Impact of Dietary and Behavioural Factors on Obesity and Response to Treatment

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Abstract

Worldwide obesity prevalence has never been so great. Deceleration of this disturbing trend is critical from a public health and economic perspective and for the individual, for whom the physiological and psychological consequences of obesity can be debilitating. The pathogenesis of obesity is multifactorial. Our genetic makeup has predisposed susceptible humans to weight gain when exposed to the modern "obesogenic" environment. Currently available medical and behavioural obesity treatments most often fail to produce sustained weight loss. Inability to maintain behaviours conducive to weight loss maintenance is a commonly cited cause. For clinically severe obesity bariatric surgery is considered the most reliable and durable intervention. Despite its growing popularity, the impact of pre- and post-operative behavioural patterns on surgical outcomes is unclear, and empirical evidence to support important aspects of dietary and behavioural management is lacking.

This thesis aimed to provide an evidence base to direct key features of pre-and post-surgical care of the bariatric surgery recipient.

Pre-operative dietary management of the bariatric surgery patient increasingly involves a very-low-energy diet (VLED) to minimize operative risk. This thesis addressed previously unexplored aspects of efficacy, acceptability and safety of pre-operative VLED. In a prospective cohort (n=32), serial abdominal imaging revealed a significant mean decline in liver volume; the greatest size reduction occurring in the first 2 weeks of weight loss. Predictors of initial liver volume and subsequent liver volume reduction were investigated. The safety of rapid weight loss in subjects at high risk of non-alcoholic steatohepatitis (NASH) was also explored. The studies suggest that VLEDs

are a safe and acceptable means of pre-operative weight loss in the majority. A modified regimen to elicit slower weight loss may be warranted in those at high risk of NASH.

A prospective study explored pre- and post-surgical dietary and behavioural patterns, and predictors of post-surgical weight loss and quality of life outcomes 12-months after Lap-band surgery (n=129). Behavioural patterns underwent marked change. Characteristics associated with positive outcomes included higher post-surgical levels of physical functioning and physical activity, lower hunger and the absence of a "grazing" pattern of eating.

To investigate the clinical significance of disordered eating patterns, cross-sectional data were collected from three groups differing in body weight and treatment-seeking status (n=431). This study helped to characterize the core behavioural features of binge eating disorder (BED) and the night eating syndrome (NES) most closely associated with psychological distress. In binge eaters, feelings of loss of control over eating appeared most significant. Among night eaters, nocturnal snacking (waking to eat) was associated with the highest level of psychopathology.

In summary, this thesis provides evidence to direct pre- and post-surgical behavioural management of the bariatric surgery recipient. The clinical significance of "disordered" eating patterns is explored, and patients who may benefit from closer monitoring or more intensive post-operative interventional therapy are identified.

General Declaration

I hereby declare that this thesis contains no material which has been accepted for the award of any other degree or diploma at any university or equivalent institution and that, to the best of my knowledge and belief, this thesis contains no material previously published or written by another person, except where due reference is made in the text of the thesis.

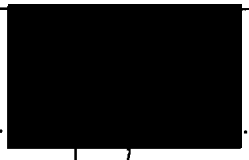
This thesis includes six original papers published in peer reviewed journals and one unpublished manuscript. The ideas, development and writing up of all the papers in the thesis were the principal responsibility of myself, the candidate, working within the Monash University Centre for Obesity Research and Education under the supervision of Professor Paul O'Brien and Associate Professor John Dixon.

The inclusion of co-authors reflects the fact that the work came from active collaboration between researchers and acknowledges input into team-based research.

My contribution to the work involved the following:

Thesis chapter	Publication title	Publication status	Nature and extent of candidate's contribution
4	Preoperative weight loss by very low calorie diet: Quantitation of changes in liver and abdominal fat by serial imaging	Published	Involved in the design of the experiment. Responsible for running the study, most data collection, tabulation, analysis of data and writing the manuscript.
5	Liver histology after VLED in morbidly obese persons at high risk for NASH: Changes and challenges	Unpublished manuscript	Involved in the design of the experiment. Responsible for running the study, most data collection, tabulation, analysis of data and writing the manuscript.
7	Night Eating Syndrome: Impact on Bariatric Surgery	Published	Collection and analysis of data and writing the manuscript.

8	Night eating syndrome and nocturnal snacking: association with obesity, binge eating and psychological distress	Published	Responsible for study design, all data collection and tabulation, analysis of data and writing the manuscript.
9	Loss of control is central to psychological disturbance associated with binge eating disorder	In Press	Responsible for study design, all data collection and tabulation, analysis of data and writing the manuscript.
11	Hunger control and regular physical activity facilitate weight loss after laparoscopic adjustable gastric banding	In Press	Responsible for study design, all data collection and tabulation, analysis of data and writing the manuscript.
12	Grazing and feelings of loss of control over eating: two high risk factors following bariatric surgery	In Press	Responsible for study design, all data collection and tabulation, analysis of data and writing the manuscript.

Signed: 

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And finally, I would like to dedicate this thesis to my Uncle Jim who passed away earlier this year. Above all others, Jim truly enjoyed discussing the intricacies of my research. For me, his wit and intelligence will never be forgotten.

Publications Arising

Colles S, Dixon J, Marks P, Strauss B, O'Brien P. Preoperative weight loss by very low calorie diet: Quantitation of changes in liver and abdominal fat by serial imaging. Am J Clin Nutr 2006; **84**(2): 304-11.

Colles S, Dixon J. Night Eating Syndrome: Impact on Bariatric Surgery. *Obes Surg* 2006; **16**(7): 811-20.

Colles S, Dixon J, O'Brien P. Night eating syndrome and nocturnal snacking: association with obesity, binge eating and psychological distress. *Int J Obes*, 2007; **31**(11): 1722-30.

Colles S, Dixon J, O'Brien P. Loss of control is central to psychological disturbance associated with binge eating disorder. In Press *Obesity* 2007

Colles S, Dixon J, O'Brien P. Hunger control and regular physical activity facilitate weight loss after laparoscopic adjustable gastric banding. In Press *Obes Surg* 2007

Colles S, Dixon J, O'Brien P. Grazing and feelings of loss of control over eating: two high risk factors following bariatric surgery. In Press *Obesity* 2007

Invited Presentations

21st Annual Scientific Meeting of the Obesity Surgery Society of Australia and NZ, Margaret River, 2007.

"Variations in adopted behaviours affect energy balance & weight loss success"

"Disordered" and "non-normative" eating and bariatric surgery: which behaviours are high risk?"

20th Annual Scientific Meeting of the Obesity Surgery Society of Australia and NZ, Noosa, 2005.

"Pre-operative Weight Loss: Why and How?"

13th Annual Scientific Meeting of the Australasian Society for the Study of Obesity, Brisbane, 2004.

"BED and NES: The role and significance of eating disorders in obesity management"

Prizes

Senior Medical Staff Prize for Clinical Research, The Alfred Hospital, Melbourne, 2006

Student prize for best oral presentation, 14th Annual Scientific Meeting of the Australasian Society for the Study of Obesity, 2005

Abstracts Presented

Oral Presentations

The 11th World Congress of the International Federation for the Surgery of Obesity, Sydney, 2006.

"Preoperative weight loss by VLCD: Quantitation of changes in liver and abdominal fat by serial imaging"

"Binge eating disorder and the night eating syndrome: prevalence in sub-groups of the Australian population, and association with body weight and psychopathology"

14th Annual Scientific Meeting of the Australasian Society for the Study of Obesity, Adelaide, 2005.

"A prospective study of the effect of a 12-week VLCD on health status, liver size and abdominal adiposity in the severely obese"

29th Annual Scientific Meeting of the Nutrition Society of Australia, Melbourne, 2005.

"A prospective study of the effect of a 12-week VLCD on health status, liver size and abdominal adiposity in the severely obese"

20th Annual Scientific Meeting of the Obesity Surgery Society of Australia and NZ, Noosa, 2005.

"A prospective study of the effect of a 12-week VLCD on health status, liver size and abdominal adiposity in the severely obese"

"Binge Eating Disorder: Prevalence and Correlates in Sub-Groups of the Australian Population"

Poster Presentations

NAASO: The Obesity Society Annual Scientific Meeting, New Orleans, 2007.

"Loss of control is central to psychological disturbance associated with binge eating disorder"

"Subjective hunger and leisure time physical activity predict weight loss 12 months after laparoscopic adjustable gastric banding"

"Grazing and feelings of loss of control over eating: two high risk factors following bariatric surgery"

15th Annual Scientific Meeting of the Australasian Society for the Study of Obesity, Canberra, 2007.

"Loss of control is central to psychological disturbance associated with binge eating disorder"

"Subjective hunger and leisure time physical activity predict weight loss 12 months after laparoscopic adjustable gastric banding"

"Grazing and feelings of loss of control over eating: two high risk factors following bariatric surgery"

The Alfred Hospital Research Week, Melbourne, 2007.

"Loss of control is central to psychological disturbance associated with binge eating disorder"

"Subjective hunger and leisure time physical activity predict weight loss 12 months after laparoscopic adjustable gastric banding"

"Grazing and feelings of loss of control over eating: two high risk factors following bariatric surgery"

The 15th European Congress on Obesity, Budapest, 2007.

"Rapid weight loss and NASH: Changes in liver histology in high risk individuals"

"Binge eating and binge eating disorder: Measures of psychological distress are graded according to binge volume and loss of eating control, but not binge frequency"

The 10th International Congress on Obesity, Sydney, 2006.

"Preoperative weight loss by VLCD: Quantitation of changes in liver and abdominal fat by serial imaging"

"Binge eating disorder and the night eating syndrome: prevalence in sub-groups of the Australian population, and association with body weight and psychopathology"

The Alfred Hospital Research Week, Melbourne, 2006.

"Preoperative weight loss by VLCD: Quantitation of changes in liver and abdominal fat by serial imaging"

"Binge eating disorder and the night eating syndrome: prevalence in sub-groups of the Australian population, and association with body weight and psychopathology"

14th Annual Scientific Meeting of the Australasian Society for the Study of Obesity, Sydney, 2005.

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20th Annual Scientific Meeting of the Obesity Surgery Society of Australia and NZ, Noosa, 2005.

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List of Abbreviations and Symbols

AGB; adjustable gastric band

ALP; alanine phosphatase

ALT; alanine aminotransferase

AD; appearance dissatisfaction

AE; appearance evaluation

AO; appearance orientation

AST; aspartate aminotransferase

Ax; assessment

B; binges

BDI; Beck Depression Inventory

BE; binge eaters, binge eating

BED; binge eating disorder

BES; Binge eating scale

BMI; body mass index

BPD; biliopancreatic diversion

BSQ; Binge scale questionnaire

CBT; cognitive behavioural therapy

CCVFFQ; Cancer Council Victoria Food Frequency Questionnaire

CHD; coronary heart disease

CHO; carbohydrate

CI; clinical interview

cm; centimetre

cm^2; squared centimetres

CRP; C-reactive protein

C/S; cross-sectional

CT; computed tomography

CV; coefficient of variation

DNA; deoxyribonucleic acid

DSM IV; Diagnostic and statistical manual of mental disorders, 4th Edition

EDE; Eating Disorder Examination

EDNOS; eating disorders not otherwise specified

EI; energy intake

FFQ; food frequency questionnaire

g; gram(s)

GBP; gastric bypass

GGT; gamma glutamyltransferase

HbA1c; glycosylated haemoglobin A_{1c}

HDL cholesterol; high density lipoprotein cholesterol

HPA-axis; hypothalamic-pituitary-adrenal axis

HQoL; health-related quality of life

IQR; interquartile range

kcal; kilocalories

kg; kilogram(s)

kg/m^2; kilograms per metres squared

kj; kilojoules

kV; kilovoltage

L; litres

LAGB; laparoscopic adjustable gastric band

LDL cholesterol; low density lipoprotein cholesterol

LFT; liver function tests

LOC; loss of control

L2–L3; second and third lumbar vertebrae

m; month

M; men

mA; milliamps

MBSRQ; Multidimensional Body Self Relations Questionnaire

MCS; mental component summary

MC4R; melanocortin 4 receptor

mg/L; milligrams per litre

MHQoL; mental health-related quality of life

Mj ; megajoules

mm; millimetre

mm^3; cubic millimetres

mmHg; millimeters of mercury

mmol/L; millimoles per litre

ms; milliseconds

MRI; magnetic resonance imaging

n; number of subjects

N/A; not applicable

NAFLD; non-alcoholic fatty liver disease

NASH; non-alcoholic steatohepatitis

NBE; non-binge eaters

NEDS; night eating/drinking syndrome

NES; night eating syndrome

NHMRC; National Health and Medical Research Council

NSRED; nocturnal sleep-related eating disorders

OSA; obstructive sleep apnoea

P; prospective

PCS; physical component summary

Q; questionnaire

QEWP-R; Questionnaire on Eating and Weight Patterns – Revised

QoL; quality of life

r; correlation

R; retrospective

RDI; recommended dietary intake

RYGB; roux-en-Y gastric bypass

s; second

SAT; subcutaneous adipose tissue

SCID; Structured clinical interview

SD; standard deviation

SF-36; Medical Outcomes Trust Short Form-36

SS CI; semi structured clinical interview

TAG; triglyceride

TFEQ; Three Factor Eating Questionnaire

umol/L; micromoles per litre

VAT; visceral adipose tissue

VBG; vertical banded gastroplasty

VLCD; very low calorie diet

VLED; very low energy diet

W; women

WHO; World Health Organization

4DFR; 4-day food record

<; less than

>; greater than

≤; less than or equal to

≥; greater than or equal to

γGT, gamma glutamyltransferase

%EWL; percentage excess weight loss

%WL; percentage weight loss

CHAPTER 1: Introduction

Thesis Rationale and Overview

The worldwide prevalence of overweight and obesity has escalated in recent decades, and is now considered a global health priority by the World Health Organization (WHO) [1]. Deceleration of this disturbing trend is critical from a public health and economic perspective, and also for the individual, for whom the physiological and psychological consequences of obesity can be debilitating. Of great concern is the fact that behavioural and lifestyle approaches to weight loss are rarely effective. This is especially true in persons with clinically severe obesity.

At present, bariatric surgery is the only reliable and durable means to attain significant weight loss in the severely obese. Despite its increasing popularity, there is little empirical data to direct important aspects of pre- and post-surgical dietary and behavioural management. This research set out to investigate several areas of uncertainty related to the dietary and behavioural management of the bariatric surgery patient. It aimed to provide a significant contribution to the evidence base supporting best practice.

There are thirteen chapters within this thesis.

Chapter 1 outlines the economic, medical, physical and psychological consequences of obesity. The efficacy of current weight loss treatments and effect of weight loss on co-morbidity of obesity are reviewed. The discussion then focuses on potential benefits and hazards of rapid pre-surgical weight loss on hepatic change. The chapter concludes with two research questions that relate to: 1) the efficacy and acceptability of a pre-operative weight loss intervention, and 2) the effect of rapid pre-operative weight loss on liver morphology in a select group of morbidly obese bariatric candidates at high risk of non-alcoholic steatohepatitis (NASH).

Chapter 2 reviews binge eating disorder (BED) and the night eating syndrome (NES); two eating-related conditions commonly found among bariatric surgery candidates. Research questions address the clinical significance of the core behavioural features of BED and NES. Other eating-related behaviours in the bariatric literature including

feelings of loss of control related to eating and "grazing", and exercise-related behaviours are reviewed. The paucity of prospective data to address the association between pre- and post-surgical behaviour is highlighted. Research questions are posed regarding the nature and extent of change in selected eating and exercise behaviours after laparoscopic adjustable gastric banding (LAGB) and the association with surgical outcome.

Chapter 3 describes the methods used in chapters 4 and 5 of this thesis to bring about pre-operative weight loss, and to assess the pattern of change in liver volume and abdominal adipose tissue with weight loss.

Chapter 4 presents a published study of 32 bariatric surgery candidates which prospectively investigates the pattern of liver volume reduction during rapid pre-surgical weight loss. This study is the first to document the pattern of liver volume decline in this setting, and to report clinical predictors of hepatomegaly and liver size reduction.

Chapter 5 presents a manuscript of a prospective study investigating the change in liver morphology with rapid weight loss in eight severely obese patients at high risk of NASH. Results are discussed within the light of problems encountered obtaining and assessing tissue samples in this population.

Chapter 6 describes the methods used to collect data on dietary composition, eating and exercise-related behaviours and markers of psychological distress for the studies detailed in chapters 8,9,11 and 12.

Chapter 7 presents a published critical analysis of current theory on NES, and its impact on bariatric surgery.

Chapter 8 presents a published cross-sectional study which investigates the clinical significance of NES and night-time snacking in a cohort of 431 subjects ranging in BMI and treatment seeking status. This study provides evidence of a strong association between NES and obesity, and is the first to compare the extent of psychological distress associated with separate behavioural features of NES.

Chapter 9 presents data from the cross-sectional sample of 431 subjects. It provides an original contribution by examining the diagnostic features of BED most strongly related

to obesity and psychological disturbance. This manuscript has been accepted for publication.

Chapter 10 outlines additional methods used to assess post-operative eating and exercise-related behaviours in chapters 11 and 12.

Chapter 11 presents a study of 129 subjects before and 12 months after LAGB. This manuscript, accepted for publication, prospectively measures a range of eating and exercise-related behaviours. It identifies a number of behavioural characteristics which are independently predictive of post-operative weight loss.

Chapter 12 presents prospective data from the same cohort, and represents one of the first attempts to characterize "non-normative" eating patterns and their influence on outcomes after bariatric surgery. This manuscript has also been accepted for publication.

Chapter 13 summarizes the findings of this thesis, and discusses opportunities for future research.

Obesity: Defining the Problem

Fat is primarily stored within the human body as triglyceride. The main reservoir for triglyceride storage is the adipocyte or fat cell. Adipocytes are predominately stored as human adipose tissue. Body fat is a potent energy store, essential for good health. Among other roles it pads and protects certain regions of the body and is the site of hormone synthesis. Body fat normally accounts for approximately 25% of the body weight of women, and 18% in men [2]. The obese state occurs when the quantity and size of fat cells increases disproportionately to the other tissues of the body.

The Rising Tide of Obesity

At no other time has the worldwide prevalence of overweight and obesity been so great. Observed initially in the industrialized world, this global trend has now extended into developing nations [1, 3] and shows no signs of abating [4]. The unprecedented rise in obesity is now so universal that it is set to overtake under nutrition and communicable diseases as the most widespread health crises [5].

Analysis of the extent of the problem in Australia reveals disturbing statistics. In 1980, the first National Heart Foundation risk-factor prevalence study found 48% of men and 27% of women aged 25-64 years living in capital cities were overweight, and 7.2% of men and 7.0% of women were obese [6]. In 2000, rates of overweight among the same population segment had risen to 65% for men and 45% for women. Most outstanding however, was the rise in obesity prevalence. Rates in men more than doubled to 17.1%, and almost tripled in women to 18.9% [7]. Data from the Australian Institute of Health and Welfare [8] and the "Ausdiab" study [9] support that between 17% to 21% of adult Australians are currently obese. Children and adolescents have suffered a similar fate. Using the new international standard definitions published by the International Obesity Taskforce, the prevalence of overweight in boys rose from 9.3% to 15%, and 10.6% to 15.8% in girls in just one decade from 1985 to 1995 [10]. Obesity prevalence more than tripled in both sexes, from 1.4% to 4.5% in boys and 1.2% to 5.3% in girls.

The prevalence of overweight and obesity in Australia is now comparable to the USA, where it has been estimated that in excess of 65% of adults are currently overweight or obese [11]. Although these conditions have risen in the general US population, the

greatest increase over the last 2 decades has been in the prevalence of extreme obesity. For example, class I obesity (BMI $\geq$30kg/m^2) rose from 15% in 1985 to over 30% in 2000 [11]. In a similar timeframe adults with a BMI $\geq$50kg/m increased by a factor of 5, from 1 in 2000 to 1 in 400 [12]. Over the past 30 years, the prevalence of overweight in paediatric groups has nearly tripled [13]. Approximately 16.1% of US adolescents (12-19 years) are now considered overweight (BMI $\geq 95^{th}$ percentile for age) [14]. Disturbingly, studies indicate that 50-77% of these adolescents will become obese adults [15, 16].

The Economic Cost of Obesity

Obesity is now considered the most significant dilemma confronting current health care systems, and has overtaken the public health burden placed on communities by smoking and alcohol abuse [17]. In Australia during 1989-1990, total direct costs (the cost to the community) and indirect costs (resulting from a reduction in goods or services, or premature death) associated with obesity were calculated at AU$736 million [18]. In the order of 60% of these costs were attributed to co-morbid diseases of obesity, namely coronary heart disease (CHD) and hypertension. Health care costs have been estimated 44% higher among patients with a BMI greater than 35kg/m^2 compared to those in the healthy weight range [19]. In 1996, experts re-estimated the direct obesity-related costs alone to be in the vicinity of AU$0.84-1.4 billion [20]. Although sizeable, Australian figures are dwarfed by estimates of the economic burden of the obesity in the USA. In 1995, direct medical costs were reckoned at US$52 billion [21]. It has been conservatively estimated that obesity costs developed nations between 2 – 7% of their overall health care expenditure [1].

Measurement of Obesity

The WHO has defined obesity as a BMI equal to or greater than 30kg/m² [1]. BMI classifications are listed in **Table 1.1**.

Table 1.1 The World Health Organisation classification of weight by body mass index [4]

Classification	BMI (kg/m²)	Risk of Co-morbidity
Underweight	<18.5	Low (but risk of other clinical problems increased)
Normal Weight	18.5 – 24.9	Average
Overweight	25 – 29.9	Increased
Obese I	30 – 34.9	Moderate
Obese II	35 – 39.9	Severe
Obese III	≥40	Very Severe

After controlling potential confounders such as cigarette smoking, age and unintentional weight loss, the risk of mortality from increasing adiposity is amplified at a BMI above 25 kg/m² [22, 23]. This risk continues to increase with increasing body fatness, and substantially so over BMI 35kg/m². Body mass index is accepted as a useful general measure of body fatness and general disease risk [18] however, on an individual basis, the application of BMI has limitations. In the elderly, BMI may lead to under-estimations of body fatness due to a relatively low lean tissue mass [24]. Persons with a high level of musculature are likely to have body fatness over-estimated [25]. Furthermore, measures of BMI do not take into account the pattern of body fat distribution. Marked visceral (central) adiposity significantly increases the risk of

numerous co-morbid diseases [26], including CHD and diabetes [28-31]. Central adiposity is a key component of the "metabolic syndrome" [27, 28]. Measurement of central adiposity minimizes the limitations of BMI as a single marker of disease risk.

Central obesity, including the relative distribution of central subcutaneous adipose tissue (SAT) and visceral adipose tissue (VAT) is most accurately measured by radiological methods. Assessment of VAT by computed tomography (CT) [29-31] and magnetic resonance imaging (MRI) [32-34] offers high accuracy, reproducibility and clinical utility. However, these methods are expensive, time consuming and can be difficult to access. In mainstream clinical practice a less expensive, more easily obtainable proxy is the measurement of waist circumference [35, 36]. Based on studies in Caucasian adults, the WHO has published waist circumference measurements indicative of an increased risk of metabolic complications of obesity [1] (**Table 1.2**).

Table 1.2 The World Health Organisation classification of waist circumference [1]

	Increased Risk	**Substantially Increased Risk**
Men	≥94 cm	≥102 cm
Women	≥80 cm	≥88 cm

The Consequences of Obesity and Benefits of Weight Loss

The disease burden of obesity is high. Excessive adiposity carries with it a heightened risk of a range of medical, physical and psychological complications and conditions comprising most of the body's organ systems. Co-morbidities such as type 2 diabetes, CHD and sleep apnoea can be debilitating and possibly life threatening. Other complications such as urinary incontinence, osteoarthritis and gastro-oesophageal reflux disease, while not life threatening, may be incapacitating or painful. Psychosocial problems including symptoms of depression and body image distress are highly

prevalent among obese persons seeking weight loss treatment. Health-related quality of life (QoL) is often lower than persons who are "normal" weight. Moreover, obesity can shorten the lifespan. The following section provides an overview of the consequences of obesity and studies that have demonstrated reversal of co-morbid disease with weight loss. Particular attention is paid to the psychological associates of obesity explored in this thesis.

Mortality

In 1999, approximately 280,000 deaths in the United States were attributed to obesity [37]. More recently, obesity has been recognized as the second leading cause of preventable and premature mortality behind smoking, estimated to cause around 385,000 US deaths per year [38]. Numerous epidemiological studies have documented a strong, positive association between adiposity and death rate [19, 23, 39, 40]. For example, compared to persons in the healthy weight range, a large US cohort showed a significantly higher risk of death from cancer in those of BMI $\geq$35kg/m^2 [19].

Studies comparing obese persons to those who have achieved sustained weight loss demonstrate a reversal of mortality risk if weight reduction can be achieved. Christou et al. reported a reduction in the relative risk of mortality by 89% in a cohort of 1,035 bariatric surgery patients who lost on average 67% of excess weight over a 5-year period [41]. Compared to matched controls, the weight-reduced group recorded significantly lower rates of cardiovascular and infectious diseases, respiratory conditions, malignancy, endocrine and musculoskeletal disorders, and psychiatric and mental problems. As expected, markedly lower rates of health care usage, hospitalization, and mean total health care costs were also observed. A very recent report compared cumulative death rates between subjects and controls in the Swedish Obese Subjects study 16 years following recruitment [42]. After adjustment for possible confounding factors, bariatric surgery in this cohort was shown to reduce the risk of death by 29%.

Medical and Physical Co-morbidity

The increased health risks associated with obesity are numerous and well documented. While the relative risk of associated co-morbid conditions varies, obesity has been related to an increased probability of:

1. Metabolic diseases such as insulin resistance, type 2 diabetes mellitus and dyslipidaemia, and the cluster of conditions known as the metabolic syndrome. The metabolic syndrome is characterised by hypertension, dyslipidaemia (raised plasma triglycerides and reduced high-density lipoprotein cholesterol), insulin resistance, impaired glucose tolerance and central obesity [43].
2. Vascular diseases such as CHD, hypertension and cerebrovascular disease.
3. Respiratory system diseases and abnormalities such as obesity-hypoventilation syndrome, obstructive sleep apnoea (OSA), asthma and breathlessness.
4. Digestive system abnormalities such as gallbladder disease, non-alcoholic fatty liver disease (NAFLD) and non-alcoholic steatohepatitis (NASH), hepatomegaly and gastro-oesophageal reflux disease.
5. Increased risk of cancers of the breast, endometrium, ovaries, gallbladder, colon and rectum, prostate and kidney.
6. Renal system abnormalities and problems such as proteinuria and urinary incontinence.
7. Reproductive system problems such as polycystic ovary syndrome, reproductive hormone abnormalities and infertility.
8. Mechanical complications such as osteoarthritis, joint (particularly knee) pain and back problems.
9. Haemostatic and fibrinolytic abnormalities.
10. Nervous system problems such as pseudotumour cerebri.
11. Immune system dysfunction.
12. Raised levels of chronic inflammatory markers.
13. Skin diseases and problems [1, 18].

Weight Loss

There is good evidence from controlled clinical trials and observational studies that weight loss reverses or reduces co-morbid disease. Behavioural treatments eliciting weight losses between 5% and 10% have demonstrated improvements in serum lipids [44, 45], and reductions in atherosclerotic lesions and CHD-related mortality [46]. Marked improvements in hypertension [47] and OSA [48] have also been demonstrated. Modest weight losses achieved through a combination of pharmacotherapy and dietary modification have also bought about improvement in medical co-morbidities [49-51]. Evidence from studies involving surgical weight loss provides further unequivocal data. A systematic review and meta-analysis of bariatric surgery showed marked post-operative improvements in insulin resistance and type 2 diabetes, hyperlipidaemia, hypertension and OSA [52]. More specifically, surgically induced weight loss has bought about either resolution or marked improvement in the clinical signs of type 2 diabetes in 90% of patients 12 months after LAGB [53]. Another prospective study with an average follow-up of 7.6 years post roux-en-Y gastric bypass (RYGB), reported normal fasting blood glucose and glycosylated haemoglobin levels in 83% of patient with pre-surgical type 2 diabetes [54]. Almost complete resolution of basal impaired glucose tolerance was also reported. Weight loss appears to reverse the course of type 2 diabetes, improving insulin sensitivity and pancreatic beta cell function [55]. Significant improvements in overall cardiac risk factor profile [56] and normalisation of dyslipidaemias and hypertriglyceridaemias are also well documented [57, 58]. The incidence and severity of bronchial asthma [59] and obesity hypoventilation syndrome reduce. Reflux oesophagitis improves [60, 61], as does polycystic ovarian syndrome [62]. Improvement in physical co-morbidities of obesity such as osteoarthritis and urinary incontinence has also been reported following surgical weight loss [63].

Psychosocial Co-morbidity

There is significant and widespread social stigma attached to obesity. Individuals suffering from obesity may be seen as unfit, lazy, lacking self-discipline, stupid and less competent [64]. These beliefs can manifest as discrimination in educational and workplace opportunities and health care provision, and influence or exacerbate feelings of poor self-esteem and low self-worth. Women in particular may be at greater risk of

negative societal and self-attitudes [65]. High levels of emotional distress are common among those seeking bariatric surgery. Following a weight loss of 45kg or more, gastric bypass patients stated that they would rather be an amputee, deaf, blind or diabetic than morbidly obese, and would reject the offer to become a multimillionaire if it entailed becoming obese again [66]. These findings support that the extent of the psychological disturbance associated with the obese state may be more disabling to the individual than related medical co-morbidity.

In this thesis symptoms of depression, body image distress and mental health-related QoL have been used as three markers of psychological distress. These markers were used to assess the extent of emotional disturbance related to body weight, to individual features of BED and NES, and to eating behaviours before and after LAGB.

Symptoms of Depression

Although inconsistently linked with obesity, symptoms of depression typically show a positive association with adiposity which is particularly evident among obese treatment seekers [67]. As a group, those who seek surgical weight loss are at very high risk of depression; particularly younger women with greater body image dissatisfaction [68]. The association between obesity and depression may relate to factors such as poor body image and self-esteem, social stigmatization, the disease burden of obesity, or the presence of disordered eating patterns such as BED.

Behavioural weight loss treatments have been associated with short-term improvements in general psychopathology and symptoms of depression, but positive changes in mood may deteriorate with weight regain [69, 70]. Marked improvement in the incidence and severity of depressive symptoms has been documented after surgically-induced weight loss [68, 71, 72]. These improvements appear to be sustained in the medium-term in those who achieve weight loss maintenance [68].

Body Image Distress

Body image refers to the perceptions, attitudes and feelings an individual experiences about their body, particularly in relation to its physical appearance. In pre-industrialized societies overweight and obesity were linked with positive characteristics such as strength, prosperity, prestige and spiritual power [73]. Westernized cultures consider

body fatness physically unattractive and ascribed with numerous undesirable character traits. This has created a cultural ideology to be thin which often becomes manifest in the early childhood years [74] and typically places more pressure on females than males.

Distress related to one's body image can have a significant effect on psychosocial functioning, and has been associated with extreme concerns about body weight and shape, symptoms of depression, poorer QoL and low self-esteem [75-77]. Extreme levels of body image disturbance are common in persons with BED [78, 79] and among bariatric surgery candidates [80-82], and may be inter-related in some persons. Negative issues surrounding body image have been shown to improve following surgically-induced weight loss [80-82]. However, even after significant weight change, measures of body image distress have not declined to the level of never-obese controls [80, 81]. This residual body image disturbance may reflect fear of weight regain or deep-seated inner beliefs that are independent of actual body weight.

Health-Related Quality of Life

Health-related QoL (HQoL) refers to an individual's personal evaluation of the influence that one or more health conditions have on their overall well-being [83]. Obesity, being associated with numerous medical and psychosocial co-morbidities, displays an inverse relationship with HQoL, decreasing as BMI increases In controlled studies, markers of health-related QoL are significantly poorer in overweight and obese individuals than normal weight controls [84-87]. Persons seeking weight loss treatments are also more likely to report poorer health-related QoL, with seekers of bariatric surgery reporting the greatest impairment [88]. The Medical Outcomes Study Short Form – 36 (SF-36) suggests that obesity impacts QoL related to physical function and fitness to a greater extent than mental health status [89-91]. Published reviews clearly show that HQoL improves following weight loss [86, 92]. The most dramatic improvements have been observed following bariatric surgery [66, 87, 93], with changes in social and physical functioning, emotional and mental health, the experience of bodily pain and energy levels being maintained alongside weight loss out to 4 post-surgical years [87].

Factors Contributing to Obesity Risk

In simplified terms the equation governing weight gain requires that energy intake exceeds expenditure. The positive energy balance which drives weight gain is often small, but occurs over extended periods of time. For example, most individuals gain weight slowly over the course of their life, accumulating less than 1kg per year; a weight gain that requires a daily positive energy balance of approximately 420kj [94]. Yet the cause of positive energy balance and pathogenesis of obesity are complex and multifactorial and involve a combination of environmental, behavioural and genetic factors [95].

Environmental Factors

The worldwide obesity epidemic has been termed a "disease of civilisation" [1]. Technological and societal changes and advances have created modern day "obesogenic" environments [96]. These environments in turn affect behaviours. For example, changes in employment patterns and urban design have decreased the need and opportunity for physical activity, and contributed to reduced levels of incidental daily activity. Migration studies also demonstrate the impact of environmental and societal change on BMI in genetically susceptible persons [97, 98], and the deleterious effects of westernization on indigenous populations such as the Native Americans and Australian Aboriginals are well documented [99, 100].

Dietary Factors

Increased energy intakes have been blamed for the rise in obesity prevalence [101]. Although the extent of this role is in question [106, 107], a range of evidence supports that high energy diets contribute to weight gain. Animal studies clearly show that lean mammals offered a palatable, high energy diet quickly gain weight and become obese [102]. Dietary fat provides more than twice the kilojoules per gram of either carbohydrate or protein. Controlled human studies demonstrate the increased likelihood of fat deposition and weight gain on a high fat, high energy diet [103-106]. While the consumption of a high fat diet does not invariably lead to obesity [107], diets high in fat are typically more energy dense, and provide higher amounts of kilojoules than low fat, complex carbohydrate diets [104, 108]. The WHO has also identified diets high in

refined carbohydrate as potential contributors to weight gain [109]. Habitually high intakes of simple sugars can result in an energy density similar to that of a high fat diet. In developing nations, increased availability and affordability of vegetable oils and refined sugars, and the displacement of traditional ethnic foods has been blamed in part for increasing obesity rates [110]. In today's "obesogenic" environment a wide range of factors may impact on dietary energy density or energy intake:

- Fats and sugars are routinely used in cooking and manufacturing practices to enhance the palatability, appearance, aroma and shelf-life of foods.
- "Fast foods" are typically energy dense, easy to access and extensively advertised [111].
- Portion sizes have increased over the last two to three decades [112], and consumers have become accustomed to "super-sized" meals.
- Less emphasis is being placed on the development of cooking skills, and less time dedicated to meal preparation.
- A greater proportion of meals are consumed outside the home [113].
- Eating in social environments can arouse appetite and delay meal termination without, or perhaps in spite of, the input of internal regulatory mechanisms [114].
- Diets generally seen to be "protective" of obesity are more costly [115, 116].
- The consumption of soft drinks sweetened with high fructose corn syrup has increased markedly, and often accompanies high fat snacks or meals [117, 118].
- Mid-meal snacking appears to be increasing, and snack foods are often high in fat and/or sugar [119].

Physical Activity and Inactivity

In pre-industrialized times, a level of physical exertion was required for food acquisition and daily subsistence. With technological advances in areas such as agricultural production, transportation and telecommunications, and time saving devices such as washing machines, cars and supermarkets, our daily food and lifestyle requirements can be met without the need to be physically active [120-122]. At the same time, sedentary

pastimes such as sitting in front of computers, in the car or behind the desk have increased. High rates of television viewing have been positively associated with obesity development in both children and adults [123-125]. Data from the United States [126] and United Kingdom [127] suggest that the average western diet has actually decreased in fat and energy density. These reports propose that similar or lower energy intakes have been countered by a greater reduction in total energy requirement. Low levels of habitual physical activity and/or a high level of sedentary behaviour are considered by some to be the most important focus of obesity intervention strategies [121, 128].

Total daily energy expenditure is accounted for by the sum of an individual's resting metabolic rate, the thermic effect of food, and the thermic effect of physical activity. Energy expended during physical activity is the most variable component of the total daily energy expenditure, and the only component at least in part under conscious control. Physical activity energy expenditure usually exists in the range of 20-30%, but may comprise near 0% (total inactivity) to greater than 50% in elite athletes. During weight bearing activities energy expenditure is directly proportional to body weight, and thus an obese individual will expend greater amounts of energy performing the same weight bearing activity as a lean individual of similar age and gender [129-131]. However, in obese persons the level of voluntary activity is often reduced. Total physical activity energy expenditure is therefore often similar or lower compared to lean individuals [132]. Physical co-morbidities of obesity such as osteoarthritis and joint pain may be a barrier to physical activity and further perpetuate weight gain or impede weight loss efforts.

Genetics

George Bray stated in 1996 that "genetics load the gun, but the environment pulls the trigger" [133]. It is now well accepted that the process of evolution has primed the human genome to meet the challenges of survival in the harsh days of the hunter-gatherer [111]. Our genes are programmed to arouse a strong drive to eat, store excess calories as adipose tissue, and conserve energy by minimising physical activity when able [114]. In modern societies our encoded genetic efficiency is at best redundant, and in fact deleterious.

Over 430 potential genes, loci and markers that promote a genetic susceptibility to obesity have been identified [134]. Single gene mutations are one known cause of human obesity. Leptin deficiency [135], produced by mutation of the leptin receptor gene, was first shown in rodent models to cause hyperphagia and obesity [136]. Targeted deletion of the melanocortin 4 receptor (MC4R) also results in hyperphagia, hyperinsulinaemia, reduced energy expenditure and obesity [137, 138]. In humans, MC4R mutations are the most common cause of monogenic obesity [172], and are present in 4-5% of children and adults with class II obesity and above [139, 140]. Mutation of this gene has been implicated in the aetiology of severe, early onset obesity [141-143], but does not appear to play a role in common, late-onset obesity [134]. Single gene mutations are too rare to explain the burgeoning obesity crisis.

It is now recognized that numerous chemicals and neurotransmitters operate synergistically through a complex interplay of central and peripheral signals that are processed by chemical receptors located in the hypothalamus and other parts of the brain [144, 145]. Known collectively as the "central control of appetite", this system regulates short-term information regarding meal-to-meal levels of hunger (which determines when, and to some degree how much, food is eaten) and satiety (the inhibition of eating during the mid-meal interval) [146], and longer-term features of energy balance. Anabolic orexigenic hormones that promote an increased energy intake include ghrelin, insulin, neuropeptide Y, agouti-related protein (AgRP) and orexins A and B. Anorectic peptides that oppose weight gain include cholecystokinin, glucagon-like peptide-1, leptin, peptide YY, pro-opiomelanocortin, alpha-melanocyte-stimulating hormone and cocaine-amphetamine-regulated transcript [147, 148]. These homeostatic mechanisms are set towards facilitating a positive energy balance. Whilst catabolic pathways may change in response to internal environmental conditions, anabolic pathways appear poorly suppressed under most circumstances [144].

In addition to the shared environmental and genetic factors, maternal and neonatal nutrition are now believed to have the ability to alter the phenotype, and possibly the genotype of the next generation. Rats fed a high-fat diet have produced offspring with a higher body-fat accumulation than rats fed a low-fat diet reared under similar conditions [149]. Controlled animal studies have also shown that pregnant rats fed a low

protein/energy diet produce hyperphagic offspring with a preference for high-fat foods [150, 151]. In pregnant women, low protein diets may result in an increased risk of childhood obesity [152]. The foetal effects of under-nutrition is a possible explanation for the high prevalence of central obesity and associated metabolic consequences in developing countries [153]. The importance of early nutrition on neonatal programming has also been highlighted in animal experiments [154]. For example, rats weaned onto highly palatable diets that subsequently became obese, were more likely to remain obese and defend this weight in adulthood than never-obese rats [155]. A recent systematic review of the effect of human infant feeding practices and obesity risk in later life concluded that breast feeding was likely to be protective against adult obesity [156]. Foetal programming and epigenetic changes highlight the importance that maternal and infant nutrition play in the future development, or prevention of obesity.

Obesity Treatments and Outcomes

Weight reduction is fundamental to the effective reversal or reduction of co-morbidity associated with obesity. Every year billions of dollars are spent on weight-loss books, plans and programs [157]. These strategies are often highly marketed, but in general offer unsubstantiated advice and claims, and will not be reviewed here. In the scientific literature, single interventions plus combinations of diet, exercise, behaviour therapy, pharmacotherapy and bariatric surgery have all demonstrated the ability to bring about degrees of weight reduction. Weight loss interventions should be based on individual requirements, taking into consideration such issues as the level of overweight or obesity, associated co-morbidity, client preferences, physical ability and level of cognition. **Table 1.3** summarizes the findings of a review of randomised controlled trials and controlled studies undertaken by the National Health and Medical Research Council (NHMRC), reported in Appendices B to G [18]. The efficacy of clinically proven weight loss treatments is based on mean % weight losses at the end of active treatments lasting between one and two years.

Table 1.3 Clinically proven weight losses using a variety of treatment modalities [18]

Weight loss treatment	Mean % weight loss	Mean % weight loss at follow-up
Bariatric surgery[1]	> -24% (range -16 to -37%)	->26% (range 19 to 37%)[2]
VLEDs	-14.7% (range -8.0 to -23.1%)	-4.0% (range -8.3 to +5.0%)[3]
Sibutramine + Lifestyle/diet	-10.7% (range -5.4 to -16.5%)	Not known
Orlistat & low fat diet	-8.6% (range -6.2 to -13.4%)	Not reported
Diet & physical activity	-8.1% (range -15.6 to -4.7%)	~60% of weight regained at 2-6 y
Energy-restricted diets	-6.9% (range -9.7 to -5.5%)	~85% of weight regained at 4-5 y
Behavioural therapy	-5.1% (range -13.2 to -0.2)	~60% of weight regained at 3-5 y
Low fat, reduced energy diets	-4.4% (range -2.9 to -7.8%)	~30% of weight regained at 3-6 y
Physical activity	-2.1% (range -6.4 to +0.8%)	~25% of weight regained at 2-6 y

[1]Studies involving laparoscopic adjustable gastric banding and roux-en-Y gastric bypass
[2]Follow-up period ranged from 3 to 14 years, median follow-up 4 years
[3]VLED without behavioural therapy, follow-up period ranged from 1 to 5 years, median follow-up 1 year

Behavioural Therapies

Behavioural approaches to weight loss aim to help individuals develop new skills to facilitate the uptake and maintenance of beneficial practices and behaviours that will reduce energy intake and maximize energy output. Principles of behavioural therapies commonly include self monitoring, goal setting, stimulus control and problem solving. Counseling often focuses on strategies to identify cues or triggers that initiate inappropriate eating patterns or behaviours, and teaches individuals how to temper and change their response to these cues [158]. Behavioural treatment studies vary, but more commonly involve weekly group meetings for 3 to 6 months, followed by fortnightly review from 6 to 12 months and monthly or bimonthly meetings out to 1 to 2 years. Although behavioural therapies can produce a modest short-term weight loss, these strategies are best combined with other weight loss interventions to produce superior results [159].

Dietary Strategies

Therapies to reduce energy intake are generally acknowledged as the foundation stone of obesity treatment [160]. Conventional strategies seek to bring about a negative energy balance, providing fewer kilojoules than the daily energy requirement. Dietary treatments most often take the form of a low energy diet (a deficit of 2 to 4Mj/day), an energy-restricted diet (providing 4 to 5Mj per day) or a very low energy diet (VLED) (providing 1.9 to 3.4Mj per day). Table 1.3 shows that low energy, ad libitum low-fat diets can produce a small weight reduction over one to two years. Weight loss is enhanced when combined with either pharmacotherapy or physical activity. A low energy diet paired with regular physical activity also facilitates weight loss maintenance. Energy-restricted diets confer greater weight loss than low energy, ad libitum diets, but are of limited value due to extensive weight regain. The very-low-energy diet (VLED) can also result in poor medium-term outcomes however, a significant benefit lies in its ability to induce marked, rapid weight loss in a short duration. Immediate weight reduction is often desirable prior to bariatric surgery when advancement to the operation may be contingent on weight loss or improvement in associated co-morbidity.

Very-Low-Energy Diets

The modern day VLED has a clear safety record and is considered an appropriate for the treatment of class I obesity and above [161]. However, the evolution of VLED was marred by nutritional inadequacy. The earliest VLED, the "protein-sparing modified fast", was introduced in the 1960s [162]. These regimes entailed partial starvation, plus provision of some dietary protein and minerals, or an infusion of amino acids [163]. In the next decade, commercially-available, protein-supplemented starvation formulae became available. These products relied on hydrolyzed protein derived from collagen or gelatin. Both of these early VLEDs lacked essential amino acids, electrolytes, vitamins, minerals and micronutrients, and resulted in severe complications, including sudden death [164]. During the late 1980s problems of nutritional inadequacy were addressed, and VLED formulations were modified to provide complete nutrition. These revisions removed the risk of severe negative nitrogen balance or electrolyte disturbances and rendered VLED suitable as a total meal replacement [165].

Modern VLEDs most commonly involve specially formulated commercial products such as reconstituted powder preparations or "snack bars". With careful planning a VLED can be undertaken using normal food. In addition to generating a large energy deficit, a number of factors can facilitate weight loss using VLED:

- The expediency of readily available meal replacements alongside strict dietary guidelines has been shown to promote dietary compliance compared to an ad-libitum, low calorie diet [166].
- The induction of ketogenesis secondary to low carbohydrate content can aid in the reduction of food preoccupation and reported hunger levels [167, 168] and further assist dietary compliance.
- The swift reduction in body weight, assisted by ketosis, can act as another important motivational factor [169].
- Improvements in the metabolic abnormalities of the metabolic syndrome can occur within the first 4 weeks of weight loss using VLED [170], which enhance general health and compliance.

Medical contraindications to VLED therapy include severe hepatic disease, advancing renal disease, pregnancy and lactation, and acute cerebrovascular or cardiovascular disease [161]. Current drug prescriptions must also be considered. Blood pressure medications may need adjustment due to reductions in hypertension secondary to increased diuresis. In persons with type II diabetes, oral hypoglycaemic agents or insulin also commonly require reduction to prevent hypoglycaemia. Other potential side-effects include postural hypotension, hyperuricaemia and gout, exacerbation of cholelithiasis, constipation, hair loss and iron deficiency in women. Close monitoring and medical supervision throughout the duration of a VLED is recommended [18, 161]. However, side-effects are generally mild and transitory [171].

In the pre-surgical setting, VLED has shown no compromise to wound healing [172] or immune function [173] following weight losses averaging 17kg and 19.6kg respectively. Drop out rates from VLED programs have reportedly ranged from 15% to 45% [161]. A lower attrition rate of 7% has been reported during a 7 to24 week VLED in group of morbidly obese instructed to lose weight prior to elective surgery [174]. From a practical standpoint, specific factors that help and hinder acceptability and compliance to a VLED in the pre-operative setting have not been investigated.

Physical Activity

Interventions to increase energy expenditure often include the establishment of a structured exercise regimen and progressive goal setting. Strategies to overcome barriers to exercise may also be addressed. Advice on how to increase "incidental activity" by incorporating more movement into everyday pursuits is a useful approach for those with poor physical fitness or ability, and the morbidly obese.

As a stand-alone intervention, evidence from predominantly observational studies shows minor weight loss can be attained through participation in regular, high level physical activity [18]. Not only does this level of weight loss not solve the problem of morbid obesity, but these small weight losses were achieved through participation in amounts and levels of physical activity beyond the capability of most persons. The induction of a sizeable energy deficit is more readily achieved through dietary restriction than increased physical activity energy expenditure [175]. Weight loss treatments involving

both diet and exercise result in greater weight loss than single strategies. The primary benefits of increased physical activity may be greater retention of fat-free mass [176, 177] a lesser reduction in metabolic rate, and an enhanced ability to undertake sufficient physical activity to facilitate weight loss maintenance [178, 179].

Pharmacotherapy

When dietary or behavioural weight loss programs are ineffective and the level of overweight or obesity is affecting the individual's health, pharmacotherapy can be considered [180]. Weight loss drugs currently available on the Australian market include noradrenergic re-uptake inhibitors (e.g., phentermine), a serotonin and noradrenergic re-uptake inhibitor (sibutramine) and an intestinal lipase inhibitor (orlistat). Selective serotonin re-uptake inhibitors (e.g., fluoxetine) have also been prescribed to assist weight management associated with low mood or depression. At present, phentermine is approved for short-term obesity management. Orlistat and sibutramine are the only currently approved weight loss medications for long-term use. A new class of appetite suppressant is the selective CB1 endocannabinoid receptor antagonist (e.g.rimonabant). This weight loss drug is not currently available in Australia, but has been approved for use in Europe since mid 2006. Other antidepressant and antiepileptic drugs are also being evaluated for weight loss efficacy [181], and development of new anti-obesity drugs to target hormones and protein receptors involved in the central control of appetite is well underway [182]. Fenfluramines were withdrawn from therapeutic use one decade ago due to associations with pulmonary hypertension and valvular disease [183].

A systematic review of clinical trials reported average weight losses over placebo after one year of 2.7kg (2.9%) and 4.3kg (4.6%) in orlistat and sibutramine, respectively [184]. Better results are achievable when drug treatments are combined with behavioural and/or dietary therapies (Table 1.3). The prescription of an appetite suppressant with cessation of VLED may assist adherence to behavioural recommendations and promote long-term success [18, 161]. Potential issues can include poor drug compliance [184], highly variable individual responses to treatment, and weight regain following cessation of the drug regimen [18].

Surgical Weight Loss Interventions

The superiority of surgical weight loss techniques over dietary and pharmacological interventions is clear. In a recent systematic review, surgical therapies facilitated sustained reductions between 25 to 75kg in the short to medium term (2-4 years) [185]. This compared to losses less than 5kg after dietary therapies and 5 to 10kg following pharmacotherapy. The marked rise in class III obesity, coupled with the poor weight loss outcomes of medical treatments, has lead to a rising demand for bariatric surgery [18, 186]. In the decade from the early 1990s to 2003, the number of bariatric procedures in the USA rose from 16,000 to over 100,000 [187]. These figures reflect a growing worldwide trend.

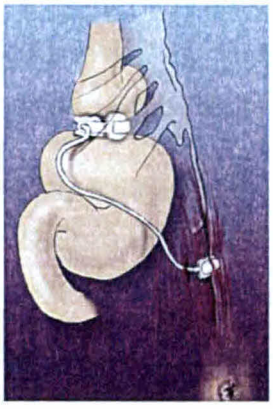
Surgery to treat obesity has existed for a number of decades. The jejuno-ileal bypass was the earliest bariatric operation [188]. This procedure markedly reduced the exposure of ingested food to digestive juices, and produced a severe malabsorption of nutrients and energy. Although most patients achieved significant weight loss, the extent of the nutrient malabsorption and irreversible nature of the operation produced unacceptably high morbidity and mortality [189]. Exclusively malabsorptive procedures are now rarely used. Current bariatric operations involve a singularly gastric restrictive component, or a combination of gastric restriction and malabsorption [190]. Surgical intervention is typically available to those with clinically severe obesity, generally defined as a BMI greater than 40kg/m^2, or BMI greater than 35kg/m^2 with significant obesity co-morbidity [186]. Eligible individuals must typically demonstrate a history of failed weight loss attempts using dietary and/or pharmacological means.

The Adjustable Gastric Band

The adjustable gastric band (AGB) is a restrictive procedure, first used in the mid-1980s [191]. The silicone elastomer band is placed around the upper part of the stomach just below the gastro-oesophageal junction to produce a small upper gastric pouch. The AGB contains an inner inflatable balloon, connected by silicone tubing to a subcutaneous access port (**Figure 1.1**). The volume of saline in the balloon can be manipulated to increase or decrease the stoma between the proximal gastric pouch and the greater part of the stomach. This ability to adjust the diameter of the band provided

a marked improvement on stomas of fixed diameter. An additional benefit is its relative simplicity and complete reversibility.

Figure 1.1 The laparoscopic adjustable gastric band



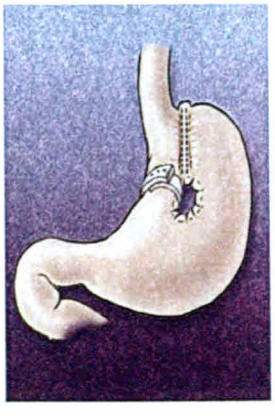
Inflation or deflation of the band should be a clinical decision based on the patient's current weight status, their dietary intake and sense of hunger [192]. Early satiation and increased feelings of mid-meal satiety are thought to be key weight loss mechanisms of the AGB [193]. The imposed gastric restriction also physically constrains the amount of solid food that can be consumed at one time. Aversive stimuli such as abdominal discomfort or regurgitation may occur if food is consumed in too great a quantity, too quickly, or is not chewed adequately. Placement of the AGB does not alter the digestion of nutrients in any way and the chance of long-term nutritional deficiencies following AGB is low. Adequate folate, B_{12} and Vitamin B_6 are however, required to maintain low homocysteine levels [194] and daily supplementation to bring intake up to recommended dietary levels (plus $\geq$400mcg of folate) with a standard multi-vitamin and mineral supplement is advised. Low dose iron supplementation may also be beneficial in pre-menopausal women. Potential complications of the AGB include band erosion or migration, gastro-oesophageal reflux disease and port-related problems [52]. The AGB was the first bariatric procedure to use the laparoscopic approach. Since that time laparoscopy has been applied to all common bariatric procedures, and appears to result in shorter recovery times while maintaining weight loss benefits [195-198].

A systematic review of the safety of bariatric procedures showed lowest rates of mortality and morbidity associated with LAGB [199]. The mortality rate of 0.05% was ten times lower than that for RYGB. Peri-operative complications following LAGB were around 10% the incidence of RYGB. Systematic review of short and medium-term weight loss outcomes shows slower initial weight loss after LAGB compared to RYGB. In the first post-surgical year the average excess weight loss (%EWL) was 42%EWL for LAGB and 62%EWL for RYGB [200]. Three to seven years after surgery weight losses are similar, averaging 53.2%EWL and 57.2%EWL in LAGB and RYGB respectively.

Other Bariatric Procedures

Vertical banded gastroplasty (VBG) entails surgical placement of a vertical staple line from the gastro-oesophageal junction along the lesser curvature of the stomach. A reinforced stoma approximately 1cm in diameter is introduced at the base of the staple line to form a small gastric pouch (**Figure 1.2**). Similar to AGB this gastric restrictive procedure induces feelings of fullness following consumption of relatively small amounts of solid food. Vertical banded gastroplasty, performed frequently in the past, is now known to induce a "maladaptive" eating pattern involving preferential and often excessive consumption of soft or liquid high energy foods.

Figure 1.2 Vertical banded gastroplasty



Caused by the lack of stoma size adjustability, this eating pattern leads to increased energy intake and decreased nutritional adequacy [201-205]. A high incidence of staple-line dehiscence [206], pouch distension and poor medium to long-term weight outcomes [201, 202, 207] have also been reported. As such VBG is largely considered an out-dated procedure.

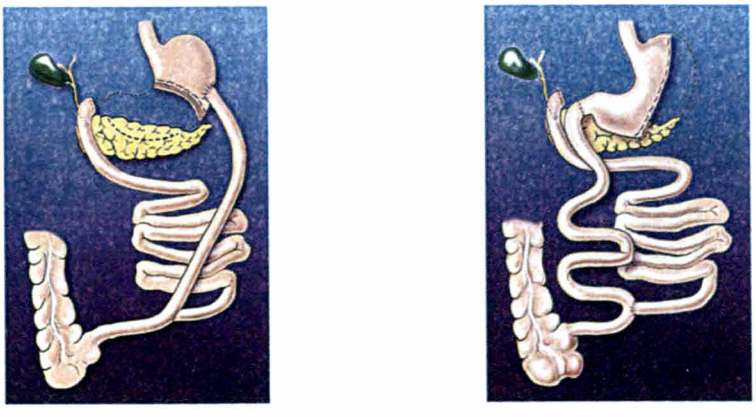
Roux-en-Y gastric bypass was first documented in 1967 [208]. This is currently the most commonly performed bariatric procedure in the USA, but has had a slower uptake in favour of gastric banding in Australia and Europe. The operation involves partial gastrectomy, and exclusion of the duodenum and a 40 to 50cm segment of the proximal jejunum from the digestive process. The 'roux-en-Y' limb of small bowel is brought to the upper abdomen and anastomosed to the small proximal gastric pouch (**Figure 1.3**). Although not technically a malabsorptive procedure, RYGB may induce a degree of malabsorption depending on the length of small bowel bypassed [209]. Weight loss after RYGB is achieved predominantly through energy restriction, decreased hunger and enhanced feelings of satiety [210]. Strong aversive stimuli such as the "dumping syndrome" can also override or diminish the willingness to eat [207] and alter dietary choices away from sweet, oily, and dairy foods [211, 212]. An alteration in circulating ghrelin levels has also been postulated to assist weight loss and improve glucose tolerance [213].

Figure 1.3 Roux-en-Y gastric bypass and the long limb RYGB

Potential risks associated with RYGB include intestinal leaks and staple line failure [52], and long-term metabolic complications involving deficiencies of iron, cyanocobalamin, folate, calcium and cholecalciferol [214, 215]. These nutrients should be supplemented daily using specialized formulations in amounts exceeding recommended dietary intakes.

Biliopancreatic diversion (BPD) involves a gastric restrictive and malabsorptive component, and is the most radical bariatric procedure used today. Food digestion and absorption are limited to a short, common segment of the ileum. The functional efficiency of the intestinal mucosa for nutrient absorption is also greatly reduced by limiting the availability of gastric acids, bile and pancreatic enzymes [216] (**Figure 1.4**). A recent variant of the BPD, the biliopancreatic diversion with duodenal switch (BPD/DS) involves a "sleeve" gastrectomy, leaving the pyloric sphincter and initial segment of duodenum intact. A lower incidence of metabolic abnormalities may occur following BPD/DS when compared to the original BPD, with similar weight loss results [217]. While these malabsorptive surgeries generate a more rapid and profound weight loss than restrictive procedures, they are associated with far greater mortality and morbidity [52]. Patients having undergone both BPD and BPD/DS are at a higher risk of metabolic complications such as vitamin and mineral deficiencies of iron, calcium, folate, fat soluble vitamins, zinc and protein-energy malnutrition [218]. Intense nutrient supplementation and monitoring are required. Limited data are available on the long-term safety of both variants of this procedure, and as such BPD is less accepted than LAGB and RYGB.

Figure 1.4 Biliopancreatic diversion and the biliopancreatic diversion with duodenal switch



The Liver in Obesity

Overview of Nonalcoholic Fatty Liver Disease

Non-alcoholic fatty liver disease is an ever more common complaint that encompasses several conditions of increasing severity. At the less severe end of the NAFLD continuum lies hepatic steatosis. Mild fatty deposition entails abnormal accumulation of lipid predominately in centri-lobular hepatocytes. With increasing fat deposits, more and more hepatocytes throughout the liver lobule accumulate lipid [219]. Liver steatosis without necro-inflammatory change is generally considered a benign condition [220]. Most patients with NAFLD are devoid of distinct clinical symptoms. Fatigue, general malaise or right upper quadrant pain may be present [221]. Hepatomegaly, found in over 50% of some patient groups, is the most common clinical sign [222-225].

Non-alcoholic steatohepatitis is a more severe form of NAFLD, involving hepatic steatosis in the presence of portal or parenchymal (lobular) inflammation, and fibrosis. Natural history studies suggest NASH can be a benign condition, but may progress slowly in disease severity [226, 227], particularly in the obese [227]. The presence of "zone 3" fibrosis or degeneration of hepatocyte ballooning, with or without Mallory bodies, predicts more aggressive liver disease and greater 10 year mortality [228]. Another 10-year study reported cirrhosis development in 21% to 28% of patients with more severe degenerative change at baseline, and higher death rates than general community controls [223]. Progression to fibrosis and cirrhosis was also evident in 4% of patients who presented with liver steatosis alone. The advancement of NAFLD to NASH and liver cirrhosis is the most common cause of liver failure [229].

Fatty change and liver inflammation have been found in lean and overweight individuals [228, 229] yet the severity of liver steatosis is linked positively with the degree of obesity [230]. In a consecutive autopsy study, 70% of obese and 35% of lean patients were found to have steatosis, and 18.5% of obese and 2.7% of lean patients were diagnosed with NASH [231]. Series of bariatric surgery candidates show consistently high rates of abnormal liver morphology. Reports range from:

- **63 to 93%** for hepatic steatosis [246-254],
- **16% to 56%** for NASH [246, 248, 250, 251, 253-255], and
- **1 to 2%** for cirrhosis [248-254].

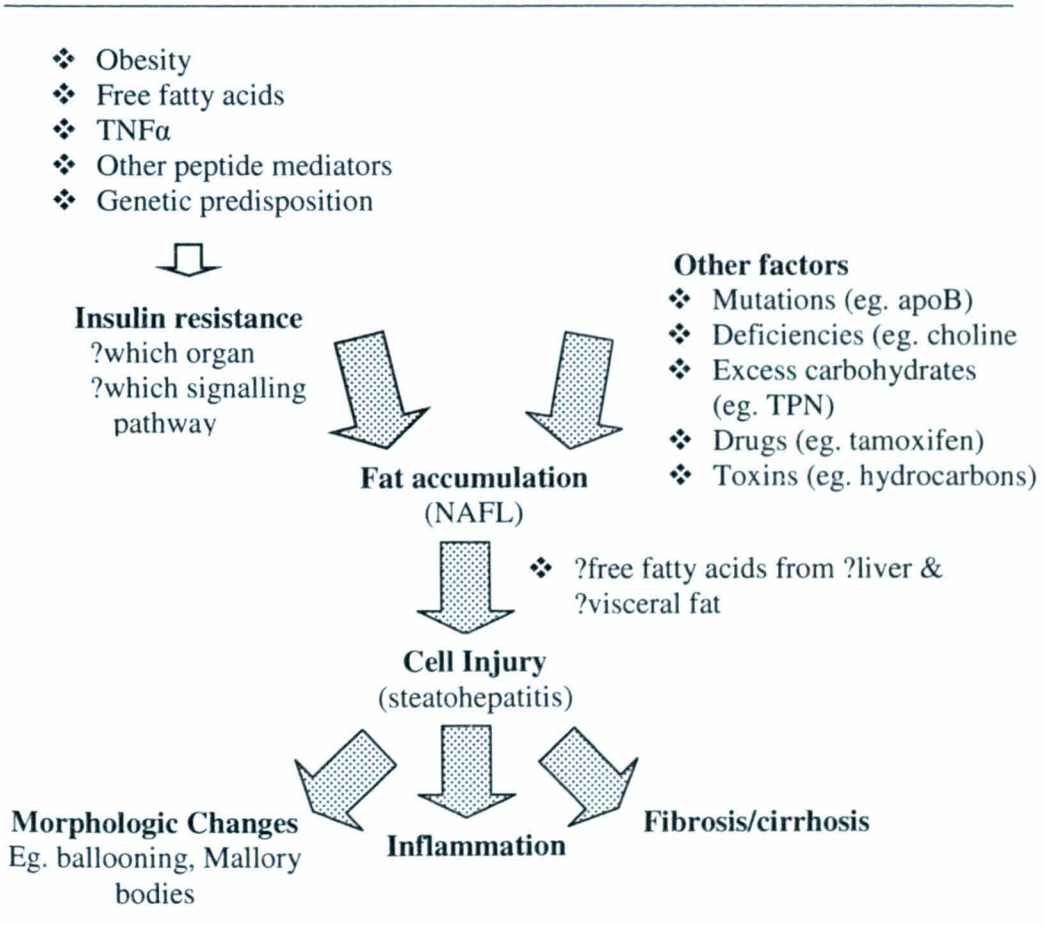
Non-alcoholic fatty liver disease is also strongly related to the metabolic and inflammatory features of the metabolic syndrome [226, 232]. Obese persons with type 2 diabetes are most at risk of NAFLD and NASH [233, 234]. Independent predictors of NASH in a series of 105 morbidly obese bariatric surgery candidates have included insulin resistance, raised alanine aminotransferase (ALT), and hypertension [232]. The occurrence of at least two of these three variables provided a sensitivity of 0.8 and specificity of 0.9 in predicting the presence of NASH. In a cohort of 144 subjects with biopsy-proven NASH, factors predictive of more histologically advanced disease included older age, obesity and type 2 diabetes [224]. Rates of liver steatosis and NASH are predicted to increase alongside the worldwide rise of obesity and diabetes [229].

