between post-intervention (12 weeks) testing and the following 12 weeks, a sustainability strategy was delivered electronically to the intervention group. This involved a fortnightly newsletter on healthy living tips from evidence-based resources.

Neither the investigators nor the participants were blinded to group allocation as this was considered impractical for the long-term investigation and limited members of the research team. However, to minimise contamination, participants in the intervention group were asked to refrain from disclosing their intervention experience to researchers assigned to data collection and/or analysis and to wait-list control participants. To further minimise bias, assessor blinding occurred within dietary measures and biochemical analyses. For the primary outcome variable of WC, measures were completed in duplicate with reported measures of reliability: coefficient of variation (CV), intraclass correlation coefficient (ICC) and measurement error (ME).

Figure 7.2. Timeline of testing for intervention and wait-list control participants



Testing measures

Survey data

A self-administered lifestyle survey was completed to provide data on (i) health status and medical conditions, (ii) nutrition (including alcohol consumption), and (iii) current physical activity habits. The lifestyle survey was developed specifically for the study and validated using the process of face validation (Gravetter & Forzano, 2012).

Anthropometric assessment

Body composition was assessed via waist circumference (WC), hip circumference, body mass index (BMI), and body mass. WC was measured to the nearest 0.1 cm in the horizontal plane at the level of the midpoint between the iliac crest and lower costal margin (Alberti et al., 2009) using a non-elastic measuring tape, with the average of two measures reported. For WC, CV = 1.26%, ICC (3, 1) = 0.986 and ME = 1.34%, which equates to an error range of ± 2.6 cm. Body mass was measured to the nearest 0.1 kg using digital scales (Tanita, Tokyo, Japan) with participants wearing light clothing and no footwear, and height was estimated to the nearest 0.1 cm using a wall-mounted stadiometer (Seca, Germany). BMI was calculated as weight (kg)/height (m^2), with overweight/obesity defined as BMI $\geq$ 25 $kg \cdot m^{-2}$ (World Health Organisation, 2006).

Metabolic syndrome markers and additional biochemical parameters

Metabolic syndrome was defined according to the most recent and unified criteria (Alberti et al., 2009), in which three of the following five markers were met: (1) waist circumference $\geq$ 80 cm, (2) serum triglycerides $\geq$ 1.7 $mmol \cdot l^{-1}$, (3) HDL-cholesterol <1.29 $mmol \cdot l^{-1}$, (4) systolic blood pressure (SBP) > 130 mmHg or diastolic blood pressure (DBP) > 85 mmHg, and (5) fasting plasma glucose $\geq$ 5.6 $mmol \cdot l^{-1}$ or previously diagnosed type 2 diabetes. Markers of insulin resistance, including fasting insulin and homeostasis model assessment of insulin resistance (HOMA-IR), and the pro-inflammatory marker high sensitivity C-reactive protein (hs-CRP), were also measured in this study.

Following an overnight fast, intravenous blood was collected (8:00-11:00am) from the antecubital vein. Blood lipid profiling of serum concentrations of triglycerides, total cholesterol and high-density lipoprotein (HDL) cholesterol were measured using the Reflotron Plus desktop analyser (Roche, Switzerland). A CV of 3.8% is reported between Refloton measurements for total cholesterol and a standardised wet-chemistry method (Statland, 1990). Fasting plasma glucose, insulin and hs-CRP concentrations were analysed by clinical pathology at a leading hospital. Insulin resistance was estimated by HOMA-IR using the equation: HOMA-IR = fasting insulin concentration (μU/mL) x fasting glucose concentration (mmol/L) / 22.5 (Matthews et al., 1985). HOMA-IR is a surrogate measure of whole body insulin sensitivity and β-cell functioning correlates (r = 0.88) well with estimates using the euglycemic clamp method (Bonora et al., 2000)' with a value ≥ 2.0 considered indicative of insulin resistance (Jensterle et al., 2008). For hs-CRP, a value > 3.0 $mg \cdot l^{-1}$ was deemed high risk (Pearson et al., 2003).

For SBP and DBP, duplicate assessments were obtained from the left arm with an automated digital sphygmomanometer (Carescape V100, Dinamap, GE technology, USA).

Health and Fitness evaluations

The YMCA graded submaximal cycle ergometer test (Golding et al., 1989) was used to estimate aerobic power (predicted VO_{2max}), where heart rate was extrapolated against work rate (W) using regression analysis. Physical activity behaviour was obtained via a 7-day recall (Sallis et al., 1993).

Within the acknowledged limitations of dietary recall (Magarey et al., 2011), participants completed a three-day food and beverage recall (including vitamins, minerals and/or supplements) on two consecutive weekdays and on either a Saturday or Sunday of their usual diet. Participants were encouraged not to alter their habitual diet during the recall period. Macro- and micro-nutrient intakes were analysed by a research dietician, blinded to grouping, using the FoodWorks® 7 Professional program (Xyris software, Highgate Hill, Queensland, Australia). An estimation of average daily energy intake was also calculated.

Intervention

The 12-wk lifestyle intervention was comprised of three main components: (1) physical activity (2) nutrition education, and (3) cognitive behavioural therapy (Table 7.1). Total time for participants in the intervention group was approximately 4.5 hours per week. Specifically, exercise participation time averaged 3 hours per week. The intervention also included 60 minutes of psychological support (CBT) plus a 30 minutes nutrition session weekly. Participants met in smaller groups for nutrition and exercise sessions while the CBT was one larger group per week. In contrast, participants in the wait-list control group (n=17) were instructed to continue existing lifestyle choices, and after 12 weeks were invited to complete the lifestyle intervention.

Physical activity

Participants undertaking the intervention completed two supervised exercise sessions (progressive circuit training) and one unsupervised, but were prescribed one home-based session (brisk walk or jog) per week. The supervised sessions were administered by a qualified Exercise Scientist and consisted of a general warm-up, a combination of aerobic activities, dynamic strength and/or resistance training, abdominal conditioning, and stretching. Session duration lasted approximately 60 min, with the intensity of the exercise increasing from 60% to 85% on the OMNI Picture System (range (Robertson, 2004), by the end of the 12-week period. The OMNI Picture System is a rating of perceived exertion (RPE) scale (ranging from 0 = extremely easy to 10 = extremely hard), with which participants were well-familiarised prior to intervention commencement. Evidence supports the use of the OMNI-RPE scale by young women (n=34, 18-36 y) to estimate RPE (Utter et al., 2004). A positive linear relationship was found between the OMNI-RPE scale and $\%VO_{2max}$ (r^2 = 0.72), and heart rate (r^2 = 0.63), respectively, during a graded treadmill exercise test (Utter et al., 2004). Intensity was verified by comparing heart rates with RPE during most exercise sessions with a Polar heart rate monitor (Polar Electro, Finland). This occurred at the completion of the aerobic component of the exercise session. The home-based, unsupervised training session involved a brisk walk or jog at an RPE of 5-7 on the OMNI Picture System (Robertson, 2004). Participants were encouraged to incorporate intermittent high-intensity intervals into their session. Duration of the session progressed from 30 minutes at

intervention commencement to 45 minutes at program completion. As a measure of compliance, participants maintained a detailed training diary including any extra activities they completed during the intervention. The Bruce protocol (Bruce et al., 1973) was completed every three weeks to ensure accuracy of progressive overload of aerobic fitness during the program. Upper (chest-press) and lower (leg-press) body strength was tested via a 5-repetition maximum test to guide the strength and resistance component of the exercise intervention (Abadie & Wentworth, 2000). Results from the Bruce protocol and strength test provided individualised heart rate and RPE zones and initial loads for the training program, respectively. To replicate community resources, sessions occurred in both the gym on campus and at a local park.

Nutrition education

Participants in the intervention group received weekly nutrition education sessions guided by a dietician about healthy eating choices from the existing Australian Dietary Guidelines (National Health and Medical Research Council, 2005). This information provided education regarding non-dieting weight management and healthy eating principles. Following baseline analysis of a three-day food and beverage recall, nutrition education topics targeted the perceived needs of the female participants, such as appropriate snacks, portion sizes, and responsible alcohol consumption.

Cognitive behavioural therapy

Within the framework of self-determination theory (Deci & Ryan, 1985), weekly 60-minute group sessions with a counsellor provided participants with psychosocial support and developed skills to overcome personal barriers to lifestyle change. Topics included changing behaviour, goal setting, self-efficacy and building self-confidence. The program aimed, ultimately, to empower individuals to develop healthier eating and physical activity patterns (Miller & Jacob, 2001).

Table 7.1. Outline of the 12-week multi-disciplinary lifestyle intervention of physical activity, nutrition education and cognitive behavioural therapy.

Week	Physical Activity			Nutrition Education	Cognitive Behavioural Therapy (CBT)
	Supervised session intensity (%)	Unsupervised session duration (mins)	Fitness testing	Weekly Topics	Weekly Topics "Mission Possible"
1	60	30	Bruce, 5-RM	Australian dietary guidelines for adults	Group formation and introductions
2	60	30		Australian physical activity guidelines for adults	Changing Behaviour: Benefits of change
3	65	30		Label reading and interpretation	Identifying strengths: Building momentum
4	65	35	Bruce, 5-RM	Serving size	Motivation: Goal setting for success
5	70	35		Glycemic index	Overcoming the barriers to change
6	70	35		Separating fact from fiction	Food for health: Making nutrition work for you
7	75	40	Bruce, 5-RM	Food variety, dietary fibre and snack choices	Letting go of the 'uncontrollable'
8	75	40		Dietary fats and take-away food	Examining self-talk and building self-confidence
9	80	40		Fluids, hydration and alcohol	Physical activity and mood
10	80	45	Bruce, 5-RM	Protein and iron	Social support
11	85	45		Fad diets and body image	Behavioural change for life
12	85	45		Dairy products and calcium	Group endings

5-RM repetition max

Statistical analyses

Data were analysed using IBM SPSS Statistics, Version 20 for Windows (SPSS Inc, Chicago IL). Data were tested for normal distribution using the Shapiro-Wilk statistic and skewness and kurtosis (Peat & Barton, 2005). Log transformation was performed with data not normally distributed. All data are presented as means ± standard deviation. Statistical significance was set at $P \leq 0.05$. A linear mixed-model analysis was used to calculate the differences between groups and across time for the intervention and control groups. Hedge's *g* effect size was used to assess the magnitude of effect. An effect size ≥ 0.2 was considered small, ≥ 0.5 medium, and ≥ 0.8 large (Cohen, 1988). Mean differences and 95% confidence intervals (CI) are reported.

Results

A total of 39 participants were included in the analysis. For reasons described in Figure 7.1, 27% of intervention participants and 35% of control participants failed to maintain study involvement beyond pre-intervention/pre-control measures. However, for those completing the intervention, compliance rates were high with 80% attendance at physical activity and nutrition sessions and 74% at CBT sessions.

A per-protocol analysis (n=30) was performed on participants who completed the entire study excluding those who withdrew (n=9). Additionally, a sensitivity analysis was conducted to compare the means of those participants (n=4) who were allocated to the wait-list control group and who then undertook the intervention. No differences were found using both analyses and the findings were not altered.

Between group differences

Table 7.2 shows the results of comparisons between the intervention and control groups before and following the intervention, using a linear mixed model analysis. With only one difference observed between groups at pre-intervention, this supports the homogeneity of the groups. The baseline difference was found in a higher resting heart rate, in the intervention group, with a moderate effect size (g=0.79). At post-intervention, only physical activity was higher in the intervention group than the control group, with a large effect size (g=2.14).

Table 7.2. Between group comparisons of cardiometabolic risk factors for the intervention and control group at pre (0 weeks) and post (12 weeks).

	Pre-control/pre-intervention (0 weeks)					Post-control/post-intervention (12 weeks)				
	Control (n=17)	**Intervention (n=26)**	***P* value**	**Effect size (Hedge's *g*)**	**Mean difference (95%CI)**	**Control (n=11)**	**Intervention (n=19)**	***P* value**	**Effect size (Hedge's *g*)**	**Mean difference (95%CI)**
Anthromometric assessment										
Body mass (kg)	86.1 ± 17.8	89.8 ± 21.1	0.564	0.18	3.7 (-9.2 to 16.6)	82.5 ± 19.5	86.9 ± 20.5	0.609	0.21	4.4 (-11.2 to 20.1)
Body mass index ($kg \cdot m^{-2}$)	31.4 ± 6.6	32.2 ± 5.9	0.674	0.13	0.8 (-3.1 to 4.8)	30.0 ± 6.6	31.3 ± 0.9	0.724	0.31	1.3 (-3.5 to 6.0)
Waist circumference (cm)	92.8 ± 10.8	93.1 ± 11.7	0.930	0.03	0.3 (-7.1 to 7.7)	87.2 ± 10.5	87.3 ± 9.8	0.910	0.01	0.1 (-7.7 to 8.0)
Hip circumference (cm)	113.8 ± 11.5	116.3 ± 13.3	0.537	0.19	2.5 (-5.7 to 10.7)	111.1 ± 11.9	114.2 ± 13.50	0.696	0.23	3.1 (-6.9 to 13.2)
Waist-hip-ratio	0.81 ± 0.03	0.79 ± 0.05	0.242	0.46	0.02 (-0.04 to 0.01)	0.78 ± 0.03	0.77 ± 0.04	0.581	0.26	-0.01 (-0.05 to 0.01)
Waist-height-ratio	0.56 ± 0.06	0.56 ± 0.06	0.989	0.00	0.0 (-0.04 to 0.04)	0.53 ± 0.06	0.53 ± 0.05	0.927	0.00	0.0 (-0.04 to 0.04)
Metabolic syndrome markers										
Systolic BP (mmHg)	119 ± 8	120 ± 11	0.669	0.10	1.0 (-5.0 to 7.8)	111 ± 12	116 ± 9	0.312	0.48	5.0 (-2.4 to 13.1)
Diastolic BP (mmHg)	64 ± 8	68 ± 6	0.115	0.10	4.0 (-0.8 to 8.1)	59 ± 5	64 ± 9	0.108	0.62	5.0 (-1.5 to 10.3)
HDL-cholesterol ($mmol \cdot L^{-1}$)	1.7 ± 0.6	1.7 ± 0.5	0.887	0.00	0.0 (-0.4 to 0.3)	2.0 ± 0.5	1.9 ± 0.5	0.706	0.19	-0.1 (-0.4 to 0.3)
Triglycerides ($mmol \cdot L^{-1}$)$^{\#}$	1.2 ± 0.4	1.3 ± 0.5	0.838	0.21	0.1 (-0.2 to 0.4)	1.5 ± 0.6	1.4 ± 0.7	0.255	0.15	-0.1 (-0.7 to 0.3)
Fasting glucose ($mmol \cdot L^{-1}$)$^{\#}$	4.5 ± 0.6	4.6 ± 0.4	0.353	0.20	0.1 (-0.2 to 0.5)	4.4 ± 0.6	4.6 ± 0.4	0.325	0.40	0.2 (-0.2 to 0.5)
Additional biochemical parameters										
Total cholesterol ($mmol \cdot L^{-1}$)	4.3 ± 0.5	4.4 ± 0.6	0.645	0.17	0.1 (-0.3 to 0.5)	4.3 ± 0.4	4.3 ± 0.8	0.746	0.00	0.0 (-0.5 to 0.6)
Fasting insulin ($mU \cdot L^{-1}$)$^{\#}$	8.1 ± 4.4	9.4 ± 4.7	0.720	0.28	1.3 (-1.9 to 4.4)	7.4 ± 2.7	8.1 ± 2.6	0.203	0.26	0.7 (-1.3 to 2.8)
HOMA-IR	1.6 ± 1.0	1.9 ± 1.0	0.331	0.29	0.3 (-0.4 to 0.9)	1.4 ± 0.5	1.6 ± 0.5	0.614	0.39	0.2 (-0.2 to 0.6)
hsCRP ($mg \cdot L^{-1}$)$^{\#}$	2.9 ± 2.6	3.5 ± 3.0	0.495	0.21	0.6 (-1.4 to 2.4)	3.9 ± 3.7	4.6 ± 4.9	0.579	0.15	0.6 (-2.9 to 4.2)
Fitness appraisal										
Resting heart rate (bpm)	67 ± 10	76 ± 12	0.019*	0.79	9.0 (0.9 to 15.8)	67 ± 9	68 ± 8	0.929	0.12	1.0 (-6.0 to 6.9)
Predicted $\dot{V}O_2$ max ($L \cdot min^{-1}$)	2.7 ± 0.2	2.4 ± 0.5	0.515	0.74	-0.3 (-0.7 to 0.1)	2.5 ± 0.6	2.8 ± 0.6	0.347	0.49	0.3 (-0.2 to 0.7)
Predicted $\dot{V}O_2$ max ($mL \cdot kg^{-1} \cdot min^{-1}$)	32.0 ± 10.3	27.9 ± 7.0	0.133	0.47	-4.1 (-9.8 to 1.5)	31.7 ± 10.9	32.6 ± 6.8	0.245	0.10	0.9 (-5.7 to 7.5)
Physical activity ($min \cdot week^{-1}$)$^{\#}$	118 ± 89	97 ± 62	0.870	0.27	21 (-73.4 to 30.9)	121 ± 81	280 ± 67	< 0.001*	2.14	159 (103.0 to 215.5)
Nutrition evaluation										
Energy (kj)	6657 ± 3310	6535 ± 2183	0.945	0.04	122 (-2501 to 2255)	5065 ± 1346	5223 ± 1725	0.743	0.10	158 (-1266 to 1581)
CHO (g)	194 ± 87	166 ± 74	0.386	0.34	28 (-88.7 to 33.7)	205 ± 101	178 ± 96	0.443	0.27	-27 (-112.1 to 59.0)
Protein (g)$^{\#}$	135 ± 93	173 ± 86	0.097	0.42	38 (-30.1 to 107.6)	137 ± 59	138 ± 63	0.857	0.01	1.0 (-53.9 to 55.0)
Total fat (g)$^{\#}$	66 ± 38	66 ± 34	0.734	0.00	0.0 (-27.9 to 27.6)	50 ± 13	55 ± 14	0.457	0.36	5.0 (-7.0 to 17.0)

Data presented as mean ± standard deviation, $^{\#}$ log10 transformation, * $P \leq 0.05$. BP blood pressure, HDL high-density lipoprotein, HOMA-IR homeostasis model assessment of insulin resistance, hs-CRP high sensitivity C-reactive protein, CHO carbohydrates. Effect size ≥ 0.2 small, ≥ 0.5 medium, ≥ 0.8 large (Vincent, 1995).

Intervention group

For the intervention group, there were positive significant ($P \leq 0.05$) changes pre-to post-intervention for WC (-6.4%), WHR (-2.5%), WHtR (-5.5%), SBP (-3.4%), DBP (-5.8%), resting heart rate (-11%), predicted VO_{2max} (+15%), physical activity (+97%) and total energy intake (-22%) (Table 7.3 and Figure 7.3). Absolute protein intake (g) decreased but this difference disappeared when the decreased total energy intake was accounted for. Many of these improvements were maintained at sustainability (24 weeks) testing, and while predicted VO_{2max} and physical activity reduced during the 12-week sustainability phase, physical activity remained greater than at pre-intervention.

Control group

Despite being requested to maintain normal lifestyle habits, the control group displayed several improvements from pre- to post-testing, including WC (-6.2%), WHR (-3.8%), WHtR (-5.5%) and SBP (-7.0%), while circulating triglycerides rose (Table 7.4 and Figure 7.3). In contrast to the intervention group, there were no changes in reported DBP, reported physical activity, predicted VO_{2max}, resting heart rate and energy intake following the 12-week control period.

Table 7.3. Within-group comparisons of cardiometabolic risk factors for the *intervention* group at pre-intervention, post-intervention, and sustainability

				P-values		
Variable	**Pre-int. (0 weeks) (n=26)**	**Post-int. (12 week) (n=19)**	**Sustainability (24 week) (n=19)**	**Pre-int. vs Post-int.**	**Pre-int. vs Sustainability**	**Post-int. vs Sustainability**
Anthropometric assessment						
Body mass (kg)	89.8 ± 21.1	86.9 ± 20.5	86.1 ± 20.3	0.791	0.408	0.369
Body mass index ($kg \cdot m^{-2}$)	32.2 ± 5.9	31.3 ± 0.9	31.0 ± 6.1	0.447	0.197	0.291
Waist circumference (cm)	93.1 ± 11.7	87.3 ± 9.8	87.8 ± 9.4	< 0.001*	0.002*	0.696
Hip circumference (cm)	116.3 ± 13.3	114.2 ± 13.50	114.5 ± 13.9	0.309	0.627	0.734
Waist-hip-ratio	0.79 ± 0.05	0.77 ± 0.04	0.77 ± 0.04	0.002*	0.018*	0.998
Waist-height-ratio	0.56 ± 0.06	0.53 ± 0.05	0.53 ± 0.05	< 0.001*	0.001*	0.841
Metabolic syndrome markers						
Systolic BP (mmHg)	120 ± 11	116 ± 9	116 ± 11	0.047*	0.131	0.967
Diastolic BP (mmHg)	68 ± 6	64 ± 9	64 ± 6	0.040*	0.050*	0.841
HDL-cholesterol ($mmol \cdot L^{-1}$)	1.7 ± 0.5	1.9 ± 0.5	1.9 ± 0.4	0.193	0.386	0.726
Triglycerides ($mmol \cdot L^{-1}$)#	1.3 ± 0.5	1.4 ± 0.7	1.5 ± 1.0	0.855	0.271	0.221
Fasting glucose ($mmol \cdot L^{-1}$)#	4.6 ± 0.4	4.6 ± 0.4	4.6 ± 0.5	0.728	0.559	0.756
Additional biochemical parameters						
Total cholesterol ($mmol \cdot L^{-1}$)	4.4 ± 0.6	4.3 ± 0.8	4.3 ± 0.6	0.542	0.671	0.937
Fasting insulin ($mU \cdot L^{-1}$)#	9.4 ± 4.7	8.1 ± 2.6	8.8 ± 4.7	0.957	0.466	0.344
HOMA-IR	1.9 ± 1.0	1.6 ± 0.5	1.80 ± 0.97	0.176	0.575	0.480
hsCRP ($mg \cdot L^{-1}$)#	3.5 ± 3.0	4.6 ± 4.9	4.7 ± 3.8	0.743	0.148	0.140
Fitness appraisal						
Resting heart rate (bpm)	76 ± 12	68 ± 8	66 ± 9	0.020*	0.004*	0.489
Predicted $\dot{V}O_2max$ ($L \cdot min^{-1}$)	2.4 ± 0.5	2.8 ± 0.6	2.5 ± 0.6	0.029*	0.471	0.179
Predicted $\dot{V}O_2max$ ($mL \cdot kg^{-1} \cdot min^{-1}$)	27.9 ± 7.0	32.6 ± 6.8	30.9 ± 9.7	0.000*	0.248	< 0.001*
Physical activity ($min \cdot week^{-1}$)#	97 ± 62	280 ± 67	143.7 ± 48.4	< 0.001*	0.002*	< 0.001*
Nutrition evaluation						
Energy (kj)	6535 ± 2183	5223 ± 1725	5538 ± 2588	0.007*	0.269	0.161
CHO (g)	166 ± 74	178 ± 96	154 ± 83	0.638	0.928	0.638
Protein (g)#	173 ± 86	138 ± 63	150 ± 86	0.012*	0.520	0.079
Total fat (g)#	66 ± 34	55 ± 14	56 ± 20	0.227	0.575	0.513

*Data presented as mean ± standard deviation, # log_{10} transformation, * $P \leq 0.05$. Int, intervention. BP blood pressure, HDL high-density lipoprotein, HOMA-IR homeostasis model assessment of insulin resistance, hs-CRP high sensitivity C-reactive protein, CHO carbohydrates.*

Table 7.4. Within-group comparisons of cardiometabolic risk factors for the *control* group at pre-control and post-control.

Variable	Pre-control (0 weeks) n = 17	Post-control (12 weeks) n = 11	*P* value
Anthropometric assessment			
Body mass (kg)	86.1 ± 17.8	82.5 ± 19.5	0.893
Body mass index ($kg \cdot m^{-2}$)	31.4 ± 6.6	30.0 ± 6.6	0.775
Waist circumference (cm)	92.8 ± 10.8	87.2 ± 10.5	< 0.001*
Hip circumference (cm)	113.8 ± 11.5	111.1 ± 11.9	0.894
Waist-hip-ratio	0.81 ± 0.03	0.78 ± 0.03	0.001*
Waist-height-ratio	0.56 ± 0.06	0.53 ± 0.06	0.011*
Metabolic syndrome markers			
Systolic BP (mmHg)	119 ± 8	110 ± 12	0.012*
Diastolic BP (mmHg)	64 ± 8	59 ± 5	0.115
HDL-cholesterol ($mmol \cdot L^{-1}$)	1.7 ± 0.6	2.0 ± 0.5	0.194
Triglycerides ($mmol \cdot L^{-1}$)#	1.2 ± 0.4	1.5 ± 0.6	0.034*
Fasting glucose ($mmol \cdot L^{-1}$)#	4.5 ± 0.6	4.4 ± 0.6	0.662
Additional biochemical parameters			
Total cholesterol ($mmol \cdot L^{-1}$)	4.3 ± 0.5	4.3 ± 0.4	0.730
Fasting insulin ($mU \cdot L^{-1}$)#	8.1 ± 4.4	7.4 ± 2.7	0.775
HOMA-IR	1.6 ± 1.0	1.4 ± 0.5	0.522
hsCRP ($mg \cdot L^{-1}$)#	2.9 ± 2.6	3.9 ± 3.7	0.727
Fitness appraisal			
Resting heart rate (bpm)	67 ± 10	67 ± 9	0.919
Predicted $\dot{V}O_2$max ($L \cdot min^{-1}$)	2.7 ± 0.2	2.5 ± 0.6	0.962
Predicted $\dot{V}O_2$max ($mL \cdot kg^{-1} \cdot min^{-1}$)	32.0 ± 10.3	31.7 ± 10.9	0.945
Physical activity ($min \cdot week^{-1}$)#	118 ± 89	121 ± 81	0.362
Nutrition evaluation			
Energy (kj)	6657 ± 3310	5065 ± 1346	0.115
CHO (g)	194 ± 87	205 ± 101	0.745
Protein (g)#	135 ± 93	137 ± 59	0.947
Total fat (g) #	66 ± 38	50 ± 13	0.213

*BP blood pressure, HDL high-density lipoprotein, HOMA-IR homeostasis model assessment of insulin resistance, hs-CRP high sensitivity C-reactive protein, CHO carbohydrates. Data presented as mean ± standard deviation, # log_{10} transformation, * $P \leq 0.05$*

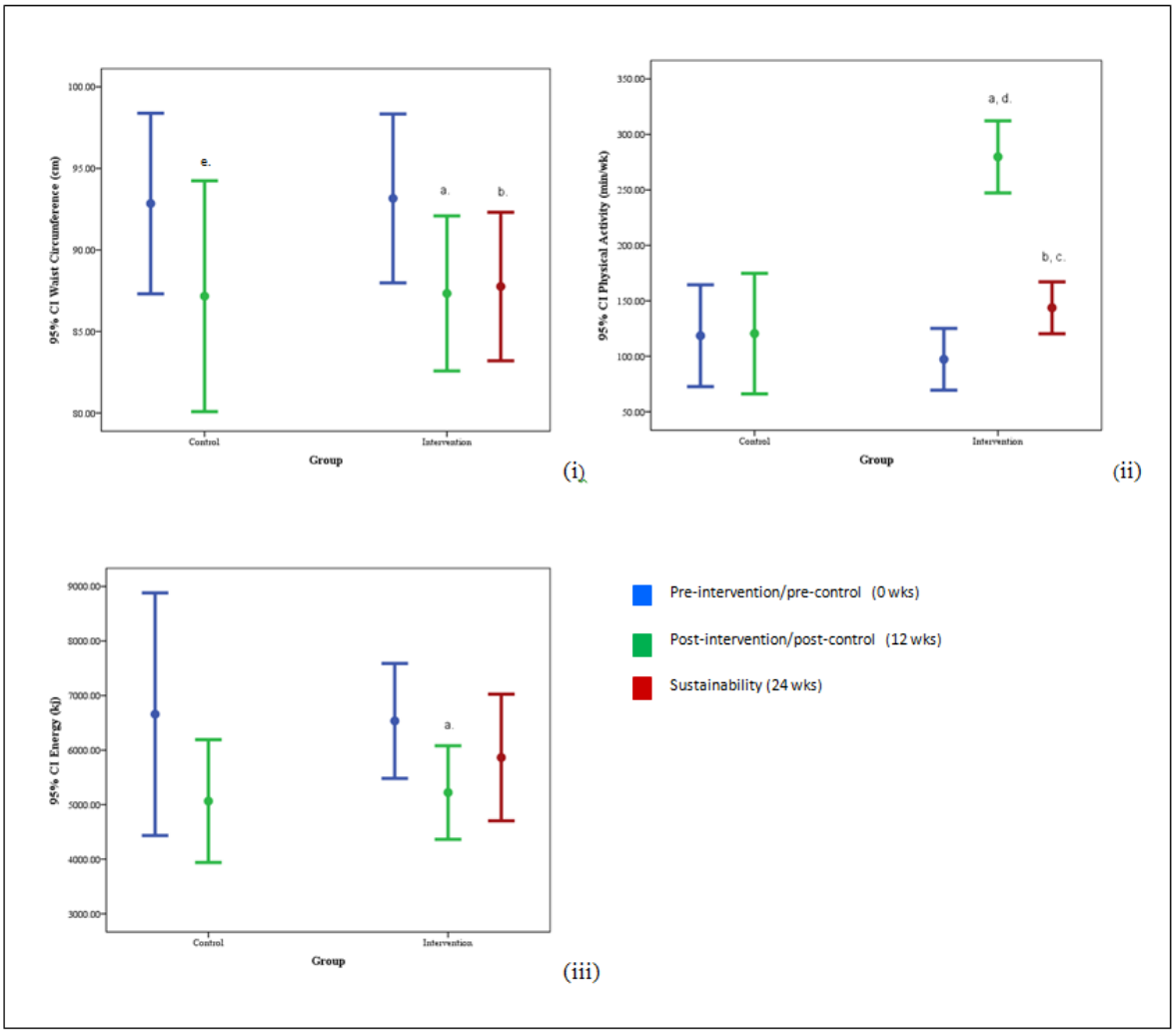


Figure 7.3. Mean and 95% CI for intervention (n=26) and control (n=11) participants during the multi-disciplinary lifestyle intervention at pre-intervention, n=26/pre-control, n=17 (0 weeks), post-intervention, n=19/post-control, n=11 (12 weeks) and sustainability, n=19 (24 weeks) for (i) waist circumference, (ii) physical activity, and (iii) energy intake.

'a' denotes. P ≤ 0.05 from pre-intervention to post-intervention.

'b' denotes. P ≤ 0.05 from pre-intervention to sustainability.

'c' denotes. P ≤ 0.05 from post-intervention to sustainability

'd' denotes. P ≤ 0.05 between intervention and control groups (at post).

'e' denotes. P ≤ 0.05 from pre-control to post-control.

Discussion

The effectiveness of the multi-disciplinary lifestyle intervention for reducing CVD risk in young women was highlighted by within-group improvements in a range of risk factors for the intervention group, with several of these improved markers retained 12 weeks after completion of the lifestyle intervention. Thus, these data suggest a relatively successful intervention for reducing CVD risk with promising sustainability. However, when between-group comparisons were made with the control group, the findings suggested a research design that was largely unsuccessful in identifying the effectiveness of the intervention phase. This raises several concerns associated with a wait-list control design when used with overweight/obese young women. Concerns from the current study support previous findings that describe more difficulties in retaining younger than older females to research trials (Hutchesson et al., 2013).

Positive changes within the intervention group were demonstrated with improvements in WC related measures, systolic and diastolic blood pressure, aerobic fitness and physical activity, and dietary energy intake. Collectively, these measures imply that the intervention produced cardiovascular, more so than metabolic, benefits for the intervention group. The use of investigative procedures such as non-invasive echocardiography or MRI may provide insight into the significance of these changes (Kosmala et al., 2008).

Improvements in fitness and physical activity and reduced energy intake also suggest that the exercise and nutrition education components of the intervention, respectively, were effective. Moreover, there was strong evidence for sustainability of intervention-induced improvements at 24 weeks, suggesting that the CBT component produced positive behavioural change in participants.

However, similar post-intervention changes in our wait-list control group, made it difficult to detect any anthropometric, biochemical, fitness or dietary differences between groups following the 12-week intervention phase. The control group in this RCT also displayed a decrease in WC that paralleled the intervention group, despite undetectable changes in self-reported physical activity and nutrition. The decreased WC of the control group is particularly difficult to explain without further investigative procedures such as accelerometry for physical activity and more rigorous dietary monitoring, but does suggest

that basic awareness of CVD risk might be enough to evoke change in targeted populations (Wake et al., 2013; Waters, George, Chey, & Bauman, 2012).

Randomised controlled trials provide the highest level of evidence for the effects of an intervention and are deemed to be scientifically rigorous (Peat, 2001), with control groups employed to provide a contrast for the experimental group (Elliott & Brown, 2002) and for establishing the efficacy of an intervention (Baucom, Hahlweg, & Kuschel, 2003). But changed outcomes that arise from a wait-list control condition can be detrimental rather than beneficial to a randomised controlled trial (Elliott & Brown, 2002), and this occurred in the current study. Therefore, wait-list control designs might not be appropriate for this population.

Retention and compliance of wait-list participants is also an issue for consideration when planning control conditions essential for maintaining the rigour of a randomised control design. In this study, more than one-third of the control group failed to return for post-testing at 12 weeks despite researcher attempts to maintain contact. In contrast, once engaged in the intervention group, retention to lifestyle change was high for at least 24 weeks. It is postulated that assigning participants to the control group decreased their motivation to participate. Thus, the duration (12 weeks) and/or conditions (no changes to existing lifestyle) of the control group do not appear suitable for women of this age group and demographic. Alternative strategies for immediate engagement, perhaps via topics of interest using multimedia such as health-related *apps* or support groups might improve commitment and maintain control group compliance. There were also some difficulties encountered with recruitment, with almost a quarter of interested and eligible participants failing to engage after initial commitment (prior to group allocation). Complexities associated with recruiting young women for weight management trials, especially from 'Generation Y', may result in smaller sample sizes and require shorter periods of engagement (Griffin et al., 2013).

Although not always the case (Crist et al., 2012), successful outcomes have been observed following lifestyle interventions with middle-aged (Irving et al., 2008) and older women (Kemmler et al., 2009). But there is a lack of effective lifestyle interventions for young adults, with no weight loss programs to date developed specifically to address the needs of this age group. Outcomes, enrolment and retention rates have been compared between younger (18-35 years, n=21) and more mature (> 35 years, n = 277) adults (66% female) engaged in similar behavioural weight loss and physical activity programs (Gokee-LaRose et

al., 2009). Results showed attendance was 30% lower in young adults and they were 30% less likely to be retained for the 6-month assessment. Weight loss and increases in total physical activity from baseline to 6 months were significantly less in the younger population. Although the number of younger adults was relatively small, these results indicated that traditional interventions were less successful in young adults (Gokee-LaRose et al., 2009). These findings are supported by results from other studies attempting to engage young adults (Chang et al., 2010; Donnelly et al., 2003; Thomson et al., 2008).

This study is not without limitations. Despite recruitment and retention strategies, the sample size, particularly in the control condition, was lower than anticipated at completion of the study, suggesting it was slightly under-powered. Additionally, the results are specific to Caucasian women at a tertiary institution. To capture any potential changes to control groups in a wait-list design, objective measures (e.g. accelerometers, fortnightly anthropometric measures) might be useful. In addition, the use of more objective measures of physical activity and dietary compliance would strengthen evidence of change in this age group of women.

Nonetheless, the study contributes to a very limited number of healthy lifestyle interventions in young adult women (< 30 years of age) with cardiometabolic risk factors (Chang et al., 2010). The multi-disciplinary lifestyle intervention confirms the potential value in health changes observed post-intervention, with favourable sustainability at a 12 weeks.

Conclusions

Within-group analysis showed that the multi-disciplinary lifestyle intervention comprising physical activity, nutrition education and CBT was positive for the reduction of CVD risk factors both immediately after and beyond the completion of the program. However, we also observed positive, but unexpected and difficult to explain, changes in the wait-list control group. Therefore, comparative lifestyle benefits for the intervention group may have been masked by undetectable weight management behaviour in the control group. When considered alongside the difficulties faced with recruitment and retention, especially in the nature of the control group, these results provide a challenge for prospective study designs with young women with cardiometabolic risk factors. Traditional RCT designs may be problematic for healthy lifestyle interventions in young women.

7.1. ADDENDUM: Perceived barriers to lifestyle change.

Introduction

While participation in regular physical activity is vital for health, women experience many and varied barriers to participating in physical activity (Yeats, 2010). In adult women, lack of time is often cited as the most prominent barrier to participation in physical activity, with work and study attributed to lack of time (Arango, Patiño, Quintero, & Arenas, 2011). Parenting/caring demands, body image and safety concerns are also highly ranked as perceived barriers for women (Yeats, 2010).

In the present study, selected psychological instruments were surveyed for a range of personal behavioural patterns. The objective was to determine the importance, motives, stage of change, and perceived barriers for participation in physical activity, together with information about perceived barriers to healthy eating.

Methods

At the pre-intervention/pre-control, post-intervention/post-control, and sustainability testing periods, participants completed three psychological instruments to address physical activity/exercise related behaviours. These inventories, described in Chapter 4, were:

1) Motives for Physical Activity Measure – Revised (MPAM-R) (Ryan et al., 1997).

2) Perceived Barriers to Activity (Booth et al., 1997; King et al., 2000).

3) Stage of Change for Exercise (B. Marcus et al., 1992).

In addition, participants specified their perception of ‘exercise importance’ and rated perceived barriers for healthy eating (Fowles & Feucht, 2004) on a 5-pointLikert-scale.

Results

Table 7.5 presents the personal behavioural patterns for the intervention and control groups at the pre-intervention/pre-control (0 weeks) and post-intervention/post-control (12 weeks) time periods. The three major barriers to physical activity and healthy eating are shown. For the motives for physical activity, the responses are ranked from most (1) to least (5) important. For the stage of change for exercise, the percentage distribution for each participant group is provided, as is the distribution of responses for perceived exercise importance, calculated from cross-tabulations. Similarly, Table 7.6 presents the responses for participants who completed the lifestyle intervention, with data gathered at the pre-intervention (0 weeks), post-intervention (12 weeks) and the 'sustainability' (24 weeks) time periods.

Table 7.5. Personal behavioural patterns: between-group comparisons for the control and intervention groups at pre-intervention/pre-control and post-intervention/post-control.

	Pre-control/pre-intervention (0 Wk)		Post-control/post-intervention (12 wk)	
Variable	**Control group (n=17)**	**Intervention group (n=19)**	**Control group (n=11)**	**Intervention group (n=19)**
Barriers to physical activity				
1	Feeling too tired (87.5%)	Feeling too tired (89%)	Feeling too tired (89%)	Feeling too tired (84%)
2	Cost of classes or venues (75%)	Unmotivated (79%)	Cost of classes or venue (78%)	Feeling self-conscious (63%)
3	Poor weather (69%)	Cost of classes or venue (74%)	Poor weather (78%)	Lack of time (58%)
Barriers to healthy eating				
1	Engaging in comfort eating (87%)	Comfort eating (100%)	Don't feel like eating healthy (100%)	Comfort eating (83%)
2	Don't feel like eating healthy (75%)	Food cravings (84%)	Comfort eating (89%)	Don't feel like eating healthy (83%)
3	Eat when I'm not hungry (75%)	Don't feel like eating healthy (79%)	Eat when I'm not hungry (67%)	Eat when I'm not hungry (72%)
Motives for physical activity				
1	Appearances	Appearance	Appearances	Fitness
2	Fitness	Fitness	Fitness	Appearance
3	Interest	Competence	Interest	Interest
4	Competence	Interest	Competence	Competence
5	Social	Social	Social	Social
Stage of Change				
Pre-contemplation	0%	0%	0%	0%
Contemplation	18%	22%	0%	0%
Preparation	64%	56%	67%	10%
Relapse	18%	22%	11%	5%
Action	0%	0%	22%	68%
Maintenance	0%	0%	0%	16%
Exercise Importance				
Very important or important	64%	50%	56%	84%
Neutral	36 %	33%	44%	16%
Very unimportant or unimportant	0 %	16%	0%	0%

Table 7.6. Personal behavioural patterns: within-group comparisons for the intervention group at pre-intervention, post-intervention, and sustainability..

Variable	Pre-intervention (n=19)	Post-intervention (n=19)	Sustainability (n=19)
Barriers to Physical Activity			
1	Feeling too tired (89%)	Feeling too tired (84%)	Feeling too tired (74%)
2	Unmotivated (79%)	Feeling self-conscious (63%)	Lack of time (63%)
3	Cost of classes or venue (74%)	Lack of time (58%)	Cost of classes or venues (58%)
Barriers to Healthy Eating			
1	Comfort eating (100%)	Comfort eating (83%)	Comfort eating (89%)
2	Food cravings (84%)	Don't feel like eating healthy (83%)	Don't feel like eating healthy (72%)
3	Don't feel like eating healthy (79%)	Food cravings (56%)	Food cravings (67%)
Motives for Physical Activity			
1	Appearance	Fitness	Appearance
2	Fitness	Appearance	Fitness
3	Competence	Interest	Competence
4	Interest	Competence	Interest
5	Social	Social	Social
Stage of Change			
Pre-contemplation	0%	0%	0%
Contemplation	22%	0%	0%
Preparation	56%	10%	37%
Relapse	22%	5%	16%
Action	0%	68%	32%
Maintenance	0%	16%	16%
Exercise Importance			
Very important or important	50%	84%	79%
Neutral	33%	16%	21%
Very unimportant or unimportant	16%	0%	0%

Discussion

An understanding of the barriers to behaviour change, and the motives and importance given to such change by individuals, is important when considering the implementation and assessment of intervention programs and their outcomes. For the young women involved in the intervention study of this thesis, the majority of participants viewed exercise as very important or important. The motives for exercise participation and the barriers to healthy lifestyle change were similar to previous reports of in adults < 40 years of age (Arango et al., 2011; Lovell, El Ansari, & Parker, 2010).

At baseline, the spread of behaviour patterns reported by participants was similar between the intervention and control groups (Table 7.5). In the present study, the primary barriers to exercise was "feeling too tired". This agrees with previous work with adults (age 37 ± 8 y, 60% female) in which the highest ranked perceived barrier to physical activity was 'lack of will power' (Arango et al., 2011). In this same study, women reported higher barrier scores than men, and obese participants reported a greater proportion of barriers than their non-obese counterparts. Thus, analysis of barriers to physical activity faced by overweight/obese women is essential when planning any strategy to increase the motivation and adherence to an active lifestyle. For motives to engage in physical activity in the present study, "fitness" was ranked second behind "appearance" as the most prominent. This is in agreement with work with non-exercising female university students (age 19 ± 1 y) who reported their greatest perceived benefit from exercise to be 'physical performance' (Lovell, El Ansari & Parker, 2010).

At baseline for "stage of change for exercise", the majority of participants in the intervention and control groups were in the contemplation/preparation. This is consistent with other work (Arango et al., 2011) with adults (age 37 ± 8 y, 60% female) where the most prevalent stage of change for exercise was 'contemplation', followed by 'preparation'. It was concluded that barriers to increased physical activity were most prominent in women and obese individuals who identified themselves as being in the 'contemplation' and 'preparation' stage of change (Arango et al., 2011). This further highlights the importance of collecting and understanding these types of semi-quantitative data when designing and implementing lifestyle programs.

Following the 12-week intervention, participants demonstrated shifts in "stage of change for exercise" ratings, from a pre-intervention value of 0% for the 'action phase' to 68% by intervention completion. The intervention group also demonstrated a change in their perspective of exercise importance, with 84% of the group expressing exercise as 'very important or important' compared with only 50% at pre-intervention. These shifts could indicate a greater knowledge in the participants of the value of exercise and of strategies for incorporating it into their lifestyle routines, as highlighted in post-intervention focus group testing and anonymous program evaluations (see Addendum 7.2 for more details). However, at the 'sustainability' testing phase at 12 weeks *after* completion of the intervention (Table 7.6), a move back towards relapse/preparation was observed. This might reflect the rebound previously reported once an intervention program has been withdrawn, even when behavioural change strategies have been implemented (Wycherley et al., 2012).

Similarly, the control group displayed a shift in "stage of change for exercise" ratings in the same direction, although to a lesser extent, as the intervention group. Specifically, 22% of the control group reported being in the 'action phase' at post-control assessment, compared with 0% at the pre-control phase. This general change from pre-contemplation/contemplation to preparation/action in the control group provided evidence of a shift in motivation to commence lifestyle change, despite instructions to maintain current behaviours for the 12-week control period. The shift might be associated with improvements observed in some CVD risk factors (in particular, waist circumference) at the post-control testing, despite no detectable changes in self-reported physical activity and nutrition behaviours (see Chapter 7).

The results of the current study have implications for the design of physical activity programs and lifestyle interventions. The analysis of barriers that hinder physical activity engagement of participants, and their stage of change for exercise, is essential if successful behavioural change strategies are to be maintained. This is of particular importance if strategies are to target overweight/obese women and if exercise is to be a component of the intervention. Therefore, results of psychological changes in the current study support the need for age- and context-specific programs when attempting to engage sedentary young women in exercise programs.

7.2. ADDENDUM: Evaluation of the program

Introduction

A RCT design is widely accepted as the most reliable method for determining effectiveness (Oakley, Strange, Bonell, Allen, & Stephenson, 2006); (Campbell et al., 2000). Additionally, if possible, a RCT should always be considered because it is the most robust method of preventing bias (Campbell et al., 2000). The present study employed a "complex intervention" design that was multi-disciplinary, with three interacting components (i.e. physical activity, nutrition education, CBT).Due to their multifaceted nature and dependence on social context, complex interventions pose methodological challenges (Medical Research Council, 2000; Oakley et al., 2006). Therefore, it has been suggested that a lack of intervention impact may reflect implementation failure rather than genuine ineffectiveness and, thus, process evaluation is needed to identify implementation problems (Medical Research Council, 2000). Including a process evaluation of a RCT intervention is recommended to explain discrepancies between expected and observed outcome, to understand how context influences outcomes, and to provide insight to direct future implementation (Medical Research Council, 2000).

In the present work, several processes were implemented with the aim to better understand the experiences of the participants and, ultimately, to inform the evaluation of the lifestyle intervention and study overall. Three methods were used for the data collection process evaluation including:

- A focus group session at the completion of the intervention.
- Anonymous completion of an evaluation form at the completion of the intervention.
- Feedback from wait-list control group participants who withdrew from the study.
- An appraisal of recruitment, attendance, and retention rates of intervention participants.

Methods

At the completion of the lifestyle intervention, a focus group was conducted to gather rich data from participants about their experiences (Appendix 16). A facilitator qualified in the area of counselling conducted a 60-minute focus group with participants from the study, selected at random (n=7). The facilitator asked a series of semi-structured questions (Table 7.7) to encourage discussion within the group. The session audio was digitally recorded and transcribed verbatim to allow for theoretical analyses. Data were categorised and coded according to the researcher's perspectives of emergent themes.

Table 7.7. Questions initiated by the facilitator used to develop discussion in the focus group.

1.	What did being involved in the study mean to you?
2.	Why did you respond to the initial email request for participants?
3.	What is your current exercise regimen?
4.	How have your nutritional choices been affected by your participation?
5.	What or who are the biggest challenges to your healthy lifestyle?
6.	What or who helps you lead a healthy lifestyle?
7.	What are your short and long term healthy lifestyle goals?
8.	What are two main things you learnt about changes you needed to make?

