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**Temporal effect of bariatric surgery on predicted ten-year and lifetime cardiovascular risk at 1 month, 6 months and 5 years following surgery: A pilot study**

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**Running Title:** Bariatric surgery and predicted CV risk

## **Abstract**

### **Background and Aims**

Cardiovascular (CV) risk equations are routinely used to predict risk in non-bariatric populations but have not been studied in depth in patients undergoing bariatric surgery and specifically those with impaired glucose regulation. The aim of this pilot study was to investigate changes in the 10-year and lifetime predicted CV risk in subjects with impaired glucose regulation before, 1 month, 6 months and 5 years after bariatric surgery.

### **Method and Results**

A non-randomized prospective study of 45 participants with impaired glucose regulation undergoing temporal assessments during follow-up. Body weight, body mass index (BMI), blood pressure, lipid profile and HbA1c were recorded pre-operatively, 1 month, 6 months and 5 years post-operatively. Preoperative and postoperative predicted CV risk was calculated using the QRISK2, QRISK lifetime and JBS3 calculators.

Follow-up rates were 93%, 91% and 71% at 1 month, 6 months and 5 years respectively. The sample had a mean age of  $48.8 \pm 7.0$  years, a mean BMI of  $53.9 \pm 11.1 \text{ kg/m}^2$ , and a mean HbA1c of  $7.5 \pm 1.7\%$ . The predicted 10-year QRISK2 score decreased by 35%, 54% and 24% at 1 month, 6 months and 5 years respectively ( $P < 0.001$ ). The predicted lifetime risk also decreased with the greatest reduction (24.5% with QRISK lifetime and 26.7% with JBS3 lifetime score) observed at 5 years even though the subjects were 5 years older.

### **Conclusion**

Bariatric surgery in patients with impaired glucose regulation is associated with a significant reduction in predicted 10-year and lifetime CV risk in a population that was 5 years older compared to baseline.

### **Key Words**

Obesity; Bariatric surgery; Type 2 diabetes; Impaired glucose regulation; Cardiovascular risk prediction

## 1. Introduction

Cardiovascular disease (CVD) including coronary heart disease (CHD) and stroke is a leading cause of mortality<sup>1</sup> with obesity being an independent and modifiable risk factor. Sjöström et al, reported that bariatric surgery was associated with a reduction in cardiovascular (CV) events in obese subjects<sup>2</sup>. However, a recent meta-analysis concluded that uncertainty remains regarding the effects of bariatric surgery on long-term CV events<sup>3</sup>. One method to predict the long-term CV outcome following bariatric surgery is to use a validated risk prediction tool. CV risk assessment tools are widely used to identify high-risk individuals and to implement timely lifestyle and therapeutic interventions for the primary prevention of CVD. Most risk prediction methods provide an absolute 10-year CV risk estimate and several studies have demonstrated that bariatric surgery is associated with a reduction in CV risk scores<sup>4-8</sup>. However, risk calculators used in most of these studies do not include body mass index (BMI) or obesity as risk factors. These CV risk calculators include the Framingham risk score (FRS), the Prospective Cardiovascular Munster Heart Study (PROCAM) score and the United Kingdom Prospective Diabetes Study (UKPDS) Risk engine<sup>4,6-9</sup>. In addition, many studies have focused on CHD risk rather than CVD risk<sup>8,9</sup>; the study samples have included the entire spectrum of bariatric patients, with little focus on those impaired glucose regulation<sup>5-9</sup>; and the follow-up has also been relatively short<sup>5-9</sup>. The study by Vogel et al, which consisted of 109 Roux-en-Y gastric bypass (RYGB) patients, reported that the Framingham CHD risk score decreased by 39% in men and 25% in women ( $P < 0.001$ ) at 17 months following surgery<sup>8</sup>. Torquati et al, also observed a 50% reduction in the Framingham CHD risk score at 1 year following RYGB<sup>9</sup>. CVD risk is a continuum and as such the consequences might not be observed for a significant period of time. Marma et al, showed that approximately 67% of adults in the United States with a low 10-year CVD risk had a high lifetime predicted risk<sup>10</sup>. A low 10-year but high lifetime CVD risk is more common in women and in younger age groups because age and gender are two of the main determinants in CVD risk prediction models<sup>10,11</sup>. Morbid obesity and bariatric surgical procedures are more frequent in females and younger age groups (<50 years), with no fewer than 70% of participants in the Swedish Obese Subjects Study (SOS) being female with a mean age of

47 years<sup>3,12</sup>. To date, no studies have examined the effect of bariatric surgery on the predicted lifetime CVD risk.