Figure 1.5 illustrates the cascade of factors thought to be involved in the pathogenesis of NAFLD and NASH. Reduced tissue sensitivity to insulin is considered a common and important precursor in the metabolic pathway to liver steatosis [235, 236]. Accrual of fat in the liver places the individual at higher risk of hepatocellular injury. Oxidative stress is thought to be a major mediator via excessive β-oxidation of free fatty acids by hepatocellular mitochondria, microsomes and peroxisomes. This gives rise to lipid peroxidation, damage to mitochondria and mitochondrial DNA, and injury-related cytokine release [236, 237]. The inflammatory response to cell injury, in concert with possible genetic or environmental factors, can lead to further detrimental morphologic change, inflammation, fibrosis, and possibly cirrhosis.

Imaging modalities such as ultrasonography, CT and MRI can be used to suggest the presence of hepatosteatosis [238]. Yet liver biopsy is the only means to assess the presence and severity of necroinflammatory change and fibrosis, and provide a definitive diagnosis of NASH [239]. Liver biopsy is required to distinguish steatosis from NASH, to estimate disease severity and track the course of the disease, and exclude

other causes of liver dysfunction. Due to the risk of injury, the value of liver biopsy in patients with a good prognosis has been questioned [240].

Figure 1.5 A proposed model for the development of NAFLD and NASH. Adapted from Neuschwander-Tetri and Caldwell [240].



Weight Loss and Hepatomegaly

Although the pathogenesis of NAFLD is somewhat in question, weight loss, and particularly loss of visceral fat [239] is a primary management aim in NAFLD associated with overweight and obesity [241, 242]. Dietary interventions [243-246] and bariatric surgery [247-251] have been shown by liver biopsy to effectively reduce levels of liver steatosis. Decreased hepatic fat storage would be expected to reduce liver size. Only two previous studies have specifically addressed the effect of weight loss on hepatomegaly. Fris employed ultrasound to assess change in the left lobe of the liver in 40 obese subjects (median BMI: 47 ± 6.8 kg/m^2) after a 2 week pre-operative VLED [252]. Mean liver volume reduced by 5.1% ($p<0.001$) and correlated with the decrease in BMI, but not estimated total fat mass assessed by bioelectrical impedance. Busetto et al. assessed liver size and body fat distribution using whole-body multi-slice MRI in 6 premenopausal women after LAGB [253]. This small sample had a mean baseline BMI of 42.6 ± 1.1 kg/m^2 and mean liver volume of 1.79 ± 0.41 L. Weight loss, liver volume, and body fat were reassessed 8 and 24 weeks after LAGB. Significant declines in body weight and total body fat occurred at both time points, while liver size ($p<0.05$) and VAT ($p<0.05$) reduced only during the first 8 weeks. Liver volume and VAT were correlated at baseline ($p<0.01$) but not thereafter.

These studies demonstrate significant reductions in liver volume and VAT with weight loss. They also suggest the most marked declines occur in the early phase of weight reduction. For the purposes of pre-operative intervention, a recommended time frame should be a judgement based on the potential for maximal reduction in liver size and weight loss, versus issues of dietary compliance and acceptability. These issues have not been explored within the setting of imminent surgery. Furthermore, identification of clinical factors that predict massive hepatomegaly would allow the surgeon to detect those at greatest risk of hepatomegaly so effective therapy can be focused on those likely to benefit most. An understanding of factors associated with liver volume reduction would also enable the surgeon to predict those likely to have successfully achieved pre-operative liver volume reduction.

Research Question #1

What is the efficacy and acceptability of pre-operative weight loss by VLED in a severely obese population?

i) What is the actual change in liver volume and the pattern of change during weight loss using VLED?

ii) What is the relative change in liver volume, body weight, and visceral adipose tissue areas?

iii) Which, if any, anthropometric, clinical, and biochemical factors predict an enlarged pre-treatment liver or predict the total change in liver volume after treatment?

iv) What is the extent of dietary acceptability and patient compliance to a pre-operative VLED, and what are the most common treatment side-effects?

Weight Loss and Non-alcoholic Steatohepatitis

In addition to decreased hepatic volume and steatosis, weight loss brings about reductions in liver inflammation and fibrosis. Due to the relative ease of obtaining a liver biopsy during upper abdominal surgery, histological change has been most frequently demonstrated after surgically-induced weight loss. Significant improvements in lobular steatosis, necroinflammatory change and fibrosis has been observed in 36 subjects 25.6$\pm$11 months after gastric banding [249]. These subjects achieved a mean drop in BMI from 47.0$\pm$10.6kg/m^2 to 34.0$\pm$5.5kg/m^2. Of 10 subjects with pre-existing severe fibrosis, seven showed resolution, two showed improvement, and one remained unchanged at repeat biopsy. Pre-existing portal abnormalities were unchanged. In another series, 70 patients underwent a repeat liver biopsy 15$\pm$9 months after surgical weight loss (RYGB, LAGB and sleeve gastrectomy) and a mean BMI reduction from 56$\pm$11kg/m^2 to 39$\pm$10kg/m^2 [250]. Baseline liver inflammation resolved in 37% and fibrosis resolved in 20%. No progression in liver inflammation or fibrosis was found.

While these studies demonstrate clear benefits to the morbidly obese patient with NASH, a potential for rapid weight loss to exacerbate hepatocellular injury has been observed. Jejuno-ileal bypass generated a substantial and immediate weight loss, which

alongside a compromised nutritional status, was associated with deterioration of the liver, and frequently, cirrhosis [254, 255]. Exacerbations in liver disease have been reported following more recent bariatric procedures. Despite a reduced incidence and severity of hepatic steatosis, an increase in inflammatory lobular hepatitis has been reported among 69 morbidly obese patients 27±15 months post gastroplasty [248]. Repeat biopsy in 104 patients 41±25 months after BPD has shown reduced liver fibrosis in 27%, no change in 33%, and increased fibrosis in 40% of subjects [256]. In this cohort worsening fibrosis was linked to pre-operative menopausal status and alcohol use, and post-operative decreases in albumin and diarrhoea.

Random investigations have assessed change in liver morphology following dietary intervention. These studies have predominantly employed strategies of energy restriction and total starvation, and are summarized in **Table 1.4**. Similar to surgical studies, predictable reductions in liver steatosis accompany dietary weight loss. Most studies also detected concurrent decreases in inflammation and fibrosis at repeat biopsies ranging from one week to 23 months.

Of note however, are reports of increased focal necrosis after fasting [257] and increased portal inflammation after VLED [245]; two weight loss modalities known to induce a rapid weight loss. A study by Anderson et al. is the only known prospective investigation of change in liver histology following weight loss by VLED [245]. Forty one patients (mean BMI 43.3kg/m^2, range 37-74) underwent VLED intervention. A median weight loss of 34kg occurred over a median duration of 261 days. Repeat biopsy an average of 76 days after treatment showed normalization of hepatic histology and improvements in steatosis in most subjects. Signs of portal inflammation and portal fibrosis were present in 5 patients who had achieved a rapid weight loss, greater than 1.6kg per week. Portal fibrosis was not observed in any patient who lost less than 1.6kg per week. Change in liver enzymes did not predict change in liver morphology.

Table 1.4 Dietary interventions and changes in biopsy proven NAFLD and NASH

Reference	Study Type	Study Criteria	Therapy	n	Duration	Weight Loss (kg)	Liver Enzymes	Histology
Rozenthal 1967	Case series	Biopsy, no exclusions	Fast	5	1 – 4wk	Mean 20.5 Range 14.4-30.4	No change	Decreased S
Drenick 1970	Case series	Biopsy	Fast	11	1.5 – 3.5m	Mean 40.9 Range 26-76.4	N/A	Decreased S Increased FN
Drenick 1970	Case series	Biopsy	Diet	7	2 – 7m	Mean 59.5 Range 32-81.8	N/A	Decreased S No change in FN
Eriksson 1986	Case series	Biopsy, clinically proven NASH	Diet	3	12m	Mean 12.7 Range 7-20	Improved	Decreased S, F, I
Keeffe 1987	Case report	Biopsy, clinically proven NASH	Modified Fast	1	4m	Total 18.2	Improved	Decreased S, I
Anderson 1991	Case series	Biopsy, excluded alcohol & diabetes & some medications	VLED	41	4 – 23m (med 261)	Median 34 Range 17-89	Improved AST	Decreased S Decreased FN Increased PF
Ueno 1997	Controlled clinical trial	Biopsy, clinically proven NAFLD	Diet and exercise	25	3m	Mean drop in BMI by 3 points*	Improved AST, ALT	Decreased S, F No change in untreated group
Huang 2005	Case series	Biopsy, clinically proven NASH	Diet	15	12m	Mean 3.3	No change	Decreased S

S, steatosis; F, fibrosis; I, inflammation; FN, focal necrosis; PF, portal fibrosis; AST, aspartate aminotransferase; ALT, alanine aminotransferase
*Weight at follow-up not provided

It has been hypothesized that the increased flux of free fatty acids during rapid weight loss exacerbates hepatocellular injury in compromised livers [258]. This swift and extensive mobilisation of free fatty acids most likely arises from liver stores and visceral adipose depots (see Figure 1.5). Persons undergoing bariatric surgery have clinically severe obesity and high levels of metabolic co-morbidity. As such they are a group at high risk of undetected NASH. An acute deterioration in liver function in the setting of imminent surgery may place the patient at higher risk of immediate complications and affect the long-term management of the disease.

Hepatomegaly and Laparoscopic Surgery

While an enlarged steatotic liver may not in itself be a critical health concern, has been identified to increase surgical risk and complexity in patients undergoing upper abdominal laparoscopic surgery [258-260]. Key elements of the two most common bariatric procedures, LAGB and RYGB, require exposure and surgery in the area of the gastro-oesophageal junction. Massive hepatomegaly has been cited as the most common cause for conversion to an open procedure from LAGB [261] and laparoscopic RYGB placement [262]. Excessive visceral adiposity, covering the structures of the left upper quadrant of the abdomen, results in a deep operative field, and provides an additional particular challenge. A close relationship between hepatomegaly and abundant visceral fat has been observed [263].

With the rising demand for laparoscopic bariatric surgery, a safe and effective intervention to reduce massive hepatomegaly and visceral adiposity should benefit surgeons and patients alike. Advantages may include:

- Increased operating space, manoeuvrability and visibility of anatomical markers [261, 264]
- Greater ease of liver retraction at laparoscopy
- Reduced risk of liver trauma and blood loss [252]
- Reduced risk of conversion to an open procedure

- Reduced operating time which may reduce other surgical risks such as venous thrombosis and pulmonary embolism

To supplement investigation of liver volume change in the severely obese, a sub-study was undertaken. This study aimed to investigate the change in liver morphology in a group of subjects at high risk for NASH during the most rapid phase of weight loss using VLED.

Research Question #2

How does rapid weight loss using VLED affect liver morphology in a select group of morbidly obese subjects at high risk of NASH?

i) What is the extent of change in hepatic steatosis, inflammation (NASH grade) and fibrosis (NASH stage)?

ii) How do changes in liver morphology relate to the absolute and relative reduction in body weight, and with changes in liver volume and VAT?

CHAPTER 2: Eating Behaviour and Obesity

Simply put, weight gain occurs when, over an extended period of time, habitual energy intake exceeds the body's actual energy requirement. Numerous internal and external factors can affect energy balance. Consumption of an energy dense diet and low levels of physical activity will facilitate weight gain in susceptible persons. These eating and exercise patterns are considered normal and conventional in modernized societies. "Non-normative" or "disordered" eating patterns extend beyond what are considered standard or typical. With worldwide rates of obesity soaring, interest in the importance of disordered eating patterns, and the hazard they impose on weight gain, has grown.

An eating disorder can be conceptualized as a recurrent pattern of eating that causes functional impairment, psychological distress, or a risk to health [265]. The Diagnostic and Statistical Manual of Mental Disorders (DSM IV) [266] currently lists three categories of eating disorder:

1. Anorexia nervosa, which involves a highly restrictive eating pattern that most often results in severe underweight.
2. Bulimia nervosa, characterized by recurrent episodes of bingeing or gorging on large amounts of food, followed by purging or other compensatory behaviours. Bulimia nervosa is predominately found in females of "normal" weight.
3. Eating disorders not otherwise specified (EDNOS) is a classification given to persons who fail to meet full diagnostic criteria for anorexia nervosa or bulimia nervosa, or engage in a range of non-specific disordered eating patterns.

Binge eating disorder (BED) is listed under the category of EDNOS. Binge eating disorder is characterized by recurrent episodes of bingeing or gorging on large amounts of food in the absence of compensatory behaviours, and is associated with weight gain and obesity. Although not yet a formal diagnosis, BED has attracted an impressive amount of research in the last decade, and in clinical practice is increasingly known and accepted.

The night eating syndrome (NES) is another pattern of eating that has been associated with weight gain and obesity. Night eating syndrome is most often characterized as a time-delayed pattern of food intake, where a proportionately greater quantity of food is eaten during the evening and night. The core behavioural features and clinical significance of NES are currently unclear, and as such, it is not a currently recognised eating disorder. High rates of concurrent BED and NES have also been reported.

Concomitant with the obesity epidemic, an increasing number of persons are seeking bariatric surgery. Binge eating disorder and NES prevalence estimates are consistently high among bariatric surgery candidates. It is common sense that the efficacy of bariatric surgery would be partially dependent on behaviour modification to facilitate the long-term change in energy balance. The impact of BED and NES on post-surgical weight loss outcomes and complication rates is a current topic of debate. Most prospective work has only assessed pre-surgical eating behaviour and its association with outcome. "Normative" and "non-normative" post-surgical eating behaviours are poorly characterised. Quantitative and qualitative accounts of post-surgical intakes and eating patterns are few. The impact of obesity surgery on the behavioural features of BED and NES is largely unexplored. There is also a paucity of data to investigate the relationship between post-operative eating behaviours and surgical outcomes. This lack of data extends to the change in physical activity levels after surgery and the association with eating behaviour and weight loss efficacy.

The following chapter reviews current theory on BED and NES. It is argued that the central behavioural features of these conditions most closely associated with obesity and psychological distress are unclear. The section on NES in this chapter is supplemented by a published review of NES presented in chapter 7. Studies in the bariatric surgery literature to investigate BED and NES, the change in energy and nutrient intakes and other aspects of pre- or post-surgical eating and exercise behaviours are reviewed. Research questions appear at the end of each section.

Binge Eating Disorder

History and Current Definition

The phenomenon of binge eating among the obese was first observed by Albert Stunkard in 1959 [267]. He described

> "...an orgiastic quality..." to food consumption, where "...enormous amounts of food may be consumed in relatively short periods...regularly followed by severe discomfort and expressions of self-condemnation".

It was not until the 1980s that a series of multi-centre field trials were conducted to investigate the prevalence and psychometric properties of the newly proposed binge eating disorder [268, 269]. These studies found a high prevalence of BED among persons seeking medical weight loss treatments, compared to the general community. Binge eating disorder was positively associated with the severity of obesity and psychological distress, and more common in females than males. Binge eating disorder was included in the 1994 edition of the DSM IV under the diagnostic category EDNOS, and as a proposed eating disorder requiring further study.

Binge eating involves consumption of an objectively large amount of food for the circumstances, accompanied by a lack of control over what or how much is being eaten. Diagnosis of BED requires binge eating to occur an average of two days per week over the previous six month period, alongside marked psychological distress, and in the absence of inappropriate compensatory behaviours [266]. The current BED diagnostic criteria are listed in **Table 2.1**.

Table 2.1 Current diagnostic criteria for binge eating disorder listed in the DSM IV [266]

A. Recurrent episodes of binge eating. An episode of binge eating is characterized by the following:

1) Eating in a discrete period of time (eg. within any 2 hour period), an amount of food that is definitely larger than most people would eat within a similar period of time under similar circumstances
2) A sense of lack of control over eating during the episode (eg. a feeling that one cannot stop eating or control what or how much one is eating)

B. The binge eating episodes are associated with three (or more) of the following:

1) Eating much more rapidly than normal
2) Eating until feeling uncomfortable full
3) Eating large amounts of food when not feeling physically hungry
4) Eating alone because of being embarrassed by how much one is eating
5) Feeling disgusted with oneself, depressed, or very guilty after overeating

C. Marked distress regarding binge eating is present

D. The binge eating occurs, on average, at least 2 days a week for 6 months

Note: The method of determining frequency differs from that used for Bulimia Nervosa. Future research should address whether the preferred method of setting a frequency threshold is counting the number of days on which binges occur or counting the number of episodes of binge eating.

E. The binge eating is not associated with the regular use of inappropriate compensatory behaviors (eg. purging, fasting, excessive exercise) and does not occur exclusively during the course of anorexia nervosa or bulimia nervosa

Although generally accepted, the ambiguous nature of several criteria may affect BED diagnosis rates [270-273]. Inconsistencies can arise from:

- Difficulty defining a binge as distinct from a period of continuous background eating or unstructured over-eating.
- Differences in the interpretation of an 'unusually large amount of food for the circumstances'. An objective bulimic (binge) episode has been defined as a LOC during the consumption of an amount of food considered abnormally large for the circumstances by both the subject and the interviewer. A subjective bulimic episode has been defined as a LOC during consumption of an amount of food considered abnormally large for the circumstances by the subject but not the interviewer [274].
- The limitation of retrospective recall of feelings of lack of control. Binge episodes have been associated with "numbing out" or escaping from awareness [275].
- Interpretation of descriptive terms such as the "marked distress", and the absence of "regular" compensatory behaviours.

Prevalence

Binge eating disorder prevalence estimates vary widely. This is due in part to differences in research methodologies and BED diagnostic measures (which are briefly reviewed in chapter 6). The prevalence of BED is also notably higher among obese treatment-seeking samples compared to general population samples. In addition to the recognized association with obesity [78, 269], higher BED prevalence are likely to be biased by the tendency for persons who suffer significant psychological distress to seek treatment [79]. **Table 2.2** provides an overview of BED prevalence in various community samples. **Table 2.3** overviews BED prevalence among groups of overweight and obese individuals seeking medical weight loss treatments. **Table 2.4** documents BED prevalence within populations of bariatric surgery candidates. In Table 2.4 binge eating behaviours that do not meet rigid DSM IV BED criteria have also been listed. Among the studies involving surgical candidates, median BED prevalence can be calculated at 29% and median binge eating estimates at 30%.

Table 2.2 An overview of studies that have assessed binge eating disorder prevalence in various community samples

Study (reference)	Sample	Sample Size (F)	Age (y)	BED Ax Method	BED Prevalence Estimate
Hay 1998 [276]	General sample	3001 (60%)	Mean 35.2	CI	1%
Ghaderi and Scott 2001 [277]	Swedish females	1157 (100%)	Range 18-30	SEDs	1.2%
Smith, Marcus et al. 1998 [278]	General sample	3948 (55%)	Range 28-40	QEWP	1.5%
Spitzer, Devlin et al. 1992 [268]	Combined community sample	1031 (62%)	33	QEWP	2.0%
Spitzer, Yanovski et al. 1993 [269]	College students	728 (79%)	Mean 22	QEWP	2.6%
Kinzl, Traweger et al. 1999 [279]	Austrian females	1000 (100%)	Range 15-85	Phone interview	3.3%
Spitzer, Williams et al. 2000 [280]	Obstetric/ Gyno O/P sample	3000 (100%)	Mean 31	PRIME-MD	4%
Spitzer, Yanovski et al. 1993 [269]	Medical centre employees	216 (70%)	Mean 34	QEWP	4.6%

CI, clinical interview; QEWP, Questionnaire on Eating and Weight Patterns; SEDS, Survey for Eating Disorders (a self-report tool based on DSM IV BED criteria)

Table 2.3 Binge eating disorder prevalence in obese samples seeking medical weight loss treatment

Study (reference)	Sample	Sample Size (F)	Mean Age (y)	Mean BMI	BED Ax Method	BED Prevalence Estimate
Vamado, Williamson et al. 1997 [281]	Obese treatment seekers	468 (84%)	~43	~35	QEWP	7.3%
Ricca, Mannucci et al. 2000 [282]	Obese outpatients	344 (83%)	44	35.8	CI	7.5%
Stunkard, Berkowitz et al. 1996 [283]	Weight loss sample	79 (100%)	39	35.3	CI	7.6%
Brody, Walsh et al. 1994 [284]	Weight loss sample	67 (87%)	~43	~30	CI	18.8%
Spitzer, Yanovski et al. 1993 [269]	Weight loss samples	1785 (89%)	43	31.0	QEWP	28.8%
Spitzer, Devlin et al. 1992 [268]	Treatment seeking samples	723 (81%)	45	29.8	QEWP	30.1%

QEWP, Questionnaire on Eating and Weight Patterns; CI, clinical interview

Table 2.4 Point prevalence of binge eating disorder and binge eating in bariatric surgery candidates

Study [reference]	Study Design	Sample Size (F)	Assessment Method	BED (%)	Binge Eating (%)	BED plus Binge Eating (%)
Glinski et al. 2001 [285]	C/S	115 (NR)	SS CI	0	10	10
Adami et al. 1996 [286]	Pros	65 (49)	CI	0	63	63
Burgmer et al. 2005 [287]	Pros	149 (68)	CI	2.0	20.1	22.1
Allison et al. 2006 [288]	C/S	210 (172)	SS CI	4.2	1.4	5.6
Busetto et al. 1996 [289]	Pros	80 (57)	CI	12.5	NR	12.5 all BED
Potoczna et al. 2004 [290]	Pros	300 (210)	CI	16	NR	16 all BED
de Zwaan et al. 2003 [291]	C/S	110 (96)	QEWP-R	17.3	21.8	39.1
Green et al. 2004 [292]	Pros	65 (48)	SCID or QEWP-R	26	25; 1B/wk	51
Wadden et al. 2001 [293]	C/S	122 ()	QEWP Int	27	14.8	41.8
Sarwer et al. 2004 [294]	Cross	90	QEWP	27	42	69
Busetto et al. 2002 [295]	Pros	260 (188)	CI	29	NR	29 all BED
Dymek et al. 2001 [296]	Pros	32 (NR)	QEWP-R	32	NR	32 all BED
Busetto et al. 2005 [297]	Pros	379 (281)	CI	34	NR	34 all BED
Hsu et al. 1996 [298]	Retro	24 (24)	EDE-CI	37.5	NR	37.5 all BED
Adami et al. 1999 [299]	Pros	63 (48)	CI	42.8	NR	43 all BED
Saunders 1999 [300]	C/S	125 (113)	QEWP	43.2	17.6; ≤1B/wk/6m	61.3
Adami et al. 1995 [301]	C/S	92 (66)	SS CI	46.7	22	68.5
Latner et al. 2004 [302]	Retro	65 (65)	EDE-CI	48	NR	48 all BED
Hsu et al. 1997 [303]	Retro	27 (27)	EDE-CI	48.1	NR	48.1 all BED
Mitchell et al. 2001 [304]	Retro	78 (65)	SS CI	49	NR	49 all BED
Hsu et al. 2002 [305]	C/S	37 (31)	EDE	NR	11; ≥2B/wk/3m 14; ≤1B/wk/3m	25
Lang et al. 2000 [306]	C/S	79 (76)	BSQ	N/A	27; ≥1B/wk/3m	27
Boan et al. 2004 [307]	Pros	40 (34)	BES (≥18)	N/A	20; score 18-26 10; score ≥27	30
Kalarchian et al. 1998 [308]	C/S	64 (49)	EDE	NR	39; ≥1B/wk/3m	39
Sabbioni et al. 2002 [309]	Pros	82	Medical history	N/A	43.2	43.2
Malone et al. 2004 [310]	Pros	109 (91)	BES (≥18)	N/A	28; ≥18-26 24; ≥27	52
Powers et al. 1999 [311]	Pros	116 (96)	BSQ	N/A	52; ≥1B/wk	52
Larsen et al. 2004 [312]	Cross	93 (77)	BES (≥18)	N/A	55.9	55.9
Lang et al. 2002 [313]	Pros	66 (58)	BSQ	N/A	63.6	63.6

SS CI, semi structured clinical interview; QEWP-R, Questionnaire of Eating and Weight Pattern – Revised; EDE, Eating Disorder Examination; SCID, Structured clinical interview; QEWP Int, QEWP-R administered during interview; BES, Binge eating scale; BSQ, Binge scale questionnaire; B, binges

Additional explanations for inconsistent prevalence estimates in surgical populations may include:

- The conscious under-reporting of disordered eating in an effort to be approved for bariatric surgery [288].
- The psychological defence mechanism of "denial" [285].
- An attenuation in the psychological distress related to binge eating, fear of weight gain or dissatisfaction with shape and weight after having made the decision to undergo obesity surgery. This may assist the control of binge-eating behaviour [288, 305].

Aetiology

As currently defined, the pathogenesis of BED appears multifactorial. Compared to healthy controls, risk factors for BED have included adverse childhood events such as sexual or physical abuse, disparaging comments from parents regarding weight, shape and eating, and poor self-esteem [78]. An association with severe and early onset obesity has also been noted [78, 269] This has lead to speculation that strict dieting behaviour may predispose the individual to "counter-regulatory eating" such as binge eating [314]. Although a popular theory, the majority of subjects report BED onset before the commencement of serious dieting [269, 315-319]. The inception of serious dieting may however, occur at a younger age in obese binge eaters than obese individuals without BED [269, 317, 319-322]. Binge eaters are more likely to have been obese as children compared to subjects with other psychiatric disorders [78].

A possible genetic predisposition to binge eating has also been identified. Mutation of the melanocortin 4 receptor (MC4R) gene is the most common known cause of monogenic obesity in humans [323]. One recent study identified 24 of 469 class III obese subjects with a mutation of the MC4R [290]. All 24 subjects were subsequently diagnosed with BED, compared to BED in 14.2% of obese, non-carrier controls.

Negative emotions may also play a role in either the onset or maintenance of binge eating. Cited triggers of a binge episode include life stress [324, 325] or intense emotions such as severe anxiety [326], anger [285], depression, and hopelessness [327].

Certain social situations, time of day and perceived overeating during a meal have also been reported to initiate a binge episode [328].

Course

The course of BED appears somewhat variable. Partial or total spontaneous remission of BED has been reported in 48% of a small cohort of women [329] and 90% of young females [330] over a 6 month and 5 year period, respectively. Reductions in binge eating frequency have been reported in wait-listed controls receiving no active treatment [331] and during a 4-week placebo run-in before the onset of drug therapy [332]. The latter study reported a reduction in the average binge frequency from 6.0 to 1.7 binge episodes per week (72%). Controlled drug trials also show a high placebo response, in some cases similar to response rates in the treatment arm [283, 333, 334]. Jacobs-Pilipski et al. further characterized placebo responders, and found that those who responded to placebo were more likely to engage in subjective binge episodes than objective binge episodes, and to place less importance on body shape [335]. These findings suggest placebo responders may possess less severe eating disorder pathology than non-responders.

The severity and incidence of binge eating and BED can also reduce following a range of direct or indirect treatments (outlined below). Yet despite reported reductions, follow-up studies identify a significant proportion of subjects who resume binge eating. Treatment studies have not defined characteristics of those more likely to resume eating disorder pathology. Binge eating may be more likely to recur in those with more severe baseline behaviours. After bariatric surgery, it is possible that severe pre-operative binge eaters with deeply internalized thought patterns may over time, still attempt to binge eat or abuse food.

Further support for the general stability of BED comes from a recent community study designed initially to determine the familial association of BED [336]. The lifetime prevalence of any eating disorder was determined by clinical interview among 888 first degree relatives of the initial cohort (which consisted of 150 subjects with BED and 150 subjects with no history of disordered eating). Mean lifetime duration of BED among the first degree relatives was 14.4 ± 13.9 years [336]. This was a significantly longer duration when compared to bulimia nervosa with a mean lifetime duration of 5.8 ± 9.1

years and anorexia nervosa at 5.9±7.4 years. Furthermore, the majority of individuals with BED reported its presence as a single, extended episode. The authors concluded that BED is an essentially stable syndrome, at least as persistent as anorexia nervosa and bulimia nervosa.

Direct Treatment of BED

Various psychological treatments, including cognitive behaviour therapy (CBT) [79, 337, 338], interpersonal therapy [331, 337] and self help [331, 339] have bought about greater reductions in binge eating than non-treatment arms. In these studies, reductions in binge frequency varied from less than 50% to greater than 90%. Importantly, 12-month follow-up studies show an increase in the incidence of binge eating with cessation of active treatment [337, 338]. For example, one year after a 36-week CBT treatment, Agras et al. found 55% of those abstinent after treatment were again bingeing at 12-month follow up [338]. The 26% who again met criteria for BED had gained 3.6 kg above their baseline weight, while those who abstained weighed 4kg less than pre-treatment [338]. While weight losses up to 5.5kg have been reported after psychological BED treatments [334, 337, 338, 340], weight loss maintenance after medical treatments is generally poor, and may be particularly so among those who fail to abstain from binge eating. The small weight reduction and the high tendency for weight regain are insufficient to address the associated problem of obesity.

Short-term pharmacological trials involving anti-depressants, appetite suppressants and anti-convulsants have also demonstrated a decline in binge frequency beyond that of the placebo arm [332-334, 341-343]. In some cases small concurrent reductions in body weight were achieved. Yet a review of current pharmacological studies highlights the short-term nature of the studies and tendency for bingeing behaviours and body weight to return to baseline with cessation of active treatment [344]. Furthermore, several recent randomized controlled trials suggest that CBT achieves significantly greater reductions in binge eating than controls or pharmacotherapy [334, 340, 345]. The unremitting and somewhat persistent nature of BED following direct treatment suggests that some affected persons require on-going follow-up and therapy. The associated problem of obesity is also not easily solved.

Indirect Treatment of BED

The dual problem of binge eating and obesity has caused controversy among clinicians regarding appropriate treatment. For obese binge eaters, an advantage of dietary interventions is their ability to bring about greater reductions in body weight, in addition to a decline in binge eating. Treatment using VLED is particularly successful at achieving rapid and significant reductions in body weight. At least in the short term, VLED therapy reduces binge eating as much as CBT and interpersonal therapy [70, 326, 346-349]. For example, 57% of subjects no longer met BED diagnostic criteria six months after VLED treatment [348].

The issue of dietary compliance and success among binge eaters has been questioned, and is a relevant consideration in the bariatric surgery recipient. Similar post-treatment reductions in body weight have been reported after 26-week VLED therapies in binge eaters compared to non-binge eaters [350, 351]. For example, Yanovski et al. reported a loss of 19.6±2.5kg (17.7±1.8% initial body weight) in baseline binge eaters, and 21.3±1.4kg (20.6±1.3% initial body weight) in non-binge eaters [350]. Wadden et al. also reported similar weight losses of 21.5±8.9kg and 21.7±8.8kg in binge eaters and non-binge eaters, respectively [351].

Most behavioural treatment studies report comparable [70, 326, 347, 351, 352], and even superior [353] retention rates and dietary adherence between pre-treatment binge eaters and non-binge eaters. Poorer compliance and higher dropout rates from obesity-directed treatments have also occurred [350, 354, 355]. Consistent with direct BED treatment studies, those who stop binge eating are more likely to stabilize their weight, while unresolved BED promotes weight regain [337, 338, 348].

Association with Obesity

The positive association between BED and obesity is now well accepted. Both obese treatment seekers and large general community samples have shown strong associations between the magnitude of binge eating behaviour and degree of adiposity [268, 269, 276]. While not all binge eaters in the general community are obese, a longitudinal study of young women found that binge eating was associated with accelerated weight gain [330]. One retrospective study also noted that weight gain and obesity occurred a few years after BED onset [315]. Most subjects reported that they started binging in

adolescence and were then of normal weight. Binge eating disorder is frequently associated with more severe and earlier onset obesity [79, 269, 272, 356]. Frequent and severe weight fluctuations and a history of extensive and unsuccessful dieting are also more common to bingers than non-bingers [268, 269, 300, 301, 321, 322].

In addition to the sizeable energy contribution of binge episodes, several laboratory studies have reported that binge eating occurs against a background tendency to overeat [357-359]. For example, obese binge eaters have consumed significantly more calories during "normal" and "binge" meals than obese non-BED [359]. In the same study, binge eaters consumed a higher percentage of energy from fat, and a lesser percentage of protein during the binge meal. Binge eating disorder is consistently characterized by higher levels of disinhibition and hunger than controls [291, 360], indicating more difficulty regulating eating behaviour.

Psychological Correlates

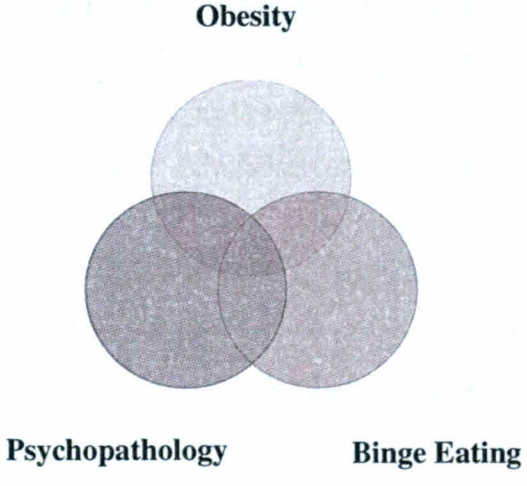
Beyond the existence of regular binge eating, and a strong tendency to weight gain and obesity, subjects with BED are quantifiably distinct from obese non-BED subjects. Common features of BED include the presence of psychiatric co-morbidity [316, 322], higher symptoms of depression [316, 361] and higher ratings of body image distress and weight and shape concern [362-364]. Self-esteem is often low [285, 321].

As a group, bariatric candidates show high levels of psychological distress. Among surgical cohorts, BED assessed by clinical interview [288, 297] and severe binge eaters assessed by questionnaire [292, 310] have shown significantly higher symptoms of depression than non-bingeing surgical candidates. However, not all reports agree [291, 305]. Body image distress and weight and shape concerns have been assessed as higher [305] and similar [308, 365] between surgery seekers who do and do not binge eat.

While a strong susceptibility to obesity and high incidence of psychopathology characterize those with BED, the causal and counter-causal nature of these associations remains largely unknown. In a group of obese female binge eaters, co-morbid psychopathologies co-varied with binge eating severity but not with body weight [366]. Immediately after bariatric surgery the incidence and severity of both binge eating behaviours and psychopathologies declines dramatically while patients are still classified

as morbidly obese [296, 367]. These findings suggest that present psychopathology is more related to the occurrence of binge eating than the problem of obesity. **Figure 2.1** is a paradigm conceived to demonstrate the interrelationship of obesity, binge eating and psychopathology in BED.

Figure 2.1 A proposed overlap between binge eating, obesity and psychopathology



Elevated psychological distress is a prerequisite for BED diagnosis. However, the nature of the association between each of the core behavioural features of BED and psychological disturbance is not established. Binge frequency, binge size and experience of loss of control (LOC) related to eating are central features of BED, and potential drivers of emotional distress. Work by Striegal-Moore et al. and Crow et al. has shown few distinctions in measures of psychological disturbance between obese subjects bingeing two or more times per week and those not meeting the BED frequency criterion [273, 368, 369]. Similar levels of depression and psychological disturbance have also been reported in subjects who differed in binge size (objectively large versus subjectively large volumes) [370].

A number of researchers have proposed a loss of control (LOC) related to eating to be the most important and consistent feature of a binge [371-373]. Work comparing full and partial syndrome bulimia nervosa suggests the experience of LOC is more strongly associated with psychological distress than binge volume [374-376]. This relationship has not been explored in BED. Women with BED have identified a binge episode by feelings of LOC, and less so by the amount of food consumed [373]. Identification of the factor(s) most strongly associated with psychological distress will further define the disorder, inform intervention strategies and improve patient management.

Binge Eating Disorder and Bariatric Surgery

Within bariatric cohorts, co-morbid psychological and psychiatric conditions occur relatively frequently, and of these, BED is among the most common [377]. A survey of clinical practice of eating disorders suggested most RYGB surgeons are aware of BED, and a proportion screen for its pre-surgical presence [378]. Yet management decisions in those identified with BED varies widely; some centres exclude binge eaters, others recommend RYGB over LAGB, and some offer pre- and/or post-operative counselling.

Obesity surgery induces a marked change in eating behaviour. In general, food is most easily tolerated when consumed as small, bite-sized pieces, chewed thoroughly, and eaten slowly. Meals should be small and the environment free from distractions and stressors. These guidelines are contrary to the erratic, excessive, and psychologically disturbing pattern of consumption that defines binge eating. Whether binge eaters are less able to adopt new eating patterns and are more prone to poor treatment outcomes remains in question [379, 380].

Does binge eating persist after bariatric surgery?

Assessment of abnormal post-operative eating behaviour is difficult due the radical change enforced by gastric restrictive surgery. Eating patterns and behaviours by necessity are different from pre-surgery, and are also different from what may be considered "normal" within the general community. There is presently no standardized or validated tool to assess "normative" or "non-normative" post-surgical eating behaviour. Recent studies to assess the prevalence of post-surgical binge eating have done so according to either:

- full DSM IV BED criteria,
- modified DSM IV criteria that omit the requirement for objective bulimic episodes, and in some cases have a reduced frequency criterion, or
- ratings of the frequency and severity binge eating symptoms as a continuous variable, rather than a set diagnosis.

Eight prospective (**Table 2.5**), three cross-sectional (**Table 2.6**) and four retrospective (**Table 2.7**) studies investigating binge eating behaviours after bariatric surgery were identified. Of these, 11 studies found evidence of post-surgical symptoms of binge eating and feelings of loss of control over eating. Two prospective studies by Adami et al. reported post-surgical BED at 2 and 3 years post-BPD [299, 381] (Table 2.5). Rates had declined significantly after surgery, yet 9% (6/65) and 2% (1/63) continued to meet BED diagnostic criteria. Post-surgical BED were most likely to have been diagnosed with BED prior to surgery [381]. In a cross-sectional study Guisado et al. diagnosed BED in 18% of subjects 18 months after VBG [382]. Mitchell et al. diagnosed full BED in 6.4% of patients who were between 12.5 to 15.6 years post RYGB [304].

Table 2.5 Summary of prospective studies to assess post-operative binge eating behaviours and other surgical outcomes. Studies are ordered according to post-surgical BED and binge eating prevalence rates*

Study reference, surgery, design	Sample	Mean Follow-up Period	Assessment materials and methods	Pre-operative binge eating		Post-operative binge eating		Post-surgical Outcomes
				BED	BE	BED	BE	
Adami, Gandolfo et al. 1996 [286], BPD, Pros	n=65 (49F), mBMI 47.6 , ma 37, att 0%	2y	BED: CI	63.1%	NR	9.2%	NR	5 (of 6) with BED also had baseline BED. BED did not predict WL.
Adami, Meneghelli et al. 1999 [299], BPD, Pros	n=63 (48F), mBMI 46.9, ma 37.6, att 0%	3y	BED: CI	42.8%	NR	1.6%	NR	No baseline BED were still BED. One subject commenced BE post-surgery. BED did not predict WL.
Latner, Wetzler et al. 2004 [302], RYGB, Pros	n=65 (65F), mBMI 54.1, ma NR, RR 43%, att 0%	16.4m	BED: abridged EDE. Post-op by phone.	48%	NR	0%	NR	No baseline BED were still BED. Pre-operative BED predicted greater BMI loss.
Dymek, le Grange et al. 2001 [296], RYGB, Pros	n=32 (26F), mBMI 56.7, ma 39.1, att 38%	6m	BED: QEWP-R TFEQ BES	32%	NR	0%	NR	No baseline BED were still BED. Pre-operative BED did predict poorer WL (38.5%EWL vs non-BED 53.9%EWL) No differences in eating behaviour or symptoms of depression b/w pre-operative BED and NBE.
Saunders 2004 [379], RYGB, Pros	n=64 (NR), mBMI NR, ma NR	3-18+m	QEWP BES Post-operative self-made survey	NR	~60% binging or grazing	NR	~48% reporting loss of control	80% of pre-operative bingers and grazers continued to report feelings of loss of control from 6 post-surgical months. Many binge eaters reported a shift to grazing.
Lang, Hauser et al. 2002 [313], LAGB, Pros	n=66 (58F), mBMI 48.1, ma 38.1, att 0%	12m	BE: BSQ TFEQ	N/A	63.6%	N/A	28.7%	16/19 of baseline binge eaters still bingeing at 12m. Binge eating did not predict WL or eating behaviour.
Kalarchian, Wilson et al. 1999 [367], RYGB, Pros	n=50 (38F), mBMI 52.8, ma 38, att 19%	4m	BED: EDE-CI TFEQ BDI	N/A	44% (≥1/ wk, 3/12)	N/A	16%[1]	Only subjective bulimic episodes reported. Pre-surgical binge eating did not predict BMI loss, eating behaviour or symptoms of depression.

Powers, Perez et al. 1999 [311], Gastric restrictive, Pros	n=116 (96F), mBMI 53.4, ma 39.6, att 34%	5.5y	BE: BSQ BES	N/A	52% (≤1/wk)	N/A	0%	No binge eating. Pre-operative binging did not predict WL. 33% were vomiting >weekly; pre-operative binge eating not related to vomiting.
Boan, Kolotkin et al. 2004 [307], RYGB, Pros	n=40 (34F), mBMI 52.9, ma 41 , att 0%	6m	BE: BES (>18) TFEQ	N/A	30	N/A	0%	No binge eating. Pre-operative binge eating was a positive predictor of WL.
Busetto, Segato et al. 2005 [297], LAGB, Pros	n=379 (281F), mBMI NR, ma NR, att 0%	5y	BED: CI	34%	NR	NR	NR	Post-op binge eating N/A. Pre-operative BED had pre-surgical therapy. Pre-operative BED did not predict WL, but required more & higher band adjustments.
Busetto, Segato et al. 2002 [295], LAGB, Pros	n=260 (188F), mBMI 46.6, ma 37.6, att 4%	3y	BED: CI	28.8%	NR	NR	NR	Pre-operative BED did not predict WL or weight regain. BED did predict increased band-related complications.
Green, Dymek-Valentine et al. 2004 [292], RYGB, Pros	n=65 (48F), mBMI 54.8, ma 39.3, att ~2%	6m	BED: SCID or QEWP-R TFEQ BES	26.2%	24.6% (1/wk)	NR	NR	Combined pre-operative BE did predict poorer WL (41.2%EWL vs 46.8%). BE had higher lower SF-36 social function, and higher disinhibition and hunger. No differences in depression.
Potoczna, Branson et al. 2004 [290], LAGB, Pros	n=300 (210F), mBMI 43.5, ma 42, att 4%	3y	BED: CI	16%	NR	NR	NR	Pre-operative BED lost less weight than non-BED. BED who were carriers of MC4R mutations had poorer outcomes than non-MC4R BED.
Busetto, Valente et al. 1996 [289], ASGB, Pros	n=80 (57F), mBMI 48, ma 36, att 0%	12m	BED: CI Vomiting diary 24-hour recall	12.5%	NR	NR	NR	Pre-operative BED did not predict WL. BED did predict increased vomiting frequency and band-related complications. No difference in total EI, macronutrient distribution, consistency of foods, food contacts/day b/w BED and NBE
Malone and Alger-Mayer 2004 [310], RYGB, Pros	n=109 (91F), mBMI ~48, ma ~45, att ~30%	12m	BE: BES (≥18)	N/A	52%	NR	NR	Binge eating did not predict WL. More severe BE showed greater improvement in depression.

*The key for tables 2.5, 2.6 and 2.7 is listed under table 2.7

Table 2.6 Summary of cross-sectional studies to assess post-operative binge eating behaviours and other surgical outcomes

Study reference, surgery, design	Sample	Follow-up Period	Assessment materials and methods	Pre-operative binge eating		Post-operative binge eating		Post-surgical Outcomes
				BED	BE	BED	BE	
Guisado Macias and Vaz Leal 2003 [382], VBG, C/S	n=25 (15F) binge eaters, mBMI NR, ma 36.5, RR NR and n=115 (95F) non-binge eaters, mBMI NR, ma 44.6, RR NR and n=115 (95F)	18m	BED: CI	N/A	N/A	18	NR	Current BED predicted poorer WL (24.5% vs 32.2%WL)
Kalarchian, Marcus et al. 2002 [383], RYGB, C/S	n=96 (77F), mBMI ~49, ma ~42, RR 51%	>2y to <7y	BED: EDE-Q TFEQ	N/A	N/A	N/A	45%[2]	Binge eating behaviour predicted weight regain (5.2 versus 2.5 BMI points) despite similar initial weight loss.
Larsen, van Ramshorst et al. 2004 [312], LAGB, C/S	n=109 (102F), mBMI 45.4, ma 41, RR 82%	>2y	BE: BES (≥18) Dutch – EDE SF-36	N/A	N/A	N/A	37%	Post-operative binge eating was associated with poorer BMI loss and poorer mental health than non-binge eaters
	n=48 (42F), mBMI 45.5, ma 40, RR ~82%	≤2y		N/A	N/A	N/A	32%	
	n=93 (77F), mBMI 46.5, ma 39, RR NR	N/A		N/A	56%	N/A	N/A	

Table 2.7 Summary of retrospective studies to assess post-operative binge eating behaviours and other surgical outcomes

Study reference, surgery, design	Sample	Mean Follow-up Period	Assessment materials and methods	Pre-operative binge eating		Post-operative binge eating		Post-surgical Outcomes
				BED	BE	BED	BE	
Mitchell, Lancaster et al. 2001 [304], RYGB, Retro	n=78 (65F), mBMI 43.8, ma 56.8, RR 91%	12.5 to 15.6y	BED: M-FED	48.7%	--	6.4%	5.1%[3]	Current binge eating increased tendency to weight regain.
Pekkarinen, Koskela et al. 1994 [384], VBG, Retro	n=27 (19F), mBMI 50, ma 36, RR 82%	5.4y	BE: BES (≥17)	N/A	N/A	N/A	37%	Post-operative binge eating was main predictor of poor WL and weight regain.
Hsu, Betancourt et al. 1996 [298], VBG, Retro	n=24 (24F), mBMI 48.8, ma 39.7, RR 20%	≤3.5y	BED: EDE-CI	37.5%	--	N/A	21%[3]	Pre-operative BED more likely to be post-operative BE. Post-operative BE associated with weight regain. Pre-operative BED was not associated with weight regain.
Hsu, Sullivan et al. 1997 [303], GBP, Retro	n=27 (27F), mBMI 48.8 , ma 40.4, RR 43%	21±11 m	BED: EDE-CI	48%	--	N/A	7%[3]	Post-surgical eating disturbance >2 years was associated with weight regain.

[1]Subjective bulimic episodes reported at a frequency of ≤1 per week. No objective binges reported.
[2]BE were defined as ≥1 episode of loss of control (objective or subjective bulimic episode) per week over the past 4 weeks
[3]Diagnostic criteria excluded the criterion for consumption of an objectively large amount of food; BE = subjective bulimic episodes only
Surgery: BPD, biliopancreatic diversion; RYGBP, roux-en-Y gastric bypass; LAGB, laparoscopic adjustable gastric band; ASGB, adjustable silicone gastric band; VBG, vertical banded gastroplasty; GBP, gastric bypass
Design: Pros, prospective; C/S, cross-sectional; Retro, retrospective
Sample: n (F), number of subjects (number of females); mBMI prior to surgery, mean BMI; ma, mean age; att, attrition; RR, response rate; NR; not reported
Assessment: CI, clinical interview; QEWP-R, Questionnaire on eating and weight patterns – revised; TFEQ, Three factor eating questionnaire; BES, Binge eating scale; BSQ, Binge scale questionnaire; SCID, structured clinical interview; EDE-Q, Eating disorder examination questionnaire; EDE-CI; Eating disorder examination clinical interview; M-FED, an interview to collect data on eating behaviour and psychopathology; N/A, not assessed

Loss of Control over Eating

A loss of control (LOC) related to eating refers to the feeling that one cannot stop eating or control what or how much is eaten. Based on clinical observation and studies of individuals with bulimia nervosa, experts have suggested feelings of LOC are the most consistent and psychologically disturbing feature of a binge.

Given the gastric restrictive component of LAGB and RYGB, a number of authors have omitted the BED criterion that stipulates consumption of an objectively large amount of food, and focussed on feelings of LOC. Using modified criteria, Kalarchian et al. reported subjective binge episodes at a frequency of $\leq$1/week in 16% of subjects as early as 4 months after RYGB [367]. In a cross-sectional design >2 and <7 years after RYGB, Kalarchian et al. reported $\geq$1 objective or subjective binge episode per week over the past 4 weeks in 45% of subjects [383].

Three studies that assessed pre-surgical BED by retrospective recall reported the continuation of subjective binge episodes at a significantly reduced rate after surgery. Recurrent feelings of LOC were diagnosed in 5.1% of patients over 12.5 years after RYGB [304], in 7% of patients around 2 years after GBP [303] and 21% of patients up to 3.5 years after VBG [298]. In all cases pre-surgical binge eaters were more likely than non-binge eaters to experience subjective bulimic episodes after surgery. Saunders also described the continuation of poorly controlled eating behaviour in 80% of those who reported difficulty before surgery [379]. Feelings of LOC reappeared around six months after RYGB.

Symptoms of binge eating severity, without the need to engage in objective binge episodes, have also been reported at 12 months following LAGB [313]. Lang et al. reported 29% of subjects with at least moderate binge eating tendencies. Over 80% of these had been binge eating prior to surgery. In a cross-sectional study, Larsen et al. reported binge eating behaviour in greater than 30% of subjects around two years after LAGB [312]. At an average of 5.4 years after VBG, 37% of subjects have also reported moderate to severe binge behaviours [384].

Subjects have also reported poor control associated with the consumption of smaller amounts of food over an extended period of time [379, 383]. This eating pattern has been termed "grazing". Given the difficulty consuming objectively large amounts of food following gastric restrictive surgery, Saunders has suggested this post-surgical pattern of eating may fulfil a similar function to binge eating [379]. The concept of grazing is discussed below.

In clinical practice self-reported loss of eating control may occur more frequently than reported. Patients may simply be too ashamed to admit these feelings to their surgeon, or be more inclined to avoid clinical follow up [379]. The relationship between post-surgical feelings of LOC and psychological health outcomes has not been investigated. Although infrequently associated with the consumption of objectively large amounts of food, post-surgical feelings of LOC may represent a psychologically disturbing behaviour that warrants clinical assessment and treatment. Studies to investigate weight loss outcomes are discussed below.

Weight Loss Outcomes

"Success" following bariatric surgery is most often judged by body weight at follow up or when weight stable. Within the surgical literature, percentage of excess weight loss (%EWL), percentage of weight loss, actual weight loss, and change in BMI are commonly used measures. A total of 19 studies that assess and compare post-operative weight change in binge eaters and non-binge eaters have been identified (Tables 2.5, 2.6 and 2.7). In pre-surgical binge eaters these investigations were approximately divided between a finding of no difference in weight outcome, and a poorer weight loss outcome. In addition two reports, a prospective study at 6 months post RYGB [307], and a retrospective study at an average of 16.4 months post RYGB [302] observed a greater weight reduction in pre-surgical binge eaters.

Importantly, the relationship between post-surgical symptoms of binge eating and weight loss outcomes appears more consistent. Most studies report a positive association between post-surgical change in binge eating behaviour or feelings of LOC and BMI.

Nine reports found similar weight outcomes in pre-surgical BED and non-binge eaters. These reports include prospective studies at 4 months post RYGB [367]; 1 year following AGB [289], LAGB [313] and RYGB [310]; 3 years post LAGB [295]; 5 years post LAGB [297] and an average of 5.5 years post 'gastric restrictive' surgery [311]. In one of the longer, larger prospective studies, Busetto et al. found a similar %EWL at all time points out to 5 years following LAGB, and no difference in the percentage of weight regain [297]. It is noteworthy that this study and an earlier study by the same group [295] provided pre- and post-surgical psychological support to persons with BED.

Two retrospective studies also reported similar weight outcomes in pre-operative binge eaters [298, 304]. However, both studies noted an association between post-operative binge eating and body weight. At 12.5 to 15.6 years following RYGB Mitchell et al. reported a wide range of weight loss outcomes (-3.6 to 93.6kg) [304]. Compared to those who had never binged and those bingeing only prior to surgery, persons who engaged in binge eating both before and after surgery had regained significantly more weight ($p<0.05$). In a small group of subjects <3.5 years post VBG, Hsu et al. also reported greater weight regain in subjects engaging in subjective binge episodes beyond 2 post-surgical years [298].

Poorer weight loss outcomes in pre-operative binge eaters are described in eight reports. Prospective studies range from 6 months post RYGB [292, 296] to 3 years following LAGB [290]. The largest of these studies diagnosed 47 of 300 (16%) consecutive LAGB candidates with BED [290]. A gene analysis undertaken in all study participants revealed that all 19 subjects (6.3%) carrying mutations of the MC4R were also part of the BED group. At 3 years follow-up BED with MC4R variants had lost approximately 18% less weight than all non-carriers ($p=0.003$). A non-significant trend to poorer weight loss was noted in the non-carrier BED group compared to non-binge eaters ($p=0.10$). A small retrospective investigation at 21 ± 11 months post GBP reported that 60% of subjects with pre-operative binge eating had begun to regain weight compared to only 14% of non-binge eaters [303]. In this study, a pre-surgical eating disturbance (BED or night eating syndrome or drinking excessive amounts of fluid) also predicted weight regain in those $\geq$2 years post surgery.

Post-surgical cross-sectional studies support of an inverse association between post-surgical binge eating behaviour and weight loss outcome. At 18 months post VBG current BED had lost 24.5% of body weight, compared to 32.2% in non-BED (p=0.001) [382]. Despite a significant overall decrease in BMI at <2 years and > 2 years after LAGB, Larsen et al. also reported a lesser reduction in post-surgical binge eaters [312]. At >2 and <7 years post RYGB, subjects reporting ≥1 episode of LOC (objective or subjective bulimic episode) per week over the past 4 weeks experienced a rise in BMI by 5.2kg/m² compared to 2.5kg/m² in non-binge eaters (p<0.001) [383]. Despite similar initial weight losses, 37% of subjects with symptoms of binge eating a mean of 5.4 years post VBG recorded 24%EWL compared with 50%EWL in non-bingers (p=0.04) [384].

Complication Rates

Five studies to compare binge eaters and non-binge eaters on various post-surgical complications were identified [289, 290, 295, 297, 311], and are listed in Table 2.5. All but one study involved the adjustable gastric band; the remainder involved unspecified "gastric restrictive" procedures [311]. All studies compared post-operative complications according to pre-operative binge status. Findings are largely inconsistent however, studies reporting vomiting frequency appeared to be positively associated with gastric or oesophageal problems. Persons with pre-operative BED may also require more intense follow-up to adjust gastric band volumes.

Differences in vomiting frequency according to binge status, which were considered in this thesis, have previously been assessed in four prospective studies. Three years after LAGB Potoczna et al. found that pre-operative BED with MC4R gene mutations vomited more often and/or with increased severity compared to non-carrier BED and non-binge eaters [290]. At 6 and 12 months post LAGB, Busetto et al. also reported that pre-operative BED vomited significantly more than non-BED [289]. A second, larger study by the same group showed no increased vomiting frequency 3 years after LAGB in pre-operative BED [295]. The authors suggested that increased pre- and post-operative psychological support may have improved this outcome. At an average of 5.5 years following gastric restrictive surgery, Powers et al. also found no association between pre-operative binge eating and post-operative vomiting [311]. In this cohort,

33% vomited weekly or more often. Vomiting was a most commonly cited response to the consumption of foods known to be difficult, or eating too great a quantity of food. Current data are limited by the small number of available studies, the failure to assess post-operative eating pathology, and the lack of research involving RYGB and BPD.

Psychological Outcomes

Psychological disturbance such as depression and body image distress are commonly associated with BED. While the causal and counter-causal nature of the relationship is unclear, those with a predisposition to eat or binge eat in times of low mood or intense negative emotion may over time still turn to food. It is conceivable that the recurrence of symptoms of binge eating or depression may instigate or perpetuate each other. Wadden et al. argue that subsequent to periods of high or low mood, an individual's disposition tends to return to an innate level [293]. This could also be true of deeply ingrained patterns of thinking and attitudes towards food [379]. Poor post-surgical weight loss or weight regain may influence psychological state and eating behaviour. Some research suggests that weight regain after behavioural weight loss therapy is associated with increased symptoms of depression and reduced self-esteem [385].

To date, a small number of studies have assessed symptoms of depression before and after surgically induced weight loss. These studies have compared outcomes in pre-operative binge eaters and non-binge eaters. Similar to the short-term effects of behavioural weight loss treatments, a significant reduction in symptoms of depression has been reported so that binge eaters and non-binge eaters were indistinguishable at an average of 6 months [292, 296] and 16.4 months after RYGB [302]. Due to higher pre-operative symptoms of depression in binge eaters, Kalarchian et al. noted that this group underwent a comparatively greater improvement in the immediate post-surgical phase [367]. In another study, despite marked improvements at 12 month follow-up, a higher depression score still defined pre-operative BED ($p<0.018$) [310].

Cross-sectional studies have found poorer weight loss and greater major depression, passive-aggressive and aggressive-sadistic personality styles, manic disorders and alcohol dependence (all $p<0.001$) in binge eaters at 18 months post VBG [382]. At >2y to <7years after RYGB, symptoms of binge eating have been associated with poorer

weight loss and higher levels of weight and shape concern (both $p<0.001$) and poorer body shape evaluation ($p<0.05$) [383]. In the first year after BPD, despite marked weight loss in the whole group, body image disturbance reduced more slowly in baseline BED [365]. Reduced anxieties over weight and shape has been advocated as an important factor contributing to a reduction in binge eating two years after BPD [381].

The post-surgical interaction between psychological stressors such as low mood and body image distress, binge eating behaviour and body weight is unclear. It is possible that over time, old eating patterns or former emotional or environmental binge triggers may lead to the recurrence of binge eating attempts and unfavourable eating patterns. Psychological, behavioural and pharmacological treatment studies suggest that BED can be unremitting and somewhat persistent in some affected persons. Surgical studies also show a tendency for pre-surgical binge eaters to continue aberrant eating behaviour at some time after surgery. Further work needs to clarify whether bariatric surgery is an appropriate and effective stand-alone or adjunctive treatment for obese persons with BED. Given the change in eating behaviour induced by gastric restrictive surgery, improved understanding of the clinical significance of feelings of LOC related eating is required. Enhanced understanding of these factors can be used to inform the management of affected individuals seeking and undergoing obesity surgery.

Research Question #3

i) Which of the three central behavioural features of BED; binge frequency, binge size or feelings of LOC are most strongly associated with psychological distress?

Research Question #4

i) What is the extent and nature of change in BED and feelings of LOC related to eating after LAGB surgery?

ii) Is there an association between pre- or post-surgical BED or feelings of LOC and surgical outcomes including weight loss, psychological well-being and complication rates?

Night Eating Syndrome

History and Description of the Syndrome

Albert Stunkard first characterized NES in 1955 as morning anorexia, evening hyperphagia and insomnia [386]. A positive association with life stress and depression was noted, along with a reduced efficacy during weight loss attempts. It was also suggested that night eating may be a response or coping mechanism in the face of negative emotions. Similar to BED, NES received little attention following its original documentation, but became the topic of renewed interest in the eighties and nineties.

As currently studied, the NES is not formally recognized as an eating or sleeping disorder. There is a distinct lack of clarity regarding the clinical significance of NES, and the lack of agreed diagnostic criteria. Although not formally validated, the majority of NES studies have based diagnosis on the three features first described by Stunkard et al. [283, 386]. These include:

1) no appetite for breakfast

2) 50% or more of food intake after 7pm, and

3) trouble getting to sleep and/or staying asleep [283].

More recent criteria proposed by Birkedvedt et al. in 1999 attempted to narrow and define the NES definition, specifying that awakenings must occur at least once per night over a 3 month period. A criterion involving consumption of high calorie snacks during night-time awakenings was also added [387]. Their research criteria include:

1) Morning anorexia, even if the subject eats breakfast

2) Evening hyperphagia, in which $\geq$50% of daily caloric intake is consumed after the last evening meal

3) Awakenings at least once per night at least 3 nights of the week

4) Consumption of high calorie snacks during these awakenings on frequent occasions

5) This pattern occurs for a period of ≥3 months

6) Subjects do not meet criteria for bulimia nervosa or binge eating disorder

The criteria by Birketvedt et al. were put forward following a small behavioural study which involved 10 overweight NES subjects (BMI 28.5kg/m², mean age 57y) and 10 controls (BMI 28.2kg/m², mean age 47y). Individuals with NES consumed significantly more of their dietary energy later in the evening than non-NES. Sleep-onset and sleep-maintenance insomnia was common, and NES subjects awoke an average of 3.6 times per night compared to 0.3 times per night in controls. Half of the awakenings of the NES subjects involved food intake, whereas no food was consumed during waking of the control group [387].

Prevalence

Prevalence estimates of NES show great variation depending on the population studied, and research methodology and NES criteria employed. **Table 2.8** lists NES prevalence estimates among general samples, and a large female sample. **Table 2.9** lists NES prevalence estimates among obese subjects seeking non-surgical obesity treatment. Compared to community samples rates of NES are notably higher yet wide ranging (median 14.5%; range 6 - 64%). Prevalence estimates among those seeking conservative weight loss treatments appear similar to morbidly obese individuals seeking surgical obesity treatment (see **chapter 7, table 7.2**). Prevalence of pre-surgical NES has been reported in the range of 8% to 31% (median 15.5%).

