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## Physical Activity in Obese Type 2 Diabetes Following Gastric Bypass or Medical Management

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### Abstract

**Purpose**—To compare effects of Roux-en-Y gastric bypass versus a multi-disciplinary, group-based medical diabetes and weight management program on physical fitness and behaviors.

**Methods**—Physical behavior and fitness was assessed in participants of the study Surgery or Lifestyle With Intensive Medical Management in the Treatment of Type 2 Diabetes (SLIMM-T2D) (NCT01073020), a randomized parallel-group trial conducted at a U.S. academic hospital and diabetes clinic with 18–24-month follow-up. Thirty-eight type 2 diabetes patients with hemoglobin A<sub>1c</sub> above 6.5% and BMI 30–42 kg/m<sup>2</sup> were randomized to Roux-en-Y gastric bypass or medical program. A six-minute-walk-test to evaluate fitness, self-reported physical activity, standardized physical surveys, and cardiometabolic risk assessment were performed at baseline and after intervention.

**Results**—Both groups similarly improved six-minute-walk-test distance, with greater improvements in oxygen saturation and reduced heart rate following surgery. Self-reported physical activity improved similarly at 18–24-months following interventions, although exercise increased gradually following surgery, whereas early substantial increases in medical group were not fully sustained. Self-reported total and physical health were similar by Short Form-36, but improved more in the Impact of Weight on Quality of Life survey following surgery. Improvement in cardiovascular risk scores, HbA<sub>1c</sub>, and BMI were greater after surgery.

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**Conclusion**—In this small, randomized study, both interventions led to therapeutic lifestyle changes and improved objective and self-reported physical fitness. Greater improvements in heart rate, oxygen saturation, and perceived impact of weight on health were seen following surgery, which could be attributable to greater weight loss. Clinical importance of these improvements with greater weight loss warrants further investigation.

### Keywords

Type 2 diabetes; obesity; physical activity; physical fitness; bariatric surgery; Roux-en-Y gastric bypass

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## Introduction

Physical activity underlies fitness and well-being, weight maintenance or loss, diabetes prevention or management, and cardiometabolic health. Exercise lowers blood pressure(1), reduces need for blood pressure and cholesterol-lowering medications(2), and may improve mortality(3–6), although controversial in type 2 diabetes(2,7). Higher exercise capacity associates with reduced mortality, myocardial infarction, and revascularization rates(6,8). Multi-disciplinary, group-based programs effectively promote weight loss in pre-diabetes and type 2 diabetes(2,9). Increased physical activity contributes to weight loss following both non-surgical(10,11) and surgical interventions(12). Thus, physical activity and fitness are important determinants of health, but it remains uncertain how different diabetes and weight loss approaches impact longer-term change.

We compared effectiveness of metabolic surgery versus non-surgical approaches to diabetes and weight management by evaluating changes in objective measures of fitness using the six-minute walk test, and self-reported physical activity and patient-reported physical health outcomes over 18–24 months following randomization to Roux-en-y gastric bypass(RYGB) surgery or intensive medical diabetes and weight management(IMWM) interventions in obese patients with type 2 diabetes. We find two vastly different approaches to diabetes management both lead to improved objective and self-reported physical fitness and behaviors over 18–24 months, with some measures improving more following RYGB.

## Patients and Methods

### Trial Design, Randomization, and Intervention

To compare changes in physical activity and function following randomized allocation to RYGB versus a multidisciplinary, group-based medical diabetes and weight management program for obese patients with type 2 diabetes, we conducted a sub-study within the study Surgery or Lifestyle With Intensive Medical Management in Treatment of Type 2 Diabetes(SLIMM-T2D)(ClinicalTrials.gov Identifier:NCT01073020), a parallel-group trial with balanced (1:1) computer generated randomization allocated in blocks of four, stratified for body mass index (BMI) above or below 35 kg/m<sup>2</sup> at an outpatient clinic and a hospital setting within one university. The protocol was approved by the Institutional Review Board. An independent data monitoring committee reviewed participant safety. Trial design, population, and one year cardiometabolic findings have been described(13). Briefly, all

participants were obese (BMI 30–42 kg/m<sup>2</sup>), had established diagnosis of type 2 diabetes for 1-year, on 1 diabetes medication with baseline hemoglobin A<sub>1c</sub> (HbA<sub>1c</sub>) 6.5%, and considered medically appropriate for surgery or unsupervised exercise.

Participants randomized to IMWM were enrolled in WhyWAIT™ (Weight Achievement and Intensive Treatment), a multidisciplinary program for weight control and intensive diabetes management(14), modeled on successful programs in diabetes treatment or prevention(2,9), with diabetes medications adjusted to simultaneously promote weight loss and glycemic goals(13,14). Key aspects of this program include twelve weekly meetings in groups of 10–15 with: a) medication adjustments, b) structured, hypocaloric diet with six initial weeks of breakfast and lunch meal replacement using Boost Glucose Control™ (Nestle Medical Nutrition Inc.) and structured dinner menus, c) cognitive behavioral intervention, d) group education, and e) up to 300 minutes/week initially of graded, balanced, individualized exercise. Exercise plans incorporated a balanced mix of aerobic, resistance, and flexibility workouts, with 12-weekly 60-minute exercise sessions under supervision. Graded exercise counseling aimed to gradually advance time and intensity of physical activity weekly(11). A maintenance phase consisted of individual monthly counseling for the remainder of the first year, with follow-up over the subsequent year according to recommendations of clinical care providers.