The aim of this pilot study was to investigate changes in the temporal 10-year and the lifetime predicted CV risk in subjects with impaired glucose regulation preoperatively and 1 month, 6 months and 5 years following bariatric surgery by using the QRESEARCH Cardiovascular Risk Algorithm (QRISK2), QRISK lifetime and Joint British Societies 3 (JBS3) score. The QRISK scores and JBS3 score are developed and validated in the United Kingdom and include BMI as a variable in their calculation<sup>11, 13-15</sup>.

## **2. Methods**

### **2.1 Participants**

Approval for the study was obtained from the Local Research Ethics Committee (South West Wales; LREC reference 06/WMW02/7) and ABM University Health Board. Participants were identified and recruited from patients undergoing a planned bariatric surgical procedure in our centre. Entry criteria at the outset included: - both genders, age 20-60 years, body mass index (BMI) >40kg/m<sup>2</sup> and physically fit for surgery. All subjects had previously diagnosed type 2 diabetes, or diagnosed during an oral 75g glucose tolerance test (OGTT) at the start of the study according to American Diabetes Association (ADA) criteria<sup>16</sup> or impaired glucose tolerance according to ADA criteria<sup>16</sup>. All participants were recruited preoperatively and followed-up post operatively at 1 month, 6 months and 5 years. This study sample has been previously described<sup>17-19</sup>.

### **2.2 Data collection**

Data was collected at baseline (preoperatively), 1 and 6 months, and 5-years postoperatively. Age, sex, ethnicity, address, medications, diabetes, cigarette smoking, family history of CVD, relevant past medical history were self-reported via standardised questionnaire. Height and weight were measured

according to local standard protocol, and BMI was calculated as  $\text{kg/m}^2$ . The percent excess weight loss (%EWL) was calculated by using the Ideal body weight at a BMI of  $25\text{kg/m}^2$ <sup>20</sup>. A single measurement of systolic and diastolic blood pressure was obtained by the same trained registered nurse. Glucose, haemoglobin A1c (HbA1c), creatinine, estimated glomerular filtration rate (eGFR), lipid profile [total cholesterol, high density lipoprotein cholesterol (HDL-C), low density lipoprotein cholesterol (LDL-C), and triglyceride] were analysed within the local hospital accredited laboratory. Diabetes remission is defined as:- (i) complete remission with a HbA1c <6% and fasting blood glucose <5.6 mmol/L and off medication (ii) partial remission with a HbA1c 6-6.4% and fasting blood glucose 5.6-6.9 mmol/L and off medication<sup>21</sup>.

### **2.3 Cardiovascular risk estimation**

Cardiovascular risk, both pre- and post-operatively were calculated by using online calculators: QRISK2-2016 ([www.qrisk.org/index.php](http://www.qrisk.org/index.php)), QRISK lifetime ([www.qrisk.org/lifetime/index.php](http://www.qrisk.org/lifetime/index.php)), accessed 01/05/2016 and JBS3 ([www.jbs3risk.com/pages/risk\\_calculator.htm](http://www.jbs3risk.com/pages/risk_calculator.htm)), accessed 15/04/2016.

### **2.4 Statistical analysis**

Statistical analysis was performed using SPSS (version 22, SPSS Inc., Chicago). Continuous data with a normal distribution are presented as mean and standard deviation, and data which did not have a normal distribution are described as median and interquartile range. A paired samples t-test, one-way repeated measure ANOVA and independent-samples t-test were used for continuous variables with a normal distribution and the Friedman's test, the Wilcoxon signed rank test and the Mann-Whitney U test were used for continuous variables which did not have a normal distribution. The Chi-squared test was used for analysis of categorical variables. In all cases a  $P \leq 0.05$  was considered statistically significant.

### **3. Results**

#### **3.1 Participant characteristics**

Of the 49 participants, 4 had pre-existing CVD preoperatively and were excluded from further analysis. Of the remaining 45 subjects, 42 and 41 participants attended the 1 and 6-month follow-up post-operative visits. At the time of manuscript preparation (February 2016), 20 participants had attended a 5-year follow up visit; 12 participants had attended a follow-up visit with their general practitioners; 8 were lost to follow-up; and 5 were deceased (Figure 1). At 5 years, data for clinical measures of obesity were available for 27 participants, HbA1c for 31 participants, lipid profile for 30 participants and medication history for 36 participants. Within the sample, 24 participants had undergone a laparoscopic sleeve gastrectomy, 12 a biliopancreatic diversion, 6 a RYGB and 3 a laparoscopic adjustable gastric banding.

#### **3.2 Changes in clinical measures of obesity**

Table 1 shows the changes in clinical measures of obesity at 1 month, 6 months and 5 years following bariatric surgery. The greatest changes were seen at 6 months postoperatively and these were maintained at 5 years. The maximum %EWL ( $45 \pm 18\%$ ) was achieved at 6 month following surgery ( $P < 0.001$ ).