In addition to the focus group, an evaluation survey was completed anonymously by all participants, to gather feedback on the lifestyle intervention program (Appendix 17). The questionnaire evaluated several aspects of the program including: characteristics of the exercise instructor (who also delivered key nutrition messages prepared by a dietician) and group CBT counsellor; attainment of personal goals; each of the three intervention components (i.e. physical activity, nutrition education, and CBT); and, if the program met personal expectations.

Throughout the course of the control period, six wait-list control participants withdrew from the study. These participants were invited to provide feedback regarding reasons for withdrawal and three participants responded. These participants were asked two questions:

1) *How did you feel when you were initially assigned to the control group?*

2) *Did your involvement in the study as a control participant trigger you to change anything about your current lifestyle?*

A record of the flow of participants through the intervention was maintained using the CONSORT guidelines (Schulz, Altman, & Moher, 2010) to detail; (i) number of initial responses to study advertisements, (ii) number of eligible and ineligible participants, (ii) participant withdrawal/retention rates for the intervention and control groups, and (iv) those participants who were represented in both the intervention and control groups. Furthermore, attendance at training sessions and the group CBT classes, together with a detailed training diary kept by all intervention participants, were used to evaluate program adherence.

Results

Focus group (intervention participants)

A record of the post-intervention focus group session, transcribed from an audio recording, was analysed for emergent themes. From this analysis, the top five emergent themes were:

1. 'OPPORTUNITY'.

   Participants enrolled in the lifestyle intervention program because they considered it an opportunity for much needed lifestyle change, and were attracted by the program's convenient location (i.e. based at on campus).

2. ‘LIFESTYLE’.

Prior to involvement in the lifestyle intervention, the greatest challenge to participating in regular physical activity included:

(i) themselves (i.e. ‘being lazy’);
(ii) feeling too tired from juggling university and work life;
(iii) leading a sedentary lifestyle that involved a lot of sitting. Moreover, participants agreed that portion size, excessive alcohol intake, and no money for ‘healthy’ food (such as vegetables) were their barriers to a healthy diet.

3. ‘ACCEPTABLE CHANGES’.

After program completion, participants now:

(i) engage in ‘active transport’ (e.g. walk rather than take the tram/bus; take the stairs rather than the elevator) as a means of incidental exercise;
(ii) structure physical activity into their daily routine;
(iii) use exercise as a means of socialising with friends (i.e. go for a walk together);
(iv) are generally more aware of portion sizes and ‘healthy’ food in general.

4. ‘WALKING’.

Walking (structured and/or incidental) as a means of physical activity was the most popular choice of exercise, performed alone or with family/friends.

5. ‘POSITIVE EXPERIENCE’.

Participants agreed that, overall, the lifestyle intervention had motivated them to be healthier, had empowered them with the skills for lifelong change, and had been a positive experience.

Anonymous evaluation (intervention participants)

Analysis of the anonymous completion by participants of the post-intervention evaluation form demonstrated that:

1. Attitudes toward exercise had changed as a result of participation in the lifestyle intervention, with the following themes emerging about feelings towards exercise participation: feeling more motivated; exercise had become an important aspect of their life; exercise is now a priority; they now enjoyed physical activity.
2. The nutrition education component appeared to have resulted in: more awareness/conscious of healthy options; eating better foods; consuming smaller portions.
3. The emotional state of participants had improved as a result of the CBT sessions, with participants feeling 'much happier' and less moody after the completion of the lifestyle intervention.
4. There was consensus that the most enjoyable part of the intervention was: training with others; social interactions; being part of a group.
5. Participants had a preference for 'more variety' in the exercise program because there was 'too much repetition'.

Reasons for withdrawal (wait-list control participants)

Of the three wait-list control participants who provided feedback regarding their withdrawal from the study:

- In response to Question 1, "*How did you feel when you were initially assigned to the control group?":*

Two participants stated that they were 'disappointed' once allocated to the wait-list control group, while the other said she was 'not fussed' by the allocation.

- In response to Question 2, "*Did your involvement in the study as a control participant trigger you to change anything about your current lifestyle?":*

One participant said she maintained her usual lifestyle habits as instructed to by the researcher. However, two participants indicated that their participation in pre-control testing triggered them to increase exercise and become more conscious about food choices, despite being allocated to the wait-list control and asked to maintain normal lifestyle habits.

Attendance, recruitment and retention rates.

Results showed that of the initial 62 women who inquired about participation in the Young Women's Heart Health Study, 63% (n=39) underwent baseline testing, with 77% of these participants (n=30) going on to complete post-intervention/post-control and sustainability testing. Retention in the intervention group was higher (73%) compared with wait-list control participants (64%). At the completion of the wait-list control period, only four women went on to complete the lifestyle intervention and associated testing. Adherence to the physical activity (80%) and CBT (74%) components of the lifestyle intervention was high.

Discussion

The appraisal of the lifestyle program by participants in this study is in line with recommendations that process evaluation of an intervention should be conducted to better understand study outcomes and to direct future implementation (Medical Research Council, 2000; Oakley et al., 2006). Collectively, the major findings from the focus group and anonymous evaluations demonstrated five emergent themes including 'opportunity', 'lifestyle', 'acceptable changes', 'walking', and 'positive experience'. This information suggested that the program had provided participants with strategies to implement both exercise and dietary planning into their behavioural routines. Moreover, the social interaction components of the intervention were expressed as critical to their enjoyment of the program.

The evaluation processes revealed that participants perceived all three components (exercise, nutrition education, CBT) of the lifestyle intervention to be of importance in fostering

positive lifestyle behaviour changes. This was most apparent in the responses regarding planning and engagement in exercise. Participants offered evidence that the program had imparted to them strategies to incorporate both incidental and structured physical activity into their current lifestyle, with walking as the principle exercise modality. Similarly, participants expressed a greater knowledge of the importance of dietary planning and of strategies to achieve improvements in their nutritional choices. The importance of socialising reported by the participants, particularly in the context of exercise, is consistent with findings in the systematic review (Chapter 3), where only studies that included contact with fitness professionals and others during the intervention phase resulted in increases in fitness or physical activity engagement (Carroll et al., 2007; Kerksick et al., 2010; Silva et al., 2010).

In contrast, although the data are from three wait-list control participants only, the responses support the notion that a RCT study design may not be appropriate when study volunteers are ready for lifestyle change. The responses of these participants provided evidence of a motivation to commence lifestyle change, despite the study requirement of maintaining current behaviours during the control period. This is supported by the "state of change for exercise" data presented in Addendum 7.1, where wait-list control participants were primarily in 'preparation' for change, similar to the participants allocated directly to the intervention phase. Similarly, the majority of wait-list control participants rated "exercise importance" as 'very important or important' (see Addendum 7.1), suggesting a desire to commence an intervention for lifestyle change. These are critical insights given that the control group demonstrated a reduction in WC and improvements in CVD risk profile (see Chapter 7) while undertaking the 'control' phase of the intervention study. This might be, in part, a response to knowledge of their pre-control test data, which was provided as a condition and incentive for taking part in the study (Appendix 20). Upon reflection, this knowledge may have influenced subsequent behaviour change, given that unanticipated weight loss is not normally observed in participants under wait-list control conditions (Waters et al., 2012).

Appraisal of recruitment rates demonstrated that the conversion rate of participants from initial recruitment to baseline testing was modest. However, the retention rate of participants in the intervention and control groups was lower than expected, with an allowance of 20% drop-out calculated to maintain sample power. In the current study, drop-out rates were 27% and 36% for the intervention and control groups, respectively. Moreover, there was evidence of poor transition from the wait-list control condition into the lifestyle intervention, with only

23% of women initially allocated to the control group completing the intervention phase. In contrast, program adherence for physical activity and CBT components was high among intervention participants. This data may provide insight into to recruitment and retention of young women with abdominal obesity to a lifestyle intervention, and important information about the behavious of participants initially allocated to a wait-list control group. Furthermore, because of the richness of data provided by process evaluation, future studies could be enhanced by the inclusion of perceptions from compliant control group members as well as intervention drop-outs.

In summary, the responses from participants who completed the lifestyle intervention indicated that its multi-disciplinary focus was a crucial feature in producing behaviour change and associated strategies for future weight control. This is in agreement with recommendations (A. Lang & Froelicher, 2006; Wing, 2002) that management strategies to address overweight and obesity should incorporate diet, exercise and behavioural therapy.

Chapter 8. Effects of a lifestyle intervention on cardiac measures in young women with abdominal obesity: A randomised controlled trial.

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Publication Statement:

This work has been prepared as a short report for submission to the *Canadian Journal of Cardiology*, please see Appendix 1.

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Abstract

Young adult women with obesity have shown subclinical cardiac dysfunction. Lifestyle interventions are recommended for prevention of cardiovascular disease in obese populations. In a randomised controlled trial using conventional, tissue Doppler imaging, and 2D speckle tracking imaging echocardiography, we assessed changes in cardiac morphology and function, including myocardial deformation and mechanical indices, in women (18-30 y) with abdominal obesity (n = 26) following a 12-week, multi-disciplinary lifestyle intervention. Echocardiographic measures at baseline and post-intervention were compared to a wait-list control group (n = 17). The 12-week lifestyle intervention did not result in significant changes in cardiac function.

Keywords: Waist circumference, speckle-tracking-imaging, echocardiography, exercise, physical activity, female

Summary

Lifestyle interventions are recommended for preventing cardiovascular disease and obesity. Abdominal obesity, even in young adults, is linked to abnormal cardiac remodelling and dysfunction. Technical advances in echocardiography can permit early detection and prevention of cardiac abnormalities using 2D speckle tracking imaging. The potential effect of lifestyle interventions on cardiovascular health of obese young women requires attention.

Introduction

Cardiovascular disease (CVD) is the leading cause of death among women (World Health Organisation, 2000), with abdominal obesity (Alberti et al., 2009) increasing the chance of developing cardiac and vascular dysfunction (Wong, Byrne, et al., 2006). In the USA, United Kingdom and Australia, 45-50% of women aged 20-39 years are overweight or obese (Australian Bureau of Statistics, 2013; Flegal et al., 2012; Health and Social Care Information Centre, 2011). Although the cardiovascular complications of obesity have been documented, efficacious lifestyle intervention strategies in obese young women are yet to be established. Understanding the impact of lifestyle interventions on cardiovascular impairment is important for lifelong cardiovascular health.

Cardiac dysfunction may be identified as changes in cardiac morphology and function using conventional techniques and tissue Doppler imaging (TDI) echocardiography. Using these techniques, previous cross-sectional work found subclinical abnormalities in left ventricular (LV) structure and function in young women (mean 32 ± 4 y; range 21-37 y) with obesity (Peterson, Herrero, et al., 2004). More recently [Share et al. (2014) *under review*], cardiac and myocardial dysfunction was explored in young women (mean 22 ± 4 y; range 18-30 y) with abdominal obesity, using a combination of these traditional echocardiographic techniques and the newer technique of 2D speckle tracking imaging echocardiography (STE), which may possess greater sensitivity for detecting early changes (K. A. Marcus et al., 2011). The women with abdominal obesity were found to display subclinical cardiac remodelling of the left atrium (LA), reduced mitral annular plane velocities, increased LA pressure surrogates, and prolonged timing measurements of diastolic dysfunction, when compared to aged-matched, non-obese controls. These women also exhibited reductions in LV longitudinal strain and systolic strain rate when using STE. These findings show that early intervention strategies in this population have emerging importance (K. A. Marcus et al., 2011), to arrest further progression of subclinical cardiac dysfunction and other markers of CVD. However, there are few randomised controlled trial (RCT) investigations (Chang et al., 2010) of such strategies in young adult women (< 30 yr), despite the increasing prevalence of overweight/obesity in this population

Therefore, the primary aim of this RCT was to examine the effects of a multi-disciplinary lifestyle intervention on measures of cardiac function, using conventional, TDI and STE echocardiography, in young adult women with abdominal obesity.

Methods

Ethics statement

Participants provided written informed consent following approval of the Australian Catholic University Human Research Ethics Committee (V2009-91). The intervention received clinical trial registration from the Australian New Zealand Clinical Trials Registry (ACTRN12612001017819). All testing was completed between August 2010 and February 2012.

Participants

Sixty-two university-enrolled women aged 18 to 30 years with abdominal obesity [waist circumference (WC) ≥ 80 cm] and leading a sedentary lifestyle (< 210 min per week of organised physical activity in the past six months (Department of Health and Ageing, 1999) were invited to participate in a randomised controlled trial. Participants were free from CVD risk factors (hypertension, diabetes, and smoking) and endocrine disorders, had not undergone bariatric surgery, and were not pregnant.

From 62 women who responded to recruitment, 11 women did not meet the inclusion criteria and a further 12 eligible participants did not complete testing (Figure 8.1). Therefore, 39 participants who underwent baseline testing were randomisation to either the intervention or wait-list control group. A wait-list (delayed-start) control design was chosen to allow *all participants* access to the lifestyle intervention.

All participants who attended two testing sessions at both pre-intervention (0 wk) and post 12-wk intervention, had refrained from strenuous physical activity in the preceding 24 hours. For the first testing session (anthropometric, blood biochemical, vascular measures), participants were in a fasted state, while for the second session (echocardiography, fitness measures), participants refrained from caffeine and alcohol in the preceding 24 hours. Wait-

list control participants were assessed at three times (0 wk; post-control period (12-wk); post 12 wk intervention).

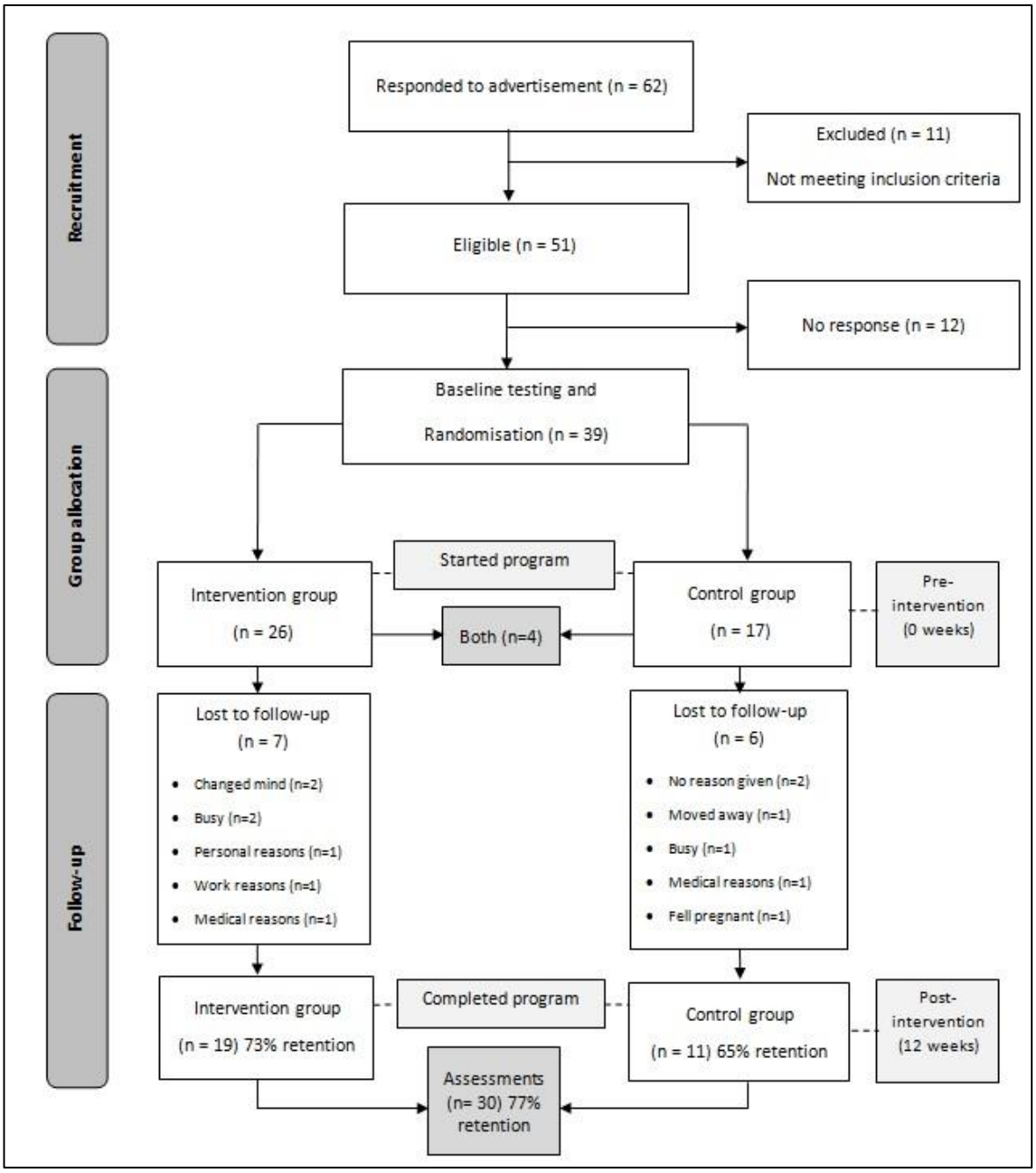

Figure 8.1. Flow diagram of participants

Metabolic and vascular characteristics

Body mass was measured to the nearest 0.1 kg (Tanita, Tokyo, Japan), and stature was measured to the nearest 0.1 cm (Seca, Germany). Body mass index was calculated (World Health Organisation, 2000) . WC was measured to the nearest 0.1 cm at the midpoint between sub-costal and supra-iliac landmarks, with the average of two measurements reported. Blood pressure and heart rate were measured in a supine position after 15 minutes rest using an automated digital sphygmomanometer (Dinamap, GE Technology, USA). Following an overnight fast, intravenous blood was collected from the antecubital vein. Blood lipids [triglycerides, total cholesterol, high-density lipoprotein (HDL)] were measured using the Reflotron Plus desktop analyser (Roche, Switzerland). Fasting plasma glucose, insulin and high sensitivity C-reactive protein (hs-CRP) concentrations were analysed in a clinical pathology laboratory. Insulin resistance (IR) was estimated by the homeostasis model assessment (HOMA-IR) (Matthews et al., 1985). A graded submaximal cycle ergometer test (Golding et al., 1989) was used to estimate cardiorespiratory fitness (Predicted VO_{2max}). Participants self-reported habitual weekly physical activity.

Ultrasonography scans for carotid intima-media thickness (c-IMT) were performed on the far (posterior) wall of the right common carotid artery. Semi-automated edge-detection wall-tracking software was used to analyse images (Chodakauskas, 2006).

Echocardiography

Standard 2D transthoracic echocardiography examination was conducted in accordance with the recommendations of the American Society of Echocardiography (R. M. Lang et al., 2005). Image acquisition was performed by the same experienced operator using a commercially available ultrasound device (Vivid i, GE Healthcare, Horten, Norway). Digital data were stored for subsequent off-line analyses (Echopac, GE Medical Systems). All measurements were the averages derived from three consecutive cardiac cycles.

M-mode measurements were obtained in the parasternal long-axis. LV volumes and ejection fraction were quantified using a Simpson's bi-plane method. Pulsed-wave Doppler-derived transmitral inflow velocities were obtained from the apical four-chamber view with the sample volume at the tips of the mitral leaflets. TDI was used to measure mitral annular

velocities. Data are reported as the average of four sites from apical 4-chamber (septal and lateral wall) and 2-chamber (inferior and anterior walls) views.

STE analysis of myocardial wall motion was performed on greyscale images acquired at a minimum frame rate of 70 Hz. The values from circumferential apical and basal views were averaged. Twist, twist/untwist rate, and apical and basal rotational mechanics of the LV were also calculated. Customised software (Scilab 4.1, Avignon University, Avignon, France) was used to normalise time sequence as a percentage of systolic duration.

Lifestyle intervention

The 12-wk multi-disciplinary lifestyle intervention comprised three main components: (1) moderate-intensity physical activity, (2) nutrition education, and (3) small-group cognitive behavioural therapy (CBT). In contrast, participants in the wait-list control group were instructed to continue existing lifestyle choices, and after 12 weeks were invited to complete the same lifestyle intervention (Table 7.1).

Statistics

Descriptive statistics are presented as mean ± SD. Following tests for normal distribution, group comparisons over time were performed using a general liner mixed-model analysis. This statistical test was chosen based on its ability to analyse unbalanced repeated measures data (Cnaan et al., 1997). IBM SPSS statistical software, Version 20 for Windows (SPSS Inc, Chicago IL) was used for analyses and statistical significance was set at $P \leq 0.05$. Hedge's *g* was used for effect size calculations. Intra- and inter-observer reliability was performed for key variables and reported as coefficient of variation (CV) (Table8.1)

Table 8.1. Reliability analyses for waist circumference and major echocardiographic parameters.

		Coefficient of variation (CV) (%)	
	n	**Intra-observer**	**Inter-observer**
Waist circumference	**20**	1.26	NA
Carotid IMT	**20**	2.26	NA
Conventional & TDI echocardiography	**10**		
LV mass		2.7	2.1
LVED diameter		1.1	2.0
IVS thickness		3.2	4.8
PW thickness		2.3	3.5
E velocity		1.9	1.6
A velocity		2.5	1.8
E/A ratio		2.5	2.0
Septal S_m velocity		1.4	2.3
Septal E_m velocity		2.2	4.0
Septal A_m velocity		1.5	4.2
Speckle tracking echocardiography	**20**		
LV L strain		5.9	5.1
LV L diastolic SR		4.3	7.8
LV L systolic SR		4.1	5.5
LV C strain		4.7	5.5
LV C diastolic SR		5.7	8.3
LV C systolic SR		5.7	5.3
Apical rotation		7.0	11.5
Basal rotation		6.5	9.7
LV twist		9.2	10.0

IMT: intima-media thickness, LV: left ventricle, LVED: left ventricular end-diastolic, IVS: inter-ventricular septum, PW: posterior-wall, L: longitudinal, C: circumferential (average of apical and basal views).

Results

Thirty-nine participants were included in the analysis. After baseline testing and commencement of the intervention period, 27% of intervention participants (n = 7) and 35% of control participants (n = 6) withdrew from the study (Figure 8.1). In contrast, compliance rates within the intervention group showed 80% attendance for the physical activity sessions and 74% for the CBT sessions.

Table 8.2 lists the anthropometric, metabolic, fitness and vascular characteristics of the intervention and control groups at pre- and post-intervention. All markers were similar between groups at baseline, with physical activity being the only between-group difference post-intervention, with an effect size (*g*) of 2.14. Within-group changes for the intervention

group from baseline to post-testing were a reduction in WC and systolic blood pressure, and improvements in markers of fitness (predicted VO_{2max} and physical activity – see table 8.2) and a Bruce treadmill protocol time increased from 10.5 ± 2.2 min to 11.8 ± 2.2 min ($P < 0.001$). The vascular measure of c-IMT was unchanged by the intervention. In the control group, despite participants reporting maintained lifestyle habits during the control period, a reduction in both WC and systolic blood pressure was observed.

Table 8.2. Metabolic and vascular characteristics for the intervention and control groups at pre-intervention/pre-control, and post-intervention/post-control.

	Pre-control/Pre-intervention (0 wk)			**Post-control/Post-intervention (12 wk)**		
	Control (n=17)	**Intervention (n=26)**	***P* value**	**Control (n=11)**	**Intervention (n=19)**	***Between group P***
Age (years)	22.8 ± 3.4	22.0 ± 3.7	0.56			
Body mass (kg)	86.1 ± 17.8	89.8 ± 21.1	0.56	82.5 ± 19.5	86.9 ± 20.5	0.61
BMI ($kg \cdot m^{-2}$)	31.4 ± 6.6	32.2 ± 5.9	0.67	30.0 ± 6.6	31.3 ± 0.9	0.72
Waist circumference (cm)	92.8 ± 10.8	93.1 ± 11.7	0.93	87.2 ± 10.5[§]	87.3 ± 9.8[§]	0.91
Systolic blood pressure (mmHg)	119 ± 8	120 ± 11	0.67	111 ± 12[§]	116 ± 9[§]	0.31
Diastolic blood pressure (mmHg)	64 ± 8	68 ± 6	0.11	59 ± 5	64 ± 9	0.11
Fasting glucose ($mmol \cdot L^{-1}$)[#]	4.5 ± 0.6	4.6 ± 0.4	0.35	4.4 ± 0.6	4.6 ± 0.4	0.32
Triglycerides ($mmol \cdot L^{-1}$)[#]	1.2 ± 0.4	1.3 ± 0.5	0.84	1.5 ± 0.6	1.4 ± 0.7	0.25
HDL-cholesterol ($mmol \cdot L^{-1}$)	1.7 ± 0.6	1.7 ± 0.5	0.89	2.0 ± 0.5	1.9 ± 0.5	0.71
Total cholesterol ($mmol \cdot L^{-1}$)	4.3 ± 0.5	4.4 ± 0.6	0.64	4.3 ± 0.4	4.3 ± 0.8	0.75
Fasting insulin ($mU \cdot L^{-1}$)[#]	8.1 ± 4.4	9.4 ± 4.7	0.72	7.4 ± 2.7	8.1 ± 2.6	0.20
HOMA-IR	1.6 ± 1.0	1.9 ± 1.0	0.33	1.4 ± 0.5	1.6 ± 0.5	0.61
hs-CRP ($mg \cdot L^{-1}$)[#]	2.9 ± 2.6	3.5 ± 3.0	0.49	3.9 ± 3.7	4.6 ± 4.9	0.58
Resting heart rate (bpm)	63 ± 12	69 ± 10	0.10	73 ± 20	67 ± 14	0.37
Predicted $\dot{V}O_2$ max ($mL \cdot kg^{-1} \cdot min^{-1}$)	32.0 ± 10.3	27.9 ± 7.0	0.13	31.7 ± 10.9	32.6 ± 6.8[§]	0.24
Physical activity ($min \cdot wk^{-1}$)[#]	118 ± 89	97 ± 62	0.87	121 ± 81	280 ± 67[§]	< 0.001[*]
Carotid IMT (mm)	0.41 ± 0.04	0.41 ± 0.03	0.43	0.40 ± 0.03	0.37 ± 0.14	0.15

Data are mean ± standard deviation. BMI: body mass index, HDL: high-density lipoproteins, HOMA-IR: homeostatic model assessment of insulin resistance, hs-CRP: high sensitivity C-reactive protein, IMT: intima media thickness. CI: confidence interval. [*] *$P \leq 0.05$.* [#] *data were log transformed before reported P-values were obtained.* [*]*between-group differences (at post) $P < 0.001$.* [§]*within-group differences $P \leq 0.05$.*

Table 8.3 shows the primary variables of interest in this study. Specifically, there were no differences between intervention and control groups for cardiac morphology, cardiac function, myocardial deformation or myocardial mechanics at baseline or post-intervention. However, a within-group change was observed for both groups, with an increase in LV mass indexed.

Table 8.3. Cardiac morphology and function, and myocardial deformation and mechanics for intervention and control groups at pre-intervention/pre-control, and post-intervention/post-control.

	Pre-control/Pre-intervention (0 wk)					Pre-control/Post-intervention (12 wk)				
	Control n = 17	**Intervention n = 26**	***Between group P***	**Hedges' *g* Effect Size**	**Mean Difference (95% CI)**	**Control n = 11**	**Intervention n = 19**	***Between group P***	**Hedges' *g* Effect Size**	**Mean Difference (95% CI)**
Cardiac morphology										
LA diameter (mm)	32.5 ± 3.8	32.9 ± 5.3	0.80	0.08	0.4 (-2.7 to 3.4)	30.8 ± 5.4	31.5 ± 3.0	0.76	0.17	0.7 (-2.7 to 3.4)
LV mass indexed ($g \cdot m^{-2.7}$)	34.1 ± 10.2	40.3 ± 10.8	0.12	0.57	6.3 (-1.3 to 13.8)	43.1 ± 9.0[§]	45.0 ± 10.5[§]	0.67	0.18	1.9 (-7.0 to 10.7)
LVED diameter (mm)	44.6 ± 2.5	43.5 ± 4.5	0.37	0.28	-1.0 (-3.7 to 1.7)	43.0 ± 5.5	41.7 ± 4.3	0.50	0.27	-1.3 (-5.1 to 2.5)
LVES diameter (mm)	29.5 ± 3.6	29.3 ± 5.0	0.96	0.04	-0.1 (-3.3 to 3.0)	28.5 ± 3.9	29.6 ± 5.1	0.45	0.22	-1.3 (-3.3 to 3.1)
LV PW thickness (mm)	9.7 ± 1.1	10.5 ± 1.6	0.31	0.55	0.8 (-0.3 to 1.8)	10.4 ± 3.7	11.5 ± 2.7	0.31	0.28	-1.1 (-3.5 to 1.7)
IVS thickness (mm)	10.3 ± 2.0	10.6 ± 1.5	0.57	0.17	0.27 (-0.9 to 1.5)	10.4 ± 1.5	11.4 ± 1.3	0.07	0.70	1.0 (-0.1 to 2.2)
Cardiac function										
LV ejection fraction (%)[#]	62.1 ± 5.8	64.1 ± 4.3	0.33	0.39	2.1 (-1.6 to 5.8)	60.3 ± 5.8	63.7 ± 6.6	0.23	0.52	3.4 (-2.4 to 9.2)
E velocity ($cm \cdot s^{-1}$)	86.1 ± 16.6	87.7 ± 13.5	0.79	0.10	1.6 (-8.2 to 11.5)	89.6 ± 21.8	89.2 ± 18.6	0.88	0.02	-0.4 (-15.8 to 14.9)
A velocity ($cm \cdot s^{-1}$)	41.3 ± 9.5	43.3 ± 12.2	0.57	0.18	2.0 (3.6 to 9.4)	40.3 ± 8.4	41.4 ± 12.4	0.81	0.09	1.0 (-7.7 to 9.7)
E/A ratio	2.2 ± 0.5	2.2 ± 0.6	0.95	0.00	0.01 (-0.4 to 0.4)	2.3 ± 0.6	2.3 ± 0.6	0.97	0.00	-0.02 -0.5 to 0.4)
S_m velocity ($cm \cdot s^{-1}$)	8.6 ± 1.2	9.4 ± 1.6	0.05	0.54	0.8 (-0.2 to 1.8)	9.0 ± 0.9	9.0 ± 1.3	0.72	0.00	0.0 (-1.0 to 1.1)
E_m velocity ($cm \cdot s^{-1}$)	14.6 ± 2.9	14.6 ± 2.6	0.96	0.00	0.0 (-2.0 to 2.0)	14.0 ± 2.2	15.0 ± 2.9	0.50	0.36	1.0 (-1.5 to 3.5)
A_m velocity ($cm \cdot s^{-1}$)	6.8 ± 1.1	7.2 ± 1.1	0.15	0.36	0.4 (-0.3 to 1.4)	7.2 ± 1.3	7.6 ± 1.1	0.27	0.33	0.4 (-0.6 to 1.5)
Myocardial deformation										
Longitudinal strain (%)	-15.9 ± 2.2	-16.3 ± 2.0	0.49	0.19	-0.5 (-2.3 to 1.4)	-16.5 ± 1.5	-17.1 ± 1.1	0.21	0.46	-0.7 (-2.0 to 0.6)
Circumferential strain (%)	-19.5 ± 2.5	-20.1 ± 3.2	0.54	0.20	0.6 (-1.6 to 2.7)	-18.3 ± 2.6	-18.8 ± 1.9	0.64	0.67	0.5 (-1.5 to 2.2)
Myocardial mechanics										
Apical rotation (˚)	4.5 ± 1.7	4.4 ± 1.4	0.73	0.06	-0.1 (-1.3 to 1.1)	4.0 ± 1.5	4.6 ± 1.7	0.29	0.35	0.6 (-0.7 to 2.0)
Basal rotation (˚)	-5.3 ± 1.9	-5.5 ± 1.8	0.87	0.10	-0.2 (-1.8 to 1.4)	-5.6 ± 1.4	-4.0 ± 2.0	0.07	0.82	1.6 -0.3 to 3.4)
Twist (˚)	6.7 ± 1.8	8.2 ± 3.3	0.10	0.53	1.6 (-0.6 to 3.7)	5.1 ± 2.5	5.2 ± 2.5	0.87	0.04	0.1 (-2.7 to 2.5)
Twist rate ($˚ \cdot s^{-1}$)[#]	68.1 ± 18.0	72.0 ± 19.9	0.63	0.20	3.8 (-11.8 to 19.5)	52.8 ± 15.6	47.3 ± 15.0	0.34	0.35	-5.4 (-18.5 to 7.7)
Untwist rate ($˚ \cdot s^{-1}$)	-58.2 ± 17.8	-65.1 ± 19.6	0.35	0.35	-6.8 (-22.3 to 8.6)	-52.4 ± 25.1	-44.4 ± 14.5	0.30	0.41	8.0 (-8.2 to 24.3)

Data are mean ± standard deviation. LA: left atrium, LV: left ventricle, LVED: left ventricular end-diastolic, LVES: left ventricle end-systolic IVS: inter-ventricular spetum, PW: posterior wall, Circumferential is the average of apical and basal views. S_m, E_m, & A_m are means of four sites at the mitral annulus from apical 4-chamber (septal, lateral) and 2-chamber views (inferior, anterior). CI: confidence interval. [#] data were log transformed before reported P-values were obtained. [*]between-group differences P ≤ 0.05. [§]within-group differences P ≤ 0.05.

Discussion

The aim of this study of young women with abdominal obesity (a group under-represented in the literature) was to examine the effects of a multi-disciplinary lifestyle intervention on cardiac, vascular and myocardial measures. Specifically, we assessed the effects of an intervention which incorporated physical activity, nutrition education and CBT, using conventional, TDI and 2D speckle-tracking echocardiographic techniques. The 12-week lifestyle intervention produced no marked changes in cardiac morphology or function, c-IMT, or myocardial deformation or mechanical indices, despite significant changes in WC, systolic blood pressure and cardiorespiratory fitness.

Similar to our study, an 8-week lifestyle intervention of exercise and diet was not associated with improvements in LV diastolic function measured using conventional and TDI makers in a cohort of obese middle-aged adults (47 ± 11 y), despite reduced body composition markers (Wong, Byrne, et al., 2006). Likewise, Millen et al. (2014) delivered a 6-week exercise program (without a dietary component) to overweight and obese middle-aged adults (42 ± 18 y) of similar WC (94 ± 18 cm) to our study. Again, the intervention failed to produce improvements in indices of LV diastolic function, including tissue velocities measured with TDI, despite improved cardiorespiratory fitness.

There are several possible reasons to explain why we observed no changes in myocardial function following the multi-disciplinary lifestyle intervention. The 12-week duration may not have been sufficient to drive significant reductions in the cardiac, vascular and myocardial measures of interest. Similarly, the intensity and/or frequency of the exercise sessions may have been too low to produce changes in these measures. In comparison, using a 12-month lifestyle intervention of daily endurance exercise and resistance training, Dutheil et al. (2013) reported that adults (59 ± 5 y) with central adiposity (WC: 102 ± 9 cm) had improved c-IMT, although their greater age and WC might be factors in the observed improvements. Similarly, Eriksson et al. (2010) conducted a 6-month, low-intensity exercise intervention with women (47 ± 8 y) with abdominal obesity (WC: 103 ± 8 cm). Again, these women were older and more obese than the women in our study. Their intervention produced improvements in longitudinal right ventricular (RV) systolic function, and small but significant changes in LV systolic and RV diastolic dimensions (), when using conventional and Doppler echocardiography.

Another reason for no changes in myocardial function could be related to the nutritional component of our study. Specifically, we provided nutrition education as a means for behaviour change in dietary habits, rather than implementing caloric restriction which may not be sustainable in the longer term (Wycherley et al., 2012). However, successful outcomes have been observed with programs based on diet restriction. For example, severely obese adolescents (15 ± 2 y) who participated in a 9-month lifestyle intervention of caloric restriction and exercise had improved LV mitral annular plane velocities, and longitudinal strain (Obert et al., 2013). However, myocardial twist mechanics and LV morphology remained unchanged following the 9-month program.

This study has some possible limitations. Firstly, there is potential masking of comparative benefits for the intervention group due to unexpected decreases in WC in the control group, despite undetectable changes in their weight management behaviour. However, these undetected changes might be a consequence of problems associated with self-reporting of nutritional and/or physical activity habits over the 12-week control period. Some may argue shortcomings associated with ultrasonography acquisition and analyses being dependent on operator skill, but intra- and inter-reliability measures for the present study were similar to previous reports (K. A. Marcus et al., 2011). Finally, central fat distribution was not measured using more precise estimations (e.g., MRI and dual energy x-ray absorptiometry), but WC does provides a level of sensitivity relevant to most clinical settings(National Health and Medical Research Council, 2005).

Conclusion

This work contributes to the limited RCT literature addressing lifestyle interventions on cardiovascular risk in young adult women, providing novel data from conventional and TDI echocardiography and STE. Although decreases in WC and increases in cardiorespiratory fitness were noted following the lifestyle intervention, there were no changes in cardiac morphology or function, or in myocardial deformation or mechanical indices.

Supplementary Material

This section contains supplementary method which will accompany the short report during submission. This information is presented in Chapters 4 and 7.

Participants

All participants attended the laboratory on two occasions at both baseline and post-intervention, and were requested to refrain from strenuous physical activity in the 24 hours prior to testing on all occasions. During the first visit participant arrived in a fasted state and clinical testing lasted 75 min. The second visit only required participants to abstain from caffeine and alcohol for 12 hr and lasted 60 min. Testing was performed at pre-intervention/pre-control (0 wks) and again at post-intervention/post-control (12 wks). All measurements were taken at the same time of day (±2 hr) and by the same researcher.

Metabolic and vascular characteristics

Blood samples were drawn from an antecubital vein into a 10 ml evacuated, lithium heparin anticoagulant vacutainer tube by a qualified phlebotomist. Blood samples were then centrifuged at 3000 rpm for 10 min (Spinton, Australia, GT-175BR) to obtain plasma for subsequent analysis by spectophotometrically using a Reflotron PLUS^{TM} analyser, and further analyses performed by pathology. The Reflotron requires a 30 µL droplet of blood placed on specialised measuring strips to be fed into the desktop analyser. Insulin resistance (IR) was estimated by the homeostasis model assessment (HOMA-IR), using the equation: HOMA-IR = fasting insulin concentration (µU/mL) x fasting glucose concentration (mmol/l) / 22.5 (Matthews et al., 1985) , with values more than 2.5 considered indicative of IR (Jensterle et al., 2008). For hs-CRP, a value of > 3.0 mg·l^{-1} was considered high risk (Pearson et al., 2003)

Echocardiography

Image acquisition was performed by the same experienced operator using a commercially available ultrasound (Vivid i, GE Healthcare, Horten, Norway) with a 3.5 MHz phased-array transducer. Participants were examined in the left-lateral decubitus position in a dark room, and connected to a 3-lead ECG. A minimum frame-rate of 70 Hz was used when acquiring gray-scale cine-loops. Digital data were stored for subsequent off-line analysis with specific software (Echopac, GE Medical Systems) by an observer blinded to subject assignment.

Speckle tracking imaging echocardiography (STE) analysis of myocardial wall motion was performed using frame-by-frame tracking of natural acoustic markers known as "speckles" in a region of interest from greyscale images. Using proprietary software (EchoPAC v108.1.5, GE Medical Systems, Horton Norway), endocardial borders were manually traced and region of interest adjusted to include all of the myocardium.

Lifestyle intervention

The 12-wk lifestyle intervention was comprised of three main components: (1) moderate-intensity physical activity (2) nutrition education, and (3) small-group cognitive behavioural therapy. In contrast, participants in the wait-list control group were instructed to continue existing lifestyle choices, and after 12 weeks were invited to complete the same lifestyle intervention.

1. Physical activity: participants completed two supervised exercise sessions (progressive aerobic and resistance training circuit) with a qualified Exercise Scientist, and one unsupervised, but prescribed home-based session (brisk walk or jog with intermittent high-intensity intervals) per week. The supervised sessions lasted approximately 60 min, with the intensity of the exercise increasing from 60% to 85% on the OMNI Picture System (Robertson, 2004), by the end of the 12-wk period. To replicate community resources, sessions occurred in both the gym on campus and at a local park. Participants maintained a detailed training diary. The standard Bruce treadmill protocol (Bruce et al.,

1973) was completed every three weeks (0, 4, 8, 12 weeks) by intervention participants to assist with prescription of progressive overload of aerobic activities during the program.

2. Nutrition education: participants in the intervention group received weekly nutrition education sessions from a dietician about healthy eating choices from the existing Australian Dietary Guidelines (National Health and Medical Research Council, 2005) . Information provided education regarding non-dieting weight management and healthy eating principles tailored to the perceived needs of the female participants.

3. Cognitive behavioural therapy (CBT): intervention participants undertook weekly 60-min group cognitive CBT sessions with a counsellor, which provided psychosocial support and developed skills to overcome personal barriers to lifestyle change. The program aimed to empower individuals to develop healthier eating and physical activity patterns

Statistics

Data were tested for normal distribution using the Shapiro-Wilk statistic and skewness and kurtosis (Peat & Barton, 2005). Log transformation was performed on data not normally distributed. Hedge's *g* calculated effect size to assess magnitude, with an effect size of ≥ 0.2 considered small, ≥ 0.5 considered medium, and ≥ 0.8 considered large (Cohen, 1988). Mean differences and 95% confidence intervals (CI) for each variable were also reported.

Where possible, measures were completed in duplicate and intra and inter-observer coefficient of variation (CV) was reported. CV was conducted on major cardiometabolic risk factors (n=20), and cardiac variables in randomly selected participants (conventional and TDI echocardiography, n=10; STE, n=20) in order to demonstrate the off-line analyses were reproducible. Variables were evaluated twice by the same observer, and once more by another experiences observer, both blinded to participant details.

8.1 ADDENDUM: Cardiac and vascular measures in young women with abdominal obesity: Short-term sustainability of outcomes following completion of a lifestyle intervention.

Introduction

The data presented in Chapter 8, entitled "Effects of a lifestyle intervention on cardiac measures in young women with abdominal obesity: A randomised controlled trial, have been prepared for submission to the *Canadian Journal of Cardiology*. In Chapter 8, pre- and post-intervention data are presented for cardiac morphology and function, myocardial deformation and mechanical indices, and carotid IMT following a 12-week, multi-disciplinary lifestyle intervention. These data were obtained from conventional, TDI, and STE-derived ultrasonography.

In this addendum, data for cardiac morphology and function, myocardial deformation and mechanical indices and carotid IMT, collected at follow-up testing performed at 24 weeks (i.e. 12 weeks *after* post-intervention testing), are presented. These within-group 'sustainability' data were collected from all participants who completed the lifestyle intervention (n=19), using conventional, TDI and STE-derived ultrasonography. These data were not included in the manuscript forming Chapter 8 given that the lifestyle intervention did not result in any significant changes in these measures at the post-intervention period compared with the control group.

Methods

The experimental methods are described in Chapters 4, 6 and 8. All data were checked for normality according to established standards (Peat & Barton, 2005) prior to statistical analyses. A linear mixed model was then computed to assess within-group comparison across time period.

Results

Table 8.4 describes and compares the cardiac and vascular data derived from ultrasonography analyses for all participants at pre-intervention (n=26) and for participants completing the intervention and returning for sustainability testing at 24 weeks (n = 19). The majority of cardiac measures did not change from pre-intervention to sustainability testing. Specifically, for cardiac morphology and function parameters measured via conventional and TDI echocardiography, there were no changes over the 24-week period. Differences in myocardial measures obtained from STE, were observed for circumferential strain and in twist and twist rate. For the vascular measure of carotid IMT, there was no change at the sustainability phase.

Table 8.4. Within-group comparisons of cardiac and vascular data collected from conventional, TDI and STE-derived ultrasonography at pre-intervention (0 week) and sustainability (24 week) for the intervention group.

Outcome measure	Pre-intervention (n = 26)	Sustainability (n = 19)
2D and m-mode		
LA diameter (mm)	32.9 ± 5.3	31.8 ± 3.6
LV mass indexed ($g/m^{-2.7}$)	40.3 ± 10.8	43.8 ± 8.9
LV end-diastolic diameter (mm)	43.5 ± 4.5	44.8 ± 3.9
LV end-systolic diameter (mm)	29.3 ± 5.0	30.2 ± 4.6
LV PW thickness (mm)	10.5 ± 1.6	11.0 ± 1.6
IVS thickness (mm)	10.6 ± 1.5	10.6 ± 1.5
LV ejection fraction (%) [#]	64.1 ± 4.3	62.4 ± 7.0
Carotid IMT (mm)	0.41 ± 0.03	0.40 ± 0.03
Pulsed-wave Doppler		
E velocity ($cm \cdot s^{-1}$)	87.7 ± 13.5	81.1 ± 14.8
A velocity ($cm \cdot s^{-1}$)	43.3 ± 12.2	42.1 ± 9.8
E/A ratio	2.2 ± 0.6	2.0 ± 0.4
Tissue Doppler imaging		
S_m ($cm \cdot s^{-1}$)	9.4 ± 1.6	8.8 ± 1.3
E_m ($cm \cdot s^{-1}$)	14.6 ± 2.6	14.7 ± 2.8
A_m ($cm \cdot s^{-1}$)	7.2 ± 1.1	7.1 ± 1.2
Speckle tracking echocardiography		
Longitudinal strain (%)	-16.3 ± 2.0	-16.6 ± 1.5
Circumferential strain (%)	-20.1 ± 3.2	-17.3 ± 4.3[*]
Apical rotation (˚)	4.4 ± 1.4	3.9 ± 1.7
Basal rotation (˚)	-5.5 ± 1.8	-4.5 ± 2.4
Twist (˚)	8.2 ± 3.3	4.8 ± 1.5[*]
Twist rate ($˚ \cdot s^{-1}$)	72.0 ± 19.9	51.1 ± 17.9[*]
Untwist rate ($˚ \cdot s^{-1}$)	-65.1 ± 19.6	-53.7 ± 20.3

Data presented as mean ± SD. IMT, intima-media thickness. [#] log10 transformation. [*] significant difference (P < 0.05). LA, left atrium. LV, left ventricular. IVS, Inter-ventricular septum. PW, posterior wall.

Discussion

At 12 weeks after completion of the lifestyle intervention (i.e. 24 weeks from study commencement), there were no changes in cardiac morphology or function or c-IMT for participants who had completed the 12-week multidisciplinary program. These within-group outcomes are consistent with the data collected immediately upon completion of the lifestyle intervention (presented in Chapter 8), with the exception of left ventricle mass indexed to height. There was an increase in mass indexed at post-intervention in Chapter 8, but at the testing scheduled for the sustainability phase of the intervention (Table 1), the increase no longer reached statistical significance. It is hypothesised that this loss in mass indexed from post-intervention could be related to a rebound in lifestyle behaviours, such as losses in physical activity and dietary improvements (see Chapters 7 and 9), when the intensive support of the intervention has ceased (Wycherley et al., 2012)

With respect to myocardial deformation and mechanical indices, three STE-derived parameters changed from pre-intervention at 24 weeks. These parameters were circumferential strain, twist and twist rate (with twist rate dependent on the 'twist' measure). These 'sustainability' changes are difficult to explain, in magnitude and direction, given that they were not different from baseline when assessed immediately post-intervention (see Chapter 8). Therefore, future CVD intervention studies should incorporate these STE-derived measures to substantiate these findings.

In summary, when the 'sustainability' data were considered alongside post-intervention data (Chapter 8), it was apparent that the 12-week intervention delivered in this thesis was not associated with improvements in echocardiographic measures or c-IMT. Some possible reasons for this are addressed in more detail in Chapter 8, including an intervention duration, exercise intensity and/or dietary component insufficient to produce significant cardiac or vascular adaptations. However, the findings of Chapter 6 should also be considered, in which women with abdominal obesity, when compared to those with a WC < 80 cm, displayed cardiac abnormalities associated with remodelling and myocardial dysfunction. These 'abnormalities' were not considered of 'clinical' consequence, given that each parameter was still within its 'normal' range. Therefore, it is possible that the degree of CVD progression in these markers, at this stage of early detection, is not substantive enough for a lifestyle intervention to demonstrate significant improvements in cardiac or vascular outcomes.