Table 2.8 Studies that have assessed the prevalence of night eating syndrome in general samples

Study reference	Sample	Sample			NES Assessment Criteria						
		n (%F)	Mean BMI	Mean Age	Morning Anorexia	Evening Hyperphagia	Poor Sleep Onset or Maintenance	Mood Disturbance	Wake to eat	Method	%NES (n) (%F)
Rand and Kuldau 1986 [388]	Normal weight volunteers	232 (62)	NR	35	Wakening with little or no appetite, not starting to eat until later in the day	Eating on and off throughout the evening	Having difficulty going to sleep	Eating without enjoyment, feeling tense upset, or anxious as bedtime neared	No	CI & Q	0.4% (1) (100%)
Rand, Macgregor et al. 1997 [389]	General population	2097 (58)	25	53	Over past 2/12: Morning anorexia, delay of eating after awakening for several hours	Excessive evening eating	Insomnia	Evening, tension and/or feeling upset	No	CI	1.5% (31) (NR)
Striegel-Moore, Dohm et al. 2005 [390]	Young female volunteers	1341 (100)	~26	21	Not eating until after 9am in the morning	Consuming nearly 50% or more of daily food intake after the evening meal	Getting up in the middle of the night at least once per week	No	At least sometimes having a snack during awakening	Q	1.6% (22) (All F)

Sample: (%F), (% of NES group who were female); NR, not reported. Method: CI, clinical interview; Q, self-report questionnaire

Table 2.9 Studies that have assessed the prevalence of night eating syndrome in obese subjects seeking non-surgical obesity treatment

Study reference	Sample	Sample			NES Assessment Criteria						
		n (%F)	Mean BMI	Mean Age	Morning Anorexia	Evening Hyperphagia	Poor Sleep onset or Maintenance	Mood Disturb-ance	Wake to eat	Method	%NES (n) (%F)
Ceru-Bjork, Andersson et al. 2001 [391]	Obesity clinic	194 (76)	40	44	No appetite in the morning	Largest food intake after 7pm	Trouble getting to or staying asleep	No	No	Q	6% (11) (82%)
Stunkard, Berkowitz et al. 1996 [283]	Obesity clinic	79 (100)	35	39	No appetite for breakfast	50% or more food intake after 7pm	Trouble getting to or staying asleep	No	No	CI	8.9% (7) (All F)
Stunkard 1959 [267]	Obesity clinic	100	NR	NR	Morning anorexia with little food intake at breakfast	>25% EI after evening meal	Sleeplessness > midnight at least half the time	No	No	Q	12% (12) (NR)
Stunkard, Berkowitz et al. 1996 [283]	Obesity clinic	102 (100)	38	39	No appetite for breakfast	50% or more food intake after 7pm	Trouble getting to or staying asleep	No	No	CI	13.7% (14) (All F)
Gluck, Geliebter et al. 2001 [392]	Weight loss	76 (70)	37	44	Skipping breakfast >4 d/wk	50% or more food intake after 7pm	Difficulty falling or staying asleep >4 d/wk	No	No	Q	14% (11) (73%)
Stunkard, Berkowitz et al. 1996 [283]	Obese drug trial	40 (100)	36	40	No appetite for breakfast	50% or more food intake after 7pm	Trouble getting to/staying asleep	No	No	CI	15% (6) (All F)
Adami, Campostano et al. 2002 [393]	Cons/ surg	166 (78)	44	NR	Morning anorexia	25% EI after the evening meal	Trouble falling or staying asleep most nights	No	No	CI	15.7% (26) (69%)
Napolitano, Head et al. 2001 [394]	Long term obesity	83 (53)	41	48	Do you typically lack an appetite in the morning?	50% or more food intake after 7pm	No	No	No	CI	43.4% (36) (50%)
Aronoff, Geliebter et al. 2001 [395]	Metab clinic	110 (62)	55	48	No appetite for breakfast	50% or more food intake after 7pm	Trouble getting to/staying asleep	No	No	CI	51% (56) (41%)
Stunkard, Grace et al. 1955 [386]	Obesity clinic	25 (92)	NR	35	Morning anorexia with low food intake at breakfast	>25% EI after evening meal	Sleeplessness > midnight at least half the time	No	No	CI	64% (16) (NR)

Sample: (%F), (% of NES group who were female); NR, not reported; Cons/ surg, mixed medical/surgical treatment group; Metab clinic, metabolic clinic.
Method: Q, self-report questionnaire; CI, clinical interview

Nocturnal snacking

There is a growing view that rising from sleep to eat is an important component of NES [272, 387, 396], or may depict a subgroup of NES with more severe symptoms [397, 398]. Two studies have described a time-delayed pattern of eating in conjunction with night-time awakenings to full consciousness and ingestion of food [387, 399]. Food diaries suggest the average night-time ingestion can be highly variable, but equates, on average, to a medium-sized snack (1134±1197kj) [387]. Other studies have focussed singularly on nocturnal eating, rather than low ratings of morning appetite or quantitation of evening energy intake. Cases of NES that involve recurrent night-time snacking share common features with the recognized sleep disorder "night eating/drinking syndrome" (NEDS). The NEDS involves repeated night-time awakenings (to full consciousness) during which food or drink is compulsively consumed, and followed by normal sleep resumption [400]. While the NEDS is classified primarily as a sleep-related issue, comparison of the two conditions suggests there are more similarities linking NEDS and NES than dividing them [391]. Studies that have assessed nocturnal snacking or NEDS are listed in **Table 2.10**. Study methods and prevalence estimates range widely (range 5.8 - 55%).

Aetiology and Course

Understanding of the pathogenesis or clinical course of NES is hampered by inconsistent characterization of the syndrome. Experts suggest NES follows a chronic course, exacerbated in times of higher stress [272]. A small number of studies have investigated circadian hormone patterns in NES and non-NES. Birkedvedt et al. assessed neuroendocrine features of NES in a small study of 10 night eaters and 21 age and BMI-matched female subjects of normal and overweight [387]. All subjects were restricted to 4 meals per day (8am, 12noon, 4pm and 8pm) each containing 400kcal (1673kj). A significant decrease in nocturnal plasma melatonin levels and attenuation of plasma leptin levels occurred in the overweight and normal weight NES subjects. The authors hypothesized that sleep onset and sleep maintenance insomnia was disrupted in NES secondary to the failure of melatonin to rise. Lower plasma leptin levels at night

Table 2.10 Studies that have assessed nocturnal eating or night-time snacking in bariatric surgery candidates and persons seeking non-surgical obesity treatments

Study reference	Sample	Sample			Night-time Eating Assessment Criteria	Method	%NES (n) (%F)
		n (%F)	Mean BMI	Mean Age			
Manni, Ratti et al. 1997 [401]	Sleep Disorder Centre	120 (57%)	NR	43	Compulsive feeding shortly after a mid-sleep awakening, in the absence of daytime eating disorders	CI&Q	5.8% (7) (71%)
Greeno, Wing et al. 1995 [402]	Obesity clinic	79 (100)	~38	~39	Subjects self-recorded details related to night-time eating patterns over 8 days (range 5-10 days). 'Night eaters' recorded ≥1 night eating episode	D	7.6% (6) (All F)
Andersen, Stunkard et al. 2004 [403]	General	2111 (50%)	NR	NR	Do you get up at night to eat?	Q	8.2% (173) (55%)
Ceru-Bjork, Andersson et al. 2001 [391]	Obesity clinic	194 (76)	40	44	Waking up at night and getting out of bed to eat or getting out of bed to eat or eating in bed	Q	10% (19) (82%)
Hsu, Sullivan et al. 1997 [303], Retro	GBP	27 (100)	49	39	At least once/week for at least 3/12	CI	33% (9) (All F)
Hsu, Betancourt et al. 1996 [298], Retro	VBG	24 (100)	49	48	No set frequency or time frame	CI	42% (10) (All F)
Latner, Wetzler et al. 2004 [302]	GBP	65 (100)	54	40	At least twice/week for previous 3/12	CI	55% (36) (All F)

Study Type: Retro, retrospective assessment. All other studies assessed present eating pathology. Sample: (%F), (% of NES group who were female); GBP, gastric bypass; VBG, vertical banded gastroplasty. Method: CI, clinical interview; Q, self-report questionnaire.

may contribute to nocturnal hunger and disrupt sleep by failing to suppress appetite. A more recent study found a reduction in serum leptin concentration related to severe sleep deprivation in 10 healthy men [404]. This suggests a reverse pathway, where sleep onset or sleep maintenance insomnia leads to suppressed leptin levels. Attenuated 24-hour plasma leptin and melatonin levels have also been observed in students who habitually stay awake until the early hours of the morning, and eat >50% of their daily energy intake in the evening [405].

Birkedvedt et al. also documented higher 24-hour plasma cortisol levels in NES [387] and attenuation of the stress-induced biological response secondary to an over-expressed hypothalamic-pituitary-adrenal axis (HPA-axis) [406]. Persistent stimulation of the HPA-axis has been linked to stress, insomnia and depression [407, 408]. The authors hypothesized that night eating is associated with chronic levels of stress. The studies by Birkedvedt et al. produced some interesting findings but are limited by small sample sizes, and study protocols and laboratory settings which may have altered hormonal responses in the night eaters. More recently, similar plasma cortisol, leptin and melatonin levels were reported in 15 NES and 14 matched controls [409]. This study also reported a lower evening ghrelin level secondary to nocturnal eating, and raised night-time insulin and glucose in concert with food intake.

Association with Obesity

The evidence linking NES and obesity has been largely based on prevalence data showing consistently higher night eating estimates in overweight and obese persons, compared to the general community. Recent studies also suggest that NES may be a risk factor for obesity development. Marshall et al. compared 40 night eaters of BMI >30kg/m^2 and 40 night eaters BMI <25kg/m^2 [410]. The obese NES were significantly older, suggesting NES contributes to weight gain over time. A large prospective study found that obese women who responded affirmatively to the question "do you get up at night to eat?", gained significantly more weight over a six year period (mean 5.2kg) compared to obese non-night eaters (mean weight gain 0.9kg) [403]. In a psychiatric population night eaters meeting a criterion of evening hyperphagia (>1/3 of calories after the evening meal) or nocturnal snacking ($\geq$3 times/week) were five times more likely to

be obese [411]. Patients attending sleep disorder clinics for problems that involve nocturnal eating often report weight gains directly linked to the onset of the sleep-related eating disorder [397, 412].

It is unclear whether NES involves a general tendency to overeat. In controlled studies, increased [387] and similar total daily energy intakes [399, 409] have been observed. A laboratory study found that NES and non-NES consumed similar amounts of a test meal during the day, despite those with NES reporting less hunger and greater pre-prandial feelings of fullness [392]. During structured dieting, obese NES have recorded poorer [386, 392, 395] and similar weight loss outcomes [413]. A propensity to background overeating or poor dietary compliance secondary to the continuation of night eating could impact on weight loss efforts following bariatric surgery.

Psychological Correlates

Altered psychological and emotional states that have been linked with NES include:

- A low mood, particularly in the evening and night [386-388, 392, 409, 414, 415].
- Symptoms of depression [392, 409, 414, 416].
- Life stress [386].
- Low self-esteem [392].
- Psychoneuroticism and bulimic behaviour [416].
- Psychological distress and anxiety [394].

Similar levels of psychological functioning between NES and non-NES have also been reported in community populations [389, 390, 417], a normal weight sample of black females [390], an obese sample [394], and a group of bariatric surgery candidates [311]. Within obese populations BED has been found to co-occur with NES [272, 393, 394, 396, 415] and nocturnal snacking [298, 303, 401, 402]. The prevalence and significance of overlap in these conditions will be discussed presently.

In general, studies examining the level and significance of psychological impairment associated with NES offer disparate findings. The lack of agreed diagnostic criteria is directly related to the uncertainty regarding which behavioural feature(s) of NES

constitute a clinically meaningful entity. These facts were highlighted in a recent review which questioned the validity of NES as a distinct eating disorder [418]. The review concluded with a number of recommendations, including the need to:

1) Develop a uniform definition.

2) Identify the core cluster of symptoms.

3) Identify clinically significant frequency thresholds for symptoms and the syndrome.

4) Attain further evidence that NES is associated with distress and dysfunction.

5) Develop reliable and valid assessment measures.

Night Eating Syndrome and Bariatric Surgery

Among obese bariatric surgery candidates, rates of NES are potentially high, and certainly greater than the general community. A total of nine studies to investigate aspects NES and bariatric surgery were identified. As is the general state of the literature, these studies showed significant heterogeneity in study methodology and design. Small sample sizes and retrospective analysis of behavioural traits further weaken the dataset. These studies are reviewed in chapter 7, and listed in **Tables 7.2 and 7.3.**

Co-morbid Binge Eating Disorder and Night Eating Syndrome

Binge eating disorder and NES share a common association with obesity [272, 415], but have been studied and described as separate entities. **Table 2.11** outlines diagnostic features that distinguish the two conditions.

Table 2.11 Clinical features defining the night eating syndrome and binge eating disorder

Clinical Features	NES	BED
Morning anorexia	Yes	Usually No
Evening hyperphagia	Yes	Possibly
Daytime food cravings	Yes (evening only)	Yes
Binges	No (snacks)	Yes
Nocturnal ingestions	Yes	Rarely
Sleep difficulties	Yes	No
Amnesia for events	No	No
Compensatory behaviours	No	No

Adapted from O'Reardon, Peshek et al. 2005 [396]

Despite differing sleep patterns, and timing and quantity of food consumption, a number of investigations have recorded significant overlap between the two conditions. **Table 2.12** lists eight studies that have assessed rates of co-morbid BED and NES in obese populations. Total group overlap varies from 0% in a group of women seeking medical weight loss treatment [283], to 15.7% in an inpatient obesity program [394]. The latter study did not include an NES criterion for sleep difficulties. Focussing only on the disordered eating groups, overlap ranged from 0% to 100%. In the studies listed in Table 2.12, a median of 36.1% of NES also reported BED and a median of 21.3% of BED had NES. Overlap between nocturnal snacking and BED has also been reported within obese populations (**Table 2.13**). Highest rates of overlap are reported by retrospective recall [298, 303] however, cross sectional studies also show high rates of nocturnal eating among persons with BED.

Table 2.12 Studies that have assessed co-morbid night eating syndrome and binge eating disorder

Study reference	Sample	n	Mean BMI	Mean age	% F	BED and NES assessment method and criteria	% NES	% BED	%NES with BED	%BED with NES	Total group overlap
Stunkard, Berkowitz et al. 1996 [283]	Weight loss	79	35	39	100 %	BED: DSM CI; NES: No appetite for breakfast, 50% or more food intake after 7pm, and trouble getting to sleep or staying asleep	8.9% (n=7)	7.6% (n=6)	0%	0%	0%
Allison, Wadden et al. 2006 [288]	Obesity Surgery	210	50	44	82%	BED: DSM CI; NES: Evening hyperphagia (<25% of intake after evening meal) and/or 3 or more nocturnal ingestions per week.	9.0% (n=19)	4.2% (n=9)	26.3% (n=5)	55.5% (n=5)	2.4%
Powers, Perez et al. 1999 [311]	Obesity surgery	116	53	40	83%	BED: BSQ using modified DSM-IV criteria, ie. binge frequency of ≥1/week; NES: Morning anor, >25% EI after eve meal, trouble sleeping	10.3% (n=12)	16.4% (n=19)	25% (n=3)	15.8% (n=3)	2.6%
Stunkard, Berkowitz et al. 1996 [283]	TV advert	102	38	39	100 %	BED: DSM CI; NES: No appetite for breakfast, 50% or more food intake after 7pm, and trouble getting to sleep or staying asleep	13.7% (n=14)	19.6% (n=20)	42.9% (n=6)	30% (n=6)	5.9%
Adami, Meneghelli et al. 1999 [299]	Obesity surgery	63	47	38	76%	BED: DSM CI; NES: Morning anorexia, 50% EI after 7pm, trouble getting to sleep or staying asleep	7.9% (n=5)	42.8% (n=27)	100% (n=5)	18.5% (n=5)	7.9%
Adami, Campostano et al. 2002 [393]	Cons/ surg [2]	166	44	NR	78%	BED: DSM CI; NES: Morning anorexia, 25% EI after the evening meal, trouble falling and/or staying asleep most nights	15.7% (n=26)	32.5% (n=54)	50% (n=13)	24.1% (n=13)	7.8%
Stunkard, Berkowitz et al. 1996 [283]	Obese BED	40	36	40	100 %	BED: DSM CI; NES: No appetite for breakfast, 50% or more food intake after 7pm, and trouble getting to sleep or staying asleep	15% (n=6)	100%[1] (n=40)	N/A	15% (n=6)	15%
Napolitano, Head et al. 2001 [394]	Inpatient Obesity clinic	83	41	48	51%	BED: DSM CI; NES: Based on 2 questions: Do you often eat >50% of calories in the evening (after 7pm)? Do you typically lack an appetite in the morning? (NB. no sleep criterion)	43.4% (n=36)	31.3% (n=26)	36.1% (n=13)	50% (n=13)	15.7%

[1]Sample group all had BED; [2]Cons/surg, a cohort seeking a combination of conservative and surgical weight loss treatment

Table 2.13 Studies that have assessed the overlap of nocturnal eating and binge eating disorder

Study Reference	Sample	n	Mean BMI	Mean age	% F	Nocturnal Eating / Night eating/drinking syndrome (NEDS)	% Nocturnal Eating (NE)	% BED	%NE with BED	%BED with NE	Total group overlap
Manni, Ratti et al. 1997 [401]	Sleep Centre	120	NR	43	57%	BED: DSM CI; Night Eating: Compulsive feeding shortly after a mid-sleep awakening, in the absence of daytime eating disorders	8.3% (n=10)	2.5% (n=3)	30% (n=3)	100% (n=3)	2.5%
Greeno, Wing et al. 1995 [402]	Obesity clinic	79 [1]	~38	~39	100%	BED: EDE CI; Night Eating: > 1 night eating episode over an average 8 day (range 5-10 days) recording period	7.6% (n=6)	51% (n=40)	100% (n=6)	15% (n=6)	7.6%
Grilo and Masheb 2004 [419]	Obese BED	207	44	35	78%	BED: DSM CI; Night Eating: ie. eating after having awoken from sleep, at least half of the time over previous 28 days	9.2% (n=19)	100%[2] (n=207)	N/A	9.2% (n=19)	9.2%
Hsu, Sullivan et al. 1997 [303], Retro	Obesity surgery	27	49	39	100%	BED: DSM CI (retrospective); Night Eating: Waking during the night and eating at least once/week for at least 3/12	33.3% (n=9)	48.1% (n=13)	44.4% (n=4)	30.1% (n=4)	14.8%
Hsu, Betancourt et al. 1996 [298], Retro	Obesity surgery	24	49	40	100%	BED: DSM CI (retrospective); Night Eating: Not defined	42% (n=10)	37.5% (n=9)	40% (n=4)	44% (n=4)	17%

[1]40 women who met criteria for BED and 39 weight and age-matched women without BED
[2]Sample group all had BED
Study Reference: Retro, retrospective assessment. All other studies assessed present eating pathology. DSM CI, Clinical Interview for BED based on Diagnostic and Statistical Manual of Mental Disorders 1994; EDE CI, Clinical Interview for BED based on Eating Disorders Examination; NR, not reported

Co-existence of BED and night eating behaviours may exacerbate associated weight gains and lead to more severe obesity [283, 394, 419]. Given the strong association between BED and psychological distress, night eaters with co-existing BED may be more likely to manifest emotional upset and symptoms of depression. Of the studies to examine the link between NES and psychological disturbance, few studies have controlled for the influence of binge eating. Reported associations between NES and depression [386, 392], self-esteem [392] and psychoneuroticism and bulimic behaviour [416] have failed to consider co-morbid BED. In studies that have considered binge eating, similar levels of psychological functioning between NES and non-NES have been reported in a normal weight sample of black females [390] and an obese sample [394]. Only one study to control for BED has reported a positive association between NES and depressive symptoms of depression [415]. This study compared weight-matched controls to obese NES defined by consumption of $\geq$25% total energy after the evening meal and/or awakenings to eat $\geq$3 times in a week. A high level of psychological disturbance has also been reported among nocturnal eaters referred to a sleep clinic for polysomnography [401]. The presence of nocturnal snacking may be an important correlate of any psychological impairment associated with NES.

Research Question #5

i) Which behavioural features of NES constitute a clinically meaningful entity with regard to the risk of obesity or psychological impairment (after controlling for overlap with BED)?

Research Question #6

i) What is the extent of change in the prevalence of NES and nocturnal snacking following LAGB surgery?

ii) Is there an association between pre- or post-surgical NES or nocturnal eating and outcomes including weight loss, psychological well-being and complication rates?

Eating and Exercise Behaviour after Bariatric Surgery

The following section outlines the proposed weight loss mechanisms of LAGB and RYGB and reviews the scientific literature that has investigated post-operative changes in dietary intake, eating behaviours and patterns, and physical activity. Particular attention is paid to LAGB, with work involving RYGB included for comparative purposes or in the absence of LAGB data.

Weight Loss Mechanisms

The primary modes of action of LAGB and RYGB are currently believed to involve:

- Physical restriction of the amount of solid food that can be consumed at any one time, resulting in an overall decrease in daily energy intake [289, 420].
- Early satiation; increased mid-meal satiety; reduced feelings of hunger [193, 421].
- Aversive stimuli such as abdominal discomfort or regurgitation that can occur if food is consumed in too great a quantity, too quickly, or is not chewed adequately [207, 289]. This may facilitate an increase in dietary restraint and reduction in disinhibited eating [421, 422].

Careful adherence to post-surgical dietary guidelines encouraging an ordered and regular meal pattern may also facilitate control over food and energy intake [423]. An attenuated pre-prandial rise in plasma ghrelin has been observed after RYGB which may assist to reduce appetite [424]. LAGB does not appear to induce hormonal change beyond the normal weight loss response [193].

Nutritional Advice

Despite growing numbers of severely obese undergoing bariatric surgery, no evidence-based guidelines support nutritional management after bariatric surgery. Dietary advice for the immediate post-surgical period often follows a similar progression, yet long-term nutritional recommendations differ between clinicians and clinics [425].

Immediately after gastric restrictive surgery, patients are instructed to consume foods and beverages of liquid consistency. Consumption of 5 to 6 small "meals" containing

protein-rich choices such as low-fat milks and yoghurts, creamy soups and protein-rich beverages such as Optifast are recommended [426]. Over the next two to three weeks, the texture of food is increased to pureed consistency (finely minced meats and vegetables, eggs, "soggy" cereals), then soft (fish, cooked vegetables) and solid foods.

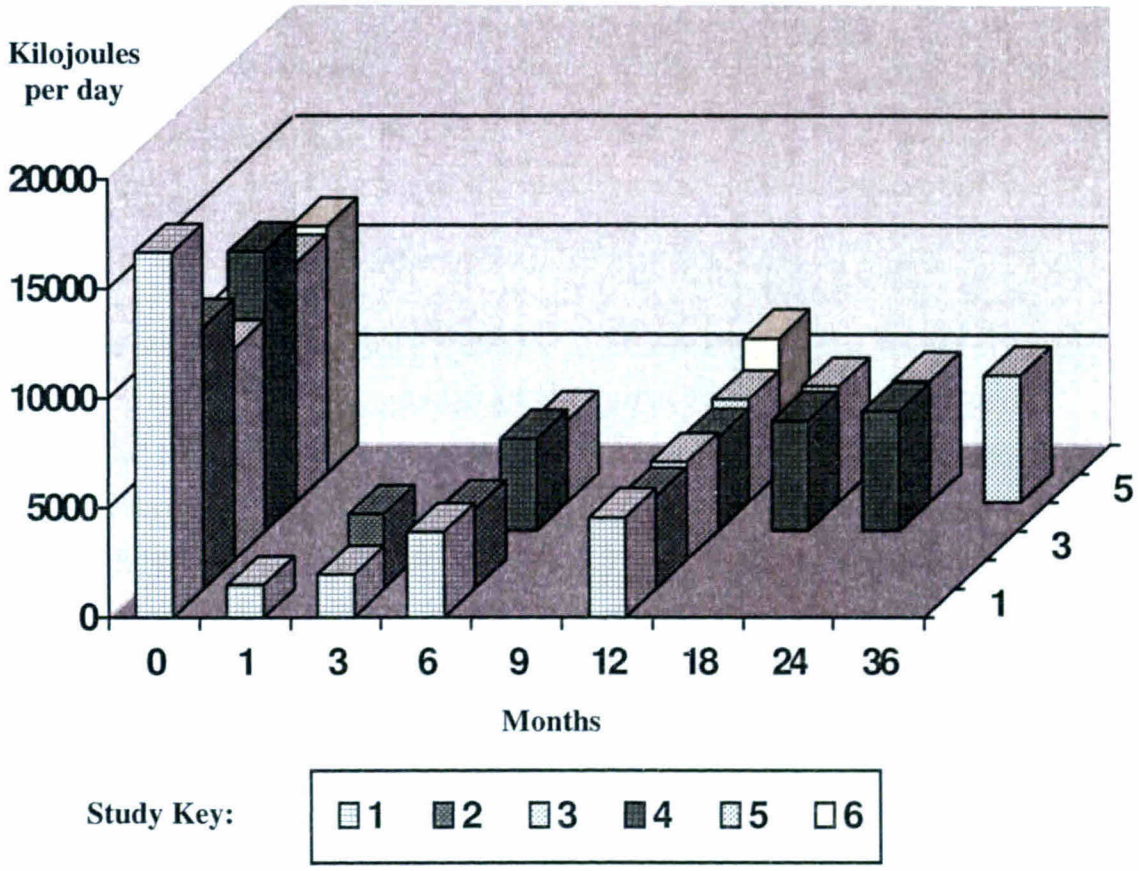
Beyond the immediate post-operative period, eating and exercise guidelines after LAGB have typically included advice to [192]:

1) Eat 3 small meals per day
2) Eat only nourishing, solid food
3) Eat slowly, stop when comfortable
4) Avoid eating between meals
5) Take no liquids with the meal
6) Consume only liquids with zero calories (dairy being an exception)
7) Exercise for at least 30 minutes per day
8) Be active throughout the day

Dietary Intake

The putative weight loss mechanisms of gastric restrictive surgery function predominately by reducing overall energy intake. Only one study has previously evaluated the change in energy intake during the first year after gastric banding [289]. In this study Busetto et al. assessed intake using the 24-hour dietary recall method. A baseline energy intake of 11.9$\pm$6.0Mj, reduced to 3.2$\pm$1.2Mj/day by three post-surgical months (p<0.001) and remained essentially stable at 4.2$\pm$1.8Mj/day by 12 months. **Figure 2.2** graphs this data alongside estimated energy intakes following RYGB.

Figure 2.2 Change in energy intake following RYGB and LAGB



Surgery/Number		Dietary Methodology
1	GBP / n=25	Dietary Recall & Checklist [212]
2	AGB / 80 Ss	24-hour dietary recall [289]
3	RYGB / n=26	4-day weighted intake [427]
4	RYGB / n=51	24-hour dietary recall [211]
5	RYGB / n=108	24-hour dietary recall [201]
6	RYGB / n=36	Semi-quantitative FFQ [420]

Figure 2.2 shows a distinct reduction in energy intake in the early post-operative period, followed by a small, gradual increase in energy intake out to three post-operative years. Mean decreases in energy intake calculated from these data are:

- 68% at 6 months
- 61% at 12 months
- 57% at 18 months
- 53% at 24 months
- 47% at 36 months

Alongside change in energy intake, Busetto et al. examined the relative change in dietary macronutrient composition after LAGB [289]. Prior to surgery, dietary composition consisted of 16.8±4.9% protein, 36.4±9.7% fat and 44.9±11.4% carbohydrate. Despite a marked reduction in total energy intake, 12 month figures remained similar to baseline; 19.2±5.3% protein, 37.8±11.2% fat and 42.7±12.3% carbohydrate. The same study assessed the qualitative change of foods of solid, soft and liquid consistency. Food choices altered and reflected a move toward liquid consistencies in lieu of solid foods. The number of "food contacts" also reduced significantly from baseline, which may indicate a lesser tendency to graze or snack.

Dietary Disinhibition, Hunger and Restraint

In general terms, higher ratings of dietary disinhibition and hunger are reported by obese individuals compared to normal weight controls [428-430]. Greater disinhibited eating and hunger have predicted higher energy intakes [429], poorer weight reduction [431] and poorer weight loss maintenance [179]. High dietary restraint may facilitate successful weight loss [432]. Bariatric surgery candidates, and particularly those who binge eat, typically show higher levels of disinhibition and hunger, and lower levels of dietary restraint than obese non-treatment seekers [291, 305]. At 12 [287] and 24 months [72] after gastric restrictive surgeries, prospective studies have demonstrated a marked reduction in dietary disinhibition and hunger, and significant increase in dietary

restraint. In both cases weight loss success was inversely correlated with reported levels of disinhibition and hunger. Two cross-sectional studies which captured data >2 and <7 years after RYGB [383] and approximately two years after LAGB [312] showed higher levels of hunger in subjects displaying post-surgical binge eating tendencies.

Grazing

Grazing has received limited attention in the medical [433, 434] and surgical [285, 287, 297, 300, 379, 435] weight loss literature. Other authors have described patterns of "nibbling" [295, 436-439] and "snacking" [440-442] in relation to energy intake and body weight. These terms are inconsistently defined, and yield variable results. As a concept "grazing" is currently poorly defined and is not listed or acknowledged as a disordered eating pattern or non-normative behaviour. In cases where grazing is associated with significant functional or psychological impairment it is possible that this pattern of eating be listed under the category of "eating disorder not otherwise specified" (EDNOS).

Among bariatric surgery candidates the prevalence of grazing and frequent snacking appears high [285, 287, 295, 297, 300, 379]. Burgmer et al. reported 19.5% of surgical candidates were grazing, in the sense of "permanent eating" [287]. Saunders defined grazing as consumption of "smaller portions of food continuously or larger amounts of food over an extended period of time", during the previous six months [300]. Sixty percent of surgical candidates were self-reported grazers, and significantly more grazers reported severe binge eating problems (43.1%) than non-grazers (19.6%; $p<0.01$). Busetto et al. assessed patterns of pre-operative nibbling and grazing [295, 297]. Nibbling, diagnosed if the patient ate "small quantities of foods repetitively between meals, typically triggered by inactivity and/or loneliness", was present in 42.5% of surgical candidates [295]. In a subsequent study, grazing defined according to similar criteria, was present in 38.3% of the total cohort, and was more prevalent among those with pre-operative BED (49.2%) than non-binge eaters (32.5%; $p<0.01$) [297]. Two of these studies compared post-operative weight losses in pre-operative grazers, finding no difference in outcome. Burgmer et al. reported similar weight loss 12 months after

gastric restrictive surgery [287]. Busetto et al. reported similar weight outcomes 3 years after LAGB [295].

Post-surgical grazing has received little attention. Saunders observed that pre-operative grazers were high risk to maintain this behaviour after surgery, and reported an element of poor control over grazing behaviour [379]. Marcus and Elkins have also noted that most patients soon become aware the consumption of small, regular amounts of food is not precluded after gastric restrictive surgery [443]. Saunders has suggested that post-surgical grazing in association with feelings of LOC may fulfil a similar function to binge eating [379]. Despite typically high rates of pre-surgical grazing, the tendency to continue grazing after surgery, and the relationship with weight and psychological outcomes has not been prospectively investigated.

Non-hungry eating

"Non-hungry" eating can be described as eating in the absence of physiological hunger. Despite marked decreases in hunger ratings following gastric restrictive surgery, it is possible that some persons may still eat or overeat for reasons other than hunger. Increased eating in response to emotional arousal such as stress, anxiety or sadness [444] has been observed among bariatric recipients [285, 445]. Immediately after RYGB, Dymek et al. reported that eating in response to anger, anxiety and depression reduced significantly and remained stable at 6 month follow-up [296]. Two or more years after surgery, higher levels of eating in response to emotions and food-related concerns have been reported in persons with binge eating tendencies [312, 383]. Grazers may also be at high risk to eat when not physically hungry. A tendency to "non-hungry" eating could circumvent a reduction in energy intake secondary to increased feelings of satiety or reduced physical hunger.

Physical activity patterns

Poor health and other physical and mental barriers to participation in physical activity are common in the obese [446]. Following obesity surgery and marked weight reduction, these barriers can reduce and facilitate increased levels of physical activity. Based on data from 1210 participants in the Swedish Obese Subjects (SOS) study, Karason et al. proposed that surgical intervention can break the obesity – physical

(in)activity cycle, with weight loss enabling greater levels of physical activity, in turn promoting better weight loss outcomes [447]. A decrease in time spent viewing television and increase in self-reported activity has been observed 6 months after RYGB [307], and 30 months after BPD [176]. The latter study reported a positive correlation between physical activity and lean body mass [176]. In the SOS study, leisure-time physical activity self-reported on a 4-point scale ranging from "sedentary activity" to "regular strenuous exercise" increased significantly 2 years after surgical intervention [447]. Those classed as physically inactive at baseline and follow-up lost less weight than those reporting a rise in post-surgical physical activity levels. The physical activity score was associated with medical health outcomes. Smaller reductions in shortness of breath and discomfort on exertion were related to lower physical activity scores [447]. Lesser improvement in physical health and ability after bariatric surgery has also independently predicted poorer weight loss outcomes after LAGB [448].

Regular involvement in physical activity facilitates weight loss during medical obesity treatments and subsequent weight loss maintenance. The benefits of regular exercise extending to greater retention of fat-free mass, lesser reduction in metabolic rate during active weight loss and improvement in metabolic health. More detailed description of the nature of change in physical activity levels following bariatric surgery, and the relationship with weight loss, physical and psychological health and eating behaviour can direct post-surgical management strategies to optimize behavioural characteristics conducive to positive surgical outcomes.

Research Question #7

i) What is the nature and extent of the change in eating patterns including energy and macronutrient intakes; food choice; dietary disinhibition, hunger and restraint and "grazing" in the first year following LAGB placement?

ii) In what measurable ways do patterns of physical activity alter in the first year following LAGB placement?

iii) Do post-operative differences in eating and exercise-related variables influence surgical outcomes including weight loss, psychological state and complication rate?

CHAPTER 3: Materials and Methods

Chapters 4 and 5 present two studies that involved dietary intervention using VLED, and radiological methods to quantitate changes in liver volume and VAT with weight loss. The following chapter provides greater detail of shared research methods, and other aspects of study design. Methods unique to a given study are detailed within that particular chapter.

The Very-Low-Energy Diet Protocol

All subjects underwent dietary weight loss intervention using a VLED (Optifast® VLCD; Novartis Consumer Health Australasia Pty. Ltd. Mulgrave, Australia). Individualized guidance and counselling were based on the recommendations of the "Optifast Clinical Treatment Protocol" (Novartis Consumer Health Australasia Pty. Ltd. Mulgrave, Australia).

In all cases subjects were instructed and encouraged to adhere to the "Intensive Phase" of this protocol. In brief this involved:

- Substitution of each meal with one or two Optifast meal replacements, depending on individual requirements. Severely obese subjects may have increased protein requirements to be met by increasing the daily number of Optifast serves to 4 or 5.

Available products included shakes, soup, mousse, and in the latter study (chapter 5) bars were also offered. Ingestion of three Optifast shakes per day provides 1906kj (456kcal), 52g of protein, 7g of fat and 45g of carbohydrate, plus the recommended daily intake of vitamins, minerals, and trace elements. Other Optifast meal replacements are of comparable nutrient content and interchangeable within the regime. One useful exception is the inclusion of 5.2 g of dietary fibre in a bar variety, compared to negligible fibre in liquid supplements.

- Subjects were encouraged to include up to 2 cups (approximately 250g) of low starch vegetables per day and one piece of "allowed" fruit.
- One teaspoon of olive oil daily was advised to contract the gall bladder and minimise the risk of gallstone formation.

The supplementary fruit, vegetables and oil provided dietary fibre plus additional nutrients, and increased the daily total energy intake to approximately 2720kj to 3030kj (650kcal to 725kcal).

- Patients were advised to drink at least 2L of water and other calorie-free beverages each day.
- Individualized advice was offered regarding physical activity. Subjects were encouraged to be physically active where able.

Subjects were seen by an experienced dietitian (Susie Colles) prior to commencement of the VLED and then fortnightly throughout the duration of the intervention.

Table 3.1 lists the nutrient content of the Optifast VLCD shake. The average daily intake of nutrients provided by 3 sachets of Optifast has been compared to the current recommended dietary intake (RDI) values for adults, derived by the National Health and Medical Research Council of Australia in 2006.

Table 3.1 Composition of Optifast VLCD compared to current recommendations for dietary intakes in adults

Nutrients	Quantity per serve (1 x 40g)	Quantity per day (3 x 40g)	RDI for adults 31-70y[1]
Energy	635 kj (152 kcal)	1905 kj (456 kcal)	N/A
Protein	17.3 gm	51.9 gm	0.75 gm/kgbw W, 0.845 gm/kgbw M
Fat, Total	2.3 gm	6.9 gm	N/A
Saturated	0.41 gm	1.2 gm	N/A
Carbohydrate	15 gm	45 gm	N/A
Sugars	9.2 gm	27.6 gm	N/A
Sodium	332 mg	996 mg	N/A
Potassium	668 mg	2004 mg	N/A
Vitamin A	332 mcg	900 mcg	700 mcg W, 900 mcg M
Vitamin C	25 mg	75 mg	45mg
Thiamin	0.5 mg	1.5 mg	1.1 mg W, 1.2 mg M
Riboflavin	0.7 mg	2.1 mg	1.1 mg W, 1.3 mg M
Niacin	6 mg	18 mg	14 mg W, 16 mg M
Calcium	300 mg	900 mg	1300 mg W, 1000 mg M
Iron	6 mg	18 mg	18 mg W, 8 mg M
Vitamin D	1.67mcg	5.9 mcg	N/A
Vitamin E	4 mg	12 mg	N/A
Vitamin B6	0.7 mg	2.1 mg	1.5 mg W, 1.7 mg M
Folic Acid	133 mcg	399 mcg	400 mcg
Vitamin B12	1 mcg	3 mcg	2.4 mcg
Phosphorus	268 mg	804 mg	1000 mg
Iodine	50 mcg	150 mcg	150 mcg
Magnesium	116 mg	348 mg	320 mg W, 420 mg M
Zinc	5 mg	15 mg	8 mg W, 14 mg M
Copper	0.8 mg	2.4 mg	N/A
Biotin	67 mcg	201 mcg	N/A
Pantothenic Acid	2.67 mg	801 mg	N/A
Vitamin K	33 mcg	99 mcg	N/A
Chloride	400 mg	1200 mg	N/A
Manganese	1 mg	3 mg	N/A
Selenium	14 mcg	42 mcg	60 mcg W, 70 mcg M
Chromium	33 mcg	99 mcg	N/A
Molybdenum	67 mcg	201 mcg	45mcg

[1]Recommended Dietary Intakes are expressed as a mean daily intake. Values are derived from National Health and Medical Research Council, Australian Government, Department of health and Ageing *Nutrient Reference Values for Australia and New Zealand* 2006. N/A indicates that there is currently no Australian RDI for this nutrient; kgbw, kg of bodyweight; W, women; M, men

Radiological Imaging

Radiological imaging was used to assess the change in liver volume, VAT area, and where possible, SAT area. All subjects underwent an abdominal CT scan before (week 0) and after weight loss (week 12). In order to control exposure to ionizing radiation, the pattern of change in liver volume and VAT during weight loss was assessed using MRI. In addition to baseline and final CT assessments, serial MRI scans were taken at weeks 2, 4 and 8 of the study protocol.

Assessment of Liver Volume by CT and MRI

The two most common and clinically useful methods of liver volume assessment are CT and MRI. Computed tomography provides a valid measure of liver volume that is highly reproducible [449-451]. Correlations between in vivo liver volume measurement by CT and direct measurement have included $r = 0.94$ for 3 bovine and 1 cadaveric human liver [449] and $r = 0.998$ for 9 fresh sheep livers [451]. An average ratio of 1.04 has also been calculated when comparing CT assessment to actual liver volume in 579 patients with liver disease undergoing transplant [450].

MRI is also a valid and reproducible method of liver volume calculation [452-454]. Series of liver transplant recipients have shown correlation coefficients of $r = 0.90$ (n=19) [453] and $r = 0.998$ (n=17) [454]. Similar variances between CT and MRI-derived liver volume calculations have been observed [452].

Imaging of Liver Volume: Computed Tomography

The paired abdominal CT scans (Asteion Multislice System; Toshiba America MRI Inc., San Francisco, CA) were undertaken in the Department of Radiology at The Avenue Hospital in Windsor, Victoria. All investigations were performed in a supine position during a single breath hold while the arms were extended overhead. Based on the procedures of Schiano et al. [450], a scout view of the upper abdomen was obtained to plan the examination. Contiguous 8mm slices were taken. This included at least one image superior to and one image inferior to the liver, to ensure the entire organ was captured. The scan was performed using a spiral sequence without contrast medium (kV = 120, mA = 250, gantry rotation = 0.75 revolution/s, table speed = 48mm/s, effective pitch = 4.5, matrix = 512x512, and field of view = 500mm).

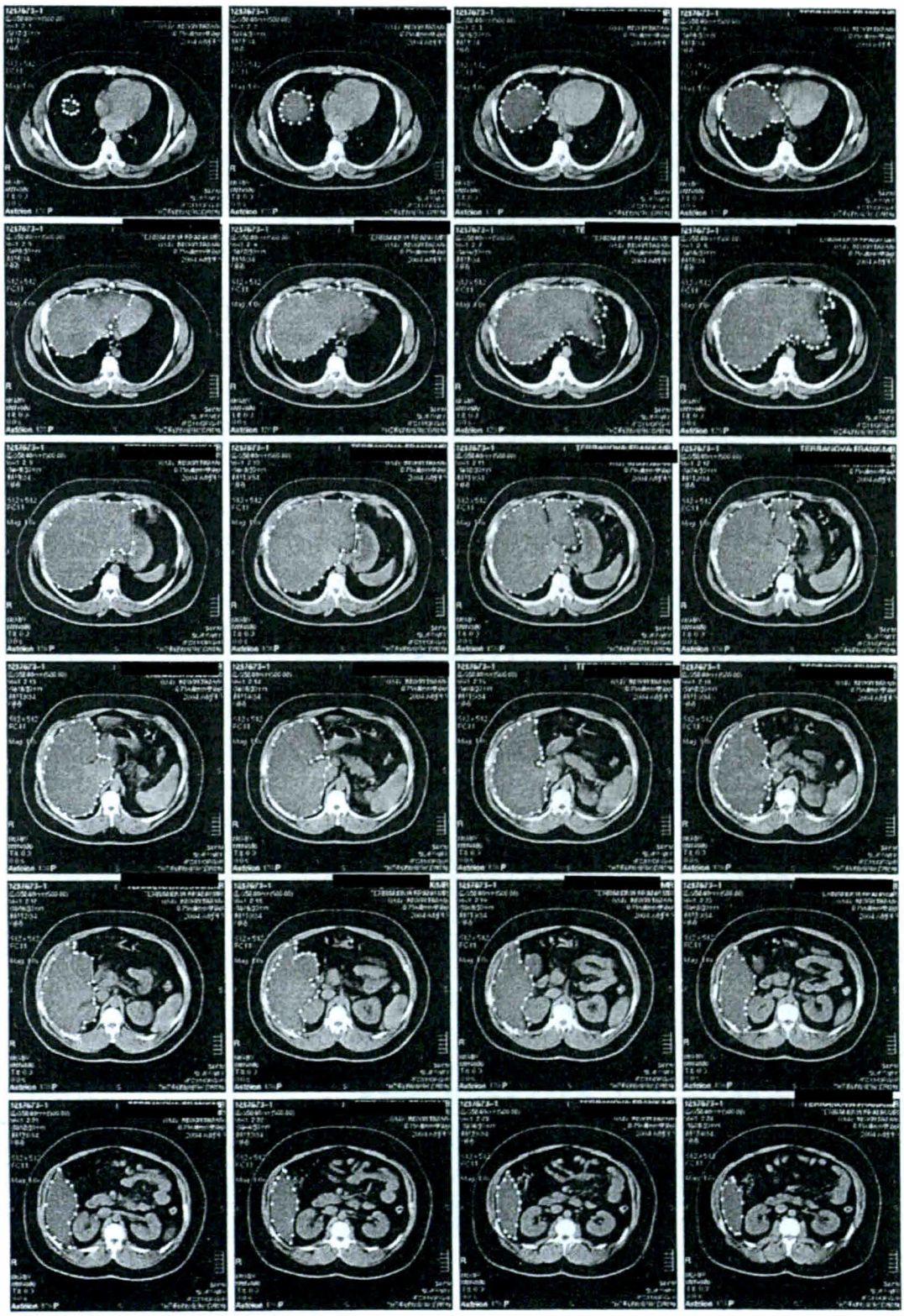
Imaging of Liver Volume: Magnetic Resonance Imaging

Magnetic resonance imaging was undertaken in the Department of Radiology at The Avenue Hospital in Windsor, Victoria. Consecutive MRI of the liver and abdomen was conducted at weeks 2, 4, 8 and 12 of the study. The primary purpose of the week 12 MRI scan was to assess the level of agreement between MRI and CT-derived images. Whenever possible, the protocol for CT and MRI was equivalent. The procedures for MRI were also based on the procedures of Schiano et al. [450] and in accordance with the methods of others who have used MRI [455]. Magnetic resonance imaging was carried out on the Signa Hi Speed Plus 1.5 Tesla (General Electric, Milwaukee, WI). As was done for CT, all investigations were performed while the subjects were in a supine position during suspended respiration with the arms raised overhead. After an initial scout view, contiguous 8mm slices were taken from the superior to the inferior aspect of the liver. The images were obtained by using a contiguous axial T1-weighted gradient echo pulse sequence (repetition time 285ms, matrix: 256x160, field of view: 480mm, flip angle: 90°).

Calculation of Liver Volume

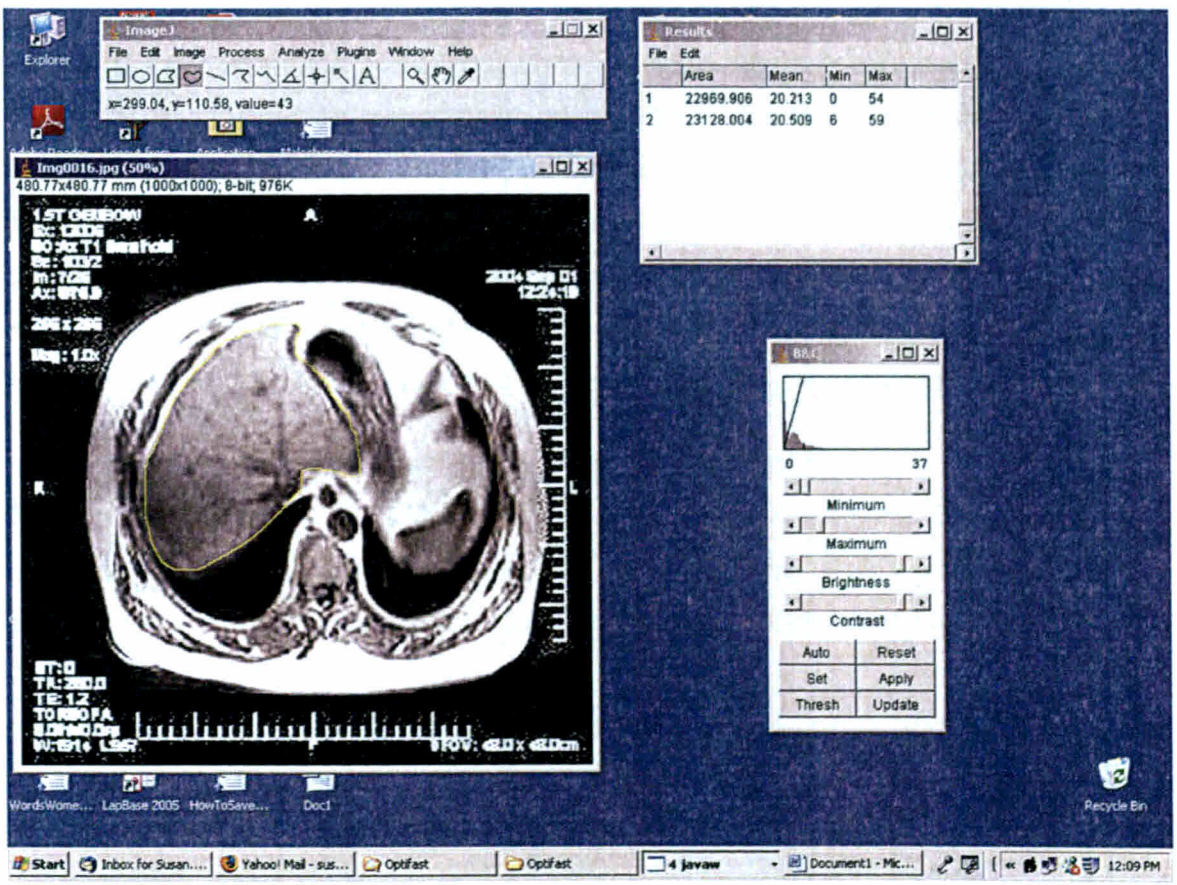
All CT scans were assessed using the software on the Asteion Multislice System software (Toshiba America MRI Inc.). To calculate actual liver volume, the planimetric technique was employed. A line was carefully drawn around the border of the liver on each contiguous scan, and the cross-sectional area within was automatically calculated. To determine the total liver volume in cubic millimetres (mm^3), the area of all slices was summed and multiplied by 0.8cm (the slice thickness). One hundred thousand mm^3 is equal to 1L. **Figure 3.1** provides an example of the planimetric technique used to assess total liver volume.

Figure 3.1 Liver volume assessment using the CT planimetric method. The cross-sectional area within each adjacent slice was calculated and summed, then multiplied by the slice thickness.



MRI sections were stored to CD-ROM, and transferred to a workstation containing a computer-based digitizing system (Image J; National Institute of Health, Bethesda, MD). Using the planimetric technique, a line was carefully drawn around the border of the liver on each contiguous scan, and the cross-sectional area within automatically calculated by the software. Measurements were undertaken by a single operator (Susie Colles). Each slice area was calculated three times, and the average value taken. The area of all slices was summed and multiplied by 0.8cm (the slice thickness) to determine total liver volume. **Figure 3.2** provides an example of the determination of tissue area using Image J.

Figure 3.2 A single MRI scan from a series of contiguous slices of the liver. A trace was carefully drawn around the border of each liver slice, and the cross-sectional area of tissue within was calculated automatically.



Assessment of Visceral Adiposity by CT and MRI

The measurement of total adipose tissue, and specific regions such as visceral and subcutaneous fat areas is commonly performed using CT and MRI techniques. The accuracy of total fat assessment by CT [31] and MRI [33, 34, 456, 457] has been validated in cadaveric and animal models. Reproducibility has also proven high [29, 458, 459].

The level of total or regional adipose tissue is most accurately determined by multi-slice imaging [460, 461]. However, multiple scanning protocols increase radiation exposure during CT [458], and elevate imaging and analysis costs associated with MRI [462]. These issues have lead to the development of protocols for measurement of VAT from a single abdominal slice. Single transaxial images at the level of the second and third, third and fourth, and fourth and fifth lumbar vertebrae, the level of the umbilicus, and other variations have been applied. Good correlations (r = 0.95-0.99) [30, 461, 463, 464] and lower correlations (r = 0.82) [465, 466] between VAT volumes obtained from multi-slice imaging and VAT area derived from a single image have been reported. Abate et al. investigated the optimal site to predict total VAT volume from a single axial image [462]. They found the level of the second and third lumbar vertebrae (L2–L3) best predicted total intra-abdominal and retroperitoneal adipose tissue (r = 0.85; p<0.001). Amounts of VAT were also greatest at this level. Agreement between measurements of VAT area assessed by CT and MRI has previously shown a spearman rank correlation coefficients of 0.89 (p<0.01) in seven healthy male volunteers [29].

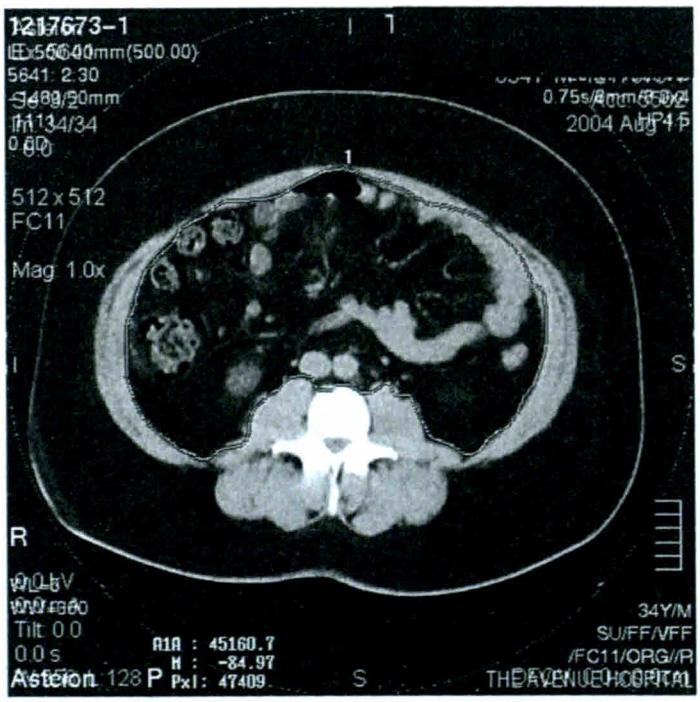
Imaging of Adipose Tissue: Computed Tomography

Paired transaxial images at the level of L2–L3 assessed the total change in VAT and SAT area. Computed tomography images were taken during each liver scan, before commencement (week 0) and at completion (week 12) of the VLED protocol.

Calculation of VAT and SAT

CT-derived VAT and SAT were measured according to the procedures of Rössner et al. [31]. A trace was drawn around the outer edge of the abdomen and total fat area determined by calculating the pixel distribution with attenuation values between –150 and –50 Hounsfield units. According to the recommendations of Shen et al. [467], a trace was then drawn inside the muscle layer of the abdominal cavity, and VAT determined by calculating the fat area encircled within. The SAT area was considered to be the adipose tissue outside the muscle layer of the abdominal cavity, derived by subtracting VAT area from the total abdominal fat measurement. Paired measurements of total and SAT area were not available for 14 subjects (44%) due to extension of the abdomen outside the field of view. **Figure 3.3** is an example of a CT image with a trace drawn inside the muscle layer of the abdominal cavity.

Figure 3.3 An abdominal computed tomography scan at the level of the second and third lumbar vertebrae, used to estimate visceral fat area



Inter- and Intra-observer Error

All CT scans and assessments were carried out by 2 skilled radiographers. Re-examination of 30% of liver volume, VAT, and SAT measurements by both technicians showed no significant differences between the initial and repeated calculations either within or between observers. Spearman's correlation coefficients between both radiographers were high at $r = 0.985$ for liver volume ($p<0.001$), $r = 0.985$ for VAT ($p<0.001$), and $r = 0.991$ for SAT ($p<0.001$). The inter-observer coefficient of variation was 1.0%, 2.1% and 1.8% for liver volume, VAT, and SAT respectively. Mean volume and area calculations of both observers were compared to the initial measurements, to yield Spearman's correlation coefficients of $r = 0.992$ for liver volume ($p<0.001$), $r = 0.982$ for VAT ($p<0.001$), and $r = 0.987$ for SAT ($p<0.001$). Intraobserver coefficients of variation based on a comparison of the initial measurements and re-measurements for each radiographer were 2.4% and 2.0% for liver volume, 2.0% and 1.7% for VAT, and 3.1 and 1.0% for SAT.

Imaging of Adipose Tissue: Magnetic Resonance Imaging

Single-slice transaxial images at the level of L2–L3 were used to assess change in the VAT compartment using the same protocol as for CT. These images were taken during the liver scan at weeks 2, 4, 8 and 12. Due to extension of the abdomen outside the field of view an accurate series of SAT measurements was obtained in 3 of the 9 subjects (33%) who completed the MRI scans. Because of this small sample size the pattern of SAT change relative to liver volume, weight and VAT was not examined.

Calculation of VAT

In order to assess VAT area, the abdominal slice at L2-L3 was identified within the sections stored to CD-ROM and transferred to a workstation containing SliceOmatic (Version 2.4, Rev-1; TomoVision, Montreal, Canada). Because of the strong signal intensity produced by adipose tissue when visualized by MRI, fat is easily differentiated from surrounding tissue. The SliceOmatic software compares the intensity of each pixel within an image to that of adjacent pixels and automatically generates a border to separate sections of the image that significantly differ in signal strength.

Figure 3.4 shows the "jig-saw" effect that is created. This enables easy identification of sections of tissue with similar pixel intensity. A mouse-click inside each piece of the VAT jig-saw colours that section of the image. Similar to the CT protocol, the inner margin of the abdominal cavity demarcated the outer border of the VAT compartment. Each scan was then manually edited within the program to ensure light sections of bowel were excluded and boundaries were clearly defined. The software determined the area of coloured VAT, providing a measurement in square centimetres.

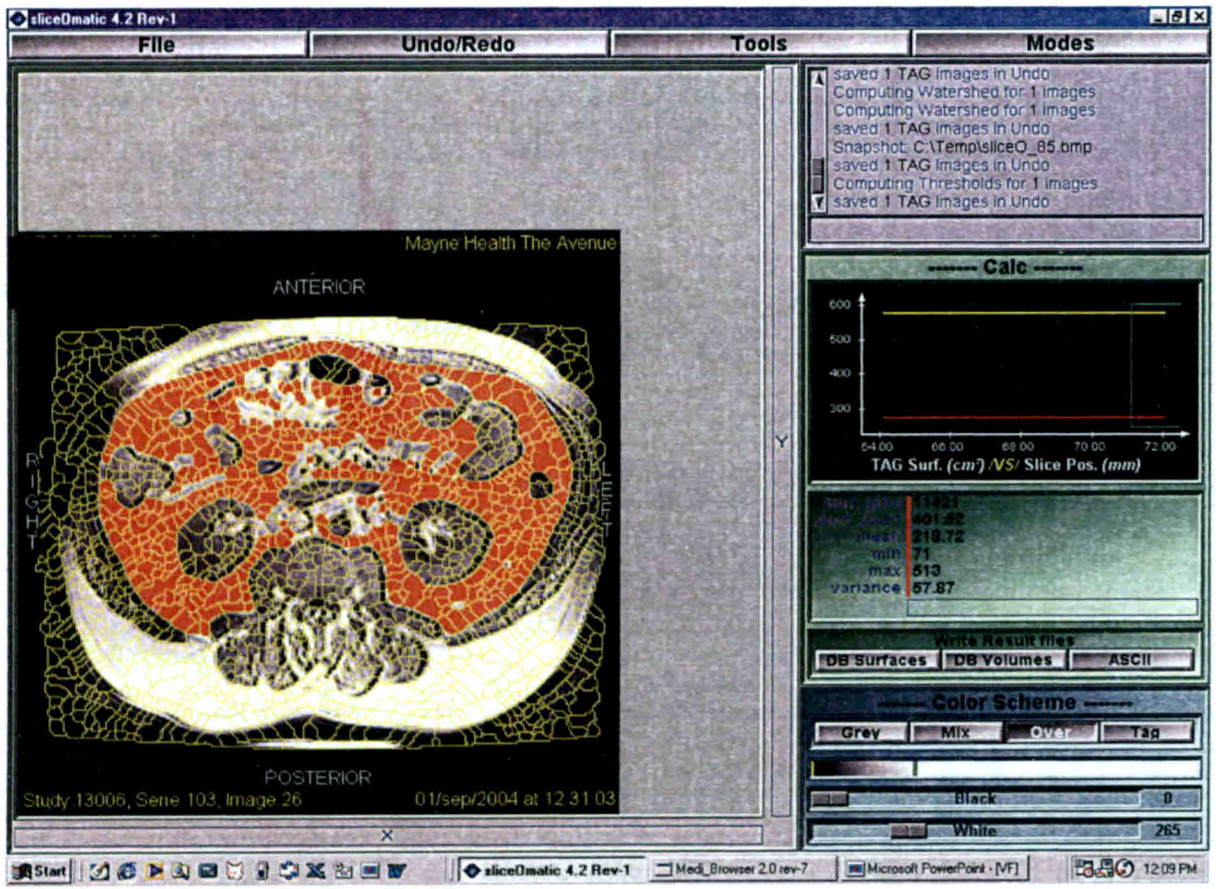
Intra-observer Error

All MRI sections were calculated by a single operator (Susie Colles). Re-examination of 30% of liver volume and VAT measurements showed no significant difference between the initial and repeated calculations. Spearman's correlation coefficients were high for liver volume ($r = 0.998$, $p<0.001$) and for VAT ($r = 0.993$, $p<0.001$). The intra-observer CV was 0.7% for liver volume and 2.4% for VAT.

Agreement between CT and MRI

To assess the level of agreement between CT and MRI-derived liver volume and VAT calculations, 11 paired measurements (2 at baseline and 9 at week 12) were available. For assessment of liver volume, the correlation between the 2 methods was high ($r = 0.989$, $p<0.001$). Analysis according the recommendations of Bland and Altman [468, 469] revealed a trivial mean bias of 0.0024L towards MRI (limits of agreement of $\pm$ 0.1736). For measurement of VAT, the correlation between the 2 methods remained high ($r = 0.866$; $p=0.001$). Bland and Altman analysis revealed a mean bias of 14.85cm^2 towards MRI (limits of agreement $\pm$ 51.2). This indicates that although the agreement between the 2 methods was very good, MRI-derived VAT measurements tended slightly higher. Neither liver volume nor VAT measurements showed any change in bias across the range of measurements.

Figure 3.4 An example of the assessment of visceral adipose tissue area using the SliceOmatic software. The area shaded orange represents visceral adipose tissue.



Data Management

Collection and Storage

Data were accumulated through clinical and radiological reports, during dietary counseling, and the assessment of MRI images. Shortly after collection, all data were transferred onto a database in the Microsoft Access® program, specially designed for the studies in this thesis. The program was devised to enable the storage of serial data, and also allow for the collation and arrangement of the records in preparation for statistical analysis. At entry into the database all participants were de-identified and provided with a unique identification number. The database was stored on a computer that required password entry. Hard copies of the study reports, documents containing personal information and the subject identification numbers were stored in a locked cabinet, and will remain so for 5 years from the date of submission of this thesis.

Data Analysis

Statistical methods are detailed within each chapter.

Declaration for Thesis Chapter 4

Declaration by candidate

In the case of Chapter 4, this work represents a manuscript that has been published in the *American Journal of Clinical Nutrition*, 2006; 84(2): 304-11. The nature and extent of my contribution to the work was the following:

Nature of contribution	Extent of contribution (%)
I was involved in the design of the experiment and study protocol. I was responsible for running the study, the majority of data collection and analysis, and writing the manuscript.	>80%

The following co-authors contributed to the work.

Name	Nature of contribution	Extent of contribution (%) for student co-authors only
Associate Professor John Dixon	Involved in the design of the experiment and study protocol. Assisted with collection and analysis of data, and writing of the manuscript.	
Dr Paul Marks	Involved in design of the experiment. Oversaw all radiological measurements, and assisted with writing of the manuscript.	
Associate Professor Boyd Strauss	Assisted with MRI analysis and with writing of the manuscript.	
Professor Paul O'Brien	Involved in the design of the experiment and study protocol. Assisted with subject recruitment and writing of the manuscript.	

Candidate's Signature	[redacted]	**Date** 5/12/07

Declaration by co-authors

The undersigned hereby certify that:

(1) the above declaration correctly reflects the nature and extent of the candidate's contribution to this work, and the nature of the contribution of each of the co-authors.
(2) they meet the criteria for authorship in that they have participated in the conception, execution, or interpretation, of at least that part of the publication in their field of expertise;
(3) they take public responsibility for their part of the publication, except for the responsible author who accepts overall responsibility for the publication;
(4) there are no other authors of the publication according to these criteria;
(5) potential conflicts of interest have been disclosed to (a) granting bodies, (b) the editor or publisher of journals or other publications, and (c) the head of the responsible academic unit; and
(6) the original data are stored at the following location(s) and will be held for at least five years from the date indicated:

Location	**The Centre for Obesity Research and Education**	
Signature 1	Associate Profes[redacted] Dixon	**Date** 7/12/07
Signature 2	Dr Paul[redacted]	7/12/7
Signature 3	Associate Professor Boyd Strauss[redacted]	5/12/07
Signature 4	Professor Paul O'Brien[redacted]	5/12/07

CHAPTER 4: Pre-operative Weight Loss by Very-Low-Energy Diet: Quantitation of Changes in Liver and Abdominal Fat by Serial Imaging

Abstract

Background: The very-low-energy diet (VLED) can achieve substantial, rapid weight loss, and is increasingly prescribed prior to obesity surgery to minimise risk and difficulty by reducing liver size and abdominal adiposity. Despite growing popularity, VLED in this setting has received little attention. The aim of this study was to investigate the efficacy and acceptability of pre-operative VLED.