#### **3.3 Changes in cardiovascular risk factors**

Table 1 shows the changes in risk factors for all available subjects at 1 month, 6 months and 5 years after bariatric surgery. Significant reductions in both systolic and diastolic blood pressures were observed at 1 month. The mean systolic blood pressure decreased by  $10.9 \pm 4.3$  mmHg ( $P = 0.02$ ) and the mean diastolic blood pressure by  $7.3 \pm 2.5$  mmHg ( $P = 0.009$ ) at 1 month. No significant changes in blood pressure were recorded at 6 months and 5 year visits.



Total serum cholesterol concentration showed a decrease at 1 month but an increase at 5 years ( $P=0.034$ ). HDL cholesterol showed a similar trend to that of total cholesterol ( $P<0.001$ ). Significant changes in serum triglyceride level were observed at 6 months but there was no significant change in LDL cholesterol level.

The greatest change in mean HbA1c was observed at 6 months ( $P<0.001$ ). Mean HbA1c decreased by 1.0%, 1.7% and 1.0% at 1 month, 6 months and 5 years respectively ( $P<0.001$ ). Of those patients with type 2 diabetes, 71% achieved the National Institute of Health and Care Excellence (NICE) recommended target HbA1c of 7% at 5 years after bariatric surgery. The prevalence of complete remission of type 2 diabetes at 1 and 6 months and 5 years postoperatively were 27%, 44.7% and 35.5%, respectively ( $P<0.001$ ). The prevalence of partial remission of T2DM was 18%, 8% and 18.5% at 1 month, 6 months and 5 years respectively ( $P<0.001$ ).

### **3.4 Changes in medications**

Table 2 shows the changes in medication following bariatric surgery. The requirement for diabetes medication was significantly lower following surgery. A decrease in antihypertensive medication was also observed (68.9% at baseline versus 39.4% at 5 years), but this was not statistically significant ( $P=0.463$ ). The proportion of participants non longer requiring lipid-lowering medication was greatest at 5 years (35.6% at baseline versus 63.9% at 5 years) but this was not again statistically significant ( $P=0.0728$ ).

### **3.5 Changes in predicted 10-year cardiovascular risk**

The preoperative and postoperative QRISK2 scores were calculated using the age at the time of the visit. A significant reduction in 10-year predicted QRISK2 scores were observed across the temporal time points ( $P<0.001$ ). Table 3 shows the percentage change in absolute risk and relative risk. The QRISK2 calculator also provides relative risk, which is calculated by dividing the subject's predicted

risk score by a healthy subject's risk. A healthy person is defined as an individual with same age, sex and ethnicity; no adverse clinical indicators; a BMI of 25kg/m<sup>2</sup>; a systolic blood pressure of 125mmHg; and a cholesterol ratio of 4. Risk groups were categorised as follows: a score of <10% as low risk; a score of 10-19% as moderate; and a score of ≥20% as high risk. Chi-squared analysis revealed there was a significant difference in distribution of low, moderate and high-risk groups before and after bariatric surgery (P=0.042) (Figure 2).

Table 3 shows changes in the 10-year JBS3 score preoperatively, 1 and 6 months, and 5 years after bariatric surgery. The predicted 10-year JBS3 score was lower at 1 and 6 months, but at 5 years the score was similar to the preoperative level. After adjusting for age, a significant change in 10-year JBS3 score was observed at 5 years (P<0.001). No significant difference in the distribution of risk groups before and after bariatric surgery was observed.

### **3.6 Changes in predicted lifetime cardiovascular risk**

We observed that bariatric surgery had a positive impact not only on predicted 10-year CVD risk but also on the lifetime CVD risk. Table 4 shows changes in the QRISK lifetime score and JBS3 lifetime score. The maximum decrease in predicted lifetime CVD risk was observed at 5 years for both risk assessment models. Mean lifetime QRISK score decreased by 10.3%, 15.9% and 24.5% at 1 and 6 months, and 5 years respectively (P<0.001). Similar observations were seen for the lifetime JBS3 score: 11.8% reduction at 1 month; 15.3% reduction at 6 months; and 26.7% reduction at 5 years (P<0.001).

### **3.7 Baseline predicted CVD risk scores between attenders and non-attenders**

Table 5 shows baseline predicted CVD risk scores between two groups defined by their 5-year status. Attenders were those who had attended follow-up visit at 5 years. Non-attenders included those who were lost to follow-up or deceased. There were no differences in baseline risk scores between two groups.