Chapter 9. Cardiovascular disease risk factor profile and lifestyle modification in young women with abdominal obesity: A one-year follow-up.

Introduction

Long-term sustainability of behaviour change addressed with lifestyle intervention programs have been met with limited success (Wycherley et al., 2012). In Chapter 3, a systematic review of the literature found only five RCT studies of premenopausal adult women (mean age $\leq$ 40 years) in the past decade investigating the effectiveness of a multi-disciplinary lifestyle intervention on CVD risk profile. Of these, three reported that follow-up testing was conducted, at 32 weeks (Chang et al., 2010), 36 weeks (Carroll et al., 2007), and 96 weeks (Silva et al., 2008) after completion of the intervention. However, only one of these studies (Chang et al., 2010) reported data from this follow-up testing. Therefore, there is a clear need for long-term follow-up to evaluate the sustainability of behaviour change and CVD risk factor modification, once the research-based delivery of a lifestyle intervention is completed.

In this supplementary chapter, data from a subsample of intervention participants who completed follow-up testing at 52 weeks post-intervention are addressed. The aim of this testing was to evaluate the sustainability of CVD risk factor improvements and lifestyle behaviour changes observed immediately post-intervention.

Methods

The 'longitudinal' follow-up was performed on a subsample of women (n=7) who completed the lifestyle intervention and were available at 52 weeks post-intervention. 'Longitudinal' testing was identical to that performed at the pre-intervention, post-intervention, and 'sustainability' phases. Briefly, metabolic, vascular and cardiac variables were collected over two laboratory sessions for the assessment of anthropometry, metabolic syndrome markers, blood biochemistry, aerobic capacity, vascular morphology, cardiac morphology and function, and myocardial deformation and mechanical indices. Data relevant to lifestyle

behaviour, including weekly physical activity, dietary habits, and stage of change were also collected. The methodological procedures for the collection of these data are reported in Chapters 4 to 8. All data were checked for normality according to established standards (Peat & Barton, 2005) prior to statistical analyses. A linear mixed model was then computed to assess within-group comparisons across the four testing periods.

Results

Tables 9.1 and 9.2 present metabolic, vascular and cardiac data for a subsample of participants (n=7) in the Young Women's Heart Health Study across four time-points (pre-intervention, 0 weeks; post-intervention, 12 weeks; sustainability, 24 weeks; longitudinal follow-up, 52 weeks). The metabolic outcome measures (Table 9.1), from pre-intervention to post-intervention, participants showed significant reductions in WC-dependent measures (WC, WHR, WHtR), increased HDL-cholesterol, improved predicted VO_{2max}, increased weekly physical activity, and a reduced daily energy intake. Some of these measures (WHR, WHtR), together with fasting glucose and resting heart rate, were significantly improved from pre-intervention to sustainability. At longitudinal follow-up, indices of WC (WC, WHR, WHtR), resting heart rate, weekly physical activity and daily energy intake were again significantly improved from pre-intervention. Additionally, body mass, BMI, WC, hip circumference and WHtR all improved from sustainability (24 weeks) to longitudinal follow-up (52 weeks).

For vascular measures (Table 9.1), blood pressure was unchanged by the intervention. Conversely, carotid IMT was significantly reduced from pre-intervention to sustainability, but was no longer different from pre-intervention at longitudinal follow-up.

Table 9.1. Metabolic, lifestyle and vascular data collected at pre-intervention (0 wk), post-intervention (12 wk), sustainability (24 wk), and longitudinal follow-up (52 wk), for a subsample (n = 7) of participants in the Young Women's Heart Health Study.

Outcome measure	Pre-intervention (0 weeks)	Post-intervention (12 weeks)	Sustainability (24 weeks)	Longitudinal (52 weeks)
Metabolic				
Body mass (kg)	85.4 ± 18.9	85.4 ± 21.3	84.7 ± 22.2	80.3 ± 17.2[b]
Body mass index (kg/m^2)	31.7 ± 4.0	31.5 ± 5.07	31.3 ± 5.6	29.8 ± 4.5[b]
Waist circumference (cm)	93.5 ± 6.8	88.9 ± 8.5[a]	90.4 ± 9.8	86.1 ± 8.9[a,b]
Hip circumference (cm)	115.8 ± 12.7	116.2 ± 14.3	116.5 ± 15.3	110.9 ± 12.3[b]
Waist-hip-ratio	0.81 ± 0.06	0.77 ± 0.05[a]	0.78 ± 0.05[a]	0.78 ± 0.05[a]
Waist-height-ratio	0.57 ± 0.02	0.54 ± 0.03[a]	0.55 ± 0.05[a]	0.53 ± 0.05[a,b]
Fasting glucose (mmol·L^{-1})	4.9 ± 0.5	4.5 ± 0.2	4.4 ± 0.2[a]	4.0 ± 1.8
Fasting insulin (mU·L^{-1})[#]	8.9 ± 3.1	8.3 ± 1.9	9.4 ± 6.5	7.4 ± 2.5
HOMA-IR[#]	2.1 ± 0.8	1.8 ± 0.4	2.1 ± 1.3	1.6 ± 0.6
Total cholesterol (mmol·L^{-1})	4.7 ± 0.6	4.4 ± 0.8	4.2 ± 0.5	4.3 ± 0.8
HDL-cholesterol (mmol·L^{-1})	1.5 ± 0.5	1.9 ± 0.5[a]	1.4 ± 0.2	1.8 ± 0.4
Triglycerides (mmol·L^{-1})	1.3 ± 0.6	1.6 ± 1.0	1.8 ± 1.5	1.7 ± 0.7
hs-CRP (mg·L^{-1})[#]	3.5 ± 1.9	3.8 ± 2.6	4.0 ± 2.3	3.3 ± 1.9
Resting heart rate (bpm)	81 ± 10	72 ± 8	65 ± 10[a]	66 ± 18[a]
Predicted VO_{2max} (mL·kg^{-1}·min^{-1})[#]	29.8 ± 8.2	31.8 ± 6.1[a]	34.5 ± 11.2	30.6 ± 5.8
Physical activity (min·wk^{-1})[#]	98.6 ± 63.3	282.8 ± 81.0[a]	159.28 ± 38.88	216.4 ± 112.9[a]
Daily energy intake (Kj)[#]	61117 ± 666	4957 ± 1315[a]	5331 ± 1175	4359 ± 745[a]
Vascular				
Carotid IMT (mm)	0.40 ± 0.02	0.42 ± 0.03	0.37 ± 0.01[a]	0.42 ± 0.03[b]
Systolic blood pressure (mmHg)	121 ± 7	117 ± 8	115 ± 12	117 ± 14
Diastolic blood pressure (mmHg)	71 ± 6	66 ± 11	63 ± 6	67 ± 10

Data presented as mean ± SD. n = 7. HOMA-IR, homeostasis model assessment of insulin resistance; HDL, high-density lipoprotein; hs-CRP, high-sensitivity C-reactive protein; IMT, intima-media thickness. #log10 transformation to satisfy Gaussian distribution prior to further statistical tests [a]significantly different to pre-intervention (P ≤ 0.05); [b]significant difference from sustainability to longitudinal (P ≤ 0.05).

Among cardiac outcomes (Table 9.2), systolic mitral annular plane tissue velocity (S_m), myocardial twist, and rate of twist/untwist were significantly reduced from pre-intervention to post-intervention. Differences from pre-intervention to sustainability were observed for increased IVRT and reduced circumferential strain. However, by longitudinal testing, no differences were present when compared with pre-intervention, nor were there changes from the sustainability phase.

Table 9.2. Echocardiographic data collected at pre-intervention (0 wk), post-intervention (12 wk), sustainability (24 wk), and longitudinal follow-up (52 wk), for a subsample (n = 7) of participants in the Young Women's Heart Health Study.

Outcome measure	Pre-intervention (0 weeks)	Post-intervention (12 weeks)	Sustainability (24 weeks)	Longitudinal (52 weeks)
Cardiac				
LA diastolic diameter (mm)	26.6 ± 12.7	31.7 ± 2.1	33.2 ± 3.5	31.0 ± 3.1
LV mass (g)	153.5 ± 39.9	175.3 ± 34.4	175.5 ± 34.6	154.9 ± 33.6
LV mass indexed ($g \cdot m^{-2.7}$)	41.4 ± 13.6	47.1 ± 11.5	48.1 ± 7.9	42.0 ± 13.9
LVED diameter (mm)	42.9 ± 4.5	41.7 ± 4.5	44.8 ± 3.1	43.0 ± 4.5
LVES diameter (mm)	27.3 ± 5.7	26.8 ± 2.8	28.4 ± 3.9	29.7 ± 4.1
LV PW thickness (mm)	10.4 ± 1.7	12.1 ± 3.3	11.2 ± 1.6	10.0 ± 2.0
IVS thickness (mm)	10.4 ± 1.7	11.9 ± 1.7	10.8 ± 1.9	11.0 ± 1.0
LV EF (%)	55.2 ± 3.1	61.9 ± 7.4	61.4 ± 3.8	66.6 ± 13.3
E velocity ($cm \cdot s^{-1}$)	84.9 ± 7.8	75.9 ± 9.4	75.3 ± 10.9	76.0 ± 13.4
A velocity ($cm \cdot s^{-1}$)	38.7 ± 11.4	31.0 ± 4.6	37.0 ± 3.5	45.2 ± 14.3
E/A ratio	2.4 ± 0.7	2.5 ± 0.3	2.1 ± 0.4	1.9 ± 0.5
IVRT (ms)	71.9 ± 31.8	94.7 ± 14.8	96.3 ± 17.6	92.4 ± 8.5
Deceleration time (ms)[#]	215.3 ±24.1	233.9 ± 69.6	276.7 ± 33.9[a]	236.0 ± 37.1
S_m velocity ($cm \cdot s^{-1}$)	9.4 ± 1.8	8.7 ± 1.5[a]	8.9 ± 1.6	9.0 ± 1.1
E_m velocity ($cm \cdot s^{-1}$)	14.9 ± 1.7	13.3 ± 2.9	13.4 ± 2.4	14.8 ± 1.0
A_m velocity ($cm \cdot s^{-1}$)	7.0 ± 1.6	7.4 ± 1.6	6.9 ± 1.6	7.3 ± 1.1
E/E_m lateral wall	5.2 ± 1.2	4.6 ± 1.2	4.4 ± 1.2	4.1 ± 0.4
Longitudinal strain (%)	-17.2 ± 2.4	-17.5 ± 0.5	-16.7 ± 1.5	-17.1 ± 2.1
Circumferential strain (%)	-19.2 ± 5.2	-19.3 ± 2.6	-18.2 ± 4.6[a]	-17.3 ± 4.5
Apical rotation (˚)	5.4 ± 2.3	4.7 ± 1.8	4.2 ± 2.4	5.1 ± 2.0
Basal rotation (˚)	-3.6 ± 3.0	-4.3 ± 1.7	-5.3 ± 3.6	-3.9 ± 0.8
Twist (˚)	9.0 ± 3.2	5.8 ± 1.5[a]	5.6 ± 2.0	6.5 ± 2.1
Twist rate ($˚ \cdot s^{-1}$)	79.5 ± 15.5	42.2 ± 22.7[a]	53.8 ± 26.8	65.1 ± 21.6
Untwist rate ($˚ \cdot s^{-1}$)	-73.0 ± 20.7	-31.6 ± 19.3[a]	-52.3 ± 28.1	-56.5 ± 10.7

Data presented as mean ± SD. n=7. S_m, E_m and A_m are means of four sites at the mitral annulus from apical 4-chamber and 2-chamber view. LA, left atrium; LV, left ventricle; LVED, left ventricle end-diastolic; LVES, left ventricle end-systolic; PW, posterior wall; IVS, inter-ventricular septum; EF, ejection fraction; IVRT, isovolumetric relaxation time; S, systolic; E, early-diastolic; A, late-diastolic; SR, strain rate. [#]log10 transformation to satisfy Gaussian distribution prior to further statistical tests. [a]significantly different to pre-intervention ($P \leq 0.05$).

Figure 9.1 presents data for "stage of change for exercise". Of note, at pre-intervention, all participants indicated that they were in 'contemplation' (n=3) or 'preparation' (n=4). However, upon completion of the lifestyle intervention at post-intervention testing, six of the seven women had moved into the 'action' phase. At sustainability, three participants were still in the 'action' phase, an indication that they had maintained exercise beyond the completion of the intervention, while the other four had returned to 'preparation'. Responses varied at longitudinal follow-up, with three participants indicating for the first time that they had entered the 'maintenance' phase. Meanwhile, one participants was in 'action', while others had returned to 'contemplation' (n=1) or 'preparation' (n=2).

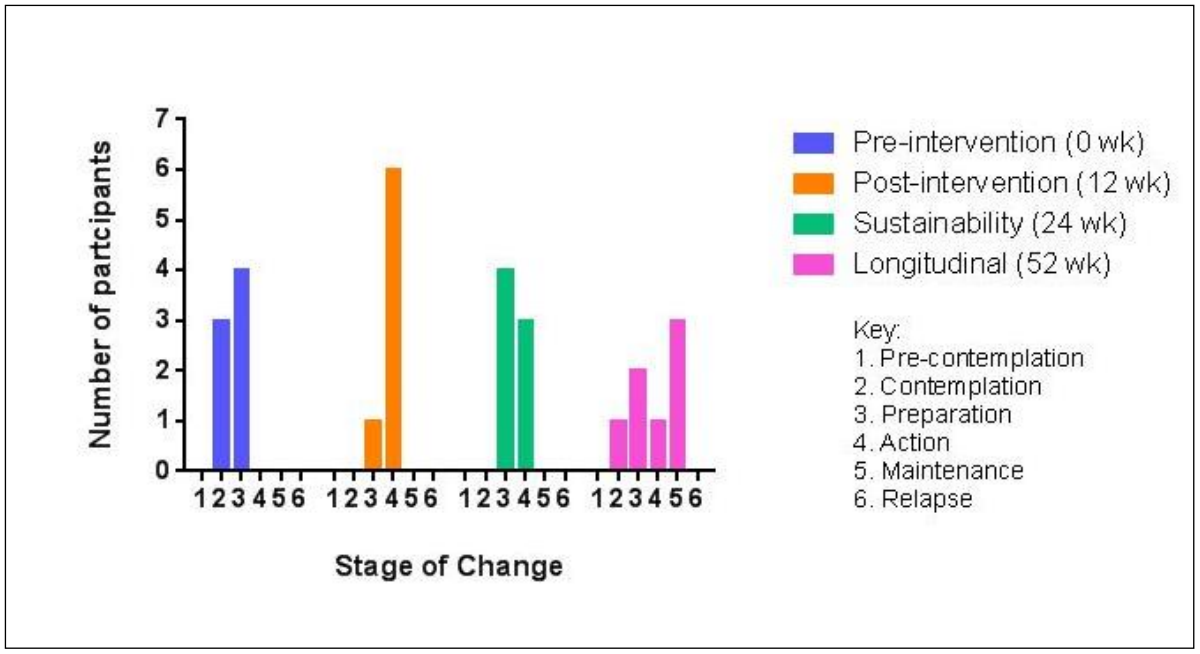

Figure 9.1. "Stage of change for exercise" for participants at longitudinal follow-up testing (n=7).

Discussion

In this supplementary study, a subsample of participants who completed the multi-disciplinary lifestyle intervention was followed up one year later. At this longitudinal follow-up, participants exhibited significant reductions in WC-dependent anthropometric measures when compared to pre-intervention values, representing a favourable change in abdominal adiposity. These women also reported increased engagement in weekly physical activity and reductions in daily energy intake, representing positive modifications to lifestyle behaviours to support weight management. However, care must be taken when interpreting these data for possible bias, given that the women returning for longitudinal testing may have been the more compliant of the intervention participants.

Immediately post-intervention (12 weeks), results for this subsample demonstrated that a short-term, multi-disciplinary lifestyle intervention was effective for reducing a number of metabolic and lifestyle risk factors, including WC-dependent anthropometric measures, fitness variables and energy intake. However, at the sustainability phase (24 weeks), an emergent 'rebound' trend was evident for several variables, with the post-intervention

improvements in WC, fitness and nutritional measures no longer different from pre-intervention. There was also a reduction in weekly physical activity by 24 weeks from post-intervention. This rebound effect is also observed in the sustainability data presented for the intervention group as a whole (n=19) in Chapter 7, and has previously been reported in adults in intervention studies investigating chronic disease (Wycherley et al., 2012). At longitudinal follow-up, WC-dependent measures, physical activity levels and energy intake displayed changes were again significantly improved compared with pre-intervention values. This is in contrast to another lifestyle intervention study with young adult women with overweight/obesity (Chang et al., 2010), where reported improvements in fruit and vegetable intake behaviour at post-intervention were no longer present at 8-month follow-up.

This rebound trend was reflected in the "stage of change" data, which showed that some participants formerly in 'action' at post-intervention had regressed to the 'preparation' phase at sustainability. However, at longitudinal follow-up, several participants returned to 'action' or 'maintenance'. It is speculated that this pattern of regression noted at sustainability testing was initiated by the suspension of supervised physical activity and CBT group sessions when the lifestyle intervention concluded (Wycherley et al., 2012). The trigger for renewed improvements in lifestyle behaviours from sustainability to longitudinal follow-up, which resulted in improvements in the WC-dependent measures, requires further investigation.

Further evidence of this 'rebound' effect is evident from individual data obtained from the primary outcome variable of WC (data not shown). It was revealed that from post-intervention to sustainability: (i) *one* participant had a reduced WC (3.0 cm); (ii) *three* participants had maintained their WC; and (iii) *three* had increased WC (range: 4.1 to 5.0 cm). In comparison, from sustainability to longitudinal follow-up: (i) *five* participants had reduced WC (range: 4.0 to 10.6 cm); and (ii) *two* participants had maintained WC. Moreover, at longitudinal testing, all but one participant displayed a WC that was less than at pre-intervention. In addition, at longitudinal follow-up, two participants were no longer considered 'abdominally obese' (i.e., their WC < 80 cm). And although not statistically different from pre-intervention, mean body mass and hip circumference had reduced by 4.5% and 5%, respectively, at longitudinal follow-up, further suggesting sustained lifestyle behaviours beyond the completion of the intervention.

There were changes observed in some cardiac and vascular (ultrasonography) markers, from pre-intervention to post-intervention and sustainability, in this subsample of seven women.

These changes are difficult to explain given that they were not observed in the post-intervention (Chapter 8) and sustainability (Addendum 8.1) data of the entire intervention cohort (n=19), except for a decrease in circumferential strain at the sustainability phase. However, by one-year follow-up, there were no differences from pre-intervention values for any cardiac or vascular measure assessed with ultrasonography.

In summary, the follow-up testing at 24 weeks provides evidence that positive behaviour modifications developed during the lifestyle intervention demonstrate a 'rebound' after withdrawal of the intervention and its intensive support. However, further follow-up testing at 52 weeks suggests that participants re-engage in positive lifestyle behaviours and, concomitantly, exhibit improvements in CVD risk factors similar to those observed immediately post-intervention. Importantly, the key improvement in CVD risk status at 52 weeks was a significant reduction in WC, representing a favourable change in abdominal adiposity. Therefore, despite a small sample size at one-year follow-up, a multi-disciplinary lifestyle intervention comprising physical activity, nutrition education and CBT can be considered an effective approach for long-term, sustained improvements in CVD risk profile for young adult women with abdominal obesity. However, it is possible that this outcome reflects a bias of only the most committed participants returning for longitudinal testing.

Chapter 10. Discussion and Conclusion

10.1. Overview

Overweight and obesity continues to escalate in developed and developing countries (Ng et al., 2014). Obesity is an independent risk factor for CVD and is associated with the progression of other risk factors that increase the chance of developing CVD (Kahn et al., 2006) in middle-aged and older adults, particularly in post-menopausal women (Galassi et al., 2006; Hubert et al., 1983; Worrall-Carter et al., 2011). Similar trends are now emerging in premenopausal women (Peterson, Herrero, et al., 2004; Peterson, Waggoner, et al., 2004). Young women in particular are at risk of future CVD events, with weight gain rising steeply between the ages of 19 to 40 years (Ng et al., 2014). Despite this, premenopausal women are under-represented in CVD research (Chomistek, Mukamal, Eliaseen, & Rimm, 2014; Hutchesson et al., 2013). Data on the prevalence, characteristics and consequences of overweight/obesity in young women are important for early detection, timely treatment and adaptation of lifestyle interventions (van Emmerik et al., 2012).

10.2. Linking of the studies

The narrative literature review (Chapter 2) highlighted an under-representation of work examining CVD risk in premenopausal adult women, with a paucity of data regarding more contemporary early detection markers such as ultrasonographic measures of cardiac and vascular risk. There was limited attention to strategies within population to address CVD risk progression, with multi-component lifestyle intervention proposed as an effective non-pharmacological approach for reducing overweight/obesity and other modifiable risk factors. The systematic literature review (Chapter 3) revealed only five RCT studies since 2004 to address the efficacy of a multi-disciplinary lifestyle intervention for reducing CVD risk in premenopausal women (≤ 40 years of age) with overweight/obesity. Of these five studies: (i) only one had a mean participant age below 36 years; (ii) none had investigated cardiac and/or

vascular measures using ultrasonography, and (iii) sustainability measures following interventions were lacking.

The series of studies described in Chapters 5 to 8 were conducted with the primary purpose of advancing the knowledge of reducing CVD risks in young women and, in particular, those with overweight/obesity. This thesis first focussed on the early identification of CVD risk factors that are modifiable, reversible and preventable, using a cross-sectional design for the assessment of metabolic, cardiac and vascular markers of CVD risk and associated lifestyle behaviours. This was followed with a RCT intervention study of lifestyle modification (intended at being realistic, sustainable, and age- and gender-appropriate) to assess its effectiveness in reducing identified risk factors, and included tracking the sustainability of any intervention-induced changes in CVD risk. These investigations of CVD risk in young adult women with overweight/obesity presented in this thesis have produced a number of notable and novel contributions towards the understanding of early detection and intervention of CVD in this population.

Research question 1: What (cardio)metabolic, cardiac and vascular risk factors are associated with overweight/obesity in premenopausal women aged 18-30 years?

It was hypothesised that young women with overweight/obesity exhibit elevated markers of CVD risk for metabolic and lifestyle factors, and display cardiac and vascular dysfunction measured by ultrasonography. These risk factors may evolve as a result of excess adiposity and lead to the development of CVD. Many risk factors are modifiable, reversible and preventable with appropriate strategies. In this thesis, waist circumference $\geq$ 80 cm as a surrogate measure of abdominal obesity was selected to define 'overweight/obesity'. Waist circumference is a reliable and inexpensive index of adiposity that correlates well with advanced measuring techniques (Goh et al., 2014; National Health and Medical Research Council, 2003). Compared with non-overweight/obese (WC < 80 cm), age-matched (18-30 years) controls, it was established that young women with abdominal obesity had elevated CVD risk in measures of insulin resistance (HOMA-IR), low-grade systemic inflammation (hs-CRP) and systolic blood pressure, and lower levels of physical activity and fitness. In contrast, traditional markers of CVD risk, such as those associated with the metabolic

syndrome (i.e., blood lipids and fasting glucose), did not differentiate between overweight/obese women and age-matched women in the healthy anthropometric range. Similarly, increased c-IMT as a vascular marker of developing atherosclerosis was not evident in the overweight/obese group. However, the elevations in HOMA-IR and systolic blood pressure for women with abdominal obesity were within 'acceptable' limits (Jensterle et al., 2008; Pearson et al., 2003), while the elevated hs-CRP was deemed 'high' risk (> 3.0 $mg \cdot l^{-1}$). But given the between-group differences, these elevated CVD risk markers might be more useful for early detection of future CVD risk in this population than those (e.g., metabolic syndrome markers) currently used in standard health checks. Moreover, the calculation of unadjusted odds ratios produced significant outcomes for insulin resistance and physical activity, indicating that a HOMA-IR score ≥ 2.0 and exercise engagement < 210 min per week were risk factors associated with overweight/obesity in this population. Therefore, *mild* abdominal obesity could be considered as among the first stages in a sequence of early markers of CVD risk.

Young women with abdominal obesity also displayed cardiac remodelling. Obesity is independently associated with increased LV mass, with eccentric hypertrophy the most common form associated with this metabolic disorder (Wong et al., 2004). In this thesis, the increased LA diameter was consistent with these findings, and has been reported to occur to compensate for a greater haemodynamic load in obesity. Thus, cardiac hypertrophy may be an early marker in the sequence of cardiac events (Wong & Marwick, 2007b). These women also displayed subtle, subclinical cardiac dysfunction, providing support to the only other study to report such measures in young obese women (Peterson, Waggoner, et al., 2004). In the present study, the overweight/obese group exhibited reduced systolic (S_m) and diastolic (E_m) mitral annular plane velocities, increased LA filling pressure surrogates (E/E_m), and prolonged timing measures of diastolic function. While the specific values for these measures in the overweight/obese group are still considered 'normal' in the clinical setting (Nagueh et al., 2009), the presence of between-group differences again suggest their usefulness as early detection markers. In addition, the advances in echocardiographic techniques over the past decade may provide avenues for earlier detection of cardiac dysfunction. In this thesis, circumferential deformation and myocardial mechanical indices (twist indices and rotation) were similar between groups. However, longitudinal deformation was impaired in women with overweight/obesity compared with controls. Similarly, reduced global longitudinal LV strain was observed in a cross-sectional study of obese children and adolescents when

compared to age-matched non-obese controls (Shah et al., 2011). These results indicate emerging systolic involvement early in the process of obesity in these young populations (Barbosa, Mota, e Silva, Maria do Carmo, & Barbosa, 2013).

Taken together, these findings suggest that WC was useful as a first-line diagnostic measure of CVD risk. Similarly, BMI ($\geq$ 25 kg/m^2) and WHtR (> 0.50) as anthropometric measures for overweight/obesity were also useful as first-line diagnostic measures of CVD risk in this age group, given they predicted CVD risk factors (i.e., insulin resistance and physical inactivity) similar to waist circumference. Anthropometric measures of abdominal adiposity have previously shown strong and positive associations with all-cause CVD mortality independent of BMI (Zhang et al., 2008). Specifically, elevated WC has been associated with increased CVD mortality even among normal-weight women (Zhang et al., 2008). Furthermore, the Emerging Risk Factors Collaboration [ERFC] (2011) showed that WC, BMI, WHtR, and WHR each had similar strengths of association with CVD risk. Therefore, data in this thesis are in agreement with previous literature, given the results of the present study found WC, BMI and WHtR each predicted similar CVD risk factors in young women, while WHR was not a strong predictor.

The detection of differences in selected metabolic and cardiac parameters in young obese women in this thesis, albeit relatively subtle, is concerning and, thus, a better understanding of heart health in these early stages of adulthood is required. When seeking deeper insight into the progression of CVD risk, measures of glycaemic control and lifestyle factors appear more informative than traditional metabolic syndrome markers at this younger age. There is also value in echocardiographic techniques for advancing this insight, given the findings of this thesis that premenopausal women with mild abdominal obesity demonstrate abnormal cardiac function at a younger age, and in earlier stages of obesity, than previously reported (Kosmala et al., 2009; Wong, Byrne, et al., 2006). In summary, the data from the cross-sectional studies of this thesis support the hypotheses that young women with overweight/obesity (compared with their non-obese counterparts) exhibit markers of CVD risk in their metabolic profile and display subclinical cardiac dysfunction measured from echocardiography. These findings demonstrated the emerging importance of early intervention strategies in this population to arrest further progression of CVD. Effective lifestyle intervention strategies that promote weight loss and reduce risk factors for CVD

through early detection and prevention will, ultimately, reduce CVD and the associated personal and financial burden of the disease on individuals and society.

Research question 2: Does a multi-disciplinary lifestyle intervention comprising physical activity, nutrition education and CBT improve CVD risk factors in young women with abdominal obesity? And if so, are these improvements sustainable beyond the completion of the program?

A number of multi-component lifestyle intervention studies have produced beneficial outcomes for body composition, fitness, and cardiometabolic parameters (Carroll et al., 2007; Dutheil et al., 2013; Irving et al., 2008). Lifestyle interventions incorporating exercise, dietary and behavioural components are considered the most successful design for health outcomes, including weight loss and reductions in CVD risk factors (Wing, 2002) As highlighted in the systematic literature review (Chapter 3), the effects and sustainability of multi-disciplinary lifestyle interventions for young adult women with overweight/obesity (particularly aged ≤ 30 years) are noticeably under-researched. In the present study, the 12-week multi-disciplinary lifestyle intervention produced some within-group improvements in CVD risk factors for young women with abdominal obesity. Interestingly, these risk factor improvements were primarily limited to the metabolic and lifestyle markers identified in the cross-sectional studies (Chapters 5 and 6) as showing poorer values in women with overweight/obesity. Specifically, anthropometric measures related to waist circumference, systolic (and diastolic) blood pressure, and measures of physical activity engagement, aerobic fitness and total energy intake improved at post-intervention. Improvements in these CVD risk factors are consistent with other RCT studies that have assessed the effectiveness of multi-disciplinary interventions with premenopausal women with overweight/obesity (Kerksick et al., 2010; Silva et al., 2010). While metabolic risk factors related to anthropometry and blood pressure improved to be better aligned with young, non-obese women (see Chapter 5), in contrast, other risk factors like fasting insulin, HOMA-IR and hs-CRP were unaffected by the intervention. Similarly, cardiac and vascular properties assessed with ultrasonography were unaffected at post-intervention. This might reflect an intervention of insufficient duration or intensity or lifestyle manipulation to drive change in many of the outcome measures. But it is also possible that this early stage of CVD progression in women

with abdominal obesity insufficiently advanced for a lifestyle intervention to generate sizeable or detectable improvements in metabolic, cardiac and/or vascular risk factors. This was supported by the between-group findings in Chapter 5, in which elevated hs-CRP in the overweight/obese women was the only risk factor deemed to be of 'high' risk. Similarly, while differences between obese and non-obese women were observed in echocardiographic markers in Chapter 6, the specific values for these measures in the women with abdominal obesity were still considered 'normal' in the clinical setting.

Once leaving the intervention program, women maintained their post-intervention improvements in anthropometric measures, blood pressure, resting heart rate and physical activity engagement at 24 weeks. Similarly, daily energy intake was still 15% lower than pre-intervention levels, although statistical significance was not reached (P = 0.269). However, levels of physical activity at 24 weeks had declined significantly from the greatly increased weekly engagement at immediately post-intervention, and this likely explains the return of aerobic fitness to a level no longer different from pre-intervention. This might reflect the frequent rebound that can occur once the intensive support of an intervention program is withdrawn, even when behavioural change strategies have been implemented (Wycherley et al., 2012). However, collectively, the maintenance of the intervention-induced improvements above suggest that the intervention produced longer lasting lifestyle modifications and, thus, its characteristics were realistic, sustainable, and age- and gender-appropriate for young, university-educated adult women.

The data collected at one-year post-intervention provide supportive evidence of an intervention that was successful in establishing sustainable lifestyle behaviours in young adult women. For the seven women who returned for this follow-up testing, the outcomes for the majority of the metabolic, cardiac and vascular measures did not differ from the pre-intervention data. This could be considered a positive outcome from the perspective of an absence of deleterious progression of CVD risk in these participants. Moreover, there was a significant decrease in all anthropometric markers at this time point, including WC, BMI, WHR, WHtR, body mass and hip circumference. These body composition changes reflect a significant decrease in general adiposity, with the reduction in waist circumference indicating a decrease in abdominal adiposity. It is predicted that these reductions in adiposity will result in positive changes in the intermediate modifiable risk factors (Bastien et al., 2014) and in circulating adipokines and inflammatory mediators (Berggren et al., 2005; Matsuzawa,

2006a). It is likely that improvements in other CVD risk markers will emerge more explicitly over a longer time period if the anthropometric corrections are maintained or further enhanced.

From a behavioural modification perspective, the seven participants at one year had substantially increased their weekly engagement in physical activity and reduced their dietary energy intake when compared to pre-intervention values. The combination of these outcomes result in a negative shift in total energy balance, which is consistent with the decreases in body mass and related anthropometry observed at this time point. These one-year post-intervention data for physical activity and dietary patterns also reversed the rebound towards pre-intervention levels observed at 24 weeks in these lifestyle behaviours. These positive lifestyle modifications developed by one year also provide evidence that the intervention delivered in this thesis was successful and sustainable long-term for this population. However, it is important to acknowledge that a possible bias exists with the seven women who returned for longitudinal testing. These women may have been more compliant than other intervention participants given their availability for one-year follow-up testing.

While within-group changes observed in the intervention group showed the lifestyle intervention to be successful in mitigating some CVD risk, between-group comparisons with the overweight/obese control group suggested a research design that was largely unsuccessful in discriminating the effectiveness of the intervention phase. In fact, only physical activity engagement was significantly different between groups, with the overweight/obese women in the wait-list control group displayed similar patterns of effect in anthropometric, biochemical, fitness and dietary measures at post-control testing. Most notable was a decrease in WC that paralleled changes in the intervention group, despite undetected changes in self-reported physical activity and nutrition behaviour of the control group participants. Unanticipated improvements in the behaviour of control participants have been observed in intervention trials targeting physical activity and chronic disease management, but weight loss improvements are not normally observed in wait-list control conditions (Waters et al., 2012). In the current study, participants appear to have experienced an increase in motivation for change simply through assignment to a control group. Therefore, a wait-list (delayed-start) control group design may not be appropriate for ‘Generation Y’ women who share urgency for feedback and success (Griffin et al., 2013) This was highlighted by the (presumed) poor compliance to pre-recruitment lifestyle behaviours, as indicated by a decrease in WC similar

to the intervention group, as well as poor continuation into the intervention phase upon completion of the control phase. These limitations and difficulties have been previously documented, with one study acknowledging that young obese women are difficult to recruit to weight management trials (Griffin et al., 2013). Young women have been identified in the research as a high risk group (Gokee-LaRose et al., 2009; Hutchesson et al., 2013), with standard weight loss programs not meeting the weight control needs of young adults and research urgently required to improve recruitment and retention efforts within this group (Gokee-LaRose et al., 2009).

In summary, results from the intervention study of this thesis support the hypothesis that a 12-week multi-disciplinary lifestyle intervention would produce anthropometric and CVD risk factor improvements, albeit subtly, in young adult women with abdominal obesity. Similarly, the behaviour change associated with the intervention was successful in sustaining several improvements in the cardiovascular health profile of these women longer term. Given the association of abdominal obesity with CVD risk, an important outcome was that the decrease in WC exhibited at the completion of the intervention phase was maintained at 24 weeks and 1 year later. However, this perspective extends from the intervention group data alone, where the intervention itself appeared appropriate to initiate improvements in CVD risk and behaviour change for the sustainability of healthier lifestyle management. In contrast, the RCT research design with its use of a wait-list control group does not appear appropriate for testing the effectiveness of an intervention when control participants are seeking change.

10.3. Practical applications

The series of studies comprising this thesis have contributed knowledge to direct future interventions and strengthen the evidence base for health promotion strategies in young women at risk of chronic disease. Moreover, the findings reported in this thesis have implications for the design and implementation of effective multi-disciplinary lifestyle interventions for young adult women. Based on the evidence from the cross-sectional studies and the intervention study, the following practical applications are recommended for the future of cardiovascular health in young women with abdominal obesity:

- Traditional markers of CVD risk, including markers of the metabolic syndrome, may not be appropriate for the early detection of risk in this age group (18 to 30 years) of women. Indicators of low-grade systemic inflammation (i.e. hs-CRP) appear more sensitive for identifying early stages of CVD progression. Indicators of insulin resistance (HOMA-IR) and physical activity engagement may also be useful adjuncts in the early detection of CVD progression, rather than metabolic syndrome markers.

- WC, BMI and WHtR all show similar risk factors for CVD in young adult women and, given their ease and cost of measurement, are useful first-line detection tools for CVD risk in clinical settings.

- The inclusion of mechanistic data obtained from cardiac and vascular imaging may improve diagnosis

Additionally, based solely on evidence obtained from the lifestyle intervention program in this thesis, the following points for the implementation of future multi-disciplinary lifestyle interventions are recommended:

1. Provide opportunities for women to develop self-efficacy for behavioural change. In this study, women were introduced to exercise techniques in training that can be implemented in everyday life.

2. Provide opportunities for social interaction and support (groups).

3. Teach women to value exercise and use the health belief model to provide experiences and empowerment in the knowledge around the importance of healthy lifestyle choices.

4. Ensure that women who exercise outdoors have access to low-cost, local locations in which they feel safe.

5. Develop age- and sex-specific approaches to prevention, diagnosis, and treatment.

10.4. Limitations

The following are potential study limitations and associated strengths, when considering the respective study designs, population, and statistical methodologies employed:

- *The lifestyle intervention sample was under-powered.*

Power calculations showed that 44 participants were required to meet appropriate power, taking into account a 20% attrition rate. From an initial recruitment of 39 women, there were 30 by program completion. This was primarily due to the greater attrition rate in control group, given that the retention rate in intervention group was as expected. This provides further support to the supposition that wait-list control designs may not be an appropriate approach for this population.

- *Intra- and inter-rater reliability for some STE parameters (e.g. rotation and twist) with a CV of 9% to 12%*

Despite this, both intra- and inter-reliability was comparable to other studies reporting similar variables (K. A. Marcus et al., 2011). Additionally, a minimum of three cycles/images were averaged for all echocardiography analyses, in order to further minimise measurement error. However, other reliability measures of STE were acceptable and well within previous reports.

- *Due to the lack of echogenicity in the study population (particularly women with abdominal obesity), clear echocardiographic imaging was difficult in some circumstances.*

This precluded accurate estimation of radial deformation and, thus, these data were not included in any analyses.

- *STE represents an objective and angle-independent modality for non-invasive quantification of LV deformation (strain and strain rate) and mechanics (rotation and twist) that play an important role in ejection and filling of the LV (ref).*

The importance of STE lies in its potential for early detection of pathology (Obert et al., 2012). However, despite STE showing excellent agreement with gold-standard heart imaging techniques such as tagged magnetic resonance imaging, it is not without its limitations. For example, preload and afterload may influence contractile responses of the myocardium and should be considered in all STE analyses (Burns et al., 2010).

- *Advanced techniques, such as DEXA, were not used for the assessment of body composition.*

Despite the popularity of weight loss among populations of young women, weight loss was not the goal of this thesis. The focus was on metabolic health outcomes and as such remained on waist circumference rather than whole body weight loss. Ideally, weight loss refers to losses of fat mass, but without a DEXA, this type of evidence was not possible. In an intervention with a high probability of increasing lean mass (at the same time as decreasing fat mass) weight changes may not have been observed. Furthermore, WC is recognised as a clinically relevant tool in the assessment of abdominal obesity (National Health and Medical Research Council, 2003). Additionally, while WC is a simple measure, it is unrelated to height, correlates closely with BMI and WHR, and is an approximate index of intra-abdominal fat mass and total body fat (Australian Institute of Health and Welfare, 2010). In this study, the intra-rater reliability for WC was very strong (CV = 1.3%), highlighting that it was reliably implemented as a tool for body composition assessment.

- *Recruitment of Caucasian participants and from middle-high socioeconomic status.*

Caution must be exercised when generalising the results of this thesis to other race/ethnic populations, given previous work highlighting differences in CVD risk between ethnicities (Ajjan et al., 2007). Additionally, participants in this study were university students, mostly residing in middle-high socioeconomic areas, non-smoking and possibly well informed about health issues. Therefore, the limit to external validity is acknowledged.

- *Validity, reliability and sensitivity of outcome measures.*

It is possible to be critical of the sensitivity to change of both the waist circumference and ultrasound measures used in this program of research. Selected outcome measures were often dependent on the available budget but could be more carefully considered in future funding initiatives. Additionally, the validity and reliability of dietary recall of the types, amounts, preparations and brands of food recall are well acknowledged in the literature (Magarey et al., 2011) and apply to the interpretation of results in the current program of research. Furthermore, despite the acknowledged rigour of assessors being blinded to group allocation, not all researchers involved in data collection in the present program of research were able to be precluded to the knowledge of the participants' grouping. As such, larger, future trials should have a greater number of staff to avoid the bias that potentially comes with knowledge of group allocation.

- *Effects of the menstrual cycle and the oral contraceptive pill on outcome measures.*

Participants were tested during the same phase of their menstrual cycle at baseline and on subsequent testing occasions but the differences in the phase of the menstrual cycle is a limitation of this protocol. Furthermore, future studies should also consider the potential limitations imposed by young women's use of oral contraception, particularly if vascular function is of interest (Minson, Halliwill, Young, & Joyner, 2000).

10.5. Future directions

Early detection or progression of CVD, may indicate that impaired endothelial function in the vascular system is the beginning of physiological event in atherogenesis, often detected before the existence of vascular plaques and the clinical detection of vascular disease (Celermajer, et al., 1992). Furthermore, endothelial dysfunction may act as a prospective indicator of increased cardiovascular risk (Kuvin, et al., 2001), and can be measured via a technique known as flow-mediated dilation, which describes the vasodilatory response of a vessel to elevations in blood flow (Pyke, & Tschakovsky, 2005). It is recommended that future studies of CVD risk incorporate markers of vascular dysfunction, including future work investigating young adult women with overweight/obesity.

The implementation of intervention studies with young adult women requires paramount consideration of the research design for targeting this population. Specifically, the use of a randomised, wait-list control design might not be appropriate for gauging the effectiveness of an intervention with this population. This is particularly important if participants recruited into a study are ready for change. Thus, knowledge of the current 'state of change' of proposed participants, as well as an understanding of their barriers to lifestyle change, will help direct the research design in order to increase the likelihood of short-term retention and long-term sustainability. Future studies with larger sample sizes should also consider stratification for age and baseline waist circumference (e.g. categories such as 80-90 cm and >90 cm). Interventions with a multi-disciplinary approach, incorporating exercise, diet and behavioural therapy components, are recommended. In addition, long-term follow-up (e.g. at one year or later) is likely to provide greater insight into the sustainability success of the intervention, rather than shorter-term follow-up only.

10.6. Conclusion

In this thesis, young adult women, a population under-represented in CVD research, were investigated from a perspective of early identification of CVD risk and progression, and from a perspective of lifestyle and behavioural change for weight loss. This involved the use of traditional and contemporary measures of metabolic, cardiac and vascular risk, including a mechanistic evaluation of cardiac function performed with traditional and advanced echocardiography techniques. It was established that young women with mild abdominal obesity have elevated markers of insulin resistance and low-grade systemic inflammation (i.e. hsCRP) as well as subclinical cardiac dysfunction, when compared with a healthy control group (defined by WC < 80 cm). However, these comparative perturbations in CVD markers were still within clinical norms, with the exception of elevated hsCRP. Despite this, the early identification of changes in CVD risk factors in young women in the current study may help guide future detection strategies. Such strategies may be critical to halting and reversing CVD development while in its earliest stages of progression. This outcome would substantially decrease the social and financial costs from the perspective of the individual, as well as the longer term burden on national health costs.

The intervention component of this thesis demonstrated that a multi-disciplinary approach to lifestyle change, incorporating exercise, nutrition and behavioural strategies, can be effective in short-term maintenance or improvements in modifiable CVD risk factors. There was also evidence, among highly compliant individuals, that this type of intervention can be effective for lifestyle behaviour modifications conducive to sustainable weight loss and, thus, improved CVD risk profile. For future implementation studies targeting young adult women, the current study provides important information when considering the features of study design. Most notably, a RCT design with a wait-list control group may not meet the needs of "Generation Y" women who share a need for urgent feedback and success.

Findings from larger, future trial, informed by this thesis will hopefully contribute to stronger clinical outcomes, translatable to the broader community.

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Appendices

Appendix 1. Research Portfolio

Publications:

This thesis contains five papers for publication in peer-reviewed journals, three of which have been published, and two that are ready for submission. All five papers are authored by Bianca Louise Share, her three supervisors and other contributing authors.

Presentations:

This thesis was presented at three international conferences, two national conferences, and two institution-facilitated conferences, as an oral presentation or poster presentation. All seven presentations were presented by Bianca Louise Share, and prepared with assistance from her three supervisors and other contributing authors.

Manuscript 1:

Cardiometabolic and behavioural risk factors in young overweight women identified with simple anthropometric measures (Chapter 5).

Bianca L Share[1] (BExSci (Hons)), Geraldine A Naughton[1,2] (PhD), Philippe Obert[3] (PhD), Jennifer K Peat[4] (PhD), Justin G Kemp[1] (PhD)

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All authors met the criteria for authorship and agreed on the final version of the manuscript. None of the authors had a conflict of interest in relation to this manuscript.

Signatures:

Bianca L Share: ..... Date: ……

As principal supervisors, I certify that the contributions below are true and correct

Justin G Kemp: ..... Date: ……

In the case of this publication, the following contributions were made:

Author	Statement of contribution
Bianca L Share	Conception and design of the study (including developing the scientific basis for the research; identification of outcome testing methodology; formulating the ethics proposal; preparation of data record forms, information and results sheets), recruitment and screening of participants, co-ordinated the study, performed all data collection (including intravenous blood draws, fitness testing, blood pressure, and anthropometric assessment), performed all data analyses (including auto-analyser biochemical analysis of blood lipids), managed the study data files, performed statistical tests (including reliability and validity analyses), interpreted the data, and co-ordinated the writing of the manuscript.
Geraldine A Naughton	Contributed to conception and study design, data interpretation, and writing of the manuscript
Philippe Obert	Contributed to conception and study design.
Jennifer K Peat	Advised statistical analyses and assisted with data interpretation.
Justin G Kemp	Contributed to conception and study design, and writing of the manuscript.

Other contributors (non-authors):

Dietitian	Analysed the 3-day food recall in FoodWorks® 7 Professional
Pathology	Performed some biochemistry analyses (glucose, insulin, hs-CRP)
Nurse	Assisted with some intravenous blood draws

Manuscript 2:

Young women with abdominal obesity have sub-clinical myocardial dysfunction (Chapter 6).

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Signatures:

Bianca L Share: ..... Date: ……

As principal supervisors, I certify that the contributions below are true and correct

Justin G Kemp: ..... Date: ……

In the case of this publication, the following contributions were made:

Author	Statement of contribution
Bianca L Share	Conception and design of the study (including developing the scientific basis for the research; identification of outcome testing methodology; formulating the ethics proposal; preparation of data record forms, information and results sheets), recruitment and screening of participants, co-ordinated the study, performed all data collection (including echocardiography and ultrasonography image acquisition, intravenous blood draws, fitness testing, blood pressure, and anthropometric assessment), performed all data analyses (including offline echocardiography image assessment, and auto-analyser biochemical analysis of blood lipids), managed the study data files, performed statistical tests (including reliability and validity analyses), interpreted the data, and co-ordinated the writing of the manuscript.
Andre La Gerche	Provided expertise in the field of echocardiography, data interpretation, and contributed to writing of the manuscript.
Geraldine A Naughton	Contributed to conception and study design, data interpretation, and writing of the manuscript
Philippe Obert	Contributed to conception and study design. Provided expertise in the field of echocardiography/ultrasonography, and contributed to writing of the manuscript
Justin G Kemp	Contributed to conception and study design, and writing of the manuscript

Other contributors (non-authors):

Dietitian	Analysed the 3-day food recall in FoodWorks® 7 Professional
Pathology	Performed some biochemistry analyses (glucose, insulin, hs-CRP)

Manuscript 3:

Effects of a multi-disciplinary lifestyle intervention on cardiometabolic risk factors in young women with abdominal obesity: A randomised controlled trial (Chapter 7).

