



# A randomized controlled trial comparing intensive non-surgical treatment with bariatric surgery in adolescents aged 13–16 years (AMOS2): Rationale, study design, and patient recruitment

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## ARTICLE INFO

### Keywords:

Adolescents  
Bariatric surgery  
Low-calorie diet  
Obesity  
Pediatric  
Roux-en Y gastric Bypass

## ABSTRACT

**Background:** Previous non-randomized studies show similar outcomes in adolescents and adults after bariatric surgery. We describe the study protocol, recruitment, and selected baseline data of patients in a randomized multi-center study, the Adolescent Morbid Obesity Surgery 2 (AMOS2).

**Methods:** Three clinics in Sweden collaborated in designing the study and recruitment of patients from August 1, 2014 to June 30, 2017. Patients were selected among adolescents 13–16 years of age attending third-level obesity care for at least one year. Patients were randomized 1:1 to bariatric surgery (predominantly Roux-en-Y gastric bypass) or intensive non-surgical treatment starting with an eight-week low-calorie-diet.

**Results:** Fifty adolescents (37 girls) were randomized, 25 (19 girls) to bariatric surgery. Mean age was 15.7 years (range 13.3–16.9), weight 122.6 kg (range 95–183.3), Body Mass Index (BMI) 42.6 kg/m<sup>2</sup> (range 35.7–54.9) and BMI-SDS 3.45 (range 2.9–4.1). One patient had type 2 diabetes mellitus, and 12/45 (27%) had elevated liver enzymes. There were no significant differences between the groups. For the 39 eligible patients who were offered but declined inclusion, BMI was not different from included patients. However, patients who declined were younger, 15.2 years ( $p = 0.021$ ). A sex difference was also noted with more of eligible girls, 37/53 (69.8%), than boys, 13/36 (36.1%), wanting to participate in the study ( $p = 0.002$ ).

**Conclusions:** This clinical trial, randomizing adolescents with severe obesity to bariatric surgery or intensive non-surgical treatment, aims at informing about whether it is beneficial to undergo bariatric surgery in early adolescence. It will also enlighten the outcome of comprehensive non-surgical treatment. The study was registered at [www.clinicaltrials.gov](http://www.clinicaltrials.gov) number NCT02378259.

**Abbreviations:** AMOS2, Adolescence Morbid Obesity Study 2, BMI, Body Mass Index, BORIS, Swedish Childhood Obesity Treatment Register, DXA, Dual Energy X-Ray Absorptiometry, GB, Roux-en-Y Gastric Bypass, LCD, Low-Calorie Diet, SOReg, Scandinavian Obesity Surgery Registry

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<https://doi.org/10.1016/j.conctc.2020.100592>

Received 12 February 2020; Received in revised form 8 June 2020; Accepted 14 June 2020

Available online 27 June 2020

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## 1. Introduction

Despite some countries reporting that obesity is leveling off, the number of adolescents with severe obesity is increasing worldwide [1–7]. Treatment with lifestyle modifications has limited effects [8].

Bariatric surgery is the standard treatment for severe obesity in adults. In Sweden, there is a strong commitment to national guidelines limiting bariatric surgery before 18 years to studies [9], although there is accumulating evidence for similar efficacy as in adult patients. In the Adolescent Morbid Obesity Surgery (AMOS) study, 81 adolescents underwent Roux-en-Y gastric bypass. They lost, on average, 36.8 kg, which was similar to matched adult controls, and improved metabolic risk factors. Gastric bypass was, however, associated with additional surgical interventions and nutritional deficiencies, and nine (11%) of the adolescent patients had lost less than 10% of their initial weight at the five-year follow up [10].

Similar marked weight loss was also demonstrated for both groups in the Teen-Longitudinal Assessment of Bariatric Surgery (Teen-LABS) study, where 161 adolescent patients were compared to an adult group who had obesity at 18 years of age. Adolescent patients were significantly more likely to have remission of type 2 diabetes and hypertension than adults [11,12]. However, an issue of concern was two deaths associated with substance abuse in the adolescent group, although no significant difference in mortality between the groups was observed. The proportion of patients that lost less than 5% of initial weight or increased in weight was significantly larger in the adolescent group [12]. In a randomized study in adolescents comparing laparoscopic adjustable gastric band and intensive conservative treatment, 84% of operated patients lost half of their excess weight in contrast to only 12% in the control group. Eight of the 25 patients needed additional revisional surgical procedures [13].