Laparoscopic RYGB was performed using standard procedures(17). Participants were advised to follow a balanced diet. Calorie goals were not provided. Exercise as tolerated was recommended as part of good medical care.

Participants were evaluated by the clinical research team at baseline prior to intervention, at 3-months or 10% weight loss-whichever occurred first(‘early’ assessment), at 12-, and 18 to 24-months follow-up, when weight loss had stabilized. Participants were weighed and had fasting laboratory and complete physical fitness assessments.

### **Six-Minute Walk Test**

To estimate functional capacity and general physical fitness, a six-minute walk test(13) was performed. Participants walked as far as possible in six-minutes at a pace not causing discomfort, with total walking distance recorded. Heart rate and oxygen saturation(GO2 Achieve Oximeter, Nonin Medical, Inc. Plymouth, MN) were measured immediately after exertion.

### **Patient-Reported Physical Activity and Health Status**

Trained study-staff systematically asked participants to describe current types(walking, treadmill, elliptical, stepper, bicycle, swimming, yoga, Pilates, strength training, and other), duration(minutes-per-session), and frequency(sessions-per-week) of exercise, using validated questionnaires from Nurses’ Health Study and Health Professionals’ Follow-up Study to determine physical activity based on North American populations(15,16).

Patient-reported health status standard surveys were administered at baseline and follow-up visits. SF-36 measures general health status in two primary domains, physical and mental health component scores, and eight subscales(physical functioning, role-physical, bodily

pain, general health, vitality, social functioning, role-emotional, and mental health)(17). IWQOL-Lite assesses effects of weight on quality of life overall and in five areas: physical function, self-esteem, sexual life, public distress, and work(18). This analysis focused on total and physical function scales.

## Calculations

Cardiometabolic risk was calculated using the United Kingdom Prospective Diabetes Study(UKPDS) risk engine(<https://www.dtu.ox.ac.uk/riskengine/download.php>, accessed December 5, 2015)(19,20).

## Statistical Analysis

Sample size was estimated for the primary parent-study outcome to test the null hypothesis of equal resolution of hyperglycemia(13). This sub-study included participants enrolled in the parent trial. Baseline characteristics are presented as mean±standard deviation(SD) or median(interquartile range IQR), and outcome data as mean±standard error. Categorical variables were analyzed using chi-square analysis or logistic regression. Continuous variables were analyzed using paired or unpaired Student's t-test, or a longitudinal mixed model including treatment, time, and interaction effects. Each outcome was adjusted for baseline. Primary analysis was intention-to-treat, involving all randomly-assigned participants with at least one post-randomization assessment(modified per-protocol analysis). Pre-specified contrasts of baseline versus follow-up visit and between-group comparisons were performed at each visit. A sensitivity assessment using last observation carried forward is also presented. Results were considered significant at  $P<0.05$ . Statistical analysis was performed using STATA version 12.1(College Station, TX).

## Results

### Patient Demographics

Thirty-eight participants (RYGB=19, IMWM=19) were randomized and initiated intervention between March 2010 and September 2011. Baseline characteristics were similar(Table 1). 18–24 month assessments, with mean of 22.9 months, were available in 18 RYGB (95%) and 14 IMWM (78%) participants, with two from IMWM declining participation in the six-minute walk test but completing all other assessments(Figure 1).

### Six-Minute Walk Test

There was no difference in improvement in covered distance during six-minute walk test between RYGB and IMWM (group effect,  $P=0.862$ ) over 18–24 months(Figure 2A). RYGB improved covered distance from baseline to 18–24 months ( $34.2\pm 17.4$  meters,  $P=0.049$ ) similar to IMWM improvements ( $38.5\pm 20.9$  meters,  $P=0.067$ ) with no difference between groups at 18–24 month assessment ( $P=0.880$ ).

Overall, change in oxygen saturation by pulse oximeter was higher following RYGB ( $P=0.0001$ ). Group differences were driven by early and sustained improvement in oxygen saturation within RYGB ( $0.98\pm 0.37\%$ ,  $P=0.007$ ) while IMWM remained unchanged from baseline ( $0.12\pm 0.47\%$ ,  $P=0.806$ )(Figure 2B).

Heart rate immediately following six-minute walk, was lower in RYGB throughout follow-up ( $P=0.004$ )(Figure 2C). At 18–24 months, RYGB tended to have lower heart rate compared to baseline by  $-5.7\pm 3.3$  beats/minute ( $P=0.080$ ) versus a numeric increase ( $+6.0\pm 3.9$  beats/minute,  $P=0.124$ ) in IMWM, such that at 18–24 month assessments difference between groups was significant ( $P=0.021$ ).

