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# Weight loss following an intensive dietary weight loss program in obese candidates for bariatric surgery: The retrospective RNPC® cohort

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ABSTRACT

*Aim:* Bariatric surgery is the most effective treatment for obesity. However, less than 1% of eligible patients undergo bariatric surgery annually. Here we evaluated the weight loss effectiveness of an intensive non-surgical weight loss program in patients that would qualify for bariatric surgery.

*Methods:* Patients eligible for bariatric surgery (n = 1460) (BMI ≥ 40 or BMI ≥ 35 kg/m$^2$ plus comorbidities) who were enrolled in a dietary weight loss intervention, the RNPC® program, were compared to a cohort of bariatric surgery patients in terms of weight loss outcome.

*Results:* The 663 patients completing the RNPC® program (35% dropout and 20% ongoing) lost 20.2 ± 11.8 kg corresponding to a reduction of 47% of the excess weight and a percentage weight loss from the initial weight of 18% after a mean period of 18.6 ± 9.1 months. Weight loss 18 months after bariatric surgery (n = 61) was 42.5 ± 15.8 kg corresponding to a reduction of 74% of excess weight and a percentage weight loss from the initial weight of 32%.

*Conclusion:* Although bariatric surgery results in a more pronounced weight loss, a clinically important weight loss can be obtained in patients that would qualify for bariatric surgery following an intensive non-surgical weight loss program. This retrospective analysis calls for randomized trials that compare the long-term cost-effectiveness between the RNPC® program and bariatric surgery.

## 1. Introduction

Given that the prevalence of overweight and obesity has reached epidemic proportions with more than half of the world's population being overweight or obese (World Health Organization, 2018), there is a need for efficacious and cost-effective weight loss interventions with long-term effects. Bariatric surgery is currently the most effective treatment for obesity and its associated co-morbidities, as it produces a greater and more sustained weight loss than other non-surgical weight loss strategies (Cummings et al., 2016; Mingrone et al., 2015; Schauer et al., 2017). Due to the cost and risk of complications following bariatric surgery, this intervention is considered a final option when conventional treatments do not result in permanent weight reductions. Behavioral approaches, such as dietary modification and exercise, should be the first-choice therapeutic option for obesity. Therefore, weight loss therapies that facilitate long-term weight loss and weight loss maintenance, to achieve a permanent weight reduction, are needed.

Patients who obtain weight loss through surgery lose on average 30% of their initial body weight within the first postoperative year, dependent on the type of surgery performed (Bergh et al., 2016; Sjöström et al., 2012). Behavioral approaches typically result in a more modest weight loss of approximately 5–10% in overweight and obese patients after an intervention period of 1–2 years (Foster et al., 2010; Wadden et al., 2009). However, when using more intensive weight loss interventions, with sustained support and nutritional guidance and focus on both weight loss and weight loss maintenance, weight loss of up to 16% have been reported in patients with severe obesity over an average period of 17 months (Anderson et al., 2007).

We recently presented weight loss outcomes from the Rééducation Nutritionnelle et Psycho-Comportementale (RNPC®) program. The RNPC® program is a novel dietary approach that involves intensive medical follow-up through blood analyses and constant interaction of the RNPC® center with patients' physician(s), frequent nutritional

*Abbreviations:* BMI, Body mass index; DXA, dual-energy X-ray absorptiometry; HDL-cholesterol, hemoglobin A1c, (HbA1c), high-density lipoprotein cholesterol; LDL-cholesterol, low-density lipoprotein cholesterol; RNPC®, Rééducation Nutritionnelle et Psycho-Comportementale; RYGB, Roux-en-Y gastric bypass

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consultations of patients and increased focus on weight loss maintenance (Thorning et al., 2018). The program is mainly intended to patients with overweight-associated diseases. When 2013 AHA/ACC/TOS Guideline for the Management of Overweight and Obesity in Adults consider that a sustained weight loss of about 5%–10% of initial body weight represents a definite degree of success (Jensen et al., 2014), the RNPC® program was effective for both short- and long-term weight loss. Weight loss of ~11% and ~17% was reported after an average period of 3.4 and 8.2 months respectively (Thorning et al., 2018). Furthermore, absolute weight loss was found to be largest among patients with larger initial BMI (Christensen et al., 2019; Thorning et al., 2018).

Therefore, the aim of the present study was to compare the weight loss effectiveness of the RNPC® program in patients that would qualify as candidates for bariatric surgery, with a group of patients undergoing bariatric surgery. Within the cohort of RNPC® patients qualifying for bariatric surgery, we furthermore investigated potential differences in changes in anthropometric and metabolic parameters between successful and less successful patients as well as potential pre-treatment factors influencing successful weight loss outcome.