Manuscript published in *PLoS One (2015)*.

Bianca L Share[1] (BExSci (Hons)), Geraldine A Naughton[1,2] (PhD), Philippe Obert[3] (PhD), Jennifer K Peat[4] (PhD), Elizabeth A Aumand[1] (MA), Justin G Kemp[1] (PhD)

[1] School of Exercise Science, Australian Catholic University, Melbourne, Australia

[2] Murdoch Childrens Research Institute, Melbourne, Australia

[3] Laboratory of Cardiovascular Pharmacology, University of Avignon, France

[4] Faculty of Health Sciences, Australian Catholic University, Sydney, Australia

All authors met the criteria for authorship and agreed on the final version of the manuscript. None of the authors had a conflict of interest in relation to this manuscript.

Signatures:

Bianca L Share: ..... Date: ……

As principal supervisors, I certify that the contributions below are true and correct

Justin G Kemp: ..... Date: ……

In the case of this publication, the following contributions were made:

Author	Statement of contribution
Bianca L Share	Conception and design of the study (including developing the scientific basis for the research; identification of outcome testing methodology; development of the exercise training protocols; formulating the ethics proposal; preparation of data record forms, information and results sheets; developing appropriate questions for the focus group), recruitment and screening of participants; co-ordinated the study (troubleshooting participant concerns; personal training for exercise groups; presented nutrition information), performed all data collection (including intravenous blood draws, fitness testing, strength assessment, blood pressure, and anthropometric assessment), performed all data analyses (including auto-analyser biochemical analysis of blood lipids), managed the study data files, performed statistical tests (including linear mixed model; reliability and validity analyses; transcribing the focus group audio recordings; program evaluation), interpreted the data, and co-ordinated the writing of the manuscript.
Geraldine A Naughton	Contributed to conception and study design, data interpretation, and writing of the manuscript.
Philippe Obert	Contributed to conception and study design, and revised the manuscript.
Jennifer K Peat	Advised statistical analyses, and assisted with data interpretation.
Justin G Kemp	Contributed to conception and study design, and writing of the manuscript

Elizabeth A Aumand	Designed and conducted the group CBT sessions, and facilitated the focus group.

Other contributors:

Dietitian	Analysed the 3-day food recall in FoodWorks® 7 Professional, delivered a one-hour tutorial, and developed the nutrition education.
Pathology	Performed some biochemistry analyses (glucose, insulin, hs-CRP)

Manuscript 4:

Effects of a lifestyle intervention on cardiac and myocardial measures in young women with abdominal obesity: A randomised controlled trial (Chapter 8).

Manuscript ready for submission to *Canadian Journal of Cardiology.*

Bianca L Share[1] (BExSci (Hons)), Geraldine A Naughton[1,2] (PhD), Philippe Obert[3] (PhD), Andre La Gerche[4] (PhD), Justin G Kemp[1] (PhD)

[1] School of Exercise Science, Australian Catholic University, Melbourne, Australia

[2] Murdoch Childrens Research Institute, Melbourne, Australia

[3] Laboratory of Cardiovascular Pharmacology, University of Avignon, France

[4] St. Vincent's Hospital, Melbourne, Australia

All authors met the criteria for authorship and agreed on the final version of the manuscript. None of the authors had a conflict of interest in relation to this manuscript.

Signatures:

Bianca L Share: ..... Date: ……

As principal supervisors, I certify that the contributions below are true and correct

Justin G Kemp: ..... Date: ……

In the case of this publication, the following contributions were made:

Author	Statement of contribution
Bianca L Share	Conception and design of the study (including developing the scientific basis for the research; identification of outcome testing methodology; development of the exercise training protocols; formulating the ethics proposal; preparation of data record forms, information and results sheets; developing appropriate questions for the focus group), recruitment and screening of participants; co-ordinated the study (troubleshooting participant concerns; personal training for exercise groups; presented nutrition information), performed all data collection (including echocardiography and ultrasonography image acquisition; intravenous blood draws; fitness testing; strength assessment; blood pressure; anthropometric assessment), performed all data analyses (including offline echocardiography image assessment auto-analyser; biochemical analysis of blood lipids), managed the study data files, performed statistical tests (including linear mixed model; reliability and validity analyses; transcribing the focus group audio recordings; program evaluation), interpreted the data, and co-ordinated the writing of the manuscript.
Geraldine A Naughton	Contributed to conception and study design, data interpretation, and writing of the manuscript.
Philippe Obert	Contributed to conception and study design. Provided expertise in the field of echocardiography/ultrasonography, and contributed to writing of the manuscript.
Andre La Gerche	Provided expertise in the field of echocardiography, data interpretation, and contributed to writing of the manuscript.

Justin G Kemp	Contributed to conception and study design, and writing of the manuscript.

Other contributors:

Dietitian	Analysed the 3-day food recall in FoodWorks® 7 Professional, delivered a one-hour tutorial, and developed the nutrition education.
Pathology	Performed some biochemistry analyses (glucose, insulin, hs-CRP)

Manuscript 5:

The effectiveness of randomised controlled trial lifestyle interventions on cardiovascular disease risk factors in premenopausal women with overweight and obesity: A systematic review (Chapter 3).

Manuscript prepared for submission to the *International Journal of Behavioral Nutrition and Physical Activity.*

Bianca L Share[1] (BExSci (Hons)), Geraldine A Naughton[1,2] (PhD), Justin G Kemp[1] (PhD)

[1] School of Exercise Science, Australian Catholic University, Melbourne, Australia

[2] Murdoch Childrens Research Institute, Melbourne, Australia

All authors met the criteria for authorship and agreed on the final version of the manuscript. None of the authors had a conflict of interest in relation to this manuscript.

Signatures:

Bianca L Share: ..... Date: ……

As principal supervisors, I certify that the contributions below are true and correct

Justin G Kemp: ..... Date: ……

In the case of this publication, the following contributions were made:

Author	Statement of contribution
Bianca L Share	Performed electronic and manual searches, journal elimination, interpreted the data, and co-ordinated the writing of the manuscript.
Geraldine A Naughton	Assisted with initial search strategy, journal elimination, and writing of the manuscript.
Justin G Kemp	Contributed to writing of the manuscript.

Appendix 2: Ethical Approval

Australian Catholic University
Brisbane Sydney Canberra Ballarat Melbourne

ACU National

Human Research Ethics Committee

Committee Approval Form

Principal Investigator/Supervisor: JUKEMP Melbourne Campus

Co-Investigators: Geraldine Naughton, Philippe Obert, Elizabeth Aumand Melbourne Campus

Student Researcher: Bianca Share Melbourne Campus

Ethics approval has been granted for the following project:
The metabolic syndrome in young women

for the period: 18.12.09 – 01.10.11

Human Research Ethics Committee (HREC) Register Number: V2009 91

The following standard conditions as stipulated in the *National Statement on Ethical Conduct in Research Involving Humans* (2007) apply:

(i) that Principal Investigators / Supervisors provide, on the form supplied by the Human Research Ethics Committee, annual reports on matters such as:
- security of records
- compliance with approved consent procedures and documentation
- compliance with special conditions, and

(ii) that researchers report to the HREC immediately any matter that might affect the ethical acceptability of the protocol, such as:
- proposed changes to the protocol
- unforeseen circumstances or events
- adverse effects on participants

The HREC will conduct an audit each year of all projects deemed to be of more than low risk. There will also be random audits of a sample of projects considered to be of negligible risk and low risk on all campuses each year.

Within one month of the conclusion of the project, researchers are required to complete a *Final Report Form* and submit it to the local Research Services Officer.

If the project continues for more than one year, researchers are required to complete an *Annual Progress Report Form* and submit it to the local Research Services Officer within one month of the anniversary date of the ethics approval.

Signed: .... Date: .....18.12.09.....
(Research Services Officer, Melbourne Campus)

F:\Bianca\PhD folder\Ethics\V2009 91 Approval Form.doc

From: Gabrielle Ryan [mailto:Gabrielle.Ryan@acu.edu.au]
Sent: Wednesday, November 23, 2011 11:30 AM
To: Geraldine Naughton; Justin Kemp; Elizabeth Aumand; Bianca Share
Subject: Extension approved

Dear Justin Guy,

V2009 91
The metabolic syndrome in young women

Thank you for returning the Ethics Progress Report for your project V2009 91 The metabolic syndrome in young women

The Deputy Chair of the Human Research Ethics Committee has approved your request to extend the period of data collection. The new expiry date for data collection is the 30/04/2012 .

We wish you well in this ongoing project.

Kind regards,
Gabrielle Ryan

Ethics Officer | Research Services
Office of the Deputy Vice Chancellor (Research)
Australian Catholic University
Locked Bag 4115, Fitzroy, VIC, 3065
T: 03 9953 3150 F: 03 9953 3315

THIS IS AN AUTOMATICALLY GENERATED RESEARCHMASTER EMAIL

Appendix 3: ANZ Clinical Trials Registration

ANZCTR
Australian New Zealand Clinical Trials Registry

Questions in **bold** text are mandatory. (*)

Request Number:	363050
Current Page:	Review

Trial from ANZCTR

Trial ID	ACTRN12612001017819
Trial Status:	Registered
Date Submitted:	18/09/2012
Date Registered:	20/09/2012
	Retrospectively registered

Page 1

Public title	The Young Women's Heart Health Study: the effects of a lifestyle intervention on cardiovascular disease risk factors in overweight women aged 18-30 years
Study title in 'Participant-Intervention-Comparator- Outcome (PICO)' format	The effects of a randomised control trial 12-week multidisciplinary lifestyle intervention on cardiovascular disease risk factors in young Caucasian women aged 18-30 years with abdominal obesity
Secondary ID [1]	Nil
UTN	U1111-1134-7515
Trial acronym	

Page 2

Health condition(s) or problem(s) studied:	
Overweight/ obesity Cardiovascular disease risk factors	
Condition category:	**Condition code:**
Cardiovascular	Other cardiovascular diseases
Diet and nutrition	Obesity

Appendix 4: Information letter to participants and informed consent - Cross-sectional Studies

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INFORMATION LETTER TO PARTICIPANTS

TITLE: The metabolic syndrome in young women

SUPERVISOR: Dr Justin Kemp

CO-SUPERVISORS: Professor Geraldine Naughton; Professor Philippe Obert

STUDENT RESEARCHER: Miss Bianca Louise Share

PROGRAM IN WHICH ENROLLED: PhD

Dear Participant,

You are invited to participate in a research study investigating early risk factors for the metabolic syndrome in young women aged 18 to 30 years. The metabolic syndrome is characterised by a combination of conditions that increase one's risk of developing cardiovascular disease and type 2 diabetes. Limited data exist in the understanding of early risk factors for the metabolic syndrome in young women. Therefore, your involvement will provide us with important data currentluy not available for this age group.

Data collection will include completion of the following:

1. Cardiovascular Risk Assessment Form
2. The Young Women's Heart Health Study Survey
3. Three-day Activity and Food Record
4. Basic body measurements of height, body mass and girth measurements. All measurements will be performed by a female researcher in a private room.
5. Measurement of blood pressure.
6. Supplying a 15 ml intravenous blood sample for established health markers of blood glucose, triglycerides, total cholesterol, HDL-cholesterol concentrations, insulin, and inflammatory markers. The sample will be collected by an individual trained in blood collection and sent to a pathology clinic for subsequent analysis. This will require abstaining from all food and beverage products, except water, for a minimum of 12 hours prior to arriving for testing (e.g. after an overnight sleep). Furthermore, you will be required to refrain from all alcoholic products and strenuous physical activity in the 24 hours prior to testing.
6. Obtaining cardiovascular information (heart structure and function) using non-invasive ultrasound techniques with simultaneous ECG trace.
7. Determination of vascular endothelial function – an early marker of cardiovascular disease – by non-invasive ultrasound techniques measuring arterial diameter and blood flow velocity at the brachial artery. The assessment of vascular endothelial function requires a pneumatic cuff to be placed around the forearm and inflated to 250 mmHg for 5 minutes whilst lying in a supine position, as well as the ingestion of 400 μg of nitroglycerin, a vasodilator substance.
8. A measure of cardiovascular endurance by performing a sub-maximal cycle ergometer stress test lasting up to 10 minutes.
9. A measure of upper and lower body strength via a five-repetition max resistance test.

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The data collection will be divided into three sessions. Each session will take approximately two hours to complete. Each data collecting session will be conducted in the School of Exercise Science at Australian Catholic University, St. Patrick's Campus, Melbourne.

Overall, this project is expected to contribute to the advancement of young women's health. It is hoped that the findings of this study will be published in peer-reviewed journals and presented at conferences in an effort to advance the knowledge of the metabolic syndrome in young women. All personal data collected will be kept confidential and only be known to the researcher. All data will be analysed collectively, thus individual data are not reported. Any published data will be anonymous and can not in any way be associated with you. You are also offered the opportunity to obtain any information regarding any aspect of the research project.

Be advised that as a participant you are free to refuse consent altogether without having to justify that decision, and if you wish to, can withdraw consent and discontinue participation in the study at any time without giving a reason. Should you have any questions regarding this project, please contact the supervisors and/or student researcher:

Dr Justin Kemp
Phone: (03) 9953 3031
(Supervisor)

Prof. Geraldine Naughton
Phone: (03) 9953 3034
(Co-supervisor)

Miss Bianca Share
Phone: (03) 9953 3225
(Student Researcher)

Address:
School of Exercise Science
Australian Catholic University
Locked Bag 4115
Fitzroy VIC 3065

Furthermore, you are warmly encouraged to apply for feedback regarding the results of the study by contacting the aforementioned supervisors and/or student researcher.

Please be advised that this study has been presented and approved by the University Human Research Ethics Committee at Australian Catholic University. In the event that you have a query or complaint about the way you have been treated during this study, you may write care of the Office of Research at the following address:

Chair, HREC
C/- Research Services
Australian Catholic University
Melbourne Campus
Locked Bag 4115
FITZROY VIC 3065
Tel: 03 9953 3158
Fax: 03 9953 3315

Any complaint or concern will be treated in confidence and fully investigated. The participant will be informed of the outcome.

Upon agreement to participate in this study please sign both copies of the Consent Form, retain one copy for your records and return the other copy to the Supervisor, Co-supervisor or Student Researcher.

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INFORMED CONSENT FORM
(Researcher Copy)

TITLE OF PROJECT: The metabolic syndrome in young women

SUPERVISOR: Dr Justin Kemp

CO-SUPERVISORS: Professor Geraldine Naughton; Professor Philippe Obert

STUDENT RESEARCHER: Miss Bianca Louise Share

I .....*(the participant)* have read and understood the information provided in the Information Letter to Participants. Any questions I have asked have been answered to my satisfaction. I agree to participate in this activity, realising that I can withdraw at any time. I agree that research data collected for the study may be published or may be provided to other researchers in a form that does not identify me in any way. I agree to participate in the following testing procedures

1. Completing the Cardiovascular Risk Assessment Form
2. Completing the Young Women's Heart Health Study Survey
3. Completing an Activity and Food Record
4. Abstaining from all food and beverage products (except water) for 12 hours prior to arriving for testing
5. Refraining from consumption of alcohol and strenuous physical activity in the 24 hours prior to testing
6. Provide measures of height, body mass and girth measurements
7. Measurement of blood pressure
8. Supplying a 15 ml intravenous blood samples for subsequent analysis of fasting plasma glucose, lipid-profiling, insulin and inflammatory markers
9. Echocardiography for analysis of cardiac structure and function (with ECG tracing)
10. Ultrasound measurements at the carotid artery for the calculation of intima-media thickness
11. Vascular endothelial function (requiring occlusion and nitroglycerin ingestion) for flow-mediated dilatation.
12. A measure of cardiovascular endurance by performing a sub-maximal cycle ergometer test
13. A measure of upper and lower body strength via a five-repetition maximal resistance test

Name of Participant:..... Phone: .....
(block letters)

Signature: ..... Date: .....

Supervisor: Dr Justin Kemp

Signature: ..... Date: .....

Co-Supervisor: Professor Geraldine Naughton

Signature: ..... Date: .....

Student Researcher: Miss Bianca Share

Signature: ..... Date: .....

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INFORMED CONSENT FORM
(Participant Copy)

TITLE OF PROJECT: The metabolic syndrome in young women

SUPERVISOR: Dr Justin Kemp

CO-SUPERVISORS: Professor Geraldine Naughton; Professor Philippe Obert

STUDENT RESEARCHER: Miss Bianca Louise Share

I ……*(the participant)* have read and understood the information provided in the Information Letter to Participants. Any questions I have asked have been answered to my satisfaction. I agree to participate in this activity, realising that I can withdraw at any time. I agree that research data collected for the study may be published or may be provided to other researchers in a form that does not identify me in any way. I agree to participate in the following testing procedures:

1. Completing the Cardiovascular Risk Assessment Form
2. Completing the Young Women's Heart Health Study Survey
3. Completing an Activity and Food Record
4. Abstaining from all food and beverage products (except water) for 12 hours prior to arriving for testing
5. Refraining from consumption of alcohol and strenuous physical activity in the 24 hours prior to testing
6. Provide measures of height, body mass and girth measurements
7. Measurement of blood pressure
8. Supplying a 15 ml intravenous blood samples for subsequent analysis of fasting plasma glucose, lipid-profiling, insulin and inflammatory markers
9. Echocardiography for analysis of cardiac structure and function (with ECG tracing)
10. Ultrasound measurements at the carotid artery for the calculation of intima-media thickness
11. Vascular endothelial function (requiring occlusion and nitroglycerin ingestion) for measures of flow-mediated dilatation.
12. A measure of cardiovascular endurance by performing a sub-maximal cycle ergometer test
13. A measure of upper and lower body strength via a five-repetition maximal resistance test

Name of Participant:…… Phone: ……..
(block letters)

Signature: ..... Date: .....

Supervisor: Dr Justin Kemp

Signature: …… Date: ……

Co-Supervisor: Professor Geraldine Naughton

Signature: …… Date: ……

Student Researcher: Miss Bianca Share

Signature: …… Date: ……

Appendix 5: Information letter to participants and informed consent – Intervention Study

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INFORMATION LETTER TO PARTICIPANTS

TITLE: The effects of a lifestyle intervention on the metabolic syndrome in young women

SUPERVISOR: Dr Justin Kemp

CO-SUPERVISOR: Professor Geraldine Naughton

STUDENT RESEARCHER: Miss Bianca Louise Share

PROGRAM IN WHICH ENROLLED: PhD

Dear Participant,

You are invited to participate in a study to determine the effects of a lifestyle intervention program on the progression of the metabolic syndrome in young women aged 18 to 30 years. The metabolic syndrome is characterised by a combination of conditions that increase one's risk of developing cardiovascular disease and type 2 diabetes. Several studies have investigated the effects of exercise on underlying risk factors leading to the development of the metabolic syndrome in older populations. However, limited data exist in the understanding of early risk factors for the metabolic syndrome in young women. Therefore, through implementation of a lifestyle intervention program of physical activity, nutrition education, and behavioural counselling, we aim to assess the influence of this program on risk factors of the metabolic syndrome and other cardiovascular and blood measures of health.

Your participation is this study will include involvement in a lifestyle intervention program, where you will engage in regular physical activity (lasting up to 60 minutes) three days per week for twelve weeks, supervised by the researchers. One exercise session may be performed unsupervised at home. You will be required to wear a heart rate monitor and a pedometer, and keep a training diary throughout the duration of the intervention. Additionally, you will engage in a weekly focus group session for health coaching about nutrition education and sustainable behavioural change, consulted by a dietician and delivered by a qualified counsellor. Following the completion of the lifestyle intervention program, you will be asked to return for a final assessment.

If you agree to participate in this study, you will be randomly assigned to either an experimental or control group. The experimental group will begin the lifestyle intervention program immediately while the control group will maintain their normal routine for 3 months, then have the opportunity to complete the lifestyle intervention program following this time period.

Throughout the study, you will be asked to attend three data collecting sessions, each separated by 12 weeks. Prior to starting the study, you will be asked to gain medical clearance from your general practitioner and complete a cardiovascular risk assessment form. On your first visit only (prior to engaging in the exercise intervention), you will be asked to complete the following documents:

1. Young Women's Heart Health Study Survey
2. Activity and Food Record

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Each of the three sessions will also involve the following testing procedures and take approximately two hours to complete:

1. Basic body measurements of height, body mass and girth measurements. All measurements will be performed by a female researcher in a private room.
2. Measurement of blood pressure.
3. Measurement of the established health markers of blood glucose, triglycerides, total cholesterol and HDL-cholesterol concentrations, obtained by the standard aseptic finger prick technique. This will require abstaining from all food and beverage products, except water, for a minimum of 12 hours prior to arriving for testing (e.g. after an overnight sleep).
4. Supplying a 10 ml intravenous blood sample for assessment of other cardiovascular health markers. The sample will be collected by an individual trained in blood collection and sent to a pathology clinic for subsequent analysis. This will require you to abstain from all food and beverage products, except water, for 12 hours prior to arriving for testing, and to refrain from consuming alcohol and exercising strenuously in the 24 hours prior to testing.
5. Supplying a 15 ml urine sample. You will be provided with a urine sample container and asked to supply a sample from the first void (urination) of the morning on the day of testing. You will be required to bring the urine sample with you to the testing session.
6. Obtaining cardiovascular information (e.g. heart structure and function; blood vessel wall thickness; blood vessel diameter; ECG) using non-invasive ultrasound techniques.
7. Determination of vascular endothelial function – an early marker of cardiovascular disease – by non-invasive ultrasound techniques measuring arterial diameter and blood flow velocity at the brachial artery. The assessment of vascular endothelial function requires a pneumatic cuff to be placed around the forearm and inflated to 250 mmHg for 4.5 minutes whilst lying in a supine position, as well as the ingestion of 400 μg of nitroglycerin, a vasodilator substance.
8. A measure of cardiovascular endurance by performing a sub-maximal cycle stress test lasting up to 10 minutes.
9. A measure of upper and lower body strength via a five-repetition max resistance test.
10. Complete five psychological inventories about personal beliefs and attitudes towards exercise.

All data collecting sessions will be conducted in the School of Exercise Science at Australian Catholic University, St. Patrick's Campus, Melbourne. You will be advised of your results following each testing session. The two supervised training sessions per week (for the 12-week exercise programme) will take place at a local park and/or gym. At the conclusion of the lifestyle intervention and all testing session, you will be rewarded with a token of appreciation for your time and commitment to the study.

The potential benefits of this research to you and to society in general include: (1) assisting young women at risk of the metabolic syndrome to engage in appropriate physical activity and provide sustainable educational advice about dietary and behavioural changes; and (2) further establish the benefits of a lifestyle intervention in the management and prevention of the metabolic syndrome and related chronic diseases. Overall, this project is expected to contribute to the advancement of young women's health. It is hoped that the findings of this study will be published in peer-reviewed journals and presented at conferences in an effort to advance the knowledge of the metabolic syndrome in young women.

All personal data collected will be kept confidential and only be known to the researcher. All data will be analysed collectively, thus individual data are not reported. Any published data will be anonymous and can not in any way be associated with you. You are also offered the opportunity to obtain any information regarding any aspect of the research project.

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www.acu.edu.au

Be advised that as a participant you are free to refuse consent altogether without having to justify that decision, and if you wish to, can withdraw consent and discontinue participation in the study at any time without giving a reason.

Should you have any questions regarding this project, please contact the supervisors and/or student researcher:

Prof. Geraldine Naughton
Phone: (03) 9953 3034

Miss Bianca Share
Phone: (03) 9953 3031
(*Student Researcher)*

Dr Justin Kemp
Phone: (03) 9953 3225

Address:
School of Exercise Science
Australian Catholic University
Locked Bag 4115
Fitzroy VIC 3065

Furthermore, you are warmly encouraged to apply for feedback regarding the results of the study by contacting the aforementioned supervisors and/or student researcher.

Please be advised that this study has been presented and approved by the University Human Research Ethics Committee at Australian Catholic University (ACU National). In the event that you have a query or complaint about the way you have been treated during this study, you may write care of the Office of Research at the following address:

Chair, HREC
C/- Research Services
Australian Catholic University
Melbourne Campus
Locked Bag 4115
FITZROY VIC 3065
Tel: 03 9953 3158
Fax: 03 9953 3315

Any complaint or concern will be treated in confidence and fully investigated. The participant will be informed of the outcome.

Upon agreement to participate in this study please sign both copies of the Consent Form, retain one copy for your records and return the other copy to the Supervisor, Co-supervisor or Student Researcher. Furthermore, please make an appointment to see your local GP and have him/her complete the Cardiovascular Risk Assessment Form during your consultation.

Yours sincerely,

Dr Justin Kemp
SUPERVISOR

Prof. Geraldine Naughton
CO-SUPERVISOR

Miss Bianca Share
STUDENT RESEARCHER

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INFORMED CONSENT FORM
(Participant Copy)

TITLE OF PROJECT: The effects of a lifestyle intervention on the metabolic syndrome in young women

SUPERVISOR: Dr Justin Kemp

CO-SUPERVISOR: Professor Geraldine Naughton

STUDENT RESEARCHER: Miss Bianca Louise Share

I ……*(the participant)* have read and understood the information provided in the Information Letter to Participants. Any questions I have asked have been answered to my satisfaction. I agree to participate in this activity, realising that I can withdraw at any time. I agree that research data collected for the study may be published or may be provided to other researchers in a form that does not identify me in any way. I agree to participate in the following testing procedures, which will last up to 2 hours in duration per session, on three separate occasions (over a six-month period):

1. Completing the Cardiovascular Risk Assessment Form (with my local GP)
2. Completing the Young Women's Heart Health Study Survey, and Activity and Food Record
3. Complete five psychological inventories about my personal beliefs and attitudes towards exercise
4. Abstaining from all food and beverage products (except water) for 12 hours prior to arriving for testing
5. Refraining from consumption of alcohol and strenuous physical activity in the 24 hours prior to testing
6. Provide measures of height, body mass and girth measurements
7. Measurement of blood pressure
8. Supplying blood samples (from a finger-prick) for analysis of fasting plasma glucose and lipid-profiling
9. Supplying 10 ml intravenous blood samples for subsequent assessment of cardiovascular risk factors
10. Supplying a 15 ml urine sample from the first urination of the morning
11. Echocardiogram images of the heart for analysis of cardiac structure and function (with ECG tracing)
12. Ultrasound measurements at the carotid artery for the calculation of intima-media thickness
13. Vascular endothelial function (requiring 4.5 min occlusion & nitroglycerin ingestion) for FMD measures
14. A measure of cardiovascular endurance by performing a sub-maximal cycle test
15. A measure of upper and lower body strength via a five-repetition maximal resistance test
16. Aerobic exercise and resistance training program (3 days per week for 12 weeks)
17. Wearing a heart rate monitor and a pedometer, and keeping a training diary
18. Participate in focus group sessions for educational coaching about nutrition and behavioural change

Name of Participant:…… (block letters) Phone: ……..

Signature: ……. Date: ……

Supervisor: Dr Justin Kemp

Signature: …… Date: ……

Co-Supervisor: Professor Geraldine Naughton

Signature: …… Date: ……

Student Researcher: Miss Bianca Share

Signature: …… Date: ……

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Telephone: 613 9953 3000
Facsimile: 613 9953 3005
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INFORMED CONSENT FORM

(Researcher Copy)

TITLE OF PROJECT: The effects of a lifestyle intervention on the metabolic syndrome in young women

SUPERVISOR: Dr Justin Kemp

CO-SUPERVISOR: Professor Geraldine Naughton

STUDENT RESEARCHER: Miss Bianca Louise Share

I .....*(the participant)* have read and understood the information provided in the Information Letter to Participants. Any questions I have asked have been answered to my satisfaction. I agree to participate in this activity, realising that I can withdraw at any time. I agree that research data collected for the study may be published or may be provided to other researchers in a form that does not identify me in any way. I agree to participate in the following testing procedures, which will last up to 2 hours in duration per session, on three separate occasions (over a six-month period):

1. Completing the Cardiovascular Risk Assessment Form (with local GP)
2. Completing the Young Women's Heart Health Study Survey, and Activity and Food Record
3. Complete five psychological inventories about my personal beliefs and attitudes towards exercise
4. Abstaining from all food and beverage products (except water) for 12 hours prior to arriving for testing
5. Refraining from consumption of alcohol and strenuous physical activity in the 24 hours prior to testing
6. Provide measures of height, body mass and girth measurements
7. Measurement of blood pressure
8. Supply blood samples (from a finger-prick) for analysis of fasting plasma glucose and lipid-profiling
9. Supply 10 ml intravenous blood samples for subsequent assessment of cardiovascular risk factors
10. Supply a 15 ml urine sample from the first urination of the morning
11. Echocardiogram images of the heart for analysis of cardiac structure and function (with ECG tracing)
12. Ultrasound measurements at the carotid artery for the calculation of intima-media thickness
13. Vascular endothelial function (requiring 4.5 min occlusion & nitroglycerin ingestion) for FMD measures
14. A measure of cardiovascular endurance by performing a sub-maximal cycle test
15. A measure of upper and lower body strength via a five-repetition max resistance test
16. Aerobic exercise and resistance training program (3 days per week for 12 weeks)
17. Wearing a heart rate monitor and a pedometer, and Keeping a training diary
18. Participate in focus group sessions for educational coaching about nutrition and behavioural change

Name of Participant:..... Phone: .....
(block letters)

Signature: ..... Date: .....

Supervisor: Dr Justin Kemp

Signature: ..... Date: .....

Co-Supervisor: Professor Geraldine Naughton

Signature: ..... Date: .....

Student Researcher: Miss Bianca Share

Signature: ..... Date: .....

Appendix 6: Cardiovascular Risk Assessment Form

AUSTRALIAN CATHOLIC UNIVERSITY

Cardiovascular Risk Assessment Form

Name: ..... **Date of Birth:**.....

Person to contact in case of emergency

Name: ..... **Relationship:**.....

Address:.....

.....

Telephone: .....(W) .....(H) .....(M)

Medical History

In the past have you ever had, or currently have.... (tick no or yes):

	No	Yes
Stroke	☐	☐
Myocardial Infarction	☐	☐
Heart Murmur	☐	☐
Heart Arrythmia	☐	☐
Congenital Heart Disease	☐	☐
Disease of the Arteries	☐	☐
Asthma	☐	☐
Other Respiratory Disease	☐	☐
Insulin Dependent Diabetes	☐	☐
Gestational Diabetes	☐	☐
Polycystic Ovarian Syndrome	☐	☐
Thyroid abnormalities	☐	☐
Liver or Kidney Disease	☐	☐
IVF treatment	☐	☐

Are you pregnant or breastfeeding? ☐ ☐

Other illness (Give Details):

.....

.....

.....

AUSTRALIAN CATHOLIC UNIVERSITY

List any prescribed medications being taken:

.....

.....

.....

Symptoms during or after exercise:

As a result of exercise, have you ever experienced any of the following:

	No	Yes
Chest pain or discomfort	☐	☐
Severe shortness of breath or problems with breathing	☐	☐
Dizziness or nausea	☐	☐
Palpitation in heart	☐	☐
Pain in the legs during mild exertion	☐	☐
Severe heat exhaustion	☐	☐

Cardiovascular Risk Factors:

Do you have.....	No	Yes	Don't Know
High blood pressure	☐	☐	☐
High blood cholesterol/triglycerides	☐	☐	☐
Diabetes	☐	☐	☐
Regular Alcohol Consumption	☐	☐	Ave./Day.....
Smoking Habit	☐	☐	Number/Day ....

Family Medical History:

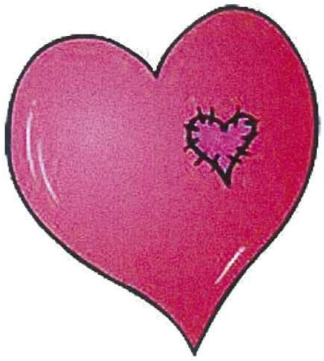
Have members of your immediate family ever had any of the following conditions. (If you answer 'Yes' or 'Don't Know', write beside this which member of the family has been affected):

	No	Yes	Don't Know	Family Member	Age	Still Alive?
Stroke	☐	☐	☐	.....	.....	.....
Myocardial Infarction	☐	☐	☐	.....	.....	.....
Angina Pectoris	☐	☐	☐	.....	.....	.....
High Blood Pressure	☐	☐	☐	.....	.....	.....
Diabetes	☐	☐	☐	.....	.....	.....
High blood cholesterol	☐	☐	☐	.....	.....	.....

Is there anything not mentioned that you believe the research staff should be aware of? If yes, please explain: .....

Appendix 7: Poster

Young Women's Heart Health Study



'Exercise training for health improvements in young women aged 18 to 30 years'

- Did you know that *moderate exercise* training can improve heart health by lowering the chances of developing cardiovascular disease and type 2 diabetes?
- The aim of the Young Women's Heart Health Study is to test the influence and sustainability of a 12-week lifestyle intervention on risk factors for heart health.

The lifestyle intervention will include the following:

- Exercise training ***2-3 days per week*** of a circuit program with gentle strength training and aerobic activities
- Nutrition advice from a qualified dietician
- Group counselling sessions aimed at helping change and social support

Are You ?

- ✓ Female
- ✓ 18 to 30 years old
- ✓ Healthy
- ✓ Have a waist circumference above 80 cm
- ✓ Not doing regular physical activity or sport - but willing to try some changes

If you would like to volunteer for this study or require further details please contact **Bianca Share**

Ph: 9953 3225 or email: bianca.share@acu.edu.au

Australian Catholic University | Exercise Science, School of Exercise Science, Australian Catholic University | centre of COPAYAL, physical activity across the lifespan | Université d'Avignon

Appendix 8: Face Validation Questions

I am undertaking the process of validating the Young Women's Heart Health Study (YWHHS) Survey, which is an important document for my PhD research project. Your contribution is greatly appreciated.

Instructions: Please take your time to complete the YWHHS Survey and answer the questions below as honestly as possible.

1. Please record the time taken to complete the survey: …….. mins
2. Is the language clear/ easy to understand? YES ☐ NO ☐

   If no, please state where the problem occurs in the survey ……..
3. Please identify any ambiguities and/or difficult questions :

……

……

.....

4. Did you answer all questions? If not, please record those you skipped and briefly explain why:

……

……

……..

5. Please provide any comments which you feel may improve this survey (i.e. suitability to the population group; ease of use etc.):

……

……

……..

Thank you for taking the time to complete my survey.

Bianca Share

Appendix 9: Custom Survey

Young Women's Heart Health Study

Survey

PERSONAL DETAILS

Your name .....

Address.....

Town/Suburb .....Postcode.....

Phone contact number/s.....

Email address (if available).....

Signature: ..... Date: .....

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Health & Lifestyle

PLEASE NOTE: This information will be held in strict confidence and will only be seen by researchers based at the Australian Catholic University.

No individuals will be identified.

BACKGROUND INFORMATION

Date of Birth: ..... **Age:** .....Years

Height: .....cm **Weight:** .....kg

How long have you lived in your local area? .....Years

Highest level of education completed? (tick one box)

- ☐ Year 10 or below
- ☐ Year 11 or 12
- ☐ Tertiary degree
- ☐ Other .....

Country of your birth?

- ☐ Australia
- ☐ Other country (please name) .....

What is the ancestry of your parents?

Mother:.....

Father: .....

PERSONAL INFORMATION

Whom are you currently living with?

- ☐ Alone
- ☐ My parents
- ☐ My parents and sibling/s
- ☐ My partner
- ☐ My partner and child or children
- ☐ My child or children only
- ☐ Relatives
- ☐ House mate/s

Do you have a child or children?

YES ☐ NO ☐

If yes, how many .....

What is your employment status? (tick all that apply)

- ☐ Unemployed
- ☐ Part-time employment
- ☐ Full-time employment
- ☐ Casual employment
- ☐ Full-time student
- ☐ Part-time student
- ☐ House duties

List your occupation:

.....

.....

FAMILY HISTORY

Has any of your close relative (parents, grandparents, aunt / uncles, siblings) suffered from the following (If yes: state their relationship to you):

	YES	NO	Don't Know	RELATIONSHIP/S (Can be more than one)
1. Obesity	☐	☐	☐	.....
2. Diabetes	☐	☐	☐	.....
3. High blood pressure	☐	☐	☐	.....
4. High cholesterol	☐	☐	☐	.....
5. Heart disease	☐	☐	☐	.....
6. Stroke	☐	☐	☐	.....
7. Mental disorder	☐	☐	☐	.....
8. Any other known hereditary diseases (Specify: .....)	☐	☐	☐	.....

DIETARY INFORMATION

Do you think you have a weight problem?

YES ☐ NO ☐ UNSURE ☐

Do you have difficulty in controlling your food intake?

YES ☐ NO ☐ SOMETIMES ☐

How many times a week do you eat out or have take away for dinner? .....

Do you eat between meals? (i.e. between breakfast, lunch and dinner)?

YES ☐ NO ☐ SOMETIMES ☐

Do you take care with your fatty food intake?

YES ☐ NO ☐ SOMETIMES ☐

HEALTH STATUS

In general, would you say your health is: (tick one only)

- ☐ Excellent
- ☐ Very good
- ☐ Good
- ☐ Fair
- ☐ Poor

In regards to your current weight, how much would you like to weigh now? (circle one only)

5 kg more | 1-5 kg more | Happy as I am | 1-5 kg less | 5 kg less

How often have you gone on a diet in order to lose weight during the last year?

- ☐ Never
- ☐ 1 to 4 times
- ☐ 5 to 10 times
- ☐ More than 10 times
- ☐ I am always on a diet to lose weight

Have you had an illness in the last 12 months that has affected your health, and in particular, your weight?

YES ☐ NO ☐

If yes, provide details: .....

Have you had any significant accidents in the last 12 months that has affected your health, and in particular you weight?

YES ☐ NO ☐

If yes, provide details: .....

MENSTRUAL STATUS

At what age did you first start menstruating? (nearest half year e.g. 12.5 yrs) .....

How regularly are you currently menstruating? (tick one)

Every two weeks	☐
Every 4 weeks	☐
Every 4-6 weeks	☐
Every 6-8 weeks	☐
> 8 weeks	☐

Is the time between your cycles predictable? (i.e. is the time between your periods the same)

YES ☐ NO ☐ SOMETIMES ☐

If you menstruate regularly, how many days between the end of your period and the start of the next period?.....

On average, how heavy is the flow of your period? (tick one)

Very light	☐
Light	☐
Moderate	☐
Heavy	☐
Very heavy	☐

On average, how long is the flow of your period? (tick one)

1-2 days	☐
2-3 days	☐
3-5 days	☐
5-7 days	☐
> 7 days	☐

Do you experience any pain or discomfort during your period?

YES ☐ NO ☐ SOMETIMES ☐

If yes, what do you do for the pain or discomfort: .....

MEDICAL HISTORY

Do you have any medical history of the following conditions? (please tick if applicable)

Breathing or respiratory conditions

- ☐ Asthma
- ☐ Bronchitis
- ☐ Other (please specify) .....

Blood disorders

- ☐ High blood pressure (hypertension)
- ☐ High cholesterol
- ☐ Anaemia

Cardiovascular system

- ☐ Heart disease or vascular conditions
- ☐ Stroke
- ☐ Chest pain
- ☐ Heart rhythm abnormalities
- ☐ Other (please specify) .....

Reproductive system

- ☐ Polycystic ovarian syndrome
- ☐ Other (please specify) .....

Metabolic

- ☐ Insulin Dependent Diabetes Mellitus/ Type 1 Diabetes
- ☐ Non Insulin Dependent Diabetes Mellitus/ Type 2 Diabetes
- ☐ Gestational diabetes (during pregnancy)
- ☐ Other (please specify) .....

Psychological

- ☐ Depression
- ☐ Anxiety disorder
- ☐ Insomnia
- ☐ Postnatal depression
- ☐ Other (please specify) .....

MEDICATION USE

Do you take prescribed medication in the past 6 months?

YES ☐ NO ☐

If yes, provide details: .....

Has your doctor ever prescribed you medication for your triglyceride levels?

YES ☐ NO ☐

If yes, are you taking it now? .....

Has your doctor ever prescribed you medication for your cholesterol levels?

YES ☐ NO ☐

If yes, are you taking it now? .....

Do you take vitamins, minerals or any other form of health preparations?

YES ☐ NO ☐ SOMETIMES ☐

If yes, provide details: .....

Do you take an oral contraceptive pill, hormone implant or injection?

YES ☐ NO ☐

If yes, please specify the brand: .....

Do you smoke cigarettes/cigars?

YES ☐ NO ☐ PREVIOUSLY ☐

If yes, how many per day: .....

If you no longer smoke indicate when you stopped: .....

SLEEP

On average, how many hours of sleep do you get per night on weekdays:

<4 hrs ☐ 4-6 hrs ☐ 6-8 hrs ☐ 8-10 hrs ☐ 10-12 hrs ☐ 12 + hrs ☐

On average, how many hours of sleep do you get per night on weekends:

<4 hrs ☐ 4-6 hrs ☐ 6-8 hrs ☐ 8-10 hrs ☐ 10-12 hrs ☐ 12 + hrs ☐

Do you snore during sleep?

YES ☐ NO ☐ SOMETIMES ☐ NOT SURE ☐

Do you stop breathing during sleep?

YES ☐ NO ☐ SOMETIMES ☐ NOT SURE ☐

Do you take sleeping pills?

YES ☐ NO ☐ SOMETIMES ☐

SCREEN TIME

On average, how many hours of TV (including DVD) do you watch per day on weekdays

< 1 hr ☐ 1 hr ☐ 2 hrs ☐ 3 hrs ☐ 4 hrs ☐ 5 + hrs ☐

On average, how many hours of TV (including DVD) do you watch per day on weekends

< 1 hr ☐ 1 hr ☐ 2 hrs ☐ 3 hrs ☐ 4 hrs ☐ 5 + hrs ☐

On average, how often do you use a computer for work or study purposes per week?

< 1 hr ☐ 1-3 hr ☐ 4-6 hrs ☐ 7-10 hrs ☐ 10-15 hrs ☐ 15 + hrs ☐

On average, how often do you use a computer (including video games and play station) for recreational purposes or in your free time per week?

< 1 hr ☐ 1-3 hr ☐ 4-6 hrs ☐ 7-10 hrs ☐ 10-15 hrs ☐ 15 + hrs ☐

Nutrition

PLEASE NOTE: This information will be held in strict confidence and will only be seen by researchers based at the Australian Catholic University.

No individuals will be identified.