### Physical Activity

Change from baseline in self-reported exercise differed between RYGB and IMWM over 18–24 months ( $P=0.003$ )(Figure 2D). At early assessment, RYGB had no change in self-reported exercise ( $P=0.345$ ), while IMWM increased exercise over 300% ( $P<0.0001$ ). Over two-years, RYGB slowly increased self-reported activity (by  $87.3\pm 38.6$  minutes/week,  $P=0.024$ ), while early increases within IMWM were incompletely sustained but remained increased from baseline ( $93.8\pm 44.9$  minutes/week,  $P=0.037$ ). At 18–24 months, there was no difference in improvement between groups ( $P=0.913$ ). At end-of-study, 41% of RYGB reported exercising equal to or more than the American Diabetes Association recommended 150 minutes/week(21), compared to 30% within IMWM ( $P=0.561$ ).

To assess relationships between weight change and improvement in measures of cardiorespiratory fitness(oxygen saturation and heart rate at end of 6-minute walk testing), we performed linear regression between these variables in the combined cohort at 18–24-months. Weight loss significantly correlated with improvement in oxygen saturation ( $R^2=0.20$ ;  $P=0.012$ ) and reduction in heart rate ( $R^2=0.18$ ;  $P=0.018$ ) after 6-minute-walk test(Figures 3A–3B, respectively).

### Patient-Reported Outcomes of Physical Health

Overall, groups differed for IWQOL-Lite scores with lower/better values in RYGB than IMWM over 18–24 months for both total and physical function subscale scores ( $P=0.0006$  and  $P<0.0001$ , Figure 4A–4B, respectively). For total IWQOL-Lite score, RYGB had a  $32.5\pm 4.0$ -point ( $P<0.0001$ ) reduction at 18–24-months, compared to a lesser, yet still highly significant decrease of  $18.3\pm 5.0$  ( $P<0.0001$ ) from baseline within IMWM. Improvement was greater for RYGB than IMWM at 18–24 months ( $P=0.025$ ). The physical function subscale mirrored this improvement with a within-group decrease of  $12.1\pm 1.4$  ( $P<0.0001$ ) for RYGB compared to the  $3.4\pm 1.6$  ( $P=0.04$ ) points decrease in IMWM, with significant difference between groups at 18–24 months ( $P=0.0001$ ).

There was no between-group difference in either SF-36 total score or its physical function scale over the study ( $P=0.614$  and  $P=0.208$ , Figure 4C–4D, respectively). For total SF-36 total score, RYGB improved from baseline ( $7.2\pm 3.4$  points,  $P=0.032$ ) compared to a smaller increase for IMWM ( $6.0\pm 4.2$  points,  $P=0.156$ ), although at 18–24 months no statistical difference between groups was observed ( $P=0.827$ ). The physical function scale paralleled the total SF-36 survey, with increase from baseline at 18–24 months in RYGB ( $13.7\pm 4.4$  points,  $P=0.002$ ) compared to no change ( $4.5\pm 5.5$  points,  $P=0.409$ ) in IMWM, with no between-group differences ( $P=0.193$ ).

## Cardiometabolic Measures

RYGB achieved a greater reduction in HbA<sub>1c</sub> ( $P=0.0003$ ) (Figure 5A) and weight ( $P<0.0001$ ) (Figure 5B) over 18–24 months. RYGB lowered HbA<sub>1c</sub> early, with sustained reductions of  $1.9\pm 0.3\%$  ( $P<0.0001$ ) at 18–24 months. Early improvements in HbA<sub>1c</sub> within IMWM were not fully sustained ( $-0.5\pm 0.4\%$ ,  $P=0.222$ ), resulting in greater reduction in HbA<sub>1c</sub> at end-of-study for RYGB ( $P=0.006$ ). RYGB had nadir weight at 12-months, which was largely sustained at 18–24 months with BMI reduction of  $-9.1\pm 0.8\text{ kg/m}^2$  ( $P<0.0001$ ). IMWM sustained early weight loss, reducing BMI to a lesser degree of  $-2.0\pm 0.9\text{ kg/m}^2$  ( $P=0.022$ ), with significant differences between groups at 18–24 months ( $P<0.0001$ ).

Additionally, patients randomized to RYGB had lower UKPDS risk scores for coronary heart disease (CHD,  $P=0.0016$ ), fatal CHD ( $P=0.002$ ), stroke ( $P=0.0065$ ), and fatal stroke ( $P=0.001$ ) at 18–24 months (Figure 5C).

## Adverse Events

No participant experienced severe hypoglycemia. Surgical arm serious adverse events included ischemic heart disease with coronary artery bypass surgery, cholelithiasis, new breast cancer, nephrolithiasis, acute kidney injury, exacerbated depression, panniculectomy, hip arthroplasty, and cervical osteophyte resection. In the nonsurgical arm, one participant had a resuscitated cardiac arrest, and three participants had presyncopal events.