#### 4. Discussion

Our pilot study has demonstrated that bariatric surgery is associated with a reduction in predicted 10-year CVD risk and predicted lifetime CVD risk despite the patients being years older. To our knowledge, no previous studies have examined the effect of bariatric surgery on predicted lifetime cardiovascular risk in individuals with impaired glucose regulation. Since the long-term effects of bariatric surgery on CVD events are unclear, there is a need to investigate the effect on predicted lifetime CVD risk following bariatric surgery. The 10-year CVD risk alone might miss a proportion of those with a high lifetime risk. Mackey et al, reported that 76% of bariatric patients with a low 10-year predicted risk had a high lifetime CVD risk<sup>22</sup>. We observed that bariatric surgery was associated with a continuous decrease in the lifetime CVD risk. Of note, age alone is a non-modifiable risk factor for the development of CVD. In a cohort of 3.6 million individuals age  $\geq 40$  years, the prevalence of any vascular disease increased significantly with each decade of life: 2% in 50 year olds, 3.5% in 60 year olds, 7.1% in 70 year olds, 13% in 80 year olds, and 22.3% in 90 year olds<sup>23</sup>. In our study, the maximum reduction in lifetime CVD risk (up to 26% reduction) was observed at 5 years despite the participants being 5 years older. We also observed a reduction in 10-year CVD risk: 54% reduction in QRISK2 score at 6 months and 24% reduction at 5 years. The relative risk reduction in QRISK2 was more pronounced at 5 years compared to absolute risk reduction (59% versus 24%). A significant reduction in predicted 10-year JBS3 score was observed at 5 years after adjusting age to baseline. Of interest, several studies have demonstrated that bariatric surgery is associated with a reduction in predicted 10-year CVD risk. The study by Batsis et al<sup>7</sup>, which included 197 RYGB patients and 163 control patients, used the FRS and the Prospective Cardiovascular Munster Heart Study (PROCAM) risk score. The 10-year FRS CVD risk score was lower at 3.3 years in the surgical group (from 7.0 to 3.5%;  $P < 0.001$ ) compared to the control group (from 7.1 to 6.5%;  $P < 0.001$ ). The PROCAM score was also lower in the surgical group (4.1 to 2.0%;  $P < 0.001$ ) when compared to the control group (4.4 to 3.8%;  $P = 0.08$ ). Aminian et al, demonstrated that RYGB was associated with a relative risk reduction of 27% for 10-year overall risk of CHD, stroke, and peripheral vascular disease; 20% for 10-year risk of CHD; 40% for 10-year risk of

myocardial infarction; 42% for 10-year risk of stroke; and 47% for 4-year risk of intermittent claudication in a cohort of 131 diabetic patients at 6 years <sup>4</sup>. Radwan et al reported that QRISK2 score were significantly lower in a cohort of 250 bariatric surgical patients at 24 months <sup>5</sup>.

The QRISK2 algorithm has been developed using routinely collected data from Primary Care practices across England and Wales. The study cohort consisted of 2.3 million patients aged 35-74 years from 531 practices. Validation studies demonstrated that QRISK2 identified high-risk patients more accurately than the modified Framingham score in the UK population <sup>14,24</sup>. Recent guidance from NICE recommends QRISK2 as the CVD risk assessment tool <sup>25</sup>. QRISK2-2016 utilises the following variables:- age, gender, ethnicity, Townsend score, smoking status, diabetes mellitus, family history of CVD, chronic kidney disease, atrial fibrillation, rheumatoid arthritis, blood pressure treatment, systolic blood pressure, total cholesterol, HDL-C and BMI <sup>26</sup>. Endpoints assessed in QRISK2 are fatal and non-fatal myocardial infarct, angina, coronary revascularization, fatal and non-fatal stroke, transient ischaemic attack and intermittent claudication. The QRISK lifetime <sup>14</sup> uses the same variables as QRISK2 and calculates cardiovascular risk up to 95 years of age. The JBS3 risk calculator was also developed in the UK and released in 2014. Variables used and endpoints assessed in JBS3 are similar as those in QRISK2 <sup>11</sup>.

Bariatric surgery aims to provide improvement in CVD risk factors and long-term weight loss. In our current study we observed a reduction of 44% in %EWL, 22.7% in body weight, 35.5% in prevalence of diabetes remission, a reduced proportion of glucose lowering medication, and improvement in CV biomarkers with an increase in HDL-C, and a decrease in total cholesterol to HDL-C ratio at 5 years. The increase in total cholesterol may be explained by the increase in HDL-C and the decrease in total to HDL-C ratio. A reduction in both systolic and diastolic blood pressure, lower anti-hypertensive medication and lipid lowering medication were observed but the differences were not statistically significant.

One of the limitations of our study is that these risk assessment tools have not previously been validated specifically in those with impaired glucose regulation and morbid obesity. Another limitation is the drop-out rate at 5 years. However, we observed no differences in baseline risk scores between participants with follow-up and those with lost-to follow-up or were deceased. In addition, significant reductions in risk scores were observed in the baseline-observation-carried-forward analysis (data not shown). A further limitation is the small number of patients included. Nevertheless, this study is the first study to examine the predicted lifetime CVD risk in bariatric surgical patients with impaired glucose regulation. We also have temporal measures from preoperative to 1 month, 6 months and 5 years postoperative period.