Studies in adolescents have also shown that longer-term weight loss seems to be driven by weight outcomes by 12 months post-surgery, whereas preoperative weight loss from time of intake to time of surgery did not show an association with weight outcomes. This suggests that adolescent patients who lose more weight pre-surgery are not necessarily the individuals who lose more weight post-surgery [14].

Regardless of weight, adolescence is a vulnerable period in life with substantial physical, social, cognitive, and psychological transformations [15,16]. Adolescents with obesity have a higher prevalence of concomitant psychiatric disease than normal-weight peers, and socio-economic disadvantages are more common [17,18]. In a review, bariatric surgery was associated with sustainable improvement of quality of life in adolescents [19]. In the AMOS-study, self-concept and self-esteem improved significantly so that adolescents achieved a level of mental health and self-concept comparable to norms two years after bariatric surgery [20]. However, one in five adolescents reported substantial mental health problems after surgery, and baseline mental health problems were associated with poor mental health after surgery [21]. Mental health problems persisted in adolescents five years after bariatric surgery despite substantial weight loss [22].

The promising results of studies on bariatric surgery are already influencing clinical practice in many countries, but questions regarding the optimal time point for bariatric surgery have been raised [23]. The effect of surgery in relation to pubertal development and growth spurt as well as mental development, autonomy, and social functions need further evaluation, and sex differences need to be explored. Therefore, we designed a randomized clinical trial to compare outcomes from intensive non-surgical treatment versus bariatric surgery for adolescents 13–16 years old with severe obesity.

## 2. Materials and methods

### 2.1. Study area

AMOS2 is a nationwide Swedish study. Three tertiary childhood obesity treatment clinics in university hospitals in the three largest cities of Sweden included patients. These clinics also accepted referrals from other parts of the country.

### 2.2. Study population

All patients between 13 and 16 years of age who had been treated for obesity for at least 12 months were screened for eligibility.

### 2.3. Recruitment procedures

Patients in the selected age group were screened for eligibility for the study in multi-professional team-based discussions. Patients were considered eligible provided: 1) 13–16 years of age 2) BMI  $\geq 35$  and 3) undergone at least 12 months of obesity treatment with insufficient effect, of which at least six months at the including clinic. Patients should be in pubertal stage Tanner 3, or higher, and obvious exclusion criteria should not be present.

Information about the study was distributed at the clinics and a study-specific webpage, [www.amos2.se](http://www.amos2.se). An adolescent or a family could also initiate an evaluation for consideration of bariatric surgery, which then was followed by the same team-discussion and screening for eligibility.

Eligible patients were informed about the study at a visit to the clinic. A thorough investigation was initiated if patients were interested in participating in the study. The investigation aimed at identifying exclusion criteria, evaluate the ability of the patient to make an informed decision, and provide information about the study design and procedures. During this investigation, patients had appointments with a pediatrician, a nurse, and a psychologist, often several times.

We informed the adolescent and their families that bariatric surgery might become a treatment alternative at some point in their life. Families were informed that the study aimed at exploring whether there are benefits from undergoing surgery in adolescence in comparison to later. Treatment arms were presented with equipoise stating that “we don't know whether it is better to undergo surgery in adolescence or later”.

Group information sessions facilitated further information exchange between clinicians and adolescents and their parents, usually with the surgeon present. Families were informed that surgery was centralized to one center (Gothenburg). For planning reasons, patients were assigned a tentative date for surgery, alternatively a date for starting the low-calorie diet for two or eight weeks, respectively, depending on randomization.