Design: A prospective observational study, 32 subjects (n=19 men and 13 women) with a mean (±SD) age of 47.9 ± 9.1y and BMI of 47.3 ± 5.3kgm^2 consumed a VLED for 12 weeks. Primary outcomes included change in liver volume (LV) and in visceral and subcutaneous adipose tissue (VAT/SAT). Changes in body weight, anthropometric measures and biochemical variables were also recorded, and compliance, acceptability and side effects of treatment were assessed. Changes in LV and VAT/SAT area were measured by computed tomography and magnetic resonance imaging at baseline, weeks 2, 4, 8, and 12.

Results: Mean (±SD) LV and VAT/SAT reduced significantly, and body weight decreased by 14.8±7.2kg (p<0.001 for all). The degree of LV reduction was directly related to the reduction in relative body weight (r = .54; p=0.001) and initial LV (r = .43; p=0.015). Eighty percent of the reduction in LV occurred between weeks 0 and 2 (p<0.001). Reductions in body weight and VAT were uniform over the 12 week period. Attrition was 14%. Acceptability was adequate but waned over time. Mild transitory side effects occurred.

Conclusions: Given the observed early reduction in LV and the progressive reduction of VAT, we suggest the minimal duration for pre-operative VLED be 2 weeks, ideally extending 6 weeks to achieve maximal LV reduction and significant reductions in VAT and body weight, without compromising compliance and acceptability.

Introduction

Non-alcoholic fatty liver disease (NAFLD), characterized predominantly by steatosis, and non-alcoholic steatohepatitis (NASH) with additional lobular inflammation and fibrosis, are strongly related to obesity and metabolic and inflammatory features of the metabolic syndrome [226, 232]. Prevalence estimates of NAFLD vary; however it has been suggested that one third of individuals with NAFLD are severely obese (BMI $\geq$35kg/m^2) [470], and rates of liver steatosis are predicted to increase alongside worldwide occurrence of obesity and diabetes [229].

Although NAFLD arises most often without clinical symptoms, an enlarged, fatty liver can increase surgical risk and complexity in patients undergoing upper abdominal laparoscopic surgery [258-260]. Key elements of the two most common obesity surgery procedures in the world today, roux-en-Y gastric bypass (RYGB) and the laparoscopic adjustable gastric band (LAGB) require exposure and surgery in the area of the gastro-oesophageal junction. Hepatomegaly has been cited as the most common cause for conversion to an open procedure from laparoscopic RYGBP [262] and LAGB placement [261]. Surgeons at our centre estimate hepatomegaly increases surgical difficulty in around 10 to 20% of cases, and excessive omental fat, covering the structures of the left upper quadrant of the abdomen, provides an additional technical challenge.

Although the aetiology of NAFLD is unclear and the most appropriate treatment option undecided, weight reduction is a primary aim in the management of NAFLD associated with overweight and obesity [241, 242]. Weight loss by obesity surgery [247, 249], low calorie diets [471], and very-low-energy diets (VLED) [245, 472] can reduce weight, liver steatosis, necro-inflammatory change, and fibrosis. In the pre-surgical setting, a VLED provides the benefit of rapid weight loss [164], with no compromise to immune function [173] or wound healing [172], and few side effects [171].

Safe and effective interventions to reduce massive hepatomegaly prior to laparoscopic surgery should benefit surgeons and patients alike. However, before this practice can be broadly considered, we need good evidence that a clinically relevant reduction in liver size can be achieved. The surgeon is also interested in identifying those at greatest risk so therapy can, if effective, be focused on those likely to benefit most. Identifying the

pattern of liver volume reduction will also guide the optimal time frame for pre-operative weight loss intervention.

The aims of this study were to investigate the efficacy and acceptability of pre-operative weight loss by VLED. Specifically, we wished to investigate in a severely obese population: 1) the actual change in liver volume and the pattern of change during weight loss by VLED, 2) the relative change in liver volume, body weight, and visceral and subcutaneous adipose tissue (VAT/SAT) areas, 3) the anthropometric, clinical, and biochemical risk factors that may predict an enlarged pre-treatment liver or predict the total change in liver volume after treatment, and 4) patient acceptability and compliance, and treatment side-effects.

Methods

Patient Selection

During May 2004 to July 2005, 37 morbidly obese (BMI >40kg/m^2) subjects were selected to undergo a 12 week VLED (Optifast® VLCD; Novartis Consumer Health Australasia Pty. Ltd. Mulgrave, Australia) intervention prior to LAGB placement, using the Lap-Band® System (Inamed Health, Santa Barbara, CA), at The Avenue Hospital, Melbourne, Australia. The study was approved by the Avenue Hospital Ethics Committee, and was carried out in accordance with the Helsinki Declaration of 1975 as revised in 1983. Informed written consent was obtained from each participant.

Men or women aged between 18 to 60 years were invited to enter the study if their body weight was $\leq$155kg (the upper weight limit of the radiological equipment) and stable within $\pm$5kg over the previous three months, with a BMI $\geq$50kg/m^2 in women and $\geq$40kg/m^2 in men. Gender-specific BMI criteria were set based on the advice of surgeons who report greater surgical difficulty in men than women between a BMI 40 and 50kg/m^2. Patients were excluded if they displayed any medical contra-indications to the use of a VLED, including severe hepatic disease, advancing renal disease, and unstable cardiac disease [161]. Persons with a "high risk" alcohol intake (based on the NHMRC Australian Alcohol Guidelines, defined as greater than 7 standard drinks per day or greater than 43 standard drinks per week for males, and greater than 5 standard

drinks per day or greater than 29 standard drinks per week for females [473]) were also excluded.

Power of the Study

The principal end point was defined as the percentage change in liver volume at 12 weeks after entry into the study. On the basis of existing data, we expected that the mean percentage change in liver volume will be 40 +/- 10%. We assumed that a difference of 30% would be clinically worthwhile, and calculated that 32 patients would need to be studied to provide a 95% confidence of detecting a difference between the final liver volume and the initial volume with a power of 0.8, using a two-tailed test. On the basis of an expected 20% loss of candidates, a total initial recruitment of 40 patients was planned.

Very-Low-Energy Diet (VLED)

Subjects consumed a VLED (Optifast® VLCD™; Novartis Consumer Health Australasia Pty. Ltd. Mulgrave, Australia) during the 12 week dietary intervention. The VLED was ceased at the end of the twelfth week, which in most cases corresponded with the day prior to surgery. Adherence to the diet was not used to assess suitability for LAGB surgery, and poor compliance was not a contraindication to surgery. There was no planned re-feeding period.

Radiological Imaging: Liver, VAT and SAT

Details of the radiological imaging techniques have been detailed earlier in chapter 3. Briefly, to assess the total change in liver volume, all subjects underwent an abdominal CT scan (Asteion Multislice System; Toshiba America MRI Inc., San Francisco, CA) prior to commencement and at completion of the 12 week VLED.

The pattern of change in liver volume during the 12 week period was assessed at weeks 2, 4, and 8 using MRI (Signa Hi Speed Plus 1.5 Tesla; General Electric, Milwaukee, WI). Magnetic resonance imaging was carried out in a subgroup of nine subjects with an initial CT-derived liver volume measurement >2.8L. An additional MRI scan was taken at completion of the 12 week VLED to assess the level of agreement between CT and MRI. Single-slice transaxial images at the level of L2–L3 were obtained during all CT and MRI scans, and used to assess change in VAT and SAT area.

Anthropometric Measurements

Weight was recorded using the electronic Tanita Wedderburn TBF-305 (Lake Worth, FL) in light clothing without shoes. Height was determined by a wall-mounted stadiometer. Neck circumference was taken immediately above the thyroid cartilage, waist circumference at the narrowest point between the lower rib margin and the iliac crest, and hip circumference at the widest point over the greater trochanters. Seated blood pressure was recorded. All measurements were taken at baseline, and then fortnightly throughout the study period by a single clinician.

Laboratory Tests

Baseline and week 12 metabolic variables were assessed using a series of biochemical and haematological tests. These included liver function tests (LFT), fasting glucose metabolism (plasma glucose, plasma insulin, and glycosylated haemoglobin A_{1c}), a fasting lipid profile (total cholesterol, LDL cholesterol, HDL cholesterol, and triglyceride), and C-reactive protein (CRP). All analyses were performed in an approved laboratory with internal and external quality control, using standard assays.

Assessment of Dietary Compliance and Acceptability

Dietary compliance was assessed by using urinary ketone reagent strips (Keto-Diastix; Bayer Diagnostics Manufacturing Ltd, Bridgend, UK) to assist on-going monitoring and counselling, and not for the purpose of predicting or testing post-surgical dietary adherence. After the first week of VLED a rise in urinary excretion of ketoacids occurs subsequent to increased fat catabolism [474]. The presence of at least a trace of ketones in the urine was considered to indicate net lipolysis. Urine samples were collected on the day of each biweekly consultation. The absence of ketones scored 0, a "trace" scored 1, "small" scored 2, and "moderate" urinary ketones scored 3 points. For the purpose of analysis, the last observation carried forward was used for a single missing value in 6 patients (<1% of total measurements). Ketone scores determined at visits every 2 weeks were summed for each patient.

Qualitative methods were used to measure product side-effects and acceptability. During counselling sessions subjects were asked to rate 6 factors on a 5-point Likert scale: product taste (1, highly unacceptable; 2, unacceptable; 3, tolerable; 4, acceptable;

5, highly acceptable), hunger (1, extreme hunger; 2, hungry most days; 3, hungry some of the time; 4, occasional hunger; 5, no hunger), nausea/vomiting (1, daily; 2, 4-6 times/wk; 3, 2-3 times/wk; 4, ≤1 time/wk; 5, none), bowels (1, constipation (no bowel movement in the last 4 days); 2, constipation (no bowel movement in the last 2-3 days); 3, normal; 4, increased frequency; 5, diarrhoea), emotional eating (1, daily; 2, 4-6 times/wk; 3, 2-3 times/wk; 4, ≤1 time/wk; 5, none) and social eating (1, daily; 2, 4-6 times/wk; 3, 2-3 times/wk; 4, ≤1 time/wk; 5, none). Emotional eating was defined as "eating foods outside the diet's guidelines, due to emotional reasons such as stress, sadness, anger or frustration". Social eating was defined as "eating foods outside the diet's guidelines, because you are in a social setting". Median group ratings for each factor at weeks 4 and 10 were compared. A person's aggregate score of each factor over all 12 weeks was also assessed against their total percentage weight loss.

Data Analysis

Effects of the 12 week VLED program were directly compared using the paired-samples *t* test for continuous variables. The pattern of liver volume, abdominal fat, and body weight change over the 12 week VLED was expressed as a percentage and plotted over time. The difference in mean liver volume, VAT, and weight measurements at baseline and weeks 2, 4, 8, and 12 was assessed by analysis of variance using Tukey's post hoc analysis and paired-samples *t* test for normally distributed data. Simple bivariate analysis assessed for correlations between initial liver volume and all baseline characteristics, the percentage change in liver volume and all other measures, the average ketone score, total acceptability scores, and cumulative weight loss. Forward and backward linear regression identified factors independently predictive of a larger liver volume, and liver volume change over the 12 week period. Two quantitative laboratory variables - fasting plasma insulin and gamma glutamyltransferase (γGT) required log-transformation prior to parametric analysis. SPSS version 12.0.1 was used for statistical analysis. A *p*-value less than 0.05 was considered statistically significant.

Results

Thirty seven subjects were recruited into the study and commenced the 12 week VLED protocol; however 5 subjects (14%) failed to establish a pattern of dietary compliance

during the first 2 weeks. Four of these subjects (80%) reported on-going taste intolerance resulting in nausea and occasionally vomiting, as the main reason for non-adherence. The other subject failed to comply primarily due to major instability in his personal life. These 5 subjects, which included 2 members of the subgroup of 12 undergoing the series of MRI scans, were excluded from further investigation. All subjects continuing past week 2 were considered part of the study. There were no other patients who revoked consent or were lost to follow up, but one subject in the MRI-subgroup chose to discontinue the additional measurements due to feelings of claustrophobia inside the MRI apparatus but remained in the study. In total, 32 subjects (86%) completed the 12 week protocol, and 9 of these subjects (75% of the initial MRI-subgroup and 28% of the final study group) underwent MRI scans weeks 2, 4, 8, and 12.

Baseline Characteristics

The subject group consisted of 19 men and 13 women with a mean (±SD) age of 47.9 ± 9.1 years. Descriptive characteristics of the 32 bariatric surgery candidates are presented in **Table 4.1**. Body weight ranged from 116 to 155 kg, and BMI category from morbidly obese to super obese (range: 40.4–61.9 kg/m^2). Computed tomography assessment showed a mean liver volume of 2.8L (range: 2.0–3.9L), a mean VAT deposition 346.3 cm^2 (range: 163.9 to 556.0 cm^2), and a mean SAT measurement of 454.53 cm^2 (range: 252.5 to 699.3 cm^2). Due to extension of the abdomen outside the field of view, paired SAT measurements were only available for 18 subjects. Thirteen of the 32 subjects had type 2 diabetes (41%), 16 were on a lipid lowering medication (50%), 24 were taking an antihypertensive agent or recorded a baseline blood pressure >140/90 mmHg (75%), and 14 had ≥1 abnormal LFT (44%). Baseline biochemical parameters are shown in **Table 4.2**.

Table 4.1 Descriptive characteristics of subjects before and after a 12-week very-low-energy diet [1]

Characteristic	Baseline [2]	After 12 Weeks [2]	Mean Change (%) [3]
Body Weight (kg)	139.8 ± 11.03	125.0 ± 11.7	-10.6 (-0.7 to -19.1)
BMI (kg/m²)	47.3 ± 5.3	42.3 ± 5.5	-10.6 (-0.7 to -19.1)
Waist circumference (cm)	140.8 ± 9.8	128.1 ± 10.0	-9.0 (0 to -19.2)
Neck circumference (cm)	45.9 ± 3.8	43.2 ± 3.2	-5.9 (+2.1 to -15.3)
Systolic BP (mmHg)	154.3 ± 18.3	136.0 ± 18.1	-11.08 (+13 to -37)
Diastolic BP (mmHg)	90.7 ± 9.8	80.9 ± 11.2	-10.24 (+22 to -34)
Liver Volume (L)	2.8 ± 0.5	2.3 ± 4.5	-18.7 (+20 to -51.6)
L2-3 VAT Area (cm²)	346.3 ± 103.3	285.1 ± 89.3	-16.9 (+11.8 to -52.6)
L2-3 SAT Area (cm²) [4]	454.5 ± 114.8	375.7 ± 109.7	-17.7 (+2.9 to -40)

[1] n = 32 paired results. A significant liver volume reduction of 0.5 L (1 SD) was achieved by 15 subjects (47%). Eleven of the 15 subjects had a baseline liver volume >2.8 L at baseline. Six of the 15 subjects achieved a reduction of 1.0 L (2 SD), all of whom had a baseline liver volume >2.8 L.
BP, blood pressure; VAT, visceral adipose tissue; SAT, subcutaneous adipose tissue.
[2] mean ± SD (all such values)
[3] All values are mean; range in parentheses. All changes are statistically significant, $p<0.001$ (paired samples t test).
[4] n = 18.

Table 4.2 Change in measures of glucose metabolism, lipids, liver function, and a marker of inflammation before and after a 12 week very-low-energy diet [1]

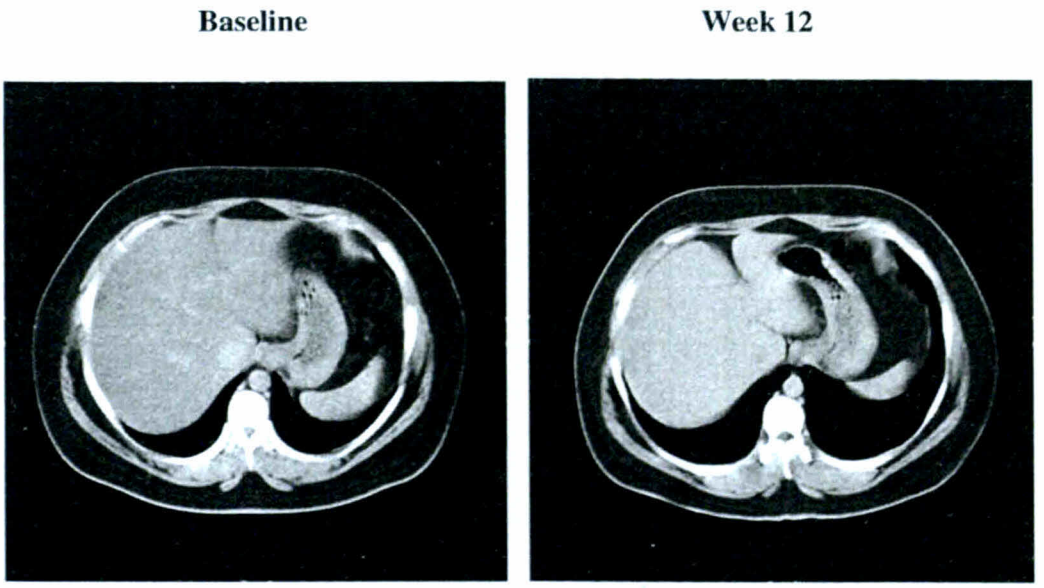
Characteristic	Baseline [2]	After 12 Weeks [2]	*p*-value [3]
ALP(U/L)	93.2 ± 31.4 (59 – 211)	84.5 ± 24.2 (52 – 159)	0.001
AST(U/L)	27.4 ± 12.7 (14 – 73)	24.8 ± 11.3 (11 – 59)	NS
ALT(U/L)	40.6 ± 23.6 (11 – 121)	32.8 ± 18.1 (9 – 105)	0.05
γGT(U/L)[4]	38.0 ± 39.0 (16 – 259)	30.0 ± 21.0 (10 – 227)	<0.001
Bilirubin (umol/L)	11.1 ± 6.5 (4 – 30)	13.0 ± 8.3 (6 – 45)	0.011
Fasting Glucose (mmol/L)	7.6 ± 3.4 (4.5 – 17.2)	6.1 ± 11.7 (3.8 – 16.4)	0.011
Fasting Insulin (mIU/L)[4,5]	24.0 ± 15.0 (11 – 164)	17.0 ± 13.0 (7 – 85)	<0.001
HbA1c (%)	7.2 ± 1.8 (5.6 – 12.7)	6.3 ± 1.1 (5 – 9.6)	<0.001
Cholesterol (mmol/L)	5.0 ± 0.95 (3 – 6.8)	4.5 ± 1.2 (2.4 – 6.5)	<0.001
Triacylglycerol (mmol/L)[5]	1.8 ± 0.68 (0.8 – 3.1)	1.5 ± 0.69 (1 – 3)	0.043
HDL cholesterol (mmol/L)	1.3 ± 0.29 (0.8 – 2.3)	1.3 ± 0.25 (0.8 – 2.0)	NS
LDL cholesterol (mmol/L)	2.9 ± 0.87 (1.1 – 4.7)	2.5 ± 1.0 (0.8 – 4.5)	0.001
CRP (mg/L)	11.4 ± 9.6 (3 – 39.1)	10.8 ± 10.0 (1 – 43.6)	NS

[1] n =31 paired results.
HbA1c, glycosylated haemoglobin A_{1c}; ALP, alanine phosphatase; AST, aspartate aminotransferase; ALT, alanine aminotransferase; γGT, gamma glutamyltransferase; CRP, C-reactive protein.
[2] mean ± SD; range in parentheses (all such values).
[3] Paired-samples t test.
[4] Denotes log-transformed data for non-normal distribution. Data presented as median + inter-quartile range (range).
[5] Denotes data for which one outlying variable has been removed and excluded from all subsequent calculations.

Changes with Weight Loss

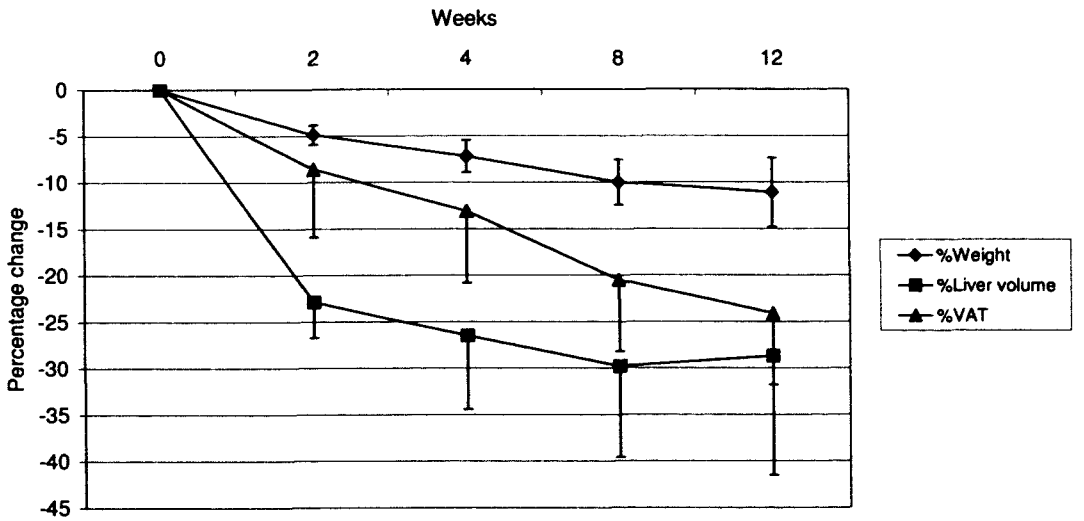
At completion of the 12 week VLED, all baseline descriptive characteristics for the 32 subjects showed a highly significant reduction (Table 4.1). Body weight decreased by 14.8 ± 7.2kg, and BMI by 5.0 ± 2.4kg/m². Liver volume diminished by 0.56 ± 0.50L, VAT by 61.2 ± 52.1cm², and SAT by 78.7 ± 50.1cm². Neither age nor gender predicted the extent of the tissue reduction. An example of a cross-sectional CT-derived image of the liver at baseline and week 12 is shown in **Figure 4.1**. Overall, there was no difference in the relative reduction of liver volume, VAT, or SAT (18.7%, 16.9%, and 17.7% respectively). Repetition of this comparative analysis in the subgroup of 18 subjects with paired SAT measurements yielded a similar reduction of 19.2% in liver volume, of 17.6% in VAT and of 17.7% in SAT.

Figure 4.1 Single cross-sectional images of the liver, performed by computed tomography at baseline and week 12 of the very-low-energy diet. These images, taken from within the series of contiguous 8mm slices used to calculate total liver volume, illustrate the extent of the change in liver volume with weight loss in a 35 year old male with an initial liver volume of 3.7L and a final liver volume of 2.4L. A 35% reduction in liver size and a weight loss of 18kg was observed.



Except for a higher initial liver volume, the baseline demographic and clinical measurements of the 9 subjects who took part in the series of MRI scans did not differ significantly from the main study group. The greater baseline liver volume of 3.4±0.42L versus 2.6±0.45L ($p<0.001$) reflects the fact that only subjects with an initial liver volume measurement >2.8 L were invited to join the MRI subgroup. Due to extension of the abdomen outside the field of view in 6 of the 9 subjects, the pattern of SAT change was not examined. The relative change in liver volume, body weight and VAT is shown in **Figure 4.2**. The total decline in liver size was 28.7%. An immediate fall in liver volume took place; 80% of the observed size reduction occurred between weeks 0 and 2 ($p<0.001$). The pattern of VAT and weight reduction showed a more progressive decline. The mean VAT decreased by 24.1% between weeks 0 and 12 ($p<0.001$). The mean total weight loss in the group of 9 was 11.1% between weeks 0 and 12 ($p<0.001$).

Figure 4.2 Relative change in liver volume, visceral adipose tissue (VAT) area and body weight during a 12-week VLED as measured by serial magnetic resonance imaging. An immediate reduction in liver volume occurred in the first 2 weeks (p<0.001) and between baseline and all other time points (p<0.001 for all). The decreases in body weight and VAT showed a more uniform change. Significant decreases in body weight (p<0.001) and VAT (p=0.001) occurred between baseline and week 12.

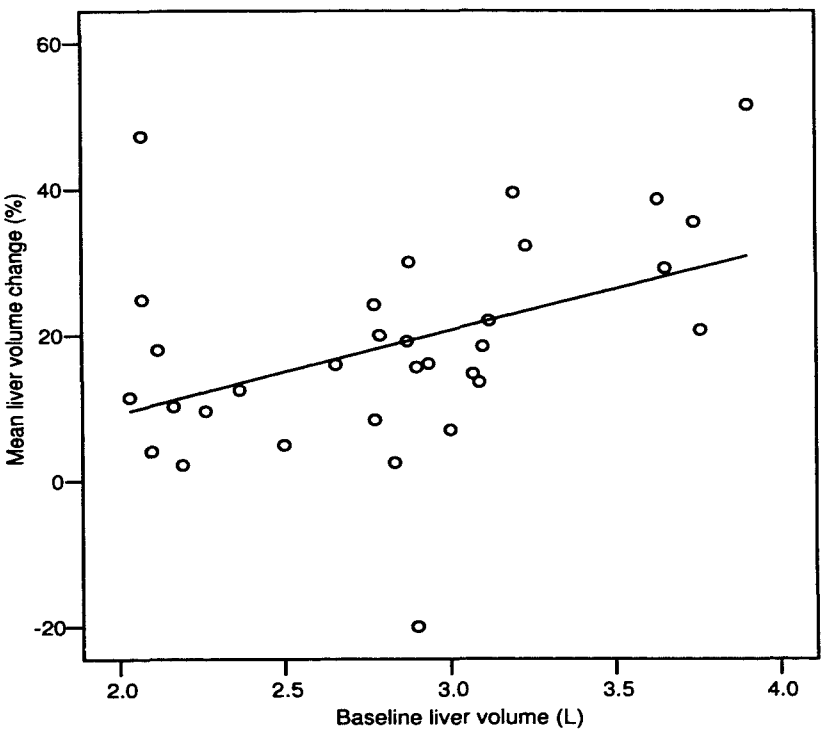


n = 9
Statistical analysis using ANOVA with Tukey's post hoc analysis and paired samples t test.

Predicting Liver Volume Loss

Focusing on the change in liver volume in the 32 subjects with paired baseline and 12 week measurements, total percentage reduction in liver volume was strongly predicted by both the relative reduction in body weight ($r = 0.54$; $p=0.001$) and the initial liver volume ($r = 0.43$; $p=0.015$). Together these variables contributed 45% of the variability in the relative change in liver volume ($p<0.001$). Subjects with a greater baseline liver volume lost proportionately more liver size over the course of the 12 week VLED, as illustrated in **Figure 4.3**. Categorization of the group into initial liver volume $\leq$2.99 L (n=20) and $\geq$3.0 L (n=12) showed a significantly greater mean size reduction in the group with larger livers (26.9% compared with 13.8%; $p=0.011$). There was no correlation between the initial VAT and SAT measurements and the relative change in VAT and SAT area, respectively.

Figure 4.3 Comparison of the mean reduction in liver volume between subjects according to initial liver size (n=32). Subjects with larger livers experienced a significantly greater decline in liver volume than those with a smaller baseline liver volume ($r = 0.43$; $p=0.015$; simple bivariate statistical analysis).



Predicting Baseline Liver Volume

Demographic characteristics of the 5 subjects who failed to establish a pattern of dietary compliance during the first 2 weeks of the study were not statistically different from the study group; therefore their anthropometric, biochemical, and radiological data were included in the assessment of factors associated with initial liver volume. When the baseline liver volume measures for the 37 subjects were corrected for age, sex and BMI, linear regression yielded 3 factors with significant independent predictive effects on baseline liver volume: triglycerides (33%; $\beta = 0.528$; $p<0.001$), diastolic blood pressure (10%; $\beta = 0.310$; $p=0.021$) and CRP (8%; $\beta = 0.297$; $p=0.025$). Together these factors contributed 51% of the variability in initial liver volume ($p<0.001$). The change in triglyceride over the 12 week VLED showed a weak relation to the change in liver volume but was not significant ($r = 0.33$; $p=0.08$).

Compliance and Acceptability

Urinary ketone analysis was performed 6 times throughout the duration of the diet in 26 subjects and 5 times in the remaining 6 subjects. The total ketone score was highly correlated with the total percentage weight reduction at completion of the diet ($r = 0.66$; $p<0.001$).

Ratings of taste acceptability in the 32 subjects averaged "acceptable" during the first 8 weeks of the diet; nevertheless, taste acceptability deteriorated over time: median scores decreased significantly from week 4 to week 10 ($p<0.001$). When the summed taste rating for each subject was compared to their total percentage weight loss, a strong inverse correlation emerged ($r = -0.57$; $p<0.001$). There were no reports of nausea or vomiting throughout the duration of the diet. At week 4 hunger ratings averaged "occasional hunger", however median hunger scores were significantly higher at week 10 ($p<0.001$). Median total hunger ratings were also inversely related to total relative weight loss ($r = -0.66$; $p<0.001$). Similar to hunger, scores for emotional eating ($p<0.001$) and social eating ($p<0.001$) increased significantly between weeks 4 and 10. Emotional eating was positively correlated with hunger score ($r = 0.72$; $p<0.001$) and inversely correlated with total percentage weight loss ($r = -0.80$; $p<0.001$). Social eating was not related to any other factor.

Biochemical Measures and Side Effects

Most biochemical measures showed improvement by completion of the study, and no deterioration in any clinical condition was observed (Table 4.2). Constipation was the most common side effect. Seven subjects (21.9%) reported "no bowel movement in the last 4 days" at some stage during the diet, and another 10 subjects reported "no bowel movement in the last 2-3 days". Constipation was usually moderated by increased fluid and vegetable intake, the addition of a fibre supplement, or the addition of a mild laxative. Other reported side effects included light headedness (16%), cold intolerance (6%), and dry skin (3%).

Finally, none of the subjects enrolled in the study presented at surgery with hepatomegaly. There were no conversions to an open procedure, no major peri-operative complications, and no prolonged hospital stays. This study however, was not adequately powered to measure a change in peri-operative complication rates, and the study design did not include a control group.

Discussion

In a severely obese population, we investigated a range of factors related to aspects of efficacy and acceptability of pre-operative weight loss using VLED. Importantly, examination of the pattern of change in liver volume showed that most of the volume reduction occurred in the first 2 weeks of weight loss, whereas VAT and body weight declined at a uniform rate over the 12 week study period. At conclusion of the diet, the average decrease in liver size was 18.7%. The change in liver volume was linearly related to initial liver volume (13.8% in livers of <3.0L and 26.9% in livers $\geq$ 3.0L) and the relative reduction in body weight. Thus, for a given weight loss, those with larger livers can be expected to undergo a preferential reduction in liver size, the preponderance of which occurs in the first 2 weeks but which continues to occur to a maximum effect at 8 weeks. Favourable and largely predictable changes with weight loss were also observed for a range of biochemical, clinical and anthropometric measures.

We found only 2 previous studies that examined changes in liver volume during weight loss. Fris [252] employed ultrasound to assess changes in the size of the left lobe of the

liver, and used bioelectrical impedance to assess total body fat in 40 obese subjects (median BMI: 47 $\pm$ 6.8 kg/m^2) after a 2 week VLED. Notwithstanding methodological differences, significant liver volume reductions were recorded which correlated with the decrease in BMI, but not estimated fat mass.

Busetto et al. [253] assessed liver size and body fat distribution via whole-body multi-slice MRI in 6 premenopausal women losing weight after LAGB. This small sample had a mean baseline BMI of 42.6 $\pm$ 1.1 kg/m^2 and mean liver volume of 1.79 $\pm$ 0.41 L. Weight loss, liver volume, and body fat reduction were reassessed at 8 weeks and 24 weeks post-LAGB. Significant declines in body weight and the total fat measurement occurred at both time points, whereas reductions in liver size and VAT occurred only in the first 8 weeks. Liver volume and VAT were significantly correlated at baseline, but no association was found between liver size and total or regional fat measurements during weight loss. We found no association between liver volume and VAT at any time point. The mechanism explaining this relative reduction relates to the disposition of fat. In mild liver steatosis, abnormal accumulation of lipid is predominately in centri-lobular hepatocytes, while with increasing steatosis, more and more hepatocytes throughout a greater area of the liver lobule accumulate lipid [219]. In severe steatosis, a greater proportion of cells can reduce their size when abnormal lipid accumulations are dissipated during weight loss. This contrasts with changes in adipose tissue; adipocytes have a more uniform reduction in size with weight loss.

To our knowledge, this is the first study to measure and compare changes in liver volume, VAT, and SAT, and the first study to investigate their pattern of change over the first 12 weeks of weight loss. Computed tomography was selected for the majority of measurements because of its proven accuracy for assessing liver volume [462, 467] and VAT [27-29], more moderate expense, and shorter acquisition time which reduces movement artefacts and affords high accuracy and precision [467]. However, the utility of CT for serial measurements is limited due to the emission of ionizing radiation. For this reason, MRI was chosen for the sequential scans to assess ongoing change. Similar to CT, MRI determination of liver volume [450, 451] and VAT [32-34] has shown high accuracy and clinical utility. Computed tomography and MRI previously showed similar variances in planimetry liver volume calculations [452], and estimation of

visceral fat areas [29]. Our own volume and area calculations supported this close agreement.

Despite the limited power of this study, we found that triglyceride showed a strong independent association with baseline liver size. The association between an elevated triglyceride concentration and liver size has not been examined, but elevated triglyceride is commonly associated with liver steatosis and liver disease; high rates of between 20% to 80% have been shown in patients with NAFLD [475]. An earlier study found a significant correlation between fasting triglyceride concentration and liver steatosis [232]. An elevated CRP concentration; a marker of non-specific inflammation, and elevated diastolic blood pressure were also positive predictors of liver volume. All 3 factors, which contributed 51% of the variability in baseline liver size, are considered to be components of the expanded metabolic syndrome [476], of which NAFLD is now also deemed a part [232, 477].

To facilitate dietary adherence and success, subjects underwent fortnightly supervision and counselling from an experienced dietitian. The close correlation between total weight reduction and urinary ketones measured during these meetings supports the use of this simple, non-invasive method to monitor on-going dietary compliance. Initially, hunger and emotional eating were well controlled in most subjects; however, in the latter stages these factors increased, and taste acceptability decreased. Reports of hunger and food cravings during a VLED appear to be less than reports during conventional low calorie diets [168]. Nonetheless, the increase over time was most likely related to boredom and fatigue with the ongoing dietary restriction.

A recommended time period for the use of a VLED prior to surgery is a judgement based on a balance between the possible benefits of small additional weight loss, versus boredom, fatigue and poor compliance. Given the early significant reduction in liver volume, and the slower more consistent reduction in weight and VAT, we suggest that the minimum time for pre-operative VLED be 2 week. Extending this dietary intervention to 6 week will achieve an optimal balance between maximal reduction of liver size, and useful reductions in VAT stores and body weight, without compromising patient compliance and acceptability.

One limitation of this study was the relatively small selected sample of morbidly obese persons seeking bariatric surgery. Secondly, different methods were used to determine the pattern of liver volume and VAT reduction; however, both techniques are highly reliable and showed a very close correlation. Finally, a liver biopsy, which is required for definitive diagnosis of fatty liver, was not performed at patient entry into the study because it would have been unethical to undertake this procedure when not clinically indicated. It was previously shown that liver size independently predicts the level of hepatic steatosis at laparoscopy [232]; therefore, the hepatomegaly identified in this study was considered to reflect a high level of fatty infiltration into the liver. In the early stages of VLED, the low carbohydrate content of the diet will also result in depletion of liver glycogen stores. The level of glycogen reserve is highly dependent on recent dietary intake [478], averaging around 400 g healthy persons [478, 479]. Each gram of stored glycogen binds 3 to 4 gm of water [480]; therefore, diminution of liver glycogen may contribute up to 40% of the observed volume reduction.

In summary, severely obese individuals who are compliant with a 12 week VLED can safely and effectively achieve significant reductions in body weight, liver volume, VAT, and SAT prior to laparoscopic surgery - improvements that are likely to diminish the degree of surgical difficulty and decrease the risk of liver trauma and blood loss. Of particular note is the fact that the greater part of liver size reduction occurs in the first 2 weeks of weight loss by VLED, whereas the reduction in VAT and body weight is more uniform over a 12 week period. Several components of the metabolic syndrome may predict the presence of an enlarged liver, but those with massive hepatomegaly will experience a liver volume loss of greater magnitude without special attention. The VLED was an acceptable means of pre-operative weight loss in the majority, and apart from mild transitory side effects no unfavourable anthropometric, biochemical, or clinical outcomes were found.

Declaration for Thesis Chapter 5

Declaration by candidate

In the case of Chapter 5, this work represents an unpublished manuscript. The nature and extent of my contribution to the work was the following:

Nature of contribution	Extent of contribution (%)
I was involved in the design of the experiment and study protocol. I was responsible for running the study, all data collection, tabulation and analysis, and writing the manuscript.	>80%

The following co-authors contributed to the work.

Name	Nature of contribution	Extent of contribution (%) for student co-authors only
Associate Professor John Dixon	Involved in the design of the experiment, and study protocol. Assisted with collection and analysis of data, and writing of the manuscript.	
Professor Prithi Bhathal	Analysed and scored all liver biopsies.	
Dr Paul Marks	Performed all baseline liver biopsies and oversaw all radiological measurements.	
Professor Paul O'Brien	Involved in the design of the experiment and study protocol. Performed all follow-up liver biopsies. Assisted with subject recruitment and writing of the manuscript.	

Candidate's Signature	[redacted]	**Date** 5/12/07

Declaration by co-authors

The undersigned hereby certify that:

(1) the above declaration correctly reflects the nature and extent of the candidate's contribution to this work, and the nature of the contribution of each of the co-authors.
(2) they meet the criteria for authorship in that they have participated in the conception, execution, or interpretation, of at least that part of the publication in their field of expertise;
(3) they take public responsibility for their part of the publication, except for the responsible author who accepts overall responsibility for the publication;
(4) there are no other authors of the publication according to these criteria;
(5) potential conflicts of interest have been disclosed to (a) granting bodies, (b) the editor or publisher of journals or other publications, and (c) the head of the responsible academic unit; and
(6) the original data are stored at the following location(s) and will be held for at least five years from the date indicated:

Location(s)	**The Centre for Obesity Research and Education**	
Signature 1	Associate Professor John [redacted]	**Date** 6/12/07
Signature 2	Professor Prithi Bhatha[redacted]	11/12/07
Signature 3	Dr Paul Ma[redacted]	7 Dec 07
Signature 4	Professor Paul O'Brie[redacted]	5/12/07

CHAPTER 5: Liver histology after VLED in morbidly obese persons at high risk for NASH: Changes and challenges

Abstract

Background: Non-alcoholic fatty liver disease (NAFLD) and its more severe form, non-alcoholic steatohepatitis (NASH) are associated with obesity and the metabolic syndrome. While slow, sustained weight loss undoubtedly improves NAFLD, some data suggest that acute, rapid weight loss can exacerbate existing liver disease. The aim of this study was to compare the liver morphology in a select group of morbidly obese persons at high risk for NASH prior to, and after 6 weeks of rapid weight loss.

Methods: A prospective observational study of 8 subjects taking a very-low-energy diet (VLED) for 6 weeks. Outcomes included change in liver histology, body weight, liver enzymes, liver volume, visceral adipose tissue (VAT) and biochemical markers of the metabolic syndrome.

Results: Subjects included 2M and 6F, average age 49.5±9.4 years and BMI 44.8±6.0kg/m^2. At baseline NASH was diagnosed in 5 subjects and cirrhosis in 1. Body weight decreased by 9.75±5.39kg (p=0.001) and mean weight loss was 1.6kg/week (range 0.03kg-3.1kg). Liver steatosis improved (p=0.038) while scores for liver inflammation and fibrosis was more variable, increasing or decreasing by 1 stage or grade in the majority. Gamma glutamyltransferase showed a consistent decline (p=0.029). Liver volume (p=0.027), VAT (p=0.029) and biochemical markers of the metabolic syndrome improved. A significant positive correlation between NASH stage score and VAT area was evident (p=0.034). A number of methodological and analytical difficulties related to liver biopsies in morbidly obese patients were encountered.

Conclusions: While sampling variability and other methodological limitations occurred, available data tends to agree that rapid weight loss in the setting of NASH or impaired hepatic reserve can aggravate inflammatory and fibrotic processes in some subjects. Rigorous monitoring and consideration of a more conservative approach to weight reduction in persons at high risk for NASH is recommended.

Introduction

Non-alcoholic steatohepatitis is a more severe and potentially progressive form of the most common hepatic ailment, non-alcoholic fatty liver disease. The advancement from NAFLD to NASH involving lobular inflammation and fibrosis, can further progress to cirrhosis, the most common cause of liver failure [229].

While NASH is found in persons of normal weight and overweight [481-483], the obese state [484] in concert with insulin resistance and other features of the metabolic syndrome, is clearly associated with the pathogenesis of NASH [232, 249, 256, 477]. Within bariatric surgical series a consistently high proportion of patients exhibit abnormal liver morphology. Reported rates of liver steatosis range from 63 to 93% [232, 234, 248, 251, 477, 485-488], NASH from 16% to 56% [232, 234, 477, 485, 487-489], and cirrhosis in the order of 1 to 2% [232, 234, 248, 251, 477, 487, 488].

Weight reduction in obese persons with NAFLD or NASH is an important aspect of treatment [240, 249]. Surgically induced weight loss has induced favourable changes in hepatic steatosis, inflammation, and fibrosis [247, 249, 251]. Yet rapid weight loss following some forms of bariatric surgery has also been shown by repeat biopsy to exacerbate liver disease. An increase in inflammatory lobular hepatitis [248], degenerative changes and worsening of steatosis [257] and fibrosis [256] have all been reported.

Changes in liver morphology following diet induced weight loss have also received some attention. Varied strategies of moderate [246] to severe caloric restriction [257] and fasting [244, 257, 490] have shown either improvement or deterioration in liver histology. In the only study achieving weight loss using VLED, normalization of liver morphology was observed in the majority [245]. However, portal inflammation and fibrosis were detected in patients with higher levels of baseline steatosis who achieved greater reduction in liver fat accompanied by faster weight loss [245].

Increasingly VLED are used to facilitate rapid reductions in body weight, liver volume and VAT in obese persons prior to laparoscopic bariatric surgery [252, 491]. The potential of adverse histological change is of particular importance in this setting of imminent surgery, in a population at high risk of NAFLD and NASH.

This study aimed to compare liver morphology in a select group of morbidly obese bariatric surgery candidates at high risk of NASH prior to and after 6 weeks of rapid weight loss using VLED. Changes in body weight, VAT, liver volume, liver enzymes and biochemical markers of the metabolic syndrome were secondary outcome measures. Preliminary data collection on ten patients was planned, with a view to extend numbers to provide adequate power for statistical analysis, if required. However during the study, methodological and analytical difficulties related to obtaining liver biopsies in morbidly obese patients and interpretation of histological findings were encountered. These factors are reported and discussed, and the study results considered within light of these limitations.

Methods

Patient Selection

Subjects were a highly selected group of morbidly obese (BMI >40kg/m^2) deemed at high risk for NASH, recruited prior to Lap-Band® System (LAGB) (Inamed Health, Santa Barbara, CA) placement at The Avenue Hospital, Melbourne, Australia. Eligible subjects were men or women aged between 18 and 65 years, with a body weight $\leq$150kg, stable within $\pm$5kg over the last 3 months. Subjects were required to fulfil the following criteria, indicating a high risk for NASH [232] and clinical indication for liver biopsy [492]:

- Waist circumference: Women $\geq$88cm, Men $\geq$102cm
- Abnormal liver function with a raised level of any of enzymes AST, ALT, or GGT ($\geq$1 abnormal parameter)
- Blood pressure $\geq$130/85, or treated hypertension
- Fasting blood glucose level $\geq$6.1mmol/L, or known type 2 diabetes

Subjects were also required to demonstrate an understanding of, and willingness to comply with the requirements of a VLED and monitoring over the 6-week period.

Individuals were not eligible for study entry if they were medically contra-indicated to use of a VLED [161]. Any person on medications known to adversely affect liver function, or reporting a "high risk" alcohol intake (based on the NHMRC Australian

Alcohol Guidelines, defined as greater than 11 standard drinks on any one day for males, and greater than 7 drinks on any one day for females [473]) was also excluded from selection.

The study was approved by the Avenue Hospital Ethics Committee, and carried out in accordance with the revised Helsinki Declaration. Each subject provided informed, written consent.

Very-low-energy diet

Subjects consumed the Optifast® VLCD (Novartis Consumer Health Australasia Pty. Ltd.) during the 6 week dietary intervention. Details of the dietary intervention are listed in chapter 3. The basic protocol required ingestion of 3 shakes per day to provide 1906kj (456kcal), 52g of protein, 7g of fat and 45g of carbohydrate. All subjects attended fortnightly dietetic counselling. The VLED was ceased at the end of 6 weeks, which in most cases coincided with the day prior to surgery.

Clinical and Laboratory Assessments

Subjects underwent a series of clinical and laboratory assessments preceding, during, and at completion of the 6-week VLED. At baseline height was determined using a wall-mounted stadiometer. Body weight was recorded initially and then biweekly on electronic scales (Tanita Wedderburn TBF-305, Lake Worth, FL 33467) in light clothing without shoes. The initial weight threshold of 150kg for study inclusion represents the upper limit of the computed tomography equipment used to assess liver volume and VAT. Seated blood pressure was also recorded biweekly.

A series of biochemical and haematological assessments were obtained prior to commencement and at completion of the 6 week diet. These included liver function tests (LFT), fasting blood glucose, serum insulin, glycosylated haemoglobin A1c (HbA1c), C-peptide, fasting lipids, homocysteine and C-reactive protein (CRP). HOMA%S, a measure of insulin sensitivity, was calculated from fasting plasma glucose and C-peptide values [493]. Liver function tests, fasting glucose and lipids, and CRP were also measured at weeks 2 and 4 of the study protocol.

Liver Biopsies and Histological Assessment

A biopsy of the liver was obtained prior to commencement and after 6 weeks of VLED. At baseline a percutaneous liver biopsy was performed under direct ultrasound vision by a single radiologist at The Avenue Hospital, Windsor. Biopsies were undertaken in the morning, followed by a recovery and observation period of at least four hours. The second biopsy was performed intra-operatively under laparoscopic view by an experienced surgeon. All liver tissue was collected using a 14-guage 200-mm Temno Biopsy needle (Allegiance; Health Care Corp, McGraw Park, IL). A specimen length of 8mm or greater and containing at least 8 portal tracts was the aim. These protocols have been used and described previously [232, 249].

All specimens were stained with hematoxylin and eosin, silver reticulin, Masson trichrome, Sirius red, and Perls stain and ubiquitin as previously described [249]. An experienced pathologist blinded to the patient's clinical condition scored all samples on two separate occasions. A difference in score was resolved during a third assessment. Scoring criteria are summarized in **Table 5.1**. Subjects were diagnosed with NASH if their histological assessment was scored 1 or above for both NASH grade (inflammation) and stage (fibrosis).

Liver Volume and Visceral Adipose Tissue Assessment

As detailed in chapter 3, all subjects underwent an abdominal CT scan (Asteion Multislice System; Toshiba America MRI Inc., San Francisco, CA) prior to commencement and at completion of the 6 week VLED to assess change in liver volume and VAT. The planimetric method was used to assess liver volume on the Asteion Multislice System software (Toshiba America MRI Inc., San Francisco, CA). A single transaxial image at the intervertebral space between the second and third lumbar vertebrae (L2–L3) [462, 494] was used to determine VAT area indicated by a pixel distribution between -150 and -50 Hounsfield units.

Table 5.1 Criteria for histological scoring of liver biopsies, based on those previously reported by Dixon et al. [249]

Steatosis	
0	No steatosis
1	<5% of lobular parenchyma involved
2	25% of lobular parenchyma involved
3	25-75% of lobular parenchyma involved
4	>75% of lobular parenchyma involved
Lobular Inflammation – NASH Grade	
0	No hepatocyte injury or inflammation
1	Sparse zone 3 inflammation
2	Mild focal zone 3 hepatocyte injury / inflammation
3	Noticeable zone 3 hepatocyte injury / inflammation
4	Severe zone 3 hepatocyte injury / inflammation
Fibrosis – NASH Stage	
0	Normal connective tissue
1	Perivenular or pericellular fibrosis in zone 3
2	Perivenular and pericellular fibrosis confined to zone 2 and 3
3	Bridging or extensive fibrosis with architectural distortion; no obvious cirrhosis
4	Cirrhosis

Data analysis:

Histologic scoring criteria were treated as ordinal categorical variables and presented as median ± interquartile range. Baseline demographic and anthropometric data are presented as mean ± SD for normally distributed continuous variables and median ± interquartile range for data not normally distributed. The effect of weight loss at each time point on clinical, demographic and biochemical parameters was assessed using either the paired-t test or Wilcoxon sign test as appropriate. Simple bivariate analysis assessed correlations between total and biweekly weight loss, NASH score, VAT area, plasma insulin and liver fibrosis score. SPSS statistical software (SPSS Inc, Chicago, IL) was used for statistical analysis. All statistical tests were two-tailed, and *p*-values less than 0.05 were considered statistically significant.

Results

Due to emerging methodological limitations the initial target of ten subjects was forgone. Between April 2005 and August 2006, eight consecutive patients who fulfilled the strict research criteria were invited to enter the study. All subjects (two men, six women) subsequently completed the 6 week protocol. During the study one subject decided against LAGB placement. This subject underwent a second percutaneous liver biopsy at 6 weeks as per the baseline protocol. There were no clinically adverse hepatic events in the peri or post-operative period.

Important considerations to come out of this study include practical challenges of liver biopsy interpretation. Sampling constraints which are universal to biopsy-diagnosed NASH bring into question the validity and reproducibility of current techniques. Histologic assessment difficulties related to the interpretation of paired biopsies, and additional constraints particular to the morbidly obese patient are discussed. These issues are summarized in **Table 5.2**. The forthcoming histologic and clinical data are presented and then reviewed within the context of these limitations.

Table 5.2 Constraints and considerations when performing serial liver biopsies

1. Sampling constraints:
    - Steatosis, inflammation and fibrosis are unevenly distributed throughout liver tissue [495, 496]
    - High sampling variability in NASH stage scores have been found in paired biopsies from different locations within the liver and over time [495]
2. Histologic assessment difficulties:
    - Significant reductions in fatty infiltration following weight loss cause marked changes to the appearance of the liver tissue
    - Assessment of inflammatory and fibrotic change in paired biopsies are hampered due to condensation of the liver tissue as lipid is dispersed
3. Safety considerations:
    - Ultrasound quality rapidly diminishes as patient size increases
    - The required needle length is increased, and needle tip control reduced
    - These factors amplify the danger of inadvertently perforating an important viscus
4. Recruitment challenges:
    - Slow recruitment due to necessarily strict inclusion criteria

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Baseline Characteristics

Baseline anthropometric, clinical and laboratory data are summarized in **Table 5.3**. Mean age was 49.5±9.4 years. Subjects were obese, had an elevated waist circumference, were on antihypertensive medication (data not shown), and subsequently met the Adult Treatment Panel III criteria for metabolic syndrome [43].

Table 5.3 Anthropometric, clinical and biochemical characteristics of individuals before and after a 6-week very-low-energy diet*

Characteristic	Baseline[1]	After 6 Weeks	*p*-Value
Body Weight (kg)	127.9 ± 25.3 (85.0 – 158.8)	118.2 ± 21.9 (78.0 – 147.5)	0.001
BMI (kg/m²)	44.8 ± 6.0 (33.2 – 52.9)	41.4 ± 5.4 (30.5 – 48.5)	0.001
Waist circumference (cm)	131.5 ± 16.4 (106 – 156)	123.9 ± 14.8 (99 – 148)	0.006
Systolic BP (mmHg)	135.1 ± 21.4 (100 – 160)	133.1 ± 22.4 (105 – 179)	NS
Diastolic BP (mmHg)	83.1 ± 7.0 (70 – 90)	72.6 ± 13.3 (56 – 91)	NS
Liver Volume (L)	2.42 ± 0.81 (1.29 – 3.97)	2.05 ± 0.59 (1.03 – 2.97)	0.027
L2-3 VAT Area (cm²)	338.4 ± 119.3 (211.7 – 564.0)	297.6 ± 89.7 (177.1 – 443.7)	0.029
ALP(U/L)[2]	86.5 ± 21.0 (59 – 145)	74.5 ± 26.0 (55 – 144)	NS
AST(U/L)[2]	37.0 ± 14.0 (31 – 96)	32.0 ± 19.0 (21 –1167)	NS
ALT(U/L)[2]	67.0 ± 34.0 (46 – 138)	49.5 ± 30 (31 – 678)	NS
γGT(U/L)	79.9 ± 32.3 (42 – 120)	54.6 ± 26.3 (29 – 106)	0.029
Bilirubin (umol/L)	10.5 ± 2.9 (6 – 15)	10.9 ± 4.9 (6 – 18)	NS
Albumin (g/L)	43.8 ± 3.6 (40 – 49)	41.3 ± 3.6 (38 – 49)	NS
Fasting Glucose (mmol/L)	10.4 ± 3.6 (6.1 – 16.9)	6.8 ± 2.1 (4.4 – 10.5)	0.022
HbA1c (%)	9.0 ± 2.1 (6.0 – 12.9)	7.3 ± 2.2 (5.1 – 12.1)	0.033
Fasting Insulin (mIU/L)	28.1 ± 10.6 (19 – 46)	24.8 ± 14.4 (7 – 48)	NS
C-peptide (nmol/L)	1.9 ± 0.27 (1.6 – 2.3)	1.7 ± 0.43 (1.04 – 2.3)	NS
Insulin Sensitivity (HOMA%S)	18.5 ± 3.8 (13.3 – 23.8)	26.9 ± 7.4 (18.2 – 37.7)	0.023
Cholesterol (mmol/L)	5.2 ± 1.0 (4.1 – 7.0)	4.4 ± 0.82 (3.5 – 5.7)	0.008
Triglyceride (mmol/L)	2.0 ± 0.58 (1.1 – 2.8)	1.6 ± 0.44 (1.0 – 2.5)	NS
HDL-C (mmol/L)	1.1 ± 0.22 (0.7 – 1.4)	1.0 ± 0.29 (0.4 – 1.3)	NS
LDL-C (mmol/L)	3.1 ± 0.78 (2.1 – 4.5)	2.7 ± 0.72 (1.9 – 3.7)	0.017
CRP (mg/L)	9.4 ± 6.9 (3 – 22.1)	6.6 ± 4.0 (3.0 – 14.9)	NS

Key over page.....

*n=8 paired results
[1]All values are mean ± SD (range) except where indicated
[2] Data not normally distributed and presented as Median ± IQR (range)
BP, blood pressure; VAT, visceral adipose tissue; ALP, alanine phosphatase; AST, aspartate aminotransferase; ALT, alanine aminotransferase; γGT, gamma glutamyltransferase; HbA1c, haemoglobin A1c; HOMA%S, a measure of insulin sensitivity calculated from fasting plasma glucose and C-peptide values; CRP, C-reactive protein
Statistical analysis using paired samples t test for normally distributed data, and Wilcoxon Signed Ranks test for data not normally distributed.

Liver Histology

Baseline liver biopsies had a mean of 13.8±5.79 portal tracts (range 6 - 25) and repeat biopsies had a mean of 18.25±8.26 portal tracts (range 10 - 34). One baseline biopsy sample contained six portal tracts which was below the target of eight. This specimen has been included in the study and the limitation noted where appropriate.

The incidence of abnormal liver morphology is listed in **Table 5.4**. Prior to weight loss hepatic steatosis was present in seven subjects (88%). The majority (6/7) had severe steatosis involving >75% of the lobular parenchyma. Differing degrees of lobular inflammation and perivenular and pericellular fibrosis were identified. Five subjects were diagnosed with NASH, and one with cirrhosis.

At conclusion of the 6 week VLED mean weight loss for the group was 9.75±5.39kg (p=0.001). The mean percentage of weight lost was 7.38%±3.45% (range 0.18–12.32%). The decline in weight was accompanied by improvement in a number of clinical and biochemical parameters including waist circumference, liver volume, VAT area, GGT, insulin resistance (HOMA%S), fasting glucose, HbA1c, cholesterol and LDL-cholesterol (Table 5.3).

Scores for steatosis, with an initial median (IQR) of 4.0 (2.0), improved to a median score of 2.0 (3.0) (p=0.038). At week 6 only two of seven subjects continued to display severe fatty infiltration. One subject who did not improve in steatosis score failed to comply with the strict guidelines of the VLED and achieved no appreciable weight loss. The other subject achieved a percentage weight loss of 7.12% and mean weekly weight loss of 1.88kg, which was near the group average.

Table 5.4 Individual liver histology scores and mean weight loss figures after a 6-week very-low-energy diet

Time	Steatosis	Hydropic Swelling	NASH Grade	NASH Stage	NASH	Total % WL	Mean WL/ Wk	Mean WL/Wk in 1st 2 Wks
Wk 0*	0	No	0	0	No			
Wk 6	0	No	0	0	No	8.45%	1.8kg	1.0kg/wk
Wk 0‡	2	No	0	0	No			
Wk 6	1	No	0	0	No	5.78%	1.0kg	2.6kg/wk
Wk 0*	4	No	1	1	Yes			
Wk 6	4	No	0	0	No	7.12%	1.9kg	3.4kg/wk
Wk 0‡	4	Yes	2	3	Yes			
Wk 6	4	Yes	2	4	Yes	0.18%	0.03kg	0.3kg/wk
Wk 0‡	4	No	0	1	No			
Wk 6	3	No	0	1	No	8.24%	1.2kg	1.4kg/wk
Wk 0‡	4	Yes	2	4	Yes			
Wk 6	2	Yes	1	4	Yes	8.55%	1.9kg	2.8kg/wk
Wk 0[1]*	4	Yes	2	1	Yes			
Wk 6	2	Yes	3	3	Yes	8.40%	2.1kg	4.8kg/wk
Wk 0‡	4	Yes	2	2	Yes			
Wk 6	2	No	1	3	Yes	12.32%	3.1kg	4.9kg/wk
Av Wk 0	**3.25**	**Yes=4**	**1.13**	**1.5**	**Yes=5**			
Av Wk 6	**2.25[2]**	**Yes=3**	**0.88**	**1.88**	**Yes=4**	**7.38%**	**1.6kg**	**2.7kg**

*Denotes subjects with impaired glucose tolerance
‡Denotes subjects with type 2 diabetes
[1]Baseline liver biopsy contained only 6 portal tracts
[2]The change in steatosis score was statistically significant (p=0.038). Statistical analysis using Wilcoxin signed ranks test for nonparametric data
Av, average; WL, weight loss

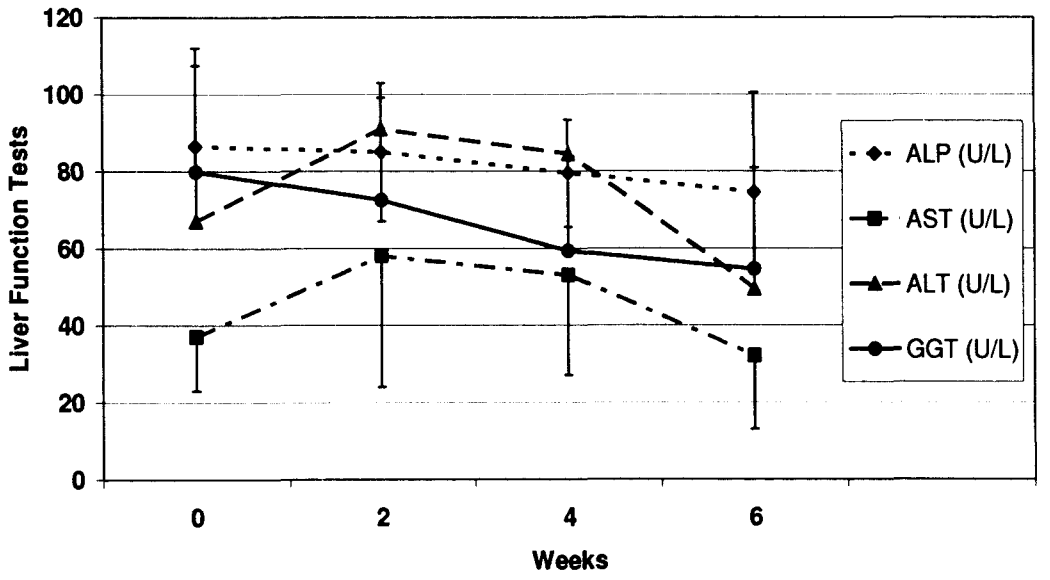
Changes in scores for liver inflammation and fibrosis were variable (Table 5.4). Three subjects were scored the same for stage and grade at both biopsies. The remaining five subjects scored one grade or stage higher or lower at the repeat biopsy. An increase of two stage scores occurred in one repeat sample however, it should be noted that the baseline biopsy contained only six portal tracts. Four of five subjects continued to be diagnosed with various degrees of lobular inflammation and fibrosis. Hydropic swelling was observed in three of four subjects who displayed these degenerative changes at baseline.

Liver Enzymes

Liver enzyme levels were assessed at weeks 0, 2, 4, and 6 of the protocol. Mean baseline and week 6 values for GGT exceeded the reference range of 0 – 35 U/L (Table 5.3), but showed a consistent, significant decline over the course of the intervention (p=0.029) (**Figure 5.1**). Median values for AST and ALT also remained above the laboratory reference range of 0 – 30 U/L (Table 5.3). A pattern of increase for both AST (p=0.042) and ALT (NS) was apparent in the first two weeks of VLED, followed by stabilisation and thereafter a pattern of decline (Figure 5.1).

One subject with normal liver histology at both biopsies developed cholecystitis and did not follow this general pattern, instead experiencing a marked rise in serum AST and ALT over the course of the VLED. The risk of cholecystitis is known to increase during VLED [472], and in this case resolved over time.