## **5. Conclusion**

In conclusion, the results of this pilot study indicate that bariatric surgery in patients with impaired glucose regulation is associated with a significant reduction in predicted 10-year and lifetime CVD risk in a population that was on average 5 years older compared to baseline. Furthermore, we observed long-term weight loss, excellent control of diabetes and less of a requirement for hypoglycaemic agents. This is a pilot study with a small sample size, and hence further studies with larger numbers are warranted.

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**Conflict of interests:** The authors declare that there is no conflict of interest associated with this manuscript.

## References

- [1] WHO. Obesity and overweight. <http://www.who.int/mediacentre/factsheets/fs311/en/>. 2015.
- [2] Sjöström L, Peltonen M, Jacobson P, Sjöström CD, Karason K, Wedel H, et al. Bariatric surgery and long-term cardiovascular events. *JAMA*. 2012;207:56-65.
- [3] Zhou X, Yu J, Li L, Gloy VL, Nordmann A, Tiboni M, et al. Effects of Bariatric Surgery on Mortality, Cardiovascular Events, and Cancer Outcomes in Obese Patients: Systematic Review and Meta-analysis. *Obes Surg*. 2016.
- [4] Aminian A, Daigle CR, Romero-Talamas H, Kashyap SR, Kirwan JP, Brethauer SA, et al. Risk prediction of complications of metabolic syndrome before and 6 years after gastric bypass. *Surg Obes Relat Dis*. 2014;10:576-82.
- [5] Radwan R, Al-Momani H, Stephens JW, Caplin S, Barry JD. Bariatric Surgery Is Associated with a Significant Reduction in 10-Year Cardiovascular Risk. *Bariatric surgical practice and patient care*. 2015;10:30-2.
- [6] Batsis JA, Romero-Corral A, Collazo-Clavell ML, Sarr MG, Somers VK, Brekke L, et al. Effect of weight loss on predicted cardiovascular risk: change in cardiac risk after bariatric surgery. *Obesity (Silver Spring)*. 2007;15:772-84.
- [7] Batsis JA, Sarr MG, Collazo-Clavell ML, Thomas RJ, Romero-Corral A, Somers VK, et al. Cardiovascular risk after bariatric surgery for obesity. *Am J Cardiol*. 2008;102:930-7.
- [8] Vogel JA, Franklin BA, Zalesin KC, Trivax JE, Krause KR, Chengelis DL, et al. Reduction in predicted coronary heart disease risk after substantial weight reduction after bariatric surgery. *Am J Cardiol*. 2007;99:222-6.
- [9] Torquati A, Wright K, Melvin W, Richards W. Effect of gastric bypass operation on Framingham and actual risk of cardiovascular events in class II to III obesity. *J Am Coll Surg*. 2007;204:776-82; discussion 82-3.
- [10] Marma AK, Berry JD, Ning H, Persell SD, Lloyd-Jones DM. Distribution of 10-year and lifetime predicted risks for cardiovascular disease in US adults: findings from the National Health and Nutrition Examination Survey 2003 to 2006. *Circ Cardiovasc Qual Outcomes*. 2010;3:8-14.
- [11] Board JBS. Joint British Societies' consensus recommendations for the prevention of cardiovascular disease (JBS3). *Heart*. 2014;100 Suppl 2:ii1-ii67.
- [12] Sjöström L, Lindroos AK, Peltonen M, Torgerson J, Bouchard C, Carlsson B, et al. Lifestyle, diabetes, and cardiovascular risk factors 10 years after bariatric surgery. *N Engl J Med*. 2004;351:2683-93.
- [13] Brindle P. QRISK2 vs Framingham. *Practitioner*. 2008;252:42.
- [14] Hippisley-Cox J, Coupland C, Robson J, Brindle P. Derivation, validation, and evaluation of a new QRISK model to estimate lifetime risk of cardiovascular disease: cohort study using QResearch database. *BMJ*. 2010;341:c6624.
- [15] Hippisley-Cox J, Coupland C, Vinogradova Y, Robson J, Minhas R, Sheikh A, et al. Predicting cardiovascular risk in England and Wales: prospective derivation and validation of QRISK2. *BMJ*. 2008;336:1475-82.
- [16] ADA. Standards of medical care in diabetes-2016. *Diabetes Care* 2016. p. S1.
- [17] Mallipedhi A, Min T, Prior SL, MacIver C, Luzio SD, Dunseath G, et al. Association between the preoperative fasting and postprandial C-peptide AUC with resolution of type 2 diabetes 6 months following bariatric surgery. *Metabolism*. 2015;64:1556-63.
- [18] Mallipedhi A, Prior SL, Dunseath G, Bracken RM, Barry J, Caplin S, et al. Changes in plasma levels of N-arachidonoyl ethanolamine and N-palmitoylethanolamine following bariatric surgery in morbidly obese females with impaired glucose homeostasis. *J Diabetes Res*. 2015;2015:680867.
- [19] Mallipedhi A, Prior SL, Barry JD, Caplin S, Baxter JN, Stephens JW. Changes in inflammatory markers after sleeve gastrectomy in patients with impaired glucose homeostasis and type 2 diabetes. *Surg Obes Relat Dis*. 2014;10:1123-8.

