

Current Research Projects

Centre for Obesity Research and
Education (CORE)

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Contents

Randomised Controlled Trials	3
Commencing in 2012	3
Currently in progress	3
Clinical Studies	6
Technical studies of the Lap-Band™	10
Commencing in 2012	10
Currently in progress	10
Psychological Studies of Obesity and Weight Loss	11
Commencing in 2012	11
Currently in progress	11
Systematic Reviews	14
Technical Studies of the Comorbidities of Obesity	16
Cost-effectiveness Evaluations	17

Randomised Controlled Trials (RCT's)

RCTs are the coin of the realm. They are the most important methods for clinical research to uncover new information in a scientific robust manner. The Australian healthcare system provides an environment that is conducive to running clinical trials with a high quality medical system, good training in scientific method, a vigorous but supportive human ethics approval process and a population who are generally pleased to act as participants. Through CORE we have conducted several RCTs to date. Two of these have become landmark studies in the medical literature – The BMI 30-35 trial, the first to compare medical and surgical treatment for obesity, and the Diabetes trial, another comparison of the best medical and surgical treatments for this particular group. We have a number of RCTS ongoing or about to begin.

RCT's Commencing in 2012

1. The Effect Of Weight Loss On Infertility Caused By Obesity: A Prospective Randomised Controlled Intervention Study Comparing In Vitro Fertilization with Substantial Weight Loss Induced By Gastric Banding

We propose a randomised controlled trial comparing IVF and LAGB as treatment for obese women who are infertile, and resistant to conservative ovulation induction programmes. Endpoints include cumulative live births rates, cumulative conception rates, complications of pregnancy and delivery, neonatal outcomes, change in maternal health and wellbeing and costs of each intervention.

Commencement Date: February 2012

2. A randomized trial of weight loss for obese people with established, inadequately controlled type 2 diabetes

Summary of Research Plan: We will randomize 60 men and women with BMI between 30 and 40, HbA1c > 7% and a history of type 2 diabetes for more than 5 years to either best possible care or best care plus LapBand surgery. Diabetes endpoints, measured at 1 and 5 years are: HbA1c, fasting glucose, 2h glucose following 75g oral glucose load and insulin AUC following IV glucose challenge. We will also determine the effects of weight loss on medication use, lipid profile and blood pressure, and the costs of each treatment.

Commencement Date: Jan 2012

RCT's currently In Progress

1. Weight loss and type 2 diabetes: A prospective randomized controlled intervention study of best practice medical management versus the additional placement of the Lap-Band™ system in overweight patients.

Summary of Research Plan: We seek to measure the effect of weight loss on the overweight patient with type 2 diabetes (T2D). The study will recruit 50 people with T2D and randomly allocate them to best medical care of their disease or to best care plus the Lap-

Band™ procedure. They will all be followed for one year at which time the benefits in terms of remission of diabetes, weight loss, other health improvements and the adverse events would be measured. We will also measure their pancreatic beta cell function and insulin resistance prior to randomization and at one year to check the magnitude of the change in those key determinants of diabetes. We will then continue following the patients for a total of 5 years to a final endpoint.

Current Status: Randomisation of the fifty participants was completed in June 2011.

Fourteen of the surgical group and 16 of the medical participants have completed the initial 12 month follow up. Compliance is generally very good with participants attending 3 monthly reviews. The first analysis of the data will occur in June 2012 after the last patient has completed one year follow up. After the last IV glucose tolerance test is done, the insulin levels from the 50 initial IVGGTs and the 12 month IVGGTs will be assayed at the one time.

2. Ten Year follow-up of a prospective randomized controlled comparison of best practice medical management versus placement of the Lap-Band™ System to effect weight loss.

Summary of Research Plan: 80 people were randomised to either a medical arm or a surgical (Lap-Band™) arm of this trial prior to Nov, 2001. We completed the two year follow up as the primary end-point of the study and published the results in Ann Int Med in 2006. We are now approaching the completion of 10 years of follow up and plan to try to review all patients and report on their long-term outcomes.