## Discussion

This study evaluated whether obese persons with type 2 diabetes undergoing structured, multi-disciplinary, group-based exercise counseling and medical intensification of diabetes control would achieve and maintain greater improvement in physical activity and fitness than patients without intensive exercise counseling undergoing RYGB. While objective measures of fitness improved similarly in both groups, quantified by distance walked during six-minutes, there were greater improvements in oxygen saturation and heart rate following RYGB, which correlated with greater weight loss after surgery. Self-reported physical activity increased dramatically during the early intensive phase of the IMWM program, but was incompletely sustained whereby self-reported physical activity increased to a similar level in both groups over longer term.

Oxygen saturation does not limit six-minute walk distance following RYGB, where despite greater improvements in oxygen saturation over time after surgery, total distance covered during the walk test did not improve more. Oxygen saturation depends on pulmonary function, circulatory capacity, and end-organ oxygen extraction and demand. Oxygen saturation integrates health status across these domains. Difference in oxygen saturation and heart rate between groups may partly be attributed to differences in achieved weight. Lower oxygen saturation after six-minute walk test occurs in obese compared to lean dogs(22).

Exercise underlies prevention and treatment of diabetes and its co-morbidities, including obesity and cardiovascular disease(23–25). Physical activity increased following bariatric surgery in the Longitudinal Assessment of Bariatric Surgery(26,27), but changes were not compared with randomized intensive non-surgical intervention. Although previous studies



demonstrate a graded dose-response effect for exercise training on fitness(28) we were not able to demonstrate this relationship in between-group comparison as both groups increased objective and self-reported activity similarly and magnitude of weight loss, not physical activity, more closely related to the quantitative measures of fitness of improved oxygen saturation and lower heart rate.

The pattern of change in self-reported exercise differed between the groups. Early assessment occurred within a short postoperative time interval with reduced physical activity during surgical recovery while IMWM were participating in weekly group and supervised exercise sessions. Participants in the IMWM group may have reported higher physical activity due to successes of weekly interventions to increase amount of exercise performed, but there may also be a tendency for bias within the group to appear compliant with program recommendations. Nonetheless, both groups appear to plateau over 18–24-months in quantitative measures of fitness assessed by distance during the walk test, oxygen saturation and heart rate, albeit with greater improvement in the latter indices following RYGB.

Patient-reported outcomes pertinent to impact of weight on quality of life improved similarly early after both interventions, but continued to improve only in RYGB. In contrast, total quality of life and physical function assessed by SF-36 were similar between groups over follow-up despite multiple greater improvements in objective measures following surgery. This may be due to lasting effects of education and support received during the IMWM program, which edifies the patient and prompts them to perceive maintaining physical ability in spite of weight regain, discordant to the programmatic teaching of the importance of physical fitness and weight maintenance or further loss for sustained improved health. Discordance between the IWQOL-Lite and SF-36 may be due to focus of the first survey on the specific role of weight on quality of life, and the second broader aspects of health. However in general, SF-36 more closely mimics self-reported changes in activity.

It is important to put the IMWM program in context as RYGB was not compared to standard of care, and physical fitness and activity were assessed following what would be considered optimal multi-disciplinary group-based program intervention. The magnitude and sustained weight loss in the IMWM group would be considered clinically successful weight management, comparable to that in the Diabetes Prevention Program and LookAHEAD studies(2,9), albeit less than for RYGB. Randomization and IMWM intervention occurred anteceding Food and Drug Administration approval of new weight loss agents including lorcaserin, the phentermine/topiramate combination, and liraglutide and similarly predating approval or widespread availability of sodium-glucose co-transporter 2 (SGLT2) inhibitors and GLP-1 agonists respectively, which can improve both weight and glycemia. It is possible physical fitness and activity would improve more with these therapeutics. Glycemic improvements were similar between groups early following intervention but sustained only in RYGB, despite the use of fewer anti-diabetic medications(13). Anecdotally, participants in the IMWM group often indicated feeling equipped with the knowledge to regain control of their diabetes through lifestyle measures and commitment to change, which appeared in some instances to delay intensification of medical management. Intensification of pharmacologies may explain the second downward trend in HbA<sub>1c</sub> beyond 18 months within IMWM.

Exercise and pharmacological interventions appear to have similar morbidity outcomes for secondary prevention of coronary heart disease(29). In contrast UKPDS risk scores for stroke and fatal coronary heart disease were lower following RYGB than IMWM(13), similar to reported non-randomized studies(30,31). The UKPDS risk equation accounts for many conventional vascular risk factors, but does not include weight loss, improved glycemic control, or changes in cardiorespiratory fitness. Thus, the UKDPS risk engine may underestimate long-term benefits of RYGB if physical activity and fitness independently contribute to further reduce cardiovascular risk.