### 2.4. Inclusion and exclusion criteria

#### 2.4.1. Inclusion criteria

- Age 13–16 years
- BMI  $> 35$  kg/m<sup>2</sup>
- Insufficient results from comprehensive treatment for obesity for at least one year
- Eligible according to the assessment of psychologist
- Pubertal stage Tanner 3 or higher

#### 2.4.2. Exclusion criteria

- Monogenic or syndromic obesity (for example Prader Willi Syndrome, Laurence Moon-Bardet-Biedl)

- Obesity secondary to brain injury
- Severe intellectual disability or other severe, pervasive developmental disorder
- Not eligible for general anesthesia
- Psychosis or other major psychiatric illness (i.e., severe depression or suicide attempt during the last year). Self-induced vomiting to regulate weight.
- Ongoing substance abuse
- Previous major gastrointestinal surgery

For safety reasons, we also excluded patients with substantial problems related to adherence, such as missing most appointments, as we anticipated severe problems in the study follow-up if they were included. A limited number of patients with manifest complications to obesity, such as type 2 diabetes mellitus, were considered ineligible for the study for ethical reasons. Instead, they were considered to have an “imperative clinical indication” for intervention. They were referred for bariatric surgery, usually at age 16–18 years, after a decision in the study steering committee.

## 2.5. Modification of protocol

Initially, we aimed at including adolescents 13–15 years of age. After six months, we changed to 13–16 years in response to the age-distribution of the patients at the clinics and their willingness to accept participation in the study. Study visits in the trial were changed from 6 weeks, 1, 2, 7, 12, and 17 years after inclusion in the original plan to 6 weeks, 1, 2, 5, 10, and 15 years after inclusion. The reason for this change was to better comply with the normal registry-based Scandinavian Obesity Surgery Registry (SOREg) intervals used for long-term follow up. The clinic in Malmö joined the study on May 1, 2015.

## 2.6. Investigations at baseline and randomization procedures

Patients who were deemed eligible by the team and accepted inclusion were scheduled for an inclusion visit. Inclusion visit lasted one or two days and included: 1) baseline investigations 2) examination by a pediatrician 3) discussion with a pediatric nurse regarding logistics and participation 4) a dietician assisted in registration of eating patterns and food choices using validated instruments and 5) a psychologist assessed psychological well-being using validated instruments. A physiotherapist assisted in performing a standardized submaximal fitness test for aerobic capacity expressed as the maximum rate of oxygen consumption ( $\text{VO}_2$  max) that was performed at two of the centers. Dual Energy X-Ray Absorptiometry (DXA) was performed for assessing body composition. Blood samples were collected for analysis and storage, and an Oral Glucose Tolerance Test (OGTT) was performed. Patients who were prescribed metformin were asked not to take the drug 1–2 days before the OGTT.

At the end of the inclusion visit, computerized randomization was performed at a research lab in Gothenburg. The center was informed over e-mail or telephone. The staff at the including center informed the patient. Randomization was performed as 1:1 in a program stratifying to ensure even numbers of surgery and non-surgery patients of both sexes at each site.

The BMI from a measurement of weight and height at the inclusion visit is the baseline BMI for each patient in the study. BMI Z scores were calculated using the IOTF-reference [24].

## 2.7. Interventions

### 2.7.1. Intensive non-surgical treatment

Patients were provided low-calorie diet (LCD) products containing 800 kcal/day using a commercial product, Modifast (Impolin AB,

Täby, Sweden), for eight weeks, free of charge. A treatment intensity of monthly interactions with members of the multi-professional team, either as physical visits or telephone contacts, was planned for the two-year study period.

### 2.7.2. Bariatric surgery

Patients were recommended LCD products containing 800 kcal/day, Modifast (Impolin AB, Täby, Sweden), for two weeks. After that, patients underwent bariatric surgery. The surgical method was decided by the surgeon after discussions with the family. Laparoscopic Roux-en-Y Gastric Bypass was performed in all cases except in two patients where sleeve gastrectomy was the preferred method. Follow-up visits were scheduled after six weeks and 6, 12, 18, and 24 months at the clinic. Seven visits were planned in the protocol over the initial study period of two years. Supplementary vitamins and minerals were provided by the study free of charge.

## 2.8. Outcome measures

The primary outcome of the study is the difference in changes in BMI over two years between the surgical and non-surgical treatment arms. The secondary outcomes will be differences in the development of cardiovascular illness and cancer, biochemical markers of metabolic health, body composition, bone health, physical fitness, quality of life, and psychological and cognitive functioning. Both the primary and secondary outcomes will be analyzed for 5-, 10- and 15-year changes.