Current Status: Of the 39 in the surgical group, 4 are lost to follow up, 4 have had explantation of the band and there has been one death from unrelated cause. The weight loss of those who are still in active follow up is 58% of excess weight at their last follow up visit. A total of 17 of the medical arm have moved to have Lap-Band™ placement since completion of the primary study. 16 of these are in active follow up and have a mean weight loss of 51%EWL at their last visit. The 10 yr follow up will be completed for all participants in November 2011 after which a report of a RCT of the long-term effects of Lap-Band™ placement will be generated.

3. A randomized controlled trial of physical activity & weight loss in LAGB patients

Summary of Research Plan: 50 patients were randomised at one month after band placement into either an intensive exercise program or a standard exercise program and were followed for three months. The %EWL was the principal outcome measure

Current Status: The study is completed and the manuscript is ready for submission.

Subjects in the intensive group achieved a higher duration of exercise than subjects in the standard group throughout the 3 months of treatment, (Intensive - 242.5 [57.7] min/wk;

Standard - 115.43 [23.2] min/wk; P=0.02). There was a significantly greater loss of excess weight in the Intensive group. Mean %EWL during the 3 month period was 39.02 % in the intensive group compared to 24.05% in the standard group, a mean difference of 15.0% (95%CI:-7.57 to -22.35) (p=0.02).

4. Randomised controlled trial of meal frequency, weight loss and dietary satisfaction in obese bariatric patients

Summary of Research Plan: Patients are recruited into the study at one month after Lap-Band™ placement and follow the protocol for three months. The %EWL is the key measured endpoint. One group will have an eating plan of an isocaloric diet taken as two meals per day. The other group will have the same energy content diet taken as 6 meals per day.

Current Status: The trial has been completed. 50 patients were randomised. Both groups were given a meal plan of 1100 kcals per day, divided into 2 or 6 meals. At 4 months after gastric banding the 2 meal per day group had lost 29.8% of their excess weight and the 6 meals per day group had lost 28.5 % of their excess weight. The difference was not significant. Satiety scores were similar between group. Both groups found the study challenging. The 2 meal per day group had difficulty eating so much food at two sittings. The 6 meals per day group just could not cope with the frequency of the meals. Further, the 6 meal per day group noted more pain and regurgitation. A manuscript of the study is in preparation.

5. Randomised controlled trial of an optimised nutrition program: weight loss and dietary satisfaction in obese bariatric patients

Summary of Research Plan: Patients were recruited into the study at one month after Lap-Band™ placement and follow the protocol for three months. The %EWL is the key measured endpoint. One group will have an eating plan in which there is no more than 30g carbohydrate per day and 40g of fat. The other group will have an eating plan of 7g fat and 43 g carbohydrate. Total calorie and protein content is held constant at 1100kcal and 50g protein.

Current Status: The study is now completed. The low carbohydrate group had lost 27.8 % of excess weight at the 4 month time point and the low fat group had lost 31.9% of excess weight. The difference was not significant (P=0.11). A number of secondary outcome measures were taken but no changes of any particular importance were noted. The manuscript is in draft form and we hope it will be ready for submission soon.

Clinical Studies

Not all questions can or need be answered by RCTs. With a large and well managed database containing many thousands of people with obesity who are losing or have lost weight CORE is well placed to conduct observational and prospective studies.

1. Long-term follow up after bariatric surgery - a case series with up to 15 year follow up and a systematic review of the literature.

Summary of Research Plan: 1. A case series of 3133 patient having LAGB and followed for up to 15 years have been reviewed with respect to weight loss and revisional surgery.

2. A formal systematic review of the literature has been conducted seeking all bariatric surgical studies which report weight loss outcome data with at least 10 years follow up.

Current Status: Participants: A total of 3235 patients were treated by primary LAGB placement. They had a mean of 47.1 years of age(range 14 - 71yr) and 78% were female. The mean initial weight was 121.7kg and initial mean BMI was 43.8 (range 30.1 - 91.2). There is 81% follow up.