This work is limited by the small number of participants. Participants were systematically questioned about type and duration of exercise in the week prior to study visits, which may not accurately reflect week-to-week variability. Pedometers or accelerometers were not used. Patients may over-report physical activity or feeling more active(32) knowing they are expected to be more active, a bias applicable to both groups. Consistent with accuracy of self-reports, objective measures of fitness assessed by distance during six-minute walk test parallel self-reported activity. Though not a focus of this study, the dietary approaches to diabetes and weight management differed fundamentally, with substantial differences between groups in regard to appetite, satiety, caloric intake, and degree of malabsorption in RYGB.

In conclusion, this study characterizes fitness and physical activity following randomization to RYGB or IMWM using subjective and objective measures. Despite 3-months of group exercise sessions and intensive coaching in IMWM, we demonstrate comparable improvements in fitness and level of physical activity, as assessed by total covered distance during six-minute walk test, self-reported physical activity, and SF-36 total and physical function scores two years following randomization to RYGB or an intensive diabetes and weight management program. Improvements in oxygen saturation and heart rate are greater after surgery, potentially related in part to the greater magnitude weight lost. Similarly, quantitative patient-reported outcomes show greater improvements in IWQOL-Lite total and physical function scores. Finally, our results demonstrate cardiometabolic risk estimates improved more after surgery. Understanding and removing barriers to develop and sustain physical activity may improve clinical management in obese patients with type 2 diabetes.

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## Abbreviations

**BMI** body mass index



<b>HbA1c</b>	hemoglobin A1c
<b>IMWM</b>	intensive medical diabetes and weight management program
<b>IWQOL-Lite</b>	Impact of Weight on Quality of Life
<b>IQR</b>	interquartile range
<b>LOCF</b>	last observation carried forward
<b>RYGB</b>	Roux-en-Y gastric bypass
<b>SF-36</b>	Short Form-36
<b>SD</b>	standard deviation
<b>SLIMM-T2D</b>	Surgery or Lifestyle With Intensive Medical Management in the Treatment of Type 2 Diabetes
<b>T2D</b>	Type 2 diabetes
<b>UKPDS</b>	United Kingdom Prospective Diabetes Study

### Additional Abbreviations in Tables

<b>M</b>	male
<b>F</b>	female
<b>W</b>	white
<b>AA</b>	African American
<b>As</b>	Asian
<b>NR</b>	not reported
<b>BPM</b>	beats per minute

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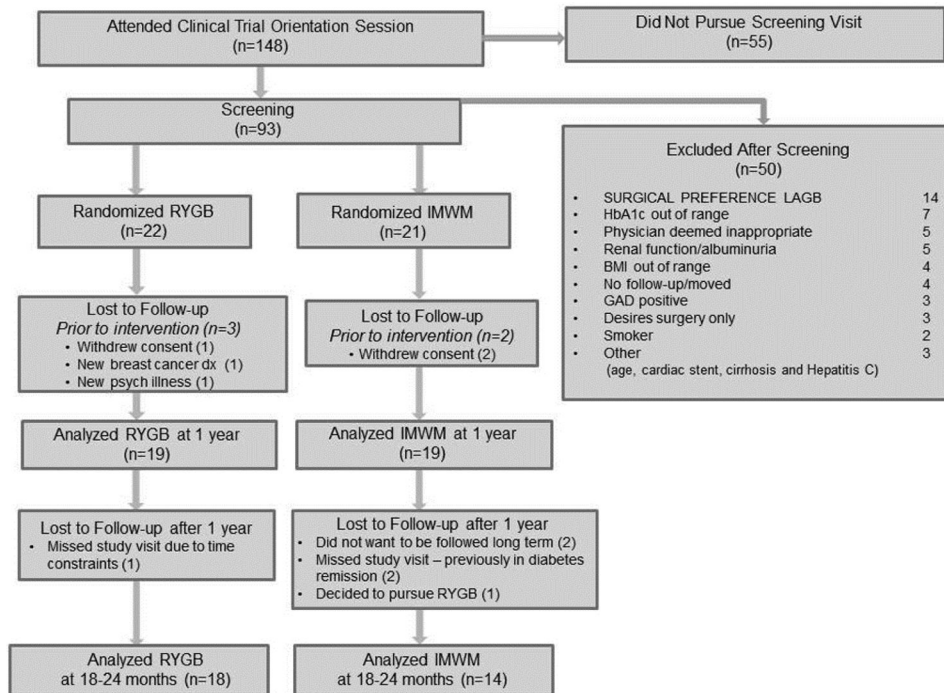
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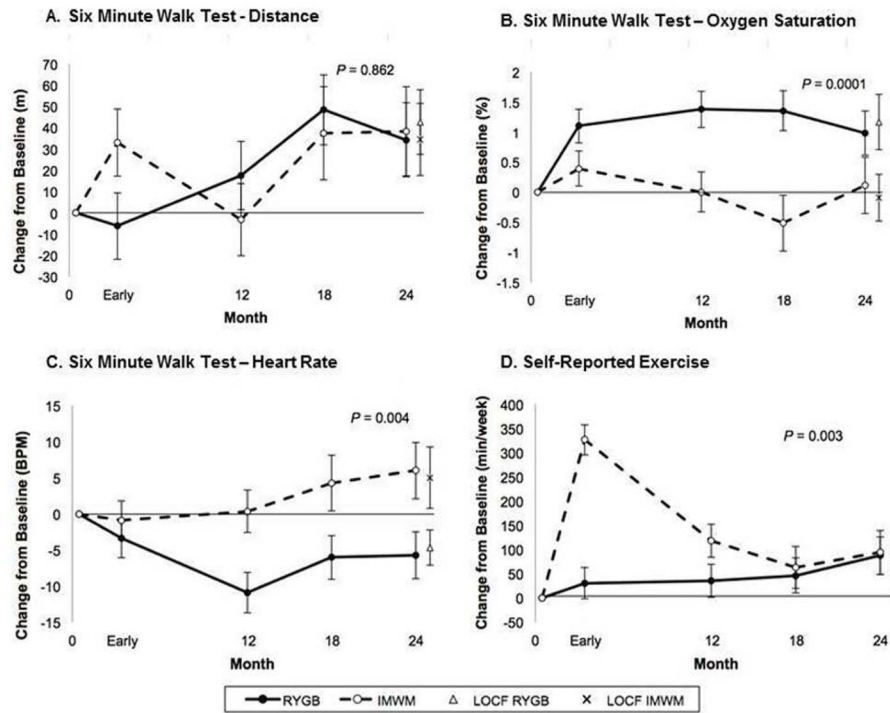
**Bullets**