- [20] SOARD. Surgery for Obesity and Related Disease. <https://www.elsevier.com/journals/surgery-for-obesity-and-related-diseases/1550-7289/guide-for-authors>.
- [21] Buse JB, Caprio S, Cefalu WT, Ceriello A, Del Prato S, Inzucchi SE, et al. How do we define cure of diabetes? *Diabetes Care*. 2009;32:2133-5.
- [22] Mackey RH, Belle SH, Courcoulas AP, Dakin G, Deveney CW, Flum DR. Distribution of 10-year and lifetime predicted risk for cardiovascular disease prior to surgery in the Longitudinal Assessment of Bariatric surgery-2 study. *Am J Cardiol*. 2012;110:1130-7.
- [23] Savji N, Rockman CB, Skolnick AH, Guo Y, Adelman MA, Riles T, et al. Association between advanced age and vascular disease in different arterial territories: a population database of over 3.6 million subjects. *J Am Coll Cardiol*. 2013;61:1736-43.
- [24] Collins GS, Altman DG. Predicting the 10 year risk of cardiovascular disease in the United Kingdom: independent and external validation of an updated version of QRISK2. *BMJ*. 2012;344:e4181.
- [25] NICE. Cardiovascular disease: risk assessment and reduction, including lipid modification. CG181. 2015.
- [26] QRISK. <http://www.qrisk.org/index.php>.

**Table 1. Changes in clinical measure of obesity and risk factors at 1 month, 6 months and 5 years following**

| Clinical measure                 | Baseline<br>(n=45) | 1 month<br>(n=42) | <sup>a</sup> p | 6 months<br>(n=41) | <sup>b</sup> p |
|----------------------------------|--------------------|-------------------|----------------|--------------------|----------------|
| Weight (kg)                      | 150.4 ±34.7        | 131.6 ±28.3       | <0.001         | 115.2 ±26.1        | <0.001         |
| BMI (kg/m <sup>2</sup> )         | 54 ±13             | 47 ±9             | <0.001         | 41 ±9              | <0.001         |
| %EWL                             |                    | 24 ±10            | <0.001         | 45 ±18             | <0.001         |
| Waist (cm)                       | 138 ±17            | 130 ±20           | 0.001          | 120 ±19            | <0.001         |
| Systolic blood pressure (mm Hg)  | 136 ±17            | 125 ±15           | 0.02           | 132 ±14            | 0.23           |
| Diastolic blood pressure (mm Hg) | 79 ±9              | 71 ±8             | 0.009          | 76 ±10             | 0.239          |
| HbA1c (%)                        | 7.3 ±1.6           | 6.3 ±0.9          | <0.001         | 5.9 ±1.0           | <0.001         |
| HbA1c (mmol/mol)                 | 56.5 ±18           | 45.4 ±9.3         | 0.001          | 41.2 ±11.1         | <0.001         |
| Total cholesterol (mmol/L)       | 4.5 ±0.9           | 4.0 ±0.9          | 0.035          | 4.4 ±1.1           | 0.610          |
| HDL cholesterol (mmol/L)*        | 1.2 (1.0-1.4)      | 1.1 (0.9-1.3)     | 0.019          | 1.2 (1.0-1.35)     | 1              |
| TC:HDL-C*                        | 3.5 (2.9-4.6)      | 3.7 (2.8-4.6)     | 1              | 3.3 (3.0-4.5)      | 1              |
| LDL cholesterol (mmol/L)         | 2.4 ±0.7           | 2.2 ±0.8          | 0.324          | 2.5 ±1.0           | 0.758          |



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|                        |               |               |   |               |       |
|------------------------|---------------|---------------|---|---------------|-------|
| Triglyceride (mmol/L)* | 1.5 (1.1-2.4) | 1.4 (1.1-2.0) | 1 | 1.2 (1.0-1.6) | 0.031 |
|------------------------|---------------|---------------|---|---------------|-------|

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Data are presented as mean  $\pm$ SD.

\*Data are presented as median and interquartile range.

<sup>a</sup>p-value comparing baseline with 1 month

<sup>b</sup>p-value comparing baseline with 6 months

<sup>c</sup>p-value comparing baseline with 5 years

BMI: body mass index; % EWL: percentage excess weight loss.