Figure 5.1 Change in liver enzymes during the 6-week very-low-energy diet



Median values and IQR shown for ALP, AST and ALP
Mean value and SD shown for GGT
ALP, alanine phosphatase; AST, aspartate aminotransferase; ALT, alanine aminotransferase; γGT, gamma glutamyltransferase

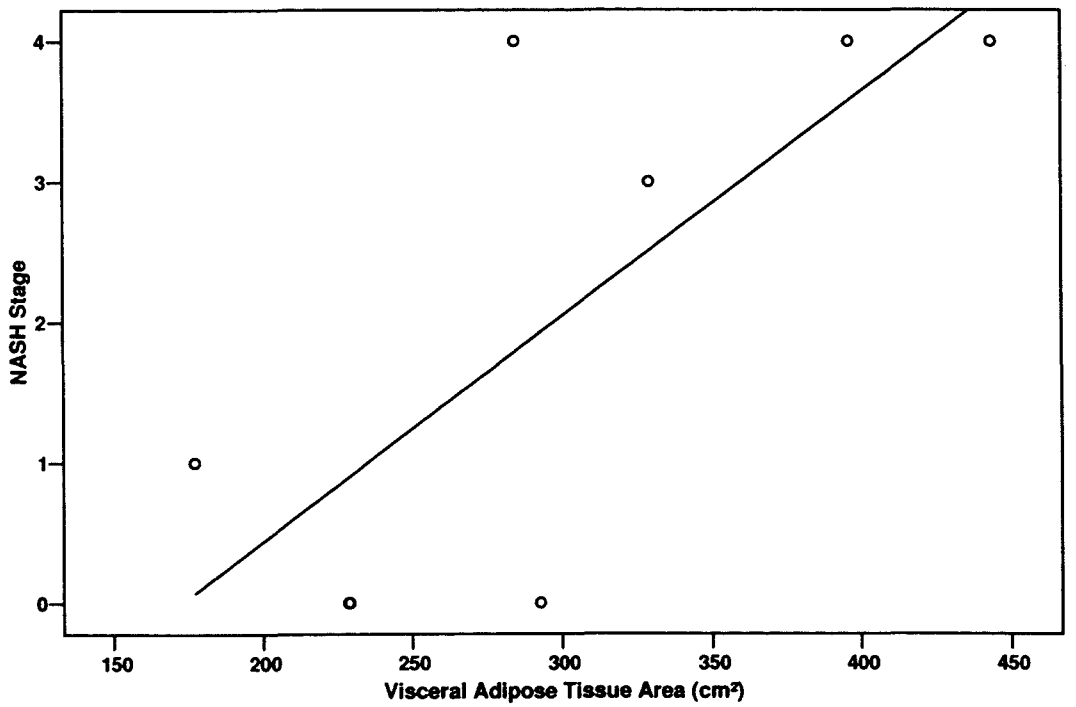
Weight Loss

Within subjects there was high variation in average weekly weight loss and average weight loss achieved in the initial two weeks of VLED (Table 5.4). The mean weekly weight loss of the group was 1.6kg, but ranged from 0.03kg to 3.1kg per week. Mean group weight loss in the first two weeks of the diet was 2.7kg, and ranged from 0.3kg to 4.9kg. Those who lost more weight in the initial two weeks were more likely to achieve a greater total weight loss, r=0.932, p=0.001. There were too few subjects to examine the affect of weight loss velocity on change in liver histology.

Associations with Liver Histology

At completion of the VLED there was a significant positive correlation between NASH stage score and VAT area at L2-L3, r=0.745; p=0.034 (**Figure 5.2**). A weak association was also apparent for baseline values, r=0.636; p=0.090. Strong baseline correlations between NASH stage and plasma insulin, r=0.830; p=0.011, and VAT area and plasma insulin, r=0.889; p=0.003 were also evident.

Figure 5.2 The association between NASH stage (level of fibrosis) and visceral adipose tissue area at completion of the 6-week very-low-energy diet



Statistical analysis using simple bivariate analysis; r=0.745, p=0.034

Discussion

This select series of morbidly obese subjects undergoing repeat liver biopsy before and after a six week VLED yielded a number of interesting findings. Despite the small sample size, change in a number of histological, clinical and biochemical parameters was observed. The median steatosis score improved significantly. Reduction in liver steatosis has been observed after diet-induced [245, 246] and surgically-induced weight loss [248-250]. During weight reduction there is a marked increase in free fatty acid release from the liver and also peripheral and visceral fat reserves. Concomitant with rapid weight loss we found a marked reduction in liver volume at week-6 of the VLED. This decline, which has been reported previously and is particularly evident in the first two weeks of weight loss [491], highlights the relative instability of the liver at this time. It has been hypothesized that this flux of fatty acids through the liver has potential to exacerbate ongoing inflammatory processes [258].

This study was the first to assess the relationship between VAT, plasma insulin and liver fibrosis. At week six of the VLED a positive association was observed between VAT area at L2-L3 and NASH stage score. Strong positive correlations at baseline between NASH stage and plasma insulin, and VAT area and plasma insulin emphasize the important relationship between abdominal adiposity, insulin resistance and liver fibrosis. Metabolic syndrome abnormalities are closely involved in the pathogenesis of NASH [240]. Weight reduction in the treatment of obese persons with NAFLD or NASH may primarily be of benefit due to improvements in insulin sensitivity.

Consistent with other studies [170, 491], markers of metabolic disease including fasting glucose, HbA1c, insulin sensitivity (HOMA%S) and serum lipids improved significantly. A steady decline in GGT also occurred over the duration of weight loss, while the pattern of change for AST and ALT tended to involve an increase followed by stabilisation and then decline. In this small cohort and a study by Anderson et al. [245], the observed change in liver enzymes was not predictive of the change in liver morphology. However, following a mean weight loss of 31.5±18kg at an average of 29.5±10 months after LAGB, we recently found a fall in GGT predicted improvement in liver inflammation, fibrosis and NASH [497]. Others have reported inconsistent

associations between LFT and severity of NAFLD in weight stable persons [240, 248, 498].

Although the histological change in inflammation and fibrosis were of primary interest, a number of methodological weaknesses limited the strength of our data. Firstly, emerging evidence of high rates of sampling variability between liver biopsies [495] draw into question the validity and reproducibility of current techniques to diagnose NASH. Recent research has observed that liver steatosis, inflammation and fibrosis are unevenly distributed throughout the liver [495, 496]. A sampling variability of 1 NASH stage score has been reported in 41% (21/51) and a difference of 2 or more NASH stage scores in 12% of subjects who underwent immediate repeat biopsy in different locations within the right lobe of the liver [495]. The authors suggest a change in NASH stage score of $\geq$2 points (based on the scoring criteria of Brunt et al [499]) as a relevant clinical end point [495]. We would require a much larger sample size to overcome this weakness.

Another difficulty was related to assessment of paired biopsies in steatotic livers. Significant reduction in fatty infiltration following weight loss results in condensation of liver tissue. These changes confound assessment and comparison of the prevalence of inflammatory and fibrotic change. Other issues presented obstacles to expansion of the sample size. Liver biopsy carries a risk of complication, particularly when obtained percutaneously in morbidly obese persons prior to any weight loss. Ultrasound quality rapidly diminishes as patient size increases. This amplifies the danger of inadvertently perforating an important viscus which can result in significant morbidity. The increased needle length also results in slight reduction in needle tip control. Finally, the necessarily strict inclusion criteria resulted in slow recruitment.

While these constraints limit our ability to draw conclusions on the direction or extent of hepatic change after rapid weight loss, three paired biopsies in this study did show evidence of decline. Only one previous study has prospectively assessed the change in liver histology following weight loss by VLED [245]. In this study, 41 patients (mean BMI 43.3, range 37-74) underwent VLED intervention over a median duration of 261 days, to produce a median weight loss of 34kg. Repeat biopsy at an average of 76 days following treatment showed normalization of hepatic histology and improvements in

steatosis in a significant number of subjects. Noteworthy however, were signs of portal inflammation and portal fibrosis in 5 patients who had achieved a more rapid weight loss of greater than 1.6kg per week. Other studies reporting a deterioration in hepatic morphology with weight loss have involved biliopancreatic diversion [256], gastroplasty [248] and total fasting [276, 506]; all of which induce a fast initial weight loss. This contrasts with modes of weight loss that achieve a more gradual decline, which chiefly report positive changes in liver histology [243, 246, 249].

In our study, the mean weekly weight loss was 1.6kg, but ranged from 0.03kg to 3.1kg, while the mean weekly weight loss over the first two weeks was 2.7kg (range 0.3kg to 4.9kg). Although small numbers preclude comparative analysis it is noteworthy that two of three subjects with a worsening in NASH stage score achieved the highest weight loss in the first two weeks of VLED.

Strengths of the study include the scoring of all paired biopsies in a standardised manner by a single experienced pathologist. Techniques used to obtain VAT area and liver volume were validated and standardized. The short duration of weight loss and biopsy interval could be viewed as a constraint, however this study was the first to investigate the acute change in liver histology following rapid weight loss by VLED. The prevalence of NASH in this study was higher than most consecutive series of bariatric surgery candidates [243, 477, 487, 488]. This indicates our inclusion criteria were useful for selecting those at high risk for NASH.

A number of limitations related to biopsy sampling and assessment of obese persons with NAFLD and NASH have been identified which limit the ability to draw conclusions on the affect of rapid weight loss on NASH. However taken together, our research and the research of others support rigorous monitoring and considerations of a more conservative approach to weight reduction in persons at high risk for NASH. VLED do bring about beneficial changes in body weight, liver steatosis, VAT area, liver volume and features of the metabolic syndrome. In the pre-surgical setting a modified VLED regime or inclusion of additional VLED serves/sachets may be more appropriate for persons at high risk of NASH. Ongoing clinical and biochemical review, in particular GGT and AST is advisable. In this cohort, repeat biopsy will be required in some cases to assess further change in liver histology and the effect of progressive

weight loss following LAGB surgery. Larger studies with longer-term assessment and monitoring following rapid weight loss are required to provide further valuable insights.

CHAPTER 6: Materials and Methods

This chapter provides details of research methods common to chapters 8, 9, 11 and 12. A number of self-report surveys were used to collect information on eating behaviour and markers of psychological distress. Data were collected from three separate groups; the general community, weight loss support group members and bariatric surgery candidates, as outlined below. Cross-sectional data from the entire study cohort have been reported in chapters 8 and 9. Prospective data, collected only from the group of bariatric surgery candidates, have been reported in chapters 11 and 12. Individual objectives and procedures are described within relevant chapters. Chapter 10 provides additional details of research methods used to collect the prospective data shared by chapters 11 and 12.

Recruitment Methods

Cross-sectional data were collected from three separate groups that differed according to weight loss intent. Each group required a slightly different recruitment approach as detailed below.

General Community Respondents

Subjects from the general community who were not actively seeking weight loss treatment were recruited through:

- flyers placed on notice boards in the general community,
- flyers placed on notice boards in 2 large metropolitan hospitals (the Alfred Hospital and the Caulfield General Medical Centre), and
- survey distribution at a large Australian university (Monash University).

The flyers explained the nature of the research and invited interested individuals to contact the research centre to arrange for the survey pack to be sent out.

Weight Loss Support Group Members

This sample provided data from overweight and obese persons involved in weight management who were not seeking bariatric surgery. Subjects were recruited from "Take Off Weight Naturally" (TOWN), a company that consists of over 130 weight loss

support groups within Victoria. Flyers detailing the nature and requirements of the study were disseminated throughout the groups. Interested individuals were asked to contact the research centre to arrange for the survey pack to be sent out.

Bariatric Surgery Candidates

Consecutive, eligible persons accepted into the bariatric surgery program at The Centre for Bariatric Surgery, Windsor, Victoria, were invited to participate in a 12 month study that involved data collection before, 4 and 12 months after LAGB. Individuals with a previous history of bariatric surgery were excluded from study involvement.

Entry into the surgical program at The Centre for Bariatric Surgery required fulfillment of the following conditions:

- Class II obesity or greater (BMI $\geq$35 kg/m^2).
- Significant medical, physical or psychological obesity-related co-morbidity.
- An extended history of at least 5 years of weight loss attempts.
- The individual indicated a willingness to adhere to the post-surgical lifestyle recommendations, and commit to life long clinical supervision.
- The individual was considered conversant with the possible risks and advantages of the procedure, and provided informed consent to proceed.

All willing persons were provided with an explanatory statement, consent form and the packet of questionnaires.

Power of the Study

The number of subjects recruited into the general community sample and weight loss support group sample was not predetermined. Within time and other logistical constraints of this thesis, the aim was to recruit the highest number possible.

The recruitment goal for the bariatric surgery candidates was driven by a principal end point of mean percentage of weight loss (%WL) 12 months after LAGB. It was expected that a 7% difference in mean %WL would be clinically significant, and calculated that a total of 110 patients would need to be studied to provide a 95% confidence of detecting a difference between the final body weight and initial body

weight with a power of 0.8, using a two-tailed test. On the basis of an expected 30% loss of candidates, an initial recruitment in excess of 145 patients was planned.

Assessment of Eating-related Behaviours

A range of eating-related behaviours were assessed by self-report survey. Diagnostic criteria for binge eating disorder (BED), feelings of loss of control (LOC) and night eating syndrome (NES) were confirmed during a clinical or phone interview. The packet of surveys provided to study participants is listed in **Appendix Ia**. The following section provides justification for the chosen tools, and details of each questionnaire.

Binge Eating Disorder

Clinical interviews and self-report methods have been used to diagnose BED. While clinical interviews are costly to administer and time consuming, the advantage lies in the interviewer's ability to probe, clarify and make consistent judgments [500]. Self-report surveys require less time commitment by the researcher/clinician and subject/patient, and are relatively inexpensive to implement. With regards to BED, more difficult concepts such as the experience of LOC related to eating show poorer correlations than more easily defined terms when comparing the questionnaire version of a diagnostic clinical interview [500-502]. Comparative studies have generally shown moderate agreement between diagnostic tools [501, 503-506]. Self-report diagnostic instruments typically yield higher rates of binge eating and BED than clinical interview, and may over-estimate actual prevalence rates [501, 507]. Fairburn and Beglin propose that it may be less embarrassing to report behaviours such as bingeing in a questionnaire [503]. Wilfley et al. suggest that the interviewer may rate a subject's response or level of associated distress lower than the subject themselves [501]. Current consensus appears to agree that self-report surveys are a useful as a screening tool to assess for the presence or absence of binge eating behaviours, rather than to provide a definitive diagnosis [501, 508].

For the purposes of this thesis the Questionnaire on Eating and Weight Patterns – Revised (QEWP-R) [268, 269] was used to screen for binge eating behaviours. The QEWP-R is a 28-item self-report instrument that has been used to assess the presence or absence of each BED criterion as delineated in the DSM IV [266]. Originally developed

to examine the proposed BED diagnostic criteria for two multi-site field trials in the early nineties [268, 269], the QEWP-R represents a revision based on this earliest version. Subjects who self-reported any characteristics of a binge underwent a semi-structured clinical (70%) or phone interview (30%) to accurately determine: 1) the amounts of food consumed during binge episodes, 2) the extent of the experience of LOC, 3) the extent of associated distress, and 4) the frequency of binge eating.

The QEWP has been validated in a community sample, in persons attending a weight control program, and among members of Overeaters Anonymous [268, 269]. The QEWP-R has also been used to diagnose BED among morbidly obese bariatric surgery candidates [291, 296, 300]. These studies support the construct validity of the QEWP-R, based on its ability to distinguish binge eaters and non-binge eaters into clinically distinct groups on a number of eating, weight-related, and psychological variables. Internal consistency for the QEWP-R was .75 in a weight control sample and .79 in a community sample [268, 269]. A 3-week test-retest reliability kappa value of .58 has likewise been calculated, indicating moderate stability of this questionnaire [509].

The level of agreement between the QEWP-R and a structured clinical DSM interview for the diagnosis of BED has yielded a kappa value of .57 [505]. A kappa of .60 was also obtained for the agreement between a clinician administered version of the QEWP and the QEWP self-report questionnaire [269]. These values represent a moderate to good level of agreement, and are comparable to ratings of agreement between diagnostic tools for other psychiatric disorders [510].

Loss of Control over eating

Numerous studies have reported binge eating in persons who do not meet BED DSM IV criteria. These studies have included normal weight and overweight subjects [268, 269, 273, 368, 370] and bariatric surgery candidates [291, 292, 300, 301, 305, 306, 308, 310-312, 381]. Many individuals who experience feelings of LOC related to eating do not consume objectively large amounts of food. Feelings of LOC during the consumption of amounts of food considered abnormally large for the circumstances by the subject but not the interviewer are known as a subjective bulimic episodes [274]. In this thesis, subjective feelings of LOC were assessed by the QEWP-R and during the semi-

structured clinical interview. In accordance with the DSM IV BED criteria, a LOC was defined as a feeling that one cannot stop eating or control what or how much one is eating. Responses to the QEWP-R have been commonly used to evaluate the prevalence of "subthreshold BED" and "eating disorders not otherwise specified" [268, 269, 291-293, 300, 511].

Night Eating Syndrome

The NES is not a currently recognized eating or sleep disorder. No universally agreed diagnostic criteria or validated diagnostic methods exist. In the literature, a brief clinical interview based on an author-developed questionnaire has most commonly been used diagnostic tool. Self-report surveys have also been used to screen [411, 413] or diagnose NES [267, 390-392].

For the purpose of this thesis, research criteria were based on those of Stunkard et al. [283]. These criteria have formed the basis of most NES prevalence studies.

Diagnosis of NES required that persons within the previous 3 month period usually:

1) had no appetite for breakfast,

2) consumed 50% or more of total energy intake after 7p.m., and

3) had trouble getting to sleep or staying asleep on 3 or more nights of the week.

Subjects were also asked if they frequently found themselves consuming snacks during night time awakenings. This behaviour was termed "nocturnal snacking". The presence of nocturnal snacking was not required for a positive NES diagnosis.

These proposed NES diagnostic criteria have not been formally validated or investigated for test-retest reliability. Persons with NES have however, been confirmed to consume greater than 50% of their caloric intake after 7pm [387, 395]. Reliability of NES assessment can be derived in a limited way from one study that prospectively assessed changes in the incidence of NES following bariatric surgery [299]. At baseline 5 of the 63 patients (8%) were diagnosed with NES by clinical interview, using similar criteria to the studies presented in this thesis. At 3 years post BPD, 3 original patients and one new patient (6.3%) were diagnosed with the syndrome.

The self-report survey screened for NES. Those reporting symptoms of the syndrome underwent the semi-structured interview to verify responses. Further details of the diagnosis of NES during the semi-structured interview are provided in chapter 8.

Anti-Cancer Council Food Frequency Questionnaire (ACCVFFQ)

A food frequency questionnaire (FFQ) was chosen to collect data on nutrient intake for a number of reasons:

1) A self-report method enabled data collection from a larger, broader range of subjects.
2) The FFQ places a low response burden on the subject compared to weighed food records or diaries, which require high subject involvement that can affect compliance and alter typical dietary habits.
3) The standardized format may facilitate the assessment of change over time.
4) A FFQ can collect both qualitative and quantitative data.
5) Data derived from a FFQ can be used effectively to rank subjects into quartiles based on low, medium or high intakes of specific foods, nutrients or food consistencies.

Obese males and females are significantly more likely to under-report their dietary intake compared to lean individuals [512]. In the large Swedish Obese Subjects study, Lindroos et al. [513] found that a semi-quantitative FFQ reduced this respondent bias, was more valid than a 4-day food record, and was similarly reproducible in normal weight and obese subjects.

In this thesis the Anti-Cancer Council Victoria Food Frequency Questionnaire (ACCVFFQ) (Copyright Anti-Cancer Council of Victoria, 1996) [514, 515] was used to assess usual dietary intake. The ACCVFFQ is an optically scannable, semi-quantitative FFQ designed for a culturally diverse Australian population. It lists 74 foods grouped into 5 categories: cereal foods, sweets and snacks, dairy products, meats and fish, fruit and vegetables. Ten food frequency options range from "never" to "3 or more times per day". Respondents are also asked to rate average portion sizes of 4 different meals based on a set of food diagrams. A "portion size factor" is then applied for each individual during nutrient analysis. This is a useful feature given the marked change in

portion size that occurs after gastric restrictive surgery. Additional questions assess the average daily consumption of commonly eaten foods such as fruit and vegetables. This acts to verify or "calibrate" later frequency responses, which may over-estimate intake of these foods [514]. Data on the individual's average alcohol intake is also collected. Nutrient intake values were calculated based on the Australian NUTTAB95 nutrient composition database [516].

The ACCVFFQ has been used in a number of epidemiological studies to assess usual dietary intake [517-520]. Its validity has been assessed relative to 7-day weighed food records [514, 515] with comparable results to other FFQ validity studies [521-523]. To control for extreme values, the top and bottom 2% of usual energy intakes calculated from the ACCVFFQ were excluded from statistical analyses.

Three Factor Eating Questionnaire (TFEQ)

The Three Factor Eating Questionnaire (TFEQ) is a 51-item self-report questionnaire that has been used to measure cognitive and behavioural components of dieting, eating and over-eating [524]. The three dimensions of human eating behaviour assessed include:

1) Dietary restraint; the amount of intentional restriction of food intake in order to control body weight and shape, the intent to diet (21 items),
2) Disinhibition; the inability to resist food stimuli or social and emotional eating cues (16 items) and
3) Hunger; subjective feelings of hunger and food cravings (14 items).

All responses are scored '0' or '1', and total scores are calculated for each factor. Higher scores indicate greater levels of dietary restraint (factor 1), disinhibition (factor 2) and hunger (factor 3).

At its conception, coefficient alpha reliabilities of 0.92 for cognitive restraint, 0.91 for disinhibition, and 0.85 for hunger were derived in a sample of normal weight and overweight dieters and free eaters [524]. Since that time a number of studies have addressed the construct validity of the 3 factors of the TFEQ, drawing various conclusions [60-62]. However, despite its on-going evaluation, the TFEQ has been

widely used among normal weight, overweight and obese populations. Its criterion validity is supported by consistent findings that severity of binge eating is correlated with dietary disinhibition and hunger, but not with dietary restraint. These findings have been reported among obese individuals seeking both conservative weight loss therapies [360, 525, 526] and bariatric surgery [72, 291, 301, 305, 308].

Assessment of Psychological Distress and Quality of Life

Several self-report surveys were used in this thesis to assess markers of psychological distress.

Beck Depression Inventory – Revised (BDI)

Symptoms of depressive illness were assessed using the revised Beck Depression Inventory (BDI) [527]. This is a 21-item self-report instrument, used for over 40 years to assess traits of depressive illness. The BDI contains the 9 distinguishing indicators of a major depressive episode listed in the DSM IV [266]. In this thesis the BDI has not been used to provide a definitive diagnosis of depression, but rather as an indication of the severity of depressive symptoms.

Each BDI item consists of 4 possible responses that are ranked in severity and awarded a score from 0 to 3 (0 = symptoms not present, 3 = symptoms strongly present). Scores for each question are tallied to provide a total figure. A higher total score indicates greater symptoms of depression. The cut-off values used to interpret total BDI scores among different groups in this thesis are based on those published by Smarr [528] (**Table 6.1**).

Table 6.1 Interpretation of Beck Depression Inventory scores [528]

Beck Depression Score	Interpretation
0 - 9	Normal
10 - 16	Mild
17- 29	Moderate Depression
30 - 63	Major Depressive Illness

The BDI has been used widely in subjects ranging from normal weight to obese. The validity and internal consistency of the BDI are well documented [527, 529], although weight ranges in study populations were not specified.

Multidimensional Body Self Relations Questionnaire (MBSRQ)

The Multidimensional Body Self Relations Questionnaire (MBSRQ) is a widely used, well-validated self-report inventory for the assessment of body image [530, 531]. The full 69-item version consists of 10 subscales with each item being scored from 1 to 5. For the purpose of this thesis a shorter version has been used. Two subscales of the MBSRQ calculated an appearance dissatisfaction (AD) score as a marker of psychological distress related to body image discontent.

The appearance orientation (AO) subscale of the MBSRQ assesses the importance an individual places on general physical appearance and presentation. A lower score indicates a general lack of concern with issues related to physical appearance. Higher scores indicate a high degree of interest and involvement in "looking good". The appearance evaluation (AE) subscale assesses how an individual evaluates their own

physical appearance and attractiveness. Lower scores indicate indifference about one's appearance, with minimal effort devoted to "looking good". Higher scores signify positive feelings and contentment with appearance. The level of AD is determined by calculating the difference between the AO and AE subscales [80]. Appearance dissatisfaction based on the assessment of these 2 subscales has been previously published in an obese population [80].

Medical Outcomes Study Short Form – 36 (SF-36)

The Medical Outcomes Trust Short Form-36 (SF-36) [532, 533] is a widely used and validated survey of general health and outcomes. The SF-36 consists of 8 domain scaled scores which include physical function, physical role, pain, general health, vitality, social functioning, emotional role and mental health. Scores from these 8 domains can be individually weighted into physical and mental components. These components are combined to calculate a physical component summary (PCS) score and a mental component summary (MCS) score [532]. The SF-36 PCS principally measures the physical dimension of health related to physical functioning and bodily pain, and to a lesser extent feelings of health and vitality. The SF-36 MCS provides a measure of self-rated psychological health and social (dis)ability due to emotional problems. Lower scores relate to poorer functioning. In this thesis the SF-36 MCS has been used as a marker of psychological distress. For the purposes of analysis these 2 health summary scores were adjusted to achieve a community mean value of 50 with a standard deviation of 10.

Data Management

Accumulated data were transferred onto the specially designed database in the Microsoft Access® program, as described in chapter 3. All study respondents were de-identified and provided with a unique identification number. Hard copies of all study questionnaires were stored in a locked cabinet, and will remain so for the next 5 years following submission of this thesis. Statistical methods used in each study are detailed within the corresponding chapter.

Declaration for Thesis Chapter 7

Declaration by candidate

In the case of Chapter 7, this work represents a manuscript that has been published in *Obesity Surgery*, 2006; 16(7): 811-20. The nature and extent of my contribution to the work was the following:

Nature of contribution	Extent of contribution (%)
I undertook the literature review and wrote the manuscript.	>90%

The following co-authors contributed to the work.

Name	Nature of contribution	Extent of contribution (%) for student co-authors only
Associate Professor John Dixon	Assisted with interpretation of the literature review, and writing of the manuscript.	
Professor Paul O'Brien	Assisted with writing of the manuscript.	

Candidate's Signature	[redacted]	**Date** 6/12/07

Declaration by co-authors

The undersigned hereby certify that:

(1) the above declaration correctly reflects the nature and extent of the candidate's contribution to this work, and the nature of the contribution of each of the co-authors.
(2) they meet the criteria for authorship in that they have participated in the conception, execution, or interpretation, of at least that part of the publication in their field of expertise;
(3) they take public responsibility for their part of the publication, except for the responsible author who accepts overall responsibility for the publication;
(4) there are no other authors of the publication according to these criteria;
(5) potential conflicts of interest have been disclosed to (a) granting bodies, (b) the editor or publisher of journals or other publications, and (c) the head of the responsible academic unit; and
(6) the original data are stored at the following location(s) and will be held for at least five years from the date indicated:

Location(s)	**The Centre for Obesity Research and Education**

Signature 1	Associate Profes [redacted]	**Date** 6/12/07
Signature 2	Professor Paul O'Brien [redacted]	5/12/07

CHAPTER 7: Night Eating Syndrome: Impact on Bariatric Surgery

Abstract

Individuals with night eating syndrome (NES) display a time-delayed pattern of food intake, outside the natural circadian rhythm. High prevalence estimates have been reported among bariatric surgery candidates, and some evidence suggests that NES is positively associated with obesity, negatively associated with weight loss efficacy, and follows a chronic course. In order to evaluate current NES theory, and the association between NES and bariatric surgery, literature searches were conducted to identify relevant literature published in English up to 2005. Due to inconsistencies in NES characterisation, and significant heterogeneity in study design and methods, a qualitative assessment of NES and its relation to bariatric surgery was then undertaken. Within the literature, variable NES definitions highlight the distinct lack of clarity as to which behavioural features constitute a clinically meaningful entity. Prevalence estimates appear high among persons seeking obesity surgery, however no consistent pre- or post-operative demographic, clinical, or psychological factors reliably differentiate NES from non-NES. Further examination of the clinical significance, correlates, and course of NES in general and surgical samples is important given the link with obesity. The ways in which NES departs from "normal" eating behaviour must be clarified. Behavioural and psychological traits of NES need elucidation, and the establishment of agreed diagnostic criteria is essential for research to move forward. Therapy options should focus on aspects of the syndrome that cause greatest impairment, distress, or health risk.

Introduction

With worldwide rates of obesity soaring [1], interest in the importance of disordered eating patterns, and the hazard they impose on weight gain, has grown. The concept of the Night Eating Syndrome (NES) in obese persons was first described in the 1950s by Stunkard et al. as the consumption of more than a quarter of daily calories after the evening meal, sleeplessness til after midnight, and morning anorexia [386]. These people experienced limited success with weight loss, and a high frequency of mid-treatment complications, including debilitating depression. Life stress and feelings of anxiety were also positively associated with night eating, suggestive of a response or coping mechanism in the face of negative emotions [267, 386].

In the last two decades, a small but growing body of research has examined various aspects of this cluster of behaviours. Of particular interest is the link with obesity, yet the exact nature of the association remains unclear [396]. Although not formally defined or recognized as an eating disorder, the occurrence of NES has increased with increasing adiposity [395], and could pose a risk for obesity development [410], although not all studies agree [393, 402]. Night eaters may possess a general propensity to overeat [387, 392], but similar total daily energy intakes in NES and non-NES have also been reported [399, 409]. Subjects with NES have yielded poorer weight losses during supervised diets [386, 392], and more complications during weight loss attempts than non-NES [386]. In addition to a time-delayed pattern of eating and hunger, night eating has been positively correlated with an irregular meal pattern, and greater delays in eating when busy [388].

Among obese treatment seekers, rates of NES are potentially high [283, 299, 302, 311, 386, 391-395, 402, 416, 534], and certainly greater than the general community [389, 390]. More and more obese persons are undergoing obesity surgery, and there is currently much interest in outcome predictors of surgical success. A recent survey suggests symptoms of night eating are assessed in some bariatric clinics prior to surgery, although management of those identified with NES varies widely [378]. In order to explore the association between NES and bariatric surgery, a review of the literature is warranted. At the outset we place the research on NES and bariatric surgery into context

with an overview of the current recognised clinical features of NES, proposed diagnostic criteria, associated factors, and treatment options. We then report on nine studies identified from the literature that investigated NES and bariatric surgery. Due to significant heterogeneity in study design and method, this paper provides a qualitative assessment and critical analysis of NES and its relation to bariatric surgery. We conclude with suggestions for future research.

Methods

Searches were conducted in Ovid MEDLINE, Web of Science, and Web of Knowledge using the search terms night eat* AND obesity, and night eat* AND surgery. Relevant literature published in English up to the end of 2005 was sought. Bibliographies of collected reports were examined, and further papers identified. Original research studies and review articles were collected for the overview of NES. Investigations of prospective, cross-sectional, and retrospective design, employing a range of NES diagnostic criteria, and all bariatric surgical techniques were collected for the review of NES and obesity surgery. Quantitative analysis of studies involving NES and bariatric surgery was not possible due to inconsistencies in NES characterization, and significant heterogeneity in study design and methods. Therefore, a qualitative assessment of NES and its relation to bariatric surgery was undertaken.

Overview of the Night Eating Syndrome

Definition of the Syndrome

Night eating syndrome is characterised by evening hyperphagia, poor sleep onset or maintenance, and morning anorexia [283]. Symptoms of mood disturbance [388, 416, 534], and more recently, a pattern of rising to eat during nocturnal awakenings [387], have also been included in some research criteria. Given no collectively agreed NES diagnostic criteria currently exist, **Table 7.1** summarises and compares three proposed NES research criteria, as well as criteria for "nocturnal sleep-related eating disorders" (NSRED), and the "night eating/drinking syndrome" (NEDS); described sleep disorders that share common features with NES.

Table 7.1 Comparison of clinical features that have been used to diagnose night eating syndrome, and the sleep disorders nocturnal sleep-related eating disorders (NSRED) and night eating/drinking syndrome (NEDS)

	Clinical Features						
	Morning anorexia	Evening hyper-phagia	Sleep Difficulty	Nocturnal snacking	Aware of waking & eating	Unaware of waking & eating	Low Mood
NES, Stunkard, Berkowitz et al. 1996 [283]	X	X	X				
NES, Rand, Macgregor et al. 1997 [389]	X	X	X				X
NES, Birketvedt, Florholmen et al. 1999 [387]	X	X		X	X		
NSRED Winkelman 1998 [535]	X			X		X	
NEDS, American Academy of Sleep Medicine [400]				X	X		

In particular, individuals who wake to consume food during the night must be distinguished from NSRED and NEDS. The NSRED is a sleep disorder that involves night-time eating during a partial or total lack of consciousness [397]. In contrast, persons with NES who night-eat have good recollection of their eating episodes. Another sleep disorder, NEDS, involves repeated night-time awakenings (to full consciousness) during which food or drink is compulsively consumed, and followed by normal sleep resumption [400]. The NEDS is classified primarily as a sleep-related issue, with diagnosis relying on a pattern of nocturnal eating rather than low ratings of

morning appetite or quantitation of evening energy intake [536]. However, in cases of NES that involve recurrent episodes of night-time eating, there are more similarities linking NEDS and NES than dividing them [391].

Variable definitions of NES within the literature highlight the distinct lack of clarity as to which behavioural features constitute a clinically meaningful entity. Morning anorexia is not considered abnormal, and most people experience sleep difficulties at some stage. The frequency and duration over which these behaviours occur should be decisive. Criteria put forward by Birkdvedt et al. [387] outlined in Table 7.1, specify awakenings at least once per night over a 3 month period. Yet it appears to be the time-delayed pattern of food intake outside the natural circadian rhythm that provides this cluster of behaviours with proposed clinical relevance [396]. An eating disorder should also occur in conjunction with a measure of distress and impairment [265], and generate a risk to health. A lack of control over this pattern of eating is also an important consideration. Night-shift workers should be excluded from diagnosis [537]. Of clinical importance is the link with obesity, and the possibility of reduced weight loss efficacy or weight loss maintenance in NES. Mood disturbance and depression, which have been consistently reported alongside NES [415], may also be of clinical significance.

There are also problems defining each behavioural feature. Debate continues over the quantity and timing of evening eating required to fulfil this criterion [390]. A specified hour of the evening may or may not include the energy content of the evening meal, which would invariably affect criteria fulfilment. This has been noted in cultures who habitually consume a late evening meal [393]. In a large cohort of teenage girls, Striegal-Moore et al. [390] found NES diagnoses differed markedly when the time, food quantity, and frequency components of evening hyperphagia were adjusted. The strictest criteria, 50% of daily energy intake consumed after dinner, was met by only 1 girl over the data collection period (approximately 1 in 2000), whilst prevalence estimates based on 50% of total daily energy intake after 7pm resulted in values around 5.5%. Persons with NES have consumed significantly greater proportions of their daily energy intake in the evening [387, 395, 399, 409], in the presence of an increased [387], or similar total daily energy intake [399, 409], and variable macronutrient composition [387, 395, 409]. Criteria put forward by Birkdvedt et al. [387] require evening

hyperphagia defined by ≥50% of daily energy intake after the last evening meal. This criterion may however be too restrictive, with recent work based on 7-day food diaries showing that, despite self-reported fulfilment of the criterion, NES consumed an average of 35% of their total energy intake after their evening meal [399]. Despite this, a definition of evening hyperphagia that is not influenced by the consumption of the evening meal moves closer towards characterising non-normative behaviour.

Prevalence

In general community samples, NES prevalence appears to occur in around 1.5% of the population [389, 390]. Prevalence estimates increase amongst obese persons seeking behavioural, medical, or surgical weight loss treatments, however results are wide ranging. Prospective and cross-sectional studies involving weight loss samples provide values from 6% to 64% (median 14.5%) [283, 299, 302, 311, 386, 391-395, 402, 416, 534]. While subjects were mainly selected cohorts of obese, middle aged women, the marked variability is most likely due to inconsistent research methods and varied diagnostic criteria. Nevertheless, the vast majority assessed components of evening hyperphagia, trouble getting to sleep or staying asleep, and morning anorexia. Although these findings are not directly comparable and cannot be generalized to wider groups, they do provide evidence that among obese treatment seekers, rates of NES are potentially high, and certainly greater than the general community.

Factors associated with NES

A low mood, particularly in the evening and night, has been associated with the NES, and although not a component of current proposed diagnostic criteria, a mood criterion is included in some research measures [389, 416, 534]. So too symptoms of depression have been positively associated with NES in some obese samples [392, 409, 414, 416]. However an obese group [311] and two community groups [389, 390] showed no correlation between depression and NES. A link between NES and elevated levels of stress [386] and anxiety [394] has also been noted, yet studies investigating cortisol levels in night eaters confer conflicting results [406, 409]. Similarly, the relationship between NES and diurnal patterns for hormones including leptin, melatonin, and ghrelin [387, 409] is currently unclear.

Binge eating disorder (BED) is a condition characterised by the consumption of abnormally large amounts of food in association with feelings of lack of control and emotional distress, and in the absence of compensatory behaviours [266]. Comparative studies show some degree of overlap between BED and NES, but this is generally small [272, 415]. Binge eaters consume far greater calories during eating episodes, and are less likely to eat at night, suffer sleep disturbance, and morning anorexia, than night eaters [396]. Persons with BED have also shown significantly higher dietary disinhibition [524], while night-eaters show similar levels of disinhibition to non-NES [393, 394].

NES treatment options

Treatment studies involving NES are few. Night eaters from the general community have recounted numerous medicinal and herbal treatments that generally had little impact on NES symptoms [538]. Frequent failed therapeutic attempts are common [536]. A controlled drug trial involving a 12 week course of the anti-depressant, sertraline, reduced night-time awakenings, night snacking, and evening energy consumption in 17 obese NES subjects [538]. Full remission of NES in 5 of the 17 subjects was associated with a weight reduction of -4.8 $\pm$ 2.6kg ($p<0.05$), compared to a weight gain of 0.6 $\pm$ 5.4kg in non-completers and those who did not achieve remission. At study conclusion, a low correlation between changes in NES and depression suggests an alternative action of sertraline, perhaps exerting an effect on food intake via an alteration of the displaced circadian rhythm [396]. A reduction in nocturnal eating has also been reported following administration of d-fenfluramine, a serotonin agonist [412], and, in some cases, a decline in stress levels has also reduced night eating severity [386, 539]. The administration of exogenous melatonin has also been proposed as a treatment option [387]. However, a review of 15 studies involving melatonin and night-time behaviours revealed limited change in only two investigations [272].

Night Eating Syndrome and Bariatric Surgery

We identified nine studies describing NES within populations of bariatric surgery patients (**Table 7.2**). Investigations were of cross-sectional [393, 416, 534], prospective [299, 311], and retrospective design [298, 302, 303], and involved a range of obesity interventions including gastric bypass (GBP) [302, 303], vertical banded gastroplasty (VBG) [298], biliopancreatic diversion (BPD) [299], gastric restrictive procedures [311], unspecified obesity surgery [416, 534], and one study comprised obese patients seeking medical and surgical weight loss [393]. There was marked heterogeneity between studies with regards to the characterisation of NES, study design, and methods. Some studies were of poor quality due to low sample size, and retrospective analysis of pre-surgical behaviours.

NES Prevalence Estimates: Pre and post-surgery

Pre-surgical NES prevalence estimates vary markedly across all nine studies, and are presented in Table 7.2. In general, prospective and cross-sectional studies involved larger sample sizes with more tightly defined NES criteria, and reported lower prevalence estimates than studies of retrospective design. Prospective and cross-sectional investigations reported that 8% of subjects consumed $\geq$50% energy intake after 7pm [299], and 10% [311] and 16 % [393] of subjects consumed $\geq$25% energy intake after the evening meal. Definitions stipulating a mood criteria while placing no numeric figure on nocturnal food consumption reported rates of 15% [416] and 25% [534]. Highest NES approximations are derived from four retrospective studies, generating figures of 31% [389], 33% [303], 42% [298] and 55% [302]. Three of these studies involved a small sample size, and employed broad definitions of night eating that did not include morning anorexia, evening hyperphagia, or specific sleep difficulties. Subjects may therefore have reported a normal variant eating pattern, or possibly a form of NEDS [298, 302, 303]. The remaining retrospective study involved NES criteria which required the presence of "excessive evening eating", rather than a set proportion of total daily intake [389].

Table 7.2 Studies involving bariatric surgery that have assessed the pre-operative prevalence of NES or night eating behaviours

Study	Study Type	Treat-ment	Sample			NES Assessment Criteria						
			n (%F)	Mean BMI	Mean Age	Morning Anorexia	Evening Hyper-phagia	Poor sleep onset or maintenance	Mood disturbance	Wake to eat	Method	%NES (n) (%F)
Adami, Meneghelli et al. 1999 [299]	P	BPD	63 (76)	47	38	Morning anorexia	50% EI after 7pm	Trouble getting to, or staying asleep	No	No	CI	**8%** (5) (NR)
Powers, Perez et al. 1999 [311]	P	Ga Res#	116 (83)	53	40	Morning anorexia	25% EI >evening meal	Trouble sleeping	No	No	CI	**10%** (12) (91%)
Kuldau and Rand 1986 [416]	C/S	Ob Surg	174 (84)	NR	36	Poor appetite, not eating til later in day	Eating throughout evening without enjoyment	Having difficulty going to sleep	Feeling tense, upset, or anxious as bedtime neared	No	CI & Q	**15%** (26) (NR)
Adami, Campostano et al. 2002 [393]	C/S	Med/ surg*	166 (78)	44	NR	Morning anorexia	25% EI after evening meal	Trouble sleeping	No	No	CI	**16%** (26) (69%)
Rand and Kuldau 1993 [534]	C/S	Ob surg	253 (75)	≥40	~37	Morning anorexia, not eating til later in day	Eating later in day, with no enjoyment	Having difficulty sleeping	Feeling tense and /or upset	No	CI	**26%** (65) (NR)
Rand, Macgregor et al. 1997 [389]	R	Ga Res	111 (93)	NR	~41	Morning anorexia, or delay of eating	Excessive evening eating	Insomnia	Evening tension and /or feeling upset	No	CI	**31%** (34) (NR)
Hsu, Sullivan et al. 1997 [303]	R	GBP	27 (100)	49	39	No	No	No	No	≥1/week for at least 3/12	CI	**33%** (9) (All F sample)
Hsu, Betancourt et al. 1996 [298]	R	VBG	24 (100)	49	48	No	No	No	No	No set frequency or time frame	CI	**42%** (10) (All F sample)
Latner, Wetzler et al. 2004 [302]	R	GBP	65 (100)	54	40	No	No	No	No	≥2/week for 3/12	Phone I'view	**55%** (36) (All F sample)

Study Type: P, prospective; C/S, cross-sectional; R, retrospective; Treatment: BPD, biliopancreatic diversion; Ga Res, surgical procedure defined only as "gastric restrictive surgery"; Ob surg, a combination of surgical procedures; *Med/surg, a cohort of subjects seeking a combination of medical and surgical weight loss treatment; GBP, gastric bypass; VBG, vertical banded gastroplasty; Sample: (%F), (Percentage of the NES group who were female); NR, not reported

Two studies also assessed the presence of post-surgical NES. A prospective study at three years following BPD, found four subjects who displayed a pattern of night eating (4/63, 6%), which was similar to baseline (5/63, 8%) [299]. The author's implied NES occurrence had remained stable. Given the low prevalence rate within a relatively small sample size there is inadequate power to justify this conclusion. The largest retrospective study also reported a small change in NES prevalence from a pre-operative 31%, to 27% at 32±30 months after gastric restrictive surgery [389]. Three small retrospective studies that only assessed night-time snacking (waking to eat), found marked declines in nocturnal eating episodes of 83% [302], 80% [298] and 67% [303] at an average of 16.4 months following GBP, ≤3.5 years post VBG, and 20.8±11 months post GBP respectively. These sizeable reductions may be overstated due to the use of broad criteria, or falsely inflated recollections of baseline night-time snacking.

Pre-surgical Factors Associated with NES

At baseline, six of nine studies assessed NES and non-NES alongside a range of demographic, behavioural, psychological, and clinical factors, and are listed in **Table 7.3**. Studies were methodologically varied, and no significant differences between NES and non-NES emerged in five of six studies. Comparable gender [393] and race distributions [534], body weights [302, 389, 393], resting energy expenditure [393], dietary restraint, hunger, and disinhibition [393], and psychological states [311] were reported. Only one study described a significant difference in measures of depression ($p<0.001$), psychoneuroticism ($p<0.01$), and bulimic behaviour ($p<0.001$) [416]. Age was inversely related to NES ($p<0.05$), and women scored higher NES symptomology than men ($p<0.01$). This study involved NES criteria stipulating "eating in the evening without enjoyment, and feeling tense, upset, or anxious" [416]. The only other study to examine NES and measure psychopathology, did not include a mood criterion, and found no association [311]. One study also assessed BED and NES concurrently, and found that half of the night-eaters also manifested BED [393]. The groups with 'BED only' and 'BED and night eating' showed significantly higher dietary disinhibition than the 'night eaters', and 'no BED or NES'.

Table 7.3 Outcomes of studies involving bariatric surgery that have assessed NES or night eating behaviours

Study	Follow Up				
	Duration	**Attrition**	**Post-op NES Assessed**	**Pre-op NES Ax Method**	**Outcomes Assessed**
Kuldau &Rand 1986 [416]	N/A	N/A	No	N/A	**Pre-op NES:** NES correlated with measures of psychoneuroticism ($p \leq 0.01$) and depression ($p \leq 0.001$), bulimic behaviour ($p \leq 0.001$). Age was inversely related to NES ($p \leq 0.05$). Women scored higher on the NES scale ($p \leq 0.01$)
Rand & Kuldau 1993 [534]	N/A	N/A	No	N/A	**Pre-op NES:** No difference in prevalence between black women, white women, and white men
Adami et al 2002 [393]	N/A	N/A	No	N/A	**Pre-op NES:** No baseline difference in: gender or weight, all scales of the TFEQ, or resting energy expenditure b/w NES and non-NES (and non-BED)
Hsu et al 1996 [298]	≤3.5y	N/A	Yes	CI	**Pre-op NES:** 10/24 subjects (42%) **Post-op NES:** 2/24 subjects (8%). Both had current bulimia nervosa
Hsu et al 1997 [303]	20.8±11m	N/A	Yes	CI	**Pre-op NES:** 9/27 subjects (33%) **Post-op NES:** 3/27 subjects (11%)
Rand et al 1997 [389]	32±30m	N/A	Yes	CI	**Pre-op NES:** 34/111 subjects (31%). Presence of NES was not related to weight **Post-op NES:** 30/111 subjects (27%)
Adami et al 1999 [299]	3y	0%	Yes	CI	**Pre-op NES:** 5/63 subjects (8%) **Post-op NES:** 4/63 subjects (6%), ie. 3 who were pre-NES and 1 new NES
Powers et al 1999 [311]	5.5y (Range 0.5 to 10.5y)	38%	No	N/A	**Pre-op NES:** Psychopathology not different to non-NES (and non-BED) **Post-op NES:** Baseline NES not related to final weight
Latner et al 2004 [302]	16.4m*	N/A	Yes	Phone Interview	**Pre-op NES:** 36/65 subjects (55%). Nocturnal eating not correlated with initial BMI **Post-op NES:** 1/65 subjects (2%) by pre-op criteria and 5/65 (8%) subjects reported nocturnal eating at lower frequency. Pre-surgical nocturnal eating not correlated with weight loss. More frequent post-surgical nocturnal eating in 6/65 subjects (10%) was associated with greater post-surgical BMI ($p<0.02$) and less treatment satisfaction ($p<0.01$)

N/A, not applicable; CI, clinical interview; TFEQ, three factor eating questionnaire; non-BED, persons without binge eating disorder
*Mean time of follow up, no SD quoted; CI; clinical interview

Post-surgical Weight Loss

Two of nine studies compared post-surgical changes in body weight between NES and non-NES (Table 7.3). A prospective study, at an average of 5.5 years following gastric restrictive surgery, found no weight difference between pre-surgical NES and non-NES [311]. A small retrospective study reported that pre-surgical nocturnal eating was not correlated with weight loss at an average of 16.4 months following GBP [302]. More frequent post-surgical nocturnal eating (which occurred in 6/65 subjects, 10%) was however associated with greater post-surgical BMI ($p<0.02$), and less treatment satisfaction ($p<0.01$). Poorly defined night eating criteria, small numbers, and retrospective analysis limits the ability to generalize these findings.

Discussion

This review considered current theory on NES, and the association between NES and bariatric surgery. The distinction between a variant of "normal eating behaviour", and a pattern that causes distress, impairment, or generates a health risk, thus constituting an eating disorder of clinical significance, appears unclear. Throughout the literature, widespread use of inconsistent NES diagnostic criteria result in the measurement of differing clinical entities, promoting disparity in the level and nature of clinical disturbance. Links between NES and obesity have been shown in some studies, but this finding is not universal. Similarly, behavioural and psychological factors associated with NES are inconsistent across studies involving random samples, weight loss samples, and persons seeking bariatric surgery. An association between NES and low mood has most consistently been reported, but the nature of the association is unclear. Current proposed treatment options are few, and differing characterization of NES may influence the definition of treatment success, or assessment of the course of the syndrome.

Studies exploring the relationship between NES and bariatric surgery are few in number, and so too provide largely fragmented and inconclusive results. In addition to the significant heterogeneity in the definition of NES, small sample sizes and retrospective analysis of behavioural traits are key methodological weaknesses, and greatly diminish the value of data. For example, of the studies to assess pre-operative NES prevalence

rates, those collecting prospective or cross-sectional data and employing more clearly defined definitions of evening hyperphagia, yielded lowest prevalence estimates. Retrospective studies using broad, poorly defined criteria, reported markedly higher rates of nocturnal eating behaviours, and must be differentiated from studies measuring characteristics of the NES.

Furthermore, following bariatric surgery, several factors may theoretically alter, and affect NES diagnosis. Hunger is greatly diminished [72, 313] and this may reduce evening eating and night-time snacks, and along with physical gastric restriction, deter a general tendency to overeat. Sleep quality also improves with weight loss, and this includes a notable reduction in the occurrence and severity of obstructive sleep apnoea (OSA) [540]. The nature or extent of the association between NES and OSA is largely unexplored [397, 541], however it is possible that the individual who achieves better sleep quality is less likely to wake and rise to eat. Symptoms of depression are also markedly improved following bariatric surgery [68], and although the nature of the relationship between NES and an altered mood state is uncertain, an overall improved disposition may reduce stress and assist behaviour change.

At present, the effect of NES, if any, on short, medium, and long-term surgical outcome remains to be determined, and the course of NES following obesity surgery is unknown. For research to move forward, the ways in which NES departs from "normal" eating behaviour must be identified. Behavioural and psychological traits of NES require elucidation, and the establishment of agreed diagnostic criteria is essential. Careful research needs to assess the clinical significance of each of the associated features of NES, and the syndrome as an entity, in order to establish a threshold at which the cluster of behaviours causes marked distress, mental or physical impairment, or generates a risk to health. Qualitative studies could assist to determine which aspects of the syndrome affected persons find most debilitating. The nature of the association between NES and psychological measures such as stress, symptoms of depression, mood state, and BED also requires investigation. The diagnostic criteria put forward by Birkdvedt et al. [387] exclude subjects who meet criteria for bulimia nervosa or BED however, greater understanding of the overlap between NES and BED is required. Assessment of BED

should be carried out according to current proposed research criteria listed in the Diagnostic and statistical manual of mental disorders: DSM-IV (4th Ed) [266].

Issues of NES causality and counter-causality need to be explored alongside factors including obesity, changes in body weight, and diurnal hormone patterns. Intervention studies that manipulate 24-hour eating patterns and assess concurrent changes in circulating hormones are required. Prospective, longitudinal studies should explore the impact of NES on outcomes of weight loss therapies. This is of particular importance to obesity surgery, given the high NES prevalence observed amongst surgical candidates. Research in this area has the potential to provide a significant contribution to the understanding of NES and its impact on weight loss outcome. Of priority however, a clear understanding of the clinical importance of NES, and agreement on the behavioural features and diagnostic criteria, are required.

Declaration for Thesis Chapter 8

Declaration by candidate

In the case of Chapter 8, this work represents a manuscript that has been published in the *International Journal of Obesity*, 2007; 31(11): 1722-30. The nature and extent of my contribution to the work was the following:

Nature of contribution	Extent of contribution (%)
I was responsible for the study design, all data collection and tabulation, analysis of data and writing the manuscript.	>85%

The following co-authors contributed to the work.

Name	Nature of contribution	Extent of contribution (%) for student co-authors only
Associate Professor John Dixon	Assisted with the study design, analysis of data, and writing of the manuscript.	
Professor Paul O'Brien	Assisted with subject recruitment and writing of the manuscript.	

Candidate's Signature [redacted] **Date** 6/12/07

Declaration by co-authors

The undersigned hereby certify that:

(1) the above declaration correctly reflects the nature and extent of the candidate's contribution to this work, and the nature of the contribution of each of the co-authors.
(2) they meet the criteria for authorship in that they have participated in the conception, execution, or interpretation, of at least that part of the publication in their field of expertise;
(3) they take public responsibility for their part of the publication, except for the responsible author who accepts overall responsibility for the publication;
(4) there are no other authors of the publication according to these criteria;
(5) potential conflicts of interest have been disclosed to (a) granting bodies, (b) the editor or publisher of journals or other publications, and (c) the head of the responsible academic unit; and
(6) the original data are stored at the following location(s) and will be held for at least five years from the date indicated:

Location(s) **The Centre for Obesity Research and Education**

Signature 1	Associate Professor Joh [redacted]	**Date** 6/12/0
Signature 2	Professor Paul O'Brien [redacted]	5/12/07

CHAPTER 8: Night eating syndrome and nocturnal snacking: association with obesity, binge eating and psychological distress

Abstract

Background: Night eating syndrome (NES) is characterized by a time-delayed pattern of eating relative to sleep, where most food is consumed in the evening and night. This study aimed to investigate the clinical significance of NES and nocturnal snacking by exploring the relationship between NES and 1) obesity, 2) binge eating disorder (BED), and 3) psychological distress.

Subjects: 180 bariatric surgery candidates, 93 members of a non-surgical weight loss support group, and 158 general community respondents (81males/350females, mean age 45.8±13.3, mean BMI 34.8±10.8, BMI range 17.7 to 66.7).

Methods: NES diagnosis required within the previous 3 months: 1) no appetite for breakfast, 2) consumption of ≥50% of daily energy after 7p.m., 3) and sleep difficulties ≥3 nights/week. Nocturnal snacking (awakening to eat) was recorded. Validated questionnaires assessed BED, symptoms of depression, appearance dissatisfaction (AD), and mental health-related quality of life (MHQoL). NES and binge eating (BE) (≥1 episode/week) were confirmed by interview.

Results: NES criteria were met by 11.1% of the total cohort. Across all groups, BE (p=0.001), BMI (p=0.003), and male gender (p=0.013) explained 10% of NES variance. Individuals with co-morbid NES and BE reported similarly elevated psychological distress as other binge eaters. NES alone was not associated with psychological distress, although those with NES who consumed nocturnal snacks reported poorer MHQoL (p=0.007) and greater depressive symptoms (p=0.039) and hunger (p=0.013) than others with NES alone. Low MHQoL (p=0.007) and male gender (p=0.022) explained 27% of the variance in the nocturnal snacking group.

Discussion: In this study, NES was positively associated with BMI, BE, and male gender. Elevated psychological distress was only apparent in those who consumed

nocturnal snacks. Further characterization and understanding of the clinical significance of NES and nocturnal snacking is required.

Introduction

The escalating worldwide prevalence of obesity has drawn attention to the association between "non-normative" eating patterns, weight gain, and obesity. Night eating syndrome (NES) is such a condition, observed most frequently among groups of overweight and obese individuals. First characterized by Stunkard et al. in 1955 [386], awareness of NES as a behavioural entity has only emerged in the last decade. Individuals with NES are characterized by a time-delayed pattern of eating relative to sleep, where most food is consumed late in the day and into the evening and night [396]. Features of the syndrome have generally included morning anorexia, evening hyperphagia, and insomnia, and more recent research criteria have stipulated the consumption of nocturnal snacks, where individuals wake from sleep to eat. Individuals with NES who report nocturnal snacking may constitute a group with more severe symptoms than those who do not wake to eat [397]. At present NES is not formally listed as an eating or sleep disorder, and no agreed diagnostic criteria exist.

NES prevalence estimates are low in community samples (range 0.4% to1.6% [400-402]) but markedly higher among groups of obese persons seeking medical or surgical weight loss (range 6% to 64%) [536]. Despite this, only one cross-sectional study has shown a positive relationship between NES and BMI [395]. Symptoms of depression are more consistently associated with NES, but may be influenced by the concurrence of binge eating disorder (BED). Binge eating disorder involves regular episodes of excessive, uncontrolled over-eating, and is strongly associated with psychological distress [266]. In obese populations BED has been linked with NES and nocturnal snacking, however the nature of the association is uncertain. It is currently unclear whether NES, as a discrete condition, is associated with emotional distress, impairment, or disability, and thereby represents an eating disorder of clinical significance. NES could simply constitute a variant of normal eating behaviour that may be linked to weight gain and obesity.

The aim of this study was to investigate the clinical significance of NES by exploring the relationship between NES and 1) BMI, 2) BED, and 3) psychological distress. Three groups differing in body weight and treatment-seeking status (bariatric surgery candidates, weight loss support group members and general community respondents) were recruited. Associations between NES and binge eating, symptoms of depression, body image/appearance dissatisfaction, mental health-related quality of life (MHQoL), and eating behaviour were investigated. It was hypothesized that:

1) NES prevalence would increase with increasing BMI;
2) NES would be associated with higher psychological distress than non-NES (and non-BED) after controlling for any distress related to age, gender and BMI;
3) individuals reporting co-morbid NES and BED would display higher levels of psychological distress than those with either NES or BED; and
4) the subgroup of NES who woke to consume nocturnal snacks would show greater overlap with BED and higher psychological distress than NES who did not wake to eat

Methods

All participants were recruited between August 2004 and January 2006. Inclusion required an age between 18 to 70 years. Subjects were excluded if they had undergone previous bariatric surgery. Six individuals were also excluded due to night-shift work [542], as was one student with a pattern of late-night studying and eating. The primary data were obtained via self-report surveys. Of 648 distributed, 431 eligible surveys were returned, representing an overall response rate of 66.5%.

The study was approved by the Monash University Standing Committee on Ethics in Research involving Humans, and was conducted in accordance with the Helsinki Declaration of 1975 as revised in 1983. All subjects were informed regarding the nature of the questionnaires and consented to study involvement.

Subjects

The majority of all respondents were white Caucasian. Ninety three percent were residents of the state of Victoria, Australia, and the remainder resided in the neighbouring states of South Australia and New South Wales.

Bariatric Surgery Candidates: This sample consisted of consecutive, eligible persons accepted into the bariatric surgery program at The Avenue Hospital, Melbourne, Australia. Two hundred and thirty of 240 subjects agreed to participate and were provided with a survey pack and consent form. Of these, 180 completed surveys and consent forms were returned; a response rate of 78%.

Weight Loss Support Group Respondents: This sample provided data from obese and overweight persons who were not seeking bariatric surgery. Subjects were recruited from "Take Off Weight Naturally" (TOWN), a weight loss company that consists of over 130 support groups within Victoria. In total, 158 survey packs were distributed, and 93 completed surveys were returned, which represents a response rate of 59%. Names and contact phone numbers were volunteered by 71% of respondents.

General Community Respondents: Subjects were randomly recruited through flyers placed on notice boards in the general community, flyers on notice boards in 2 large metropolitan hospitals, and through survey distribution at a large Australian university. Of 260 distributed packs, 158 completed surveys were received; a response rate of 61%. Names and contact phone numbers were volunteered by 72% of respondents.

Measures/Materials

A cover sheet on the weight loss support group and general community surveys requested respondent's age, home post code and contact phone number (both optional), height, weight and date this weight was last checked (The cover sheet and survey pack appear in Appendix I). Although based solely on self-report, 87% of subjects from the support group and general community stated that they had weighed themselves within the previous month. The surgical group consented to have demographic and anthropometric information obtained from clinic notes. All survey packs were otherwise identical and consisted of a questionnaire on NES, and 5 validated surveys listed below.

Eating Disorder Diagnoses and Eating Behavior

A self-report survey screened for NES diagnostic criteria based on those published by Stunkard et al. in 1996 [283]. The survey informed subjects that the questions related to past 3 months only. Six questions requiring a yes/no response were listed:

1) Do you usually have no appetite for breakfast?
2) Do you skip breakfast on 3 or more days of the week?
3) Do you usually eat the majority of your food intake, ie. greater than half of the calories that you would eat over a 24 hour period, after 7pm?
4) Do you have trouble getting to sleep and/or staying asleep on 3 or more days of the week?
5) Have you experienced awakenings during the night on at least 3 nights of the week over the last 3 months?
6) When you awaken during the night, do you find yourself frequently consuming snacks?

NES diagnosis required that persons within the previous three month period usually:

1) had no appetite for breakfast,
2) consumed 50% or more of total energy intake after 7p.m., and
3) had trouble getting to sleep or staying asleep on three or more nights of the week.

The Questionnaire on Eating and Weight Patterns – Revised (QEWP-R) [268, 269] was used to screen for characteristics of binge eating. The QEWP-R also collects data on weight and shape concerns and symptoms of bulimia nervosa.

Following completion of the NES questionnaire and the QEWP-R, all surgical candidates participated in a short semi-structured interview, and community respondents and support group members who reported characteristics of binge eating or night eating

underwent a semi-structured phone interview. The purpose of the semi-structured clinical and phone interviews was to verify survey responses. The interview moved systematically through both surveys, repeating all questions. Subjects were provided with fuller descriptions of difficult concepts such as the experience of loss of control. During the interview, a brief diet history by an experienced dietitian (SLC) determined whether subjects usually ate greater than half their dietary energy after 7p.m.

Eating behaviours and cognitions were further assessed using **The Three Factor Eating Questionnaire** (TFEQ) [524]. This widely used tool contains 51 items that measure three dimensions of human eating behaviour: 1) dietary restraint, 2) disinhibition of eating and 3) subjective feelings of hunger. Scores increase with increasing eating pathology.

Psychological Health and Quality of Life

Symptoms of depressive illness were assessed using the revised **Beck Depression Inventory** (BDI) [527]. Within a possible range of 0 and 63, a score of 0-9 was considered 'Normal'; 10-16 'Mild'; 17-29 'Moderate'; and 30-63 'Severe depression' [528].

The Multidimensional Body Self Relations Questionnaire (MBSRQ) [530] was used to calculate an appearance dissatisfaction (AD) score, as a measure of body image distress. The level of AD was determined by calculating the difference between the appearance orientation (AO) and the appearance evaluation (AE) subscales [80].

The Medical Outcomes Trust Short Form-36 (SF-36) [532, 533] assessed health-related QoL. The physical component summary (PCS) and mental component summary (MCS) scores were calculated. A lower MCS indicates poorer self-rated psychological health and more social disability due to emotional problems. The SF-36 MCS was used as a measure of psychological distress, labelled as mental health-related quality of life (MHQoL).

Data Analyses

Descriptive statistics were used to calculate the mean ± SD for continuous variables when the total study group was divided according to recruitment origin, and to define

'NES only', 'BE only' and 'Co-morbid NES and BE'. Two control groups matched for age, gender, BMI, and 'recruitment origin' to 'NES only' and 'BE only' were derived from persons in the 'No NES or BE' group. These matched control groups were also presented as mean ± SD. Binary logistic regression identified factors independently predictive of NES. Factors entered into the model included 'recruitment origin', gender, BMI, age, depression score, SF-36 MCS and PCS, AD score, and BE. The difference in mean values for 'NES only', 'BE only' and their matched controls, and 'NES only', 'BE only' and 'Co-morbid NES and BE', was assessed using independent t-tests, and chi-square analysis for gender. Characteristics of the subgroups of NES who did, and did not consume nocturnal snacks were also compared using independent t-tests, and chi-square analyses for gender and BE. Finally, within all NES and within the total cohort, binary logistic regression and linear regression identified factors predictive of nocturnal snacking. Factors entered into the models included 'recruitment origin', gender, BMI, age, depression score, SF-36 MCS and AD score. SPSS version 12.0.1 was used for statistical analysis.

Results

Non-responders

There was no difference in gender, age or BMI between participants and non-responders in the surgical group. Due to the anonymity of the surveys disseminated to the community groups, differences between responders and non-responders could not be assessed.