1. **How many pieces of fresh fruit do you usually eat per day?**
   (count ½ cup of diced fruit, berries or grapes as one piece)
   - ☐ I don't eat fruit
   - ☐ Less than 1 piece of fruit per day
   - ☐ 1 piece of fruit per day
   - ☐ 2 pieces of fruit per day
   - ☐ 3 pieces of fruit per day
   - ☐ 4 or more pieces of fruit per day

2. **How many different vegetables, including potatoes, do you usually eat per day?**
   (count all types, fresh, frozen or tinned)
   - ☐ I don't eat vegetables
   - ☐ Less than 1 vegetable per day
   - ☐ 1 vegetable per day
   - ☐ 2 vegetables per day
   - ☐ 3 vegetables per day
   - ☐ 4 vegetables per day
   - ☐ 5 vegetables per day
   - ☐ 6 or more vegetables per day

3. **What type of milk do you usually use?**
   - ☐ None
   - ☐ Full cream milk
   - ☐ Reduced fat / skim milk
   - ☐ No fat milk
   - ☐ Lactose free milk
   - ☐ Soya milk

4. **What type of bread do you usually eat?**
   - ☐ I don't eat bread
   - ☐ High fibre white bread
   - ☐ White bread
   - ☐ Wholemeal bread
   - ☐ Rye bread
   - ☐ Multi-grain bread

5. **What type of spread or oil do you usually put on your bread?**
   - ☐ None
   - ☐ Margarine
   - ☐ Butter
   - ☐ Nuttelex
   - ☐ Olive oil
   - ☐ Pro Activ
   - ☐ Soy
   - ☐ Sterol

6. **On average, how many eggs do you usually eat per week?**
   - ☐ I don't eat eggs
   - ☐ Less than 1 egg per week
   - ☐ 1 to 2 eggs per week
   - ☐ 3 to 5 eggs per week
   - ☐ 6 or more eggs per week

7. **What type of cheese do you usually eat?**
   - ☐ I don't eat cheese,
   - ☐ Hard cheese e.g. parmesan, romano
   - ☐ Firm cheese, e.g. cheddar, edam
   - ☐ Soft cheese, e.g. cabembert, brie
   - ☐ Ricotta or cottage cheese
   - ☐ Cream cheese
   - ☐ Low fat cheese

8. **On average, how many times per week do you eat breakfast?**
   - ☐ Never
   - ☐ 1 to 2 days per week
   - ☐ 3 to 4 days per week
   - ☐ 5 to 6 days per week
   - ☐ Everyday

9. **On average, how many glasses of <u>regular</u> carbonated soft drink do you drink per <u>day</u>?** (these include Coca-Cola, Pepsi, Solo, lemonade and flavoured mineral water, but not unflavoured mineral water or soda water)

375 ml can = 2 glasses
750 bottle = 4 glasses
1.25 litre bottle = 7 glasses
1.5 litre bottle = 8 glasses
2 litre bottle = 11 glasses

- ☐ None
- ☐ Less than 1 glass per day
- ☐ 1 glass per day
- ☐ 2 glasses (or 1 can) per day
- ☐ 3 glasses per day
- ☐ 4 glasses per day
- ☐ 5 glasses per day
- ☐ 6 glasses per day
- ☐ 7 glasses per day
- ☐ 8 glasses per day
- ☐ 9 glasses per day
- ☐ 10 or more glasses per day

10. **On average, how many glasses of <u>diet</u> carbonated soft drink do you drink per <u>day</u>?**

- ☐ None
- ☐ Less than 1 glass per day
- ☐ 1 glass per day
- ☐ 2 glasses (or 1 can) per day
- ☐ 3 glasses per day
- ☐ 4 glasses per day
- ☐ 5 glasses per day
- ☐ 6 glasses per day
- ☐ 7 glasses per day
- ☐ 8 glasses per day
- ☐ 9 glasses per day
- ☐ 10 or more glasses per day

11. **On average, how many times per <u>month</u>, per <u>fortnight</u>, per <u>week</u> or per <u>day</u> do you drink the following beverages?**

ALCOHOLIC BEVERAGES	Never	1-2 times per month	1-2 times per f/night	1-3 time per week	4-6 times per week	1 time per day	2-3 times per day	4+ times per day
Beer (low alcohol)	☐	☐	☐	☐	☐	☐	☐	☐
Beer (full strength)	☐	☐	☐	☐	☐	☐	☐	☐
Red wine	☐	☐	☐	☐	☐	☐	☐	☐
White wine (incl. sparkling wine)	☐	☐	☐	☐	☐	☐	☐	☐
Fortified wines, port, sherry etc.	☐	☐	☐	☐	☐	☐	☐	☐
Spirits, liqueurs	☐	☐	☐	☐	☐	☐	☐	☐

HOT BEVERAGES	Never	1-2 times per month	1-2 times per f/night	1-3 time per week	4-6 times per week	1 time per day	2-3 times per day	4+ times per day
Coffee	☐	☐	☐	☐	☐	☐	☐	☐
Decaffeinated coffee	☐	☐	☐	☐	☐	☐	☐	☐
Tea	☐	☐	☐	☐	☐	☐	☐	☐
Herbal tea	☐	☐	☐	☐	☐	☐	☐	☐
Chi latte	☐	☐	☐	☐	☐	☐	☐	☐
Hot chocolate	☐	☐	☐	☐	☐	☐	☐	☐

12. **On average, how many times per <u>month</u>, per <u>fortnight</u>, per <u>week</u> or per <u>day</u> do you eat the following:**

CEREAL-BASED FOODS	Never	1-2 times per month	1-2 times per f/night	1-3 time per week	4-6 times per week	1 time per day	2-3 times per day	4+ times per day
Porridge	☐	☐	☐	☐	☐	☐	☐	☐
Breakfast cereal	☐	☐	☐	☐	☐	☐	☐	☐
Rice	☐	☐	☐	☐	☐	☐	☐	☐
Pasta or noodles (including lasagna)	☐	☐	☐	☐	☐	☐	☐	☐
Crackers, crispbread, dry biscuits	☐	☐	☐	☐	☐	☐	☐	☐
Sweet biscuits	☐	☐	☐	☐	☐	☐	☐	☐
Cakes, tarts or sweet pastries	☐	☐	☐	☐	☐	☐	☐	☐

DAIRY FOODS and FATS	Never	1-2 times per month	1-2 times per f/night	1-3 time per week	4-6 times per week	1 time per day	2-3 times per day	4+ times per day
Margarine or butter	☐	☐	☐	☐	☐	☐	☐	☐
Oil (for cooking)	☐	☐	☐	☐	☐	☐	☐	☐
Salad dressing	☐	☐	☐	☐	☐	☐	☐	☐
Mayonnaise	☐	☐	☐	☐	☐	☐	☐	☐
Ricotta or cottage cheese	☐	☐	☐	☐	☐	☐	☐	☐
All other cheeses	☐	☐	☐	☐	☐	☐	☐	☐
Cream or sour cream	☐	☐	☐	☐	☐	☐	☐	☐
Ice-cream	☐	☐	☐	☐	☐	☐	☐	☐
Yoghurt	☐	☐	☐	☐	☐	☐	☐	☐
Milkshake or thick-shake	☐	☐	☐	☐	☐	☐	☐	☐
Custard	☐	☐	☐	☐	☐	☐	☐	☐

13. **On average, how many times per <u>month</u>, per <u>fortnight</u>, per <u>week</u> or per <u>day</u> do you eat the following:**

MEATS and FISH	Never	1-2 times per month	1-2 times per f/night	1-3 time per week	4-6 times per week	1 time per day	2-3 times per day	4+ times per day
Beef or veal	☐	☐	☐	☐	☐	☐	☐	☐
Chicken	☐	☐	☐	☐	☐	☐	☐	☐
Lamb	☐	☐	☐	☐	☐	☐	☐	☐
Pork	☐	☐	☐	☐	☐	☐	☐	☐
Sausages or frankfurts	☐	☐	☐	☐	☐	☐	☐	☐
Processed meats (e.g ham, slami)	☐	☐	☐	☐	☐	☐	☐	☐
Bacon	☐	☐	☐	☐	☐	☐	☐	☐
Fried fish	☐	☐	☐	☐	☐	☐	☐	☐
Steamed, grilled or backed fish	☐	☐	☐	☐	☐	☐	☐	☐
Tinned fish (e.g salmon, tuna)	☐	☐	☐	☐	☐	☐	☐	☐

MISCELLANEOUS FOODS	Never	1-2 times per month	1-2 times per f/night	1-3 time per week	4-6 times per week	1 time per day	2-3 times per day	4+ times per day
Pizza	☐	☐	☐	☐	☐	☐	☐	☐
Pastries with cheese (e.g quiche)	☐	☐	☐	☐	☐	☐	☐	☐
Meat pies, pasties, sausage rolls	☐	☐	☐	☐	☐	☐	☐	☐
Hamburgers with a bun	☐	☐	☐	☐	☐	☐	☐	☐
Chocolate	☐	☐	☐	☐	☐	☐	☐	☐
Confectionary	☐	☐	☐	☐	☐	☐	☐	☐
Peanuts or peanut butter	☐	☐	☐	☐	☐	☐	☐	☐
Other nuts	☐	☐	☐	☐	☐	☐	☐	☐
Corn chips or potato chips	☐	☐	☐	☐	☐	☐	☐	☐
Jam, marmalade, syrups or honey	☐	☐	☐	☐	☐	☐	☐	☐
Vegemite, Promite or Marmite	☐	☐	☐	☐	☐	☐	☐	☐
Tomato sauce or ketchup	☐	☐	☐	☐	☐	☐	☐	☐

Questions adapted and revised from:

The cancer Council Victoria. Dietary Questionnaire for Epidemiological studies (Version 3.1)

14. **How much do you agree or disagree with the following statements:**

	Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
I don't have time to prepare and eat healthy meals	☐	☐	☐	☐	☐
My lack of cooking skills limits what I can eat	☐	☐	☐	☐	☐
Sometimes I don't have enough money to purchase food	☐	☐	☐	☐	☐
My lifestyle habits mean I often skip meals	☐	☐	☐	☐	☐
Sometimes I just don't feel like eating healthy	☐	☐	☐	☐	☐
I get food cravings throughout the day	☐	☐	☐	☐	☐
Sometimes I engage in comfort eating	☐	☐	☐	☐	☐
I only eat when I feel hungry	☐	☐	☐	☐	☐
I always eat good nutritious meals	☐	☐	☐	☐	☐
I don't like fruit and vegetables	☐	☐	☐	☐	☐
Healthy food isn't always available where I work/study	☐	☐	☐	☐	☐
Someone else cooks for me so I don't have a choice	☐	☐	☐	☐	☐
My religion / culture has a strong effect on the way I eat	☐	☐	☐	☐	☐

Questions adapted and revised from:
Fowles, E., & Feucht, J. (2004). Testing the Barriers to Healthy Eating Scale. *Western Journal of Nursing Research, 26*(4), 429-443.

Physical Activity

PLEASE NOTE: This information will be held in strict confidence and will only be seen by researchers based at the Australian Catholic University.

No individuals will be identified.

1. **Please complete the following table to help us understand the activity patterns that you have done during the past <u>week</u>:**

Day of the week	Type of activity (e.g. cycling, swimming, walking)	Where the activity happened, and who it was with	How long the activity went for	Approximate intensity (e.g. easy, moderate, hard)
Monday				
Tuesday				
Wednesday				
Thursday				
Friday				
Saturday				
Sunday				

Adapted and revised from:
Sallis, J., Buono, M., Roby, J., Micale, F., & Nelson, J. (1993). Seven-day recall and other physical activity self—reports in children and adolescents. *Medicine and science in Sport and Exercise, 25*(1), 99-108.

2. **Please state how many times you did each type of activity and how much time you spent altogether doing each type of activity <u>last week</u>.**

If you did not do an activity, please write "0" in the boxes

	Number of times	Time in minutes
Walking briskly (e.g. recreational, exercise, travel)		
Moderate leisure activity (e.g. social tennis, swimming, dancing)		
Vigorous leisure activity (that which makes you breathe hard)		
Vigorous household or gardening chores (that which makes you puff and pant)		

3. **The following items are about activities that you might do during a typical <u>day</u>. Does your health limit you in these activities? If so, how much?**

	Yes, limited a lot	Yes, limited a little	Not limited at all
Vigorous activities	☐	☐	☐
Moderate activities	☐	☐	☐
Lifting or carrying groceries	☐	☐	☐
Climbing several flights of stairs	☐	☐	☐
Bending or kneeling	☐	☐	☐
Walking several blocks	☐	☐	☐
Bathing or dressing yourself	☐	☐	☐

4. **How often do you do each of the following?** (mark one on each line)

	Never	Once per month	1-3 times per month	Once per week	More than once per week
Take a dog for a walk	☐	☐	☐	☐	☐
Walk, swim, cycle for exercise or fitness	☐	☐	☐	☐	☐
Go to a gym, do aerobics or other classes	☐	☐	☐	☐	☐
Do yoga, Tai Chi or similar activities	☐	☐	☐	☐	☐
Play competitive sport (e.g netball, tennis)	☐	☐	☐	☐	☐

5. **How important is it for you to set time aside for regular physical activity?** (tick one box please)

Very important	Important	Neither important nor unimportant	Unimportant	Very unimportant
☐	☐	☐	☐	☐

6. **What physical activities would you like to do regularly?**

.....

.....

Psychosocial Inventories

PLEASE NOTE: This information will be held in strict confidence and will only be seen by researchers based at the Australian Catholic University.

No individuals will be identified.

STAGE OF CHANGE FOR EXERCISE

Instructions: Please read each of the following statements and indicate which best describes your current exercising habits.

Note: regular exercise = 3 or more times per week for 20 minutes or more each time

	YES	NO
I currently do NOT exercise, and I do NOT intend to start exercising in the next 6 months	☐	☐
I currently do NOT exercise, but I am thinking about starting in the next 6 months	☐	☐
I currently exercise some, but not regularly	☐	☐
I currently exercise regularly, but I have only begun in the last 6 months	☐	☐
I currently exercise regularly, and I have done so for longer than 6 months	☐	☐
I have exercised regularly in the past, but I am not doing so regularly	☐	☐

Reference: Marcus, B., Selby, V., Niara, R., & Rossi, J. (1992). Self-efficacy and the stages of exercise behavior change. *Research Quarterly for Exercise and Sport, 63 (1)*, 60-66.

MOTIVES FOR PHYSICAL ACTIVITY – REVISED (MPAM-R)

Instructions: The following is a list of reasons why people engage in physical activities, sport and exercise. Please respond to each question on the basis of how true that response is for you.

I engage in physical activity because…..	1 Not at all true for me	2 Sometimes	3 Moderately Often	4 Often	5 Very true for me
I want to be physically fit	☐	☐	☐	☐	☐
It's fun	☐	☐	☐	☐	☐
I like engaging in activities which physically challenge me	☐	☐	☐	☐	☐
I want to obtain new skills	☐	☐	☐	☐	☐
I want to lose or maintain weigh so I look good	☐	☐	☐	☐	☐
I want to be with my friends	☐	☐	☐	☐	☐
I like to do physical activity	☐	☐	☐	☐	☐
I want to improve existing skills	☐	☐	☐	☐	☐
I like the challenge	☐	☐	☐	☐	☐
I want to define my muscles so I look better	☐	☐	☐	☐	☐
It makes me happy	☐	☐	☐	☐	☐
I want to keep up my current skill levels	☐	☐	☐	☐	☐
I want to have more energy	☐	☐	☐	☐	☐
I like activities which are physically challenging	☐	☐	☐	☐	☐
I like to be with others who are interested in physical activity	☐	☐	☐	☐	☐

Please continue on next page

I engage in physical activity because…..	1 Not at all true for me	2 Sometimes	3 Moderately Often	4 Often	5 Very true for me
I want to improve my cardiovascular fitness	☐	☐	☐	☐	☐
I want to improve my appearance	☐	☐	☐	☐	☐
I think it's interesting	☐	☐	☐	☐	☐
I want to maintain my physical strength to live a healthy life	☐	☐	☐	☐	☐
I want to be attractive to others	☐	☐	☐	☐	☐
I want to meet new people	☐	☐	☐	☐	☐
I enjoy this activity	☐	☐	☐	☐	☐
I want to maintain my physical health and well-being	☐	☐	☐	☐	☐
I want to improve my body shape	☐	☐	☐	☐	☐
I want to get better at my activity	☐	☐	☐	☐	☐
I find this activity stimulating	☐	☐	☐	☐	☐
I will feel physically unattractive if I don't	☐	☐	☐	☐	☐
My friends want me to	☐	☐	☐	☐	☐
I like the excitement of participation	☐	☐	☐	☐	☐
I enjoy spending time with others doing this activity	☐	☐	☐	☐	☐

Reference: Ryan, R., Frederick, C., Lepes, D., Rubio, N., & Sheldon, K. (1997). Intrinsic motivation and exercise adherence. *International Journal of Sport Psychology, 28*, 335-354.

PERCIEVED BARRIERS TO ACTIVITY

Instructions: What prevents you from doing the physical activities that you would like to do? Please respond to each of the items below.

Barriers to you being physically active	1 Never	2 Sometimes	3 Neutral	4 Often	5 very often
Not having a safe place to exercise	☐	☐	☐	☐	☐
Poor weather	☐	☐	☐	☐	☐
No other people to be active with	☐	☐	☐	☐	☐
High cost of classes or venues	☐	☐	☐	☐	☐
Lack of transport	☐	☐	☐	☐	☐
Lack of time	☐	☐	☐	☐	☐
Nowhere to be active	☐	☐	☐	☐	☐
Having other people discourage you	☐	☐	☐	☐	☐
Feeling self-conscious about looks	☐	☐	☐	☐	☐
Being afraid of injury	☐	☐	☐	☐	☐
Feeling too tired	☐	☐	☐	☐	☐
Poor health in the past 4 months	☐	☐	☐	☐	☐
I find it hard to want to be active	☐	☐	☐	☐	☐
I find it difficult to be motivated for activity	☐	☐	☐	☐	☐
Caring for children	☐	☐	☐	☐	☐

Questions adapted and revised from: Booth et al., 1997; King et al., 2000.

Food Recall

TWO week days &

ONE weekend day

PLEASE NOTE: This information will be held in strict confidence and will only be seen by researchers based at the Australian Catholic University.

No individuals will be identified.

INSTRUCTIONS

- This food recall is to be completed on two consecutive weekdays and one weekend day (either Saturday or Sunday)
- Please write down everything you eat and drink for the same three days that you keep your activity record
- This is not a test. There are no right or wrong answers. Please do not report the foods you think you should be eating

HOW TO FILL IN YOUR RECORD

- Fill in the date and day of the week at the top of the record sheet
- Use as many pages as you need for each day's record (number each page)
- Start a new page for a new day

Column 1 – Time

- Every time you have something to eat or drink, write down the time you started
- Write down « am » for morning and « pm » for afternoon or evening

Column 2 – What you are measuring

Name and full description of all food and drink.

- Write down everything you eat and drink (This include snacks, water, vitamins and mineral supplements).
- For each food and drink use a new line
- Measure each food individually, for example, bread and margarine are each separate foods and are recorded on separate lines.
- Always record cooking methods such as boiling, frying, etc.
- Write down a cut of meat, that is lamb loin chop, chicken leg, rump steak etc.
- Write down if the fat on meat or skin on chicken was eaten or not eaten
- Give a detailed description of the food or drink and brand names, for example : Arnott's Milk arrowroot Biscuit; Tip Top White Bread

Column 3 – Amount eaten

- In order to get the best estimate of your nutrient intake we need an accurate estimate of quantities of food and drink consumed.
- Estimate everything as accurately as possible in either **metric cups or spoonfuls** eg teaspoons, tablespoons (level or rounded) such as for breakfast cereal, rice, vegetables or spaghetti, or use a **metric measuring tape or ruler** to give length and width such as for sausage rolls, bananas, etc.

RECIPES

This includes mashed potato, mixed vegetables dishes, gravies and sauces.

- On a separate page record the individual ingredient with quantities. Report the total amount made and the amount of total recipe consumed. See example attached on blue paper.

EATING OUT

- Estimate food eaten as described above.
- Record the main ingredients in the food if recipe is unknown.
- Record where the food came from, such as McDonald's.
- Record weights on wrappers, drink cans and other food containers.

DRINKS

- Measure these in **metric cups or in litre measurements**.
- For cordial, measure the volume of cordial concentrate first then the volume of water added.
- If diluting fruit juice, measure fruit juice and water separately.

EXAMPLE

Column 1 Time	**Column 2** Name, type, brand cooking method	**Column 3** Amount	**Leave blank**
7.30am	Cornflakes, Kellogs	1 cup	
	Lite white milk, Dairy Farmers	½ cup	
	White sugar, CSR	1 teaspoon	
11.00am	Chocolate Big M milk	300 ml	
12.30pm	1 cheese sandwich		
	White bread, Sunblest	2 slices	
	Margarine, unsalted, spread thinly		
	Cheese, Kraft	1 slice	
	Uncle Toby's muesli bar	31 grams	
	1 banana	12 cm long	
	Sultanas	½ cup	
4.00pm	1 junior burger, McDonalds		
	1 small diet coke, McDonalds		
7.00pm	Spaghetti bolognese		
	Boiled spaghetti, no frills	2 cups	
	Bolognese sauce (this goes in recipe section)		
	Parmesan cheese, Kraft	1 teaspoon	
	Orange juice, Berri	1 glass	
8.30pm	Wheatmeal biscuits, Arnotts	2	
	Tea (black), Tetley	1 cup	
	White sugar, CSR	1 teaspoon	

DATE :_____DAY OF WEEK : _____

Column 1 Time	Column 2 Name, type, brand cooking method	Column 3 Amount	Leave blank

RECIPE SHEET

Name of recipe : _____

Individual Ingredients	Weight or metric measure

Final total cooked weight or amount:

.....

Appendix 11: Training Diary – during lifestyle intervention

Training Diary

PLEASE NOTE: This information will be held in strict confidence and will only be seen by researchers based at the Australian Catholic University.
No individuals will be identified.

Training Days

Instructions: Please complete the table (below) on your *training days*. Make a list of those activities you undertook (i.e. other than your structured training sessions) during these days (e.g. gardening, housework, walked the dog, rode to work etc.).

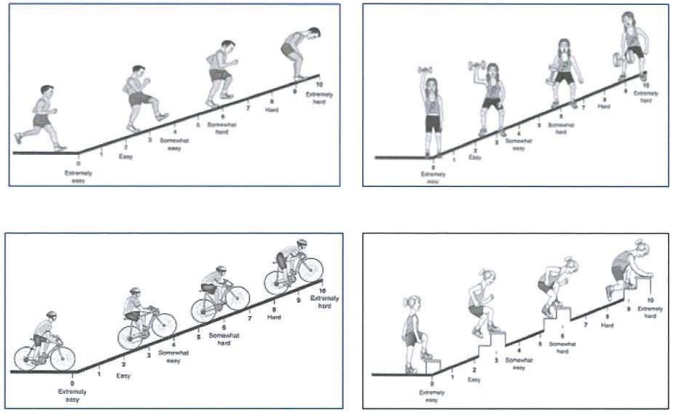
Date	Physical Activity	Duration (mins)	Intensity (RPE)

Non-Training Days

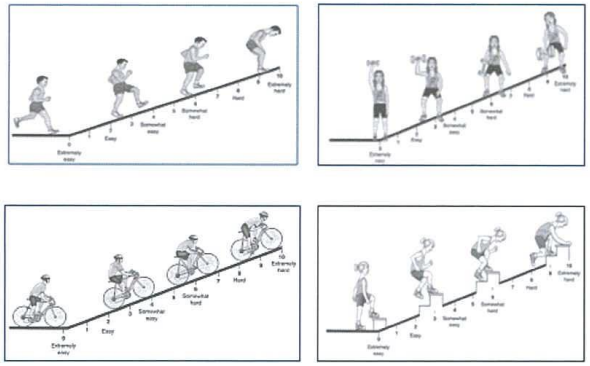
Instructions: Please complete the table (below) on your *non-training days*. Make a list of those activities you undertook during these days (e.g. list your daily duties, work activities, incidental exercise etc.).

Date	Physical Activity	Duration (mins)	Intensity (RPE)

Use these RPE images as a guide for intensity (Robertson, 2004):



Activity Record



PLEASE NOTE: This information will be held in strict confidence and will only be seen by researchers based at the Australian Catholic University.

No individuals will be identified.

Instructions: Please make a list of those activities (i.e. structured exercise and incidental activities) you undertook during the week.

Day	Physical activities	Duration (mins)	Intensity (RPE)
Mon			
Tues			
Wed			
Thurs			
Fri			
Sat			
Sun			

Note: use the Ratings of Perceived Exertion (RPE) images on the previous page as a guide for intensity (Robertson, 2004)

Appendix 13: Report

Information to assist with the interpretation of your results

The following literature has been provided to assist you in the understanding of your results. Should you require further information regarding your current health status please contact your local GP or healthcare professional for additional information. Refer to the attached document for your individual data.

Introduction

The aim of the Young Women's Heart Health Study was to assess the influence and sustainability of a 12-week lifestyle intervention on risk factors of cardiovascular disease (CVD) in young Caucasian women aged 18 to 30 years. To date, limited data exist in the understanding of early risk factors for CVD in young women. Therefore, your involvement as a participant will provide data which is not available for this age group. Furthermore, the outcomes of this work aim to advance the understanding of cardiovascular health in young women.

Participants

Healthy Caucasian women aged between 18 and 30 volunteered for this study. Exclusion criteria for the study included current smoking, pregnant or lactating, liver, kidney or respiratory disease, heart arrhythmia, insulin dependent diabetes mellitus, gestational diabetes, polycystic ovarian syndrome, thyroid abnormalities and medication treatment for lipid abnormalities.

The metabolic syndrome

The metabolic syndrome is characterised by a combination of risk factors (Table 1) that include elevated waist circumference (WC), raised serum triglyceride levels, reduced high-density lipoprotein (HDL) cholesterol, elevated fasting plasma glucose concentrations, and elevated blood pressure, which increase the chances of developing CVD (IDF, 2006).

Table 1. Components of the metabolic syndrome (IDF, 2006)

Component	Threshold
Abdominal obesity	WC ≥ 80cm
Raised serum triglyceride levels	≥1.7 mmol·L^{-1}
Reduced HDL-cholesterol	<1.29 mmol·L^{-1}
Raised blood pressure	Systolic ≥130 mmHg or diastolic ≥85 mmHg
Elevated plasma glucose concentrations	Fasting plasma glucose ≥5.6 mmol·L^{-1}

Lipid profile

High cholesterol is a key risk factor for coronary heart disease and stroke (AHA, 2010) (Table 2).

Table 2. Total cholesterol (NCEP, 2002).

Level (mmol/L)	Category
< 5.17	Desirable
5.18 – 6.18	Borderline High
≥ 6.20	High

hs-CRP: high sensitive C-reactive protein is an inflammatory biomarker that has proven to be a strong independent predictor of diabetes and CVD (Pearson, et al, 2003). According to the American Heart Association elevated levels of hs-CRP in the bloodstream (> 3.0 mg/L) is associated with an increased chance of CVD (Pearson, et al., 2003).

- < 1.0 mg/L low risk
- 1.0-3.0 mg/L Average risk
- > 3.0 mg/L High risk

BMI: Body mass index is a simple index of weight-for-height that is commonly used to classify underweight, overweight and obesity in adults. BMI does not distinguish between weight associated with muscle and weight associated with fat (WHO, 2000). A BMI within the range of 18.5-24.9 kg·m^2 is classified as desired and healthy (refer to Table 3).

BMI is defined as: weight (kg) / height (m)^2 (WHO, 2000).

Table 3. Classification of adults according to BMI (WHO, 2000).

BMI (kg·m^2)	Category
<18.5	Underweight
18.5–24.9	Normal range
≥ 25	Overweight
25-29.9	Pre-obese
30-34.9	Obese class I
35-39.9	Obese class II
≥ 40	Obese class III

WC: waist circumference is a simple measure used as an approximate index of central adiposity. An increased risk of metabolic complications is associated with a raised WC ≥ 80cm in women. Meanwhile, a WC ≥ 88cm represents substantially increased risk (IDF, 2006).

WHR: waist-to-hip ratio is a useful measure of overweight and obesity (WHO, 2000). WHR is obtained by dividing waist circumference - halfway between the lower border of the ribs, and the iliac crest - and hip circumference - the widest point over the buttock (Norton & Olds, 1996).

- WHR 0.80-0.84 Overweight
- WHR ≥ 0.85 Obese

WHtR: waist-to-height ratio can be used as a predictor of CVD and diabetes. WHtR is calculated by dividing WC by height. A ratio of 0.5 is indicative of increased risk (Browning, Hseigh & Ashwell,2010).

HOMA-IR: homeostasis model assessment of insulin resistance (HOMA-IR) is used as a relative index of insulin resistance. The model yields an estimate of insulin sensitivity and β-cell function from fasting plasma insulin and glucose concentrations (Matthews, et al, 1985). HOMA-IR is calculated from the following formula: fasting glucose (mM) x fasting insulin (μU/mL)/22.5 Insulin resistance can be measured using the euglycemic hyperinsulinemic clamp technique, which is regarded as the reference method for an accurate assessment of insulin sensitivity,

however the use of HOMA-IR (in which only a fasting blood sample is used) has shown to be a reliable technique (Bonora, et al. 2000). A HOMA-IR Score ≥2.0 is considered insulin resistance (Jensterl et al., 2008).

VO_2max: submaximal tests attempt to predict functional capacity from the heart rate response during a submaximal bout of exercise. Submaximal tests rely on the nearly linear relationship between oxygen consumption and heart rate. Functional capacity measured on the bicycle ergometer is typically 8-15% lower than on a treadmill. Factors that impact on heart rate (e.g. caffeine, medications, illness etc.) may also affect the result obtained (Brooks, Fahey, & Baldwin, 2005). See table 4 for fitness classifications.

Table 4. Cardiorespiratory fitness classifications of maximal oxygen consumption ($ml \cdot kg^{-1} \cdot min^{-1}$) for women aged 30 years and under (Brooks, Fahey, & Baldwin, 2005).

Category	*VO2 ($ml \cdot kg \cdot min^{-1}$*
Very Low	< 24
Low	24-30
Moderate	31-37
High	38-48
Very High	> 48

c-IMT: carotid intima-media thickness has become a standard for assessing arteriosclerosis and is recommended by the American Heart Association for the non-invasive assessment of cardiovascular risk. A normal c-IMT range for the right common carotid artery for women < 30 years is: 0.39-0.43 mm (Chodakauskas, 2006).

Appendix 14: Graphs

Chapter 5.

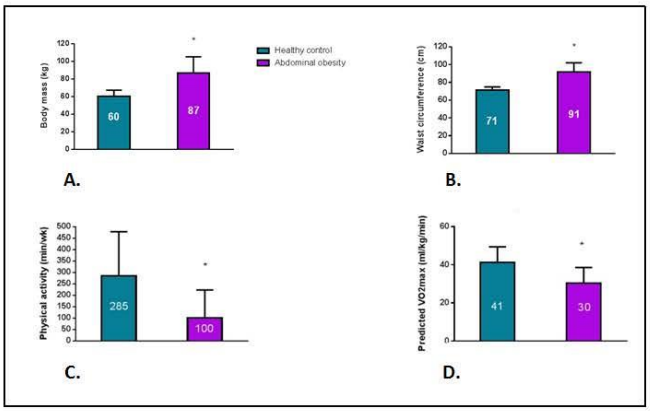


Figure 1. Cross-sectional data of statistically significant cardiometabolic variables. *P≤0.05. Green, control (WC < 80 cm); pink, women with abdominal obesity (WC ≥ 80 cm) for **A.** body mass; **B.** waist circumference; **C.** physical activity; **D.** predicted VO_{2max}

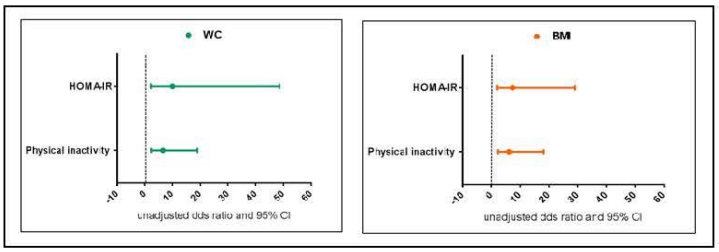


Figure 2. Cross-sectional data of WC (green) and BMI (orange) independent predator of IR and physical inactivity in young women, with unadjusted odds ratios.

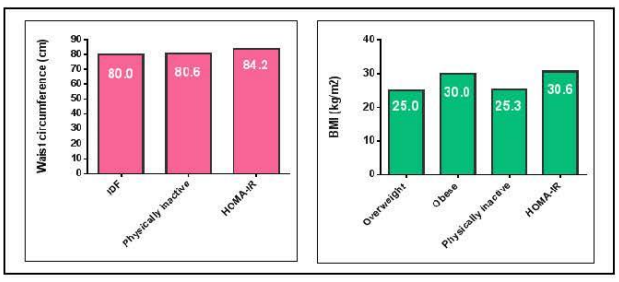
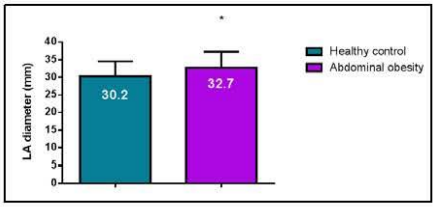


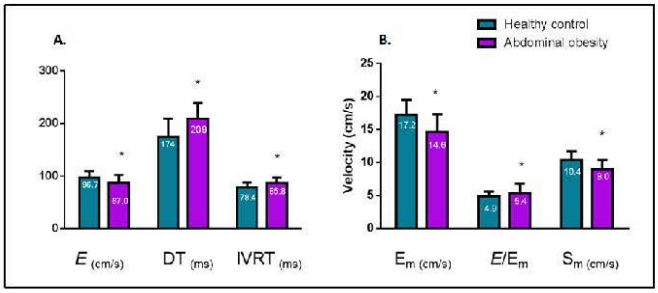
Figure 3. Cross-sectional data of dichotomization cut-off points for WC (pink) and BMI (green) in young women, from ROC curves.

Chapter 6.

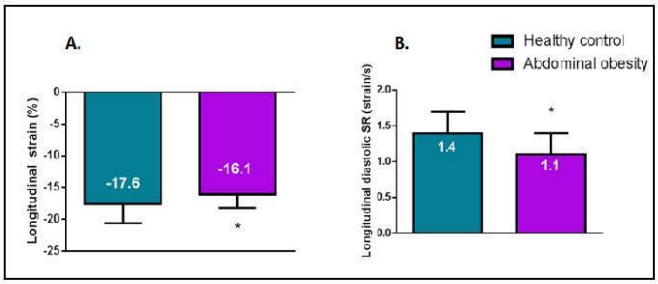
Cross-sectional data of statistically significant cardiac variables. *P≤0.05.
Green, control (WC < 80 cm); pink, women with abdominal obesity (WC ≥ 80 cm).
A. LA diameter; **B.** Indicators of diastolic function; **C.** Myocardial deformation



A.



B



C.

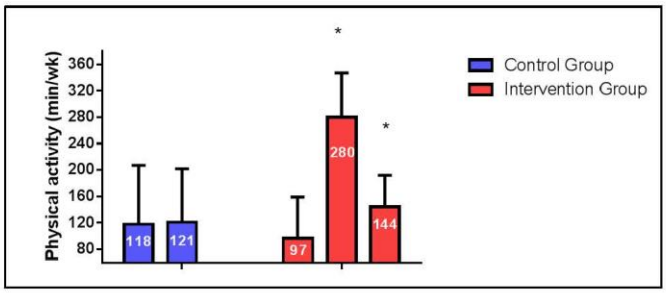


Figure 4. Between- and within-group differences for the control group (blue) at pre/post, and the intervention group (red) at pre/post/sustainability for physical activity. *P≤0.05

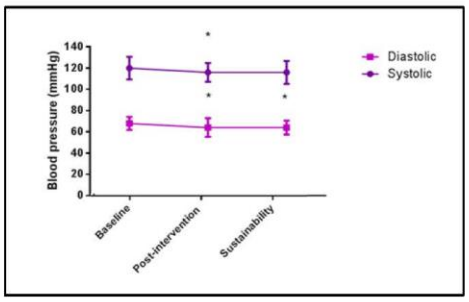


Figure 5. Within-group changes for the *intervention group.* at pre/post/sustainability for blood pressure. *P≤0.05

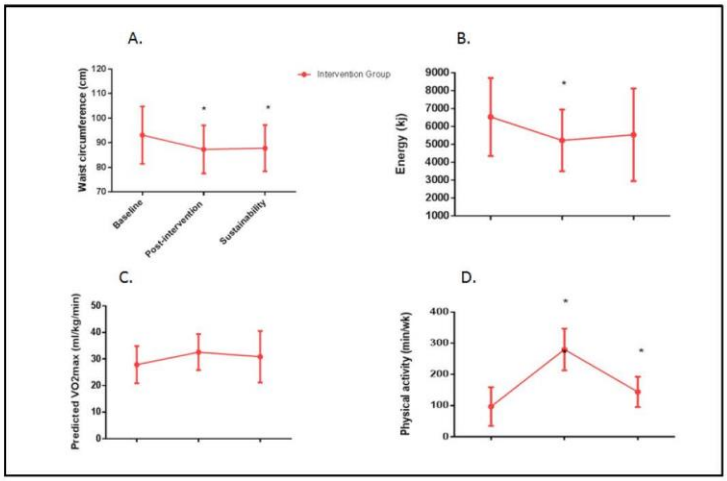


Figure 6. Within-group changes. for the *intervention group.* at pre/post/sustainability for: A. waist circumference, B. Energy, C. Vo2max, D. physical activity. *P≤0.05.

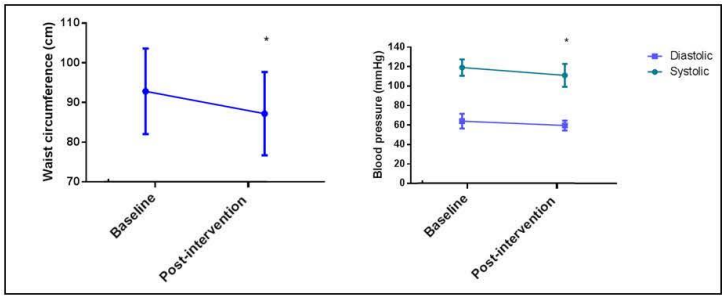


Figure 7. Within-group changes for the control group at pre/post for waist circumference and blood pressure. *P≤0.05.

Chapter 8.

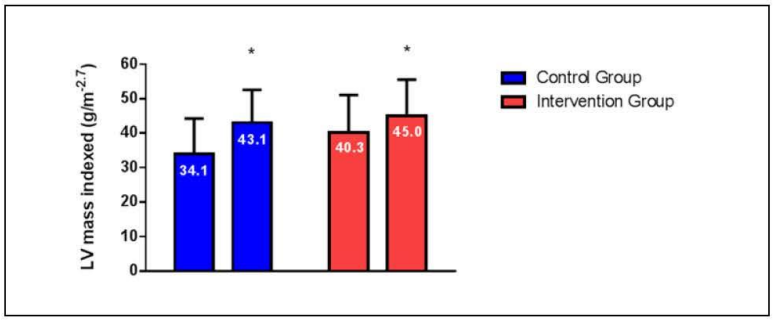


Figure 8. Within-group changes for the control (blue) and intervention (red) groups for LV mass indexed from pre to post intervention. *P≤0.05.

Appendix 15: Published Manuscripts

Journal of Science and Medicine in Sport 17 (2014) 656–661

Contents lists available at ScienceDirect

Journal of Science and Medicine in Sport

journal homepage: www.elsevier.com/locate/jsams

Original research

Cardiometabolic and behavioural risk factors in young overweight women identified with simple anthropometric measures

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Body mass index
Waist-to-height ratio
Cardiovascular disease
Physical activity

ABSTRACT

Objectives: This study aimed to (1) investigate cardiometabolic risk markers in young women (18–30 years) with overweight/obesity, and (2) establish whether the measures of waist circumference and body mass index possess similar associations of cardiometabolic risk.
Design: Cross-sectional.
Methods: Cardiometabolic risk factors including, anthropometric, metabolic syndrome markers, biochemical, and other health/fitness indicators were assessed in women when classified as overweight/obese by waist circumference [waist circumference 91.9 ± 10.1 cm, age 22.3 ± 3.5 years, $n = 38$] versus control [$n = 30$, waist circumference 71.4 ± 3.5 cm, age 20.1 ± 0.9 years], and when classified by body mass index [$n = 35$, body mass index 32.2 ± 5.2 kg m^2, age 22.5 ± 3.6 years] versus control [body mass index 21.7 ± 1.9 kg m^2, age 20.1 ± 0.9 years, $n = 33$].
Results: Compared with controls, women with overweight/obesity (classified by waist circumference or body mass index) displayed elevated body mass, systolic blood pressure and homeostasis model assessment of insulin resistance, and reduced estimated VO_{2max} and weekly physical activity, with no differences in self-reported energy intake. The unadjusted odds ratio of being classified with overweight/obesity and an elevated homeostasis model assessment of insulin resistance and/or less than recommended physical activity ranged between 5.1 and 10.0. Receiver operator characteristic curves indicated waist circumference, body mass index and waist-to-height ratio cut-off points of ≥84.2 cm, ≥30.6 kg m^{-2} and ≥0.5, respectively, for homeostasis model assessment of insulin resistance, and ≥80.6 cm, ≥25.2 kg m^{-2} and ≥0.46, respectively, for less than recommended physical activity.
Conclusions: Waist circumference and body mass index have similar associations with cardiometabolic risk, with greater homeostasis model assessment of insulin resistance and lower physical activity, rather than differences in traditional metabolic syndrome markers, observed in young women with overweight/obesity.

1. Introduction

In Australia, the prevalence of overweight/obesity is 35% for women aged 18–24 years, and 42% for women aged 25–34 years.[1] However, cardiometabolic risk data are more frequently described in adolescents[2] and even more so in older people,[3] with women in young adulthood under-represented. The gains in weight in young adult women are paralleled by substantial declines in physical activity,[4] with the greatest declines occurring between 25 years and 34 years of age.[1] When assessed against current National Physical Activity Guidelines,[5] 59% of Australian women aged 18–34 years failed to achieve recommended weekly amounts (210 min) of moderate exercise,[6] while the Australian Longitudinal Study on Women's Health found that 45% of overweight/obese women aged 18–23 years performed none or very low levels of daily physical activity.[7] A better understanding of cardiometabolic risk factors in this age group is important for early detection of chronic disease risk, especially given the rise in overweight/obesity and low prevalence of physical activity of young women.

With overweight/obesity being a modifiable risk factor for cardiovascular disease (CVD), Type 2 diabetes mellitus, and the metabolic syndrome,[8] simple anthropometric measures of body mass index (BMI) and waist circumference (WC) are in frequent clinical use. BMI is an estimate of total fat mass and has been used as a predictor of health risk.[9] For adults, a BMI of 25.0–29.9 kg m^{-2}

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is classified as overweight, and a BMI ≥ 30 kg m^{-2} is classified as obese.[10] Correspondingly, centrally distributed (abdominal) obesity using WC has gender and ethnic-specific criteria available.[8] For Caucasian women, abdominal obesity is defined as a WC ≥ 80 cm.[8] Given the differing criteria for BMI and WC in classifying overweight/obesity in young women, it is important to establish whether these anthropometric measures identify the presence and/or similar relative risk of other markers of cardiometabolic risk.

Therefore, the aims of this study were to: (1) investigate blood-borne and lifestyle markers of cardiometabolic risk in young women (18–30 years) with overweight/obesity classified by clinically useful methods, and (2) establish whether WC and BMI possess similar associations of cardiometabolic disease risk in these women. For comparative purposes, waist-to-height ratio (WHtR) was included in some statistical analyses.

2. Methods

Ninety-three university-enrolled participants responded to recruitment advertisements and emails. Of these, 11 did not meet the inclusion criteria (below) and a further 14 eligible participants did not continue through testing. Therefore, 68 Caucasian women aged 18–30 years completed all testing, between 2010 and 2012. Participants were divided into two groups: (1) an "elevated" waist circumference ≥80 cm [n = 38, abdominal obesity, mean ± standard deviation, WC 91.9 ± 10.1 cm, age 22.3 ± 3.5 years], or (2) a waist circumference < 80 cm control group [n = 30, WC 71.4 ± 3.5 cm, age 20.1 ± 0.9 years]. There was no difference between groups in socio-economic status [χ^2 (4, n = 66) = 0.42, p = 0.382], with 51.4% of participants in the elevated WC group and 62.1% of participants in the control group living in metropolitan suburbs of the most advantaged quintile of socio-economic status.[11] Exclusion criteria included being pregnant or breastfeeding, liver or kidney disease, heart arrhythmia, insulin dependent diabetes mellitus, gestational diabetes, polycystic ovarian syndrome, thyroid abnormalities and a history of bariatric surgery or liposuction. All participants were non-smokers. For additional analysis, the same 68 participants were divided into two groups according to the classifications of BMI, resulting in participants being classified as either overweight/obesity [n = 35, defined as a BMI ≥ 25 kg m^{-2}, BMI 32.2 ± 5.2 kg m^{-2}, age 22.5 ± 3.6 years] or normal BMI [n = 33, BMI 18.5–24.9 kg m^{-2}, BMI 21.7 ± 1.9 kg m^{-2}, age 20.1 ± 0.9 years].

Following approval by the University Human Research Ethics Committee (V2009-91), written informed consent was obtained and all participants completed a Cardiovascular Risk Assessment Form prior to testing. Participants arrived at the laboratory following a 12 h fast. They were also requested to refrain from strenuous physical activity in the 24 h prior to testing.

Waist circumference (WC) was measured[8] to the nearest 0.1 cm using a non-elastic measuring tape, with the average of two measurements reported. The coefficient of variation for WC, assessed from duplicate measures, was 1.26%, with an intra-class correlation (ICC, 2, 1) of 0.986 and measurement error of 1.34%, which equates to an error range of ± 2.6 cm. Body mass was measured to the nearest 0.1 kg using digital scales (Tanita, Tokyo, Japan). Height was measured to the nearest 0.1 cm using a wall-mounted stadiometer (Seca, Germany). Body mass index (BMI) (weight [kg]/height [m^2]), was defined as overweight BMI 25.0–29.9 kg m^{-2} and obese BMI ≥ 30.0 kg m^{-2}.[10] Participants were dichotomised by waist-to-height ratio (WHtR) using WC divided by height. A ratio of 0.5 was defined as the boundary value.[12]

Metabolic syndrome was defined according to the most recent and unified criteria,[8] where three of the following five are met: (1) waist circumference ≥ 80 cm, (2) raised serum triglycerides ≥ 1.7 mmol l^{-1}, (3) reduced HDL-cholesterol < 1.30 mmol l^{-1}, (4) raised systolic blood pressure ≥ 130 mmHg or raised diastolic blood pressure ≥ 85 mmHg, and (5) elevated fasting plasma glucose ≥ 5.6 mmol l^{-1} or previously diagnosed type 2 diabetes. No participants in this study were taking medication to treat elevated triglycerides or reduced HDL-cholesterol, which is considered an alternative indicator of abnormal levels.[8] Additional measurements of insulin resistance, including fasting insulin and HOMA-IR, and the pro-inflammatory marker high sensitivity C-reactive protein (hs-CRP) were also measured in participants.

Intravenous blood sampling provided blood lipid profiles: serum concentrations of triglycerides, total cholesterol and high-density lipoprotein (HDL) cholesterol (Reflotron Plus, Roche, Switzerland). A CV of 3.8% was found between Refloton measurements for total cholesterol and a standardised wet-chemistry method.[13] Fasting plasma glucose, insulin and hs-CRP concentrations were analysed by a pathology unit at a leading hospital (reagents Beckman Coulter, assays on Olympus AU2700, Abbott Architect i1000, and Olympus AU640 analyser). Insulin resistance was estimated by the homeostasis model assessment (HOMA-IR), using the equation: HOMA-IR = fasting insulin concentration (μU/mL) × fasting glucose concentration (μU/mL)/22.5.[14] HOMA-IR was used as a surrogate measure of whole body insulin sensitivity and β-cell functioning and has been shown to correlate well with estimates using the euglycemic clamp method (r = 0.88).[14,15] A HOMA-IR value ≥ 2.0 was considered indicative of insulin resistance.[16] For hs-CRP, a value of >3.0 mg l^{-1} was deemed high risk.[17] Blood pressure was obtained with an automated digital sphygmomanometer (Dinamap, GE technology, USA).

The YMCA submaximal cycle ergometer test[18] was used to estimate maximal oxygen uptake (predicted VO_{2max}). After completing a short submaximal warm-up, participants cycled (Monark, Ergomedic 838E, Sweden) for three consecutive 3-min work rates at a constant cadence of 50 rpm, and an initial power output of 25 W, resulting in a total test time of 9 min. Heart rate during the last 15 s of stage one was used to determine subsequent work loads. At the completion of the test, heart rate was extrapolated against work rate (W) using regression analysis to estimate maximal aerobic capacity.

Within the acknowledged limitations of dietary recall,[19] participants completed a three-day food diary of food and beverage intake on two weekdays and one weekend day. Macro and micro nutrients, and average daily energy intake were estimated (FoodWorks® 7 Professional) by a research dietician, blinded to grouping.

Participants completed a self-administered lifestyle survey addressing (i) health status and medical conditions, (ii) self-reported physical activity and exercise, (iii) nutrition habits, and (iv) perceived barriers to physical activity.[20] Additionally, type, frequency and duration of typical leisure and/or sporting activities were confirmed during an interview with the researcher.

Data were analysed using IBM SPSS Statistics, Version 19 for Windows (SPSS Inc., Chicago, IL) and first tested for normal distribution using the Shapiro–Wilk statistic and skewness and kurtosis values.[21] Log transformation was used when data were not normally distributed. All data are presented as mean ± standard deviation, with the exception of medians [interquartile range] for non-normally distributed data, reported prior to log transformed treatment. An alpha level of p < 0.05 was used to determine significance. Group comparisons were performed using independent t-tests. Due to uneven group size, Hedge's g calculated effect size. An effect size of ≥0.2 was considered small, ≥0.5 was considered medium, and ≥0.8 was considered large.[22] The mean difference between overweight/obesity and control participants for each cardiometabolic risk factor included 95% confidence intervals.

Unadjusted odds ratios were used to estimate disease risk given exposure and describe the strength of association between

overweight/obesity (classified by WC, BMI and WHtR) and cardiometabolic risk factors. Continuity correction was used to establish significance.[21]

Receiver operating characteristic (ROC) curves were plotted to determine the point that maximises the likelihood ratio and cut-off points for WC, BMI and WHtR. Furthermore, the positive likelihood ratio was computed for each cut-off point. Pearson's Chi-square analysis was used to compare the frequency of scores for barriers to being physically active between the two groups.

3. Results

Anthropometric and cardiometabolic data are shown in Tables 1 and 2. Compared with controls, women with abdominal obesity (WC ≥ 80 cm) had greater body mass, body mass index, waist circumference and waist-to-height ratio ($p < 0.001$). Similar differences were observed for BMI.

None of the women with overweight/obesity were diagnosed with the metabolic syndrome.[8] Of the metabolic syndrome

Table 1
Cardio-metabolic risk factors in subjects with and without abdominal obesity, as defined by waist circumference.

Variable	Control WC < 80 cm ($n = 30$)	Abdominal obesity WC ≥ 80 cm ($n = 38$)	p value	Effect size Hedge's g	Mean difference	95% CI
Anthropometric assessment						
Body mass (kg)	60.34 ± 6.68	86.74 ± 18.35	<0.001*	1.61	26.40	19.93, 32.86
Stature (m)	1.67 ± 0.06	1.66 ± 0.06	0.311	0.15	−0.01	−0.44, 0.01
Body mass index (kg m^{-2})	21.59 ± 1.94	31.47 ± 5.54	<0.001*	2.00	9.88	7.93, 11.82
Waist circumference (cm)	71.38 ± 3.48	91.87 ± 10.10	<0.001*	2.28	20.49	16.95, 24.02
Waist-to-height ratio (WHtR)	0.43 ± 0.02	0.55 ± 0.06	<0.001*	2.41	0.13	0.11, 0.15
Metabolic syndrome markers						
Systolic BP (mmHg)	114.63 ± 8.30	120.29 ± 8.37	0.007*	0.60	5.66	1.59, 9.72
Diastolic BP (mmHg)	67.30 ± 8.16	66.92 ± 6.68	0.834	0.04	−0.38	−4.07, 3.31
HDL-cholesterol (mmol l^{-1})	1.50 ± 0.32	1.63 ± 0.51	0.241	0.26	0.13	−0.08, 0.33
Triglycerides (mmol l^{-1})	1.12 ± 0.35	1.19 ± 0.37	0.400	0.17	0.07	−0.10, 0.25
Fasting glucose (mmol l^{-1})	4.83 ± 0.36	4.67 ± 0.52	0.152	0.29	−0.16	−0.39, 0.06
Additional biochemical parameters						
Total cholesterol (mmol l^{-1})	4.60 ± 0.98	4.39 ± 0.62	0.313	0.26	−0.21	−0.64, 0.21
Fasting insulin (mU l^{-1})#	5.00 [2.25]	8.00 [5.00]	<0.001*	0.84	3.68	1.99, 5.38
HOMA-IR#	1.14 [0.53]	1.75 [1.12]	<0.001*	0.75	0.74	0.35, 1.12
hsCRP (mg l^{-1})#	1.38 [1.36]	1.93 [3.49]	0.024*	0.46	1.20	0.16, 2.23
Health and fitness evaluation						
Predicted VO_{2max} (ml kg^{-1} min^{-1})	41.35 ± 8.14	30.41 ± 8.21	<0.001*	1.61	11.03	7.04, 15.02
Physical activity (min wk^{-1})#	285 [193.75]	100 [123.75]	<0.001*	1.11	−193.37	−275.36, −111.37
Daily energy intake (KJ)	5797 ± 1421	6263 ± 2478	0.343	0.187	−466.37	−1443.34, 510.58

Data presented as mean ± SD or median [IQ range].
$\log_{10}$ transformation.
* $p \leq 0.05$.
Blood pressure (BP); high-density lipoprotein (HDL); high sensitive C-reactive protein (hs-CRP); and homeostasis model assessment of insulin resistance (HOMA-IR).