**Table 2. Changes in medications**

|                                      | Baseline  | 1 month   | 6 months  | 5 years   | P value |
|--------------------------------------|-----------|-----------|-----------|-----------|---------|
| <b>Anti-diabetic medications</b>     |           |           |           |           |         |
| n                                    | 40        | 38        | 35        | 30        | 0.00073 |
| None (%)                             | 8 (20)    | 20 (52.6) | 21 (60)   | 19 (63.3) |         |
| Oral agents (%)                      | 18 (45)   | 14 (36.8) | 11 (31.4) | 7 (23.3)  |         |
| Insulin (%)                          | 9 (22.5)  | 3 (7.9)   | 3 (8.6)   | 1 (3.3)   |         |
| GLP-1 (%)                            | 8 (20)    | 1 (2.6)   | 0         | 3 (10)    |         |
| <b>Anti-hypertensive medications</b> |           |           |           |           |         |
| n                                    | 45        | 38        | 35        | 33        | 0.463   |
| None (%)                             | 14 (31.1) | 18 (47.4) | 18 (51.4) | 20 (60.6) |         |
| Monotherapy (%)                      | 13 (28.9) | 10 (26.3) | 7 (20)    | 6 (18.2)  |         |
| Dual therapy (%)                     | 11 (24.4) | 6 (17.1)  | 7 (20)    | 3 (9.1)   |         |
| Combinations (%)                     | 7 (15.6)  | 4 (10.5)  | 3 (8.6)   | 4 (12.1)  |         |
| <b>Lipid lowering medications</b>    |           |           |           |           |         |
| n                                    | 45        | 38        | 36        | 36        | 0.0728  |
| No (%)                               | 16 (35.6) | 19 (50)   | 20 (55.6) | 23 (63.9) |         |
| Yes (%)                              | 29 (64.4) | 19 (50)   | 16 (44.4) | 13 (36.1) |         |

P values calculated from Chi-squared analysis.

**Table 3. Changes in predicted 10-year CVD risk at 1 month, 6 months, and 5 years**

|                              | QRISK2 (n=29)      |                       |                        |         | QRISK2 (n=29)    |                       |                        |         |                   |
|------------------------------|--------------------|-----------------------|------------------------|---------|------------------|-----------------------|------------------------|---------|-------------------|
|                              | Absolute risk      | Change from baseline* | % change from baseline | P value | Relative risk    | Change from baseline* | % change from baseline | P value |                   |
| Baseline                     | 15.1<br>(9.8-17.4) |                       |                        |         | 4.8<br>(2.9-9.7) |                       |                        |         | 8.1<br>(5.1-11.1) |
| 1 month                      | 9.7<br>(5.0-12.8)  | 4.9<br>(0.2-6.7)      | 35<br>(4-59)           | 0.009   | 3.1<br>(1.6-6.8) | 1.7<br>(0.1-3.9)      | 35<br>(2-59)           | 0.026   | 4.8<br>(3.1-7.5)  |
| 6 months                     | 7.4<br>(3.0-14.2)  | 4.8<br>(1.4-9.5)      | 54<br>(11-69)          | <0.001  | 2.3<br>(1.4-3.6) | 1.7<br>(0.5-5.2)      | 52<br>(10-69)          | 0.001   | 4.9<br>(3.0-8.2)  |
| 5 years                      | 9.1<br>(5.9-14.2)  | 2.7<br>(0.6-7.9)      | 24<br>(5.5-53)         | 0.022   | 1.8<br>(1.2-3.1) | 3.2<br>(1.0-5.5)      | 59<br>(35-75)          | <0.001  | 8.0<br>(4.4-12.0) |
| 5 years<br>(age<br>adjusted) |                    |                       |                        |         |                  |                       |                        |         | 5.1<br>(2.3-12.0) |

**Table 4. Changes in predicted lifetime CVD risk at 1 month, 6 months and 5 years**

|          | QRISK lifetime (n=27) |                            |             | JBS3      |                            |
|----------|-----------------------|----------------------------|-------------|-----------|----------------------------|
|          | Mean ± SD             | Mean difference<br>(95%CI) | % reduction | Mean ± SD | Mean difference<br>(95%CI) |
| Baseline | 45.8±12.2             |                            |             | 48.4±13.1 |                            |
| 1 month  | 41.1±12.7             | 4.7 (2.2-7.1)*             | 10.3        | 42.7±13.5 | 5.7 (3.2-8.2)*             |
| 6 months | 38.5±11.7             | 7.3 (4.8-9.8)*             | 15.9        | 41.0±12.9 | 7.4 (4.9-9.9)*             |
| 5 years  | 34.6±8.7              | 11.2 (7.1-15.3)*           | 24.5        | 35.4±8.8  | 12.9 (8.8-17.0)*           |

Data are presented as mean ±SD.

\* A one-way repeated measures ANOVA followed by paired t-test revealed significant changes in predicted lifetime CVD risk at 1 month, 6 months and 5 years (p<0.001).