Outcomes: There were no deaths associated with either the primary LAGB placement or any subsequent revisional procedure. There have been no late deaths attributable to the procedure. There was 52.4%EWL at 3yr (N=1,973), 49.8%EWL at 6 yr (N=1,399), 47%EWL at 10 yr (N=642), 47%EWL at 12 yr (N=293) and 48% EWL at 15 yr (N=27). At 15 yr follow up, 14 patients (52%) had lost more than 50% of excess weight.

Revision of band placement for proximal enlargements has occurred in 424(45%) of those treated in the perigastric era (1994 - 2000), 255(27%) of those treated in the pars flaccida era (2001 -2005) and 33(2.6%) of those treated in the Lap-Band™ AP era (2006 onwards). Erosions occurred in 8.5% of group 1, 1.9% of group 2 and 0.6% of group 3. A total of 163 (5.0%) explants have occurred. The weight loss of the patients having revision for enlargements or erosions was not different from the overall group. Systematic review: A total of 9 studies have been identified so far that provide some quantitative weight loss data at 10 years or beyond.

2. The control of diabetes through weight loss in Indigenous Australians

Summary of Research Plan: We will perform an observational study and will estimate the treatment effect by controlling bias due to the differences of the observed covariates estimated using propensity scoring. A total of 30 participants will be sought. They would be Indigenous men and women, aged between 20 and 60, who have had type 2 diabetes diagnosed within the last ten years. They will be treated with Lap-Band™ placement at the Goulburn Valley Hospital and will be followed up at the Rumbalara Health Service for a two year period. The primary outcome measure will be status of their diabetes. Secondary

outcomes will include weight change, change in other health problems, quality of life, adverse events and costs of the treatment program.

Current Status: This trial is progressing well. All patients have been entered and completed operation. There was one serious adverse event in the perioperative period with intra abdominal sepsis and band explantation in a young man with chronic renal failure. In general there has good weight loss and control of diabetes. All have now completed one year of follow up. There has been a mean excess weight loss of 51%. At this stage 19 patients(63%) are in remission of their diabetes (normal biochemistry and no treatment), 8 remain on oral hypoglycaemics and 3 require insulin. A number of issues re compliance and acceptance have been identified. Completion of the two years of follow up will begin occurring in November, 2011 and will be completed in August 2012.

3. The Impact of treatment of obesity on cancer incidence and survival

Summary of Research Plan:

Study Population: *Surgical Weight Loss Cohort* - The surgical weight loss cohort is a series of consecutive patients treated with a laparoscopic adjustable gastric band in Melbourne between June 1994 and December 2009. Their details have been recorded on LapBase, a clinical management database in Access, designed to monitor clinical outcomes, complications & comorbidities of bariatric surgery patients.

Community Control Cohort - The Melbourne Collaborative Cohort Study (MCCS) provides a community control cohort, recruited between 1992 and 1994. Their information is recorded as individual level data of a research cohort in a statistical database (STATA), with the purpose of investigating the relationship between diet & lifestyle & cancer, cardiovascular disease & type 2 diabetes.

Current Status: Writing literature review for submission for publication. Data obtained from MCCS, Cancer Registry & NDI. Data analysis underway.

Analysis of the impact of weight loss on the metabolic syndrome

Summary of Research Plan: The metabolic syndrome consists of a cluster of risk factors that predict progression to type II diabetes and coronary heart disease. There are differing definitions of the metabolic syndrome; however, the central feature of these definitions is insulin resistance, which is a common complication of obesity. We have previously shown in Randomised Controlled Trials a clear relationship between weight loss and the resolution of the metabolic syndrome. However, it is not known exactly how much weight loss is required to achieve resolution of metabolic syndrome. In addition, the roles of gut hormones and adipokines in this process are not known. Understanding more about the process of

resolution of metabolic syndrome may enable us to set better targets for our patients, and lead to novel treatment of this common problem.