## 2. Subjects, materials and methods

### 2.1. The RNPC® program

#### 2.1.1. Design

The RNPC® program is a novel ongoing weight loss program managed by 71 RNPC® centers distributed across France and has previously been described (Thorning et al., 2018). During the program, frequent measurements and nutritional consultations of patients are carried out every second week at the RNPC® center with a trained dietician. The program starts with a weight loss phase where a rapid weight loss is achieved. The patient determines his/her target weight loss in agreement with the dietician and the physician. When the objective is reached, the weight loss phase is followed by a weight stabilization phase, during which energy intake is gradually increased in five steps. Between each of the five steps of the stabilization phase, energy intake is increased according to the calculation: next energy level = previous energy level + (post-weight loss energy requirement – weight loss energy intake)/5. Post-weight loss energy requirement was determined by the Black's formula (Black et al., 1996) using a sedentary physical activity level of 1.375. At the last stabilization phase, energy intake matches the post-weight loss energy requirement thereby energy balance is achieved. The phases of the RNPC® program are designed to be of individual-specific time-duration depending on the size of the achieved weight loss. For each one kg body weight lost during the initial weight loss period, one week is added to the weight stabilization phase. For example, a person achieving a 15-kg weight loss during the weight loss phase would have three weeks in each of the five steps in the stabilization phase, thus a total of 15 weeks in the stabilization phase. The RNPC® program was designed to be very dynamic and manageable in real life, in order to support the patients in completing the program and hence achieving weight loss and weight loss maintenance. Therefore, in case of weight regain during the program, the patients were allowed to relapse to an earlier energy level of their program. In addition, more than one weight loss phase could take place if needed, and patients could participate in the program more than once.

#### 2.1.2. Patients

The majority of the patients in the RNPC® program were referred to the program by their physicians, because of overweight or obesity while having at least one body weight-related co-morbidity. However, patients could also join the program through word of mouth, flyers, or the RNPC® Internet site, followed by written consent from the patient's physician.

There were no exclusion criteria based on medication or medical conditions in the RNPC® program. The only exclusion criterion was pregnancy. However, patients with age < 18 and > 65 years, BMI < 35, or < 40 without hypertension or diabetes were excluded in the current analyses to obtain a cohort of subjects that would be suitable as candidates for bariatric surgery.

#### 2.1.3. Diet

The RNPC® weight loss diet is composed of daily intake of vegetables, animal protein (from meat, fish, eggs or shellfish), and commercially available meal supplements in the form of snacks (biscuits, cereal bars, bread, crackers, soups, omelets, drinks and desserts) which the patients can eat whenever they want. The weight loss diet targets an energy intake of 800 kcal/day in women and 1000 kcal/day in men, and a macronutrient composition of 60% proteins (1.5 g/kg in men and 1.2 g/kg in women), 25% low-GI carbohydrates, and 15% fats. The RNPC® meal supplements were selected to support a high level of high-quality proteins (containing an average of 110 kcal, 15.8 g proteins, 2.4 g carbohydrates, 5.4 g fats, and 2.3 g fibers, for an average serving size of 30 g) in the diet and these were fortified with vitamins and minerals in order to avoid deficiencies caused by a low energy intake. In addition, the products comply with the requirements specified by the European Food Safety Authority (EFSA Panel on Dietetic Products Nutrition and Allergies (NDA), 2015). During the weight loss phase, the RNPC® meal supplements contribute approximately 40% of the total energy intake. During the weight stabilization phases of the RNPC® program, the intake of meal supplements gradually decreases as the patients' normal diet was reintroduced by the dieticians; however, with an increased focus on dietary sources of high-quality proteins. Energy percentage from dietary proteins gradually decreases during the course of the weight stabilization phase, and macronutrient composition of 25% proteins, 45% carbohydrates and 30% fats is targeted at the end of the weight stabilization phase. The cost for the RNPC® program for the patients corresponded to the price of the meal supplements, and the individual consultations was included in this price.

#### 2.1.4. Measurements and calculations

Body weight and body fat percentage were measured at baseline, as well as at each follow-up visit at the dieticians by use of a calibrated bioelectrical impedance scale (Beurer BG42, Ulm, Germany). The percentage of body weight lost as fat-free mass was calculated as: (Δfat-free mass/Δweight) x 100%. Height was measured to the nearest cm at baseline using a height gauge. Body mass index (BMI) was calculated with the formula: body weight [kg]/(height [m])$^2$. Loss of excess weight (%) was calculated with the formula: (Δweight/excess weight) x 100%, where excess weight was defined as the baseline weight minus ideal body weight based on BMI of 25 kg/m$^2$. We defined successful weight loss as excess weight loss ≥ 60%, and less successful weight loss as excess weight loss ≤ 30%. Waist circumference was measured to the nearest cm at the natural waist. However, for patients with abdominal adiposity with no visible natural waist, the measurement was taken at the level midway between the lowest rib and the iliac crest, approximately 2–5 cm above the navel.

A 12-h fasting blood sample was drawn at baseline and after the weight-stabilization phase. The blood samples were analyzed for plasma glucose, hemoglobin A1c (HbA1c), high-density lipoprotein cholesterol (HDL-cholesterol), low-density lipoprotein cholesterol (LDL-cholesterol), total cholesterol, and triglycerides. Methods used for blood sample analyses were all validated according to the general requirements defined by the NF EN ISO 15189 and NF EN ISO/IEC 17025 standards for routine blood sample analysis. All data was entered in MySQL 5.7 database, and the database was managed by the IT consultant company Oriolis (Villeurbanne, France).