Assessments are scheduled at 1, 2, 5, 10, and 15 years from baseline, including team-visits for assessment of secondary outcome measures: general health, quality of life, physical performance, bone health by DXA, biochemical metabolic situation, psychosocial variables, cognitive functioning, mental health, addictive behavior, dietary intake, and eating patterns. In addition, data from mandatory central registries for assessment of health care consumption and socioeconomic development will be collected. We will also assess how many patients in the non-surgical treatment group that chose to undergo bariatric surgery later, as well as long-term cardiovascular events, cancer incidence, and overall mortality.

### 2.9. Patients declining participation in the study

Data regarding patients who were offered but declined participation in the study was registered in their clinical records as part of the screening procedure and clinical treatment. For this study, we categorized the main reason for not wanting to participate into five broad categories: 1. “not interested” (including those who did not return for appointments); 2. perceiving surgery as “too drastic”; 3. “it works fine as it is”; and 4. “could not handle LCD for eight weeks” and 5. “not interested in randomization to LCD”, where the last two categories might be overlapping.

### 2.10. Financing

The study was financed by a grant from Sweden's innovation agency Vinnova (T. Olbers, 2012-34346-95933-20). The grant required a formalized partnership with participating university hospital, making costs equally shared to encompass that the patients in the study were already actively treated at the clinics. Surgeries were provided free of charge, both for the public health care system and the patients, by the non-profit hospital Carlanderska, Gothenburg, Sweden.

### 2.11. Registration

The study was registered at [www.clinicalTrials.gov](http://www.clinicalTrials.gov) number NC-T02378259.

### 2.12. Study management

Besides the principal investigator, a steering committee with participants from all centers and representing various professions was making decisions in the trial. Monthly telephone-conferences supported decisions about all inclusions in the study. Investigators' meetings were held twice a year for sharing study experiences and minimizing protocol deviations.

### 2.13. Statistics

The primary conclusions from this study will be based on analyses conducted under the principle of intention-to-treat. Thus, all randomized patients will be included in the analyses, and it is assumed that all randomized patients receive the treatment for which they were randomized. For the sample size calculation, we assumed a 2-year reduction in BMI of 15 kg/m<sup>2</sup> in the surgery group based on the results of the AMOS-study [10] with standard deviation (SD) 7 kg/m<sup>2</sup>. Further, we assumed a reduction in BMI of 5 kg/m<sup>2</sup> in the intensive non-surgical treatment group with SD 7 kg/m<sup>2</sup>. Based on these assumptions, a total sample size of 50 (25 in each group) will provide >95% power at 0.01 significance level to demonstrate a difference in BMI-change over two years between the groups. In addition, the sample size was chosen to allow assessment of differences in cardiovascular risk factors and differences in quality of life and cognitive functions.

For comparison between groups at baseline, an independent Student's *t*-test was performed, and results are presented as means with standard deviation and range. For further analyses, a difference in treatment effect will be evaluated with the hazard ratio between the treatment groups, and the corresponding confidence interval will be calculated. The difference in BMI-changes between the groups will be estimated with a multilevel mixed-effect regression model utilizing BMI measurements at all available time points. This model considers the repeated measurements nested within persons over time. All randomized patients except those who will withdraw their consent will be included in this analysis.

### 2.14. Register-based data collection

All patients participated in the Swedish Childhood Obesity Treatment Register (BORIS) [36]. Patients undergoing bariatric surgery were registered in SOReg. The Swedish National Patient Register collects data for in-patient as well as out-patient hospital care.

### 2.15. Ethics

This multicenter study was approved by the ethical board in Gothenburg with no 578–13.

## 3. Results

The study protocol was designed and revised, as stated above, and the study steering committee proved to be a useful forum for collaboration. Recruitment was continuous, as was the acceptance of new patients at the respective center. The number of screened patients was estimated to be around 500 (Fig. 1). The number of patients 13–16 years of age with obesity defined as IOTF-BMI > 30 [25] at three clinics measured as a point-measurement on January 1, 2016 were 473 of whom 219 were girls (46.3%). The respective size of the clinics was

126 (66 girls) in Gothenburg, 222 (97 girls) in Malmö and 125 (56 girls) in Stockholm.