- Type 2 diabetes patients randomized to gastric bypass surgery or multidisciplinary, group-based medical diabetes and weight management based interventions similarly improved fitness, measured by six-minute-walk-test distance, self-reported physical activity, and total and physical health scores by Short Form-36 over 18–24 months follow-up.
- Improvements in oxygen saturation and heart rate recovery following six-minute-walk-test, Impact of Weight on Quality of Life survey responses, HbA<sub>1c</sub>, BMI, and cardiometabolic risk scores were greater after surgery.



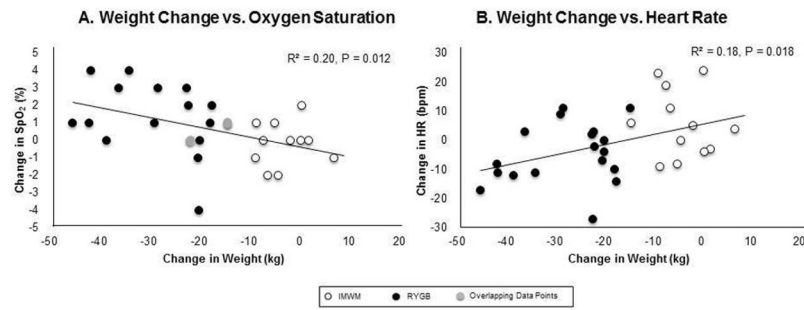
**Figure 1. Enrollment, Randomization, and Retention of the Study Participants**

Consort diagram detailing enrollment, randomization, and retention of participants. All participants randomized and initiating intervention in the primary trial were eligible for the ancillary investigation on physical activity in this report. Abbreviations used in reasons for exclusion after screening: LAGB indicates laparoscopic adjustable gastric band; HbA<sub>1c</sub>, hemoglobin A<sub>1c</sub>; BMI, body mass index; GAD, antiglutamic acid decarboxylase antibody-positive.