### 2.2. The bariatric surgery program

We included two cohorts of Roux-en-Y gastric bypass (RYGB) and sleeve gastrectomy patients – the ERGEM cohort and the GO Bypass cohort (Christensen et al., 2018; Schmidt et al., 2016). Patients were enrolled in the bariatric surgery program from 2009 to 2015 at two different bariatric clinics in Denmark, Køge Hospital and Hvidovre Hospital. The program included a mandatory 8% preoperative weight loss as preparation for bariatric surgery and nutritional counseling both before and after receiving bariatric surgery. The ERGEM cohort was randomized to follow a low-calorie diet (four powder meals, skimmed milk, vegetables, and low-fat yoghurt, ~1030 kcal/d) for 7 or 11 weeks in order to obtain the 8% weight loss before surgery. No specific diet was prescribed to the GO Bypass cohort.

Besides contraindications for bariatric surgery, exclusion criteria based on medication or medical conditions included diabetes mellitus, thyroid dysfunction, hypothalamic or known genetic etiology of obesity in the ERGEM cohort. There were no exclusion criteria based on medication or medical conditions in the GO Bypass cohort.

Body weight, height, waist circumference, and body composition using dual-energy X-ray absorptiometry (DXA) were measured before the preoperative 8% weight loss and 18 months after surgery. Body weight was measured to the nearest 0.1 kg, waist circumference was measured twice to the nearest 0.5 cm and the average was used, and height was measured to the nearest 0.5 cm using a wall-mounted digital stadiometer. DXA measurements were made using half-body scans (Lunar iDXA, Encore software version 12.3). Excess weight loss was calculated with ideal body weight defined as a BMI of 25 kg/m$^2$.

#### 2.2.1. Statistical methods

Baseline characteristics were summarized as mean ± standard deviation (SD), median (interquartile range [IQR]), or as proportions. Differences in baseline characteristics between subjects achieving a successful and less successful weight loss were assessed using a two-sample *t*-test, a non-parametric test or a chi$^2$-test (categorical data). Changes in anthropometric and metabolic parameters among RNPC patients with successful weight loss and RNPC patients with less successful weight loss were analyzed using linear mixed models with a time-group interaction and included subject and RNPC site as random effects. Simple linear regressions were used to test the association between several baseline characteristics and excess weight loss and percentage of weight loss of initial weight. Weight loss outcomes in RNPC® and bariatric surgery patients were summarized as mean ± SD and median (IQR), whereas the remaining results are reported as mean ± standard error or mean with 95% confidence intervals. *P*-values less than 0.05 were considered significant. Statistical analyses were carried out using R (R, n.d.) and RStudio version 1.1.383 (www.rstudio.com).

## 3. Results

### 3.1. Patients

Of the > 10.000 patients enrolled in the RNPC® program (Thorning et al., 2018), 1460 patients would qualify for bariatric surgery based on BMI, age, and comorbidities. Of these, 506 (35%) dropped out during the program, and 291 (20%) were still ongoing in the program, resulting in 663 (45%) patients completing the program that would have been considered potential candidates for bariatric surgery. Of these, 189 (29%) obtained a successful weight loss defined as excess weight loss ≥60% while 179 (27%) obtained a less successful weight loss, defined as excess weight loss ≤30% (Supplemental Fig. 1). Baseline characteristics of the included patients and patients divided into successful weight losers and less successful weight losers are shown in Table 1. Patients obtaining a successful weight loss were higher, had lower BMI and HbA1c as well as higher LDL-cholesterol compared to patients obtaining a less successful weight loss (all P ≤ 0.03).

Baseline characteristics for dropouts and patients ongoing in the program are shown in Supplemental Table 1. Dropouts had higher fat mass percentages, higher fasting glucose and HbA1c, and a larger proportion of the patients were medicated for type 2 diabetes compared to patients completing the program. However, a larger proportion of the patients completing the program were medicated for hypertension compared to dropouts (all P ≤ 0.02).

Data on weight loss outcome after 18 months were available for 61 bariatric surgery patients, 51 RYGB patients and 10 sleeve gastrectomy patients (80% females). Mean BMI when entering the program was 45.2 ± 5.9 kg/m$^2$ and mean age was 40.4 ± 9.6 years (Supplemental Table 2).

### 3.2. Weight loss through diet or surgery

The mean weight loss for patients completing the RNPC® program was 20.2 ± 11.8 kg after an average period of 18.6 ± 9.1 months, resulting in a reduction of 47% of the excess weight and a percentage weight loss from the initial weight of 18%. Following the bariatric surgery program, mean weight loss was 42.5 ± 15.8 kg approximately 18 months after surgery, resulting in a reduction of 74% of the excess weight and a percentage weight loss from the initial weight of 32%. The mean relative loss of fat-free mass was 36.1 ± 29.1% in the RNPC® cohort and 19.7 ± 8.7% in the bariatric surgery cohort (Supplemental Table 3).

Following both interventions, the degree of weight loss varied greatly among individuals as seen in Fig. 1. Following the RNPC® program the proportion of patients who lost 30% or less of the excess weight was 27% versus 1.6% following the bariatric surgery program. The proportion of patients who lost 60% or more of the excess weight was 29% following the RNPC® program versus 75% following the bariatric surgery program (Fig. 2).