Fifty adolescents (37 girls, 74%) fulfilled the inclusion criteria and had no exclusion criteria, and expressed an autonomous decision about willingness to participate in this trial. In addition, consent was obtained from their parents or guardians. There were no conflicting opinions between adolescents and parents or guardians in any of the included cases.

For included patients, the mean age was 15.7 years, weight 122.6 kg (range 95–183.3), and BMI 42.6 kg/m<sup>2</sup> (range 35.7–54.9), corresponding to a mean BMI SDS of 3.45 (Table 1). The recruitment process in the three clinics was similar, however not identical. The Gothenburg clinic included 19 patients, Malmö 22, and Stockholm 9 patients. Of included participants, 21 (42%) had at least one parent who had undergone bariatric surgery. For patients below 15 years, 7/11 (63.6%) had at least one parent who had undergone bariatric surgery (Table 2) in contrast to 14/39 (35.8%) of patients >15 years, but this difference was not statistically different (*p* = 0.1).

Following thorough investigations by the obesity team, 14 patients who were initially considered eligible were excluded before randomization (Fig. 1). The reasons for exclusion were related to criteria, such as having a limited autonomy and ability to make a well-informed decision about the study, or investigations revealed disturbed eating patterns, manifest or suspected substance abuse, or severe problems with compliance being likely to affect adherence to the intervention and follow-up.

Thirty-nine patients were offered inclusion in the study but declined participation. The proportion accepting an offer to participate in the study varied significantly between genders; 37/53 (69.8%) of girls offered inclusion, and 13/36 (36.1%) of boys offered inclusion agreed to participate (*p* = 0.002).

The main reason for not wanting to participate was for 25/39 (64.1%) categorized as “not interested”. Surgery was perceived “too drastic” for 7/39 (17.9%), whereas 5/39 (12.8%) said that “it works fine as it is”. One patient said “could not handle the LCD for eight weeks”, and one patient would not accept the 1:1 randomization to the non-surgical treatment. Patients declining participation were significantly younger, 15.2 years ( $\pm 1.17$ , range 12.7–16.9) (*p* = 0.021). However, the mean BMI was 41.3 kg/m<sup>2</sup> ( $\pm 5.20$ , range 35.6–52.3), which was not significantly different from included patients (*p* = 0.193).

Thirteen patients below 17 years of age with metabolic complications to obesity, such as type 2 diabetes, were offered bariatric surgery on a clinical indication during the study period and were thus not included in AMOS2. Ten of these patients were 16–17 years old, and three patients were below 16 years at the time of surgery.

### 3.1. Baseline investigations

Background data (mean and SD) are shown in Table 1. Of included (*n* = 50) patients, 29/50 (58%) had impaired glucose tolerance (fp-glucose > 5.6 mmol/l) and 12/45 (27%) had affected liver samples (alanine aminotransferase > 0.9  $\mu$ kat/l). In total, 33/50 (66%) had some metabolic impairment, measured as either impaired glucose tolerance or elevated liver enzymes. There was no difference between the groups, with 16 patients with affected metabolic status in the non-surgical treatment group and 17 in the surgical treatment group.

## 4. Discussion

This article presents the design, patient recruitment, and inclusion process for a randomized controlled trial comparing bariatric surgery and intensive non-surgical treatment for adolescents with severe obesity (AMOS2). Randomization resulted in similar groups regarding