**Table 5. Baseline risk scores between attenders and non-attenders**

| Risk score      | Attenders (n=32) | Non-attenders (n=13) | P value |
|-----------------|------------------|----------------------|---------|
| QRISK2*         | 12.8 (9.7-17.4)  | 14.9 (7.1-19.5)      | 0.822   |
| JBS3 (10-year)* | 6.6 (4.0-11.0)   | 5.0 (3.6-9.6)        | 0.462   |
| QRISK lifetime  | 45.1 ±11.3       | 41.8 ±9.8            | 0.352   |
| JBS3 lifetime   | 47.9 ±11.8       | 48.1 ±11.8           | 0.951   |

Data are presented as mean ±SD.

\* Data are presented as median and interquartile range.

Figure 1

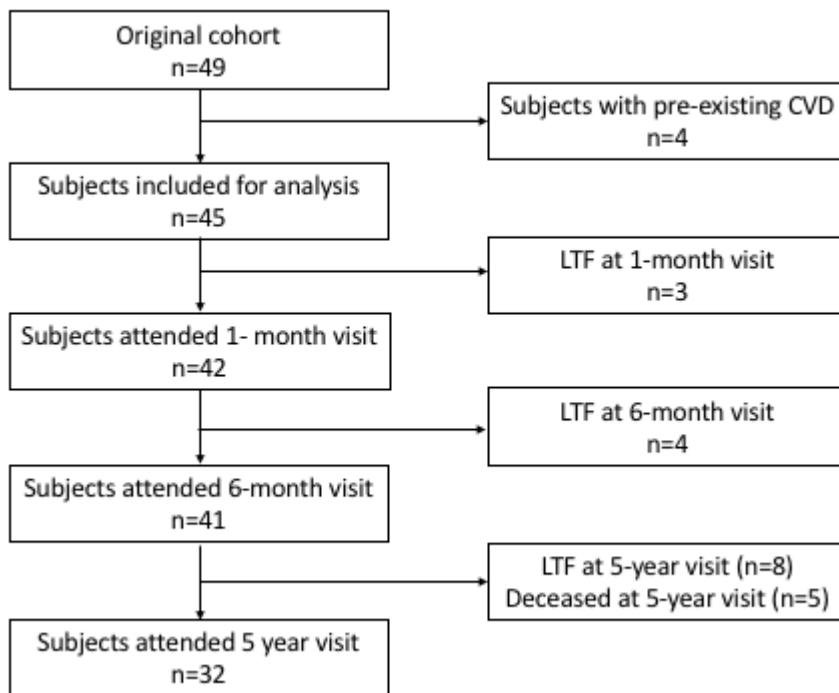
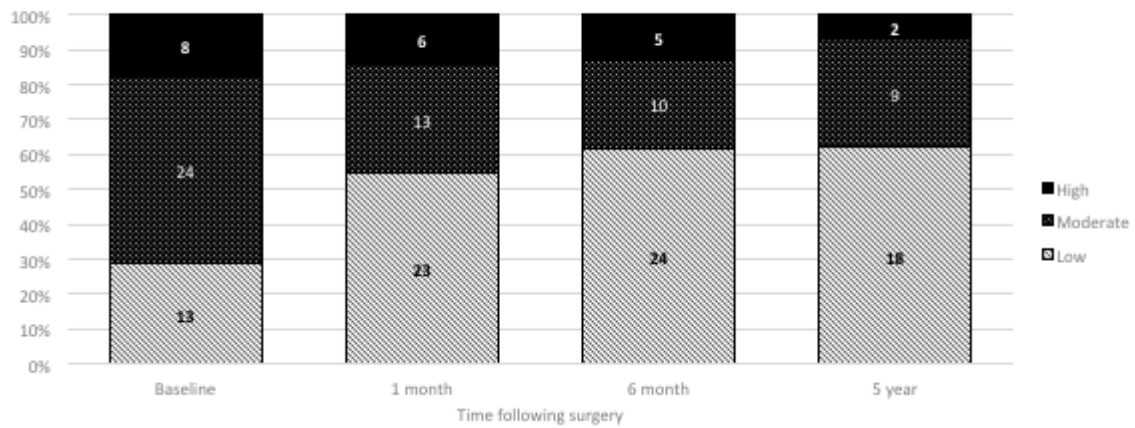


Figure 2



## Figure Legends

**Figure 1. Flow chart showing number of attenders and non-attenders at each visit**

LTF: Loss to follow-up

**Figure 2. Distribution of risk groups classified by QRISK2 score, before and 1 month, 6 months and 5 years after bariatric surgery**

Chi-squared analysis revealed a significant difference in distribution of risk groups before and after bariatric surgery (P=0.042).

Low risk group: score <10; Moderate risk group: score 10-19; High risk group: score  $\geq$ 20.