Weight loss in patients who dropped out of the RNPC® program was 14.1 ± 9.2 kg (median [IQR]: 12.6 [6.9; 19.8]) resulting in a mean percentage weight loss from initial weight of 12%. The mean duration in the program was 11.2 ± 8.3 months (median [IQR]: 8.5 [4.6; 13.4]). Weight loss for both completers and patients who dropped out was 17.5 ± 11.2 kg (median [IQR]: 15.7 [9.6; 23.1]) resulting in a mean weight loss of 15% of initial body weight, for a mean duration of 14.8 ± 9.7 months (median [IQR]: 13.5 [8.2; 19.6]).

### 3.3. Metabolic and anthropometric changes in successful and less successful patients

The mean duration of the RNPC® program did not differ between patients with successful and patients with a less successful weight loss (549 ± 20 and 592 ± 20 days, P = 0.13). Thus, weight loss velocity was higher in patients with successful weight loss compared to patients with less successful weight loss (0.48 ± 0.01 and 0.13 ± 0.01 kg/week, P < 0.001). As expected, patients with successful weight loss had a larger reduction in waist circumference and absolute and relative amount of fat mass (all P < 0.001) compared to patients with less successful weight loss. Fat-free mass also decreased more in patients with successful weight loss (P < 0.001); however, relative fat-free mass loss did not differ between groups (successful: 37.1 ± 2.6% and less successful: 33.6 ± 2.8%, P = 0.35) (Table 2).

Patients with successful weight loss had a larger reduction in plasma concentrations of total cholesterol, LDL-cholesterol, and triglycerides, and a larger improvement in HDL-cholesterol compared to patients with a less successful weight loss (all P ≤ 0.01).

### 3.4. Weight loss predictors

The following factors were associated with higher excess weight loss in a univariate analysis: higher initial BMI, lower HbA1c levels and higher LDL-cholesterol levels (all P ≤ 0.03). The association between

**Table 1**
Baseline characteristics among patients completing the weight loss and weight stabilization phases of the RNPC® program (n = 663) and divided into patients with successful weight loss (n = 189) and patients with less successful weight loss (n = 179).

| | n | All | n | Patients with successful weight loss, EWL ≥ 60% | n | Patients with less successful weight loss, EWL ≤ 30% | P-value[a] |
|---|---|---|---|---|---|---|---|
| Gender (female) | 663 | 62% | 189 | 65% | 179 | 65% | 0.99 |
| Age (years) | 663 | 56.0 (49.0; 61.0) | 189 | 56.0 (48.0; 61.0) | 179 | 56.0 (50; 61) | 0.69 |
| Height (cm) | 663 | 167 ± 10 | 189 | 168 ± 9 | 179 | 166 ± 10 | 0.03 |
| Body weight (kg) | 663 | 111.7 (102.0; 113.6) | 189 | 110.9 (102.0; 123.4) | 179 | 114.6 (104.0; 124.6) | 0.15 |
| Body mass index (kg/m$^2$) | 663 | 40.1 (36.9; 42.8) | 189 | 39.6 (36.5; 42.3) | 179 | 41.0 (37.9; 45.0) | < 0.001 |
| Waist circumference (cm) | 661 | 124 ± 11 | 189 | 124 ± 11 | 177 | 125 ± 12 | 0.62 |
| Fat mass (%) | 646 | 43.9 ± 4.4 | 185 | 43.9 ± 4.2 | 172 | 44.3 ± 4.8 | 0.36 |
| Fat mass (kg) | 646 | 48.8 (44.1; 54.3) | 185 | 48.9 (44.2; 53.0) | 172 | 50.0 (45.2; 56.7) | 0.05 |
| Fat free mass (kg) | 646 | 62.5 (55.5; 71.0) | 185 | 62.4 (54.2; 71.0) | 172 | 63.5 (56.7; 70.9) | 0.48 |
| Diabetes treatment (Yes) | 663 | 30% | 189 | 26% | 179 | 35% | 0.09 |
| Hypertension treatment (Yes) | 663 | 67% | 189 | 59% | 179 | 65% | 0.32 |
| Fasting glucose (g/L) | 620 | 1.06 (0.96; 1.24) | 181 | 1.08 (0.95; 1.21) | 162 | 1.05 (0.97; 1.30) | 0.69 |
| HbA1c (%) | 356 | 6.16 (5.70; 6.80) | 98 | 6.00 (5.50; 6.40) | 105 | 6.20 (5.70; 7.20) | 0.01 |
| Total cholesterol (g/L) | 644 | 2.02 ± 0.39 | 182 | 2.05 ± 0.34 | 173 | 1.97 ± 0.41 | 0.08 |
| HDL-cholesterol (g/L) | 641 | 0.49 ± 0.12 | 182 | 0.49 ± 0.12 | 172 | 0.48 ± 0.13 | 0.73 |
| LDL-cholesterol (g/L) | 636 | 1.25 ± 0.34 | 180 | 1.28 ± 0.35 | 172 | 1.20 ± 0.34 | 0.02 |
| Triglycerides (g/L) | 644 | 1.32 (1.03; 1.81) | 181 | 1.28 (0.99; 1.69) | 173 | 1.32 (1.06; 1.76) | 0.40 |

Abbreviations: EWL: excess weight loss; HbA1c: Hemoglobin A1c; HDL: High-density lipoprotein; LDL: Low-density lipoprotein.
Data are presented as proportions (%), mean ± SD or median (interquartile range) and analyzed by a two-sample *t*-test, a non-parametric test or a chi$^2$-test (categorical data).