Current Status:

- We have 107 patients who consented to the study. Ongoing follow up progresses - 93 (86%) patients have 12 months follow up. Ongoing analysis of 12 month data, looking at resolution of metabolic syndrome and quartiles of weight loss. Data collection will be complete at the end of March, 2012.
- Collaborations with Department of Pharmacology looking at pharmacokinetics and renal function in obesity.
- Lipidomic studies, looking at the ratios of different lipid species in adipose tissue macrophages, and correlating these with markers of inflammation in adipose tissue, and degree of insulin resistance in an obese population.
- Calculation of the alteration in cardiovascular risk profile, utilising a Framingham based Australian Cardiovascular Risk calculator, in a well characterised obese population, who have lost weight using the laparoscopic adjustable lap band.

4. Evaluation of the Intensive Care program: Does more intensive assessment and more intensive therapy improve the outcomes for the weight loss failure patient

Summary of Research Plan: A consecutive group of patients who have not achieved 25% EWL after 2 years post LAP-BAND, have been selected. There is an intensive focus on 1) correcting any anatomical or device problems, such a slippage or enlargements or tubing breaks, 2) ensuring the patient is educated in the rules of eating and exercise 3) optimizing adjustment of the band 4) frequent visits with modest weight loss aims. Weight loss achieved is used as the measure of success. Importantly, we have set a realistic expectation with a target rate of weight loss of 1 kg per month.

Current Status: A total of 38 patients were included in the study. They were on average 7.5 years from the initial Lap-Band™ procedure. At entry into the intensive care study, they had lost a mean of 12.2% of excess weight. Over a mean of 7 months intensive care, they lost 6.6 kg, 14.8 % of excess weight to achieve a final weight loss of 26.9 %of excess weight. Eight of the 34 have already achieved in excess of 40%EWL and 16 of the 34 are currently achieving a rate of weight loss of 1 kg per month. Only two patients have put on weight during the process.

Longer follow up and more patients are needed but the strong trend of the data indicates that we can achieve valuable improvement in outcomes by following our intensive care algorithm.

5. Influence of visit and adjustment frequency and nature after Laparoscopic Adjustable Gastric Banding

Summary of Research Plan: A cohort of patients has been identified and the weight loss, number of visits and number of adjustments has been measured. If there is an association between the aftercare program and the weight loss, it will reinforce the importance of this aspect of the Lap-Band™ process.

Current Status: Data collection is complete and data analysis is nearing completion. In summary, the key finding to date is that patients who had at least 3 visits in every year of follow-up had superior weight loss (63.1% EWL, N=50) to patients with less than 3 visits (46.3% EWL, N=136) or patients who had more than 6 visits each year (52.6% EWL, N=54) at 3 years of follow-up. Post-hoc comparison applying the Bonferroni test indicated that this difference was significant ($P < 0.001$). This study is in the writing up phase.

Technical studies of the Lap-Band™

We are defining the physiology critical to success with the LAGB in terms of luminal compliance and dilatation as well as evaluating mechanisms of testing reflux in gastric band patients.

Commencing in 2012

1. Determining the significance of luminal compliance in success and failure of Lap-Band™ surgery

Summary of Research Plan: To determine the compliance of the lumen above the Lap-Band™ in patients with a successful outcome following Lap-Band™ surgery, gastroscopies will be performed on 10 successful and 10 unsuccessful patients.

Commencement Date: 2012

Currently in progress

1. Evaluating Bravo and other mechanisms of testing reflux in gastric band patients

Summary of Research Plan: Undertake a pilot study of the use of BRAVO capsules in Lap-Band™ patients

Current Status: Obtained equipment and preparing for first implants. First implants have been successful and tolerated by patients. We will now look towards a prospective study of the effect of the Lap-Band™ on gastro-oesophageal reflux disease.

This is a significant study as gastro-oesophageal reflux is currently deemed a contra-indication to Lap-Band™ placement by the FDA.

2. Outcomes of luminal dilatation following Lap-Band™ surgery

Summary of Research Plan: Retrospectively review 400 Lap-Band™ patients and identify those who have sustained a luminal dilatation following surgery. Determine the treatment pathways and weight loss in patients

Current Status: Completed data collection, presented at IFSO and manuscript complete and currently being edited in preparation for submission.