Table 2
Cardio-metabolic risk factors in subjects with and without overweight/obesity, as defined by body mass index.

Variable	Control BMI <24.9 kg m^{-2} ($n = 33$)	Overweight/obesity BMI ≥25.0 kg m^{-2} ($n = 35$)	p value	Effect size Hedge's g	Mean difference	95% CI
Anthropometric assessment						
Body mass (kg)	60.81 ± 6.60	88.56 ± 17.96	<0.001*	2.00	27.74	21.11, 34.37
Stature (m)	1.67 ± 0.05	1.65 ± 0.06	0.254	0.36	−0.02	−0.05, 0.01
Body mass index (kg m^{-2})	21.75 ± 1.90	32.17 ± 5.20	<0.001*	2.60	10.42	8.50, 12.34
Waist circumference (cm)	72.51 ± 4.78	92.56 ± 10.29	<0.001*	2.44	20.06	16.13, 23.98
Waist-height-ratio (WHtR)	0.43 ± 0.03	0.56 ± 0.05	<0.001*	3.09	0.12	0.10, 0.15
Metabolic syndrome markers						
Systolic BP (mmHg)	115.15 ± 8.42	120.28 ± 8.42	0.014*	0.60	5.13	1.05, 9.21
Diastolic BP (mmHg)	66.81 ± 7.86	67.34 ± 6.87	0.770	0.07	0.52	−3.04, 4.09
HDL-cholesterol (mmol l^{-1})	1.49 ± 0.32	1.66 ± 0.52	0.114	0.38	0.17	−0.04, 0.38
Triglycerides (mmol l^{-1})	1.16 ± 0.39	1.16 ± 0.33	0.959	0.01	−0.00	−0.18, 0.17
Fasting glucose (mmol l^{-1})	4.75 ± 0.43	4.72 ± 0.48	0.811	0.06	−0.03	−0.25, 0.20
Additional biochemical parameters						
Total cholesterol (mmol l^{-1})	4.66 ± 0.94	4.34 ± 0.60	0.128	0.40	−0.32	−0.73, 0.09
Fasting insulin (mU l^{-1})#	5.00 [3.00]	8.00 [5.00]	<0.001*	1.00	0.23	0.13, 0.34
HOMA-IR#	1.07 [0.72]	1.81 [1.08]	<0.001*	1.00	0.74	0.34, 1.14
hs-CRP (mg l^{-1})#	1.43 [2.00]	1.98 [2.95]	0.079	0.43	0.98	−0.11, 2.07
Health and fitness evaluation						
Predicted VO_{2max} (ml kg^{-1} min^{-1})	40.87 ± 8.76	30.00 ± 7.66	<0.001*	1.31	10.87	6.89, 14.85
Physical activity (min wk^{-1})#	260 [220]	100 [112.50]	<0.001*	1.13	−179.00	103.19, 256.81
Daily energy intake (KJ)	6164 ± 1615	5946 ± 2434	0.671	0.10	218.14	−804.52, 1240.80

Data presented as mean ± SD or median [IQ range].
$\log_{10}$ transformation.
* $p \leq 0.05$.
Blood pressure (BP); high-density lipoprotein (HDL); high sensitive C-reactive protein (hs-CRP); and homeostasis model assessment of insulin resistance (HOMA-IR).

Table 3
Associations between cardio-metabolic risk factors and overweight/obesity.

Variable	% diagnosed in exposed group	% diagnosed in non-exposed group	Unadjusted odds ratio (95% CI)	*P* value
Waist circumference	WC ≥ 80 cm	WC < 80 cm		
HOMA-IR	41.7%	6.7%	10.0 (2.1, 48.6)	0.003
Physical activity (min wk^{-1})	78.9%	36.7%	6.5 (2.2, 19.0)	0.001
Body mass index	BMI ≥ 25 kg m^{-2}	BMI ≤ 24.9 kg m^{-2}		
HOMA-IR	42.4%	9.1%	7.4 (1.9, 29.1)	0.005
Physical activity (min wk^{-1})	80.0%	39.4%	6.1 (2.1, 18.2)	0.002
Waist-to-height-ratio	WHtR ≥ 0.5	WHtR < 0.5		
HOMA-IR	40.6%	11.0%	5.1 (1.4, 18.0)	0.016
Physical activity (min wk^{-1})	82.0%	38.2%	7.6 (2.4, 23.1)	0.001

A participant with a HOMA-IR score of ≥2.0 or physical activity levels of ≤210 min per week was allocated to the exposed group.
Note. Two data sets for HOMA-IR were unavailable due to compromised samples.

markers, only systolic blood pressure was higher than controls in participants with overweight/obesity, regardless of classification. The proportion of women in the intervention and control groups, respectively exhibiting each of the metabolic syndrome markers were: WC (100%, 0%); triglycerides (8%, 6%); HDL-cholesterol (32%, 27%); systolic blood pressure (10%, 3%); diastolic blood pressure (0%, 0%); glucose (3%, 0%).

Again, independent of the classification used, the two predictors of glycaemic risk, fasting insulin and HOMA-IR were more elevated in participants with a raised WC and/or BMI > 25 kg m^{-2} than controls (Tables 1 and 2).

The pro-inflammatory marker hs-CRP was significantly (40%) higher in women with elevated WC than controls but did not differ when using BMI thresholds. Additionally, the prevalence of elevated hs-CRP > 3 mg l^{-1} was[17] 35% for women with overweight/obesity compared with 20% in the control group, for WC [χ^2 (1, n = 67) = 1.20, p = 0.274] and BMI [χ^2 (1, n = 67) = 0.22, p = 0.642].

Aerobic fitness estimated from a submaximal cycling protocol was 26% lower in participants with elevated WC than controls. Similarly, subjective approximations of weekly physical activity were 63% less in women with elevated WC than controls. Estimated daily energy intake did not differ between groups. Similar results were observed using BMI (Tables 1 and 2).

HOMA-IR, fasting insulin, hs-CRP and physical activity were used as dependent variables and anthropometric measures of WC, BMI and WHtR were the independent variables in calculating unadjusted odds ratios. From this analysis only HOMA-IR and physical activity produced significant unadjusted odds ratios (Table 3). Approximately 41% of participants in the exposed group (overweight/obesity – classified by WC, BMI and WHtR) and 6.7–11.0% in the non-exposed group (controls) were diagnosed with elevated HOMA-IR. Furthermore, the unadjusted odds ratio for the association between overweight/obesity and elevated HOMA-IR ranged between 5.1 and 10.0. The percentage of less than recommended physical activity levels in the exposed group (approximately 80%) was double that of the non-exposed group (approximately 40%) (Table 3).

ROC curves determined the cut-off point for three anthropometric (WC, BMI, WHtR) measures. The area under the curve (AUC) for elevated HOMA-IR was 0.79 (p < 0.001) and a cut-off value of 84.25 cm when calculated for WC. Additionally, the positive likelihood ratio was 2.9. Less than recommended physical activity produced a value of 0.72 for the AUC (p = 0.002), with a cut-off value of 80.65 cm and a positive likelihood ratio of 3.3 for WC. For BMI, HOMA-IR produced a value of 0.82 for the AUC (p < 0.001), with a BMI cut-off value of 30.61 kg m^{-2}, and a positive likelihood ratio of 4.9. Moreover, the AUC for less than recommended physical activity levels was 0.73 (p = 0.002), with a BMI cut-off of 25.25 kg m^{-2}, and a positive likelihood ratio of 3.7. For WHtR, HOMA-IR value for AUC was 0.76 (p < 0.001), with a WHtR cut-off value of 0.50, and a positive likelihood ratio of 1.2. Additionally, the AUC for less than recommended physical activity levels was 0.71 (p = 0.003), with a WHtR cut-off of 0.46, and a positive likelihood ratio of 2.8.

Participants completed a questionnaire, rating their perceived barriers to physical activity. Chi-square frequencies revealed 84% of participants agreed that exercise was important to them. Despite this, 65% of women with elevated WC or BMI > 25 kg m^{-2} shared difficulties in motivation for physical activity (17% in controls), however both groups ranked feeling too tired as their number one barrier (Supplementary Table 1). Additionally, 56% of participants with elevated WC or BMI > 25 kg m^{-2} reported that being self-conscious about their looks was a major barrier to regular physically active (3% in controls).

Supplementary material related to this article can be found, in the online version, at http://dx.doi.org/10.1016/j.jsams.2013.09.011.

4. Discussion

Data on the prevalence, characteristics and consequences of overweight/obesity in young women are important for providing an indication of the need for early detection, timely treatment, and the adaptation of lifelong interventions.[23] In this study, classification of overweight/obesity using WC and BMI were associated with similar cardiometabolic risk. Risk markers commonly used in standard health checks did not differentiate between women with overweight/obesity and those in healthy anthropometric ranges, while women with overweight/obesity did display higher markers of insulin resistance (fasting insulin and HOMA-IR) and lower estimates of physical activity (weekly exercise duration and aerobic fitness). This finding suggests that anthropometric measures are useful first-line diagnostic measures of cardiometabolic risk, with insulin resistance and lifestyle factors providing deeper insight into this risk for young adult women than traditional metabolic syndrome markers.

No individual was diagnosed with the metabolic syndrome[8] and, as a group mean, none of the markers (i.e., other than WC) was elevated to that of the current metabolic syndrome definition. In contrast, data from the Australian Diabetes, Obesity and Lifestyle Study (AusDiab) reported the prevalence of the metabolic syndrome in women aged between 25 years and 34 years to be 6%.[24] Given the younger age of our participants (22.3 ± 3.5 years) compared with those in the AusDiab Study,[24] these data suggest that traditional metabolic syndrome markers may not be sufficiently sensitive to indicate cardiometabolic risk in young adulthood (<30 years). Therefore, markers of insulin resistance may be more useful indicators of future cardiometabolic risk in younger women with overweight/obesity than markers currently used in the metabolic syndrome definitions and during standard health checks.

As a marker of insulin dysfunction, elevated HOMA-IR ≥ 2.0,[16] was present in more than 41% of women with overweight/obesity in the present study, compared with 6.7–11.0% of the control group. Moreover, the odds ratio for the association between overweight/obesity and an elevated HOMA-IR score was large, suggesting a strong relationship between these two variables. Raised concentrations of circulating hs-CRP were also present in women with an elevated WC, in agreement with previous reports.[25,26] These raised hs-CRP concentrations could have contributed to higher HOMA-IR scores in the overweight/obesity group, given that hs-CRP disrupts insulin signalling and action.[25]

Similar predictors of cardiometabolic risk were found when using WC and BMI as proxy measures of overweight/obesity, suggesting that both are useful markers for potential insulin resistance in young women. This agrees with previous results showing WC and BMI have a similar strength of association with CVD risk in adults, when assessed using individual records from 58 cohorts.[27] Results from ROC curves showed that the WC cut-off point for determining increased risk of insulin resistance, as measured by both fasting insulin and HOMA-IR, was ≥84 cm. This value is higher than current guidelines of ≥80 cm for Caucasian females.[8] Similar trends were observed for the cut-off point for classifications of BMI, in which a measure of ≥30.0 kg m^{-2}, rather than ≥25 kg m^{-2}, was identified an increased risk of elevated HOMA-IR. In contrast, the dichotomization cut-off points for cardiometabolic risk associated with low physical activity (≤210 min of weekly exercise) in our study were determined to be ≥80 cm for WC and ≥25.25 kg m^{-2} for BMI, strongly supporting the probability of risk within the existing overweight/obesity classification scores.[8,10]

The use of WHtR may also be a suitable and easy to administer anthropometric screening tool for the prediction of cardiometabolic outcomes applicable to a variety of populations.[12] ROC curves showed that the WHtR margin for determining increased risk of insulin resistance, as measured by HOMA-IR, was ≥0.5, strongly supporting the current global boundary value.[12] Additionally, a cut-off value of ≥0.46 was determined for cardiometabolic risk associated with low physical activity (≤210 min of weekly exercise), which is lower than the current threshold. Furthermore, the unadjusted odds ratios of WHtR in predicting risk factors are comparable to WC and BMI.

In the present study, 80% of women with overweight/obesity failed to achieve minimum weekly exercise recommendations compared with 35% of the control group, while 3-day dietary recall data showed no differences in daily energy intake between the groups. Although dietary recall has limitations, these data show insufficient energy expenditure from physical activity relative to energy intake appears to be a significant factor in weight gain in the young women in our study. From data reported in a qualitative questionnaire, a prominent barrier to being active for the overweight/obesity women was self-conscious feelings about their own appearance. Therefore, lifestyle interventions for the prevention/reduction of overweight/obesity need to address psychological barriers to physical activity.

The study has several limitations. The cross-sectional design could conceivably be a weakness, but it provided proof of concept prior to larger trials. Future studies using a prospective design could provide predictive data that addresses WC/BMI and the development of cardiometabolic disease. Ideally, central fat distribution would be measured using MRI, but waist circumference still provided a level of sensitivity relevant to most clinical settings.[9] Additionally, the results are specific to Caucasian women at a tertiary institution and largely from suburbs in the most advantaged quintile of socio-economic status. Given this however, our data raise concerns that key health promotion messages are either poorly sourced or understood, and/or are very difficult to apply. When more educated, advantaged young women have difficulties, it may be assumed that individuals from less advantaged backgrounds may at least share these health issues.

5. Conclusion

This study supports the use of WC and BMI as first-line diagnostic measures of cardiometabolic risk. However, risk markers beyond the traditional metabolic syndrome blood-borne criteria, such as fasting insulin and HOMA-IR, may be required when screening further for cardiometabolic risk in young women. A higher order of investigation (e.g., blood sampling) may help convince young women of the need to take action. Furthermore, sedentary behaviour in young women with overweight/obesity is a lifestyle risk factor of concern, with a need for addressing identified age- and gender-specific barriers to engagement. The value of additional research into managing cardiometabolic risk in young women cannot be understated.

Practical implications

- In young adult women, WC and BMI as measures of overweight/obesity have similar associations with other cardiometabolic risk factors.
- Markers of insulin and HOMA-IR may be useful indicators of future cardiometabolic risk in younger women with overweight/obesity.
- The first line of treatment for cardiometabolic risk should be centred on modifiable lifestyle changes, such as those associated with sedentary behaviour through increased physical activity.
- Given the poor engagement in physical activity in our study population, the approach to engagement should be age and gender appropriate, and take into account perceived barriers to physical activity.

Conflict of interest

None.

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Basic Research

Young Women With Abdominal Obesity Have Subclinical Myocardial Dysfunction

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ABSTRACT

Background: Abdominal obesity is an independent risk factor for cardiovascular disease. The effect of abdominal obesity on myocardial function in young obese women remains unknown. Therefore, we aimed to investigate cardiac morphology and function, myocardial deformation, and mechanical indices, in young women with and without abdominal obesity.

Methods: Cross-sectional analyses of 39 women with abdominal obesity (waist circumference $\geq$ 80 cm) and 33 nonobese control subjects (waist circumference $<$ 80 cm) aged 18-30 years underwent conventional echocardiographic measures of cardiac morphology and function together with tissue Doppler, and 2-dimensional speckle tracking measures of myocardial deformation and mechanics. Cardiometabolic risk factors including anthropometric, hypertension, biochemistry, and fitness were also assessed.

Results: Standard echocardiography results for cardiac morphology and function were similar between groups, with the exception of larger left atrial dimensions in women with abdominal obesity ($P \leq 0.05$).

RÉSUMÉ

Introduction : L'obésité abdominale est un facteur de risque indépendant de la maladie cardiovasculaire. Nous ignorons les conséquences de l'obésité abdominale sur la fonction du myocarde chez les jeunes femmes obèses. Par conséquent, notre but était d'examiner la morphologie et la fonction cardiaque, la déformation du myocarde et les indices mécaniques chez les jeunes femmes souffrant ou non d'obésité abdominale.

Méthodes : Les analyses transversales de 39 femmes souffrant d'obésité abdominale (tour de taille $\geq$ 80 cm) et 33 sujets témoins non obèses (tour de taille $<$ 80 cm) qui étaient âgées de 18 à 30 ans ont subi des mesures échocardiographiques traditionnelles de la morphologie et de la fonction cardiaque par Doppler tissulaire et des mesures par échocardiographie bidimensionnelle *Speckle Tracking* (suivi de pixel) de la déformation et de la mécanique du cœur. Les facteurs de risque cardiométabolique, y compris l'anthropométrie, l'hypertension, la biochimie et la condition physique ont également été évalués.

Obesity is an established independent risk factor for cardiovascular disease (CVD), with prevalence reaching epidemic proportions.[1] In countries such as Australia, the prevalence of obesity in young women appears to be increasing at an exponential rate.[2] Increased waist circumference (WC) is a reliable anthropometric index of abdominal obesity[3] that allows early identification of CVD risk.[4] However, the cardiac consequences of risk factors are poorly understood in young women; a population emerging as highly vulnerable to cardiometabolic disorders.

Young women specifically continue to be underrepresented in cardiac research,[5] perhaps because of the misperception that women are 'protected' against CVD via the role of estrogen in premenopausal women.[6] Additionally, enrollment of women in clinical and epidemiological research remains relatively low in studies of populations with chronic disease.[7]

Obesity can unfavourably alter left ventricular (LV) morphology and function with greater LV hypertrophy and cardiac remodelling observed in adolescent,[8] middle-aged women,[9] and older female populations.[10] Early detection of myocardial abnormalities in obese individuals might represent a critical and cost-effective strategy to attenuate the time-related consequences of CVD.[10] Despite this, the understanding of the effects of obesity on CVD risk in women is largely limited to middle-aged and older individuals with scarce attention to young obese women.[11-13] Therefore, it remains unclear whether obesity in young women is associated with cardiac dysfunction. As such, identification of subclinical disease such as myocardial dysfunction in young women with obesity would highlight a group in which targeted interventions might have the greatest effect.

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Compared with control subjects, women with abdominal obesity also demonstrated reduced systolic and diastolic mitral annular plane velocities, increased left atrial pressure surrogates (E/diastolic mitral annular plane velocity), and prolonged timing measures of diastolic function including isovolumic relaxation time and transmitral deceleration time ($P \leq 0.05$). In addition, longitudinal strain and diastolic strain rate were reduced in women with abdominal obesity ($P \leq 0.05$) but circumferential deformation and myocardial mechanics (twist indices and rotation) were preserved. Markers of abdominal obesity retained an independent direct correlation with parameters of cardiac dysfunction, explaining 12%-39% of the overall variability.

Conclusions: A young, otherwise healthy group of women with abdominal obesity displayed subclinical cardiac dysfunction indicated using selected tissue Doppler imaging and speckle tracking echocardiography measures.

Résultats : Les résultats de l'échocardiographie standard de la morphologie et de la fonction cardiaque étaient similaires entre les groupes, à l'exception des dimensions plus grandes de l'oreillette gauche chez les femmes souffrant d'obésité abdominale ($P \leq 0,05$). Comparativement aux sujets témoins, les femmes souffrant d'obésité abdominale démontraient également une réduction des vitesses systoliques et diastoliques du plan de l'anneau mitral, une augmentation des substituts de la pression auriculaire gauche (E/vitesse diastolique du plan de l'anneau mitral) et des mesures prolongées de la durée de la fonction diastolique, y compris le temps de relaxation isovolumique et du temps de décélération du flux transmitral ($P \leq 0,05$). De plus, la déformation longitudinale et le taux de déformation diastolique étaient réduits chez les femmes souffrant d'obésité abdominale ($P \leq 0,05$), mais la déformation circonférentielle et la mécanique du myocarde (indices de torsion et rotation) étaient préservées. Les marqueurs de l'obésité abdominale conservaient une corrélation directe indépendante avec les paramètres de la dysfonction cardiaque, ce qui explique 12 % à 39 % de la variabilité globale.

Conclusions : Un groupe de femmes jeunes, mais en santé, souffrant d'obésité abdominale montraient une dysfonction sous-clinique cardiaque selon les mesures de l'imagerie Doppler tissulaire et de l'échocardiographie *Speckle Tracking* (suivi de pixel).

Subclinical cardiac dysfunction can be detected using noninvasive conventional and tissue Doppler imaging (TDI) echocardiography.[14] However, speckle tracking echocardiography (STE), a deformation imaging technique, was developed to address potential limitations in the sensitivity of existing measures for detecting subtle myocardial dysfunction.[15,16]

The aim of this study was to investigate cardiac morphology and function, myocardial deformation, and mechanical indices, in a cross-sectional profile of young women with and without abdominal obesity using traditional and advanced techniques of echocardiography.

Methods

Participants

Ninety-three university-enrolled participants responded to recruitment advertisements that specifically sought Caucasian women aged 18-30 years. Participants were free of hypertension, diabetes, smoking, endocrine disorders, had not undergone bariatric surgery, and were not pregnant or breastfeeding. Eleven women did not meet the inclusion criteria and 10 eligible participants did not complete testing. Therefore, 72 women completed testing between August 2010 and February 2012. Participants were divided into 2 groups: (1) 39 women with abdominal obesity defined by a WC $\geq$ 80 cm; and (2) 33 women without abdominal obesity (WC $<$ 80 cm). Five women in the abdominal obesity group were previously pregnant to full-term ($\geq$ 1.5 years ago). Participants arrived at the laboratory after a 12-hour fast and were requested to refrain from strenuous physical activity in the 24 hours before testing.

The study was approved by the Australian Catholic University Human Research Ethics Committee (V2009-91), and participants provided written informed consent.

Cardiometabolic risk factors

A range of clinical characteristics were assessed to profile the population including anthropometric, blood pressure, blood biochemistry, and fitness variables (see the *Cardiometabolic Risk Factors* section of the Supplementary Material).

Echocardiography examination

Participants underwent a standard 2-dimensional transthoracic echocardiography examination for the assessment of global and regional ventricular function in accordance with the American Society of Echocardiography.[17] Image acquisition was performed by the same experienced operator using commercially available ultrasound equipment (Vivid *i*, GE Healthcare, Horten, Norway) with a 3.5 MHz phased-array transducer. Participants were examined in the left lateral decubitus position in a dark room and connected to a 3-lead electrocardiogram. A minimum frame rate of 70 Hz was used during acquisition of greyscale cine loops. Digital data were stored for subsequent off-line analyses with specific software (EchoPAC v108, GE Medical Systems, Horton, Norway) by an observer blinded to group assignment. All reported measurements were averaged from 3 consecutive cardiac cycles (see the *Echocardiography Examination* section of the Supplementary Material).

Statistics

Data were analyzed using IBM SPSS Statistics, Version 20 for Windows (Chicago, IL). Log transformation was used when qualitative variables were not normally distributed.[18] Group comparisons were performed using independent *t* tests. Hedge *g* was used to calculate magnitudes of differences ($\geq$ 0.2, small; $\geq$ 0.5, medium; and $\geq$ 0.8, large).[19] A power analysis determined the power achieved for effect size on variables that were statistically significant. Multiple linear regression analysis based on a stepwise algorithm was used to

detect independent predictors of variability in cardiac parameters. Partial correlation was used to assess the degree of association between dependent variables (cardiac parameters) and independent variables (cardiometabolic risk factors) in the final model. An α level of $P < 0.05$ was considered statistically significant. Intra- and interobserver reproducibility were estimated for major cardiac variables in randomly selected participants (see the *Reliability* section of the Supplementary Material).

Results

Cardiometabolic risk factors

No differences were found for height, blood pressure, triglycerides, high-density lipoprotein cholesterol, or resting heart rate in a comparison of women with abdominal obesity (WC range, 80.5-123.0 cm) and control subjects (WC range, 63.6-77.8 cm; Supplemental Table S1). Women with abdominal obesity had greater body mass, body mass index, WC, hip circumference, waist-to-hip ratio, waist-to-height ratio, increased levels of fasting insulin, homeostasis model assessment of insulin resistance, and high sensitivity C-reactive protein than those in the control group. The mean homeostasis model assessment of insulin resistance values remained within the normal range but increased levels of high sensitivity C-reactive protein in the women with abdominal obesity was deemed 'high' risk. Women with abdominal obesity performed 63% less weekly physical activity and had reduced aerobic capacity. Control participants had increased fasting glucose and total cholesterol levels but notably values remained within normal ranges.

Cardiac morphology and function

Women with abdominal obesity displayed greater left atrial (LA) dimensions than control subjects. No differences were found for LV ejection fraction or LV structural parameters (Table 1).

Women with abdominal obesity displayed impaired LV diastolic parameters (decreased transmitral *E*, diastolic mitral annular plane velocity [E_m], and increased E/E_m, isovolumic relaxation time [IVRT], and deceleration time), and reduced systolic tissue velocity than control subjects. Although these values remained within ranges that would be considered "normal" in clinical settings, statistically significant differences were supported by moderate effect sizes. No differences were found between groups for *E/A* ratio, and parameters of late-diastolic function.

Myocardial deformation and mechanics

Women with abdominal obesity had lower longitudinal strain and diastolic strain rate (SR) than control subjects (Table 2). Circumferential strain and SR, apical and basal rotation, and twist/untwist parameters were not different between groups.

Relationship between cardiac parameters and cardiometabolic risk factors

Multivariate analyses showed that anthropometric markers of obesity were the strongest predictors of variability in cardiac parameters (Supplemental Table S2). Physical activity was not an independent predictor of cardiac dysfunction and was consequently eliminated from the model. Overall, cardiometabolic risk factors (predictors) explained approximately 12%-39% of cardiac dysfunction.

Discussion

We investigated measures of cardiac morphology and function, myocardial deformation, and mechanical indices in young women with and without abdominal obesity. We showed that young women with abdominal obesity displayed subtle early myocardial impairment identified using traditional and advanced echocardiography measures compared with control subjects. These data advance the understanding of CVD risk factors in a population that is currently underrepresented in the literature. Specifically, our findings demonstrated that young women with abdominal obesity displayed some markers of: (1) subclinical cardiac abnormalities associated with remodelling; and (2) myocardial dysfunction. We can confirm, for the first time in this population, the presence of subtle early myocardial dysfunction in the longitudinal axis but preserved circumferential deformation and twist mechanics—identified using STE—of young women with abdominal obesity.

Effects of obesity on subclinical cardiac abnormalities in cardiac morphology

Women with abdominal obesity had larger LA dimensions but otherwise cardiac morphology was similar. The left atrium enlarges in response to increases in LV pressure due to impaired LV filling, making it a useful adjunct in the assessment of chronic diastolic dysfunction.[20] Abnormalities in LA diameter have been linked to obesity in a group of young women (29 ± 10 years of age; $n = 48$) with isolated obesity,[21] in a population of slightly older (32 ± 4 years of age) obese young adults,[11] and in obese middle-aged adults,[10,22] with normal ejection fraction. This finding from our study is potentially of even greater concern in a population of women who were notably younger and had milder obesity than in these previously reported studies. Mechanisms behind this link might occur as a consequence of the hemodynamic changes associated with obesity.[23]

Effects of obesity on subclinical cardiac abnormalities in cardiac function

Obesity impairs cardiac loading.[22] In our study, conventional load-dependent parameters of LV diastolic function, indicators of filling and relaxation, and measures of LV stiffness were observed in women with abdominal obesity. Previous literature has shown underlying abnormalities in relaxation and/or myocardial compliance in obese individuals without hypertension or cardiac hypertrophy.[24] However, this is the first study to identify diastolic impairment in such a young group of women.

In the present study, women with abdominal obesity also demonstrated attenuated TDI-derived velocities. The TDI echocardiography parameters of systolic mitral annular plane velocity, E_m, and E/E_m have established independent prognostic value in a wide variety of cardiac disorders and are powerful predictors of cardiac mortality.[25] We reported

Table 1. Cardiac morphology and function parameters in participants with and without abdominal obesity

	Control; WC < 80 cm (n = 33)	Abdominal obesity; WC ≥ 80 cm (n = 39)	*P*	Hedge *g* effect size	Power (1-β)	Mean difference (95% CI)
Age, Years	20.0 ± 0.7	22.4 ± 3.5	0.002*	0.87	0.95	2.4 (−3.39 to −0.80)
WC, cm	72.5 ± 4.8	92.5 ± 10.6	< 0.001*	2.34	1.00	20.0 (16.2-23.8)
Cardiac morphology						
LA diameter, mm	30.2 ± 4.3	32.7 ± 4.6	0.02*	0.55	0.60	2.5 (0.04-0.5)
LV mass, g	148 ± 31	149 ± 40	0.98	0.03	-	1.0 (−17.8 to 18.1)
LV mass indexed, g/m$^{2.7}$	37.5 ± 7.4	40.5 ± 7.0	0.11	0.41	-	3.0 (−0.7 to 6.6)
LVED diameter, mm	44.4 ± 4.5	44.0 ± 3.8	0.71	0.09	-	0.4 (−0.2 to 0.2)
LVES diameter, mm	28.8 ± 3.5	29.4 ± 4.4	0.55	0.15	-	0.6 (−0.1 to 0.2)
LV posterior wall thickness, mm	9.7 ± 1.4	10.3 ± 1.7	0.12	0.38	-	0.6 (−0.02 to 0.1)
IVS thickness, mm	10.0 ± 1.4	10.5 ± 1.7	0.21	0.31	-	0.5 (−0.03 to 0.1)
Cardiac function						
LV shortening fraction, %	34.9 ± 5.7	32.7 ± 6.9	0.17	0.34	-	−2.2 (−5.3 to 1.0)
LV ejection fraction, %	64.0 ± 8.1	61.0 ± 10.2	0.09	0.32	-	−3.0 (−0.6 to 6.7)
Stroke volume, mL	58.8 ± 16.0	53.7 ± 12.7	0.16	0.35	-	−5.1 (−12.3 to 2.0)
E velocity, cm/s	96.7 ± 13.0	87.0 ± 14.7	0.01*	0.70	0.87	−9.7 (−0.2 to −0.03)
A velocity, cm/s	44.7 ± 12.0	42.4 ± 11.0	0.40	0.20	-	−2.5 (−0.08 to 0.03)
E/*A* ratio	2.3 ± 0.7	2.2 ± 0.6	0.44	0.15	-	−0.1 (−0.4 to 0.2)
Deceleration time, ms	174.4 ± 34.9	209.0 ± 29.8	< 0.001*	1.06	1.00	34.6 (19.2-50.1)
IVRT, ms	78.4 ± 9.9	85.8 ± 10.7	0.01*	0.71	0.87	7.4 (2.5-12.4)
S_m velocity, cm/s	10.4 ± 1.3	9.0 ± 1.4	< 0.001*	0.94	0.99	−1.4 (−0.02 to −0.01)
E_m velocity, cm/s	17.2 ± 2.3	14.6 ± 2.7	< 0.001*	1.10	1.00	−2.6 (−0.04 to −0.01)
A_m velocity, cm/s	6.9 ± 1.2	6.9 ± 1.1	0.99	0.00	-	0.0 (−0.01 to 0.01)
E/E_m lateral wall	4.9 ± 0.7	5.4 ± 1.4	0.04*	0.47	0.60	0.5 (0.02 to 1.1)

Data are presented as mean ± SD, except where otherwise noted. S_m, E_m, and A_m are means of 4 sites at the mitral annulus from the apical 4-chamber and 2-chamber views.

A_m, late-diastolic mitral annulus tissue velocity; CI, confidence interval; E_m, early-diastolic mitral annulus tissue velocity; IVRT, isovolumic relaxation time; IVS, interventricular septum; LA, left atrium; LV, left ventricle; LVED, left ventricular end-diastolic; LVES, left ventricle end-systolic; S_m, systolic mitral annulus tissue velocity; WC, waist circumference.

*$P \leq 0.05$.

decreased S_m indicating systolic mitral annular plane velocity indicating systolic dysfunction in women with abdominal obesity. Additionally, low early-diastolic (E_m) values might be indicative of abnormal LV relaxation, and have previously been reported to correlate with IVRT. In our study, IVRT was elongated and E_m reduced, albeit only minimally, which might link to early onset of cardiac dysfunction. Despite significant differences between groups, women with abdominal obesity displayed normal "within range" LV filling pressure, indicated by the E/E_m ratio of ≤ 8.[26] Thus, early but not late diastolic dysfunction was associated with obesity among the young women in the present study.

The negative effect of obesity on early diastolic function has been reported but, again, these results were found in older, less healthy adults. A group of 29 middle-aged adults (49 ± 8 years) with isolated obesity, had reduced E_m velocity, and significantly increased IVRT, deceleration time, and E/E_m ratio than 20 aged-matched nonobese control subjects.[10] Similar results have also been reported in adolescents. Obese participants (n = 37; 14.6 ± 1.5 years of age) who were free of diabetes and hypertension had significantly reduced TDI systolic and diastolic velocities and increased E/E_m compared with their lean counterparts (n = 24; 14.0 ± 1.5 years of age).[8] It might be possible that the observed dysfunction is part of a disease progression from subtle myocardial dysfunction and atrial remodelling to eventually involve structural remodelling of the ventricles. Longitudinal studies are required to investigate this question further. A focus on weight reduction, including the prevention and early detection of cardiometabolic risk factors in young obese adults, might be advantageous for inducing positive reversible changes in cardiac morphology and function.

Effects of obesity on myocardial dysfunction via deformation

Noninvasive ultrasound techniques such as conventional and TDI echocardiography have a major role in the diagnosis and management of CVD. An inability to accurately differentiate actively contracting myocardium from passive myocardial motion is one of the principal limitations of conventional and TDI echocardiography.[27] The innovation of STE enables unique acoustic speckles within the myocardium to be tracked thereby permitting analysis of the relative regions of the myocardium, thus separating deformation from passive motion.[28] In some settings, STE has enabled early diagnosis of systolic and diastolic dysfunction, even when conventional and TDI echocardiography parameters of LV function remain within the normal range.[12,26] In our study, we confirmed and extended previous data by demonstrating that young women with abdominal obesity displayed impaired longitudinal myocardial dysfunction, but preserved circumferential function, compared with control subjects. Although the exact mechanisms behind this remain unclear, the finding is consistent with previous studies in older, disease-free populations.[24] The reduced longitudinal strain and SR in our women with abdominal obesity highlight early diastolic and systolic dysfunction that could be explained by depressed relaxation and contractile properties of myocardial fibres. It is possible that increases in ventricular and atrial filling pressure are a cause and a consequence of reduced myocardial deformation.

Reduced LV strain observed in our women with abdominal obesity has been reported previously. A study of obese middle-aged women (n = 663; 47.8 ± 13.6 years of age;

Table 2. Myocardial deformation and mechanics measured in participants with and without abdominal obesity

	Control; WC < 80 cm (n = 33)	Abdominal obesity; WC ≥ 80 cm (n = 39)	*P*	Hedge *g* effect size	Power (1-β)	Mean difference (95% CI)
Myocardial deformation						
L strain, %	−17.6 ± 3.0	−16.1 ± 2.1	0.05*	0.55	0.60	−1.5 (−0.01 to 3.0)
L systolic SR, strain/s	−0.9 ± 0.2	−0.9 ± 0.1	0.18	0.00	-	0.0 (−0.03 to 0.1)
L diastolic SR, strain/s	1.4 ± 0.3	1.1 ± 0.3	0.01*	0.87	0.94	−0.3 (−0.5 to −0.1)
C strain (%)	−20.8 ± 2.4	−19.8 ± 2.9	0.15	0.37	-	−1.0 (−0.4 to 2.3)
C systolic SR, strain/s	−1.3 ± 0.2	−1.3 ± 0.2	0.19	0.00	-	0.0 (−0.03 to 0.1)
C diastolic SR, strain/s	2.0 ± 0.3	1.8 ± 0.3	0.08	0.66	-	0.2 (−0.3 to 0.02)
Myocardial mechanics						
Apical rotation, degree	4.6 ± 1.8	4.7 ± 1.9	0.78	0.05	-	0.1 (−0.8 to 1.1)
Basal rotation, degree	−5.6 ± 2.3	−5.8 ± 2.3	0.85	0.09	-	0.2 (−1.5 to 1.3)
Twist, degree	6.2 ± 2.7	7.2 ± 3.1	0.26	0.34	-	1.0 (−0.8 to 2.8)
Twist rate, degree/s	68.8 ± 22.1	70.3 ± 18.8	0.80	0.07	-	1.5 (−10.4 to 13.4)
Untwist rate, degree/s†	−76.8 ± 39.1	−62.2 ± 18.8	0.11	0.48	-	−14.6 (−2.8 to 32.0)

Data are presented as mean ± SD. Four data sets were excluded from speckle tracking echocardiography analysis in the abdominal obesity group because of poor image quality.

C, circumferential (average of apical and basal); CI, confidence interval; L, longitudinal; SR, strain rate; WC, waist circumference.

*$P \leq 0.05$.

† Log transformed.

WC, 88.5 ± 11.7 cm) showed a strong relationship between increased WC and reduction in LV strain.[29] Similarly, research has shown reduced strain indices and reduced *E* velocity in 26 middle-aged women (49 ± 8 years of age) with isolated obesity (WC, 105 ± 7.0 cm), compared with 18 age-matched nonobese control subjects.[10] Comparable to the present study, depressed longitudinal LV strain but preserved circumferential strain was observed in a group of 37 obese adolescent participants (aged 14.6 ± 1.5) compared with 24 lean control subjects (aged 14.0 ± 1.5 years).[8] Identification of these preclinical myocardial abnormalities in young obese women provides a marker that could be followed through treatment interventions; we postulate that weight reduction and increased physical activity might attenuate further decline in myocardial function. Weight reduction has been associated with improvements in measures of LV function in some studies,[30] but has proven disappointing in others.[31] However, the efficacy of a lifestyle intervention in preventing overt cardiac dysfunction in young overweight women has not been tested.

Effects of obesity on myocardial dysfunction via mechanics

Myocardial mechanics such as twist and twist rate describe the torsional rotation of the heart produced by the helical structure in which the myocardial fibres are arranged.[14] Twist and the rate of untwist have been promoted as sensitive determinants of cardiac performance, particularly during diastolic relaxation and filling.[32] However, their acceptance in clinical practice has been limited by reproducibility issues.[32]

Nevertheless, the role of LV twist as a major contributor to LV filling has generated much interest. Reductions in diastolic and systolic LV twist and basal rotation showed a stronger correlation with WC ($r = -0.24$; $P < 0.05$) in obese middle-aged (aged 44 ± 10 years) participants compared with non-obese control subjects.[14] Similarly, obese adolescents had more pronounced LV twist and greater apical rotation than lean control subjects, confirming the feasibility of detection in younger populations.[8] It was postulated that the greater LV twist in the obese individuals could be viewed as a compensatory phenomenon for their depressed longitudinal function, critical for LV filling and ejection.[8] Rotational indices of twist/untwist rates were not supported by the results from the present study. Variability might have limited accurate conclusions from these results. Discrepancies in twist mechanics between obese and control subjects could also be related to difficulties in imaging capacities, particularly for apical rotation.[32]

In our study, changes in cardiac and myocardial parameters were accompanied by some biological markers in women with abdominal obesity compared with control subjects. However, the correlations between significant markers of TDI and STE with biomarkers of CVD risk were only moderate. We propose that obesity is directly related to a sequence of yet to be clarified early markers of cardiac risk.

Study limitations

The study design means that we cannot address changes in myocardial function over time. However, this novel demonstration of myocardial dysfunction in a young population provides necessary motivation for longitudinal interventional studies. Although physical activity was not found to be an independent predictor of variability in cardiac dysfunction, the between-group differences in habitual physical activity cannot be discounted as a confounder in myocardial function. Objective measures of physical activity could clarify this relationship in future studies. We did not assess right ventricular function or myocardial reserve and hemodynamic responses during exercise. Central fat distribution could have been more ideally measured using more precise estimations. Despite this, WC as a measure of abdominal obesity is widely recognized as a reliable tool.[33]

Conclusion

Young women with abdominal obesity displayed larger LA dimensions and reduced measures of diastolic and systolic myocardial function, compared with nonobese control subjects. Low-grade systemic inflammation was also present in young women with abdominal obesity. These findings might

provide important insights into the links between obesity and the increased incidence of cardiometabolic disease.

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RESEARCH ARTICLE

Effects of a Multi-Disciplinary Lifestyle Intervention on Cardiometabolic Risk Factors in Young Women with Abdominal Obesity: A Randomised Controlled Trial

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Abstract

Background

Young women are under-represented in cardiovascular disease research, with obesity and cardiometabolic risk factor interventions generally targeting older adults. Furthermore, appropriate study designs for young women remain uncertain. This study aimed to assess the impact of a 12 week multi-disciplinary lifestyle intervention on cardiometabolic risk factors in premenopausal women with abdominal obesity.

Methods

Women aged 18–30 y with abdominal obesity [waist circumference (WC) $\geq$ 80 cm] were randomised to a 12 week lifestyle intervention (n = 26) of physical activity, nutrition education and cognitive behavioural therapy, or a wait-list control group (n = 17). Both groups completed anthropometric, biochemical, nutrition and fitness testing, at pre (0 weeks) and post (12 weeks), with intervention participants completed follow-up testing at 24 weeks.

Results

Results from a linear mixed model showed no between-group differences, other than increased physical activity in the intervention group, at post. In the intervention group alone, positive within-group changes were observed in WC, waist-hip-ratio (WHR), waist-height-ratio (WHtR), resting heart rate, blood pressure, predicted VO_{2max}, and total energy intake. Most changes were maintained at 24 weeks post-intervention. Similar within-group improvements were observed in control participants in WC, WHR, WHtR, and systolic blood pressure but no changes were detected in physical activity and nutrition.

Conclusions

Cardiometabolic risk factors were decreased as a result of a lifestyle intervention in young women with abdominal obesity. It is difficult to describe observations in the control group without greater understanding of the behaviour of wait-list participants.

Trial Registration

Australian New Zealand Clinical Trials Registry ACTRN12612001017819

Introduction

Cardiovascular disease (CVD) represents a major health threat to women worldwide [1], consequently placing substantial burden on public health systems. Most risk factors for CVD, including overweight/obesity and physical inactivity, can be modified through lifestyle interventions [2,3]. The rising prevalence of overweight and obesity is a worldwide concern among young women from developed and developing nations [4]. Currently, 51% of non-hispanic white American women aged 20–39 years are either overweight or obese [5], while prevalence among women in the United Kingdom [6], and Australia [7] aged 25–34 years are 47% and 42%, respectively. An average weight gain of 6 to 12 kg between the ages of 20 to 30 years was noted in a large longitudinal study of women's health [8], and this weight gain was more than for any other age group [8,9]. Concurrently, sedentary behaviour is increasing in young women [10], with 85% of women aged 18–35 years reporting inactive lifestyles and decreased physical activity [9]. Among women, weight gain is not only a risk factor for CVD but increases the risk of the metabolic syndrome [11], type 2 diabetes mellitus, depression, polycystic ovarian syndrome, infertility and adverse pregnancy outcomes [12].

Despite global strategies for preventive health, there is poor understanding of early risk factors (cardiometabolic risk factors) in young women, and lifestyle interventions can improve health outcomes. Moreover, research assessing the effectiveness of weight management interventions specifically targeting young women is relatively recent [13]. Effective age-appropriate interventions for improving cardiometabolic risk are required for young adults born between 1977 to 1994 ("Generation Y") who share an urgency for feedback and success [14,15]. The limited research that has been conducted in young overweight/obese women suggests they are difficult to recruit for weight management trials, with high attrition and limited success in losing weight compared with older populations [16]. Furthermore, limited evidence exists to inform the implementation of lifestyle intervention programs targeting young women [17].

Poorer retention but greater success has been reported when results of an online team-based weight loss lifestyle intervention were compared in younger and older adults [17]. However, not all studies of weight loss in young adults following lifestyle interventions report statistical significance [18]. To date, the effectiveness and long-term success of multi-disciplinary lifestyle interventions delivered face-to-face that directly target weight loss in young women remain uncertain [19]. Nonetheless exercise interventions appear to require strong familiarisation of the required physical activity along with some formal contact with the participant. Also, exercise alone is less likely to be effective in weight loss than when combined with some nutrition and psychological support [20].

Therefore, the primary aim of this study was to assess the effectiveness of a lifestyle intervention for reducing CVD risk in young women with abdominal obesity, using a randomised

controlled trial (RCT) design. Specifically, the RCT involved a 12-week multi-disciplinary program (physical activity, nutrition education, cognitive behavioural therapy) with Caucasian women aged 18 to 30 years, who shared the cardiometabolic risk factor of abdominal obesity [elevated waist circumference (WC) $\geq$ 80 cm]. A secondary aim was to examine the effectiveness of the intervention through an improved understanding of the sustainability of any changes. It was hypothesised that the lifestyle intervention would be effective (and sustainable) in reducing cardiometabolic risk in young women with abdominal obesity.

Materials and Methods

The study protocol was approved by the Australian Catholic University Human Research Ethics Committee (V2009-91) on December 18th 2009 (S1 and S2 Texts). The authors confirm that all ongoing and related trials for this intervention are registered with the Australian New Zealand Clinical Trials Registry (Identifier: ACTRN12612001017819) and the CONSORT reporting guidelines for clinical trials were followed (S1 Table). Data were collected between August 2010 and February 2012. Written informed consent was obtained from all participants.

Participants

Sixty-two female Caucasian tertiary students at risk of CVD volunteered for this study. Advertisements for recruitment specifically sought young women with abdominal obesity (WC $\geq$ 80 cm), who were also leading a sedentary lifestyle. Included were women aged 18 to 30 years; with a waist circumference $\geq$ 80 cm, and who were physically inactive (< 210 minutes per week of organised physical activity in the past six months). Exclusion criteria were being pregnant or breastfeeding; a history of bariatric surgery; and/or having a diagnosis of liver or kidney disease; heart arrhythmia; insulin dependent diabetes mellitus; polycystic ovarian syndrome; thyroid abnormalities. All participants were non-smokers.

A power analyses estimated that 18 participants per group would provide the appropriate sample size to detect a large between-subject difference of 1.0 standard deviation (β = 80%, alpha $P < 0.05$) in waist circumference from pre-intervention to post-intervention. To allow for 20% attrition, there was an attempt to recruit an initial sample size of 44 participants (22 per group). Fig 1 shows the participation of individuals in this study. From 62 women who responded to the recruitment strategy, 11 prospective participants were excluded, and a further 12 did not respond to preliminary contact. Therefore, 39 willing participants underwent pre-intervention/pre-control testing, after which group (block) randomisation occurred via a central administrator who allocated participants to either the intervention group or wait-list (delayed-start) control group. A wait-list control design was chosen because the investigators desired an ethically-sound model which provided all participants with access to the lifestyle intervention. Also, a wait-list control group was considered more appropriate than a passive control group given that health risks were comparable in both groups. After allocation to the wait-list control group for 12 weeks, only four participants continued into the lifestyle intervention phase. Participants were not blinded to their group, but where possible assessors were blinded to group allocation.