[a] Test for difference between patients with successful weight loss and patients with less successful weight loss.

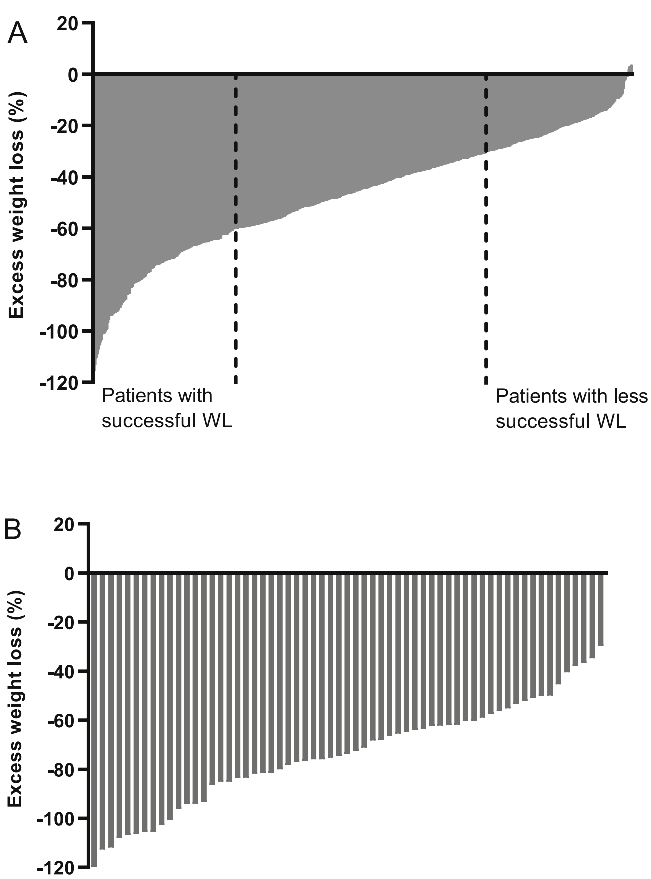


**Fig. 1.** A) Individual percentages excess weight loss (%) among patients who completed the RNPC® program and who would have been qualified for bariatric surgery. Patients are divided into patients with successful weight loss (excess weight loss ≥60%, n = 179) or patients with less successful weight loss (excess weight loss ≤30%, n = 189). B) Individual percentages excess weight loss (%) 18 months after Roux-en-Y gastric bypass and sleeve gastrectomy surgery. WL: weight loss.

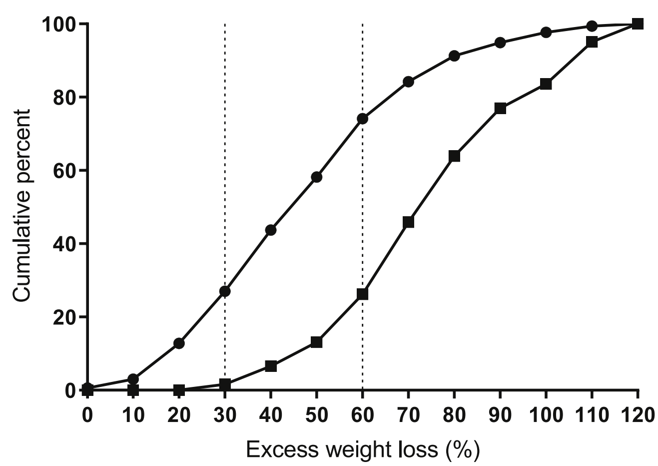


**Fig. 2.** Cumulative percentages weight loss for the 663 patients completing the RNPC® program (black line with circles) and the 60 bariatric surgery patients (black line with squares).

HbA1c and LDL-cholesterol levels and excess weight loss remained the same after adjusting for initial BMI (both P ≤ 0.03). Lower age and HbA1c levels, and higher initial BMI, waist circumference, fat mass, fat-free mass, and LDL-cholesterol levels were associated with higher percentages weight loss of initial body weight (all P ≤ 0.04). The association between HbA1c and LDL-cholesterol levels and percentages weight loss remained the same after adjusting for initial BMI (all P ≤ 0.03). However, the association between percentage weight loss and age, waist circumference, fat mass, and fat-free mass disappeared after adjusting for initial BMI (all P ≥ 0.11) (Table 3).