Participant description

Data were obtained from persons of a wide BMI range. The final groups comprised the surgery candidates (n=180, BMI range 31.9 to 66.7), weight loss support group members (n=93, BMI range 21.3 to 60.2), and community respondents (n=158, BMI range 17.7 to 45.5). **Table 8.1** lists descriptive features of each group.

Table 8.1 Descriptive characteristics and comparison of the three original recruitment groups that differed in obesity treatment-seeking status

	Group 1: General Community Respondents	Group 2: Weight Loss Support Group	Group 3: Bariatric Surgery Candidates	*P* values[1]
Male/Female	34/124	8/85	39/141	0.018
Mean Age	41.3 ± 13.5^{a}	55.1 ± 12.4^{b}	44.8 ± 11.2^{c}	0.000^{ab} 0.026^{ac} 0.000^{bc}
Mean BMI	24.8 ± 5.1^{a}	32.7 ± 7.3^{b}	44.5 ± 6.8^{c}	0.000^{ab} 0.000^{ac} 0.000^{bc}
NES[2]	9 (5.7%)	4 (4.3%)	35 (19.4%)	0.000
NES+snacks[2]	2 (1.3%)	1 (1.1%)	13 (7.2%)	0.005
Nocturnal snacks[2]	6 (3.8%)	4 (4.3%)	20 (7.0%)	0.016
BE[2]	3 (1.9%)	5 (5.4%)	44 (24.4%)	0.000
BDI Depression Score	5.5 ± 5.5^{a}	9.4 ± 7.3^{b}	16.8 ± 9.0^{c}	0.000^{ab} 0.000^{ac} 0.000^{bc}
MBSRQ-AD Score[3]	0.14 ± 1.0^{a}	1.0 ± 0.88^{b}	1.8 ± 1.0^{c}	0.000^{ab} 0.000^{ac} 0.000^{bc}
SF-36 MCS	49.7 ± 6.5^{a}	49.8 ± 6.9^{b}	46.3 ± 8.2^{c}	NS^{ab} 0.000^{ac} 0.001^{bc}
SF-36 PCS	53.2 ± 8.1^{a}	46.2 ± 10.9^{b}	36.9 ± 9.5^{c}	0.000^{ab} 0.000^{ac} 0.000^{bc}
TFEQ Restraint	8.5 ± 4.9^{a}	12.6 ± 3.9^{b}	8.2 ± 3.9^{c}	0.000^{ab} NS^{ac} 0.000^{bc}
TFEQ Disinhibition	5.7 ± 3.6^{a}	9.0 ± 4.0^{b}	11.7 ± 3.3^{c}	0.000^{ab} 0.000^{ac} 0.000^{bc}
TFEQ Hunger	4.4 ± 3.2^{a}	6.0 ± 3.4^{b}	8.8 ± 3.6^{c}	0.001^{ab} 0.000^{ac} 0.000^{bc}

[1]Paired superscript letters indicate to which variables each *p*-value belong
[2]Results presented as number of subjects (percentage of each recruitment group)
[3]MBRSQ-AD, Multidimensional body self relations questionnaire - Appearance dissatisfaction (calculation of the difference between the Appearance orientation and Appearance evaluation subscales); NES, night eating syndrome; BE, binge eaters; BDI, Beck depression inventory; MCS, mental health component score; PCS, physical component score; TFEQ, Three factor eating questionnaire
Statistical analysis using ANOVA with Tukey post-hoc analysis for continuous variables and presented as mean±SD, and Chi-square for categorical variables and presented as n (% of original recruitment group)

Prevalence of Eating Pathology

Based on responses to the self-report questionnaire, 62 persons met NES criteria. Following the confirmatory clinical or phone interview this number reduced to a final group of 48. Rates of NES were significantly different between groups at 19.4% in the surgery candidates, 4.3% in the support group, and 5.7% in the community, $\chi^2(2, n = 428) = 11.33, p<0.001$ (Table 8.1). A subgroup of NES also reported nocturnal snacking (NES+snacks). This occurred in 7.2%, 1.1%, and 1.3% of each recruitment group respectively, and was also statistically different between groups $\chi^2(2, n = 428) = 5.43$, $p=0.005$. In particular, rates of NES and nocturnal snacking were higher among the surgical candidates than the support and community groups.

When binge eaters who reported one binge episode per week (n=14) were compared to those reporting two or more binges per week (n=38), both groups showed similar demographic, psychological, and behavioural characteristics (data not shown). These two groups were therefore combined and collectively termed binge eaters. Prevalence of BE varied between recruitment groups, at 24.4% in the surgery candidates, 5.4% in the support group, and 1.9% among the community respondents $\chi^2(2, n = 428) = 25.14$, $p<0.001$). Co-existing NES and BE was present in 4.4% of the total cohort. No subject met criteria for bulimia nervosa.

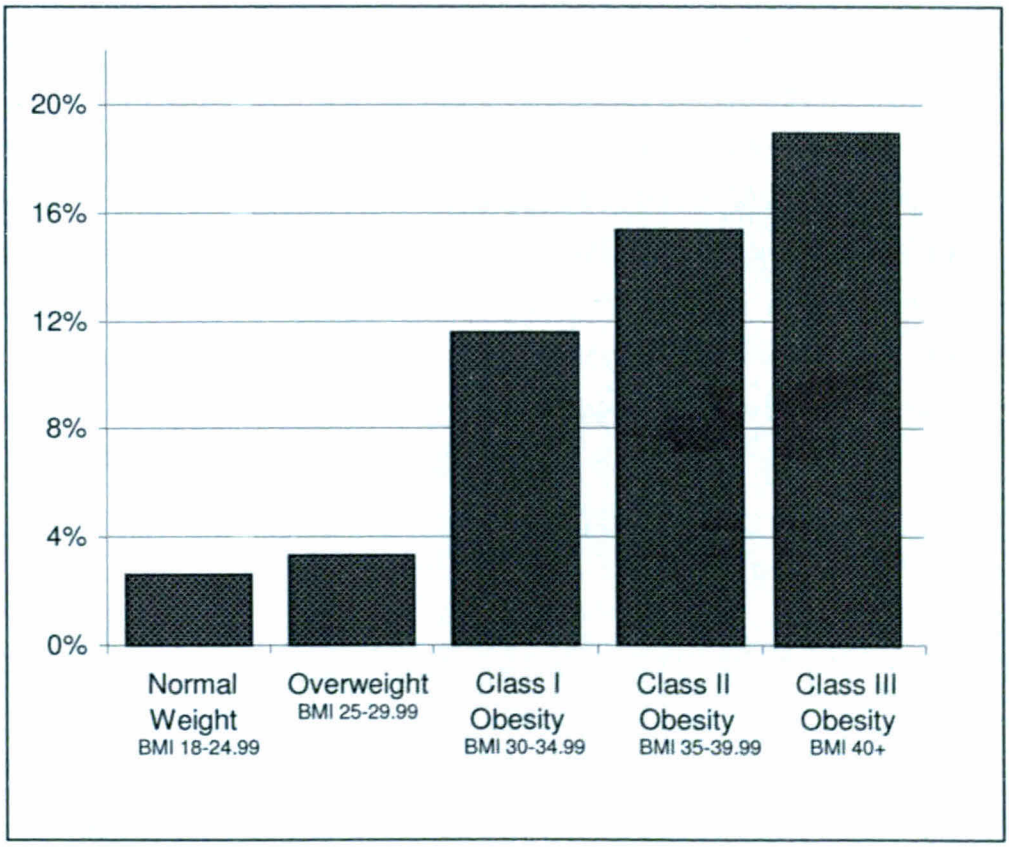
Correlates and Characteristics of NES

The effect of age, gender, BMI, and 'recruitment group' on the presence of NES was assessed in a binary logistic regression model. In the analysis BMI ($p<0.001$) and male gender ($p=0.034$) explained a significant proportion of the variance in NES diagnosis ($r^2=0.049$). **Figure 8.1** illustrates NES prevalence according to BMI category. Chi square analysis showed there was a significant difference in NES prevalence across five BMI categories, $\chi^2(4, n = 48) = 22.71, p<0.001$.

A second binary logistic regression model explored the association between NES and psychological distress while controlling for BMI and gender. Factors entered included BDI depression score, SF-36 MCS, AD score, and BE. Binge eaters were almost 7 times more likely to manifest NES (Odds Ratio 6.9; 95% CI 3.5 – 13.7). Overall, BE status ($p=0.001$), BMI ($p=0.003$), and male gender ($p=0.013$) explained 10% of the

variance in NES diagnosis. Chi-square analysis confirmed the strong association between NES and BE, $\chi^2(1, n = 431) = 38.56$, $p<0.001$, and showed a positive trend toward NES and male gender, $\chi^2(1, n = 431) = 3.81$, $p=0.051$.

Figure 8.1 Distribution of all subjects with NES according to BMI category. Across five BMI categories the prevalence of NES increased with increasing BMI.



The group containing 'NES only' (n=29) was matched for age, gender, BMI, and 'recruitment origin' to a comparison group derived from persons in the 'No NES or BE' category. The 'BE only' (n=33) were also compared to a matched group of subjects without NES or BE. **Table 8.2** demonstrates there was no statistical difference between the 'NES only' group and matched controls for all psychological or behavioural variables. In contrast, binge eaters showed significantly higher scores for symptoms of depression, SF-36 MCS, weight and shape concern, dietary disinhibition, and hunger, compared to the matched control group of non-binge eaters.

Characteristics of subjects with 'Co-morbid NES and BE' (n=19) were also assessed (Table 8.2). In total, 40% of those with NES manifested BE, and a similar proportion of binge eaters also manifested NES (37%). Weight-related variables, measures of psychological distress, and eating behaviours of 'Co-morbid NES and BE' were compared to 'NES only' (n=29) and 'BE only' (n=33) using independent t-tests. Table 8.2 illustrates that weight-related variables were similar between the three eating disordered groups. Yet importantly the 'Co-morbid NES and BE' and 'BE only' groups scored similarly high on all psychological variables. Comparison of the 'Co-morbid NES and BE' and 'NES only' groups revealed significantly lower psychological distress among those with 'NES only'. Symptoms of depression measured by the revised BDI, AD score, dietary disinhibition and hunger, and importance of weight and shape were all significantly lower in the 'NES only' group.

Table 8.2 Comparison of 'NES Only' and 'BE Only' with control groups matched for age, gender, BMI and recruitment group, derived from 'No NES or BE'. Comparison of 'Co-morbid NES & BE' with 'NES Only' and 'BE Only'

	NES Only (a)	Control Group	*P* Val -ue	BE Only (b)	Control Group	*P* Val -ue	Co-morbid NES & BE (c)	*P* Value (a)&(c) / (b)&(c)[1]
n	29	29		33	33		19 (4%)	
Male/Female	11/18	11/18	NS	5/28	5/28	NS	3/16	0.099 / NS
Mean Age	47.4±10.7	47.0±11.3	NS	42.2±8.6	42.3±8.4	NS	42.1±7.8	0.071 / NS
Mean BMI	40.2±10.4	39.2±9.0	NS	43.7±8.7	42.8±7.7	NS	43.7±7.3	NS / NS
Current Weight	117±30.8	110.2±29.1	NS	119±27.0	116±22.4	NS	120±24.5	NS / NS
BDI Score	13.9±11.1	10.3±6.9	NS	21.5±9.8	14.0±8.8	0.002	20.8±9.9	0.033 / NS
AD Score	1.1±1.5	1.2±1.2	NS	2.1±0.9	1.6±1.1	NS	2.0±0.90	0.032 / NS
Weight / Shape	2.6±0.84	2.4±0.8	NS	3.3±0.7	2.9±0.8	0.030	3.3±0.73	0.005 / NS
SF-36 PCS	40.8±9.5	43.4±11.5	NS	39.8±11.0	39.7±10.9	NS	34.5±8.9	0.031 / 0.089
SF-36 MCS	47.1±10.2	48.8±6.8	NS	42.0±7.4	47.6±7.8	0.004	43.9±7.4	NS / NS
Restraint	8.1±4.4	8.3±4.4	NS	8.0±4.1	8.1±4.7	NS	9.0±2.9	NS / NS
Disinhibition	9.9±3.7	9.6±4.0	NS	14.0±1.7	9.9±3.8	<0.001	14.4±1.4	<0.001 / NS
Hunger	7.5±3.7	7.5±3.7	NS	10.5±3.1	7.9±3.7	0.004	10.8±2.5	<0.001 / NS

[1]*p*-values = (a)&(c), 'NES Only' & 'Co-morbid NES & BE; (b)&(c), 'BE Only' & 'Co-morbid NES & BE
NES, night eating syndrome; BE, binge eaters; BDI, beck depression inventory; NS, not significant; AD, appearance dissatisfaction; PCS, physical component score; MCS, mental health component score
Statistical analysis using independent t-tests for continuous variables and presented as mean±SD, and Chi-square for categorical variables

Comparison of groups who did, and did not consume nocturnal snacks

Characteristics of the subgroup of NES who consumed nocturnal snacks (NES+snack; n=16) were compared with NES who did not report this behaviour (NES-no snack; n=32). Mean BMI was similar in both groups, t(46) = -.92, p=0.362. Gender distribution was not statistically different, $\chi^2(1, n = 48) = 2.47$, p=0.116, however males comprised 44% of 'NES+snacks' compared to 22% of the 'NES-no snack' group. Binge eating was not more prevalent in the 'NES+snacks' (43.8%) than 'NES-no snack' group (37.5%), $\chi^2(1, n = 48) = 0.17$, p=0.676, therefore binge eaters were not excluded from subsequent analysis of psychological traits. The 'NES+snack' group showed significantly higher symptoms of depression on the revised BDI, t(43) = -2.13, p=0.039, a lower SF-36 MCS score, t(43) = 2.83, p=0.007, and greater TFEQ hunger score, t(46) = -2.59, p=0.013. In a binary logistic regression model, low SF-36 MCS (p=0.007) and male gender (p=0.022) explained 27% of the variance in the 'NES+snacks' group.

Finally, within the total cohort (n=431), the characteristics of 30 individuals who reported the consumption of nocturnal snacks were explored. Of this group n=16/30 also reported full NES criteria, ie. the 'NES+snacks' group, and n=14/30 were not diagnosed with NES. Significantly more males comprised the small group of nocturnal snackers, $\chi^2(1, n = 431) = 4.467$, p=0.035, with 12.3% of all males reporting nocturnal snacking compared to 5.7% of females. In the binary logistic regression model, male gender, (p=0.002), the revised BDI score, (p=0.019) and SF-36 MCS score, (p=0.038) explained 7.3% of the variance in nocturnal snacking behavior. The average score on the revised BDI for the nocturnal snackers was 19.3$\pm$11.4 compared to 10.3$\pm$8.5 in the remainder of the cohort. **Table 8.3** presents the results of a linear regression analysis to assess factors driving the three measures of psychological distress. Nocturnal snacking within the total cohort was positively associated with BDI score and negatively associated with MHQoL. Again, NES was not associated with any psychological measure. Binge eating was strongly related to all three measures.

Table 8.3 Factors within the total cohort associated with the three measures of psychological distress

	Symptoms of Depression (Revised BDI)	Mental Health-Related QoL (SF-36 MCS)	Appearance Dissatisfaction (MBSRQ)
Age	NS	β=0.11; p=0.019	NS
Female Gender	β=-0.16; p<0.001	β=0.13; p=0.004	β=-0.27; p<0.001
BMI	β=0.43; p<0.001	β=-0.10; p=0.042	β=0.49; p<0.001
NES	NS	NS	NS
Nocturnal snacks	β=0.18; p<0.001	β=-0.19; p<0.001	NS
BE	β=0.26; p<0.001	β=-0.20; p<0.001	β=0.15; p<0.001
Total Variance[1]	39%	14%	36%

[1]Combined R square value
BDI, Beck Depression Inventory; SF-36 MCS, The Medical Outcomes Trust Short Form-36 Mental Health Component score; MBSRQ, The Multidimensional Body Self Relations Questionnaire; NES, night eating syndrome; BE, binge eaters; NS, not significant
Statistical analysis using linear regression. Beta values and p-values are provided for significant associations

Discussion

This study compared NES in a large cohort of persons ranging widely in BMI and treatment-seeking status. Characteristics of NES were contrasted with non-NES and with persons manifesting BE and co-morbid NES and BE. The clinical significance of nocturnal snacking was also explored. Of primary interest were differences in BMI and markers of psychological distress. Importantly, regardless of weight control endeavours, NES prevalence was positively associated with BMI. Until now, this association has been generally accepted due to consistently higher NES prevalence estimates in cohorts of overweight and obese when compared to the general community. Only one cross-sectional study has directly supported the positive relationship between NES and BMI [395], while the majority have shown no connection [389, 391-393]. The lack of association may be the result of a small BMI range within homogenous populations, and inadequate power to detect group differences. The current data, collected specifically to provide BMI values across a broad spectrum, clearly show a strong, independent association between NES and BMI.

Binge eating behaviour was also closely linked with NES. Most strikingly, binge eaters were almost 7 times more likely to manifest NES than non-binge eaters. Co-morbid NES and BE was 4% in the total cohort. Yet in the NES group, 40% reported BE, and among the group of binge eaters, 37% also reported NES. These findings represent similar rates of co-morbid NES and BE to other obese study groups [295, 311, 405], however higher [394] and lower [283, 311] rates have also been reported. Overlap between nocturnal snacking and BED has also been reported within obese populations [298, 303, 401, 402]. While BED and NES have been studied and described as separate entities [272, 415], these data highlight that co-occurrence of the two conditions is common. Similarities may exist in the consumption of an objectively large amount of food for the circumstances, and BE, which can extend over several hours, is common in the late afternoon and evening. While a perceived lack of control during a binge is essential, night eating behavior may also be under poor self-control [543].

Yet despite some behavioural similarities between BE and night eating, associated levels of psychological distress appear markedly different. The group with NES scored low on

all psychological measures, and was comparable to persons without NES. This was in sharp contrast to the BE group who yielded significantly higher symptoms of depression and AD, more weight and shape concern, dietary disinhibition and hunger, and lower MHQoL than matched non-bingeing controls. Furthermore, when NES and BE co-occurred, BE was the factor clearly associated with elevated psychological distress.

A number of studies have examined the link between NES (diagnosed according to various criteria) and associated psychological disturbance. However few studies have controlled for the influence of BE. Those that have controlled for bingeing behaviours have reported similar levels of psychological functioning between NES and non-NES in a normal weight sample of black females [390] and an obese sample [394]. Another study, which notably diagnosed NES by consumption of $\geq$25% total energy after the evening meal and/or awakenings to eat $\geq$3 times in a week (nocturnal snacking), did report a positive association between NES and symptoms of depression in obese NES compared to weight-matched controls [415]. A high level of psychological disturbance (and concurrent BE) have also been reported among nocturnal eaters referred to a sleep clinic for polysomnography [401].

The present study was the first to examine differences between subgroups who did, and did not consume nocturnal snacks. Frequent nocturnal snackers reported higher symptoms of depression and hunger, and lower MHQoL compared to the NES who did not wake to eat. This association between nocturnal snacking and psychological distress provides clinical significance to the behavioural feature of waking to eat, and supports the proposal that nocturnal snackers are a group with more severe impairment [397]. This also highlights the hitherto lack of distinction regarding the status of NES as an eating disorder or variant of normal eating behaviour. Night eating syndrome as defined in the present study appeared to be an extension of normal eating behaviour linked with weight gain and obesity. Further examination is required, and should also consider the level of control over nocturnal eating and the time-delayed pattern of eating, and the link between NES and stress [387, 406, 539].

Nocturnal snackers also tended to be male. Although gender differences in nocturnal snackers have not previously been assessed, one other study of morbidly obese treatment

seekers has observed an increased risk of NES in males [395]. In contrast, similar gender distributions between NES and non-NES have been found in surgical populations [393, 534], and obese [391, 392] and general samples [388, 391, 392]. Although limited by a relatively small male sample, our findings suggest that depressed men are more likely to engage in nocturnal snacking behaviour. While there are no clear explanations, work-related stress [544], obstructive sleep apnoea [401, 545] or another sleep-related disorder such as sleepwalking or restless legs syndrome [401] are possible correlates. Waking to use the bathroom [543], or insomnia, where eating acts as a "time killer" [401] are other factors that may lead to nocturnal snacking. The identification and treatment of low mood could assist to alleviate nocturnal snacking, and reduce the associated risk of weight gain.

Finally, lower evening leptin levels may contribute to night-time hunger and stimulate nocturnal snacking. Low circulating leptin has been observed in normal weight and obese NES, compared to weight-matched non-NES [387], although similar leptin levels have also been reported [409]. The present study did not specifically measure evening hunger, but found elevated hunger ratings in nocturnal snackers using a general measure of self-reported hunger.

A strength of the current study is the inclusion of a large cohort of subjects comprising a broad BMI range, recruited from geographically similar locations within the same timeframe. Body mass index was derived from clinic measurements of weight and height in the obese surgical candidates, and self-report in the community and weight loss support groups. Although self-report weights tend toward under-estimation, particularly as body weight increases [546], the majority of our overweight and obese respondents were weighed manually. Furthermore, self-reported weights in a general population have shown adequate sensitivity and good specificity when compared to actual weight [547]. Although the recruitment methods differed slightly and the three original groups possessed distinct characteristics, our methods of statistical analyses controlled for possible confounders, in particular differences in BMI and the presence of BE.

Another potential limitation of this study was the collection of data by self-report questionnaire. To minimize this weakness the surveys selected had been validated

previously within a range of population groups. Furthermore, the QEWP-R and NES survey were used as a screening tool [508] and research criteria for BED and NES were verified by either clinical or phone interview. An on-going limitation of research involving NES is the lack of formally validated diagnostic criteria and assessment methods. This study employed the most commonly applied criteria [283] and validated self-reported behavior in an interview. Nocturnal snacking, which is emerging as an important component of NES, was also considered.

Night eating syndrome as defined in this study showed a strong positive association with obesity, while frequent nocturnal snacking conferred an elevated risk of psychological disturbance. These findings highlight two clinically significant relationships, and importantly, provide a step toward differentiating a variant of normal eating behaviour from disordered eating associated with emotional distress or impairment. The high degree of overlap between NES and BE is also noteworthy and merits additional study. Finally, we suggest that male gender may be a risk factor for NES and nocturnal snacking. Awareness of NES and nocturnal snacking and the risks they impose on weight gain and psychological distress are still little known in general practice. Future work should further define NES features of clinical importance in order to guide the development of agreed diagnostic criteria, and develop targeted intervention strategies.

Declaration for Thesis Chapter 9

Declaration by candidate

In the case of Chapter 9, this work represents a manuscript that has been accepted for publication in *Obesity*, 2007. The nature and extent of my contribution to the work was the following:

Nature of contribution	Extent of contribution (%)
I was responsible for the study design, all data collection and tabulation, analysis of data and writing the manuscript.	>85%

The following co-authors contributed to the work.

Name	Nature of contribution	Extent of contribution (%) for student co-authors only
Associate Professor John Dixon	Assisted with the study design, analysis of data, and writing of the manuscript.	
Professor Paul O'Brien	Assisted with subject recruitment and writing of the manuscript.	

Candidate's Signature [redacted] **Date** 5/2/07

Declaration by co-authors

The undersigned hereby certify that:

(1) the above declaration correctly reflects the nature and extent of the candidate's contribution to this work, and the nature of the contribution of each of the co-authors.
(2) they meet the criteria for authorship in that they have participated in the conception, execution, or interpretation, of at least that part of the publication in their field of expertise;
(3) they take public responsibility for their part of the publication, except for the responsible author who accepts overall responsibility for the publication;
(4) there are no other authors of the publication according to these criteria;
(5) potential conflicts of interest have been disclosed to (a) granting bodies, (b) the editor or publisher of journals or other publications, and (c) the head of the responsible academic unit; and
(6) the original data are stored at the following location(s) and will be held for at least five years from the date indicated:

Location(s) **The Centre for Obesity Research and Education**

Signature 1	Associate Professor John D [redacted]	**Date** 6/12/07
Signature 2	Professor Paul O'Brien	5/12/07

CHAPTER 9: Loss of control is central to psychological disturbance associated with binge eating disorder

Abstract

Objective: Binge eating disorder (BED) is positively associated with obesity and psychological distress, yet the behavioural features of BED driving these associations are largely unexplored. The primary aim of this study was to investigate which core behavioural features of binge eating are most strongly related to psychological disturbance.

Research Methods and Procedures: A cross-sectional study involving 180 bariatric surgery candidates, 93 members of a non-surgical weight loss support group, and 158 general community respondents (81M/350F, mean age 45.8±13.3, mean BMI 34.8±10.8, BMI range 17.7 to 66.7). Validated questionnaires assessed BED and binge eating, symptoms of depression, appearance dissatisfaction (AD), quality of life (QoL) and eating-related behaviours. Features of binge eating were confirmed by interview. BMI was determined by clinical assessment and self-report.

Results: The loss of control (LOC) related to eating, that is, being unable to stop eating or control what or how much was consumed, was most closely associated with psychological markers of distress common in BED. In particular, those who experienced severe emotional disturbance due to feelings of LOC reported higher symptoms of depression ($p<0.001$), AD ($p=0.009$), and poorer mental health-related QoL ($p=0.027$).

Discussion: Persons who report subjective binge episodes or do not meet BED frequency criteria for objective binge episodes may still be at elevated risk of psychological disturbance, and benefit from clinical intervention. Feelings of LOC could drive binge eaters to seek bariatric surgery in an attempt to gain control over body weight and psychologically disturbing eating behaviour.

Introduction

An 'eating binge' is characterised by the uncontrolled consumption of an objectively large amount of food [266]. Binge eating disorder (BED) is a recognised eating disorder where bingeing occurs at an average frequency of 2 days per week over the previous 6 months. A strong relationship with psychological markers of distress and self-condemnation characterizes BED [78, 266, 267]. Higher general psychopathology [316], elevated symptoms of depression and higher ratings of body image distress and weight and shape concern are common associates. Prevalence estimates are typically high among bariatric surgery candidates, and the association with severe emotional disturbance occurs beyond that produced by the obese state [291]. Quality of life (QoL) may also be reduced [548], but not all reports agree [549].

The increased risk of obesity and psychological distress in BED is established. What is not established is the association between the specific diagnostic features of BED and markers of psychological disturbance. The binge frequency, binge size and experience of loss of control (LOC) over eating are all potential causes of distress. Striegal-Moore et al. [273, 368] considered binge frequency but found few distinctions in measures of psychological disturbance between obese subjects bingeing ≥ 1 to <2 versus ≥ 2 binges per week. Niego et al. [370] compared persons differing in binge size (objectively large versus subjectively large volumes) but also reported similar levels of depression and psychological disturbance. The relationship between the LOC related to eating and psychological distress has also received little attention in those with BED. However, women with BED have identified a binge episode by feelings of LOC, and less so by the amount of food consumed [373]. Work comparing full and partial syndrome bulimia nervosa suggests that the experience of LOC is more strongly associated with psychological distress than binge volume [374-376]. A number of researchers have proposed a LOC to be the most important and consistent feature of a binge [371-373].

Improved understanding of the link between BED and psychological distress will inform intervention strategies and patient management. The present study investigated inter-relationships between the central behavioural features of BED and three markers of psychological distress; symptoms of depression, appearance

dissatisfaction (AD), and mental health-related QoL (MHQoL). Subjects included three community groups varying in BMI and current weight control endeavours. Additional data were collected on usual dietary intake and other aspects of eating behaviour. The association between features of binge eating and BMI was also considered. We hypothesized that psychological distress related to BED and binge eating would be most closely associated with the LOC over eating.

Research Methods and Procedures

Subjects

Participants were recruited between August 2004 and January 2006 in a cross-sectional design. Data were obtained from 3 separate groups. 1) Members of the general community who were not trying to lose weight. These participants responded to flyers placed on notice boards in 2 large metropolitan hospitals and a large Australian university. 2) Persons attending a weight loss support group ("Take Off Weight Naturally" (TOWN), a company consisting of over 130 support groups within Victoria). These participants responded to flyers posted at group meetings. And 3) bariatric surgery candidates who were accepted into the surgical program at The Centre for Bariatric Surgery, The Avenue Hospital, Melbourne, Australia. One stipulation for program inclusion was a BMI greater than 40kg/m^2, or BMI greater than 35kg/m^2 with significant co-morbid disease [186]. These participants were invited to join the study at the time of acceptance into the surgical program.

Subjects were male or female aged between 18 to 70 years, and were excluded if they had undergone previous bariatric surgery. Six hundred and forty eight survey packs were distributed. A total of 431 eligible surveys were returned representing an overall response rate of 66.5%. The study was approved by the Monash University Standing Committee on Ethics in Research involving Humans, and conducted in accordance with the Helsinki Declaration of 1975 as revised in 1983. All subjects were informed regarding the nature of the questionnaires and consented to study involvement.

Anthropometry

Heights and weights reported by the surgery candidates were verified against recent clinic measurements. Demographic data from the community respondents and support group were based on self-report. Within these 2 groups 87% stated they had weighed themselves within the previous month.

Binge Eating Disorder

The Questionnaire on Eating and Weight Patterns – Revised (QEWP-R) was used to screen for binge eating behaviours. Subjects who reported any characteristics of a binge underwent a semi-structured clinical (70%) or phone interview (30%). This interview aimed to accurately determine: 1) the amount consumed during self-reported binge episodes, 2) the experience of LOC, 3) the extent of associated distress, and 4) the frequency of binge eating. A single experienced clinician (Susan Colles) conducted all interviews according to DSM IV criteria [266]. Subjects were provided with fuller descriptions of difficult concepts such as the experience of LOC, that is, feelings that they couldn't stop eating or control what or how much they were eating. To assess the extent of the distress associated with feelings of LOC related to eating, subjects self-rated their emotional disturbance between a score of 1 (no disturbance) to 5 (extreme disturbance). The interviewer was not blinded to recruitment group.

Subjects were subsequently divided into 3 groups:

1) 'Full BED': persons reporting a frequency of $\geq$2 objective binge episodes/week in association with significant psychological distress related to overeating and/or feelings of the LOC, as indicated by a response of 4 or 5 to criterion C1 or C2 (**Table 9.1**). An objective bulimic (binge) episode was defined as a LOC during the consumption of an amount of food considered abnormally large for the circumstances by both the subject and the interviewer [274].

Table 9.1 Binge eating disorder diagnostic criteria and the distribution of central behavioural features within the 'Full BED' and 'Subjective LOC' groups

BED Criterion	Description	Full BED* n=38	Subjective LOC† n=46
A1	Consume a truly large amount of food	100%	0%
A2	Loss of control (LOC) / unable to stop eating	100%	100%
B1	Eating more rapidly than usual	87%	57%
B2	Eating until uncomfortably full	92%	74%
B3	Eating when not physically hungry	82%	76%
B4	Eating alone because embarrassed	76%	52%
B5	Feeling disgusted / depressed / guilty	97%	85%
C1‡	How upset by perceived overeating	4.0 (4-5)	3.5 (3-4)
C2‡	How upset by LOC related to eating	5.0 (4-5)	4.0 (3-4)
D	Objective binges/ week in last 6 months§	3.6±0.8	0
	Average episodes LOC/wk in last 6 months§	3.6±0.8	2.1±1.2
E	Regular compensatory behaviours	No	No
	Commonest time of day episode began	Evening (7 - 10pm)	Afternoon (4 - 7pm)
	How long since last meal or snack§	2.6±2.3 hours	2.2±2.2 hours
	Average length of eating episode§	2.0±2.0 hours	1.1±0.7 hours

*Diagnosis required positive responses to criterion A1, A2, B (3 or more), C (a rating of 4 or 5 for either statement), D (>2days/week), E (absence of compensatory behaviours)
†Diagnosis required a positive response to criterion A2 and the absence of objective bulimic episodes
‡Categorical data, presented as median±IQR.
For items C1 and C2; 1=not at all, 2=slightly, 3=moderately, 4=greatly, 5=extremely
§Data presented as mean±SD

2) 'Subjective Loss of Control' (Subjective LOC): persons experiencing feelings of LOC during subjective bulimic (binge) episodes (Table 9.1). A subjective bulimic episode was defined as a LOC during the consumption of an amount of food considered abnormally large for the circumstances by the subject but not the interviewer [274]. No minimum criterion for subjective binge frequency was set. This group did not include persons reporting objective bulimic episodes.

3) Non-binge eaters (NBE): persons reporting no sense of LOC associated with consumption of either subjectively or objectively large amounts of food.

It should be noted that 40 subjects reported a LOC related to eating but did not meet any subgroup criteria. For example, some subjects reported objective binge episodes at a frequency of less than two per week. Others reported objective or subjective bulimic episodes which were not accompanied by significant psychological distress. These 40 subjects were excluded from binge eating subgroups and were not considered non-binge eaters, but have been included in some subsequent analyses where indicated in the text.

Other Eating Behaviour

The Three Factor Eating Questionnaire (TFEQ) [524] collected information on three dimensions of human eating behaviour; 1) dietary restraint (the amount of intentional restriction of food intake; the intent to diet), 2) disinhibition of eating (the inability to resist social, emotional, or external eating cues), and 3) subjective feelings of hunger.

The Anti-Cancer Council Victoria Food Frequency Questionnaire (ACCVFFQ) [532, 533] was used to assess subject's usual dietary intake. The ACCVFFQ is an optically scannable, semi-quantitative FFQ which lists 74 foods grouped into 5 categories. Respondents choose from 10 food frequency options and are also asked to rate average portion sizes based on a set of food diagrams.

Psychological Health and Quality of Life

The Beck Depression Inventory (BDI) [527] assessed for the presence of symptoms of depressive illness.

The Multidimensional Body Self Relations Questionnaire (MBSRQ) [530] provided a measure of appearance dissatisfaction (AD), or body image distress.

The Medical Outcomes Trust Short Form-36 (SF-36) was used to assess health-related quality of life (QoL) [532, 533]. The SF-36 mental component summary (MCS) score was considered a measure of MHQoL and used as a measure of psychological distress.

Data Analyses

Descriptive statistics were used to express the mean ± SD for all continuous variables. Recruitment groups were considered in an ordinal manner at analysis: community = 1, support group = 2, and those seeking surgery = 3. One-way analyses of variance (ANOVA) with Tukey post-hoc analyses were conducted to assess differences between the recruitment groups and between the three eating subgroups. Chi-square analyses assessed for differences between categorical values, and the Kruskal-Wallis test for ordinal data. The 'Full BED' and 'Subjective LOC' subgroups were compared to groups matched for gender, BMI, age, and 'recruitment origin' from NBE using independent t-tests, chi-square analysis and the Mann-Whitney test as appropriate. Binary logistic regression explored to what extent recruitment origin predicted membership of the binge eating subgroups. Factors entered into the model included 'recruitment origin', gender, BMI and age. Within the total cohort linear regression identified which BED diagnostic criteria were independently predictive of higher BDI and AD scores, a lower SF-36 MCS score, and increasing BMI. Factors entered stepwise into the models included age, gender, 'recruitment origin', BMI, BDI score and AD score as appropriate, and all BED diagnostic criteria as binary, ordinal or continuous variables. Diagnostic criteria that did not contribute to the predictive model were systematically removed. All variables were normally distributed except BDI score which required log transformation. SPSS version 12.0.1 was used for statistical analysis. A p-value of less than 0.05 was considered statistically significant. A p-value of greater than 0.05 and less than 0.10 was considered a statistical trend.

Results

Participant description

The three recruitment groups differed according to intent to lose weight; 1) community respondents not actively seeking weight loss (BMI range 17.7 to 45.5

kg/m²), 2) weight loss support group members (BMI range 21.3 to 60.2 kg/m²) and 3) bariatric surgery candidates (BMI range 31.9 to 66.7kg/m²). As anticipated, demographic, clinical and psychological features varied between groups (**Table 9.2**).

The distribution of binge eating subgroups within the original recruitment groups are also shown in Table 9.2. Rates of 'Full BED' were significantly higher among bariatric surgery candidates compared with the two other recruitment groups. The distribution of those reporting a 'Subjective LOC' did not differ between groups. A binary logistic regression model which included 'recruitment origin', gender, BMI and age showed that membership to the surgical group explained 8% ($p<0.001$) of the variance in the 'Full BED' subgroup.

Characteristics of the Binge Eating Subgroups

The mean demographic, clinical, behavioural and psychological characteristics of the three binge eating subgroups are listed in **Table 9.3**. The BMI range for 'Full BED' was 22.2 to 62.1kg/m²; 20.1 to 66.6kg/m² among 'Subjective LOC' and 17.7 to 66.7kg/m² in NBE. Mean BMI differed between all subgroups. Body mass index was highest in 'Full BED'; the 'Subjective LOC' subgroup had a higher BMI than NBE. There was no difference in gender distribution or age between the three subgroups (shaded columns in Table 9.3). Appearance dissatisfaction and the emotional upset associated with feelings of LOC were highest among 'Full BED' and differed between all groups. Mental health-related QoL was also highest in 'Full BED', but did not differ between 'Subjective LOC' and NBE. The BDI score did not differ significantly between 'Full BED' and 'Subjective LOC', although the median score for 'Full BED' was in the range for 'moderate' depressive symptoms, compared to 'mild' in 'Subjective LOC'.

The 'Full BED' and 'Subjective LOC' groups were matched to comparison groups derived from NBE (Table 9.3). Both groups were carefully matched for recruitment origin, BMI, age and gender. Compared to matched controls 'Full BED' reported significantly higher symptoms of depression, greater AD, and poorer MHQoL. The median BDI depression score for the 'Full BED' group was 20.0, representing moderate depressive symptoms. The median score for the control group was 12.0, which represents 'mild depression'. 'Full BED' reported higher emotional distress

Table 9.2 Descriptive characteristics and comparison of the three original recruitment groups that differed in obesity treatment-seeking status*

	Group 1: General Community Respondents	Group 2: Weight Loss Support Group	Group 3: Bariatric Surgery Candidates	*p*-value
n	158 (36%)	93 (22%)	180 (42%)	
Male/Female	34/124	8/85	39/141	0.018
Mean Age	41.3 ± 13.5^{a}	55.1 ± 12.4^{b}	44.8 ± 11.2^{c}	<0.001
Mean BMI	24.8 ± 5.1^{a}	32.7 ± 7.3^{b}	44.5 ± 6.8^{c}	<0.001
Non-binge Eaters	139 (88.0%)	74 (79.6%)	94 (52.2%)	<0.001
Subjective LOC	12 (7.6%)	10 (10.8%)	24 (13.3%)	0.089
Full BED	3 (1.9%)	3 (3.2%)	32 (17.8%)	<0.001
BDI Score†	$4\ (1\text{-}8)^{a}$	$8\ (5\text{-}12)^{b}$	$15\ (10\text{-}22)^{c}$	<0.001
AD Score	0.14 ± 1.0^{a}	1.0 ± 0.88^{b}	1.8 ± 1.0^{c}	<0.001
Importance of Weight / Shape	2.2 ± 0.78^{a}	2.5 ± 0.69^{b}	3.0 ± 0.87^{c}	<0.001
SF-36 MCS	49.7 ± 6.5^{a}	49.8 ± 6.9^{a}	46.3 ± 8.2^{b}	<0.001
SF-36 PCS	53.2 ± 8.1^{a}	46.2 ± 10.9^{b}	36.9 ± 9.5^{c}	<0.001
Restraint	8.5 ± 4.9^{a}	12.6 ± 3.9^{b}	8.2 ± 3.9^{a}	<0.001
Disinhibition	5.7 ± 3.6^{a}	9.0 ± 4.0^{b}	11.7 ± 3.3^{c}	<0.001
Hunger	4.4 ± 3.2^{a}	6.0 ± 3.4^{b}	8.8 ± 3.6^{c}	<0.001

Data presented as mean±SD except where indicated
Binge eating groups presented as n (% of recruitment group)
*40 subjects did not meet criteria for any binge eating subgroup but have been included in this descriptive analysis
†Data log transformed for analysis and presented as median (IQR)
Statistical analysis using ANOVA with Tukey post-hoc analysis for continuous variables and Chi-square for categorical variables.
^{abc} Means with different superscript letters differ significantly
LOC, loss of control; BED, binge eating disorder; BDI, beck depression inventory; AD, appearance dissatisfaction; MCS, mental health component score; PCS, physical component score

Table 9.3 Comparison between the 3 eating subgroups (shaded columns) **and comparison between eating subgroups and control groups**. In general the 'Full BED' scored highest on psychological and eating-related measures, and 'Non-binge eaters' scored lowest. Comparison between 'Full BED' and 'BED Control Group' showed many psychological and behavioural differences. Comparison between 'Subjective LOC' and 'LOC Control Group' showed no distinctions in markers of psychological distress.

	Full BED	BED Control Group[1]	Subjective LOC	LOC Control Group[1]	Non-binge Eaters
n	38	38	46	46	307
Male/Female	7/31	7/31	7/39	7/39	58/249
Mean Age	42.7±8.2	43.9±8.5	46.8±14.0	47.6±13.8	46.1±14.0
Mean BMI	42.8±8.1[a]	42.6±7.6	37.0±10.4[b]	37.4±10.3	32.5±10.6[c]
Current Weight	118.6±24.3[a]	117.8±20.5	101±27.1[b]	103±27.8	90.3±29.7[c]
BDI Score†	20 (15-31)[a]	12 (6-16)***	12 (6-18)[a]	7.5 (3-15)*	7 (3-13)[b]
AD Score	2.1±0.84[a]	1.4±1.2**	1.5±1.1[b]	0.84±1.3*	0.75±1.2[c]
Emotional upset re: LOC‡	5 (4-5)[a]	3 (2-4)***	3.5 (3-4)[b]	2 (2-3)***	2 (1-3)[c]
SF-36 PCS	37.5±9.7[a]	42.0±11.1	42.9±11.5	45.4±10.5	47.0±11.5[b]
SF-36 MCS	41.9±7.4[a]	47.3±6.1**	47.5±8.1[b]	48.8±7.4	49.3±6.6[b]
Restraint	8.2±3.9	9.0±4.6	9.4±4.8	8.9±4.6	9.5±4.8
Disinhibition	14.3±1.5[a]	9.6±3.7***	12.0±3.0[b]	8.1±3.7***	7.4±4.1[c]
Hunger	11.2±2.6[a]	7.2±3.8***	8.4±3.4[b]	5.6±4.1**	5.5±3.6[c]
Energy (kj)	11693±4634[a]	7710±2413***	8794±3013[b]	7834±3463	7672±2861[c]
CHO (gm)	282±124[a]	187±70.0***	221±73.4[b]	177±67.5**	189±72.5[c]
Fat (gm)	124±56.3[a]	73.5±27.7***	82.9±34.6[b]	77.3±39.8	71.2±31.7[b]
Protein (gm)	129±47.3[a]	92.2±28.3***	100±33.1[b]	99±63.1	91.3±38.7[b]

[1]Control groups are 'Non-binge eaters' matched for age, gender, BMI and recruitment origin
†Data log transformed for analysis and presented as median (IQR), otherwise data presented as mean±SD
‡Categorical data analysed using Mann-Whitney test and presented as median (IQR) for paired groups and Kruskal-Wallis test for the 3 eating subgroups
BED, binge eating disorder; LOC, loss of control; BDI, beck depression inventory; AD, appearance dissatisfaction; MCS, mental component score; PCS, physical component score; CHO, carbohydrate
Statistical analysis between eating subgroups and their matched controls using Independent t-tests for continuous variables, and Chi-square for categorical variables; *$p<0.05$; **$p<0.01$; ***$p<0.001$
Statistical analysis between the 3 eating subgroups using AVOVA with Tukey post-hoc analysis; [abc] Means with different superscript letters differ significantly at or greater than $p<0.05$

related to feelings of LOC. Dietary disinhibition, hunger and usual dietary intake were also increased.

Higher levels of psychological distress were also apparent when the 'Subjective LOC' group were compared to matched controls (Table 9.3). The 'Subjective LOC' group showed higher symptoms of depression, more appearance-related distress, far greater emotional upset related to their perceived LOC related to eating and higher dietary disinhibition and hunger. In order to further explore the emotional upset related to LOC, the 'Subjective LOC' subgroup were divided into those with 'great' or 'extreme' emotional disturbance due to feelings of LOC (score 4 or 5 for criterion C2) and those reporting 'no' to 'moderate' disturbance (score 1, 2 or 3 for criterion C2 in Table 9.1). The group with more severe emotional disturbance related to feelings of LOC (n=23) scored higher on the BDI (Median (IQR); 15 (12-21) versus 7 (6-12); $p<0.001$) and AD scales (1.9$\pm$0.8 versus 1.1$\pm$1.2; $p=0.009$). Mental health-related QoL assessed by the SF-36 MCS was significantly poorer (44.9$\pm$8.6 versus 50.2$\pm$6.8; $p=0.027$).

Psychological Distress and Binge Eating

Linear regression was used to explore which central behavioural features of binge eating (listed in Table 9.1) best predicted an elevated BDI and AD score, and lower SF-36 MCS score (**Table 9.4**). The total cohort of 431 was used in the analysis. This included all subjects in the 3 binge eating subgroups, plus the 40 subjects with characteristics of binge eating who did not meet any subgroup criteria. Without controlling for demographic or psychological factors, higher ratings of emotional distress related to being unable to "stop eating or control what or how much" was consumed (criterion C2) best predicted BDI, AD and SF-36 MCS scores. Higher ratings of emotional distress for criterion C1; "eating more than you think is best for you" also contributed to BDI and AD scores. The SF-36 MCS was associated with the frequency of objective bulimic episodes. Gender, age, BMI and recruitment origin were entered into the regression equation. Higher ratings of emotional distress due to feelings of LOC continued to predict a proportion of variance in all three markers of psychological distress. The frequency of objective bulimic episodes also continued to predict a degree of variance in the SF-36 MCS.

Table 9.4 Central behavioural features of binge eating predicting an elevated BDI or AD score, or low SF-36 MCS score in the total cohort of 431

	BDI Score (n=417)	AD Score (n=418)	SF-36 MCS
	Analysis with no controlling variables		
C2 Upset by feelings of LOC	β=.32, p<0.001	β=.34, p<0.001	β=-.29, p<0.001
C1 Upset by Overeating	β=.18, p=0.034	β=.26, p=0.001	NS
Frequency Objective Binges	NS	NS	β=-.11, p=0.023
Total Variance (r^2)	**22.7%**	**33.6%**	**12.1%**
	Analysis controlling for gender, age, BMI and recruitment origin		
Age	β=.15, p<0.001	NS	β=.15, p=0.001
Female Gender (F=1, M=2)	β= -.08, p=0.05	β=-.18, p<0.001	β=.11, p=0.015
Higher BMI	β=.14, p=0.049	β=.13, p=0.040	NS
Recruitment Origin	β=.22, p=0.003	β=.33, p<0.001	β=-.22, p<0.001
Sub Total of Variance (r^2)	**27.6%**	**41.0%**	**7.1%**
C2 Upset by feelings of LOC	β=.27, p<0.001	β=.29, p<0.001	β=-.26, p<0.001
Frequency Objective Binges	NS	NS	β=-.10, p=0.041
Additional Variance	**4.7%**	**5.5%**	**6.5%**
Total Variance (r^2)	**32.3%**	**46.5%**	**13.6%**

BDI, beck depression inventory; AD, appearance dissatisfaction; MCS, mental component summary score; LOC, loss of control; NS, not significant
Statistical analysis using linear regression

BMI and Binge Eating

Data in this study confirms the strong positive association between BED and BMI. In a similar way, linear regression was used to explore the association between the central behavioural features of binge eating and increasing BMI. Without controlling for demographic and psychological factors, higher ratings of emotional distress for criterion C2, the experience of being unable to "stop eating or control what or how much", predicted most variance in BMI (β=.23; p=0.006). Higher ratings of emotional distress for criterion C1, "eating more than you think is best for you" (β=.17; p=0.030), and criterion C3, eating when not physically hungry (β=.15; p=0.002), also predicted a proportion of variance in BMI (Total Variance (r^2) = 22.5%). Due to the significant co-linearity between BMI and membership of the bariatric surgical group, the subsequent linear regression analysis controlled for gender, age, BDI score and AD score, but not recruitment group. The central behavioural features of binge eating that contributed to the association with BMI were higher ratings of emotional distress for criterion C2 (β=.19; p<0.001) and criterion A1, consumption of a truly large amount of food (β=.16; p<0.001).

Discussion

The primary aim of this study was to explore the relationship between the central behavioural features of binge eating and markers of psychological distress in BED. In support of our hypothesis, the feeling of LOC related to eating was the factor most closely associated with psychological disturbance. Persons who experienced 'great' or 'extreme' emotional disturbance due to feelings of LOC reported significantly higher symptoms of depression, greater dissatisfaction with appearance, and MHQoL. The association between feelings of LOC and psychological disturbance was highest among those meeting full BED diagnostic criteria, but was also elevated in persons reporting subjective bulimic episodes.

Although binge frequency and binge size (objectively or subjectively large) were less strongly associated with psychological distress, after controlling for co-variables, a higher objective binge frequency was associated with poorer MHQoL. Poorer MHQoL also occurred among those with BED when compared to matched controls, and was

positively associated with emotional disturbance related to LOC. This supports the notion that frequent objective bulimic episodes inherent in BED have the potential to negatively influence QoL, independent of the burden of obesity. This relationship may also occur in reverse, where persons with lower psychological well-being are more susceptible to binge eating.

In research and clinical practice the diagnostic features of BED and the robust association with psychological disturbance are increasingly recognized. Yet this is the first empirical evidence to support the greater potential significance of feelings of LOC as an associate of psychological distress in BED. Those who report subjective bulimic episodes or who do not meet the frequency criteria for objective bulimic episodes may still be at elevated risk of psychological disturbance.

As a single group, those experiencing a 'Subjective LOC' reported higher symptoms of depression, more dissatisfaction with appearance, and greater emotional distress related to feelings of LOC than NBE. In particular, those who were emotionally disturbed by their experience were a subgroup with distinctly higher psychological impairment. Persons who engage in subjective bulimic episodes also appear vulnerable to weight gain and obesity. However, in this study the risk of significant psychological dysfunction and extreme obesity was lower in those reporting a 'Subjective LOC' than persons meeting full BED criteria. Nevertheless, individuals who experience repeated feelings of LOC may be still benefit from clinical assessment and intervention. Furthermore, the assessment of eating behaviour and perceived control related to eating may benefit the clinical investigation of psychological disturbance.

In this cross-sectional study those with BED constituted a distinctive group. They were more prevalent among obese bariatric surgery candidates than members of a weight loss support group and community controls not seeking weight loss. Compared to matched controls binge eaters were severely distressed about their recurrent loss of eating control, had more symptoms of depression, higher AD and poorer MHQoL. Their hunger drive was elevated and they reported a reduced ability to resist social, emotional, or external eating cues. The BED group also reported a higher usual energy and macronutrient intake. All of these characteristics would tend to generate weight gain, and have a

negative impact on efforts to control or lose weight. Those with BED may therefore be more inclined to undergo bariatric surgery in an attempt to gain control over their body weight and control over adverse, psychologically disturbing eating behaviours.

Debate persists over the suitability of bariatric surgery in persons with BED [290, 383]. Based on the findings of this study it could be hypothesized that surgically augmented eating control may contribute to the reliable improvement in psychological state that occurs following surgery [68, 72]. However feelings of LOC can continue after surgical intervention [312, 367, 379, 550] even though the ability to eat objectively large amounts of food is altered substantially. The relationship between perceived control over food intake after surgery, and body weight and psychological status is not known.

In this study a number of robust associations emerged however, the cross-sectional design of the study does not allow the determination of causality. Binge eating and feelings of LOC were carefully assessed using the QEWP-R as a screening tool, as previously suggested [508]. The extent of disordered eating was then determined in a semi-structured clinical or phone interview. Although the three original recruitment groups differed, this diversity highlighted the setting in which binge eating is more likely to occur, and the disparity between recruitment groups was statistically controlled.

In conclusion, the feature of binge eating most strongly associated with psychological disturbance was the emotional upset driven by feelings of LOC over eating. Persons who engage in subjective bulimic episodes were also at elevated risk for psychological distress, particularly if their experience of perceived LOC was accompanied by strong feelings of upset and remorse. Clinicians and researchers should be aware of the potential relationship between feelings of LOC related to eating and psychological disturbance. It is also possible that the uncontrolled eating patterns inherent in BED, along with the burden of obesity, may drive individuals with BED towards surgical weight loss intervention.

Future studies could investigate variations in the experience of LOC, and the association with psychological impairment. For example, if long-term binge eaters who accept their inevitable binges are less distressed than persons who attempt failed restraint. Prospective research should also assess the association between pre-surgical BED and

feelings of LOC, and post-surgical control over eating behaviour, weight outcomes and psychological state.

CHAPTER 10: Materials and Methods

Chapters 11 and 12 report on the findings of a prospective observational study. This study examined the direction, extent and correlates of change in a range of eating- and exercise-related behaviours before and 12 months after LAGB. The bariatric surgery candidates outlined in chapter 6 were invited at recruitment to take part in prospective data collection. This methods chapter details the surgical intervention, plus research tools used in chapters 11 and 12 that are in addition to those outlined in chapter 6.

Surgical Intervention

All subjects underwent surgical placement of the Lap-Band® System (Allergan Health, Irvine, CA).

Pre-surgical Evaluation

Prior to any pre-surgical evaluation, candidates were required to attend a "patient information evening" as part of their information gathering process. After this all interested candidates attended a clinical assessment by the surgeon (Paul O'Brien) on one or more occasions. Eligibility criteria for entry into the surgical program have been outlined in chapter 6. Following acceptance, most patients were assessed by a general physician, a respiratory/sleep physician and an endocrinologist. Patients considered at high risk for hepatomegaly, or with severe OSA were also referred to the dietitian for pre-operative weight loss.

The Surgery

The Lap-Band® System (Allergan Health, Irvine, CA) comprises a band of silicone elastomer with an inflatable inner lining that is connected by silicone tubing to an access port placed under the abdominal rectus sheath. In all cases, a single experienced surgeon placed the Lap-Band System along the pars flaccida pathway. The laparoscopically placed band sits approximately 1cm below the gastro-oesophageal junction, creating a small proximal gastric pouch. The volume of saline in the inner balloon can be inflated or deflated via the access port to offer more or less gastric restriction without altering the digestion or absorption of nutrients in any way.

Post-surgical Follow-up

The Centre for Bariatric Surgery employed a standardized peri-operative and follow-up program. A fluid diet was initiated and maintained for the first 2 post-operative weeks, followed by a 3 week progression back to solid foods. At week-5 all patients were seen by a dietitian (Susie Colles). A diet history was used to assess the usual (pre-operative) diet. Personalized advice was then provided to facilitate adherence to the clinic's eating and exercise guidelines. These guidelines are listed in chapter 11. In general, no further dietary intervention was undertaken by the dietitian throughout the remainder of the year.

The basis of post-operative care at The Centre for Bariatric Surgery was on-going physician review and volume adjustment. Volume adjustment was a clinical decision made in consultation with the patient, and determined according to the patient's weight status, their sense of satiety and satiation, and difficulty or ease of eating. In most instances volume adjustments were performed by the consulting physician without the assistance of radiological imaging. Patients were encouraged to attend the clinic at least monthly for the first 6 post-surgical months. During the next 6 months, the frequency remained constant, or reduced to bi-monthly or quarterly, as appropriate. Beyond this, attendance at least once per year was strongly recommended.

Assessment of Eating-related Behaviours

The following factors were assessed in the bariatric surgery group in addition to the measures described in chapter 6. At 12 post-surgical months, all eligible subjects were notified by phone prior to sending the follow-up surveys, and then contacted by phone to prompt survey completion between one and three times.

Anti-Cancer Council Victoria Food Frequency Questionnaire

The ACCVFFQ was used to assess habitual dietary intake at baseline, and also 4 and 12 months after LAGB. In addition to mean energy and macronutrient values, foods were analysed according to "solid", "soft" and "liquid" textures to compare the mean percentage change in food consistency. Based on the definition of Busetto et al. [289], solid food was defined as "all food requiring chewing before swallowing", soft food as

"all solid foods and viscous liquids not requiring mastication before swallowing" and liquid food as "all caloried liquids".

No validation study has assessed the suitability or reliability of nutrient intake assessed by FFQ following bariatric surgery. For this reason, a subgroup of subjects was invited to complete a 4-day food record at the time the 4-month ACCVFFQ was completed. Written and verbal instruction for the food diary included:

1. Record ALL that you eat and drink from the time you wake until the time you go to sleep.
2. Complete the diary as you eat and drink through out the day.
3. Write down the type of food, and where possible the brand name – try to be as descriptive as possible.
4. Foods were to be recorded by weight or by household measure
5. Where possible, weigh food portions before consuming, but don't forget to subtract any of the portion that is uneaten.
6. For each entry subjects recorded the time, place, description of the food, cooking method, and weight or household measure.

An aim to compare 30% (n=39) of subjects on both measures was set. However of the 40 4-day food records distributed, a total of 18 paired food records and FFQs were returned (14%). The 4-day food diaries were manually analyzed using Foodworks (Xyris Software, Australia Pty Ltd) which derives its nutrient intake values from the Australian NUTTAB95 nutrient composition database [516]. This same nutrient database was used to analyse the ACCVFFQ. The two measures were compared with regards to total energy and macronutrient composition. All data were normally distributed. **Table 10.1** compares the values calculated for the ACCVFFQ and 4-day food record using Pearson correlation coefficients. All values were significantly correlated.

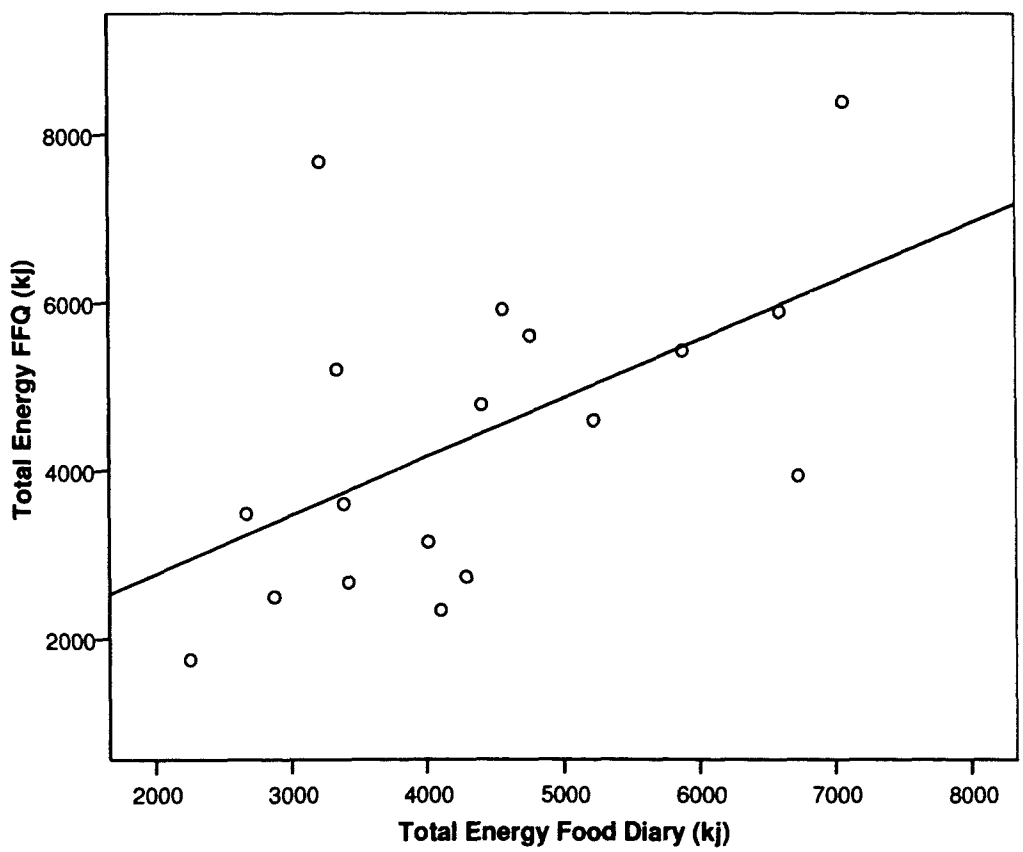
Table 10.1 Comparison of energy and nutrient values derived from the Anti-Cancer Council VictoriaFood Frequency Questionnaire and a 4-day food record at 4 months after LAGB[1]

Nutrient	Mean ± SD	Range	Correlation; *p*-value
Energy – FFQ	4423 ±1853 kj	1749 – 8383 kj	*r* = .540;
Energy – 4DFR	4383 ± 1436 kj	2257 – 7073 kj	0.021
Total Fat – FFQ	38.1 ± 20.9 gm	9.2 – 81.1 gm	*r* = .504;
Total Fat – 4DFR	38.1 ± 18.2 gm	11.3 – 74.0 gm	0.033
Total Protein – FFQ	59.2 ± 29.9 gm	29.4 – 100 gm	*r* = .494;
Total Protein – 4DFR	61.7 ± 15.3 gm	40.1 – 96.0 gm	0.05
Total CHO – FFQ	112.1 ± 48.2 gm	54.8 – 221 gm	*r* = .607;
Total CHO – 4DFR	110.2 ± 39.0 gm	46.4 – 195 gm	0.008

[1] *n*=18 paired responses
FFQ, food frequency questionnaire; 4DFR, 4-day food record; CHO, carbohydrate
Statistical analysis using Pearson's correlations

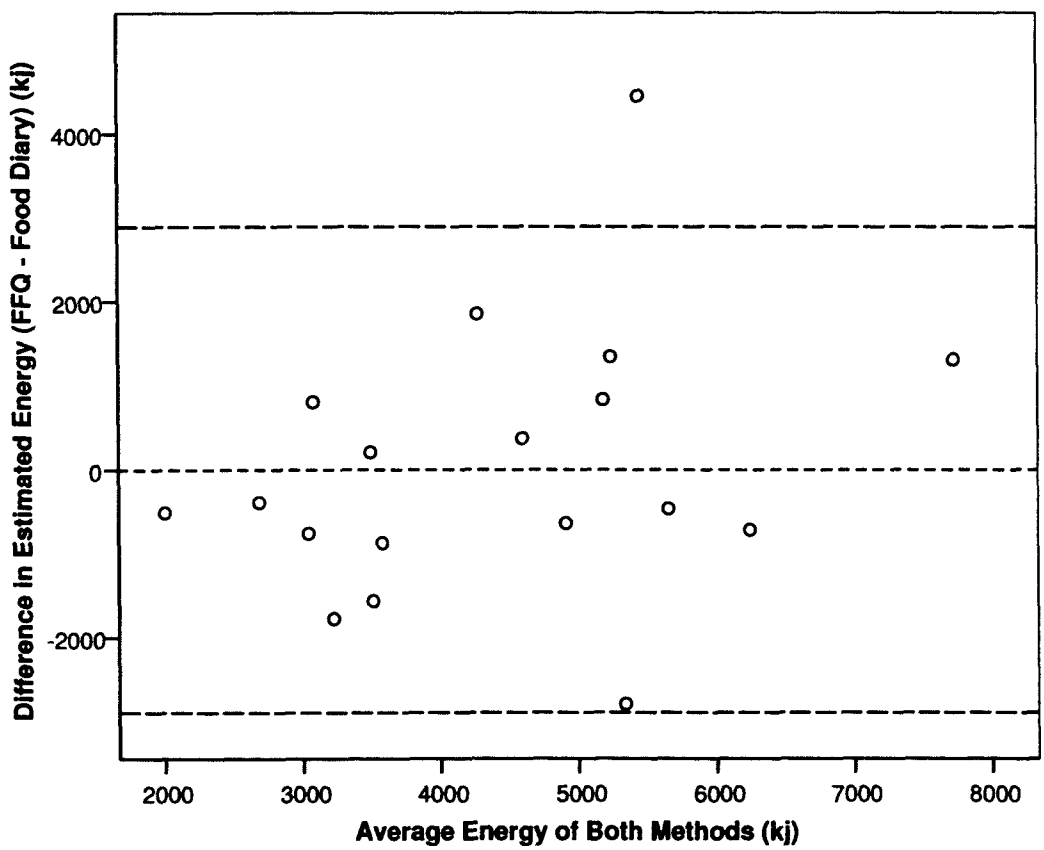
The positive correlation between estimates for total energy intake derived by both methods is graphed in **Figure 10.1**. Mean values showed a correlation of r = .540 (p=0.021).