Experimental design

For each testing period (0, 12, 24 weeks), participants attended the laboratory on two occasions. They were requested to refrain from strenuous physical activity in the 24 hours prior to all laboratory sessions. The first visit required the participant to arrive in a fasted state and clinical testing lasted 75 minutes. The second visit of 60 minutes required participants to abstain from caffeine and alcohol for 12 hours.

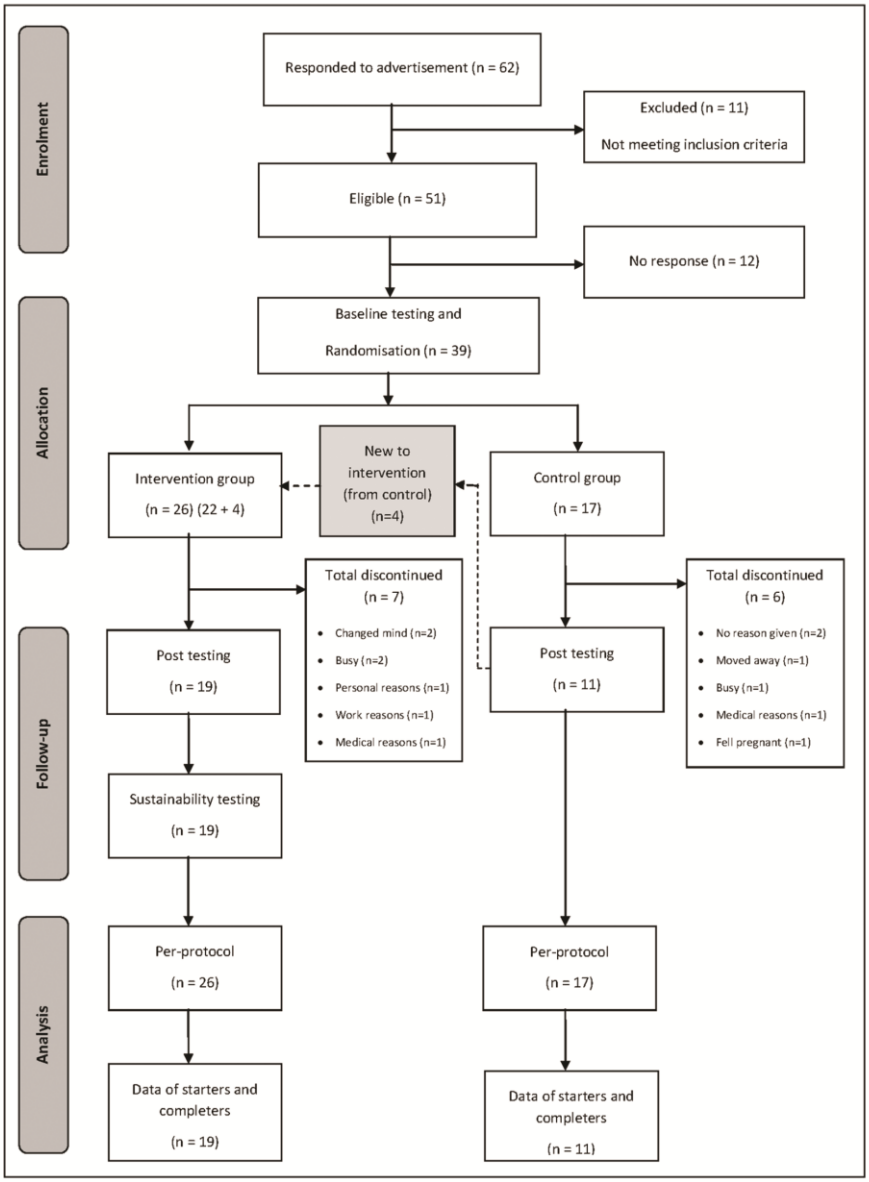

Fig 1. CONSORT participant flow-chart of intervention and control participants.

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For the intervention group, testing of cardiometabolic risk factors was performed at pre-intervention (0 weeks), post-intervention (12 weeks) and following a short-term sustainability phase (24 weeks). The control group underwent testing at pre-control and post-control (12 weeks) time periods only. For all testing, measurements were taken at the same time of day (±2 hours) and by the same researcher. For participants in the control group, monthly contact was made to remind them of the control criteria. For the sustainability phase between post-intervention (12 weeks) testing and the following 12 weeks, a sustainability strategy was delivered electronically to the intervention group. This involved a fortnightly newsletter on healthy living tips from evidence-based resources.

Neither the investigators nor the participants were blinded to group allocation as this was considered impractical for the long-term investigation and limited members of the research team. However, to minimise contamination, participants in the intervention group were asked to refrain from disclosing their intervention experience to researchers assigned to data collection and/or analysis and to wait-list control participants. To further minimise bias, assessor blinding occurred within dietary measures and biochemical analyses. For the primary outcome variable of WC, measures were completed in duplicate with reported measures of reliability: coefficient of variation (CV), intraclass correlation coefficient (ICC) and measurement error (ME).

Testing measures

Survey data. A self-administered lifestyle survey was completed to provide data on (i) health status and medical conditions, (ii) nutrition (including alcohol consumption), and (iii) current physical activity habits. The lifestyle survey (S3 Text) was developed specifically for the study and validated using the process of face validation [21].

Anthropometric assessment. Body composition was assessed via waist circumference (WC), hip circumference, body mass index (BMI), and body mass. WC was measured to the nearest 0.1 cm in the horizontal plane at the level of the midpoint between the iliac crest and lower costal margin [11]. For WC, CV = 1.26%, ICC (3, 1) = 0.986 and ME = 1.34%, which equates to an error range of ± 2.6 cm. Body mass was measured to the nearest 0.1 kg using digital scales (Tanita, Tokyo, Japan), and height was estimated to the nearest 0.1 cm using a wall-mounted stadiometer (Seca, Germany). BMI was calculated, with overweight/obesity defined as BMI $\geq$ 25 $kg{\cdot}m^{-2}$ [1]. Waist-to-hip ratio (WHR), and waist-to-height ratio (WHtR) were calculated by dividing participants WC (cm) by their hip circumference (cm) and height (cm), respectively (Browning 2010; WHO, 2000).

Metabolic syndrome markers and additional biochemical parameters: Metabolic syndrome was defined according to the most recent and unified criteria [11]. Markers of insulin resistance, including fasting insulin and homeostasis model assessment of insulin resistance (HOMA-IR), and the pro-inflammatory marker high sensitivity C-reactive protein (hs-CRP), were also measured in this study.

Following an overnight fast, intravenous blood was collected Blood lipid profiling of serum concentrations of triglycerides, total cholesterol and high-density lipoprotein (HDL) cholesterol were measured using the Reflotron Plus desktop analyser (Roche, Switzerland). Fasting plasma glucose, insulin and hs-CRP concentrations were analysed by clinical pathology at a leading hospital. Insulin resistance was estimated by HOMA-IR using the equation [22]. For hs-CRP, a value > 3.0 $mg{\cdot}l^{-1}$ was deemed high risk [23].

After 10 minutes of rest in a quiet, temperature controlled room SBP and DBP were obtained in duplicate from the left arm with an automated digital sphygmomanometer (Carescape V100, Dinamap, GE technology, USA) with the participant in the supine position.

Health and fitness evaluations. The YMCA graded submaximal cycle ergometer test [24] was used to estimate aerobic power (predicted VO_{2max}), where heart rate was extrapolated against work rate (W) using regression analysis. Physical activity behaviour (S3 Text) was obtained via a 7-day recall [25].

Within the acknowledged limitations of dietary recall [26], 100% of participants completed a three-day food and beverage recall on two consecutive weekdays and on either a Saturday or Sunday of their usual diet. Instructions were provided on how to complete the diary and diagrams of portion sizes were also shown and discussed (S3 Text). Participants were encouraged not to alter their habitual diet during the three day recall period. Macro- and micro-nutrient intakes were analysed by a research dietician, blinded to grouping, using the FoodWorks7 Professional program (Xyris software, Highgate Hill, Queensland, Australia). An estimation of average daily energy intake was also calculated.

Intervention

The 12-wk lifestyle intervention was comprised of three main components: (1) physical activity (2) nutrition education, and (3) cognitive behavioural therapy (S2 Table). In contrast, participants in the wait-list control group (n = 17) were instructed to continue existing lifestyle choices, and after 12 weeks were invited to complete the lifestyle intervention.

Physical activity. Participants undertaking the intervention completed two supervised exercise sessions (progressive circuit training) and one unsupervised, but were prescribed one home-based session (brisk walk or jog) per week. All sessions were devised and administered by a qualified Exercise Scientist who has experience in exercise prescription for elite and healthy populations. The supervised sessions consisted of a general warm-up, a combination of aerobic activities, dynamic strength and/or resistance training, abdominal conditioning, and stretching. Session duration lasted approximately 60 min, with the intensity of the exercise increasing from 6.0 to 8.5 on the OMNI Picture System (ranging from 0 = extremely easy to 10 = extremely hard)[27], by the end of the 12-week period. Intensity was verified during most exercise sessions with a Polar heart rate monitor (Polar Electro, Finland). The home-based, unsupervised training session involved a brisk walk or jog at an RPE of 5–7 on the OMNI Picture System [27]. Participants were encouraged to incorporate intermittent high-intensity intervals into their session. Duration of the session progressed from 30 minutes at intervention commencement to 45 minutes at program completion. As a measure of compliance, participants maintained a detailed training diary including any extra activities they completed during the intervention. The Bruce protocol [28] was completed every three weeks to ensure accuracy of progressive overload of aerobic fitness during the program. Upper (chest-press) and lower (leg-press) body strength was tested via a 5-repetition maximum test to guide the strength and resistance component of the exercise intervention [29]. Sessions occurred in both the gym on campus and at a local park.

Nutrition education. Participants in the intervention group received weekly nutrition education sessions guided by a qualified dietician about healthy eating choices from the existing Australian Dietary Guidelines [30]. This information provided education regarding non-dieting weight management and healthy eating principles. Following baseline analysis of a three-day food and beverage recall, nutrition education topics (S2 Table) targeted the perceived needs of the female participants. As such, nutrition was a workshop (educational focus) and did not prescribe a specific caloric intake nor ask participants to monitor their nutritional intake during the intervention.

Cognitive behavioural therapy. Within the framework of self-determination theory [31], weekly 60-minute group sessions with a qualified counsellor provided participants with

psychosocial support and developed skills to overcome personal barriers to lifestyle change (S2 Table). The program aimed, ultimately, to empower individuals to develop healthier eating and physical activity patterns [32].

Statistical analyses

Data were analysed using IBM SPSS Statistics, Version 20 for Windows (SPSS Inc, Chicago IL). Data were tested for normal distribution [33], with log transformation performed on data not normally distributed. All data are presented as means ± standard deviation. Statistical significance was set at $P \leq 0.05$. A linear mixed-model analysis was used to calculate the differences between groups and across time for the intervention and control groups. Hedge's *g* effect size was used to assess the magnitude of effect. An effect size ≥ 0.2 was considered small, ≥ 0.5 medium, and ≥ 0.8 large [34]. Mean differences and 95% confidence intervals (CI) are reported. An additional linear mixed-model calculation was determined for only the participants in each group who started and completed the study. No differences were found using both models. An independent t-test was used to compare differences between the two groups in changes from baseline to 12 weeks.

Results

A total of 39 participants were included in the linear mixed-model analysis. For reasons described (Fig 1), 27% of intervention participants and 35% of control participants failed to maintain study involvement beyond pre-intervention/pre-control measures. However, for those completing the intervention, compliance rates were high with 80% attendance at physical activity sessions and 74% at CBT sessions.

Between group differences

Table 1 shows the results of comparisons between the intervention and control groups before and following the intervention, using a linear mixed model analysis. With only one difference observed between groups at pre-intervention, this supports the homogeneity of the groups. At baseline none of the participants were classified as having the metabolic syndrome [11] however, a baseline difference was found in a higher resting heart rate, in the intervention group, with a moderate effect size ($g = 0.79$). With the exception of WC and weekly physical activity most cardiometabolic risk factors were within normal limits for the population at baseline testing (see footnotes Table 1). At post-intervention, only physical activity was higher in the intervention group than the control group, with a large effect size ($g = 2.14$). Similarly, both the absolute and percentage change in physical activity from pre to post testing were greater for the intervention group, as were the absolute and percentage changes in predicted VO_{2max} when compared to controls.

Intervention group

For the intervention group, there were positive significant ($P \leq 0.05$) changes pre-to post-intervention for WC (-5.8 cm, -6.4%), WHR (-0.02, -2.5%), WHtR (-0.03, -5.5%), SBP (-4 mmHg, -3.4%), DBP (-4.0 mmHg, -5.8%), resting heart rate (-8.0 bpm, -11%), predicted VO_{2max} (+4.7 $ml \cdot kg^{-1} \cdot min^{-1}$, +15%), physical activity (+183 $min \cdot week^{-1}$, +97%) and total energy intake (-1312 kj, -22%) (Table 2). Absolute protein intake (g) decreased but this difference disappeared when the decreased total energy intake was accounted for.

Many of the improvements observed at post-intervention were maintained at sustainability (24 weeks) testing including, WC, WHR, WHtR, DBP and resting heart rate (Table 2). The

Table 1. Between-group comparisons of cardiometabolic risk factors for the intervention and control group at pre (0 weeks) and post (12 weeks).

	Pre-control/pre-intervention (0 weeks)					Post-control/post-intervention (12 weeks)				
	Control (n = 17)	Intervention (n = 26)	*P* value	Effect size (Hedge's *g*)	Mean difference (95%CI)	Control (n = 11)	Intervention (n = 19)	*P* value	Effect size (Hedge's *g*)	Mean difference (95%CI)
Body mass (kg)	86.1 ± 17.8	89.8 ± 21.1	0.564	0.18	3.7 (-9.2 to 16.6)	82.5 ± 19.5	86.9 ± 20.5	0.609	0.21	4.4 (-11.2 to 20.1)
Body mass index ($kg \cdot m^{-2}$)	31.4 ± 6.6	32.2 ± 5.9	0.674	0.13	0.8 (-3.1 to 4.8)	30.0 ± 6.6	31.3 ± 0.9	0.724	0.31	1.3 (-3.5 to 6.0)
Waist circumference (cm)	92.8 ± 10.8	93.1 ± 11.7	0.930	0.03	0.3 (-7.1 to 7.7)	87.2 ± 10.5§	87.3 ± 9.8	0.910	0.01	0.1 (-7.7 to 8.0)
Hip circumference (cm)	113.8 ± 11.5	116.3 ± 13.3	0.537	0.19	2.5 (-5.7 to 10.7)	111.1 ± 11.9	114.2 ± 13.50	0.696	0.23	3.1 (-6.9 to 13.2)
Waist-hip-ratio	0.81 ± 0.03	0.79 ± 0.05	0.242	0.46	0.02 (-0.04 to 0.01)	0.78 ± 0.03§	0.77 ± 0.04	0.581	0.26	-0.01 (-0.05 to 0.01)
Waist-height-ratio	0.56 ± 0.06	0.56 ± 0.06	0.989	0.00	0.0 (-0.04 to 0.04)	0.53 ± 0.06§	0.53 ± 0.05	0.927	0.00	0.0 (-0.04 to 0.04)
Systolic BP (mmHg)	119 ± 8	120 ± 11	0.669	0.10	1.0 (-5.0 to 7.8)	111 ± 12§	116 ± 9	0.312	0.48	5.0 (-2.4 to 13.1)
Diastolic BP (mmHg)	64 ± 8	68 ± 6	0.115	0.10	4.0 (-0.8 to 8.1)	59 ± 5	64 ± 9	0.108	0.62	5.0 (-1.5 to 10.3)
HDL-cholesterol (mM; $mg \cdot dL^{-1}$)	1.7 ± 0.6	1.7 ± 0.5	0.887	0.00	0.0 (-0.4 to 0.3)	2.0 ± 0.5	1.9 ± 0.5	0.706	0.19	-0.1 (-0.4 to 0.3)
	65.6 ± 23.1	65.6 ± 19.3			0.0 (-15.4 to 11.6)	77.2 ± 19.3	73.3 ± 19.3			-3.8 (-15.4 to 11.6)
Triglycerides (mM $mg \cdot dL^{-1}$)#	1.2 ± 0.4	1.3 ± 0.5	0.838	0.21	0.1 (-0.2 to 0.4)	1.5 ± 0.6§	1.4 ± 0.7	0.255	0.15	-0.1 (-0.7 to 0.3)
	106.2 ± 35.4	115.0 ± 44.2			8.8 (-17.7 to 35.4)	132.7 ± 53.1	123.9 ± 61.9			-8.8 (-61.9 to 26.5)
Fasting glucose (mM; $mg \cdot dL^{-1}$)#	4.5 ± 0.6	4.6 ± 0.4	0.353	0.20	0.1 (-0.2 to 0.5)	4.4 ± 0.6	4.6 ± 0.4	0.325	0.40	0.2 (-0.2 to 0.5)
	81.1 ± 10.8	82.9 ± 7.2			1.8 (-3.6 to 9.0)	79.3 ± 10.8	82.9 ± 7.2			3.6 (-3.6 to 9.0)
Total cholesterol (mM $mg \cdot dL^{-1}$)	4.3 ± 0.5	4.4 ± 0.6	0.645	0.17	0.1 (-0.3 to 0.5)	4.3 ± 0.4	4.3 ± 0.8	0.746	0.00	0.0 (-0.5 to 0.6)
	166.0 ± 19.3	169.9 ± 23.1			3.8 (-11.6 to 19.3)	166.0 ± 15.4	166.0 ± 30.9			0.0 (-19,3 to 23.2)
Fasting insulin ($mU \cdot l^{-1}$)#	8.1 ± 4.4	9.4 ± 4.7	0.720	0.28	1.3 (-1.9 to 4.4)	7.4 ± 2.7	8.1 ± 2.6	0.203	0.26	0.7 (-1.3 to 2.8)
HOMA-IR	1.6 ± 1.0	1.9 ± 1.0	0.331	0.29	0.3 (-0.4 to 0.9)	1.4 ± 0.5	1.6 ± 0.5	0.614	0.39	0.2 (-0.2 to 0.6)
hsCRP ($mg \cdot l^{-1}$) #	2.9 ± 2.6	3.5 ± 3.0	0.495	0.21	0.6 (-1.4 to 2.4)	3.9 ± 3.7	4.6 ± 4.9	0.579	0.15	0.6 (-2.9 to 4.2)
Resting heart rate (bpm)	67 ± 10	76 ± 12	0.019*	0.79	9.0 (0.9 to 15.8)	67 ± 9	68 ± 8	0.929	0.12	1.0 (-6.0 to 6.9)
Predicted $\dot{V}O2max$ ($l \cdot min^{-1}$)	2.7 ± 0.2	2.4 ± 0.5	0.515	0.74	-0.3 (-0.7 to 0.1)	2.5 ± 0.6	2.8 ± 0.6 £	0.347	0.49	0.3 (-0.2 to 0.7)
Predicted $\dot{V}O2max$ ($ml \cdot kg^{-1} \cdot min^{-1}$)	32.0 ± 10.3	27.9 ± 7.0	0.133	0.47	-4.1 (-9.8 to 1.5)	31.7 ± 10.9	32.6 ± 6.8 £	0.245	0.10	0.9 (-5.7 to 7.5)

(*Continued*)

Table 1. (*Continued*)

	Pre-control/pre-intervention (0 weeks)					Post-control/post-intervention (12 weeks)				
	Control (n = 17)	Intervention (n = 26)	*P* value	Effect size (Hedge's *g*)	Mean difference (95%CI)	Control (n = 11)	Intervention (n = 19)	*P* value	Effect size (Hedge's *g*)	Mean difference (95%CI)
Physical activity (min·week^{-1})#	118 ± 89	97 ± 62	0.870	0.27	21 (-73.4 to 30.9)	121 ± 81	280 ± 67 ¥	< 0.001*	2.14	159 (103.0 to 215.5)
Energy (kj; kcal)	6657 ± 3310	6535 ± 2183	0.945	0.04	122 (-2501 to 2255)	5065 ± 1346	5223 ± 1725	0.743	0.10	158 (-1266 to 1581)
	1591 ± 791	1518 ± 522			29 (-598 to 539)	1210 ± 322	1248 ± 412			38 (-302 to 378)
CHO (g)	194 ± 87	166 ± 74	0.386	0.34	28 (-88.7 to 33.7)	205 ± 101	178 ± 96	0.443	0.27	-27 (-112.1 to 59.0)
Protein (g)#	135 ± 93	173 ± 86	0.097	0.42	38 (-30.1 to 107.6)	137 ± 59	138 ± 63	0.857	0.01	1.0 (-53.9 to 55.0)
Total fat (g)#	66 ± 38	66 ± 34	0.734	0.00	0.0 (-27.9 to 27.6)	50 ± 13	55 ± 14	0.457	0.36	5.0 (-7.0 to 17.0)

Data presented as mean ± standard deviation

log10 transformation;

**between-group* difference, P ≤ 0.05;

§*within-group* difference for control group (pre to post), P ≤ 0.05.

Greater change from baseline to 12 weeks in the intervention versus control group at ¥ P ≤ 0.01 and £ P ≤ 0.05.

BP blood pressure, HDL high-density lipoprotein, HOMA-IR homeostasis model assessment of insulin resistance, hs-CRP high sensitivity C-reactive protein, CHO carbohydrates.

Number of participants who were outside the normal range (see Table 2 for values) for adult women at baseline: BMI n = 35, WC n = 39, WHR n = 16, WHtR n = 25, SBP n = 1, HDL-cholesterol n = 7, triglycerides n = 3, total cholesterol n = 1, HOMA-IR n = 13, hsCRP n = 11, predicted $\dot{V}O_2$max (ml·kg^{-1}·min^{-1}) n = 28, physical activity n = 39.

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aforementioned cardiometabolic markers were significant from pre-intervention to sustainability testing (i.e. maintenance had occurred) but no further improvements were seen between post-testing to sustainability testing. In fact, predicted VO_{2max} and physical activity reduced during the 12-week sustainability phase however, physical activity remained greater than at pre-intervention.

Control group

Despite being requested to maintain normal lifestyle habits, the control group displayed several improvements from pre- to post-testing, including WC (-5.6 cm, -6.2%), WHR (-0.03, -3.8%), WHtR (-0.03, -5.5%) and SBP (-8.0 mmHg, -7.0%), while circulating triglycerides rose (Table 2). In contrast to the intervention group, there were no changes in reported DBP, reported physical activity, predicted VO_{2max}, resting heart rate and energy intake following the 12-week control period.

Discussion

The effectiveness of the multi-disciplinary lifestyle intervention for reducing CVD risk in young women was highlighted by within-group improvements in a range of risk factors for the

Table 2. Within-group comparisons of cardiometabolic risk factors for the intervention group at pre-intervention, post-intervention, and sustainability.

				P-values			
Variable	**Pre-int. (0 weeks) (n = 26)**	**Post-int. (12 week) (n = 19)**	**Sustainability (24 week) (n = 19)**	**Pre-int. vs Post-int.**	**Pre-int. vs Sustainability**	**Post-int. vs Sustainability**	**Population norms/range for adult women**
Body mass (kg)	89.8 ± 21.1	86.9 ± 20.5	86.1 ± 20.3	0.791	0.408	0.369	-
Body mass index ($kg \cdot m^{-2}$)	32.2 ± 5.9	31.3 ± 0.9	31.0 ± 6.1	0.447	0.197	0.291	18.5–24.9 [1]
Waist circumference (cm)	93.1 ± 11.7	87.3 ± 9.8	87.8 ± 9.4	< 0.001*	0.002*	0.696	≤ 80 [11]
Hip circumference (cm)	116.3 ± 13.3	114.2 ± 13.50	114.5 ± 13.9	0.309	0.627	0.734	-
Waist-hip-ratio	0.79 ± 0.05	0.77 ± 0.04	0.77 ± 0.04	0.002*	0.018*	0.998	< 0.80 [1]
Waist-height-ratio	0.56 ± 0.06	0.53 ± 0.05	0.53 ± 0.05	< 0.001*	0.001*	0.841	< 0.50 [35]
Systolic BP (mmHg)	120 ± 11	116 ± 9	116 ± 11	0.047*	0.131	0.967	≤ 130 [11]
Diastolic BP (mmHg)	68 ± 6	64 ± 9	64 ± 6	0.040*	0.050*	0.841	≤ 85 [11]
HDL-cholesterol ($mM; mg \cdot dL^{-1}$)	1.7 ± 0.5	1.9 ± 0.5	1.9 ± 0.4	0.193	0.386	0.726	≥ 1.29 [11]
	65.6 ± 19.3	73.5 ± 19.3	73.5 ± 15.4				≥ 49.8
Triglycerides ($mM; mg \cdot dL^{-1}$)#	1.3 ± 0.5	1.4 ± 0.7	1.5 ± 1.0	0.855	0.271	0.221	≤ 1.7 [11]
	115.0 ± 44.2	123.9 ± 61.9	132.7 ± 88.5				≤ 150.4
Fasting glucose ($mM; mg \cdot dL^{-1}$)#	4.6 ± 0.4	4.6 ± 0.4	4.6 ± 0.5	0.728	0.559	0.756	≤ 5.6 [11]
	82.9 ± 7.2	82.9 ± 7.2	82.9 ± 9.0				≤ 100.9
Total cholesterol ($mM;mg \cdot dL^{-1}$)	4.4 ± 0.6	4.3 ± 0.8	4.3 ± 0.6	0.542	0.671	0.937	< 5.5 [36]
	169.9 ± 23.1	166.0 ± 30.9	166.0 ± 23.1				< 212.3
Fasting insulin ($mU \cdot l^{-1}$)#	9.4 ± 4.7	8.1 ± 2.6	8.8 ± 4.7	0.957	0.466	0.344	-
HOMA-IR	1.9 ± 1.0	1.6 ± 0.5	1.80 ± 0.97	0.176	0.575	0.480	< 2.0 [37]
hsCRP ($mg \cdot l^{-1}$)#	3.5 ± 3.0	4.6 ± 4.9	4.7 ± 3.8	0.743	0.148	0.140	< 3.0 [23]
Resting heart rate (bpm)	76 ± 12	68 ± 8	66 ± 9	0.020*	0.004*	0.489	-
Predicted $\dot{V}O_2$max ($l \cdot min^{-1}$)	2.4 ± 0.5	2.8 ± 0.6	2.5 ± 0.6	0.029*	0.471	0.179	-
Predicted $\dot{V}O_2$max ($ml \cdot kg^{-1} \cdot min^{-1}$)	27.9 ± 7.0	32.6 ± 6.8	30.9 ± 9.7	0.000*	0.248	< 0.001*	≥ 31.0 [38]
Physical activity ($min \cdot week^{-1}$)#	97 ± 62	280 ± 67	143.7 ± 48.4	< 0.001*	0.002*	< 0.001*	≥ 210 [39]
Energy (kj; kcal)	6535 ± 2183	5223 ± 1725	5538 ± 2588	0.007*	0.269	0.161	-
	1562 ± 522	1248 ± 412	1324 ± 618				
CHO (g)	166 ± 74	178 ± 96	154 ± 83	0.638	0.928	0.638	-
Protein (g)#	173 ± 86	138 ± 63	150 ± 86	0.012*	0.520	0.079	-
Total fat (g)#	66 ± 34	55 ± 14	56 ± 20	0.227	0.575	0.513	-

Data presented as mean ± standard deviation

$\log_{10}$ transformation

* $P \leq 0.05$.

Int, intervention. BP blood pressure, HDL high-density lipoprotein, HOMA-IR homeostasis model assessment of insulin resistance, hs-CRP high sensitivity C-reactive protein, CHO carbohydrates.

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intervention group, with several of these improved markers retained 12 weeks after completion of the lifestyle intervention. Thus, these data suggest a relatively successful intervention for reducing CVD risk with promising sustainability. However, when between-group comparisons were made with the control group, the findings suggested a research design that was largely unsuccessful in identifying the effectiveness of the intervention phase. This raises several concerns associated with a wait-list control design when used with overweight/obese young women. Concerns from the current study support previous findings that describe more difficulties in retaining younger than older females to research trials [13].

Positive changes within the intervention group were demonstrated with improvements in WC related measures, systolic and diastolic blood pressure, aerobic fitness and physical activity, and dietary energy intake. Collectively, these measures imply that the intervention produced cardiovascular, more so than metabolic, benefits for the intervention group. The use of investigative procedures such as non-invasive echocardiography or MRI may provide insight into the significance of these changes [40].

Improvements in fitness and physical activity and reduced energy intake also suggest that the exercise and nutrition education components of the intervention, respectively, were effective. Moreover, there was strong evidence for sustainability of intervention-induced improvements at 24 weeks, suggesting that the CBT component produced positive behavioural change in participants. It has been shown that poor adherence to behavioural programs is a barrier to successful long-term weight maintenance beyond the completion of the intervention [41]. In the present study, adherence to the physical activity component and attendance at the CBT sessions was high amongst intervention participants. This might explain the success in maintenance of some cardiometabolic risk factors observed during the short-term sustainability phase. Additionally, it has been suggested that improvements in maintenance might be achieved through incorporating technology to monitor weight, physical activity and behaviour [42]. This type of innovation could be easily integrated into a population of young adults.

However, similar post-intervention changes in our wait-list control group, made it difficult to detect any anthropometric, biochemical, fitness or dietary differences between groups following the 12-week intervention phase. The control group in this RCT also displayed a decrease in WC that paralleled the intervention group, despite undetectable changes in self-reported physical activity and nutrition. The decreased WC of the control group is particularly difficult to explain without further investigative procedures such as accelerometry for physical activity and more rigorous dietary monitoring, but does suggest that basic awareness of CVD risk might be enough to evoke change in targeted populations [43,44].

Randomised controlled trials provide the highest level of evidence for the effects of an intervention and are deemed to be scientifically rigorous [45], with control groups employed to provide a contrast for the experimental group [46] and for establishing the efficacy of an intervention [47]. But changed outcomes that arise from a wait-list control condition can be detrimental rather than beneficial to a randomised controlled trial [46], and this occurred in the current study. Therefore, wait-list control designs might not be appropriate for this population.

Retention and compliance of wait-list participants is also an issue for consideration when planning control conditions essential for maintaining the rigour of a randomised control design. In this study, more than one-third of the control group failed to return for post-testing at 12 weeks despite researcher attempts to maintain contact. In contrast, once engaged in the intervention group, retention to lifestyle change was high for at least 24 weeks. It is postulated that assigning participants to the control group decreased their motivation to participate. Thus, the duration (12 weeks) and/or conditions (no changes to existing lifestyle) of the control group do not appear suitable for women of this age group and demographic. Alternative

strategies for immediate engagement, perhaps via topics of interest using multimedia such as health-related *apps* or support groups might improve commitment and maintain control group compliance. There were also some difficulties encountered with recruitment, with almost a quarter of interested and eligible participants failing to engage after initial commitment (prior to group allocation). Complexities associated with recruiting young women for weight management trials, especially from 'Generation Y', may result in smaller sample sizes and require shorter periods of engagement [16].

Although not always the case [48], successful outcomes have been observed following lifestyle interventions with middle-aged [2] and older women [3]. Furthermore, a large scale success of weight loss has been observed in a recent eight year study of adults aged 45–65 years showing an 8.5% mean body weight loss after year one of a lifestyle program [49]. Subsequent monitoring indicated maintenance of approximately 4–5% over the 7 years. However difficulties in the external validity amongst younger adults (21–44 years) was acknowledged [19]. Moreover, there is a lack of effective lifestyle interventions for young adults, with no weight loss programs to date developed specifically to address the needs of this age group. Outcomes, enrolment and retention rates have been compared between younger (18–35 years, n = 21) and more mature (> 35 years, n = 277) adults (66% female) engaged in similar behavioural weight loss and physical activity programs [15]. Results showed attendance was 30% lower in young adults and they were 30% less likely to be retained for the 6-month assessment. Weight loss and increases in total physical activity from baseline to 6 months were significantly less in the younger population. Although the number of younger adults was relatively small, these results indicated that traditional interventions were less successful in young adults [15]. These findings are supported by results from other studies attempting to engage young adults [50–52].

This study is not without limitations. Despite recruitment and retention strategies, the sample size, particularly in the control condition, was lower than anticipated at completion of the study, suggesting it was slightly under-powered. Additionally, the results are specific to Caucasian women at a tertiary institution. To capture any potential changes to control groups in a wait-list design, objective measures (e.g. accelerometers, fortnightly anthropometric measures) might be useful. In addition, the use of more objective measures of physical activity and dietary compliance would strengthen evidence of change in this age group of women. In agreement with previous reports, not all food and activity diaries were completed with precision. Future researchers may benefit from the use of diet quality changes rather than diet intake.

Nonetheless, the study contributes to a very limited number of healthy lifestyle interventions in young adult women (< 30 years of age) with cardiometabolic risk factors [50]. The multi-disciplinary lifestyle intervention confirms the potential value in health changes observed post-intervention, with favourable sustainability at a 12 weeks.

Conclusions

Within-group analysis showed that the multi-disciplinary lifestyle intervention comprising physical activity, nutrition education and CBT was positive for the reduction of CVD risk factors both immediately after and beyond the completion of the program. However, we also observed positive, but unexpected and difficult to explain, changes in the wait-list control group. Therefore, comparative lifestyle benefits for the intervention group may have been masked by undetectable weight management behaviour in the control group. When considered alongside the difficulties faced with recruitment and retention, especially in the nature of the control group, these results provide a challenge for prospective study designs with young women with cardiometabolic risk factors. Traditional RCT designs may be problematic for healthy lifestyle interventions in young women.

Supporting Information

S1 Table. CONSORT checklist.
(DOC)

S2 Table. Lifestyle intervention: Outline of the 12-week multi-disciplinary lifestyle intervention of physical activity, nutrition education and cognitive behavioural therapy.
(DOC)

S1 Text. Application for ethical approval of research projects with human participants.
(DOC)

S2 Text. Summary of research for ethics application.
(DOC)

S3 Text. Lifestyle survey.
(DOC)

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Author Contributions

Conceived and designed the experiments: BLS GAN PO JGK. Performed the experiments: BLS EAA. Analyzed the data: BLS JKP. Wrote the paper: BLS GAN JGK.

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Focus Group responses

- **Facilitator. Why did you initially respond to study recruitment?**
- **MT.** Um well for me it was, it was an opportunity. You know, I knew I had to do something about my weight and my lifestyle. I had just started uni and come out of a relationship; it was time for change. So I just, I felt like it was an opportunity to do that. And to help BS (researcher) and for her to help me, you know.. and It was good to meet other people as well.
- **Facilitator.** Ok. What other responses?
- **KC.** Yeah, I agree, it was a number of things. It was the whole lifestyle, it was free, she (BS (researcher)) was offering to give up her time and you know, use of the gym and pretty much a free personal training program. But also because she is a student and she does need participants that was an aspect of it as well… being a student yourself you can kinda identify the need to get the experience. But also my personal interest in women's health as well.. So there was a few different aspects.
- **Facilitator.** Ok.
- *Silence… laughing…*
- **BP.** Yeah, I found um a selling point for me was all the cardiac testing because I am a really big nursing nerd and I wanted to see how all the tests work, like the echos and stuff. And also I was really interested to find out how my cardiac health was because I have a family history of cardiac issues so it was a good opportunity for that as well as everything else obviously.
- **Facilitator.** Ok.
- **KP.** Yeah, I just like that it was free. That was like the thing with the email it was like "free personal training that's awesome" *(laughing)*. That's why I initially responded so It was like you have to do something and that was available.
- **Facilitator.** Great.
- **RB.** Yeah, I think I agree with KP. It was an opportunity that you really couldn't like say no to basically because what it was offering and all those kind of things, especially knowing where your fitness level was at… etcetera.
- TC. I just find It really funny because I was going through all my emails… you get so many emails from uni ..you just like click through them all. I just ignored it and turned my computer off then I was watching TV and I said "wait a second". So I turned my computer back on and I was like "whoa"... so I sent an email back to BS (researcher). I was pretty unhappy with my weight but I had never really considered doing anything about it. But, yeah, I had never considered joining a gym or anything.
- **Facilitator.** So that was like a really quick mental check of wow this is an opportunity. Interesting.
- **BP.** Yeah, I had a similar experience because BS (researcher) came and talked in my lecture and I was like 'oh yeah that sounds interesting' but didn't actually think I would fit the requirements. Then I went home and found my tape measure and discovered that I really, really did fit the requirements *(laughing)* and then like scoured through my emails to try and find it because I hadn't really taken any notice at the beginning so.
- **Facilitator.** Wow! Very good.
- **RB.** Come to think about it, I think that's when I first.. I think it was in one of the biology lectures, so yeah, I saw her in the lecture I think then I went back and looked for the email after she spoke in the lecture.
- **Facilitator.** Ok. ER, anything different for you?
- **ER.** No, same think, I was like 'oh hello, free personal training' *(laughs)*.
- **Facilitator.** So it was like the convenience of having something that was free. It was perhaps that 'wow' opportunity; take it. So even if you, like TC you said, you weren't even been thinking about changing anything but then the opportunity presented itself and you jumped.
- **ER.** It was really interesting as well sort of like the most exciting part for me was getting the ultrasounds and stuff on my heart and looking at it on the screen. It was so oooo, it's cool *(laughs)*.
- **KC.** I really liked the wholistic approach. You know, it wasn't just we're going to go jump rope for an hour, it was like the CBT, and it was you know the education, and working in small groups. We had BS (researcher) working with our small group. If you went to the gym you wouldn't have a trainer or you couldn't afford it or you get lost in a giant class. We wouldn't be doing things properly.
- **MT.** It was motivation too because you know, you had BS (researcher) and you had other girls in the group so that helped. Because if you join a gym, you just join a gym… it's like, am I going to go because I don't know anyone who is going to encourage me to go. So I found that was the difference that made me want to go
- **RB.** I was going to say, it was a massive convenience because you were going to uni anyway so to add in an extra session is not that hard. Whereas instead of going out of

your way to go to a gym or something like that which is fairly boring environment which you personally don't like.

- **Facilitator.** Yep, yep.
- **KP.** I think you know, it gave me focus because at the start the only reason I went was because I knew people would notice me like not going *(laughing)*.
- **Facilitator.** Right, ok!
- **KC**. There was definitely a level of obligation *(laughing)*.
- **BP.** To see people also, you know.
- **Facilitator.** Social accountability?
- **BP.** Yeah, the social aspect definitely.
- **Facilitator. Ok. Umm, just to get a sense of where we are at currently, who is exercising now? And what are you doing? Just go ahead and say it.**
- **KC**. Well, umm, I started doing more during the holidays especially when the gym at uni was still open because I mean I live in Brunswick and the gym is still open but there is like nobody there. Me and one of the other girls from uni we went there about two times per week.
- **Facilitator**. Yep.
- **KC**. Mainly just doing strength stuff, like not much cardio cos I hate it *(laughs)* but I'm walking to school now like two or three times per week which is like an hours walk.
- **Facilitator**. Brilliant.
- **KC**. Which I actually quite enjoy now. When I first started I was like I'm having a heart attack just from walking (*laughs)* because I walk pretty fast but now its actually like therapeutic in a way which is really good.
- **BP.** Yeah, I've been going to the gym a bit sort of end and flows a little bit and obviously it was really good because after I was in the first group I went to a lot of sessions with the third group so that was really good to get back on that and yeah, I go to the gym probably only once or twice per week but I walk a lot as well and my job is quite physical so it's a lot of running around.
- **Facilitator.** So are you making some conscious decisions to be active when you can like for example at work?
- **BP.** So yeah, my work is about a 25-30 minute walk from home so I always walk there and back.
- **Facilitator.** Great. What else? What else are people doing?
- **ES.** Just like walking in parts where you would have normally taken the tram. Instead of, like, I used to take the tram into the city and now I just walk into the city instead. And like every morning I walk to class instead of like getting on the tram. So it's like small.
- **Facilitator.** Ok, great.
- **KC.** The tram from school to Parliament? Yeah. *(Laughing)*.
- **Facilitator.** But that conscious choice to take that effort. Well, does anybody else have anything?
- **RB.** Umm,. I still like do my bicycle commuting but I also make those conscious choices to go and like go for a swim or go out for a 'walk/jog' I like to call it *(laughing)*… umm but also now I don't really care about if I'm out there and people see me.. yeah, so I just go out and not worry about that kind of stuff.
- **Facilitator.** Good. And you used to worry?
- **RB.** Yes, yep.
- **Facilitator.** Forbid someone sees me running in the park because what would they think? *(laughing)*.. oooo, there's an active girl! *(laughing)*.
- **Facilitator.** Umm, ok, so we've go a few people who are still using the gym. Anybody intending on doing more physical activity?
- **MT.** Yeah, well after I finished the study I joined belly dancing classes but I had trouble because after last year my teacher moved interstate.. so she's not doing class anymore, so I have to find another class and with uni back I haven't really made that a priority but yeah I want to do that because that sort of gave me, like if I wasn't pushing myself at least I had that hour, hour and a half class.
- **Facilitator.** Yep, ok, yep.
- **MT.** But yeah, like other people I'm sort of like instead of taking the tram I'm walking.
- **Facilitator.** Yep, great.
- **MT.** I try and fit it in when I can but id like to make it more a stable thing now that I know my timetable and everything.
- **Facilitator.** Great. Belly dancing; chat with MT (*laughs)*. Is anybody else doing a class or have a class that they are thinking about doing?
- **KP.** I'm going to start doing more Zumba… I really like it. It's really hard *(laughs)*. Are you (RB) going to come back with me?
- **RB.** Umm, *(laughs) (laughing)*

- **KP.** It's at a gym, that's quite cheap so I'm going to try and incorporate it into my life and with my boyfriends… like if he's going to go and workout or whatever, I'll go along to a class and try to go like three times per week. We've just come back from Europe so it's our plan.
- **Facilitator. Umm, ok. What or who are the biggest challenges to your healthy lifestyle?**
- **RB.** Me… *laughing*
- **Facilitator.** Why are you the biggest challenge?
- **RB.** For me, umm, it's like my brain… yeah, basically.
- **Facilitator.** What does the 'me' say?
- **RB.** I'm cold, I'm tired, I want to stay in bed *(laughing)*. Yeah, I think that is always a struggle but at least you know about it now and are a little bit more like…
- **Facilitator.** You feel more powerful against that me?
- **RB.** Yeah! Definitely.
- **ER.** My biggest struggle is work because like, well when I got back from Europe I was really motivated to keep up walking a lot because I lost like 25kg when I was over there because I was walking all the time… umm, and so when I got back I was walking everyday and being really active and stuff and then I started working these 10 hour shifts for my job which is like 12 o'clock until 10.30pm and then you don't get home until like 12 and you know, the next morning you wake up and have to sleep in a bit because you got home so late and then you know, you have to be back at wok at 12 again so that's the biggest thing for me. And then my job is just sitting down all day… on the phone.
- **Facilitator.** Ok, yep.
- **MT.** I find that too. Work and study.. trying to juggle both I'm finding that I'm needing to sort of try and find time with that and at the moment I'm having family issues so that goes on top of it so yeah.. but I think it can be done… even like what we learnt you know through CBT and that sort of thing about how to deal with these issues. I need to go back to that and have a look at that. But yeah, look It can be done, I know it can but at the time, like you say, 10 hour work day and that sort of thing it seems like you cant fit it in.. at the time, but you can.
- **ER.** Like I could get up early and go for a walk like easily because I don't start until 12 so I'd have plenty of time to go for a walk but it's just a matter of then by the time I get home at the end of the night id be dead *(laughs)*.

- **Facilitator.** What about some of you guys? What's your biggest challenge?
- **BP.** Being lazy. Like if I don't do something straight away when I get home and I sit down, there is no way it's going to happen. It's the same with exercise and like meal planning and cleaning.. it's all the same, if I don't do either first thing in the morning or first thing when I get home I will lay down or sit down and then I'll be there for three hours *(laughing)*.
- **Facilitator.** So the planning component is still that organisation component is something to work on.
- **ES.** I do the thing where I'm like as I'm walking home I'm like 'ok, when I get home I'll do this, this and this'… and then It's like you get home and its like awww but I'm tired from that walk.. it was like four minutes so I'll sit down now *(laughing)*.
- **Facilitator.** Ok. *(laughs)*. TC, what about you? I saw you nodding.
- **TC.** Yeah, I think yeah it's pretty much just laziness and business as well… and I know in my head that obviously that is really important and probably should be a high priority but at the time like when you're trying to fit all you stuff in and then you're like 'aw, I should be doing my uni work' but yeah, I'm going to start to be more regular. Now that uni is back I'm going to start to use the gym a bit.
- **Facilitator.** Ok, so when I asked the 'who' is the greatest challenge we had a couple of people say 'me'. Anyone else have somebody else that would be somebody in your life? Is there a 'who' that is a greater challenge to your lifestyle change?
- **MT.** Yes, my mother! She sabotages *(laughing)*
- **Facilitator.** Ok.
- **MT.** She'll cook like cakes and things.. but then she'll do the double standards thing where she'll say "have it because I've cooked it"… and then you have it… "well you should not have had that because you're meant to be watching your weight" *(laughing)*. Yeah, she does it all the time, I know she does but I fall into the trap.
- **BP.** My housemate started baking which is very dangerous so there is always like a bowl of something on the bench which you have to walk past like to go to the fridge *(laughing)* which is very tempting and she is very talented *(laughing)*.
- **Facilitator.** Mmm, mmm, interesting. Ok, so moving into nutrition, what have some of the nutritional changes been that you've made?
- **ER.** I think my main thing was portion sizes. My portion sizes are a lot smaller now… umm, yeah, and that's made a huge difference.

- **BP.** Yeah, I bulk out my meals with vegetables instead of carbs… and umm… eat slower. I put down my folk between each bite. You know, and I find I can eat a lot less and still feel full because my brain has time to catch up.
- **Facilitator.** Ok.
- **MT.** My biggest thing - which I'm still doing BS (researcher) – is light beer *(laughing)*. When she showed me the calorie content… well anyone who drinks cider that has a lot of calories in it so I've made that change all the time. But also I think just um, I try and judge things when I'm deciding on what to have or buying something out or whatever, I try and think to myself I'm hungry but instead of going to a café and buying something I think "am I really hungry or can I wait like another hour?" so I try and do that so I'm not eating so much, you know?
- **Facilitator.** Yep, yeah.
- **RB.** I probably drink less. I'm not a huge alcohol drinker; I don't even like the feeling the next day when your drinking but I've probably reduced it even more because I'm a lot more conscious about like what you're putting in.
- **KP.** Yeah, I don't think I even thought about alcohol before. Like I knew it was bad but for a multitude like calorie content as well as metabolism and everything but like I didn't really think about it until we got that sheet *(laughs)*… and I was just thinking 'oh my God'. Yeah I don't really drink anymore… I mean there are different reasons for that but yeah, that is just one.
- **Facilitator.** Right, ok.
- **RB.** As I said, the thing with nutrition I suppose is that, the big thing for me I suppose is that, umm, I used to eat bad food but then I used to feel incredibly bad afterwards but nowadays I still eat bad food or I still overeat or something but I tend to be a bit more like not so like negative about yourself right afterwards or the next day, it's like why don't you enjoy it. I probably don't obsess over food as much as I used too, even though I know I'm overweight Its not a massive factor in my life. I prefer to get out there a lot more because I find that I'm getting out there a lot more and when you're really social you go out for drinks with people, you go out for coffee and dinner and stuff like that and instead of like reducing by saying 'oh, I cant go out because I'm too fat tonight' or something like that I just go. And now I find that I don't really think about the whole food thing that much to be honest.
- **Facilitator.** Ok.