## 4. Discussion

Patients that would qualify for bariatric surgery based on BMI, age and comorbidities lost 20.2 ± 11.8 kg or 18% when following an intensive weight loss and weight loss maintenance program for an average period of 18.6 ± 9.1 months. RYGB and sleeve gastrectomy surgery resulted in a weight loss of 42.5 ± 15.8 kg or 32% of initial body weight approximately 18 months after surgery. Within the RNPC® cohort, 29% of the patients obtained a successful weight loss while 27%

**Table 2**
Changes in anthropometric and metabolic parameters after the RNPC® program among patients with successful weight loss and patients with less successful weight loss.

| | Patients with successful weight loss, EWL≥60% (n = 189) | | | Patients with less successful weight loss, EWL≤30% (n = 179) | | | |
|---|---|---|---|---|---|---|---|
| | Before Mean ± SEM | After Mean ± SEM | Δ(After-Before) Mean (95% CI) | Before Mean ± SEM | After Mean ± SEM | Δ(After-Before) Mean (95% CI) | P-value Time*group |
| Weight (kg) | 113.1 ± 1.2 | 80.7 ± 1.2 | −32.5 (−34.2; −30.8) | 116.0 ± 1.2 | 106.6 ± 1.2 | −9.2 (−10.9; −7.4) | < 0.001 |
| Weight loss (%) | – | 28.2 ± 0.4 | – | – | 7.8 ± 0.4 | – | < 0.001 |
| Weight loss period (days) | – | 213 ± 8 | – | – | 223 ± 9 | – | 0.42 |
| Weight loss + stabilization period (days) | – | 549 ± 20 | – | – | 592 ± 20 | – | 0.13 |
| Weight loss velocity (kg/week) | – | −0.48 ± 0.01 | – | – | −0.13 ± 0.01 | – | < 0.001 |
| Waist circumference (cm) | 123.6 ± 0.9 | 94.7 ± 0.9 | −29.0 (−30.4; −27.5) | 124.9 ± 1.0 | 114.5 ± 1.0 | −10.4 (−11.9; −8.9) | < 0.001 |
| Fat mass (%) | 43.9 ± 0.4 | 36.5 ± 0.4 | −7.4 (−8.0; −6.8) | 44.6 ± 0.5 | 43.0 ± 0.5 | −1.6 (−2.2; −1.0) | < 0.001 |
| Fat mass (kg) | 49.0 ± 0.6 | 29.1 ± 0.6 | −20.0 (−21.0; −18.9) | 50.9 ± 0.6 | 45.2 ± 0.6 | −5.7 (−6.8; −4.6) | < 0.001 |
| Fat free mass (kg) | 63.3 ± 0.9 | 51.0 ± 0.9 | −12.3 (−13.3; −11.3) | 63.8 ± 0.9 | 60.5 ± 0.9 | −3.3 (−4.4; −2.3) | < 0.001[a] |
| Relative FFM loss (%)[b] | – | 37.1 ± 2.6 | – | – | 33.6 ± 2.8 | – | 0.35 |
| Fasting glucose (g/L) | 1.13 ± 0.02 | 0.95 ± 0.02 | −0.18 (−0.25; −0.11) | 1.18 ± 0.03 | 1.05 ± 0.03 | −0.13 (−0.20; −0.06) | 0.20 |
| HbA1c (%) | 6.14 ± 0.09 | 5.24 ± 0.11 | −0.90 (−1.17; −0.63) | 6.54 ± 0.09 | 5.85 ± 0.10 | −0.69 (−0.93; −0.45) | 0.13 |
| Total cholesterol (g/L) | 2.05 ± 0.03 | 1.86 ± 0.03 | −0.19 (−0.27; −0.11) | 1.99 ± 0.03 | 1.93 ± 0.04 | −0.06 (−0.14; 0.03) | < 0.01 |
| HDL-cholesterol (g/L)[c] | 0.49 ± 0.01 | 0.55 ± 0.01 | 0.06 (0.04; 0.08) | 0.49 ± 0.01 | 0.51 ± 0.01 | 0.03 (0.002; 0.05) | 0.02 |
| LDL-cholesterol (g/L)[d] | 1.28 ± 0.03 | 1.16 ± 0.03 | −0.12 (−0.19; 0.06) | 1.21 ± 0.03 | 1.19 ± 0.03 | −0.01 (−0.08; 0.06) | < 0.01 |
| Triglycerides (g/L) | 1.44 ± 0.05 | 0.76 ± 0.05 | −0.67 (−0.81; −0.54) | 1.51 ± 0.05 | 1.13 ± 0.05 | −0.37 (−0.51; −0.24) | < 0.001[a] |

Abbreviations: EWL: excess weight loss; FFM: fat-free mass; HbA1c: Hemoglobin A1c; HDL: High-density lipoprotein; LDL: Low-density lipoprotein.

Analyzed by linear mixed models with a time-group interaction and included subject and RNPC site as random effects.

[a] Logarithm transformed. Estimates, SE and CI's are reported on a non-logarithm transformed model.

[b] Excluded one observation of 5433%.

[c] Excluded one observation of 9.99 mmol/L.

[d] Excluded one observation of 84 mmol/L.