Figure 10.1 Estimates for total energy intakes derived from the Anti Cancer Council Food Frequency Questionnaire and the 4-day food diary



To further assess the level of agreement, paired estimates for total energy intake were analysed according to the recommendations of Bland and Altman [468, 469]. This analysis revealed a mean bias of 40.5 kj (limits of agreement ± 3238), which indicates very good agreement between the two methods. ACCVFFQ-derived estimates tending slightly higher, however the difference was not statistically significant from zero (one-sample t-test, p=.92). **Figure 10.2** shows the scatter of values. All but one value fell within the limits of agreement. The scatter of values "fans out" slightly as energy estimates increase, which suggests that the residuals may increase as the mean values increase.

Figure 10.2 Limits of agreement for the two estimates of total energy intake assessed using the methods of Bland and Altman



Grazing

A pattern of "grazing" was measured primarily to investigate the association between eating small amounts of food over continuous periods, and post-surgical energy intakes and weight loss outcomes. The definition of "grazing" used in this thesis was based on that reported by Saunders [300, 379]. Grazing was defined as the consumption of "smaller amounts of food continuously over an extended period of time, eating more than you think is best for you". At baseline and 12 months after LAGB subjects were asked if they had often engaged in a grazing pattern of eating during the previous 6 months. Grazing was confirmed by interview.

Non-hungry Eating

For the purpose of this thesis, "non-hungry" eating has been described as eating in the absence of physiological hunger. At 12 months after LAGB a self-made questionnaire asked a series of questions related to non-hungry eating. Subjects were asked:

1. Do you know the difference between "physical" and "emotional" hunger? (Yes/No)
2. Do you know when you are full, or experience a feeling of fullness? (Yes/No)

   And, if so, are there times when you continue to eat anyway? (Yes/No)
3. Do you experience cravings for certain foods? (Yes/No)

   And if so, which foods? (Extended response)
4. Are there any situations where, or reasons why you are more likely to eat types of foods or quantities of food that you know is not best for you? (Yes/No)
   - i. When I feel anxious
   - ii. When I feel tired
   - iii. When I feel bored
   - iv. When I feel stressed
   - v. When I feel angry
   - vi. When I feel depressed/upset
   - vii. Out of habit
   - viii. When socialising
   - ix. Other

Factors 4.i to 4.vi were considered emotional triggers to eating. An affirmative response to one or more of these variables was regarded as a marker of eating in response to emotional cues.

Other Eating-Related Factors

At 4 and 12 post-surgical months subjects were asked how many times a day they ate, considering all meals and snacks a separate "eating episode".

At 12 month follow-up subjects were asked:

1. Do you notice any of your old eating habits, that is, patterns of eating present before your Lap-band placement, returning? (Yes/No)
2. Do you fear/feel anxious about achieving a poor weight loss, or weight regain? (Yes/No)

Gastrointestinal Symptoms

The frequency of gastrointestinal symptoms was assessed at 4 and 12 post-surgical months. Based on the definition of Busetto et al. [289], vomiting was defined as disgorging the contents of the stomach or oesophagus through the mouth. Obstruction was defined as a temporarily blockage of the Lap-band outlet.

Subjects indicated either:

1) no symptoms in the last month,
2) between 1 to 5 episodes in the last month,
3) between 5 to 20 episodes in the last month, or
4) more than 20 episodes in the last month.

At analysis the reported frequency of both symptoms were combined.

Assessment of Exercise-related Behaviours

Physical activity patterns before and 12 months after surgery were measured using a self-report questionnaire and a 7-day pedometer diary. Completion of the pedometer diary was encouraged but not mandatory. The type and number of barriers to participation in physical activity was also assessed. The surveys used to collect this data are listed in **Appendix 1b**.

The physical component summary (PCS) score derived from the Medical Outcomes Trust Short Form-36 (SF-36) [532] was outlined in chapter 6. The SF-36 PCS was also used as a measure of physical ability and well-being related to self-assessed physical capability, the presence/absence of bodily pain, and feelings of health and vitality. This questionnaire is listed in Appendix 1a.

Baecke Physical Activity Questionnaire

The Baecke Physical Activity Questionnaire is a popular 16-item survey that assesses habitual physical activity over the previous 12 months [551]. Subjects respond to a 5-point scale with descriptors ranging from "never" (1 point) to "always" (5 points). A separate score, or "index", is calculated for work, sport and leisure-time physical activity, as well as a total score.

Validity studies have shown a strong correlation between the total Baecke score and physical activity levels assessed by doubly labelled water ($r = 0.69$) [552]. Three month reliabilities have been measured at $r = 0.88$ for work, $r = 0.81$ for sport, and $r = 0.74$ for leisure time indices [551]. Total and leisure time scores have also shown a strong relation to light intensity leisure activity measured by a 4-week physical activity history [553]. Jacobs et al. noted the ability of the Baecke Questionnaire to accurately analyse light activities, which is of particular importance among obese populations [553].

Seven-day Pedometer Diary

The pedometer is a basic motion sensor used to measure objective changes in ambulatory activities [554]. Pedometers can detect variations and subtle differences in patterns of sporadic and inconsistent physical activity that have not been revealed by questionnaire [555]. Convergent validity has been demonstrated in cross-sectional studies where daily pedometer values have been positively associated with time spent in leisure time activity [556] and physical fitness level [557], and negatively associated with percentage overweight [132]. It should however be noted that errors in step count have been observed at slower walking speeds [558, 559], and elevated but admissible error has been observed in persons over BMI 30 kg/m^2 [560]. Accumulation of 10,000 steps per day is recommended to assist with health-related parameters [561].

For the purpose of this thesis, subjects were provided with a pedometer (Sportline 330, Manufactured by Sportline Inc., Hazleton, PA 18202) and asked to maintain a 7-day pedometer diary before, and 12 months after LAGB. Participants were instructed to securely fix the pedometer at the waist over the hip above their dominant leg. Step counts were to be recorded as soon as they were dressed each morning until last thing at night for 7 consecutive days. Participants were told to maintain their usual leisure time or sporting activities during this week.

Barriers to Physical Activity

A self-made questionnaire collected information on 11 potential barriers to regular physical activity. Options were listed and respondents could choose more than one alternative including:

1) Fear of injuring myself (Yes/No)
2) I don't enjoy exercising (Yes/No)
3) I don't want to exercise (Yes/No)
4) I have ankle/knee/back pain (Yes/No)
5) Lack of time (Yes/No)
6) Lack of confidence (Yes/No)
7) Poor weather/too dark/too hot or cold (Yes/No)
8) I feel physically unable to exercise (Yes/No)
9) Too expensive (Yes/No)
10) I don't have access to facilities (Yes/No)
11) I'm too tired (Yes/No)
12) Other (Extended response)

Data Management

Accumulated data were transferred onto the specially designed database in the Microsoft Access® program, as described in chapter 3. Statistical methods used are detailed within each chapter.

Declaration for Thesis Chapter 11

Declaration by candidate

In the case of Chapter 11, this work represents a manuscript that has been accepted for publication in *Obesity Surgery*, 2007. The nature and extent of my contribution to the work was the following:

Nature of contribution	Extent of contribution (%)
I was responsible for study design, all data collection and tabulation, analysis of data and writing the manuscript.	>85%

The following co-authors contributed to the work.

Name	Nature of contribution	Extent of contribution (%) for student co-authors only
Associate Professor John Dixon	Assisted with the study design, analysis of data, and writing of the manuscript.	
Professor Paul O'Brien	Assisted with subject recruitment and writing of the manuscript.	

Candidate's Signature [redacted] **Date** 5/12/07

Declaration by co-authors

The undersigned hereby certify that:

(1) the above declaration correctly reflects the nature and extent of the candidate's contribution to this work, and the nature of the contribution of each of the co-authors.
(2) they meet the criteria for authorship in that they have participated in the conception, execution, or interpretation, of at least that part of the publication in their field of expertise;
(3) they take public responsibility for their part of the publication, except for the responsible author who accepts overall responsibility for the publication;
(4) there are no other authors of the publication according to these criteria;
(5) potential conflicts of interest have been disclosed to (a) granting bodies, (b) the editor or publisher of journals or other publications, and (c) the head of the responsible academic unit; and
(6) the original data are stored at the following location(s) and will be held for at least five years from the date indicated:

Location(s)	The Centre for Obesity Research and Education

Signature 1	Associate Professor John D [redacted]	**Date** 6/12/07
Signature 2	Professor Paul O'Brien [redacted]	5/12/07

CHAPTER 11: Hunger control and regular physical activity facilitate weight loss after laparoscopic adjustable gastric banding

Abstract

Background: Bariatric surgery facilitates substantial and durable weight loss however outcomes vary. In addition to physiological and technical factors, weight loss efficacy is dependent on modification of behaviour to maintain a long-term change in energy balance. This study aimed to assess the extent and nature of change in energy intake and physical activity, and identify factors associated with percentage weight loss (%WL) 12 months after LAGB.

Methods: 129 bariatric surgery candidates (26males/103females, mean age 45.2±11.5, mean BMI 44.3±6.8, range 31.9 to 66.7) completed the study. Data were collected at baseline and 12 months. Validated questionnaires included the Anti-Cancer Council Victoria Food Frequency Questionnaire, Three Factor Eating Questionnaire, SF-36, Baecke Physical Activity Questionnaire and Beck Depression Inventory. Symptoms of "non-hungry eating", "emotional eating" and "grazing" were also assessed.

Results: Mean %WL was 20.8±8.5% and %EWL was 50.0±20.7 ($p<0.001$). Mean total energy intake reduced from 9991±3986kj to 4077±1493kj ($p<0.001$). Average leisure time and sport-related physical activity scores increased (both $p<0.001$). Regression analysis identified baseline BMI ($\beta=0.241$; $p=0.002$), subjective hunger ($\beta=-0.275$; $p=0.001$), physical function ($\beta=0.309$; $p<0.001$) and leisure time physical activity ($\beta=0.213$; $p=0.010$) as independent predictors of %WL; explaining 33.7% of variance in weight loss outcome. Higher "non-hungry eating" and symptoms of depression were also related to poorer %WL.

Conclusion: LAGB affects marked behaviour change and facilitates substantial weight loss in the first 12 months. However, variations in adopted behaviours can affect energy balance and weight loss success. Achievement and maintenance of favourable behaviours should be an important consideration during on-going post-surgical review and counselling. Management should include adequate band adjustment to control

physical hunger, optimization of physical function and activity, and reinforcement of strategies to reduce energy intake.

Introduction

The utilization of LAGB is increasing throughout the world in response to escalating rates of class II and III obesity. Laparoscopic adjustable gastric banding facilitates substantial and durable weight loss however outcomes vary. Pre-surgical factors predicting poorer weight reduction include increasing age, higher baseline BMI, insulin resistance and low self-reported physical ability [448]. Mechanical factors such as port leakage have predicted weight regain following LAGB [295]. In addition to physiological and technical factors, the efficacy of bariatric surgery is dependent on modification of behaviour to bring about a long-term change in energy balance [205].

Gastric restrictive surgery facilitates a reliable reduction in energy intake within the first post-operative year [289, 420]. Yet the excessive consumption of high energy liquids and soft foods following vertical banded gastroplasty has been associated with inferior weight outcomes [201, 202]. An increase in liquid calories and decrease in solid foods has been observed after LAGB [289], but the association with weight outcome is unexplored. A preference for sweets does not result in inferior weight loss [562]. Poorer 12 month weight outcomes have however, been associated with greater subjective hunger and dietary disinhibition [287]. High levels of depression [68] and eating in response to emotional cues [445] are also found among bariatric surgery candidates. While pre-operative depression has not predicted poorer weight loss at one year [448], the association between post-surgical mood, eating behaviour and weight outcome is unknown. A "grazing" pattern of eating has also been observed after surgery [379] but the prevalence and significance of this eating behaviour requires elucidation. Following surgery physical activity levels appear to increase and contribute positively to lean tissue mass [177]. Yet objective measures of the change in physical activity have not been undertaken, and the nature of any association with other post-surgical behaviours is unexplored.

The identification of behavioural factors associated positively and negatively with post-surgical weight loss may help us modify current lifestyle guidelines, and identify patients who need more intensive interventional therapy. This study aimed to explore

the nature and extent of change in 1) patterns of dietary intake and 2) patterns of physical activity 12 months after LAGB, and associations with surgical outcome. Assessment of dietary patterns included prospective measurement of energy and macronutrient intake, food consistency and eating behaviour. Self-reported physical activity, physical functioning and pedometer step-counts before and after surgery were assessed. Factors most closely associated with the percentage of weight lost were of primary interest.

Methods

Subjects

Consecutive, eligible subjects were recruited upon acceptance into the bariatric surgery program at The Avenue Hospital, Melbourne, Australia, prior to Lap-Band® System (Allergan Health, Irvine, CA, USA) placement. Eligible individuals were male or female aged between 18 to 65 years, with no previous history of bariatric surgery. All subjects provided written informed consent before taking part in the study, which was approved by the Monash University Standing Committee on Ethics in Research involving Humans.

During pre and post-surgical appointments subjects were provided with standard advice regarding recommended post-operative eating behaviours and exercise patterns. The topics of education and discussion which were covered extensively and repeatedly included: 1) eat 3 small meals per day, 2) eat only good, solid food, 3) eat slowly, stop when comfortable, 4) avoid eating between meals, 5) take no liquids with the meal, 6) consume only liquids which contain zero calories, 7) exercise for at least 30 minutes per day, 8) be active throughout the day, 9) aim for 10,000 (pedometer-recorded) steps per day, 10) take a daily multivitamin and mineral supplement.

Study Design

The study was of a prospective, observational design. Baseline and follow-up data at 4 and 12 post-surgical months were primarily obtained via validated self-report questionnaire.

Anthropometry

Weight was recorded at baseline, 4 and 12 months to the nearest 0.1kg using the electronic Tanita Wedderburn TBF-305 (Lake Worth, FL 33467) in light clothing without shoes. Height was determined at baseline to the nearest millimetre using a wall-mounted stadiometer. The main outcome measure was the percentage of weight lost at 12 months after LAGB placement (%WL). The percentage of excess weight loss (%EWL) has also been reported. The %EWL was calculated by dividing weight loss in kilograms by excess weight (the initial weight minus weight at BMI 25), and multiplying this figure by 100.

Assessment of Eating Behaviour

The Anti-Cancer Council Victoria Food Frequency Questionnaire (ACCVFFQ) [514] was used to record subject's usual dietary intake at baseline, 4 months and 12 months. The ACCVFFQ is an optically scannable, semi-quantitative assessment tool which lists 74 foods with 10 frequency options. To control for extreme values, the top and bottom 2% of usual energy intakes for the baseline, 4 month and 12 month questionnaires were excluded from all statistical analyses. To compare different consistencies, foods were divided according to "solid", "soft" and "liquid" textures. Based on the definition of Busetto et al. [289], solid food was defined as "all food requiring chewing before swallowing", soft food as "all solid foods and viscous liquids not requiring mastication before swallowing" and liquid food as "all caloried liquids".

The Three Factor Eating Questionnaire (TFEQ) [524] assessed dietary restraint, disinhibition and hunger at baseline and 12 months. A self-made questionnaire collected additional data on eating behaviour. At baseline, 4 months and 12 months subjects were asked how many times a day they ate, considering all meals and snacks as a separate "eating episode". At 12 months a series of questions also obtained information on subjective feelings of fullness, the return of "old eating habits" and situations or emotions considered by the subject to stimulate eating or overeating.

Assessment of Depression

The Beck Depression Inventory (BDI) [527] assessed symptoms of depressive illness at baseline and 12 months. A score of 0-9 was considered "normal"; 10-16 "mild depression"; 17-29 "moderate depression"; and 30-63 "severe depression" [528].

Assessment of Physical Activity

The Physical Component Summary (PCS) score of the Medical Outcomes Trust Short Form-36 (SF-36) [532] was used as a measure of well-being related to physical function. This health summary scale was adjusted to achieve a community mean value of 50 with a standard deviation of 10. The Baecke Physical Activity Questionnaire assessed habitual physical activity over the previous year at baseline and 12 months [551]. Separate work, sport and leisure index scores were calculated, plus a total score. A self-made questionnaire also assessed the presence of 11 possible barriers to regular physical activity. Participants were encouraged to record pedometer step counts (Sportline 330, Manufactured by Sportline Inc., Hazleton, PA 18202) at baseline and 12 months in a 7-day pedometer diary. Maintenance of a pedometer diary was not mandatory.

Data Analyses

All continuous variables were normally distributed except the BDI score at baseline and 12 months and the TFEQ hunger score at 12 months, which required log transformation. Descriptive statistics were used to express the mean $\pm$ SD for continuous variables and median (IQR) for categorical variables and data not normally distributed. Paired student's t-tests compared continuous variables between baseline, 4 months and 12 months as appropriate. Independent samples t-tests compared continuous variables divided into respondents and non-respondents, quartiles and eating categories. The Chi square test assessed for differences between categorical variables. Simple bivariate correlations assessed the strength of the association between two continuous behavioural variables. Mann-Whitney U tests assessed for differences between categorical and ordinal data. Linear regression, using forwards and backwards modelling, assessed for predictors %WL. Factors were grouped into 1) age, gender, baseline BMI and insulin resistance (controlling variables), 2) energy and macronutrient intake, 3) eating behaviour, 4) psychopathology and 5) physical activity-related variables. SPSS version

12.0.1 was used for statistical analysis. A p-value of less than 0.05 was considered statistically significant. A p-value of greater than 0.05 and less than 0.10 was considered a statistical trend.

Results

Subject Characteristics

Of 180 baseline respondents, 6 subjects did not undergo LAGB and 1 subject with a past history of heart disease died of a related cardiac illness 3 months after surgery. At 12 months, 129 surveys from a possible 173 subjects were returned; a response rate of 75%. Non-respondents had achieved a lower %WL, 16.0±8.9% versus 20.8±8.5% (p=0.002) and had attended less clinic appointments during their first post-operative year; median (IQR) 10 (8-12) versus 12 (9-14) (p=0.015). Gender and age distribution did not differ. The median (IQR) number of band adjustments was also similar at 7 (5-9) in non-respondents and 7 (5-10) in study participants. In the combined group of respondents and non-respondents (n=173) there was a positive correlation between the annual number of clinic visits and %WL, r=0.16, p=0.045. The number of band adjustments was strongly associated with clinic visits, r=0.76, p<0.001, but did not correlate with %WL. In the first year after surgery 85.5% of the original cohort (n=148 of 173) achieved greater than a 10%WL.

In the final group of 129 anterior prolapse of the band occurred in 2 subjects (1.6%) and port-related problems in 3 subjects (2.4%) during the first year. Once diagnosed, all fluid was removed from the Lap-band system. Fluid removal commonly results in increased hunger, and some weight regain can be expected prior to re-operation. Revisional surgery was undertaken in all cases.

Tables 11.1 and 11.2 list a range of demographic, anthropometric and behavioural characteristics at baseline and 12 months after LAGB. Body weight reduced significantly between baseline and 4 month, and 4 month and 12 month follow-up. This

Table 11.1 Demographic, anthropometric and eating-related traits at baseline, 4 and 12 months after LAGB

	Baseline n=129	4 months after LAGB n=93 (72%)	12 months after LAGB n=129
Mean Age (years)	45.2±11.5	--	--
Male/Female	26/103	8/85	26/103
Mean Weight (kg)	122.2±20.5	105.7±17.1***	96.5±18.2***
Mean BMI (kg/m²)	44.3±6.8	38.3±5.9***	35.0±6.0***
Mean %WL	--	13.3±5.1%	20.8±8.5%***
Mean %EWL	--	32.2±13.0	50.0±20.7***
Total Energy (kj)[1]	9991±3986	4104±1504***	4077±1493
Total Fat (gm)	98.5±42.6	34.1±15.9***	34.6±16.1
Total Protein (gm)	113.8±40.6	54.0±19.7***	52.2±18.7
Total CHO (gm)	233.0±93.4	100.4±39.4***	98.5±40.6
% Energy from Fat	36.6±5.3	30.1±6.2***	30.8±6.8
% Energy from Protein	20.1±3.4	22.7±3.9***	22.1±4.3
% Energy from CHO	37.9±5.6	39.6±7.1*	38.8±7.3
% Solid Foods	56.7±11.6	44.6±11.8***	39.7±13.8**
% Soft Foods	12.5±5.9	12.7±7.0	13.0±7.9
% Liquid Foods	30.9±13.2	42.7±14.0***	47.3±16.1**
No. of Eating Episodes	5.0±3.0	4.0±3.0***	4.0±3.0
TFEQ Restraint	8.3±3.9	--	13.0±4.2***
TFEQ Disinhibition	11.5±3.4	--	6.2±3.9***
TFEQ Hunger[2]	9 (6-12)	--	2 (1-5)***
BDI Depression Score[2]	15 (10-21)	--	7 (4-11)***

Continuous variables presented as mean±SD except where indicated

[1]The highest and lowest 2% of total reported energy intake have been excluded from analysis

Dietary comparisons based on 85 subjects who completed a questionnaire at baseline, 4 and 12 months

[2] Data log transformed for analysis and presented as median (quartile range)

BMI, body mass index; %WL, percentage weight loss; %EWL, percentage excess weight loss; TFEQ, Three factor eating questionnaire; BDI, Beck depression inventory

Student's t-tests assessed for differences between baseline and 4 months, 4 months and 12 months and baseline and 12 months as appropriate

Wilcoxin Signed Ranks test assessed for differences between categorical data at baseline and 4 months and 4 months and 12 months

*$p<0.05$, **$p<0.01$, *** $p<0.001$

Table 11.2 Change in physical function and activity levels during the first post-operative year

	Baseline	12 months after LAGB
SF-36 PCS Score	37.2±10.0	49.2±9.8***
Pedometer Step Count [1]	6061±2740	8716±5348**
Highest Day's Step-count [1]	8571±3511	11312±4438***
Lowest Day's Step-count [1]	3926±2246	5148±2772**
Baecke Work Index Score	2.49±0.64	2.46±0.57
Baecke Sport Index Score	1.69±0.50	2.11±0.61***
Baecke Leisure Index Score	2.11±0.60	2.74±0.66***
Beacke Total Score	6.30±1.17	7.32±1.27***
Total Barriers to Exercise	3.44±1.75	2.27±0.64***

Continuous variables presented as mean±SD
n=129 except where indicated
[1]n=48
PCS, Physical component summary
Student's t-tests assessed for differences between scores at baseline and 12 months
**p<0.01, *** p<0.001

corresponded to a mean reduction in BMI of 6.0±2.8kg/m² and 9.3±4.5kg/m², respectively. Marked change across a range of eating- and exercise-related variables was also evident.

Change in Energy, Macronutrient Intake, Food Consistency & Associated Factors

Average energy and macronutrient intakes as measured by the CCVFFQ are listed in Table 11.1. Mean total energy intake decreased significantly from 9991kj at baseline to 4104kj at 4 months. At 12 months the average energy intake of 4077kj did not differ from the 4-month value. By 4 post-surgical months the percentage of energy derived from fat had reduced significantly, and the proportion of energy from protein and carbohydrate (CHO) increased. Total energy intake at 12 months was positively associated with the percentage of energy derived from fat, r=0.19, p=0.035, and negatively associated with the percentage of energy derived from protein, r=-0.25, p=0.006. Total energy intake was not associated with the proportion of dietary CHO, r=-0.08, p=0.37.

Food choice also altered following surgery. The proportion of total energy derived from solid foods reduced significantly between baseline and 4 months, and reduced further by 12 months (Table 11.1). Equally, the proportion of total energy intake derived from liquid foods increased between baseline and 4 months, and continued to increase to12 months. The mean percentage of soft foods did not change. A higher proportion of protein (p=0.002) and CHO (p=0.048) was consumed by those in the highest quartile of solid food intake compared to the lowest.

At 12 months, total energy intake was positively correlated with hunger, r=0.29, p=0.001 and disinhibition scores, r=.229, p=0.011 and symptoms of depression, r=0.27, p=0.003. Total energy intake was inversely associated with dietary restraint, r=-0.23, p=0.013, SF-36 PCS score, r=-0.17, p=0.05 and Baecke Leisure Index Score, r=-0.22, p=0.014. Eating in response to anxiety (p=0.050) and fatigue (p=0.028) was related to a higher energy intake, and those conscious of the frequent recurrence of "old eating patterns" (n=35) also consumed more energy than those who reported no difficulty maintaining behavioural change (p=0.009).

Change in Physical Activity Levels and Associated Factors

Throughout the study period voluntary activity assessed by the Baecke Work Index remained constant. Baecke Leisure and Sport Index scores increased, contributing to an improvement in Baecke Total score (Table 11.2). At 12 months the Baecke Leisure Index score was positively correlated with %WL (see below) and dietary restraint, r=0.20, p=0.022, and negatively related to total energy intake, dietary disinhibition, r=-0.28, p=0.002, hunger, r=-0.29, p=0.001 and the number of perceived barriers to exercise, r=-0.22, p=0.015. Those reporting the return of "old eating habits" (p=0.003) and overeating due to stress (p=0.05) also reported a lower Leisure Index score. A trend toward lower Leisure Index scores was also noted in those who ate when depressed/upset (p=0.072) and anxious (p=0.072).

The mean SF-36 PCS score increased significantly in the first 12 months following LAGB (Table 11.2). The SF-36 PCS was positively associated with the Baecke Total score, r=0.23, p=0.008 and Baecke Leisure Index score, r=0.20, p=0.024. Inverse relationships were seen between the SF-36 PCS and dietary disinhibition, r=-0.21, p=0.016 and hunger, r=-0.20, p=0.026, and BDI score, r=-0.33, p<0.001.

Paired 7-day pedometer diaries were returned by 48 subjects (37.2%). In this group, daily step-counts rose by 2655 steps to an average of 8716 (Table 11.2). After surgery, walking further on a given day was positively associated with the Baecke Leisure Index score, r=0.34, p=0.016. It is possible that those who failed to return the paired pedometer diaries were more likely to walk less regularly or had not significantly altered their physical activity patterns from baseline. However, the correlation between poorer %WL and lower daily step counts still suggests that regular walking is associated with better weight outcomes.

Factors Associated with %WL

Five subjects (3.9%) required re-operation in the first year for either band prolapse or port-related problems. These subjects lost significantly less weight (10.1±5.7% versus 21.1±8.4%) than the remainder of the cohort (p=0.010).

At 12 months, total energy intake was negatively correlated with %WL, r=-0.23, p=0.009. Those in the highest quartile for total energy intake, consuming a reported

5898±1009kj/day achieved a significantly poorer %WL than those in lowest quartile, consuming a reported 2334±304kj/day (p=0.005). The highest quartile for total fat intake, consuming >41.1gm/day, also lost a lower %WL than those in the lowest quartile, consuming <22.9gm/day (p=0.029). With regards to food consistency, a trend toward poorer weight loss was apparent only in those who consumed more soft foods, r=-0.16, p=0.075.

Not surprisingly, there was a high overlap between behaviours influencing %WL and total energy intake. The %WL was positively associated with dietary restraint, r=0.22, p=0.014, SF-36 PCS, r=0.38, p<0.001 and Baecke Leisure Index score, r=0.32, p<0.001. Inverse associations were noted for disinhibition, r=-0.39, p<0.001 and hunger scores, r=-0.43, p<0.001, eating in response to anxiety (p=0.006), the frequent recurrence of "old eating patterns" (p<0.001) and symptoms of depression (p=0.005). The magnitude of change in total energy intake, r=-0.22, p=0.020, TFEQ hunger, r=-0.30, p<0.001, disinhibition, r=-0.36, p<0.001, and dietary restraint, r=0.20, p=0.025, SF-36 PCS, r=-0.33, p<0.001, Baecke Leisure Index Score, r=0.33, p<0.001, Baecke Total Score, r=0.21, p=0.020 and BDI score, r=-0.22, p=0.016 was also related to %WL. Less weight loss was also recorded in those who admitted eating despite feeling full (61%) (p=0.018) and eating when depressed/upset (p=0.008), and in those who recorded a lower minimum pedometer step-count, r=0.30, p=0.032, and higher number of barriers to physical activity, r=-0.20, p=0.021. Subjects who ate four or more times per day (n=43) lost a similar amount of weight to those who ate one to three times/day (n=86). There was no statistically significant correlation between the %WL and band fill volume for either the 10cm or VG Lap-Band® system.

Behavioural Predictors of %WL 12 Months Following LAGB

A linear regression model identified four independent predictors a greater %WL 12 months after LAGB. Higher baseline BMI, β=0.241, p=0.002, lower 12 month hunger score, β=-0.275, p=0.001, higher 12 month SF-36 PCS, β=0.309, p<0.001 and higher 12 month Baecke Leisure Index score, β=0.213, p=0.010 predicted 33.7% of total variance in %WL.

Discussion

This study measured a range of eating and exercise-related behaviours before and 12 months after LAGB. The nature and extent of behavioural change and the association with weight loss were the main focus. Over the study period mean BMI and %WL reduced significantly. This marked change in weight was accompanied by a sizable reduction in energy intake, comparable to that observed by Busetto et al. using 24-hour recall [289]. Significant increases in physical functioning and activity level were also reported, suggesting a favourable change in energy balance via reduced intake and increased expenditure. Significant improvements in a number of eating-related behaviours and a mood-related measure were also evident. However, across all variables a range of outcomes occurred. Factors most strongly predicting a greater 12 month %WL included higher baseline BMI, lower 12 month subjective hunger, higher 12 months QoL related to physical function and higher 12 month leisure time activity.

Consistent with our findings, others have reported superior weight loss associated with marked reductions in subjective hunger at 12 [287] and 24 [72] after gastric restrictive surgery. Diminished hunger implies an increased sense of satiety; the inhibition of hunger and eating during the mid-meal interval [146]. The results of this study support that lower subjective ratings of hunger are directly associated with a reduction in total energy intake, which is in turn associated with greater weight loss. We have previously found an optimally adjusted Lap-band produced significantly higher ratings of satiety in the fasting state compared to unrestricted bands and obese non-banded controls [193]. A physiological response to restriction at the gastro-oesophageal junction [193, 289, 421] that over-rides the characteristic hormonal response to weight loss [148, 563] is one possible mechanism.

Appropriate band-fill volumes are clearly critical to achieve and maintain an increased sense of satiety and reduced hunger. Excessive energy intake may in part reflect inadequate band adjustment. However, higher subjective hunger measured by the TFEQ was also related to symptoms of "non-hungry eating" and depression. The TFEQ measures elements of "emotional" hunger and food craving. Eating in response to negative emotional states and continuing to eat despite feeling full are forms of non-hungry eating related to higher reports of hunger and poorer weight outcomes. Others

have observed eating in response to emotions among bariatric patients [285, 445], and in non-surgical populations, an increased propensity for fatty and sweet foods [564, 565]. It has been suggested that "emotional eaters" have difficulty articulating negative emotions. Eating may provide a transient shelter to avoid confronting difficult feelings [285]. Recognition and management of those who engage in non-hungry eating appears important to optimize weight loss outcomes and psychological well-being.

Following surgery, poorer QoL related to physical function and a lower physical activity level, particularly during leisure time, were clearly related to less weight loss. Although both physical activity measures increased markedly, lower 12 month scores and lesser improvements over the year were associated with poorer weight loss. Instruction to walk regularly, which is the most common and practical form of leisure time activity among overweight and obese persons, appears important. Pedometers can be useful self-monitoring and motivational tools [566], especially if participants are keeping records, and working towards set goals [567]. Barriers to physical activity and inactive pursuits such as watching television should be minimised. Moreover, improvements in physical activity appeared to cluster with favourable eating behaviours. This relationship has been observed during a behavioural weight loss program, and may highlight a more motivated group [568]. Regular physical activity is also considered one of the strongest predictors of long-term weight loss maintenance [179].

In this study, features of depression and several eating-related behaviours were inversely associated with physical functioning and leisure time physical activity. Physical activity is beneficial in the primary and secondary prevention of depression [569, 570], while a low mood can lead to isolation and immobilization. Regular exercise may also help manage negative emotions, rather than turning to food.

During the first post-operative year the percentage of solid foods reduced, liquid foods increased and soft foods remained stable, in a pattern similar to that reported previously [289]. Dietary consistencies were not related to energy intake or weight outcome however, diets proportionately higher in soft foods were associated with higher fat intakes and a trend toward poorer weight loss. Likely explanations for modifications in food consistency are fear of adversive stimuli and failure to maintain advice recommending slow, thorough mastication of small bite-sized pieces of solid food.

Non-compliance with these guidelines increases the risk of gastrointestinal symptoms [207]. Those in the lowest quartile for fat intake lost significantly more weight the highest quartile. The intake of high fat foods and cooking methods should be minimised. Diets containing a higher percentage of solid foods contained more protein, and were lower in energy than diets higher in fat or CHO. After surgery the percentage of energy derived from protein increased however, the mean daily protein intake could still be considered less than average recommendations [571, 572]. A recent systematic review of change in fat-free mass during various weight loss interventions [573] and comparison of change in protein metabolism following LAGB and a medical weight loss intervention [574] have both shown favourable results following LAGB. Nevertheless, particularly during active weight loss adequate dietary protein is an important consideration. Dietary protein is a vital macronutrient that should be consumed in preference to CHO and fat.

On-going assessment, counselling and guidance following surgery are clearly essential. In this study, subjects who attended a higher number of clinic visits lost a greater %WL. Regular clinic attendance enables adequate band adjustment to facilitate increased feelings of satiety and reduced hunger. Reinforcement and good understanding of behavioural advice, and effective strategies to implement favourable behaviours should contribute to reduced energy intake and increased physical activity, which in turn influence weight loss and mood. Regular clinic contact also provides the opportunity to identify potentially detrimental factors and behaviours such as high "physical" or "emotional" hunger, non-hungry eating, poor physical ability/mobility, or low mood. Interventions and professional counselling can then be provided as appropriate.

Several factors must be considered in the interpretation of this study. Non-respondents (25%) were distinguished by a poorer %WL and fewer clinic visits, supporting the observation that patients who do more poorly are less inclined to attend follow-up [379]. Biased weight outcomes in study participants affect the ability to generalize our results, and suggests the actual prevalence of unfavourable behaviours and/or low mood may have been higher. Despite this limitation participants displayed a range of weight loss outcomes. Numbers were ample to find robust associations between %WL and data collected by validated questionnaires. The assessment of habitual dietary intake using a

FFQ may decrease under-reporting in obese individuals [429] however, this method may have lacked the sensitivity to detect differences in 4 month and 12 month energy intakes.

This study highlights a range of post-operative behaviours associated with variations in energy balance and weight outcomes 12 months after LAGB surgery. **Table 11.3** provides a summary of behavioural recommendations based on study findings. Although these subjects had undergone LAGB, low physical function and activity, elevated hunger and non-hungry eating, symptoms of depression and higher intakes of energy and fat are universal possibilities following any bariatric procedure. Identification of any or a combination of these characteristics can highlight persons who may need more intensive interventional therapy. Regular clinic contact and band volume adjustment is vital to optimise weight loss following LAGB. Controlled studies are required to define optimal management strategies by testing the impact of approaches such as cognitive behavioural therapy and intensive exercise therapy after LAGB and other bariatric procedures.

Table 11.3 Recommendations to direct behavioural management of the LAGB patient

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Eating-related behaviours that can facilitate weight loss after LAGB:

1) Manage physical hunger. Encourage regular clinic attendance for band volume reviews and adjustments.
2) Assess for signs of "non-hungry eating". For example, a tendency to eat when upset, anxious or tired, or eating despite feeling full.
3) Encourage appropriate "solid" foods that are high in protein, in preference to soft foods.
4) Provide advice and encouragement to minimize the proportion of fat in the diet.

Exercise-related behaviours than can facilitate weight loss after LAGB:

1) Assess for signs of poor physical function or bodily pain. Where possible, assist patients to overcome these problems.
2) Encourage regular participation in physical activity, such as walking during leisure time, and as a form of transport.
3) A pedometer may be a useful motivation tool.
4) Minimise inactive pursuits such as watching television.
5) Assess and work to overcome barriers to participation in regular physical activity.

Declaration for Thesis Chapter 12

In the case of Chapter 12, this work represents a manuscript that has been accepted for publication in *Obesity*, 2007. The nature and extent of my contribution to the work was the following:

Nature of contribution	Extent of contribution (%)
I was responsible for study design, all data collection and tabulation, analysis of data and writing the manuscript.	>85%

The following co-authors contributed to the work.

Name	Nature of contribution	Extent of contribution (%) for student co-authors only
Associate Professor John Dixon	Assisted with the study design, analysis of data, and writing of the manuscript.	
Professor Paul O'Brien	Assisted with subject recruitment and writing of the manuscript.	

Candidate's Signature [redacted] **Date** 6/12/07

Declaration by co-authors

The undersigned hereby certify that:

(1) the above declaration correctly reflects the nature and extent of the candidate's contribution to this work, and the nature of the contribution of each of the co-authors.
(2) they meet the criteria for authorship in that they have participated in the conception, execution, or interpretation, of at least that part of the publication in their field of expertise;
(3) they take public responsibility for their part of the publication, except for the responsible author who accepts overall responsibility for the publication;
(4) there are no other authors of the publication according to these criteria;
(5) potential conflicts of interest have been disclosed to (a) granting bodies, (b) the editor or publisher of journals or other publications, and (c) the head of the responsible academic unit; and
(6) the original data are stored at the following location(s) and will be held for at least five years from the date indicated:

Location(s) **The Centre for Obesity Research and Education**

Signature 1	Associate Professor John D [redacted]	**Date** 6/12/07
Signature 2	Professor Paul O'Brien [redacted]	5/12/07

CHAPTER 12: Grazing and loss of control over eating: two high risk factors following bariatric surgery

Abstract

Background: Gastric restrictive surgery induces a marked change in eating behaviour. However, the relationship between pre- and post- operative eating behaviour and weight loss outcome has received limited attention. This study assessed a range of eating behaviours before and one year after laparoscopic adjustable gastric banding (LAGB), and explored the nature and extent of change in eating patterns, their clinical associates, and impact on weight loss.

Subjects: n=129 subjects; 26M/103F, mean age 45.2±11.5 and BMI 44.3±6.8.

Methods: A 12 month observational study that assessed pre- and post-surgical binge eating disorder (BED), uncontrolled eating, night eating syndrome (NES), grazing, nutrient intake and eating-related behaviours and markers of psychological distress.

Results: Pre-surgical BED, uncontrolled eating and NES occurred in 14%, 31% and 17.1% of subjects, and reduced after surgery to 3.1%, 22.5% and 7.8%, respectively (p=0.05 for all). Grazing was prevalent before (26.3%) and after surgery (38.0%). Pre-operative BED most frequently became grazers (p=0.029). The average %WL was 20.8±8.5%; range -0.67–50.0% and %EWL 50.0±20.7%; range -1.44 to 106.9% (p<0.001). Uncontrolled eating and grazing following surgery showed high overlap and were associated with poorer %WL (p=0.008 and p<0.001, respectively) and elevated psychological distress.

Conclusion: Consistent with recent studies, uncontrolled eating and grazing were identified as two high risk eating patterns after surgery. Clearer characterisation of favourable and unfavourable post-surgical eating behaviours, reliable methods to assess their presence, and empirically tested post-surgical intervention strategies are required to optimise weight loss outcomes and facilitate psychological well-being in at-risk groups.

Introduction

The two most common bariatric procedures today are laparoscopic adjustable gastric banding (LAGB) and roux-en-Y gastric bypass (RYGB). Both surgeries involve a

gastric restrictive component that generates a predictable reduction in total energy intake, and a reliable, though variable, weight loss in the first post-operative year and beyond [52]. In the case of LAGB, the primary weight loss mechanism is thought to be the induction of satiety [193]. A marked reduction in hunger has also been reported [287]. Increased feelings of satiety and low hunger levels would facilitate the sustained behaviour modification that is required to achieve a long-term change in energy balance [211, 312]. It is currently in question whether certain pre-operative eating behaviours render affected individual less responsive to these effects, and influence the efficacy of bariatric surgery [575].

Binge eating disorder (BED) has been the focus of most studies to examine links between pre-operative eating patterns and surgical outcome. Binge eating disorder involves repeated uncontrolled episodes during which objectively large amounts of food are consumed, in association with marked emotional disturbance [266]. Prospective studies to assess pre-operative BED reveal no consistent predictors of post-surgical weight loss [301, 302, 307, 309]. Following gastric restrictive the ability to consume objectively large amounts of food in a single sitting is impeded, and BED prevalence is greatly diminished [296, 367]. Yet feelings of loss of control (LOC) related to eating can still persist [379, 383]. It is uncertain whether pre-operative binge eaters are more likely to experience post-surgical feelings of LOC, or how recurrent episodes of LOC influence weight loss and psychological state. We have previously found that emotional disturbance related to feelings of LOC, even while eating subjectively large amounts of food, was common among surgical candidates, and predicted by markers of psychological distress [576].

The night eating syndrome (NES), characterized by morning anorexia, evening hyperphagia and sleep difficulty, and more recently by recurrent awakenings from sleep to eat [577], has received limited attention [299, 311, 389]. This pattern of eating appears associated with obesity and prevalent among obese treatment seekers, yet the impact of NES on bariatric surgery is unknown [577].

The consumption of smaller amounts of food over extended periods of time has also been described prior to [285, 287, 295, 297, 300, 379] and after obesity surgery [379]. This eating pattern has been commonly termed "grazing". Pre-operative binge eaters

may be high risk to convert to post-operative grazing [297, 379]. As an eating pattern and a potential contributor to weight gain, grazing has received minimal attention. This is particularly surprising in the surgical sphere given the consumption of small amounts of food continuously over extended periods is not precluded following bariatric surgery.

This study prospectively assessed characteristics of BED, uncontrolled eating, NES and grazing, before, and one year after LAGB. We aimed to explore the nature and extent of change in these eating patterns following surgery. The impact of pre- and post surgical eating behaviour on weight loss was the primary outcome measure. Any associations between eating behaviour and markers of psychological distress were also of interest. To provide further description, energy intake and additional eating-related factors were recorded.

Methods

Study Design

The study was of a prospective observational design. Data were collected primarily via a series of self-report questionnaires, completed prior to and 12 months after LAGB. At baseline, confirmation of the presence of features of BED, feelings of LOC, NES and grazing took place during a semi-structured clinical interview. At 12 month follow-up eating behaviours were confirmed during a semi-structured phone interview.

The study was approved by the Monash University Standing Committee on Ethics in Research involving Humans, and was conducted in accordance with the Helsinki Declaration of 1975 as revised in 1983.

Subjects

Between August 2004 and December 2005, morbidly obese persons accepted into the bariatric surgery program at The Avenue Hospital, Melbourne were invited to participate. Subjects were male or female aged between 18 to 65 years. Individuals were not eligible to take part if they had undergone previous bariatric surgery. All participants provided informed, written consent.

A single experienced surgeon placed the Lap-Band® System (Allergan Health, Irvine, CA) along the pars flaccida pathway. The band was secured around the upper part of the stomach just below the gastro-oesophageal junction to create a small upper gastric

pouch. After a 5 week peri-operative period the balloon of the band was gradually inflated to induce gastric restriction and promote feelings of between-meal satiety and early satiation [192]. According to standard clinic protocol, in the first year subjects were encouraged to visit the clinic every 2 weeks for the first 1 to 2 months, then monthly, and quarterly as required.

Measures/Materials

Anthropometry

Height was recorded at baseline to the closest millimetre using a wall-mounted stadiometer. Body weight was recorded at baseline, 4 and 12 post-surgical months to the nearest 0.1kg using the electronic Tanita Wedderburn TBF-305 (Lake Worth, FL 33467) in light clothing without shoes. Weight loss was reported as the percentage weight loss (%WL) at 12 months after LAGB. For further description, the percentage of excess weight loss (%EWL) has also been reported. The %EWL was calculated by dividing the weight loss in kilograms by the excess weight (the initial weight minus weight at BMI 25), and multiplying this figure by 100.

Assessment of Binge Eating Disorder and a Loss of Control over eating

The Questionnaire on Eating and Weight Patterns – Revised (QEWP-R) [268, 269] was used to screen for binge eating behaviour. Subjects who reported any characteristics of a binge underwent a semi-structured clinical interview at baseline, and a phone interview at 12-month follow-up. A single, experienced clinician performed all interviews. The quantity of food consumed, whether a sense of LOC was present, the extent of the associated distress, and the frequency of objective and subjective binge episodes was established. To assess the extent of distress associated with feelings of LOC related to eating, subjects self-rated their emotional disturbance on a scale measuring distress. Scores ranged from 1 (no disturbance) to 5 (extreme disturbance). A score of 4 or 5 was considered to indicate a high level of self-reported emotional disturbance [576].

Before and after surgery, 'Full BED' subjects met all diagnostic criteria for BED as outlined in the Diagnostic and Statistical Manual of Mental Disorders: DSM-IV (4th Edition) [266]. They reported a frequency of $\geq$2 objective bulimic episodes/week over the previous 6 months in association with behavioural markers of LOC and significant

psychological distress. The term 'Uncontrolled Eaters' was given to the group who experienced feelings of LOC during the consumption of either a subjectively or objectively large amount of food at a frequency of ≥1/week over the previous 6 months, but did not meet full BED criteria. The level of psychological distress associated with the bulimic episodes was variable. After re-assessment of eating behaviour at 12 months, the few subjects who met full BED were combined with those meeting the criteria for 'Uncontrolled Eaters'. The post-surgical group was labelled 'Uncontrolled Eaters_12'. 'Uncontrolled Eaters_12' represented a group who experienced post-surgical feelings of LOC related to eating. 'Non-binge eaters' (NBE) reported no sense of LOC during the consumption of either subjectively or objectively large amounts of food.

The Night Eating Syndrome

A self-made survey screened for NES based on the proposed diagnostic criteria of Stunkard et al. in 1996 [283]. NES diagnosis required that persons usually: 1) had no appetite for breakfast, 2) consumed 50% or more of total energy intake after 7p.m., and 3) had trouble getting to sleep or staying asleep on three or more nights of the week within the previous three month period. The consumption of nocturnal snacks during night-time awakenings was also assessed. NES behaviours were confirmed by interview.

"Grazing" Behaviour

A pattern of "grazing" was measured primarily to investigate the association between small amounts of food eaten over continuous periods, and post-surgical energy intakes and weight loss outcomes. The definition of grazing was based on that reported by Saunders [300, 379]. Grazing was defined by the consumption of smaller amounts of food continuously over an extended period of time, eating more than the subject considers best for them. At baseline and follow-up, subjects were asked if they had often engaged in a grazing pattern of eating during the previous 6 months. Grazing was confirmed by interview.

Other Eating Behaviour

The Anti-Cancer Council Victoria Food Frequency Questionnaire (ACCVFFQ) [514] was used to assess subject's usual dietary habits and derive a total energy intake at baseline, 4 and 12 post-surgical months. Validity of the ACCVFFQ relative to 7-day food records has proven acceptable [514]. The highest and lowest 2% of calculated energy intakes at each time point were excluded from statistical analysis. The Three Factor Eating Questionnaire (TFEQ) [524] collected information on cognitive dietary restraint, disinhibition of eating and subjective feelings of hunger at baseline and 12 months. A series of multiple choice questions and dichotomous response items collected additional information. Before and after surgery subjects indicated how many times a day they ate, considering all meals and snacks as a separate "eating episode". The frequency of gastrointestinal symptoms after surgery was also assessed. Based on the definition of Busetto et al. [289], vomiting was defined as disgorging the contents of the stomach or oesophagus through the mouth. Obstruction was defined as a temporarily blockage of the Lap-band outlet. At analysis the reported frequency of both symptoms were combined. After surgery, subjects were asked to indicate from a list, situational or emotional factors that predisposed them to consume types of foods or quantities of food they knew to be not best for them. The fear of weight regain and the perceived return of "old eating habits" were also assessed. At 4 post-surgical months subjects were sent a short questionnaire which included the ACCVFFQ, and a survey asking how many times a day they ate and the frequency of gastrointestinal symptoms. Failure to return the 4-month questionnaires did not result in study exclusion.

Psychological Health and Quality of Life

The Beck Depression Inventory (BDI) [527] assessed for the presence of symptoms of depressive illness. A score of 0-9 was considered "normal"; 10-16 "mild depression"; 17-29 "moderate depression"; and 30-63 "severe depression" [528]. The Multidimensional Body Self Relations Questionnaire (MBSRQ) [530] provided a measure of body image distress. The difference between the appearance orientation (AO) subscale (how one values physical appearance in general) and the appearance evaluation (AE) subscales (how one rates their own physical appearance) was used to indicate the degree of appearance dissatisfaction (AD) [80]. The Medical Outcomes Trust Short Form-36 (SF-36) was used to assess health-related quality of life (QoL)

[532, 533]. Results of the survey are presented as the SF-36 physical (PCS) and mental (MCS) summary scales [533].

Post-surgical Complications

Any band slippage and port access problems requiring revisional surgery were noted.

Data Analyses

Descriptive statistics were used to express the mean ± standard deviation (SD) for continuous, normally distributed variables. Baseline and 12 month BDI scores and the TFEQ hunger score at 12 months were not normally distributed and required log transformation. Differences between anthropometric, psychological and eating-related measures before and after surgery were tested using paired Student's t-tests for continuous variable and Chi-square test for categorical variables. Differences between respondents and non-respondents (those who did not return the 12 month survey), and between the eating subgroups and the remainder of the cohort were tested using Independent t-tests for continuous variables, Chi-square test for categorical values, and Mann-Whitney U-test for ordinal data. The change in eating category before and after surgery, and differences in post-surgical emotional and situational eating triggers between groups were assessed using the Chi-square test. Forwards and backwards linear regression explored which pre- and post-operative factors predicted weight loss outcome. Both models controlled for age, gender, baseline BMI and insulin resistance [448]. Key variables were grouped according to post-operative eating pathology, energy intake, eating behaviour and markers of psychological distress. SPSS version 12.0.1 was used for statistical analysis. A p-value of less than 0.05 was considered statistically significant. A p-value of greater than 0.05 and less than 0.10 was considered a statistical trend.

Results

Respondents and Non-respondents

Of 180 subjects recruited at baseline, 6 did not go on to have surgery, 1 died of myocardial infarction, and 44 failed to return the 12-month survey. All eligible subjects (n=173) were notified by phone before the 12-month survey was sent, and then contacted by phone to prompt survey completion between one and three times. In total

129 subjects returned the baseline and 12 month surveys, representing a response rate of 75%. The post-operative survey was returned on average 12.29±1.1 months after surgery. Comparison of eligible subjects who did and did not return the final questionnaires showed a lower %WL (p=0.009) in non-responders. This group was also more likely to have been diagnosed with BED pre-operatively (p=0.033) and to have attended less clinic appointments (p=0.017).

Participant Description

Mean age of the participants was 45.2±11.5 years, with a gender distribution of 103 females (80%) and 26 males. **Table 12.1** lists clinical, behavioural and psychological characteristics of subjects at baseline and 12 months. Over the first post-surgical year mean body weight reduced from 122.2±20.5kg (range 75.1 to 201.2kg) to 98.5±18.2kg (range 56.8 to 152.9kg) (p<0.001). The mean %WL was 20.8±8.5% (range -0.67 to 50.0%) and mean %EWL was 50.0±20.7% (range -1.44 to 106.9%). Concurrent with the average decline in body weight, the prevalence of BED and NES, and severity of subjective hunger and dietary disinhibition, symptoms of depression and AD all reduced significantly. Dietary restraint and health-related QoL increased. The prevalence of grazing did not alter.

Table 12.1 Clinical, behavioural and psychological characteristics of the total cohort before and 12 months after LAGB

n=129	Baseline	12 Months
Mean BMI	44.3±6.8†	35.0±6.0***
Binge Eating Disorder	18 (14.0%)	4 (3.1%)*
Uncontrolled Eaters	40 (31.0%)	29 (22.5%)*
Night Eating Syndrome	22 (17.1%)	10 (7.8%)*
Grazer	34 (26.4%)	49 (38.0%)
BDI Score	15.0 (10 – 21)‡	6.0 (4 – 11)‡***
AD Score	1.7±1.0	0.91±1.0***
App. Orientation	3.5±0.69	3.5±0.64
App. Evaluation	1.8±0.66	2.6±0.82***
SF-36 MCS	46.9±8.1	48.9±7.3*
SF-36 PCS	37.2±10.0	49.2±9.8***
Restraint	8.3±3.9	13.0±4.2***
Disinhibition	11.5±3.4	6.2±3.9***
Hunger	9.0 (6 – 12)	2.0 (1 – 5)‡***

†mean ± SD (all such values)
‡Data presented as median (IQR); analysis based on log transformed values
BDI, Beck depression Inventory; AD, appearance dissatisfaction; App appearance; MCS, mental health component score; PCS, physical component score
Statistical analysis using paired Student's t-tests for continuous variables and Chi-square for categorical variables
*p<0.05, **p<0.01, *** p<0.001

Subjects attended clinic 11.75±3.7 times, and underwent 7.88±3.4 band adjustments. The annual number of clinic visits or band adjustments did not differ according to baseline or post-surgical eating pathology. Anterior prolapse of the band occurred in 2 subjects (1.6%) and port access problems requiring replacement occurred in 3 subjects (2.4%). The complication rate was too low to assess for any association with eating behaviour.

The Nature and Extent of Change in Eating Behaviour

Baseline Binge Eating Disorder

At baseline BED was diagnosed in 18 study participants (14%). When compared to the remainder of the cohort, baseline binge eaters were distinguished by higher symptoms of depression (p=0.033), AD (p=0.05), dietary disinhibition (p<0.001) and hunger (p<0.001). They reported more frequent daily eating episodes (p=0.001) and consumed a higher usual energy (p=0.023) and percentage fat (p=0.006) intake compared to the remainder of the cohort. Despite these initial differences, the group with baseline BED were not characterized by any eating-related or psychological measure after surgery. A statistical trend towards a higher monthly frequency of gastrointestinal symptoms (vomiting or obstruction) was evident at 4 post-surgical months (p=0.068), but not at 12 months. Baseline BED achieved a similar weight loss to the remainder of the cohort (%WL 21.9±11.1% versus 20.6±8.1% and %EWL 52.5±25.8% versus 49.6±19.8%). After surgery the majority of baseline BED (n=11; 61.1%) were newly categorized as 'grazers', and 8 subjects (44%) were classified as 'Uncontrolled Eaters_12' (**Table 12.2**). Seven of the eight 'Uncontrolled Eaters_12' were also classed as post-operative grazers. One third of baseline BED (n=6) reported no post-surgical eating pathology.

Post-surgical Binge Eating Disorder

Twelve months after surgery four subjects (3.1%) met full BED criteria. Two subjects had been diagnosed with baseline BED, and two had not. As this number was too few for statistical analysis, those with BED were combined with 'Uncontrolled Eaters_12'.

Table 12.2 Overlap between pre and post-surgical eating behaviours

	Pre-surgical BED n=18	**Uncontrolled Eaters n=40**	**Pre-surgical Grazer n=34**
Post-surgical BED n=4	n=2 p=0.035	n=1 NS	n=3 p=0.025
Uncontrolled Eaters_12* n=33	n=8 p=0.048	n=14 p=0.018	n=22 p<0.001
Post-surgical Grazer n=49	n=11 p=0.029	n=16 NS	n=32 p<0.001
Post-surgical Upset re: LOC n=25	n=5 NS	n=10 NS	n=10 (p=0.085)
No Grazing or LOC after surgery n=73	n=6 p=0.032	n=20 NS	n=1 p<0.001

*Group numbers include 4 subjects with post-surgical BED
BED, binge eating disorder; LOC, loss of control; NS, not significant
Statistical analysis using Chi square for categorical variables

Baseline Uncontrolled Eaters

'Uncontrolled Eaters' were common prior to surgery (31%). This group reported elevated pre-operative hunger ($p<0.001$) and disinhibition ($p<0.001$), consumed a higher usual energy intake ($p=0.035$) and tended to a higher percentage fat intake ($p=0.068$) compared to NBE. No pre-surgical psychological or weight-related measures distinguished 'Uncontrolled Eaters' however, Table 12.2 shows that a significant percentage of this group were identified with this eating pattern after surgery. Ten of the 14 subjects who continued uncontrolled eating after surgery also met criteria for grazing. Baseline 'Uncontrolled Eaters' lost a similar %WL to NBE.

Post-surgical Uncontrolled Eaters

After surgery 29 subjects (22.5%) reported feelings of LOC >1/week during the consumption of a subjectively or objectively large amount of food, during the previous 6 months. This group and the 4 subjects with BED were combined and labelled 'Uncontrolled Eaters_12'. **Table 12.3** shows that 'Uncontrolled Eaters_12' were a distinctive group who achieved a significantly lower weight loss, equating to a mean loss of 21.6kg versus 26.7kg in the remainder of the group. The 'Uncontrolled Eaters_12' consumed a higher usual energy intake and percentage of energy as fat, and ate more often over the day. They reported less dietary restraint, and greater hunger and disinhibition. Importantly, symptoms of depression were also higher and mental health-related QoL was poorer compared to the remainder of the cohort. Results were similar when the 4 subjects with BED were excluded from analysis (data not shown).

Severe Distress Related to Uncontrolled Eating

Twenty five subjects (76% of 'Uncontrolled Eaters_12') reported a high level of emotional disturbance related their feelings of LOC. This subset of 'Uncontrolled Eaters_12' was significantly younger than the remainder of the cohort; mean age 39.1 ± 12.4 years compared to 46.7 ± 10.8 years ($p=0.003$). They also reported great dissatisfaction with appearance ($p<0.001$), recorded a higher BMI at every time point (all $p<0.05$) and showed a statistical trend toward female gender ($p=0.090$).

Table 12.3 Comparison of the group who reported uncontrolled eating with the remainder of the cohort 12 months after LAGB

	Uncontrolled Eaters_12	Remainder of Cohort
n	33 (25.6%)	96
Male/Female	4/29	22/74
Age (years)	44.1±11.8‡	45.6±11.4
BMI at 0mon (kg/m²)	44.8±6.9	44.1±6.8
BMI at 4mon (kg/m²)†	39.2±6.5	38.1±5.6
BMI at 12mon (kg/m²)	37.0±7.1	34.3±5.4*
%WL	17.4±8.2	22.0±8.3**
%EWL	52.6±19.4	42.5±22.6**
BDI Score§	9 (5-19)	6 (3-10)**
AD Score	1.0±1.0	0.86±1.0
App. Orientation	3.3±0.69	3.6±0.64**
App. Evaluation	2.3±0.85	2.8±0.76**
SF-36 PCS	47.5±9.3	49.9±10.0
SF-36 MCS	46.5±7.8	49.8±6.9*
Restraint	10.9±3.7	13.7±4.1**
Disinhibition	10.1±3.1	4.8±3.2***
Hunger	6 (3-9)§	2 (1-4)§***
Energy (Kj)	4370±1544	3807±1356*
% Fat	34.3±5.6	30.3±6.4**
% Protein	21.3±3.3	22.8±4.5
% CHO	39.1±5.6	39.3±7.4
Eat per day@4m§ II	3.0 (2.5-4)	3.0 (2-3)*
Eat per day@12m§ II	3.0 (3-4)	3.0 (2-4)*

†n=93
‡mean ± SD (all such values) unless specified
§Data presented as median (IQR)
II Frequency of daily eating episodes at 4 months (4m) and 12 months (12m)
Mon, months; %WL, percentage of weight lost; %EWL, percentage of excess weight lost; BDI, Beck depression Inventory; AD, appearance dissatisfaction; App, appearance; MCS, mental component summary score; PCS, physical component score; CHO, carbohydrate
Statistical analysis using Independent t-tests for continuous variables, chi square for categorical variables, and Mann-Whitney U test for ordinal variables.
*p<0.05, **p<0.01, *** p<0.001

Baseline Night Eating Syndrome

At baseline 22 subjects (17.1%) fulfilled NES criteria and 10 subjects (7.8%) reported frequent nocturnal snacking. Men were more likely to be night eaters than women (p=0.008), and NES was commonly associated with BED (p=0.048), as previously reported [578]. Baseline NES were not distinguished from the remainder of the cohort by any psychological or eating-related measure, and lost a similar %WL. Baseline NES did not predict post-surgical night eating, uncontrolled eating or grazing (data not shown).

Post-surgical Night Eating Syndrome

Ten subjects (7.8%) reported NES at 12 months (Table 12.1). Of these, only 4 were baseline NES (18.1%), and an additional 6 subjects began experiencing this cluster of behaviours after surgery. There were no gender differences in this post-surgical group, however they reported lower cognitive restraint (p=0.042) and a lesser consumption of 'hard' foods (p=0.032) and protein (p=0.05). Weight loss was not statistically significantly different to non-NES yet the mean %WL in night eaters was 16.9% compared with 21.1%WL in non-NES, and 43.3%EWL versus 50.6%EWL, respectively. A statistical trend toward fewer band adjustments in NES was noted (p=0.069). Reports of nocturnal snacking reduced to 4 subjects (3.1%) post-operatively (p=0.033).

Baseline Grazing

Prior to surgery 34 subjects (26.4%) reported a grazing pattern of eating. Grazing was associated with lower dietary restraint (p=0.025), higher dietary disinhibition (p<0.001) and hunger (p=0.034) and more frequent daily eating episodes (p=0.05). At 12-month follow-up, baseline grazers reported significantly more symptoms of depression (p=0.033), and had lost less weight (%WL 15.7$\pm$7.8% versus 22.6$\pm$8.0% and %EWL 37.3$\pm$19.0% versus 54.6$\pm$19.3%) compared to the remainder of the cohort (p<0.001). Pre-surgical grazers were highly likely to continue grazing and to experience feelings of LOC over eating after surgery (Table 12.2). In addition to post-surgical grazing, 65% of baseline grazers also met criteria for 'Uncontrolled Eaters_12'.

Post-surgical Grazing

After surgery 49 subjects (38%) reported grazing (Table 12.1). Although this figure was not statistically different to baseline, it represents an increase in grazing prevalence by 31%. At 12 months the overlap between the grazers and 'Uncontrolled Eaters_12' was high, with 26 subjects (20.2% of the total cohort) meeting criteria for both categories ($p<0.001$). This number represents 53.1% of the post-surgical grazers and 78.8% of 'Uncontrolled Eaters_12'. As a result these two groups shared many characteristics. Compared to the remainder of the cohort, grazers lost a lower %WL; 17.3±7.6% versus 22.9±8.4% and %EWL 40.9±18.6% versus 55.6±20.0% ($p<0.001$). They reported less dietary restraint ($p=0.031$), greater hunger ($p<0.001$) and disinhibition ($p<0.001$), a higher number of daily eating episodes ($p=0.005$) and showed a statistical trend toward a higher total energy intake ($p=0.057$). More symptoms of depression ($p=0.024$) and poorer mental health-related QoL ($p=0.027$) were also reported. Unlike 'Uncontrolled Eaters_12', grazers reported a higher number of gastrointestinal symptoms at 12-month follow-up ($p=0.013$).