Psychological Studies of Obesity and Weight Loss

Commencing in 2012

1. The effect of early psychological intervention on weight loss in LAGB patients at risk of poor weight loss.

Summary of Research Plan: This study will be based on findings from the psychological assessment study and previously identified factors as being predictive of outcome following gastric banding. Entry into this study will take place 6 months after surgery with patients invited to participate in a psychological therapy program alongside their standard care at CBS. We will need a comparison group and discussion is continuing whether this can be a RCT or not. Therapy will be based on CBT, motivational interviewing and psycho-educational techniques and last for 6 months. The therapy will be weekly for the first 8 weeks, then fortnightly for the next 3 months, then monthly for 2 months. Sessions will last for one hour and take place in small groups. Follow-up contact will occur at 9 months and 12 months via phone. Outcomes will be measured at 6 and 12 months and at 2 years. Power analysis indicates 31 patients are needed for each arm. It is anticipated that based on a sample of 62 patients, recruitment will take 12 months.

Commencement Date: 2012

Currently in progress

1. The Efficacy and Cost Efficacy of Gastric Banding and/or Cognitive Behaviour Therapy in the Treatment of Severely Obese Adults with Major Depressive Disorder. A Randomised Controlled Trial

Summary of Research Plan: Obese patients with Major Depressive Disorder (MDD) and seeking obesity surgery will be randomly allocated to one of four treatment arms: laparoscopic adjustable gastric banding (LAGB), cognitive behaviour therapy for depression (CBT-D), LAGB plus CBT-D, or a community care comparison treatment as usual condition (COMP). Primary outcomes are the 2-year treatment efficacy and cost-efficacy for obesity and depression.

Current Status: Protocol for pilot study being finalised

2. The role of psychological assessment in bariatric surgery

Summary of Research Plan: 200 consecutive new patients from the Centre for Bariatric Surgery will be recruited into the study. The study will involve the completion of a battery of psychological questionnaires prior to surgery and again at 12 and 24 months. In addition a psychological assessment will also be conducted at baseline and 24 months. This will

include a SCID interview to identify DSM-IV AXIS-I disorders and discuss their weight and weight loss with surgery.

Current Status: - The 2-year follow up is now nearing completion with the final two patients to be interviewed in October 2011. The follow-up rate for the interviews at 2 years is 75% and for the questionnaires is slightly less at 70%. Analysis of baseline results is currently being conducted with the first publications in submission and another ready to be submitted: several more are in preparation (see following).

Hayden, M.J., Brown, W.A., Brennan, L. & O'Brien, P.E. Validity of the Beck Depression Inventory as a screening tool for depression in bariatric surgery candidates. In submission to Obesity, September 2011

The primary objective of this paper was to assess if the BDI is a good measure of clinical depression in bariatric surgery candidates using the SCID(31) to diagnose depression. Given the widespread usage of both the BDI-IA and the BDI-II in bariatric research, the study aimed to investigate the validity and reliability of both versions. Furthermore, the research was extended to include the BDI score and the three factors identified in previous research.

Hayden, M.J., Brown, W.A., Smith, A., & O'Brien, P.E. Psychopathology of Australian obese patients undergoing gastric banding. Submitted to Obesity, October 2011.

It has been suggested that the prevalence of psychological illnesses in obese is higher than in the general population. The aim of this study was to characterize the prevalence and severity of AXIS I disorders in Australian preoperative patients presenting for gastric banding. Almost half the patients presenting for gastric banding had a current AXIS I disorder, with depression the most prevalent. Prevalence rates were significantly greater than in the general population and psychopathology did not increase with a higher BMI in those seeking surgery.

Four more papers are in early stages of preparation:

1. Psychological characteristics of bariatric surgery candidates

- This paper will aim to investigate if there are distinct clusters of groups within bariatric surgery candidates based on psychopathology and psychological symptoms (mood, cognitive style, relationships and support, and coping style). Collation of data as been completed and analysis is currently under way.