**Table 3**
Potential baseline predictors of excess weight loss and percentage total weight loss of initial body weight after the RNPC® program (n = 663).

| | Excess weight loss (%) | | | Total weight loss (%) | | |
|---|---|---|---|---|---|---|
| | β (95% CI) | $R^2$ | P-value | β (95% CI) | $R^2$ | P-value |
| Age (years) | −0.11 (−0.31; 0.10) | < 0.01 | 0.32 | −0.10 (−0.18; −0.02) | < 0.01 | 0.01 |
| Height (cm) | 0.08 (−0.11; 0.27) | < 0.01 | 0.40 | −0.01 (−0.08; 0.06) | < 0.01 | 0.79 |
| Body weight (kg) | −0.07 (−0.18; 0.04) | < 0.01 | 0.22 | 0.08 (0.04; 0.12) | 0.02 | < 0.001 |
| Body mass index (kg/m²) | −0.59 (−1.00; −0.17) | 0.01 | 0.01 | 0.42 (0.26; 0.59) | 0.04 | < 0.001 |
| Waist circumference (cm) | −0.05 (−0.20; 0.11) | < 0.01 | 0.55 | 0.11 (0.05; 0.17) | 0.02 | < 0.001 |
| Fat mass (%) | −0.04 (−0.45; 0.37) | < 0.01 | 0.84 | 0.20 (0.04; 0.36) | < 0.01 | 0.02 |
| Fat mass (kg) | −0.16 (−0.40; 0.09) | < 0.01 | 0.21 | 0.24 (0.14; 0.33) | 0.04 | < 0.001 |
| Fat free mass (kg) | −0.04 (−0.20; 0.12) | < 0.01 | 0.65 | 0.07 (0.003; 0.13) | 0.07 | 0.04 |
| Fasting glucose (g/L) | −2.95 (−6.94; 1.03) | < 0.01 | 0.15 | −1.55 (−3.12; 0.02) | < 0.01 | 0.05 |
| HbA1c (%) | −4.03 (−6.37; −1.68) | 0.03 | < 0.001 | −1.52 (−2.43; −0.61) | 0.03 | 0.001 |
| Total cholesterol (g/L) | 3.36 (−1.19; 7.91) | < 0.01 | 0.15 | 1.02 (−0.79; 2.83) | < 0.01 | 0.27 |
| HDL-cholesterol (g/L) | −0.32 (−15.27; 14.63) | < 0.01 | 0.97 | 0.35 (−5.59; 6.28) | < 0.01 | 0.91 |
| LDL-cholesterol (g/L) | 5.98 (0.72; 11.24) | 0.01 | 0.03 | 2.18 (0.09; 4.27) | < 0.01 | 0.04 |
| Triglycerides (g/L) | −1.63 (−3.96; 0.71) | < 0.01 | 0.17 | −0.84 (−1.77; 0.09) | < 0.01 | 0.08 |

Abbreviations: HbA1c: Hemoglobin A1c; HDL: High-density lipoprotein; LDL: Low-density lipoprotein.
Analyzed with simple linear regressions.

obtained a less successful weight loss defined as excess weight loss ≥60% and ≤30% respectively. Patients that obtained a more successful weight loss outcome had better anthropometric and metabolic improvements after the weight loss compared to less successful patients. Furthermore, a higher initial BMI, higher LDL-cholesterol levels and lower HbA1c levels predicted a more successful percentage weight loss, although with low predictive power.

As expected, bariatric surgery produced a greater weight loss compared to a non-surgical weight loss program. This is in line with other studies comparing intensive behavioral weight loss programs with that of bariatric surgery. In a 12-month study, weight loss outcome after RYGB was compared to three different intensive lifestyle interventions in severely obese patients: a weight loss camp, a residential intermittent program, and a hospital outpatient program. Weight loss was higher in the surgery group when compared to the three non-surgical programs (30.5% vs. 14.8%, 13.0% and 5.3% for the weight loss camp, the residential program, and the hospital outpatients program respectively) (Martins et al., 2011). Furthermore, RYGB was still superior to the three intensive lifestyle interventions at 5-year follow-up (Øvrebø et al., 2017). Other studies found similar results, with reported weight loss of 3–12% following a 12-24-month lifestyle intervention in moderately and severely obese patients compared to a weight loss of approximately 30% following bariatric surgery (Burguera et al., 2015; Hofsø et al., 2010; Sanchis et al., 2015; Tur et al., 2013). Thus, despite intensive treatment strategies with focus on nutritional counseling, physical activity, and behavioral therapy, bariatric surgery is superior in terms of weight loss success. However, it is important to note that not all patients with moderate and severe obesity are eligible for bariatric surgery, and not all patients want surgery due to the risk of complications and the life-changing aspect of this solution. Less than 1% of eligible patients with obesity undergo bariatric surgery annually (Buchwald and Oien, 2013; Funk et al., 2015), and bariatric surgery is thereby a highly underutilized treatment option for obesity. Furthermore, even in patients who undergo bariatric surgery, the degree of weight loss varies considerably among individuals (Adams et al., 2017; Peterli et al., 2018), as also shown in the present study. Furthermore, long-term studies have identified that a significant numbers of patients regain weight post-operatively (Magro et al., 2008; Monaco-Ferreira and Leandro-Merhi, 2017). This is a medical, economic and ethical problem, and this emphasizes the importance of including lifestyle interventions as part of the surgical program in order to optimize the success of bariatric surgery for all individuals. Thus, lifestyle interventions are the cornerstone of obesity treatments, and there is a need for effective weight loss programs in moderately and severely obese patients.

The RNPC® program was associated with a weight loss of 18%. Other studies evaluating the effect of a 12-24-month intensive lifestyle intervention in moderately and severely obese patients report weight loss of 3–18% of initial body weight (Anderson et al., 2007; Hofsø et al., 2010; Martins et al., 2011; Sanchis et al., 2015; Shadid et al., 2015; Tur et al., 2013; Winkler et al., 2013). The weight loss programs reporting greater weight loss outcomes include frequent nutritional consultations and increased focus on weight stabilization and maintenance to ensure long-term weight loss (Anderson et al., 2007; Winkler et al., 2013).