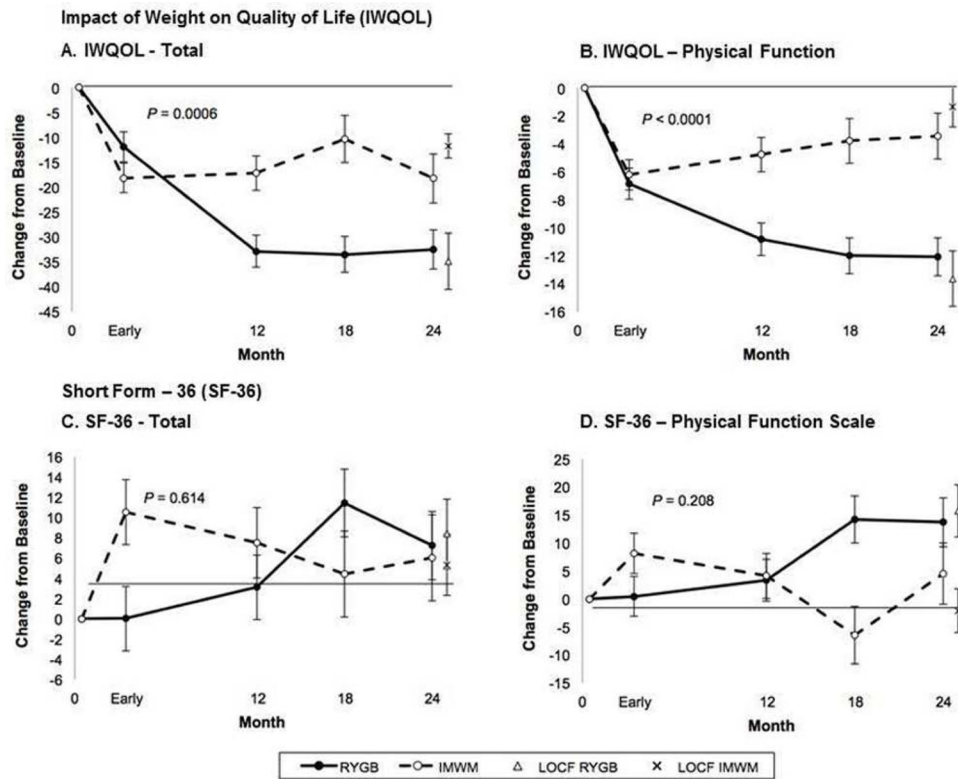
**Figure 2. Changes in Six Minute Walk Test and Self-Reported Exercise Measures**  
 (A) Six Minute Walk Test – Distance. Difference in walking distance in meters, (B) Six Minute Walk Test – Oxygen Saturation. Change in oxygen saturation (SpO<sub>2</sub>, %), and (C) Six Minute Walk Test – Heart Rate. Change in heart rate in beats per minute, immediately after 6-minute walk test and (D) Self-Reported Exercise. Self-reported exercise in minutes per week, at early, 12-month, 18-month, and 24-month time points compared between patients participating in the intensive medical and weight management or undergoing RYGB surgery. Note: “Early” time point is defined in “Trial Design, Randomization, and Intervention” section as after participants lost 10% of their baseline weight or at the 3-month mark, whichever occurred first. Mean and standard error are shown. (●) Roux-en-Y gastric bypass (RYGB), (○) Intensive medical weight management (IMWM), (X) Last observation carried forwards (LOCF) for RYGB group, (◇) Last observation carried forwards (LOCF) for IMWM group. Abbreviations: beats per minute (BPM), meters (m), minutes per week (min/week). P-values represent the difference between groups over 24 months in mixed model analysis.





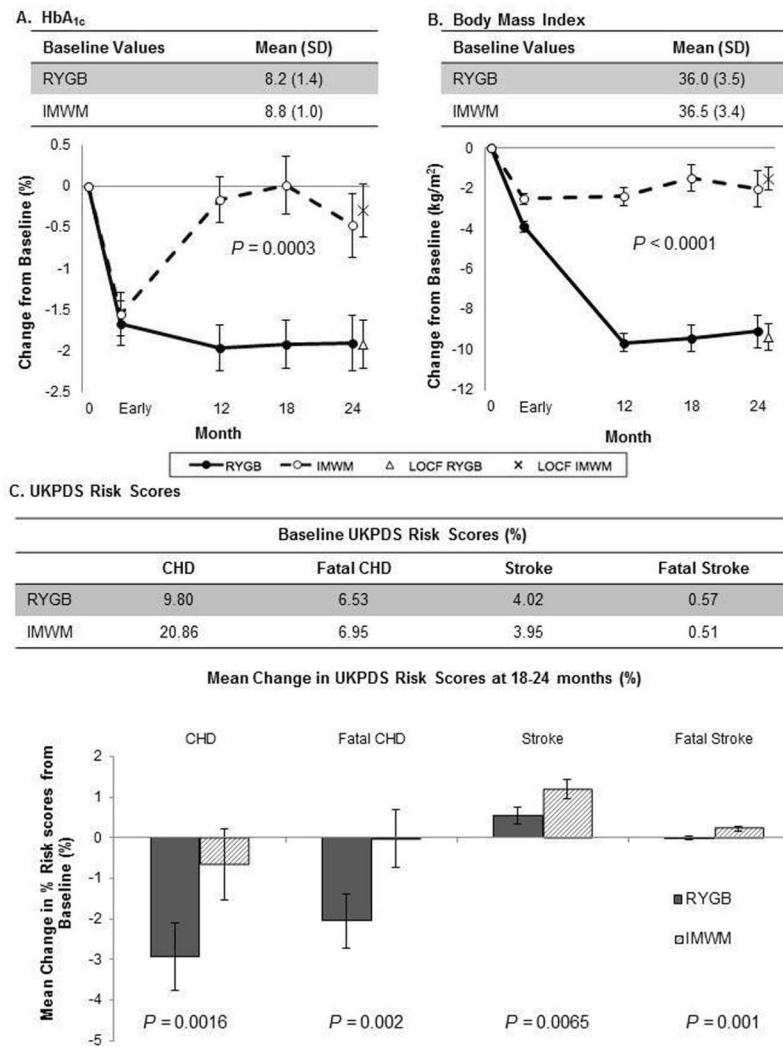
**Figure 3. Association Between Weight Change and Improvement in Measures of Cardiorespiratory Fitness**

(A) Weight Change vs. Oxygen Saturation. Association between change in weight and change in oxygen saturation immediately following six-minute walk test between 18 and 24 months from intervention in both groups. (B) Weight Change vs. Heart Rate. Association between change in weight and heart rate immediately following six-minute walk test between 18 and 24 months from intervention in both study groups. (●) Roux-en-Y gastric bypass (RYGB), (○) Intensive medical weight management (IMWM), (●) Overlapping data from two participants, one from RYGB, one from IMWM.