2. Binge Eating

- The binge eating paper will aim to address the following questions. a) Is a poor body image associated with increased binge eating, increased emotional eating and depressive symptomatology? b) Does binge eating/emotional eating behaviour change following surgery and are there differences based on weight loss? c) Can the binge eating scale (BES) be used to accurately assess binge eating disorder (BED). Statistical analysis is currently underway with preliminary analysis indicating poor reliability between SCID and BES.

3. Psychological predictors of outcome following surgery

- This paper will address the following questions; a) Does AXIS I psychopathology predict WL outcomes at 2 years; b) Does AXIS I psychopathology predict attendance, # of visits, # of adjustments; c) Predictors, based on questionnaires and characteristics, of weight loss? (2 year data); d) Is group membership (psychological characterisation) predictive of outcome. Statistical analysis has begun with preliminary analysis AXIS I not predictive of WL at 2 years – completed

4. Change in psychosocial comorbidities following weight loss

- The aims of this paper will assess if AXIS I psychopathology changes following weight loss (compare baseline and 2 year SCIDs), is there are relationship between weight loss and 2 year psychopathology (success vs failure) and is 2 year psychopathology indicative of adherence to WL program

3. The relationship between pre-surgical antidepressant use and post-surgical weight loss.

Summary of Research Plan: This study will use a clinical file review methodology. De-identified data including age, sex, height, weight and antidepressant use pre and post surgery for (1) all patients who report antidepressant use during standard pre-surgical clinical assessment and (2) a matched sample (matched on age, sex, BMI) that did not report antidepressant use will be extracted and analysed. This study will examine whether pre-surgical antidepressant use is associated with poorer post-surgical weight loss.

Current Status: Awaiting ethics approval.

4. Characterising disordered eating and maladaptive eating following bariatric surgery

Summary of Research Plan: Measures of disordered eating have been added to the standard questionnaire package given to patients to assess the prevalence of upper gastrointestinal symptoms in Lap-Band™ patients, as well as their association with weight loss and indices of quality of life and depression.

Current Status: Data collection underway.

5. Validation of the Beck Depression Inventory in Obesity Surgery Patients using Rasch Analysis

Summary of Research Plan: Beck Depression Inventory data previously collected in CORE research trials and as part of clinical practice at the Centre for Bariatric Surgery will be used to conduct Rasch analyses to assess its factor structure.

Current Status: Awaiting ethics approval.

Systematic Reviews

There is a wealth of information hidden within the mountains of published but unsorted data. Systematic review seeks to find the nuggets of gold within the mountain. The following systematic reviews are in preparation:

1. A systematic literature review of the relationship between physical activity and weight loss in bariatric surgical patients.

Summary of Research Plan: A systematic literature search, establishment of selection criteria and tabulation of eligible studies. From the pooled studies a discussion of the role of and efficacy of physical activity in aiding weight loss in bariatric surgery patients.

Current Status: The manuscript for this study has been accepted for publication by Obesity Surgery - October, 2011.

2. A systematic review of studies looking at eating patterns and nutritional intake in patients undergoing weight loss programs and their relationship to outcomes.

Summary of Research Plan: The review will focus on the role of and efficacy of an optimized nutrition regime in patients having received Lap-Band™ surgery previously. Aim is to determine the optimal program of diet which would result in the greatest loss of excess weight in our patient population

Current Status: Manuscript is ready for submission as chapter in a PhD thesis. It will then be remodelled to be suitable for publication.

3. A systematic review of meal frequency, weight loss and dietary satisfaction in obese bariatric patients

Summary of Research Plan: A systematic literature search, establishment of selection criteria and tabulation of eligible studies. From the pooled studies a discussion of the best evidence regarding meal frequency, weight loss and dietary satisfaction.

Current Status: Manuscript is nearly ready for submission as chapter in a PhD thesis and possibly journal publication.

4. A systematic review of intragastric erosions after laparoscopic adjustable gastric banding.

Summary of Research Plan: A systematic literature search, establishment of selection criteria and tabulation of eligible studies. From the pooled studies a discussion of predictors of occurrence and common approaches to management of erosions will be generated.

Current Status: Published: Egberts K, Brown WA, O'Brien PE. Systematic Review of Erosion after Laparoscopic Adjustable Gastric Banding. Obesity Surgery. 2011. 21(8):1272-1279.