- **KC.** I've found that I've become more aware of how the food I'm eating makes me feel like emotionally and physically. Like I haven't actually changed my diet because I already had a really good diet previous to all, this I was just bone-idle and now if I do eat something, you know, a little bit on the fatty side or fried side, it's like afterwards I most of the time I do feel a bit crap… not emotionally but actually found myself feeling really tired and really lethargic and you build this up like 'I'm gonna eat this cake and it's going to be the best thing ever' then you eat it and it's like oooh. Yeah, it's not as good as I thought it was going to be *(laughs)*. That's probably the main thing that has changed… how I feel and think and address what I'm going to eat a little bit more.
- **ER.** That's so true because I feel as if before I was eating so badly like all of the time but I didn't notice any changes in feeling like bloated or sluggish but now because I don't eat as much as I used to like when ever I do eat, like say a meal of pasta like I can tell the difference which is like so bizarre for me because I like never noticed that before about food *(laughs)*.
- **Facilitator.** So an awareness?
- **ER.** Yeah.
- **Facilitator.** Ok, ok. Anything else about the diet side, the nutrition side? Very good.
- **Facilitator. What are your short and long-term healthy lifestyle goals? What would you say? So short term, what are your short-term goals with your lifestyle? Like say, even just this semester?**
- **KP.** Yeah, I want to try and just make it part of my life… that's my short term and my long term goal I thing cos to reach a point where it's just something that I do. It's just like I am healthy, im not thinking about it and like a decision for everything its just what your life is.
- **BP.** Yeah, I'd like to be able to like plan when I'm going to exercise in a week and actually do it *(laughing)*.. so I started writing stuff in my diary and sometimes it happens and sometimes it doesn't happen *(laughing)*.
- **Facilitator.** Yep, yep.
- **BP.** Because I'm so busy with different commitments I really do need to schedule it in and I also need to stick to it.
- **MT.** And I think, well I suppose this could be a short term.. but finding social connections to do something.
- **Facilitator.** Yeah, yeah.

- **MT.** Because that's the best for me. I wont do something unless I'm doing it with someone else. So that's why classes work for me. I think If I sort of had people that I could regularly go for a walk with at the park or whenever someone had a break at the same time because you can do a lot from uni like if you have a one hour break and fitting that in… I think that may be an option or me.
- **Facilitator.** I'm hearing a healthy lifestyles club… at ACU *(laughs)*… sounds great!
- **KC.** You're so right though, like having someone to do it with even though, you know you do have to be self-motivated, does help you along, because if I do go to the gym without Steph who is the girl I have been going with I will go and do stuff but I probably wont do half as much if she wasn't there putting me in check. You know what I mean?
- **Facilitator.** Hmm, yep.
- **RB.** I think short term, to keep exercising is not perceived as a chore and almost try and not see it as something you have to do or you have to plan and almost something that you can do like because you want to do it with your friends or something.. because you want to go swimming, you want to walk, you want to ride to uni or something like that.
- **Facilitator.** It's a bit of me time.
- **RB.** Yeah, and just using it more as a relaxation technique I think because I'm going to start work this year, soon, and it's going to be shift work so I want to use it as a relaxation technique, something I REALLY want to do.
- **Facilitator.** Great. Because it feels good and you feel great about yourself after.
- **RB.** Long term; no heart attack or diabetes *(laughing)*.
- **Facilitator.** Are those in your family?
- **RB.** Umm, oh, diabetes is but not really heart attack because of living a healthy life. Living, you know like when you're eighty not having arthritis would be good, that type of thing.
- **Facilitator.** Ok, what else? What about you?
- **ES.** Umm, yeah, just like what everyone said, just to be healthy and after like when you first start doing exercise like afterwards you feel really, really bad… like I want to get to that period where I just feel like really good and healthy and just like fit, not crap.
- **KC.** Yep, dieing in the locker rooms *(laughs)*.
- **ES.** Like be able to train for like an hour or two hours and then at the end of it not go well now I want to go to sleep and die
- **Facilitator.** Ok. Any other short-term or long-term aspirations?

- **KC.** I think just maintain; keeping it going because I know we were doing all our exercise before Christmas then I had a month off from doing gym stuff over Christmas; the first gym session back I like died… I probably should have eased into it but I had the worst muscle pain I have ever had in my life the following week afterwards and I was like oh my goodness that's only like a month off. It's so much easier just to keep it up and keep it going then stop and start all over again. Like I really noticed it and it really surprised me, like I couldn't pick anything up off the ground.. there was all this stuff on the ground and my husband came home and I was like help me! *(laughing)*, I cant do anything by myself. Yeah, it was pretty bad.
- **BP.** Yeah, I think for me, definitely maintaining the healthy lifestyle when I go into shiftwork next year because it could be so easy just to let things slide when you are doing shifts and knights and you know, afternoons and stuff so if I can develop it now…
- **KC.** The endurance for during nursing and midwifery, totally.
- **BP.** Yep, and just strength as well.
- **KC.** It's physically demanding *(laughing)*.
- **ES.** And I want to kinda do exercise that feels like exercise. I just walk around and stroll around and I do it for like an hour or two hours or three hours but it doesn't actually feel like exercise because you like walk and then you sit down and then you walk and then you sit down for a while and you stand around looking at things (laughing). I want like exercise, exercise.
- **Facilitator. Ok. Very good. So if we think about the next six months then what's one thing your planning on integrating into your repetatur of activity?**
- **ER.** Walking every day.
- **Facilitator.** Walking every day. Ok, for how long?
- **ER.** An hour.
- **Facilitator.** An hour, wow.
- **ER.** Because that's what I was doing (laughs).
- **KP.** I should be walking to uni because I only live in Brunswick as well. It's not that far; it's actually quite a nice walk, it's flat.
- **Facilitator.** Ok, great
- **KP.** Like I was on the tram this morning and I thought I should have walked it.
- **Facilitator.** Even just a couple of times per week. you know, just start small and build. Cool. What about you BP?

- **BP.** Umm, definitely walking more but I really would like to go to the gym a bit more.
- **Facilitator.** Ok. Do you have a membership?
- **BP.** Yep, and I always try and go at least once per week otherwise I feel like I'm wasting my money that I'm paying but yeah, maybe go like once a week and do gym once a week or a class or something. If I can have the class set the same time every week then there is more chance.
- **Facilitator.** Brilliant. What about you TC?
- **TC.** Yeah, I'd really like to start walking more. Like I live in Williamstown and it's right on the beach so I shouldn't have any excuses.
- **Facilitator.** Ok. So you're going to walk and or how long?
- **TC.** Everyday… for four hours *(laughing)*. Nah, everyday for half an hour I guess.. maybe that could be like my short-term goal. By the end of six months I'll be doing that.
- **Facilitator.** Do you think is a smart idea to perhaps start smaller than that, so you know, like once or twice per week? Just to begin with then keep on bumping it up. Yeah, because I think that is the other thing to really be mindful of. What about you (Facilitator) ES?
- **ES.** Um, yeah, just like make sure that I have a walk like every single day. Like some days, Mondays, im at uni from 9am until 8pm, so like I cant do it on Mondays but..
- **Facilitator.** Any breaks?
- **ES.** Yeah, I have like a three hour break… so like the gym there.
- **Facilitator.** You could use the ACU gym.
- **ES.** Yeah, like use the gym every time I have a break. Because sometimes I'll have a break and I'll be like oh, I'll just sit in the library and just play on the compute.
- **Facilitator.** Ok.
- **ES.** But um, going to the gym every single time I have a break and like sometimes I get like when I'm by myself at the gym I get really off-put by all the boys. They are like doing massive things and I sit there on the bicycle (laughing). Um and I feel like more confident in the gym I think.
- **Facilitator.** And what could you do to be able to just be in your zone? Because everybody is in their own zone, when they are working out it's not as though they are watching you, you know.
- **ES.** Maybe just putting music in and ignoring it.
- **Facilitator.** Yeah, absolutely.
- **ES.** Try and think positive.
- **Facilitator.** Absolutely. Ok. And you also said something about exercising besides walking. What is something you think you could do?
- **ES.** Umm, my gym just got a new pool and I really love swimming. I want away and I swam like every single day and after you swim you just feel really fit and healthy and awesome so I just want to go there and like swim as often as I can or I'll get my mum to put a pool in the house *(laughing)*.
- **Facilitator.** Good-o. ok, KC what about you?
- **KC.** What was the question?
- **Facilitator.** Um, in the next six months, what's one thing that you could do in terms of physical activity?
- **KC.** Well, keep up the walking. Keep on doing it about two or three times per week.
- **Facilitator.** Is that the walking to and from uni?
- **KC.** Yeah. Ah, probably just one direction. I did to and from uni last week and died so I probably wont be doing that again *(laughs)* so probably… the Brunswick baths are getting a revamp, which is like across the road from my house so I might join there because they have pretty good rates for students but I'm not a giant gym person, like wont go there and use all the machines or anything like that, mainly just or classes, like having that structured coach sort of fitness. You know, like pilates or body pump. That would be really good.
- **Facilitator.** Ok, great.
- **BP.** Body balance is really good at the Brunswick baths
- **KC.** body balance? Yeah, I've got a friend who does that. Its like pilates and yoga combined. It's good.
- **Facilitator.** MT, what about you?
- **MT.** Um, my thing is the class. You know, just one class, I'm not going to aim for something everyday, just the one class, and my other thing is nutrition. I want to plan what I am eating more because being at uni I've got rally full days. At the moment I get home and I don't want to cook anything so I'll just get something that is easy and not necessarily healthy. So I want to sort of yeah, do that a bit more, plan that a bit more. So plan my meals and the class.
- **Facilitator.** Ok, good. RB, what about you?

- **RB.** Well I'm starting nursing in two weeks so basically I've planned to ride from Northcote to Peter Mac each day which will be nearly twenty minutes one way. I've never really classed commuting as exercise because it doesn't really increase your heartrate a lot whereas I know if I want to get my endorphins or serotonin kicking I need to be sweating so basically because I'm starting shift work I'll be riding and hopefully I'm going to try and go to the Fitzroy pool and go for a swim once or twice a week or something like that. Then get into a routine a bit, so if I've got a PM, swimming before then going to work of if I've got AM, swimming after work. But I'm also going to Melbourne Uni bush walking club on Tuesday night to have a look because at different stages of my life I've really enjoyed gym and it's been really good but I suppose this time I realise I'm not really a fan of being inside and with the gym I find it quite boring so I've actually been doing some hiking with friends and I really want to get out there so I'll check that club out hopefully. They organise trips throughout the year, so um, join up with them. Also because I'm starting work I'm going to organise getting a veggie box delivered.
- **Facilitator.** Oh wow.
- **RB.** Plus my dairy and stuff delivered through Farm Australia because the first thing people tell you is that first year you're just so tired because of the work and it's an easier way to cope. You have to plan your meals a lot and make it as easy as possible.
- **Facilitator.** Wow, that's great.
- **Facilitator. What or who is going to help you lead this healthier lifestyle that you have planned… that you are currently engaging in. So what or who?**
- **ER.** Me.
- **Facilitator.** Ok, so obviously you.
- **ES.** My dog.
- **Facilitator.** Ok, so having the dog.
- **ES.** Whenever I don't take him for a walk he gets really annoyed and comes and jumps on me.
- **Facilitator.** Ok, so a great reminder.
- **ES.** Yeah. And whenever we are walking he always runs away. He sees something and he runs so I have to like run after him *(laughing)*. So that's like a good little pusher.
- **Facilitator.** Ok, ok, very good. What else?

- **KP.** I know my boyfriend will be. I know like together we are both either, like we help each other be either healthy or unhealthy *(laughs)*, so I guess we are both like on the thing together but he is really focused at the moment and because we have just been away both of us are seeing the trip as like when you get back that is when you really have to change I guess and he is really linear so I think I'll just go along with him *(laughing)*. So hopefully we can keep each other on track and try to make a difference.
- **Facilitator.** Ok. Anybody else have a...
- **BP.** The kids I wok with because I have to exercise a lot to keep up with them *(laughing)*.
- **Facilitator.** Ok, ok. Yep.
- **TC.** My little sister wants to start exercising more regularly so she is pulling me along.
- **Facilitator.** Yep. A bit of social support. Ok. Anybody else have a what or who that helps you? Does everybody need a what or who?
- **KC.** my husband is pretty supportive, but he is generally supportive of anything I decide we are doing *(laughs)*. We have a pretty god diet and everything but I have been dragging him to the park and playing Frisbee and stuff like that… more exercise through play rather than making it a drag like we go and grab some friends and so we go for a bike ride or play in the park.
- **Facilitator.** Active activities.
- **KC.** Active activities, yeah, that's right! So now we have a couple of friends who came back from Berlin in winter and now they are all happy its summer so we're going out together all the time… instead of going to the bub or whatever we just go and, if it's a nice day, it's not too hot or raining we just go to the park and hang out.
- **Facilitator.** Lovely.
- **RB.** The what for me would be like goals, so over the holidays I went and rode the east cost of Tassie and I know the west side and south west side of Tassie has lovely walks and stuff like that and because I love hiking and I love cycling I want to be able to do those and I know I have to be at a certain fitness level to be able to do them. And just to live a lifestyle that I want to live which includes those types of activities you have to be, you know, responsible for something like that and I also think a few of my friends that I have become good friends with over the past year like who are very much into hiking and stuff like that and I have similar sort of ideas about what is fun like camping and stuff like that and its easier to go out when you have people to do that with.

- **Facilitator.** So finding people, being around people that share some of your similar passions and similar interests. Really helpful. Good.
- **Facilitator. Alright. Um so, just in general, what did being apart of this experience mean to you or do for you? Just reflect a little on where you think you are now compared to where you were at the beginning. What do you have?**
- **KC.** Well it's totally given me motivation. It's totally kicked me into gear. Like it is one thing sitting on the couch going 'yes, I think I might do some exercise and actually making the choice to go and do it and then keep at it. It's two completely different. Like thinking about exercising is not the same as going out and exercising so that has done it. And you just have to get on with it you can't dwell on 'oh, this is going to hurt so much, it' going to be horrible', you just have to suck it up really and get on with it.
- **Facilitator.** And did you have the, you know, were you able to get on with it when BS (researcher) was giving you…
- **KC.** yeah, like when I first started out, there was a couple of moments where I thought oh crap, I'm going to throw up or pass out or something as equally embarrassing but that passes, the first couple of weeks were hard because your body wasn't used to it but then you got better, and better and better and now I do realise that it is just so much easier to keep on doing it then to get back to that stage and have another quarter life crisis and do it all over again.
- **BP.** Yeah, I've found it's made me a lot more self aware and confident as well about what I need to do and what I can do and also because we had such a close group of people I've got a whole new support system of people and friends and that's been really beneficial having people around me that have similar goals and understand what it's like to have to have a lifestyle change.
- **Facilitator.** Absolutely, absolutely.
- **ER.** The program made me like just more aware of like what food and exercise actually do to your body… like biologically *(laughs)*. You know, like id never really thought about it before and like I didn't know the difference between cardio and fitness and stuff like that and like learning what actually is beneficial and you know, like how long you have to exercise for and um, that kind of thing that actually makes an impact. I had no idea.
- **Facilitator.** Ok, so some education? Lots and lots

- **KP.** Yeah like I thought about having high cholesterol and like what's its doing to your heart and all that sort of stuff but never really thought about the actual numbers and the actual thing. Like I knew if you were healthy then that stuff is better but I never really thought about what makes an impact on that.
- **RB**. I think for me it was being less obsessed about the whole.. I think being a lot more positive towards yourself and less obsesses, like I don't really think about weight these days and like I know I'm overweight but I've seen BS (researcher) and she said I've got good cholesterol level and I think as long as those things are ok your weight isn't going to drastically change by the next day if you exercise but it's a long term thing and I think it's very good to be in a very good headspace. When I started I wasn't in a really good headspace at all whereas now I'm a lot more positive and I think one thing can follow the other thing so when you're more positive you're more likely to get out there and all this kind of stuff. I'm a great believer in that rather than thinking always along the lines of how much you weigh or what you're eating because in the end, for me that personally gets me down further so I don't say 'ah, you're terrible because you didn't go for a walking today', it's more like you get up and go 'cool, I can go for bike ride with my friends today'. The mind has changed I think.
- **MT**. I found that too because my sister recently went interstate but she was saying to me a few months ago 'oo, I just ate chocolate, I'm so bad and blah, blah, blah' so I said you know, yes, you had chocolate but that doesn't mean that you have to have it tomorrow, you can go and exercise tomorrow, you can do something else tomorrow, just don't see that food as negative, as bad…
- **RB**. Enjoy it.
- **MT**. It's like, food is food at the end of the day, it's how you use it… so I got that. And I also, you know, lost just under 10kg throughout the program because I was dedicated and I haven't put that back on so I've seen that as a positive because it does change, like if you loose ten percent of your body weight which I think is what it was for me, um, it makes you change, like you feel a lot more like you can do..
- **Facilitator**. Empowered?
- **MT**. Yeah! Absolutely. So that's been a positive in making me maintain what I'm doing.
- **ER**. And just getting back to what RB said about focusing on your weight and being down on your weight and stuff like that, like when BS (researcher) measured my heartarte the other day she was like 'whoa, it's really good compared to what it was before', you

know, it was way down and that is fantastic because you forget that it's not only what you can see that is really important, it's the other stuff. Um, and that was really cool.

- **Facilitator**. So the weight, the number isn't your value as a person? I think that is a great thing to take away
- **ES**. I found that, um, I rode the hight after like doing exercise, because after I'd do exercise I felt so good that I wanted to do exercise the next day to keep feeling good and the day that I'd miss exercise I'd start feeling bad so I'd have to do more exercise to feel good again.
- **KC**. Yeah, you start craving it a little bit don't you?
- **ES**. Exactly. I remember I was talking to KP and she said her boyfriend always thought she was cranky when she wasn't doing exercise and I realised that I found that. Until that point I hadn't really realised that on days when I wasn't doing exercise I was like meaner or I'd snap at people.
- **KC**. I'm a much nicer person as well after I exercise.
- **Facilitator. Anything else that you think you have to say about your experiences or learning?**
- **TC**. It's just really great to know that we can do it… like I've done health kicks before and I've never actually seen any difference at all and then gave up after a few weeks… so yeah, it was awesome! You know, like I can exercise three times per week for a long period of time and loose weight and notice a difference and feel better.
- **MT.** Yeah, and there is other ways that you can loose weight. For me, I've always struggled with my weight and id go through stages where id say 'I'm not going to eat anything' and that's how I'm going to loose weight and then you do things the unhealthy way. I think it's the fact that I did loose weight and I do feel better about myself and you know physical changes as well as mental changes, doing it where I was eating healthy and exercising proved to me that I can do it that way… I don't have to do it the unhealthy way.
- **RB.** I think learning about those fad diets and stuff like that was really important because you know how they were saying you go on this health kick and it never lasts and you put on weight and then you put more weight on top of what you were originally.
- **KC.** Yeah, it was really good to address that unhealthy but easy way to loose weight; like the fad diets and you know, drink nothing but maple syrup or lemon juice or whatever *(laughing)*… it's just ridiculous… and people think that is the easy way but actually you can, you know, just eat normal food and just move around a little bit and that's all you have to do to loose weight and that is the easiest thing to do, you're not going to starve yourself, you don't have to run yourself ragged and sweat. You know, it's about being kind to yourself… and dieting is not *(laughs)*.
- **Facilitator.** Yeah, yeah.
- **RB.** I know one of my friends little sister is on weight watchers and stuff and maybe that is good for her to a degree but I was like that is so limiting on your social. When I'm at home with friends I don't want to count it because I would find it really socially limiting.
- **KC.** Your little book… your little points book.
- **RB.** Like I've done it before and I know it doesn't suit me because once I stop.
- **KC.** It's like a bandaid solution a lot of those things, like weight watchers, it's just giving people instruction but once they get out of it they may not have the skills to actually keep it up on their own *(laughs)*. I had a friend who did Tony Ferguson and lost heaps of weight and looked so good.
- **KP.** Isn't that like a shake diet though?
- **KC.** Yeah, and like heaps of vegetables.
- **RB.** But like you obsess over the wrong things again… you start obsessing over the food where I think it's more getting out there and socialising.
- **KC.** But he never develops the skills to cook proper meals anyway. I was having weird frozen Tony Ferguson meals which I think is just yuck.
- **Facilitator.** So that is a really great point because do you guys think that you have the skills? So even if life is busy and you perhaps have to make changes to the amount of physical activity you are doing do you still feel like you have learned some skill and learned you know, just a healthy way to move forward?
- **Group.** Yep.
- **Facilitator.** And does that feel powerful? Does that feel like the power you have perhaps not had previously?
- **BP.** Yep, I think it really shower, for me I found it really good because I obviously lost a certain amount of weight throughout the study but I was really fit for about six months after and continued to just keep going and have then have sort of maintained it since then. Because I got to do the second half myself, you know, it gives you a lot of strength to know you can do it if you fall backwards.

- **Facilitator.** Great. Well I think you guys should really tap into this momentum and exchange emails and numbers and BS (researcher) I think we should seriously look at starting some kind of club or maybe there are walks that people are doing at lunchtime, or bushwalks because this momentum is awesome.

END

Lifestyle Intervention Evaluation

Please rate each of the following sections by using a number from 0 to 10

No, Not at all **Yes, Definitely**

0 1 2 3 4 5 6 7 8 9 10

1. Trainer Characteristics	**Ratings**
Had useful knowledge about exercise programming	.....
Had a positive, constructive attitude	.....
Made my exercise experience fun	.....
Provided me with the appropriate support	.....

Did Not Like **Liked Very Much**

0 1 2 3 4 5 6 7 8 9 10

2. Rate your experience	**Ratings**
Frequency of training	.....
Length of training	.....
Variety of activities during training	.....
Location of training (i.e. ACU gym, Fitzroy gardens)	.....
The social aspect of training	.....

3. **How has your attitude towards exercise changed as a direct result of this lifestyle intervention?**

4. **How has your attitude towards food/nutrition changed as a direct result of this lifestyle intervention?**

5. **How has your emotional state and general wellbeing changed as a direct result of this lifestyle intervention?**

6. What were your main physical activity goals at the start of the program?

7. What were your main nutrition goals at the start of the program?

8. Did you have any other goals?

9. Did you achieve these goals? **YES** ☐ **NO** ☐

10. If yes, please elaborate:

11. If no, what do you think prevented you from achieving your goals?

12. What did you enjoy and find *most* helpful about the physical activity component? Please comment below.

13. What did you find *least* enjoyable or least helpful about the physical activity component? Please comment below.

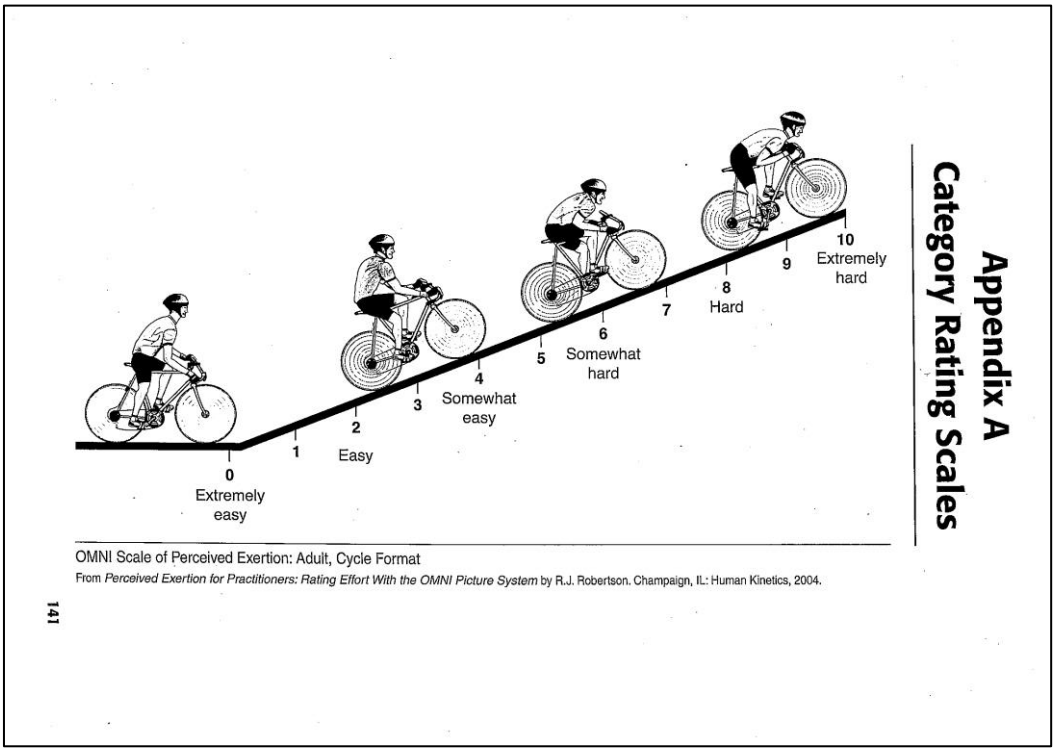
14. What did you enjoy and find *most* helpful about the nutrition education component? Please comment below.

15. What did you find *least* enjoyable or least helpful about the nutrition education component? Please comment below.

16. Please provide any recommendations for how to improve the quality or effectiveness of the lifestyle intervention.

17. Please provide any additional feedback or comments you may have?

Appendix 18: OMNI Scale of Perceived Exertion



OMNI Scale of Perceived Exertion: Adult, Cycle Format

From *Perceived Exertion for Practitioners: Rating Effort With the OMNI Picture System* by R.J. Robertson. Champaign, IL: Human Kinetics, 2004.

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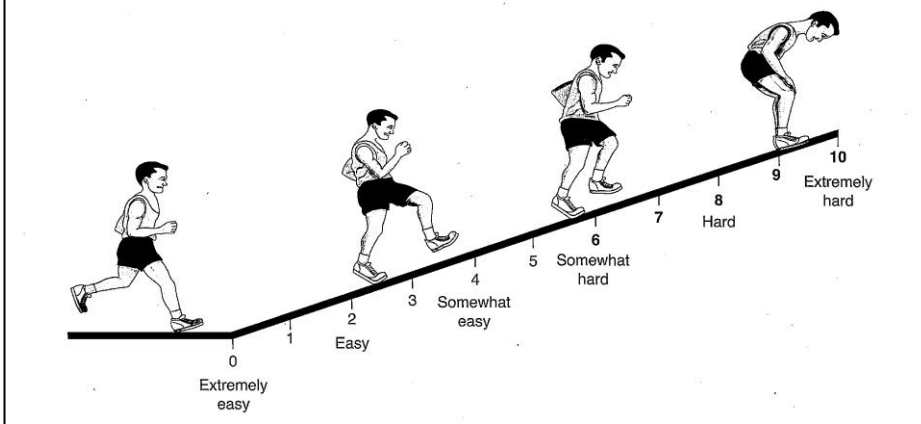
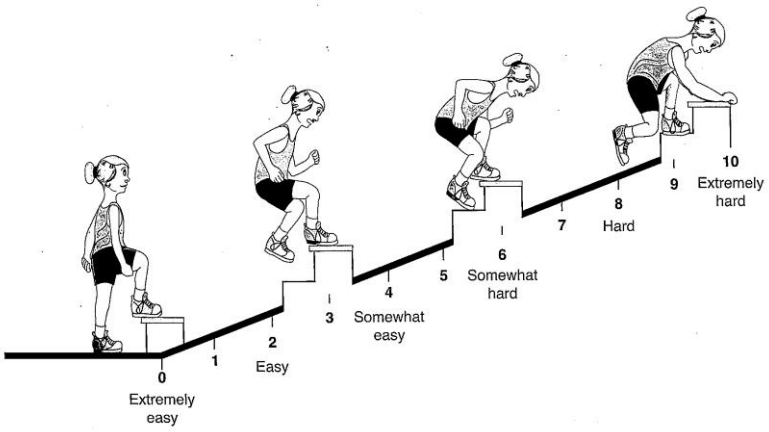
Appendix A
Category Rating Scales



OMNI Scale of Perceived Exertion: Adult, Walking to Running Format

From *Perceived Exertion for Practitioners: Rating Effort With the OMNI Picture System* by R.J. Robertson. Champaign, IL: Human Kinetics, 2004.



OMNI Scale of Perceived Exertion: Adult, Step Format

From *Perceived Exertion for Practitioners: Rating Effort With the OMNI Picture System* by R.J. Robertson. Champaign, IL: Human Kinetics, 2004.

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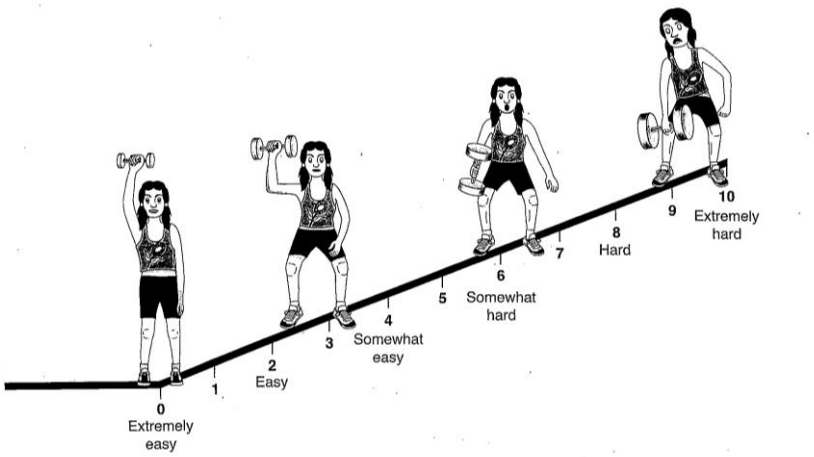
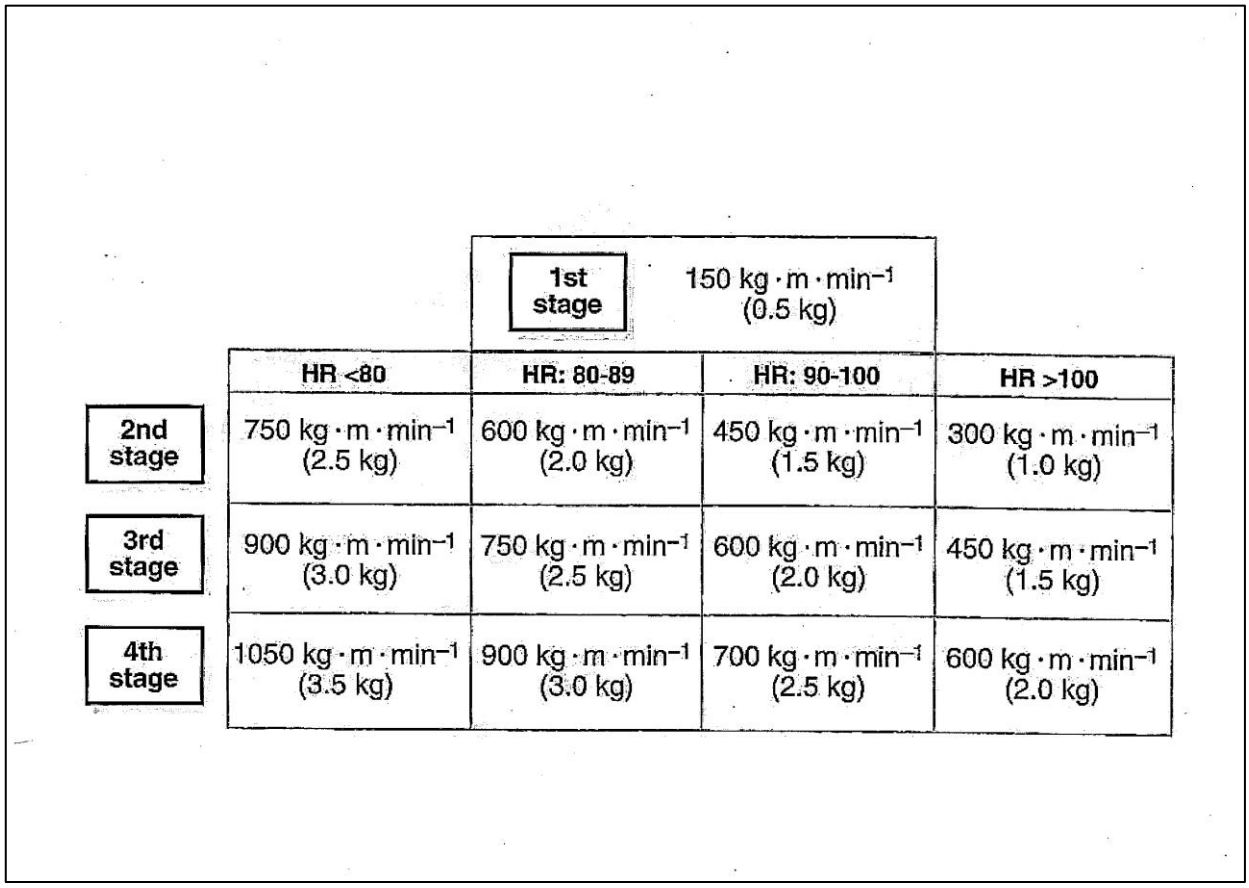


OMNI Resistance Exercise Scale: Female Child

From *Perceived Exertion for Practitioners: Rating Effort With the OMNI Picture System* by R.J. Robertson. Champaign, IL: Human Kinetics, 2004.

Appendix 19: YMCA Submaximal Cycle Ergometer Protocol



1st stage	150 kg · m · min^{-1} (0.5 kg)			
	HR <80	**HR: 80-89**	**HR: 90-100**	**HR >100**
2nd stage	750 kg · m · min^{-1} (2.5 kg)	600 kg · m · min^{-1} (2.0 kg)	450 kg · m · min^{-1} (1.5 kg)	300 kg · m · min^{-1} (1.0 kg)
3rd stage	900 kg · m · min^{-1} (3.0 kg)	750 kg · m · min^{-1} (2.5 kg)	600 kg · m · min^{-1} (2.0 kg)	450 kg · m · min^{-1} (1.5 kg)
4th stage	1050 kg · m · min^{-1} (3.5 kg)	900 kg · m · min^{-1} (3.0 kg)	700 kg · m · min^{-1} (2.5 kg)	600 kg · m · min^{-1} (2.0 kg)

Appendix 20: Example of Participant Results

BP

Table I. Metabolic syndrome data

Metabolic Syndrome (IDF)	Recommendations	Pre-Intervention	Post-Intervention
Waist circumference	≤ 80 cm	90.3 *	81.4 *
Blood pressure	≤ 130/85	116/69	108/59
Fasting glucose	≤ 5.6 mmol·L^{-1}	4.9	4.2
HDL-Cholesterol	≥ 1.29 mmol·L^{-1}	1.4	2.1
Triglycerides	≤ 1.7 mmol·L^{-1}	1.2	1.0

Table II. Anthropometric and additional biochemical data

Anthropometry	Recommendations	Pre-Intervention	Post-Intervention
BMI	18.5-24.9 kg·m^2	26.0 *	24.0
WHR	< 0.80	0.88 *	0.82 *
Body mass	N/A	67.9 kg	63.7 kg
Biochemical			
Hs-CRP	< 3.0 mg·L^{-1}	4.4 *	2.0
HOMA-IR	< 2.0	1.1	1.1
Insulin	< 10	6.0	5.0
Total cholesterol	< 5.5	5.4	4.7

Table III. Fitness data

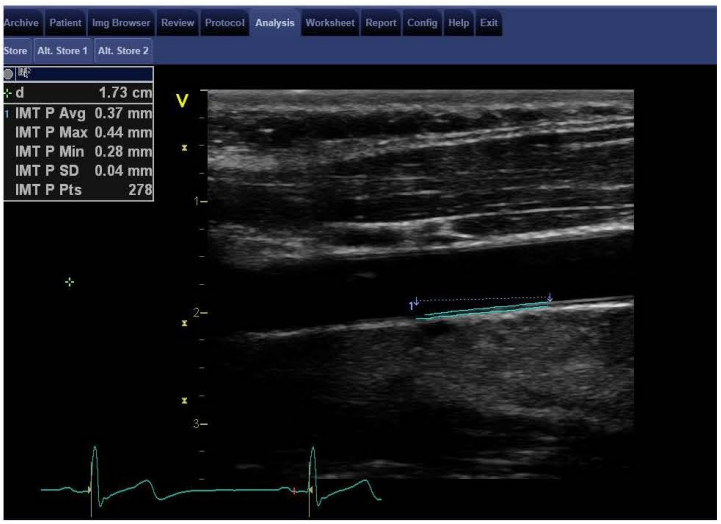
Fitness	Pre-Intervention	Post Intervention
Resting HR	71 bpm	65 bpm
Predicted VO_{2max}	29.5 ml·kg^{-1}·min^{-1}	39.5 ml·kg^{-1}·min^{-1}

* Your results for this variable are outside the recommendations. There may be nothing to worry about but should you be concerned please consult your local GP or healthcare professional.

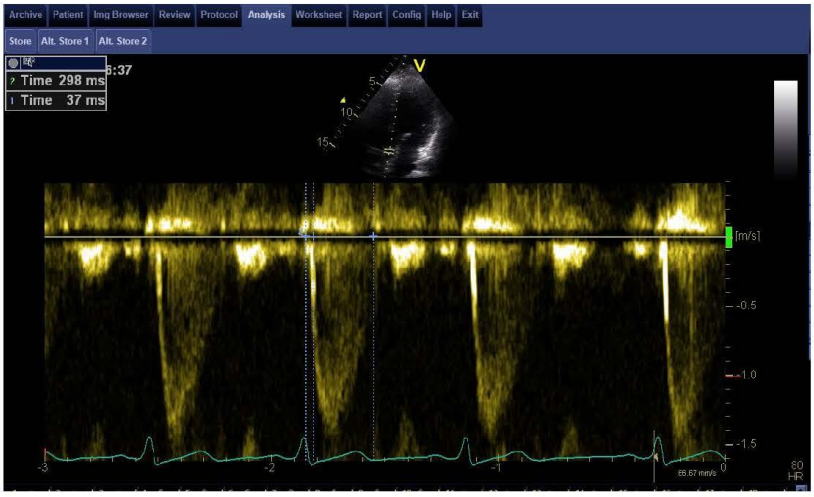
Table 1. Normality. Pre and Post-intervention. Cardiometabolic and fitness data.

	Pre (n = 30)						Post (n = 30)					
Variable	**Shapiro-Wilk**	***df***	**Skewness**	**Kurtosis**	**Group Mean (SD)**	**Group median**	**Shapiro-Wilk**	***df***	**Skewness**	**Kurtosis**	**Group Mean (SD)**	**Group median**
Body mass (kg)	0.055	30	0.588	-0.664	85.31 (19.16)	80.90	0.106	30	0.627	-0.397	85.29 (19.94)	80.55
Body mass index (kg/m^2)	0.090	30	0.500	-0.778	31.00 (5.94)	30.11	0.159	30	0.551	-0.551	30.83 (6.10)	29.95
Waist circumference (cm)	0.019	30	0.863	-0.051	91.27 (10.39)	87.65	0.027	30	0.906	0.218	87.27 (9.93)	85.15
Hip circumference (cm)	0.075	30	0.664	-0.468	113.42 (12.66)	110.35	0.126	30	0.589	0.281	113.05 (12.81)	111.10
Waist-hip-ratio	0.709	30	0.181	-0.372	0.80 (0.04)	0.80	0.479	30	0.374	-0.559	0.77 (0.04)	0.77
Systolic BP (mmHg)	0.678	30	0.129	-0.130	118.16 (9.89)	118.50	0.342	30	0.635	0.294	114.30 (10.17)	113.50
Diastolic BP (mmHg)	0.250	30	0.121	-1.039	65.40 (7.11)	66.00	0.001	30	1.225	0.772	62.37 (7.84)	59.50
Resting heartrate (bpm)	0.912	30	-0.038	-0.173	71.60 (12.24)	71.00	0.364	30	0.213	-0.627	67.83 (8.19)	67.00
Total cholesterol (mmol/l)	0.768	30	0.140	-0.565	4.40 (0.57)	4.31	0.655	30	0.437	0.469	4.31 (0.69)	4.28
HDL-chol (mmol/l)	0.014	30	0.392	-0.1255	1.76 (0.50)	1.63	0.081	30	-0.160	-1.105	1.94 (0.48)	1.91
Triglycerides (mmol/l) #	0.000	30	1.510	1.524	1.29 (0.51)	1.06	0.000	30	1.567	2.912	1.42 (0.67)	1.11
Fasting glucose (mmol/l) #	0.000	30	-3.759	17.862	4.44 (0.94)	4.65	0.737	30	0.346	0.873	4.54 (0.47)	4.60
Fasting insulin (mU/l) #	0.024	30	1.217	2.867	8.64 (5.06)	8.00	0.025	30	0.771	0.093	7.83 (2.64)	7.00
HOMA-IR #	0.030	30	1.152	2.346	1.77 (1.07)	1.70	0.129	30	0.303	-0.084	1.58 (0.54)	1.51
hs-CRP (mg/l) #	0.005	30	0.980	0.320	3.68 (3.05)	2.61	0.000	30	1.455	1.436	4.34 (4.47)	2.76
Predicted VO_{2max} (l/min)	0.036	30	-0.795	3.525	2.40 (0.72)	2.36	0.590	30	0.252	0.009	2.67 (0.59)	2.66
Physical activity (m/wk) #	0.032	30	0.740	-0.367	105.00 (77.46)	87.50	0.543	30	-0.188	-0.650	221.33 (105.66)	227.50

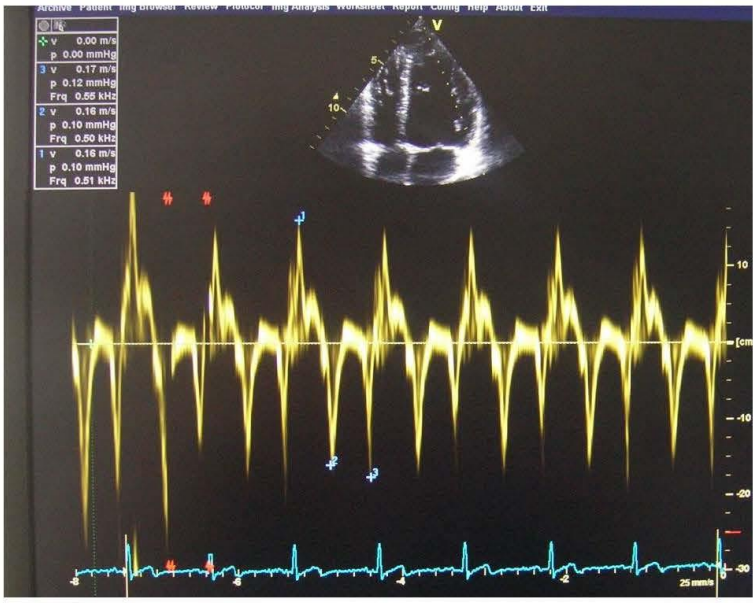
Appendix 22: Example Output from EchoPac Analyses



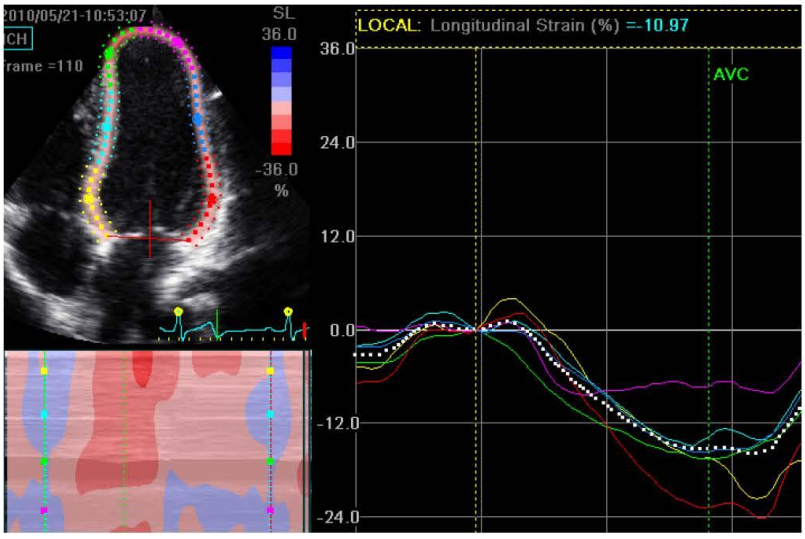
A. Intima-media thickness



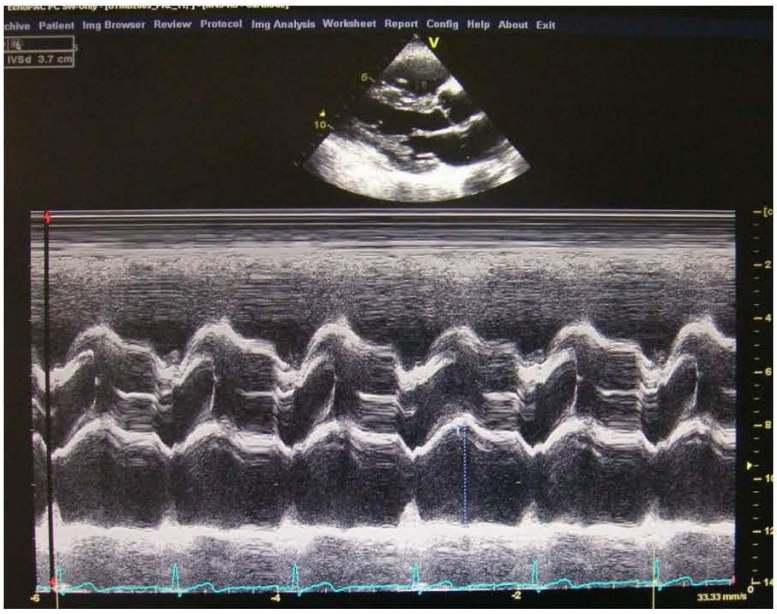
B. Pulsed Doppler



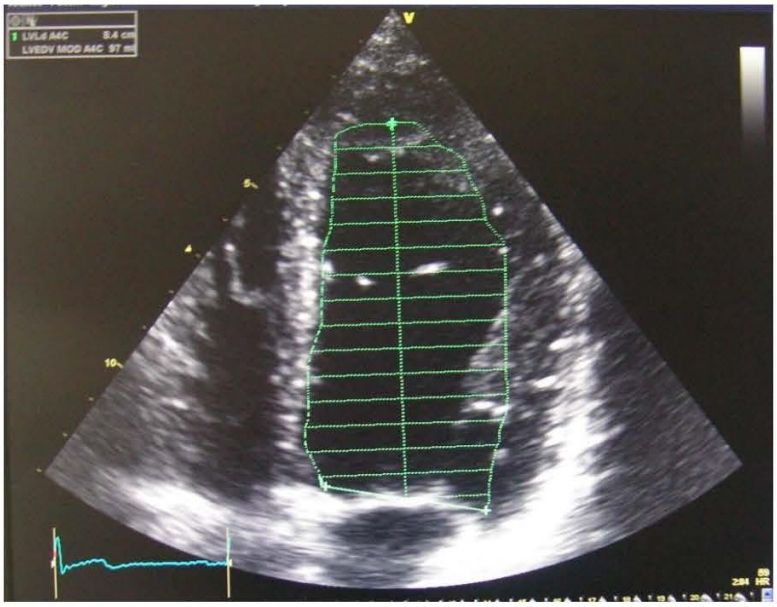
C. Tissue Doppler Imaging



D. Longitudinal strain



E. M-Mode chamber quantification



F. Simpson's bi-plane ejection fraction

END OF DOCUMENT