Post-surgical Emotional and Situational Eating Triggers

Table 12.4 shows the extent to which different emotions and situations triggered eating in certain groups, compared to the remainder of the cohort. Fear of weight regain and the perceived return of old eating habits were also assessed. Those who reported baseline grazing remained a distinctive post-surgical group who (over)ate in response to numerous emotional triggers, continued eating regardless of feeling full, were aware of the return of old eating habits and fearful of weight regain. Of the post-surgical groups, the 'Uncontrolled Eaters_12' and the subset with a high level of emotional disturbance related to feelings of LOC reported eating in response to emotional triggers, ignoring satiety cues and difficulty maintaining behaviour change. Those with NES at 12 months were also more likely to eat in social situations and when tired.

Table 12.4 Situations where, or reasons why the disordered eating groups were more likely to consume types of foods or quantities of food they knew to be not best for them, 12 months following LAGB*

	Baseline BED	Uncontrolled Eaters_12	12-month Upset re: LOC	12-month NES	Baseline Grazer	12-month Grazers
Anxiety	NS	9.89, p=0.002	16.52, p<0.001	NS	10.26, p=0.001	6.33, p=0.012
Fatigue	4.46, p=0.035	15.01, p<0.001	NS	4.48, p=0.034	16.33, p<0.001	NS
Boredom	NS	13.48, p<0.001	8.41, p=0.004	NS	12.21, p<0.001	NS
Stress	NS	18.77, p<0.001	13.61, p<0.001	NS	13.30, p<0.001	3.68, p=0.05
Anger	NS	11.60, p=0.001	6.38, p=0.012	NS	13.02, p<0.001	NS
Upset/ Depression	NS	9.48, p=0.002	14.09, p<0.001	NS	4.97, p=0.026	NS
Habit	16.20, p<0.001	NS	NS	NS	NS	NS
When socialising	NS	NS	NS	8.32, p=0.004	NS	NS
Continue to eat when full	NS	26.69, p<0.001	18.96, p<0.001	NS	30.71, p<0.001	3.70, p=0.05
Return of old patterns	NS	7.52, p=0.006	NS	NS	10.73, p=0.001	NS
Fear weight gain	NS	10.36, p=0.001	15.53, p<0.001	NS	11.25, p=0.001	8.25, p=0.004

*Each group has been compared to the remainder of the cohort.
BED, binge eating disorder; LOC, loss of control; NES, night eating syndrome; NS, not significant
Statistical analysis using chi square

Pre-surgical Factors Predicting %WL

A linear regression model was used to determine pre-surgical factors predicting %WL. After controlling for baseline BMI, age, gender and an indirect measure of insulin resistance, all baseline eating pathology groups, followed by baseline energy intake, then eating-related behaviours, and finally psychological variables were entered into the model. Forwards and backwards linear regression identified baseline grazing, β=-0.385, p<0.001 as an independent predictor of %WL. In addition to a higher baseline BMI, β=0.236, p=0.008, pre-operative grazing predicted 19.5% of variance in %WL.

Post-surgical Factors Predicting %WL

A linear regression model determined post-operative factors most strongly predicting %WL. Baseline BMI, age, gender and insulin resistance were entered as controlling variables. Higher appearance dissatisfaction, β=-0.278, p=0.002, subjective hunger, β=-0.254, p=0.006, post-surgical grazing, β=-0.186, p=0.032 and total energy intake β=-0.182, p=0.041 all independently predicted a poorer %WL. In addition to baseline BMI, β=0.194, p=0.029, these post-operative factors predicted 29.6% of variance in %WL.

Discussion

This study assessed a range of eating behaviours before and 12 months after LAGB. Associations between pre- and post-surgical eating patterns, weight loss outcome and psychological distress were investigated. Firstly, irrespective of measured eating behaviour, all groups achieved a significant weight loss, far in advance of that achievable by behavioural [579, 580] and medical [184] weight loss therapies. Secondly, while variance in eating behaviours was evident and linked with significant differences in weight outcomes, the extent of these differences may not always be *clinically* significant.

Baseline BED as a distinct group, were not associated with poorer post-operative weight loss. This finding agrees with most, but not all [290, 292, 296] prospective studies. However, pre-operative BED were at higher risk of post-surgical uncontrolled eating and grazing, and many reported a combination of these behaviours. Over 60% of baseline BED reported recurrent grazing and 44% were considered uncontrolled eaters during the first 6 to 12 post-surgical months. More than one third of baseline BED met

criteria for both post-operative eating patterns. Several other studies support this tendency for pre-operative binge eaters to continue aberrant eating behaviours after surgery [297, 303, 313, 367, 379]. Given the difficulty consuming objectively large amounts of food following gastric restrictive surgery, Saunders has suggested that post-surgical grazing may fulfil a similar function to binge eating [379].

Feelings of LOC over eating have been reported as early as 4 post-surgical months [367], and as late as 13.8 mean years after bariatric surgery [581]. Kalarchian et al. observed greater weight regain in 46% of subjects who reported feelings of LOC associated with either objective or subjective bulimic episodes between 2 and 7 years after RYGB [383]. In the current study the number of 'Uncontrolled Eaters' reduced after surgery however, one quarter of subjects were classified as 'Uncontrolled Eaters_12' after LAGB. As a group, 'Uncontrolled Eaters_12' lost significantly less weight. A number of factors may have influenced this outcome. The 'Uncontrolled Eaters_12' consumed more energy and proportionately more fat; reported higher hunger and disinhibition; less dietary restraint and more frequent eating episodes. A higher frequency of eating in response to emotional triggers was also reported. Others have observed this tendency toward "emotional eating" among surgical patients [285, 445]. Eating in response to emotions may stimulate a preference for fatty and sweet foods [564, 565, 582].

Three quarters of 'Uncontrolled Eaters_12' reported a high level of emotional disturbance directly related to the experience of loss of eating control. We have previously reported that emotional disturbance related to feelings of LOC was associated with markers of psychological distress [576]. This association was consistent in persons reporting objective or subjective bulimic episodes. In the present study, this post-operative subgroup was distinguished by poorer weight loss, younger age, higher dissatisfaction with appearance, and a tendency to be female. The causality versus counter-causality of the association remains in question however these findings suggest that uncontrolled eating after bariatric surgery is relatively common and linked with poorer weight and psychological outcomes.

After surgery, a significant number of subjects (20.2% of the total cohort) were identified as both uncontrolled eaters and grazers. This highlights a significant

proportion of persons who are likely to experience feelings of poor control related to eating behaviours which include both larger portions of food within distinct periods and smaller portions of food over extended periods. Saunders has also observed an element of poor control over grazing and defined this eating pattern as "smaller, subjective episodes of overeating" [379]. Among other factors, elevated hunger, which was identified as an independent risk factor for poorer weight loss, was greater in persons reporting these behaviours. Hunger suppression and increased satiety are important weight loss mechanisms after LAGB. Frequent clinic follow-up and band adjustments to manage hunger are of prime importance. However, not all LAGB recipients achieve optimal hunger control. Higher markers of psychological distress and eating in response to emotional cues were also present among uncontrolled eaters and grazers who were disturbed about their feelings of LOC. It is possible that those with poorly controlled physical or emotional hunger are more likely to graze and experience a LOC over eating. These factors may in turn promote a poorer psychological state.

Grazing was common before and after surgery. All but 2 (5.9%) pre-operative grazers continued this eating pattern after LAGB. Although not statistically significant, grazing prevalence was 31% higher after surgery compared to baseline. Not only does gastric restriction permit the repeated intake of smaller amounts of food, it may facilitate this eating pattern. Furthermore, both pre- and post-operative grazing independently predicted poorer post-surgical weight loss. At 6 months after RYGB Saunders has also described persistent grazing among those who reported this pre-surgical behaviour [379]. Burgmer et al. reported the prevalence of pre-operative grazing ("permanent eating") was 19.5% among a cohort seeking gastric restrictive surgery [287]. Although this figure is similar to ours, no difference in mean weight loss was found between pre-operative grazers and the remainder of the group one year after surgery. Busetto et al. defined grazing by consumption of "small quantities of foods repetitively between meals, typically triggered by inactivity and/or loneliness" [295]. This pattern was present in 42.5% of surgical candidates, but did not predict 3 year weight outcomes after LAGB.

After surgery, the incidence of NES and nocturnal snacking reduced significantly. The presence of baseline NES was not associated with post-operative NES or any other eating pattern. Interestingly, 6 of 10 subjects with post-surgical NES commenced night eating after surgery. Adami et al. prospectively assessed NES using similar criteria [299]. Their baseline prevalence estimate of 8% was similar to the 6% reporting NES three years following BPD. Our findings do not support the supposition of Adami et al. that NES remains stable following obesity surgery. Research involving NES is in its infancy and currently thwarted by inconsistent diagnostic criteria [577].

This manuscript represents one of the first attempts to measure changes in eating behaviour, and characterize "non-normative" eating patterns after bariatric surgery. Given that this was a primary aim, the lack of agreed group definitions and substantial overlap between some groups is a limitation. This study used a self-report survey followed by a semi-structured phone interview to assess eating behaviour after surgery. Although clinical interview may be considered the method of choice to assess "disordered" eating behaviour [583], Saunders [379] notes that patients could be too ashamed to admit feelings of LOC or aberrant eating behaviours to their surgeon. Individuals experiencing a LOC may also be more inclined to avoid clinical follow up. In the present study we found 12 month non-respondents were more likely to have reported pre-surgical BED, to have lost less weight and attended fewer clinic appointments. Although this bias affects the ability to generalize our results, it skews the study participants toward less post-surgical eating pathology. The actual incidence of deviant eating behaviours may have been higher. Strengths of this study include the measurement of body weight in a clinical setting; the use of validated questionnaires; paired measurement of a wide range of eating patterns and behaviours; and inclusion of several measures of non-eating-related psychological distress.

Limitations notwithstanding, this study highlights that aberrant eating patterns before and after bariatric surgery are associated with poorer post-operative outcomes. However, it is important to acknowledge that all groups achieved a significant weight reduction, and good evidence supports that LAGB and RYGB facilitate excellent sustained weight loss in the medium term [200]. Furthermore, the difficulty of achieving and maintaining even minor weight loss in those with BED is well

documented [346, 352]. Therefore the best opportunity to attain a significant weight change in obese binge eaters may be bariatric surgery. The focus on, and sometimes exclusion of pre-surgical BED appears misdirected. Yet pre-operative binge eaters are a group at high risk to become post-operative grazers and uncontrolled eaters, and as such should receive close on-going monitoring after surgery. Young females may be a group at higher risk of uncontrolled eating and psychological distress linked with poorer weight outcomes.

On-going post-operative review, band adjustments and clinical management are imperative to optimise weight loss outcomes and facilitate psychological well-being after LAGB. Clearer characterisation of favourable and unfavourable post-surgical eating behaviours, and further definition of the clinical significance of different patterns of uncontrolled eating and grazing, is required. Future research should include subjects undergoing other bariatric procedures, and address the need for reliable methods to assess post-surgical eating behaviour, and empirically tested post-surgical intervention strategies to manage at-risk populations.

Conclusions and Avenues for Future Research

This chapter returns to the research questions, discusses the unique findings of the studies in this thesis, reviews the limitations of the research and considers implications for future investigation.

As discussed in chapters 1 and 2, numerous behavioural characteristics relating to patterns of eating and exercise are associated either positively or negatively with changes in body weight. The number of surgical weight loss procedures is increasing annually however the association between pre- and particularly post-operative behavioural patterns and surgical outcome has remained largely unexplored. There are few available studies to guide behavioural management of the bariatric surgery patient.

The main aim of this thesis was to to provide an evidence base to direct key features of pre-and post-surgical care of the bariatric surgery recipient.

Major Findings and Implications

Through its series of studies, this thesis has provided new empirical evidence to guide the implementation of weight loss strategies prior to surgery, and highlight behavioural characteristics associated with patient outcomes after surgery. The benefits of this work extend to the bariatric surgeon, allied health professionals including physicians, dietitians and psychologists, and to the patient. The overall thesis design has generated several major findings, which will be addressed in turn.

The first major study quantified the extent and pattern of change in liver volume during a 12-week dietary intervention (chapter 4). Paired radiological images in 32 subjects demonstrated a mean total change in liver volume of -18.7%. Serial imaging in a subset of subjects revealed that 80% of liver volume reduction occurred in the first two weeks of weight loss. Previous work by Fris [252] reported a significant reduction in liver volume after a 2-week VLED. Busetto et al. [253] assessed liver size during weight loss after LAGB at two time points, 8 and 24 post-operative weeks. Significant reductions in liver volume occurred only in the first 8 weeks. Collectively these studies confirm that weight loss reduces hepatomegaly associated with severe obesity. The serial imaging used in this thesis further identified the first 2 weeks of weight loss as the time of the

greatest relative liver volume reduction. This study has been the first to use serial imaging to follow the change in liver volume with time during preoperative weight loss.

Several additional factors of benefit to the bariatric surgeon and physician were identified. Approximately 50% of the variability in initial liver volume was predicted by components of the metabolic syndrome and inflammatory markers, including raised plasma triglyceride level, diastolic blood pressure and C-reactive protein. Similarly, almost half of the variability in liver volume reduction was predicted by a greater relative decline in body weight and higher initial liver volume. Body weight and VAT showed a significant but more gradual decline during the 12-week VLED. From a practical standpoint, the VLED was an acceptable means of pre-operative weight loss in the majority. Patient compliance reduced as the duration of the diet increased. In order to achieve useful reductions in liver volume, body weight and VAT a pre-operative intervention period extending between two to six weeks has been recommended.

Chapter 1 reviewed hepatomegaly and NASH and the hepatic effects of rapid weight loss. This led to a smaller sub-study (n=8) which aimed to investigate the affect of rapid weight loss on liver morphology. This study (chapter 5) showed a significant reduction in hepatic steatosis however, changes in NASH grade (inflammation) and stage (fibrosis) were variable. The study findings were limited by a series of sampling constraints, histologic assessment difficulties, safety considerations and recruitment challenges. However taken together, our research and the research of others support rigorous monitoring, and consideration of a more conservative approach to weight reduction in persons at high risk for NASH.

Reviews in chapters 2 and 7 identified high prevalence rates of NES and BED among bariatric surgery candidates. The second major study in this thesis involved a cross-sectional investigation of 431 subjects exploring the clinical significance of the central behavioural features of these two "disordered" eating patterns. The large cross-sectional study in described chapter 8 showed a strong positive association between NES and obesity. Previously this association has lacked empirical evidence, but has been generally accepted due to consistently higher NES prevalence estimates in cohorts of overweight and obese when compared to the general community. This study was also

the first to examine differences between subgroups that did and did not consume nocturnal snacks. The subgroup of night eaters who engaged in frequent nocturnal snacking were most at risk of psychological disturbance. A high degree of overlap between NES and binge eating, and a higher risk of NES and nocturnal snacking in males were additional findings. The study reported in chapter 9 identified feelings of loss of control related to eating as the behavioural feature of BED most closely associated with psychological impairment. A number of researchers have proposed loss of control to be the most important and consistent feature of a binge [371-373]. To date this thesis has been the first to address this issue in BED. In particular, persons who experienced severe emotional disturbance related to their feelings of loss of control were at greatest risk of psychological distress.

A review of studies investigating eating and exercise-related behaviours after bariatric surgery (chapter 2) highlighted the lack of quantitative and qualitative data in this area. The third major study in this thesis, a 12-month observational study involving 129 subjects, addressed this issue. Marked change was evident across a range of eating- and exercise-related variables 12 months after LAGB (chapter 11). Mean total energy intake decreased significantly by 4 post-surgical months and remained stable at follow-up. By 4 post-surgical months the percentage of energy derived from fat had reduced, and the proportion of energy from protein and carbohydrate increased. Food choice altered throughout the duration of the study to include fewer foods of solid consistency and more of liquid consistency, in a pattern similar to that reported by Busetto et al. [289]. Dietary disinhibition and hunger reduced after surgery and dietary restraint increased in a pattern similar to previous reports [72, 287], suggestive of improved control related to eating behaviour. Subjective and objective measures showed a significant increase in physical activity level. The strongest behavioural predictors of greater post-operative weight loss were a lower 12 month hunger score, higher physical functioning and higher leisure time physical activity. Together with a higher baseline BMI these variables predicted one third of the variance in percentage of weight loss.

The study described in chapter 12 also measured the nature of change in "disordered" eating patterns and a "grazing" pattern of eating after LAGB. Grazing was identified in the review (chapter 2) to occur commonly among bariatric surgery candidates. A

reduction in symptoms of NES, with no important association between NES and post-surgical weight or psychological outcomes, or any other behavioural characteristics, was observed. At 12 post-surgical months, the prevalence of BED had also reduced significantly, however in contrast to NES, the majority of baseline BED were newly categorized as either an "uncontrolled eater", a grazer, or both.

Collectively, available studies offer support to the notion that pre-surgical binge eaters are at higher risk of aberrant post-operative eating behaviours. However, results from this thesis, and the majority of available prospective studies, do not show poorer weight loss or mental health outcomes in pre-operative BED. In general after surgery, eating behaviour occurs across a spectrum, and appears to alter somewhat unpredictably between individuals. A number of pre-operative binge eaters did not report deviant eating behaviours following surgery. A significant minority of former non-binge eaters were newly classified as uncontrolled eaters or grazers or both. Robust associations were observed between post-surgical characteristics of uncontrolled eating and grazing, and poorer weight loss outcome, lower mood, and a range of unfavourable behavioural features. The potential for a sense of loss of control related to eating to affect severe emotional disturbance in some persons (chapter 9) provides this subjective feeling with further significance. A tendency to "non-hungry" eating and eating in response to emotional cues was also identified, and deserves further attention given that this may confound the important bariatric weight loss mechanism of hunger suppression. The study has highlighted pre- and post-operative behavioural factors that can influence the post-surgical course of weight loss and quality of life outcomes.

This study was the first to measure the change in a grazing pattern of eating after bariatric surgery. Importantly, pre-surgical grazers showed an extremely strong tendency to continue grazing after surgery. Both pre- and post-surgical grazing was independently associated with poorer weight loss. Saunders has also described persistent grazing at 6 months after RYGB among those who reported this pre-surgical behaviour [379]. Two previous studies which measured pre-operative grazing according to variable criteria failed to detect associations with weight loss outcome [287, 295].

Limitations and Future Directions

Several limitations of this thesis may inform future research.

This thesis explored the benefits of pre-operative weight loss, and supported the use of VLED to facilitate a significant reduction in liver volume prior to bariatric surgery (chapter 4). Although a concurrent reduction in surgical risk and complexity was inferred, the study was not powered to detect a change in operative times or peri-operative complication rates. A query also remains over the absolute safety of rapid weight loss in persons with compromised liver function (chapter 5). Study constraints included high sampling variability in liver biopsies and difficulty in the assessment of inflammatory and fibrotic change in paired biopsies due to condensation of the liver tissue as lipid is dispersed. Safety and ethical considerations further limit the ability to carry out necessary research. To assess the true risk, larger studies with longer-term assessment and monitoring would be required.

By nature, behavioural characteristics are challenging to measure objectively and reliably. A number of the eating behaviours assessed in this thesis, namely binge eating, NES, nocturnal snacking, grazing, post-surgical uncontrolled eating and symptoms of "non-hungry eating" have been inconsistently defined in the literature. Definitions in this thesis were based on previously published criteria which have not been formally validated. To assist identification of "at risk" patients, future work needs to clearly characterize favourable and unfavourable post-surgical eating behaviours and develop agreed diagnostic criteria to define aberrant eating behaviours. Constructs should include important behavioural features, standards for the duration and frequency of symptoms, and objective measurement of the quantity of food or energy consumed. The extent and nature of the differences and similarities in post-surgical eating behaviour produced by current bariatric surgeries needs further exploration. Reliable clinical assessment tools are also required, and would most likely need adjustment for individual bariatric procedures.

Due to practical time constraints, this thesis had a 12-month follow-up period for the behavioural studies. This timeframe could be extended in the future to assess longer-term outcomes. Although the findings of this thesis demonstrated significant differences

in weight and other outcomes according to post-surgical behavioural patterns, these associations may alter over time. Studies are required to map medium and long-term associations between eating behaviour and surgical outcome, and define the benefit of assessment and on-going behavioural monitoring after bariatric surgery. To this end, randomized controlled trials that test the efficacy of intervention strategies (e.g. cognitive behavioural therapy) to manage aberrant eating behaviour, and the best time point (pre- and/or post-operative) to apply the intervention, would be beneficial. Ideally these studies should involve both LAGB and RYGB.

Conclusions

The findings of this thesis provide evidence to direct important areas of pre- and post-operative behavioural management of the bariatric surgery patient. The benefits of pre-operative weight loss were explored and recommended intervention strategies proposed. Behavioural patterns after LAGB showed significant change. "At risk" behavioural characteristics among bariatric patients were defined. This thesis also contributed to understanding the clinical significance of NES and BED. Future work should define normative and non-normative eating behaviour after bariatric surgery, and investigate the benefits of monitoring and intervention strategies on long-term patient outcomes.

Appendices

Appendix 1a: Eating-related and Psychological Surveys

Survey cover sheet for the two community groups

General Information

We would greatly appreciate it if you would fill in the following details before completing the questionnaires. All responses are confidential. No individual data will be analysed, as all information obtained will be analysed in a group format.

You may complete the questionnaires in one sitting, or over several days or a week, as time allows. Please read the directions for each questionnaire before commencing, as some questions relate to your behaviours in the last **3, 6** or **12** months.

Date: ...../...../.....

Gender: Male / Female **Age**: ..... years

Home Post Code: .....

Your height in cm or feet: .....

Your current body weight in kg or lbs: .....

Is this an estimate? Yes / No

How long ago did you last weigh yourself? .....weeks / months / years

Are you currently trying to lose weight? Yes / No

If yes, what steps are you taking to try to achieve this? *Please circle*

a. Dieting, ie. cutting out certain foods and/or reducing food portions
b. Trying to exercise regularly
c. A combination of a. and b.
d. Using a liquid diet replacement
e. Attending a weight loss clinic for supervised weight loss
f. Other. Please specify .....

I **agree / do not agree** (delete as relevant) to be contacted on the following number if issues of concern are raised in my responses. **Tel** _____. The caller should ask for _____ (my given name).

I understand I do not need to give my name or telephone number.

Survey common to both community groups and the surgical group

The Questionnaire on Eating and Weight Patterns

Directions: Please circle the appropriate number or response, or write in information where asked. Please try to answer every question, however you may miss a question if you do not understand, or do not wish to answer. If you are hesitating over a question or response, just choose the response that you feel is the *most correct.*

1) What has been your highest weight ever (when not pregnant)?
_____kg or _____lb

2) How old were you when you were first overweight (by at least 4.5kg (10lb) as a child or 7kg (15lb) as an adult? If you are not sure, what is your best guess?
_____ years old

3) How many times (approximately) have you lost 9kg (20lb) or more – when you weren't sick – and then gained it back?
1 Never
2 Once or Twice
3 Three or Four times
4 Five or more times

4) During the **past six months**, did you often eat within any two-hour period what most people would regard as an unusually large amount of food?
1 Yes
2 No

IF NO: MOVE TO QUESTION 9

5) During the times when you ate this way, did you often feel you couldn't stop eating or control what or how much you were eating?
1 Yes
2 No

IF NO: MOVE TO QUESTION 9

6) During the **past six months**, how often, on average, did you have times when you ate this way – that is, large amounts of food **plus** the feeling that your eating was out of control? (There may have been some weeks when it was not present – just average those in).
1 Less than one day a week
2 One day a week
3 Two or three days a week
4 Four or five days a week
5 Nearly every day

7) Did you **usually** have any of the following experiences during those occasions? Please circle:
a. Eating much more rapidly than usual?..... Yes No
b. Eating until you felt uncomfortably full? ..... Yes No
c. Eating large amounts of food when you didn't feel physically hungry? ..... Yes No
d. Eating alone because you were embarrassed by how much you were eating?..... Yes No
e. Feeling disgusted with yourself, depressed, or feeling very guilty after overeating?..... Yes No

8) Think about a typical time when you ate this way – that is, large amounts of food **plus** the feeling that your eating was out of control.

a) What time of day did the episode start?
1 Morning (8am to 12 noon)
2 Early afternoon (12 noon to 4pm)
3 Late afternoon (4pm to 7pm)
4 Evening (7pm to 10pm)
5 Night (After 10pm)

b) Approximately how long did this episode of eating last, from the time you started to eat to when you stopped and didn't eat again for at least 2 hours?
_____ hours _____ minutes

c) As best you can remember, please list everything you might have eaten or drunk during that episode. If you ate for more than two hours, describe the foods eaten and liquids drunk during the two hours that you ate the most. Be specific – include brand names if possible, and amounts as best you can estimate.

---

d) At the time this episode started, how long had it been since you had previously finished eating a meal or snack?
_____ hours _____ minutes

9) In general, during the **past six months**, how upset were you by overeating (eating more than you think is best for you)?
1 Not at all
2 Slightly
3 Moderately
4 Greatly
5 Extremely

10) In general, during the **past six months**, how upset were you by the feeling that you couldn't stop eating or control what or how much you were eating?
1 Not at all
2 Slightly
3 Moderately
4 Greatly
5 Extremely

11) During the **past six months**, how important has your weight or shape been in how you feel about or evaluate yourself as a person – as compared to other aspects of your life, such as how you do at work, as a parent, or how you get along with other people?
1 Weight and shape were **not very important**
2 Weight and shape **played a part** in how you felt about yourself
3 Weight and shape **were among the main things** that affected how you felt about yourself
4 Weight and shape **were the most important things** that affected how you felt about yourself

12) During the **past three months**, did you ever make yourself vomit in order to avoid gaining weight after binge eating?

1 Yes
2 No

IF YES: How often, **on average**, was that?

1 Less than once a week
2 Once a week
3 Two or three times a week
4 Four or five times a week
5 More than five times a week

13) During the **past three months**, did you ever take more than twice the recommended dose of laxatives in order to avoid gaining weight after binge eating?

1 Yes
2 No

IF YES: How often, **on average**, was that?

1 Less than once a week
2 Once a week
3 Two or three times a week
4 Four or five times a week
5 More than five times a week

14) During the **past three months**, did you ever take more than twice the recommended dose of diuretics (water pills) in order to avoid gaining weight after binge eating?

1 Yes
2 No

IF YES: How often, **on average**, was that?

1 Less than once a week
2 Once a week
3 Two or three times a week
4 Four or five times a week
5 More than five times a week

15) During the **past three months**, did you ever fast – not eat anything at all for at least 24 hours – in order to avoid gaining weight after binge eating?

1 Yes
2 No

IF YES: How often, **on average**, was that?

1 Less than once a week
2 Once a week
3 Two or three times a week
4 Four or five times a week
5 More than five times a week

16) During the **past three months**, did you ever exercise for more than an hour **specifically** in order to avoid gaining weight after binge eating?

1 Yes
2 No

17) During the **past three months**, did you ever take more than twice the recommended does of a diet pill in order to avoid gaining weight after binge eating?
1 Yes
2 No

IF YES: How often, **on average**, was that?
1 Less than once a week
2 Once a week
3 Two or three times a week
4 Four or five times a week
5 More than five times a week

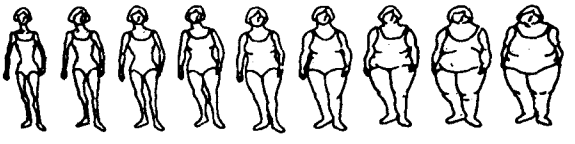
18) Since you have been an adult – over 18 years old – how much of the time have you been on a diet, been trying to follow a diet, or in some way been limiting how much you were eating in order to lose weight or keep from regaining weight you had lost? Would you say.....?
1 None or hardly any time at all
2 About a quarter of the time
3 About half of the time
4 About three-quarters of the time
5 Nearly all of the time

19) MISS THIS QUESTION IF YOU *NEVER* LOST AT LEAST 4.5KG (10lb) BY DIETING
How old were you the first time you lost at least 4.5kg (10lb) by dieting, or in some way limiting how much you ate? If you are not sure, what is your best guess?
_____ years old

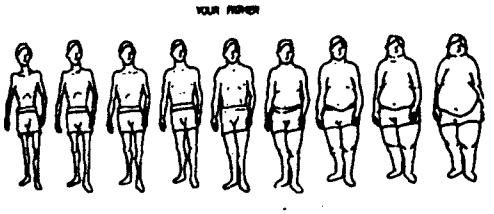
20) MISS THIS QUESTION IF YOU'VE NEVER HAD EPISODES OF EATING UNUSUALLY LARGE AMOUNTS OF FOOD ALONG WITH THE SENSE OF LOSS OF CONTROL: How old were you when you first had times when you ate large amounts of food and felt that your eating was out of control? If you are not sure, what is your best guess?
_____ years old

21) Please take a look at these silhouettes. Put a circle around the silhouette which most resembles the body build of your natural father and mother **at their heaviest**. If you have no knowledge of your biological father and/or mother, don't circle anything for that parent.

YOUR MOTHER



YOUR FATHER



The Anti Cancer Council Food Frequency Questionnaire

Dietary Questionnaire

Questions about what you usually eat and drink

Please fill in the date you completed this questionnaire:

DAY	MTH	YEAR
	○ JAN	○ 1996
	○ FEB	○ 1997
⓪ ③	○ MAR	○ 1998
① ①	○ APR	○ 1999
① ②	○ MAY	○ 2000
① ③	○ JUN	○ 2001
	④ ○ JUL	○ 2002
	⑤ ○ AUG	○ 2003
	⑥ ○ SEP	○ 2004
	⑦ ○ OCT	○ 2005
	⑧ ○ NOV	○ 2006
	⑨ ○ DEC	○ 2007

INSTRUCTIONS:

This questionnaire is about your **usual** eating habits **over the past 12 months**. Where possible give only **one answer per question** for the type of food you eat **most often.** (If you can't decide which type you have most often, answer for the types you usually eat.)

- Use a soft pencil only, preferably 2B.
- Do not use any biro or felt tip pen.
- Erase mistakes fully.
- Make no stray marks.

Please MARK LIKE THIS: ○●○○

NOT LIKE THIS: ✓ ✗ ⊖ ◯

1. How many pieces of fresh fruit do you usually eat per day? *(Count 1/2 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 do you usually eat per day? *(Count all types, fresh, frozen or tinned.)*

- ○ 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 milk
- ○ skim milk
- ○ soya milk

4. How much milk do you usually use per day? *(Include flavoured milk and milk added to tea, coffee, cereal etc.)*

- ○ none
- ○ less than 250 ml *(1 large cup or mug)*
- ○ between 250 and 500 ml *(1-2 cups)*
- ○ between 500 and 750 ml *(2-3 cups)*
- ○ 750 ml *(3 cups)* or more

5. 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

6. How many slices of bread do you usually eat per day? *(Include all types, fresh or toasted and count one bread roll as 2 slices.)*

- ○ less than 1 slice per day
- ○ 1 slice per day
- ○ 2 slices per day
- ○ 3 slices per day
- ○ 4 slices per day
- ○ 5-7 slices per day
- ○ 8 or more slices per day

7. Which spread do you usually put on bread?

- ○ I don't usually use any fat spread
- ○ margarine of any kind
- ○ polyunsaturated margarine
- ○ monounsaturated margarine
- ○ butter and margarine blends
- ○ butter

8. On average, how many teaspoons of sugar do you usually use per day? *(Include sugar taken with tea and coffee and on breakfast cereal etc.)*

- ○ none
- ○ 1 to 4 teaspoons per day
- ○ 5 to 8 teaspoons per day
- ○ 9 to 12 teaspoons per day
- ○ more than 12 teaspoons per day

9. 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

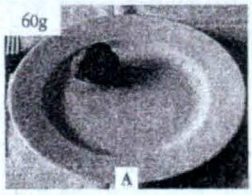
10. What types of cheese do you usually eat?

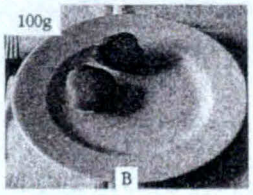
- ○ I don't eat cheese
- ○ hard cheeses, e.g. parmesan, romano
- ○ firm cheeses, e.g. cheddar, edam
- ○ soft cheeses, e.g. camembert, brie
- ○ ricotta or cottage cheese
- ○ cream cheese
- ○ low fat cheese

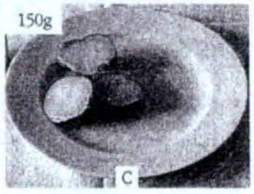
For each food shown on this page, indicate ***how much on average you would usually have eaten at main meals during the past 12 months.*** *When answering each question, think of the* ***amount*** *of that food you usually ate, even though you may rarely have eaten the food on its own.*

If you usually ate more than one helping, fill in the oval for the serving size closest to the ***total amount*** *you ate.*

11. **When you ate potato, did you usually eat:** ○ I never ate potato

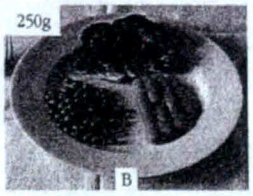


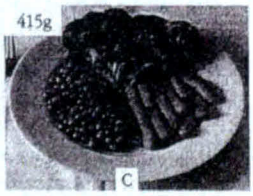




○ Less than A ○ A ○ Between A & B ○ B ○ Between B & C ○ C ○ More than C

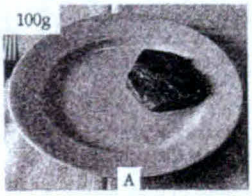
12. **When you ate vegetables, did you usually eat:** ○ I never ate vegetables

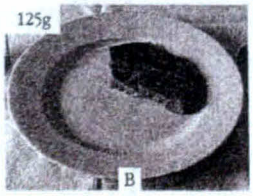


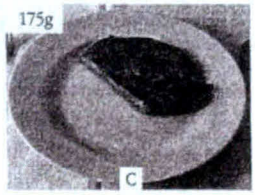


○ Less than A ○ A ○ Between A & B ○ B ○ Between B & C ○ C ○ More than C

13. **When you ate steak, did you usually eat:** ○ I never ate steak

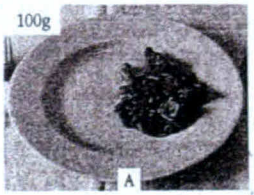


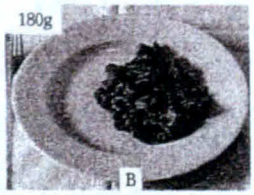


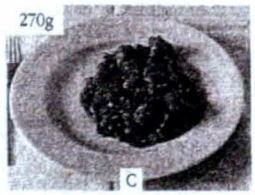


○ Less than A ○ A ○ Between A & B ○ B ○ Between B & C ○ C ○ More than C

14. **When you ate meat *or* vegetable casserole, did you usually eat:** ○ I never ate casserole







○ Less than A ○ A ○ Between A & B ○ B ○ Between B & C ○ C ○ More than C

2

15. **Over the last 12 months, on average, *how often* did you eat the following foods?** *Please completely fill one oval in every line.* Please MARK LIKE THIS: ○ ● ○ ○ NOT LIKE THIS: ✓ ✗ ⊖ ○

Times You Have Eaten	NEVER	less than once	1 to 3 times	1 time	2 times	3 to 4 times	5 to 6 times	1 time	2 times	3 or more times
		per month		per week				per day		
CEREAL FOODS, SWEETS & SNACKS										
All Bran™	○	○	○	○	○	○	○	○	○	○
Sultana Bran™, FibrePlus™, Branflakes™	○	○	○	○	○	○	○	○	○	○
Weet Bix™, Vita Brits™, Weeties™	○	○	○	○	○	○	○	○	○	○
Cornflakes, Nutrigrain™, Special K™	○	○	○	○	○	○	○	○	○	○
Porridge	○	○	○	○	○	○	○	○	○	○
Muesli	○	○	○	○	○	○	○	○	○	○
Rice	○	○	○	○	○	○	○	○	○	○
Pasta or noodles (include lasagne)	○	○	○	○	○	○	○	○	○	○
Crackers, crispbreads, dry biscuits	○	○	○	○	○	○	○	○	○	○
Sweet biscuits	○	○	○	○	○	○	○	○	○	○
Cakes, sweet pies, tarts and other sweet pastries	○	○	○	○	○	○	○	○	○	○
Meat pies, pasties, quiche and other savoury pastries	○	○	○	○	○	○	○	○	○	○
Pizza	○	○	○	○	○	○	○	○	○	○
Hamburger with a bun	○	○	○	○	○	○	○	○	○	○
Chocolate	○	○	○	○	○	○	○	○	○	○
Flavoured milk drink (cocoa, Milo™ etc.)	○	○	○	○	○	○	○	○	○	○
Nuts	○	○	○	○	○	○	○	○	○	○
Peanut butter or peanut paste	○	○	○	○	○	○	○	○	○	○
Corn chips, potato crisps, Twisties™ etc.	○	○	○	○	○	○	○	○	○	○
Jam, marmalade, honey or syrups	○	○	○	○	○	○	○	○	○	○
Vegemite™, Marmite™ or Promite™	○	○	○	○	○	○	○	○	○	○
DAIRY PRODUCTS, MEAT & FISH										
Cheese	○	○	○	○	○	○	○	○	○	○
Ice-cream	○	○	○	○	○	○	○	○	○	○
Yoghurt	○	○	○	○	○	○	○	○	○	○
Beef	○	○	○	○	○	○	○	○	○	○
Veal	○	○	○	○	○	○	○	○	○	○
Chicken	○	○	○	○	○	○	○	○	○	○
Lamb	○	○	○	○	○	○	○	○	○	○
Pork	○	○	○	○	○	○	○	○	○	○
Bacon	○	○	○	○	○	○	○	○	○	○
Ham	○	○	○	○	○	○	○	○	○	○
Corned beef, luncheon meats or salami	○	○	○	○	○	○	○	○	○	○
Sausages or frankfurters	○	○	○	○	○	○	○	○	○	○
Fish, steamed, grilled or baked	○	○	○	○	○	○	○	○	○	○
Fish, fried (include take-away)	○	○	○	○	○	○	○	○	○	○
Fish, tinned (salmon, tuna, sardines etc.)	○	○	○	○	○	○	○	○	○	○
FRUIT										
Tinned or frozen fruit (any kind)	○	○	○	○	○	○	○	○	○	○
Fruit juice	○	○	○	○	○	○	○	○	○	○
Oranges or other citrus fruit	○	○	○	○	○	○	○	○	○	○
Apples	○	○	○	○	○	○	○	○	○	○
Pears	○	○	○	○	○	○	○	○	○	○
Bananas	○	○	○	○	○	○	○	○	○	○
Watermelon, rockmelon (cantaloupe), honeydew etc.	○	○	○	○	○	○	○	○	○	○
Pineapple	○	○	○	○	○	○	○	○	○	○
Strawberries	○	○	○	○	○	○	○	○	○	○
Apricots	○	○	○	○	○	○	○	○	○	○
Peaches or nectarines	○	○	○	○	○	○	○	○	○	○
Mango or paw paw	○	○	○	○	○	○	○	○	○	○
Avocado	○	○	○	○	○	○	○	○	○	○

Times You Have Eaten CONTINUED

	NEVER	less than once	1 to 3 times	1 time	2 times	3 to 4 times	5 to 6 times	1 time	2 times	3 or more times
		per month		per week				per day		
VEGETABLES (INCLUDING FRESH, FROZEN AND TINNED)										
Potatoes roasted or fried (include hot chips)	○	○	○	○	○	○	○	○	○	○
Potatoes cooked without fat	○	○	○	○	○	○	○	○	○	○
Tomato sauce, tomato paste or dried tomatoes	○	○	○	○	○	○	○	○	○	○
Fresh or tinned tomatoes	○	○	○	○	○	○	○	○	○	○
Peppers (capsicum)	○	○	○	○	○	○	○	○	○	○
Lettuce, endive, or other salad greens	○	○	○	○	○	○	○	○	○	○
Cucumber	○	○	○	○	○	○	○	○	○	○
Celery	○	○	○	○	○	○	○	○	○	○
Beetroot	○	○	○	○	○	○	○	○	○	○
Carrots	○	○	○	○	○	○	○	○	○	○
Cabbage or Brussels sprouts	○	○	○	○	○	○	○	○	○	○
Cauliflower	○	○	○	○	○	○	○	○	○	○
Broccoli	○	○	○	○	○	○	○	○	○	○
Silverbeet or spinach	○	○	○	○	○	○	○	○	○	○
Peas	○	○	○	○	○	○	○	○	○	○
Green beans	○	○	○	○	○	○	○	○	○	○
Bean sprouts or alfalfa sprouts	○	○	○	○	○	○	○	○	○	○
Baked beans	○	○	○	○	○	○	○	○	○	○
Soy beans, soy bean curd or tofu	○	○	○	○	○	○	○	○	○	○
Other beans (include chick peas, lentils etc.)	○	○	○	○	○	○	○	○	○	○
Pumpkin	○	○	○	○	○	○	○	○	○	○
Onion or leeks	○	○	○	○	○	○	○	○	○	○
Garlic (not garlic tablets)	○	○	○	○	○	○	○	○	○	○
Mushrooms	○	○	○	○	○	○	○	○	○	○
Zucchini	○	○	○	○	○	○	○	○	○	○

16. Over the last 12 months, how often did you drink beer, wine and/or spirits?

Times That You Drank

	NEVER	less than once a month	1-3 days per month	1 day per week	2 days per week	3 days per week	4 days per week	5 days per week	6 days per week	every day
Beer (low alcohol)	○	○	○	○	○	○	○	○	○	○
Beer (full strength)	○	○	○	○	○	○	○	○	○	○
Red wine	○	○	○	○	○	○	○	○	○	○
White wine (include sparkling wines)	○	○	○	○	○	○	○	○	○	○
Fortified wines, port, sherry, etc.	○	○	○	○	○	○	○	○	○	○
Spirits, liqueurs, etc.	○	○	○	○	○	○	○	○	○	○

When answering the next two questions, please convert the amounts you drink into glasses using the examples given below. For spirits, liqueurs, and mixed drinks containing spirits, please count each nip (30 ml) as one glass.

1 can or stubby of beer = 2 glasses
1 large bottle beer (750 ml) = 4 glasses
1 bottle wine (750 ml) = 6 glasses
1 bottle of port or sherry (750 ml) = 12 glasses

17. Over the last 12 months, on days when you were drinking, how many glasses of beer, wine and/or spirits altogether did you *usually* drink?

TOTAL NUMBER OF GLASSES PER DAY	1	2	3	4	5	6	7	8	9	10 or more
	○	○	○	○	○	○	○	○	○	○

18. Over the last 12 months, what was the *maximum* number of glasses of beer, wine and/or spirits that you drank in 24 hours?

MAXIMUM NUMBER OF GLASSES PER 24 HOURS	1-2	3-4	5-6	7-8	9-10	11-12	13-14	15-16	17-18	19 or more
	○	○	○	○	○	○	○	○	○	○

Thank You for completing this questionnaire

The Three Factor Eating Questionnaire

Directions: Please circle either 'true' or 'false' with regards to the following statements. Please try to answer every question, however you may miss a question if you do not understand, or do not wish to answer. If you are hesitating over a question or response, just choose the response that you feel is the *most correct*.

1) When I smell a sizzling steak or see my favourite food, I find it very difficult to keep from eating, even if I have just finished a meal..... True / False

2) I usually eat too much at social occasions, like parties and picnics ..... True / False

3) I Am usually so hungry that I eat more than three times a day ..... True / False

4) When I have eaten my quota of calories, I am usually good about not eating any more .....True / False

5) Dieting is so hard for me because I just get so hungry .....True / False

6) I deliberately take small helpings as a means of controlling my weight .....True / False

7) Sometimes things just taste so good that I keep on eating even when I am no longer hungry ..... True / False

8) Since I am often hungry, I sometimes wish that while I am eating, an expert would tell me that I have had enough or that I can have something more to eat ..... True / False

9) When I feel anxious, I find myself eating ..... True / False

10) Life is too short to worry about dieting ..... True / False

11) Since my weight goes up and down, I have gone on reducing diets more than once ..... True / False

12) I often feel so hungry that I just have to eat something .....True / False

13) When I am with someone who is overeating, I usually overeat too .....True / False

14) I have a pretty good idea of the number of calories in common food .....True / False

15) Sometimes when I start eating, I just can't seen to stop ..... True / False

16) It is not difficult for me to leave something on my plate .....True / False

17) At certain times of the day, I get hungry because I have gotten used to eating then ..... True / False

18) While on a diet, if I eat food that is not allowed, I consciously eat less for a period of time to make up for it ..... True / False

19) Being with someone who is eating often makes me feel hungry enough to eat also ..... True / False

20) When I feel blue, I often overeat ..... True / False

21) I enjoy eating too much to spoil it by counting calories or watching my weight ..... True / False

22) When I see a real delicacy, I often get so hungry that I have to eat right away ..... True / False

23) I often stop eating when I am not really full as a conscious means of limiting the amount that I eat ..... True / False

24) I get so hungry that my stomach often feels like a bottomless pit .....True / False

25) My weight has hardly changed at all in the last ten years ..... True / False

26) I am always hungry so it is hard for me to stop eating before I finish the food on my plate ..... True / False

27) When I feel lonely, I console myself by eating ..... True / False

28) I consciously hold back at meals in order not to gain weight ..... True / False

29) I sometimes get very hungry late in the evening or at night ..... True / False

30) I eat anything I want, any time I want ..... True / False

31) Without even thinking about it, I take a long time to eat ..... True / False

32) I count calories as a conscious means of controlling my weight ..... True / False

33) I do not eat some foods because they make me fat ..... True / False

34) I am always hungry enough to eat at any time ..... True / False

35) I pay a great deal of attention to changes in my figure ..... True / False

36) While on a diet, if I eat a food that is not allowed, I often then splurge and eat other high calorie foods ..... True / False

Directions: Please answer the following questions by circling the number above the response that is appropriate to you.

37) How often are you dieting in a conscious effort to control your weight?

1	**2**	**3**	**4**
Rarely	Sometimes	Usually	Always

38) Would a weight fluctuation of 2.5kg (5lb) affect the way you live your life?

1	**2**	**3**	**4**
Not at all	Slightly	Moderately	Very much

39) How often do you feel hungry?

1	**2**	**3**	**4**
Only at Mealtimes	Sometimes between meals	Often between meals	Almost always

40) Do your feelings of guilt about overeating help you to control your food intake?

1	**2**	**3**	**4**
Never	Rarely	Often	Always

41) How difficult would it be for you to stop eating halfway through dinner and not eat for the next few hours?

1	**2**	**3**	**4**
Easy	Slightly difficult	Moderately difficult	Very difficult

42) How conscious are you of what you are eating?

1	**2**	**3**	**4**
Not at all	Slightly	Moderately	Very much

43) How frequently do you avoid 'stocking up' on tempting foods?

1	**2**	**3**	**4**
Almost never	Seldom	Usually	Almost always

44) How likely are you to shop for lower calorie foods?

1	2	3	4
Unlikely	Slightly likely	Moderately likely	Very likely

45) Do you eat sensibly in front of others and splurge alone?

1	2	3	4
Never	Rarely	Often	Always

46) How likely are you to consciously eat slowly in order to cut down on how much you eat?

1	2	3	4
Unlikely	Slightly likely	Moderately likely	Very likely

47) How frequently do you skip dessert because you are no longer hungry?

1	2	3	4
Almost never	Seldom	At least once a week	Almost every day

48) How likely are you to consciously eat less than you want?

1	2	3	4
Unlikely	Slightly likely	Moderately likely	Very likely

49) Do you go on eating binges though you are not hungry?

1	2	3	4
Never	Rarely	Sometimes	At lease once a week

50) On a scale of zero to five, where zero means no restraint in eating (that is, eating whatever you want, whenever you want it) and five means total restraint (that is, constantly limiting food intake and never 'giving in'), what number would you give yourself?

0	Eat whatever you want, whenever you want it
1	Usually eat whatever you want, whenever you want it
2	Often eat whatever you want, whenever you want it
3	Often limit food intake, but often 'give in'
4	Usually limit food intake, rarely 'give in'
5	Constantly limiting food intake, never 'giving in'

51) To what extent does this statement describe your eating behaviour? 'I start dieting in the morning, but because of any number of things that happen during the day, by evening I have given up and eat what I want, promising myself to start dieting again tomorrow'.

1	2	3	4
Not like me	Little like me	Pretty good description of me	Describes me perfectly

General Eating Patterns Questionnaire

Directions: The following questions refer to your *usual* meal and eating patterns. Please circle the appropriate number or response, or write in information where asked. Please try to answer every question, however you may miss a question if you do not understand, or do not wish to answer. If you are hesitating over a question or response, just choose the response that you feel is the *most correct.*

1) Please state what you would consider to be your **ideal weight**. That is, the most desirable and *realistic* weight that you would like to achieve and maintain? _____

2) The following questions are concerned with the **PAST 3 MONTHS ONLY**

a) Do you usually have no appetite for breakfast? ..... Yes / No

b) Do you skip breakfast on 3 or more days of the week? ..... Yes / No

c) Do you usually eat the majority of your food intake, ie. greater than half of the calories that you would eat over a 24 hour period, after 7pm? ..... Yes / No

d) Do you have trouble getting to sleep and/or staying asleep on 3 or more days of the week? ..... Yes / No

e) Have you experienced awakenings during the night on at least 3 nights of the week over the last 3 months? ..... Yes / No

f) When you awaken during the night, do you find yourself frequently consuming snacks? ..... Yes / No

g) If you answered *'Yes'* to the above question, please list the foods, and the quantities of these foods that you would most often eat:

Type of food	Quantity
Eg. Jam & margarine on wholemeal toast	2 slices, thickly spread

3) How many times a day do you eat? *Include all meals, snacks, biscuits with coffee breaks etc. as a separate eating episode.*

1 One or two times per day
2 Three times per day
3 Four times a day
4 Five times a day
5 Six or more times a day

4) Do you like to have a drink with, or just after your breakfast, lunch or dinner?

1 Yes, I have a drink with or just after all of my meals
2 I would usually drink with or just after a meal
3 Sometimes I drink with or just after a meal
4 I don't usually drink with or just after a meal

5) During the **PAST SIX MONTHS**, did you often eat smaller amounts of food continuously over an extended period of time; eating more than you think is best for you?

1 Yes
2 No
3 Occasionally

6) Do you take a multivitamin and mineral supplement? Please circle the appropriate response.

1 Yes, I take one daily
2 Yes, I take one every few days
3 Yes, I take one a few times over the month
4 No, I don't take one

a) If you do take a Multivitamin and mineral supplement, please specify which one:

---

7) Are your bowel actions regular? Please circle the most appropriate response.

1 I use my bowels daily
2 I use my bowels once every 2-3 days on average
3 I use my bowels once every 4 or more days on average
4 I tend to have loose bowels

a) Do you use laxatives to keep your bowels regular? ..... Yes / No

The Rand 36-Item Health Survey 1.0

Directions:: Please answer all questions by circling ONE number for each question. Do not leave questions blank or circle more than one response to each question.

1. In general, would you say your health is:

(circle one number)

Excellent	1
Very good	2
Good	3
Fair	4
Poor	5

2. Compared to one year ago, how would you rate your health in general now?

(circle one number)

Much better	1
Somewhat better	2
The same	3
Somewhat worse	4
Much worse	5

The following questions are about activities you might do during a typical day. Does your health now limit you in these following activities, if so how much?

(circle one number on each line)		**Yes limited a lot**	**Yes limited a little**	**No, not limited at all**
3.	Vigorous activities, such as running, lifting heavy objects, participating in strenuous sports.	1	2	3
4.	Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf.	1	2	3
5.	Lifting or carrying groceries	1	2	3
6.	Climbing several flights of stairs	1	2	3
7.	Climbing one flight of stairs	1	2	3
8.	Bending, kneeling or stooping	1	2	3
9.	Walking more than one kilometer	1	2	3
10.	Walking half a kilometer	1	2	3
11.	Walking 100 metres	1	2	3
12.	Bathing or dressing yourself	1	2	3

During the past **4 weeks**, have you had any of the following problems with your work or other regular daily activities as a result of your **PHYSICAL** health?

	(circle one number on each line)	Yes	No
13.	Cut down the amount of time you spent on work or other activities.	1	2
14.	Accomplished less than you would like.	1	2
15.	Were limited in the kind of work or other activities.	1	2
16.	Had difficulty performing work or other activities, (for example it took extra effort)	1	2

During the past **4 weeks**, have you had any of the following problems with your work or other regular daily activities as a result of any **EMOTIONAL** problems (such as feeling depressed or anxious)?

	(circle one number on each line)	Yes	No
17.	Cut down the amount of time you spent on work or other activities.	1	2
18.	Accomplished less than you like.	1	2
19.	Didn't do work or other activities as carefully as usual.	1	2

20. During the past **4 weeks**, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours or group (circle one number).

1	Not at all
2	Slightly
3	Moderately
4	Quite a bit
5	Extremely

21. How much bodily pain have you had during the past 4 weeks

1	None
2	Very mild
3	Mild
4	Moderate
5	Severe
6	Very severe

22. During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)

1	Not at all
2	A little
3	Moderately
4	Quite a bit
5	Extremely

The following questions are about how you feel and how things have been with you during the past **4 weeks**. For each question, please give the one answer that comes closest to the way you have been feeling.

How much of the time during the last 4 weeks . . . . .

		All The Time	Most of the Time	A good bit of Time	Some of the Time	A little of the Time	None of the Time
23.	Did you feel full of life	1	2	3	4	5	6
24.	Have you been a very nervous person	1	2	3	4	5	6
25.	Have you felt so down in the dumps that nothing could cheer you up.	1	2	3	4	5	6
26.	Have you felt calm and peaceful	1	2	3	4	5	6
27.	Did you have a lot of energy?	1	2	3	4	5	6
28.	Have you felt down.	1	2	3	4	5	6
29.	Did you feel worn out?	1	2	3	4	5	6
30.	Have you been a happy person	1	2	3	4	5	6
31.	Did you feel tired.	1	2	3	4	5	6

32. During the past **4 weeks** how much of the time has your physical health or emotional problems interfered with your social activities (like visiting friends, relatives, etc)?

(circle one number)		
	All of the time	1
	Most of the time	2
	Some of the time	3
	A little of the time	4
	None of the time	5

How true or false is each of the following statements for you?

	(circle one number)	Definitely True	Mostly True	Don't Know	Mostly False	Definitely False
33.	I seem to get sick a little easier than other people	1	2	3	4	5
34.	I am as healthy as anybody I know	1	2	3	4	5
35.	I expect my health to get worse	1	2	3	4	5
36.	My health is excellent	1	2	3	4	5

Multi-Dimensional Body Self Relations Questionnaire

Directions: The following section contains a series of statements about how people might think, feel, or behave. Indicate the extent to which each statement pertains to you personally. Circle the most appropriate number on the scale below for each question.

1 = Definitely disagree
2 = Mostly disagree
3 = Neither agree nor disagree
4 = Mostly agree
5 = Definitely agree

1.	1 2 3 4 5	Before going out in public, I always notice how I look
2.	1 2 3 4 5	I am careful to buy clothes that will make me look my best
3.	1 2 3 4 5	My body is sexually appealing.
4.	1 2 3 4 5	I like my looks just the way they are
5.	1 2 3 4 5	I check my appearance in a mirror whenever I can.
6.	1 2 3 4 5	Before going out, I usually spend a lot of time getting ready.
7.	1 2 3 4 5	Most people would consider me good-looking
8.	1 2 3 4 5	It is important that I always look good
9.	1 2 3 4 5	I use very few grooming products.
10.	1 2 3 4 5	I like the way I look without my clothes
11.	1 2 3 4 5	I am self-conscious if my grooming isn't right
12.	1 2 3 4 5	I usually wear whatever is handy without caring how it looks.
13.	1 2 3 4 5	I like the way my clothes fit me.
14.	1 2 3 4 5	I don't care what people think about my appearance.
15.	1 2 3 4 5	I take special care with my hair grooming.
16.	1 2 3 4 5	I am physically unattractive
17.	1 2 3 4 5	I never think about my appearance
18.	1 2 3 4 5	I am always trying to improve my physical appearance.

The Beck Depression Questionnaire

Directions: Please circle the most appropriate response

1. (0) I do not feel sad
(1) I feel sad
(2) I am sad all the time and I can't snap out of it.
(3) I am so sad or unhappy that I can't stand it

2. (0) I am not particularly discouraged about the future
(1) I feel discouraged about the future
(2) I feel I have nothing to look forward to
(3) I feel the future is hopeless and that things cannot improve.

3. (0) I do not feel like a failure
(1) I feel I have failed more than the average person
(2) As I look back on my life, all I can see is a lot of failures.
(3) I feel I am a complete failure as a person.

4. (0) I get as much satisfaction out of things as I used to.
(1) I don't enjoy things the way I used to.
(2) I don't get real satisfaction out of anything any more
(3) I am dissatisfied or bored with everything

5. (0) I don't feel particularly guilty.
(1) I feel guilty a good part of the time
(2) I feel quite guilty most of the time.
(3) I feel guilty all of the time

6. (0) I don't feel I am being punished
(1) I feel I may be punished.
(2) I expect to be punished.
(3) I feel I am being punished

7. (0) I don't feel disappointed in myself
(1) I am disappointed in myself
(2) I am disgusted with myself.
(3) I hate myself

8. (0) I don't feel I am any worse than anybody else
(1) I am critical of myself for my weaknesses or mistakes
(2) I blame myself all the time for my faults.
(3) I blame myself for everything bad that happens.

9. (0) I am no more irritated now than I ever am.
(1) I get annoyed or irritated more easily than I used to.
(2) I feel irritated all the time now.
(3) I don't get irritated at all by the things that used to irritate me.

10. (0) I have not lost interest in other people.
(1) I am less interested in other people than I used to be.
(2) I have lost most of my interest in other people..
(3) I have lost all of my interest in other people.

11. (0) I make decisions about as well as I ever could.
(1) I put off making decisions more than I used to.
(2) I have greater difficulty in making decisions than before
(3) I can't make decisions at all anymore

12. (0) I don't feel I look any worse than I used to.
(1) I am worried that I am looking old or unattractive.
(2) I feel that there are permanent changes in my appearance that make me look unattractive
(3) I believe that I look ugly.

13. (0) I can work about as well as before.
(1) It takes an extra effort to get started at doing something
(2) I have to push myself very hard to do anything.
(3) I can't do any work at all

14. (0) I can sleep as well as usual
(1) I don't sleep as well as I used to
(2) I wake up 1-2 hours earlier than usual and find it hard to get back to sleep.
(3) I wake up several hours earlier than I used to and I cannot go back to sleep.

15. (0) I don't get more tired than usual.
(1) I get tired more easily than I used to.
(2) I get tired from doing almost anything.
(3) I am too tired to do anything

16. (0) My appetite is no worse than usual.
(1) My appetite is not as good as it used to be.
(2) My appetite is much worse now.
(3) I have no appetite at all any more

17. (0) I don't have any thoughts of killing myself.
(1) I have thoughts of killing myself but I would not carry them out.
(2) I would like to kill myself.
(3) I would kill myself if I had the chance

18. (0) I don't cry any more than usual.
(1) I cry more now than I used to.
(2) I cry all the time now.
(3) I used to be able to cry, but now I can't cry even though I want to.

19. (0) I am no more worried about my health than usual.
(1) I am worried about physical problems such as aches and pains; or upset stomach; or constipation.
(2) I am very worried about physical problems and it is hard to think of much else.
(3) I am so worried about my physical problems that I cannot think about anything else.

20. (0) I haven't lost much weight, if any, lately.
(1) I have lost more than 5 pounds.
(2) I have lost more than 10 pounds.
(3) I have lost more than 15 pounds.

21. (0) I have not noticed any recent change in my interest in sex.
(1) I am less interested in sex than I used to be.
(2) I am much less interested in sex now.
(3) I have lost interest in sex completely.

Appendix 1b: Exercise-related Surveys

Name:_____

Pedometer Diary

Directions:

1) Ensure your pedometer is attached to the waistband of your clothing above you dominant leg (ie. your right leg if you are right handed) as soon as you are dressed every morning, for 7 days in a row
2) Keep the pedometer on you all day, and remove it as you go to bed, to ensure that every step throughout the day is counted
3) Record the date, and the number of steps for that day in the table below
4) Reset your pedometer, ready to use again tomorrow
5) Note down the major physical activities that you were involved in for that day, eg. Walking, gardening, housework, cycling, playing with the kids, swimming, golf

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Date							
Number of Steps							
Activity Types							

Please feel free to make any comments:

Thank you for completing this pedometer diary.

In order to keep progressing your 'step count' towards 10,000+ steps per day, we recommend that you use your pedometer regularly, as a measurement and motivation tool.

The Baecke Physical Activity Questionnaire

Directions: The following questionnaire refers to your *usual* level of physical activity in the **last 12 months.** Please fill in the answer or circle the most correct response. If you are hesitating over a question or response, just choose the response that you feel is the *most correct.*

1) What is your main occupation? (includes housewife/home duties, retirees, unemployed)

_____

2) At work I sit.....Never / Seldom / Sometimes / Often / Always

3) At work I stand..... Never / Seldom / Sometimes / Often / Always

4) At work I walk..... Never / Seldom / Sometimes / Often / Always

5) At work I lift heavy loads.....Never / Seldom / Sometimes / Often / Very often

6) After working I am tired.....Very often / Often / Sometimes / Seldom / Never

7) At work I sweat..... Very often / Often / Sometimes / Seldom / Never

8) In comparison with others my own age I think my work is physically.....

Much heavier / Heavier / As heavy / Lighter / Much Lighter

9) Do you play sport?..... Yes / No

a) **If yes:** which sport do you play most frequently? _____

How many hours per week?..... 1 or less / 1-2 hours / 2-3 hours / 3-4 hours / 4 or more

How many months per year?... 1 or less / 1-3 mon / 4-6 mon / 7-9 mon / 9 or more

b) If you play a second sport:

Which sport is it? _____

How many hours per week?..... 1 or less / 1-2 hours / 2-3 hours / 3-4 hours / 4 or more

How many months per year?... 1 or less / 1-3 mon / 4-6 mon / 7-9 mon / 9 or more

10) In comparison with others my own age I think my physical activity during leisure time is.....

Much more / More / The same / Less / Much less

11) During leisure time I sweat.....Very often / Often / Sometimes / Seldom / Never

12) During leisure time I play sport...Never / Seldom / Sometimes / Often / Very often

13) During leisure time I watch TV/Video....Never / Seldom / Sometimes / Often / Very often

14) During leisure time I walk.....Never / Seldom / Sometimes / Often / Very often

15) During leisure time I cycle.....Never / Seldom / Sometimes / Often / Very often

16) How many minutes do you walk and / or cycle per day to and from work, school and shopping?

5 or less / 5-15 minutes / 15-30 minutes / 30-45 minutes / 45 or more

Assessment of Barriers to Physical Activity

17) Please place a cross in the box next to any factors that you consider to have limited your participation in physical activity in the last 12 months. You may choose more than 1 response.

- ☐ Fear of injuring myself
- ☐ I don't enjoy exercising
- ☐ I don't want to exercise
- ☐ I have ankle/knee/back pain
- ☐ Lack of time
- ☐ Lack of confidence
- ☐ Poor weather/too dark/too cold
- ☐ I feel physically unable to exercise
- ☐ Too expensive
- ☐ I don't have access to facilities
- ☐ I am too tired
- ☐ Other .....

18) Do you own or rent and use a piece of home exercise equipment? ?.....Yes / No

a) If yes: please indicate what type of equipment.

- ☐ Walking machine / Treadmill
- ☐ Exercise bike
- ☐ Other .....

b) In general: how often do you use your piece of home exercise equipment for:

How many hours per week?.....1 or less / 1-2 hours / 2-3 hours / 3-4 hours / 4 or more

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