**Figure 4. Patient Reported Outcomes of Physical Health**

Change in patient-reported impact of weight on quality of life (IWQOL) and Short Form-36 (SF-36) total scores and physical function domains over time in Roux-en-Y gastric bypass (RYGB) and intensive medical weight management (IMWM) groups. (A) IWQOL total score and (B) IWQOL physical functioning subscale, and (C) SF-36 total score and (D) SF-36 physical function subscale at early, 12-month, 18-month, and 24-month time points in both study groups. Note: “Early” time point is defined in “Trial Design, Randomization, and Intervention” section as after participants lost 10% of their baseline weight or at the 3 month mark, whichever occurred first. Mean and standard error are shown. (●) Roux-en-Y gastric bypass (RYGB), (○) Intensive medical weight management (IMWM), (X) Last observation carried forwards (LOCF) for RYGB group, (◇) Last observation carried forwards (LOCF) for IMWM group.  $P$ -values represent the difference between groups over 24 months in mixed model analysis.



**Figure 5. Cardiometabolic Changes Following RYGB and Intensive Medical Weight Management**

(A) Change in Hemoglobin A<sub>1c</sub> and (B) Body Mass Index at early, 12-month, 18-month, and 24-month time points in patients randomized to RYGB or the intensive medical and weight management program. Note: “Early” time point is defined in “Trial Design, Randomization, and Intervention” section as after participants lost 10% of their baseline weight or at the 3 month mark, whichever occurred first. Mean and standard error are shown. (●) Roux-en-Y gastric bypass (RYGB), (○) Intensive medical weight management (IMWM), (X) Last observation carried forwards (LOCF) for RYGB group, (◇) Last observation carried forwards (LOCF) for IMWM group. *P*-values represent the difference between groups over 24 months in mixed model analysis. (C) UKPDS Risk Scores at 18–24 months in the two study cohorts. Baseline scores are indicated in the table at top, and change scores (baseline to 18–24 months) in the bar graphs below. *P*-values indicate differences in change scores between groups.

**Table 1**

## Baseline Demographics and Clinical Characteristics

	<b>RYGB</b>	<b>IMWM</b>
<b>Gender (M/F)</b>	6 / 13	9 / 10
<b>Age (yr)</b>	50.7 ± 7.6	52.6 ± 4.3
<b>Race (W/AA/As/NR)</b>	14 / 3 / 1 / 1	11 / 8 / 0 / 0
<b>BMI (kg/m<sup>2</sup>)</b>	36.0 ± 3.5	36.5 ± 3.4
<b>Weight (kg)</b>	104.6 ± 15.5	102.7 ± 17.0
<b>T2D duration (yr)</b>	10.6 ± 6.6	10.2 ± 6.1
<b>HbA<sub>1c</sub> (%)</b>	8.2 ± 1.4	8.8 ± 1.0
<b>Exercise (minutes/week)<sup>a</sup></b>	37.5 (0–135)	0.0 (0–60)
<b>6 minute walk test</b>		
<b>Distance (meter)</b>	458.7 ± 65.5	466.7 ± 55.9
<b>Oxygen Saturation (%)<sup>b</sup></b>	96.5 ± 1.4	96.2 ± 2.1
<b>Heart Rate (bpm)<sup>b</sup></b>	106.4 ± 16.7	103.5 ± 16.1
<b>Quality of Life measures</b>		
<b>IWQOL – Total</b>	81.5 ± 26.4	68.7 ± 17.7
<b>IWQOL – Physical Function</b>	28.7 ± 9.6	22.9 ± 7.0
<b>SF-36 – Total</b>	66.2 ± 17.7	71.6 ± 12.4
<b>SF-36 Physical Function</b>	61.3 ± 19.7	68.6 ± 13.2

All data are mean ± SD, unless noted. Groups were similar at baseline and each measure's outcome analysis was adjusted for baseline.

<sup>a</sup>Minutes of exercise was reported as median (25th percentile – 75th percentile)

<sup>b</sup>Oxygen saturation and heart rate were measured immediately following the 6-minute walk.

Abbreviations in order of appearance: M –male, F –female, W - white, AA - African American, As - Asian, NR - not reported, BMI - body mass index, T2D - type 2 diabetes, HbA<sub>1c</sub> - hemoglobin A<sub>1c</sub>, BPM –beats per minute, IWQOL - Impact of Weight on Quality of Life-Lite, SF-36-Short Form-36