Note also that sister publication of erosion clinical series has also been submitted to Obesity Surgery and has now been suggested for resubmission after comments.

5. Predictors of dropout in weight loss interventions: A systematic review of the literature

Summary of Research Plan: Develop systematic review protocol, conduct systematic literature search, extract relevant information from eligible studies, summarise extracted data, develop manuscript. The manuscript will summarise results and draw conclusions regarding factors contributing to attrition in weight loss interventions and discuss the implications for clinical and research practices.

Current Status: Electronic publication ahead of print: Moroshko I, Brennan L, O'Brien P. Predictors of dropout in weight loss interventions: a systematic review of the literature. Obesity Reviews. 2011 Aug 5. [DOI: 10.1111/j.1467-789X.2011.00915.x]

Technical Studies of the Comorbidities of Obesity

1. Effects of weight loss on pericardial fat and left ventricular mass assessed with Cardiac Magnetic Resonance imaging in morbid obesity

Summary of Research Plan: Cardiac MRI, ECHO and ECG assessment of cardiac function, and the collection of various weight parameters. Blood tests will also be performed to identify co-morbidities.

Current Status: The following report is in press in the International Journal of Clinical Medicine, 2011: Effects of weight loss on pericardial fat and left ventricular mass assessed with Cardiac Magnetic Resonance imaging in morbid obesity.

Stephan M, Schneider MD, Warriner R, Lefkovits L, Laurie C, O'Brien PE, Taylor AJ.

2. Role of adipose tissue immune cells in obesity-associated insulin resistance.

Summary of Research Plan: We have recently shown that adipose tissue explants stimulated with macrophage and T-cell stimulants release factors that impair insulin action in vitro. We plan to identify the factor or factors mediating this effect using anti-cytokine antibodies and by fractionating explant-conditioned media and performing mass spectrometry on active fractions. The macrophage study showed crown macrophages activate adipose T-cells. These studies may identify novel immune mediators of human insulin resistance that could serve as targets for improved diabetes therapies.

Current Status: We have established the in vitro assay of insulin action and shown that the inhibitory effects of explant-conditioned medium are not affected by blockade of either TNF- α or IL-1 β , two macrophage-derived cytokines that potently inhibit insulin action. Fractionation of conditioned medium is underway.

Cost-effectiveness Evaluations

The identification and characterization of safe and effective treatments are no longer sufficient. We must also evaluate the cost of the different options. The randomised controlled trials each have involved the collection of cost data and a comparison of the cost-effectiveness of the two arms of each study can be performed.

1. Cost-efficacy of weight loss for obese adolescents: a randomized controlled trial of Lap-Band™ placement versus optimal medical therapy

Summary of Research Plan:

All trial health costs have been collected and cost per unit weight loss calculated .

Incremental cost efficacy ratio (ICER) is then calculated

Phase 2: Cost efficacy – To include Medicare and Pharmaceutical Benefits Scheme costs

Current Status: The study is complete. Fifty adolescents (aged 14 -18 years) participated in the study. At the end of the two year trial period the LAGB group had a mean direct cost per patient of Australian dollars (AUD) \$15,335. The lifestyle group had a mean per patient cost of AUD\$3,526. The ICER for the LAGB group was AUD\$374 per additional kg of weight loss compared to the lifestyle group. The ICER for the lifestyle group compared to no therapy, in which we assume no cost and no benefit, was AUD\$1,132 per kg weight loss.

2. Effectiveness and Cost-Effectiveness of Intensive Aftercare for Gastric Banding Patients with Poor Weight Loss.

Summary of Research Plan: As a part of the evaluation of the Intensive Care program for weight loss failure, we are measuring all costs associated with increased care so that the cost per additional kg weight loss can be calculated and compared with the cost in primary Lap-Band™ care and with non-surgical programs of weight loss

Current Status: Data collection on the initial 34 patients is complete. We need to determine if we write up the data at this stage or collect longer follow up data and more patients before submitting a manuscript. We are bringing together the existing data to enable us make that decision.