Weight loss success varied significantly between patients in the RNPC® cohort. Some patients lost above 100% of excess weight while few actually gained weight during the program. Yet, 96% of the patients did obtain a weight loss of at least 5% of initial body weight, which has been shown to be beneficial for metabolic conditions (Magkos et al., 2016). As expected, patients with excess weight loss ≥60% had better metabolic and anthropometric improvements compared to patients with excess weight loss of ≤30%. One such anthropometric improvement worth highlighting was a 5.8 %-point larger reduction in percentage of fat mass. However, even the less successful patients obtained a mean weight loss of 7.8% and improved fasting glucose, HbA1c, HDL-cholesterol and triglycerides levels. The greater fat-free mass loss following the RNPC® program compared to the bariatric surgery program (39.4% versus 18.2%) is a concern due to the metabolic activity of fat-free mass. Adding physical activity to the program could help spare the loss of fat-free mass (Knuth et al., 2014). However, the bioelectrical impedance method used to estimate body composition in the RNPC® cohort affects the interpretation of this result. Several factors are known to limit this method as a valid predictor of fat mass and fat-free mass, especially in the severely obese state (Coppini et al., 2005).

Initial BMI, HbA1c, and LDL-cholesterol were identified as independent pretreatment determinants linked to weight loss outcome in the RNPC® cohort. The fact that a higher initial BMI predicted a more successful relative weight loss is likely due to higher weight loss goals among patients with higher initial BMI. Furthermore, lower HbA1c levels predicted a better weight loss outcome. This result is in agreement with studies reporting that the presence of diabetes mellitus is associated with less successful weight loss after bariatric surgery (de Hollanda et al., 2015; Erlanson-Albertsson, 2005). However, it should be noted, that the identified pretreatment determinants only explained ≤4% of the variation in percentage weight loss.

There is general agreement, that weight loss maintenance is the main challenge in obesity management, especially in regards to weight loss obtained through non-surgical methods. Thus, the long-term benefits of the RNPC® program must be interpreted with caution. Another weakness of our study is that the selection of patients in the RNPC cohort that would be eligible for bariatric surgery based on BMI 35–39.9 kg/m$^2$ only included information on hypertension and type 2 diabetes since this was the only available information. It is thereby possible that we excluded patients with BMI 35–39.9 kg/m$^2$ that would have been eligible for surgery based on other comorbidities such as sleep apnea or osteoarthritis. Furthermore, we only reported weight loss outcomes in patients completing the RNPC® program. Patients who dropped out of the program lost 12% of initial body weight over a mean period of 11.2 ± 8.3 months. The dropout rate of 35% in the present study is comparable to another large intensive weight loss program with an average duration of ~17 months (Anderson et al., 2007), and is also comparable to the dropout rate following the bariatric surgery program (Christensen et al., 2018; Schmidt et al., 2016).

Although bariatric surgery results in a more pronounced weight loss, a clinically important weight loss can be obtained in patients with moderate and severe obesity following an intensive behavioral weight loss program. In the RNPC® program, the degree of weight loss had an impact on the degree of metabolic improvements. However, even patients with less successful weight loss outcome showed beneficial metabolic improvements.

## Statement of ethics

The data used in the present manuscript was originally collected as part of clinical practice. Therefore, no protocol has been approved by any institute committee on human research, and patients were not asked to give their informed content. However, according to French law, since the patient has been informed that his/her data could be used for research, we are allowed to use them after they have been anonymized.


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AA is consultant for Groupe Éthique et Santé, and chairman of their scientific advisory board. He is consultant or member of advisory boards for Dutch Beer Institute, NL, Feast Kitchen A/S, DK, McCain Foods Limited, USA, Nestlé Research Center, Switzerland, Weight Watchers, USA; Gelesis, USA, BioCare Copenhagen, Zaluvida, Switzerland, Basic Research, USA, Beachbody, USA, Novo Nordisk, DK, Saniona, DK, & Scandinavian Airlines System, DK. AA's current research is in part funded by grants from Arla Foods, DK, Danish Dairy Research Council, & Gelesis, USA. AA is co-author of a number of diet/cookery books, including personalized nutrition for weight loss, published in several languages. He is co-owner and member of the Board of the consultancy company Dentacom Aps, co-founder and co-owner of UCPH spin-out companies Mobile Fitness A/S, Flaxslim ApS, and Personalized Weight Management Research Consortium ApS (Glucodiet.dk). MFH and MSN reports grants from Groupe Éthique et Santé during the conduct of the study. OF is employed at the Groupe Éthique et Santé. RL is CEO and founder of Groupe Éthique et Santé. AS declare no conflict of interest.


## Author contributions

MFH, RL, and OF conceived the idea of the current analysis. MSN and MFH discussed the overall analytical strategy and content of the manuscript. MSN analyzed the data and wrote the first draft of the paper. All authors have reviewed the manuscript critically and approved the final manuscript. MSN had primary responsibility for the final content.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.obmed.2019.100127.

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