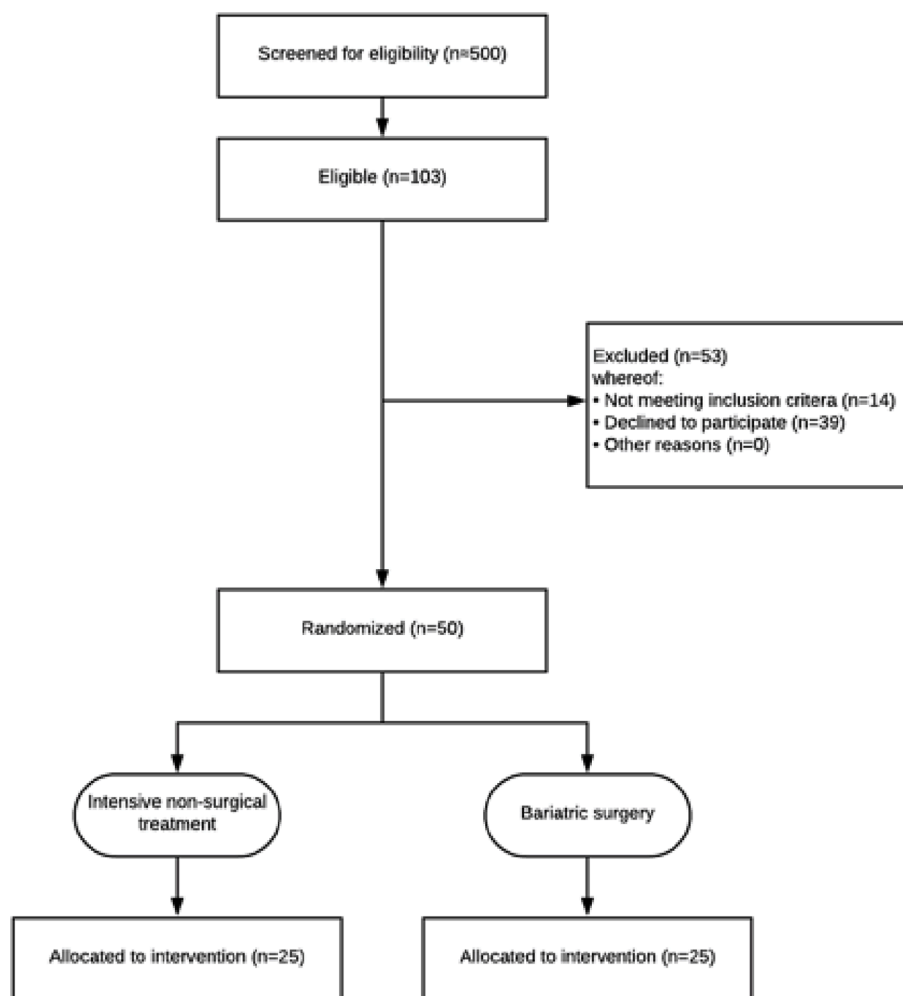


Fig. 1. Consort schedule showing flow of patients in the study Adolescent Morbid Obesity Surgery 2.

Table 1

Background data of included patients.

|                             | Total        | Intensive non-surgical treatment | Bariatric surgery |    |    |
|-----------------------------|--------------|----------------------------------|-------------------|----|----|
|                             |              |                                  |                   | n  | n  |
| Number (female)             | 50 (37)      | 25 (19)                          | 25 (18)           |    |    |
| Age (SD) years              | 15.7 (1.0)   | 15.9 (0.8)                       | 15.6 (1.1)        | 25 | 25 |
| Height (SD) cm              | 169.4 (8.2)  | 168.7 (8.2)                      | 170.2 (8.0)       | 25 | 25 |
| Weight (SD) kg              | 122.6 (17.5) | 120.9 (21.6)                     | 124.3 (14.6)      | 25 | 25 |
| BMI (SD) kg/m <sup>2</sup>  | 42.6 (5.4)   | 42.3 (5.5)                       | 42.9 (5.0)        | 25 | 25 |
| BMI SDS [24] (SD)           | 3.45 (0.3)   | 3.43 (0.32)                      | 3.48 (0.27)       | 25 | 25 |
| Waist circumference (SD) cm | 122 (11.9)   | 123.9 (15.5)                     | 120.2 (11.5)      | 25 | 25 |

SD = Standard deviation, Sign = Significance, BMI = Body Mass Index.

Table 2

Age distribution of included patients and number of patients where at least one parent has undergone bariatric surgery.

| Age (years)                                | 13–13.9 | 14–14.9 | 15–15.9 | 16–16.9 |
|--|---------|---------|---------|---------|
| Number of patients (female)                | 3 (1)   | 8 (6)   | 15 (13) | 24 (17) |
| At least one parent with bariatric surgery | 1       | 6       | 5       | 9       |

age, BMI, and prevalence of metabolic disturbances between treatment arms.

Although a handful of outcome studies are available in adolescent bariatric surgery, little is known about adolescents' pathway to obesity surgery. An interesting observation in our study was that 42% of the included patients had at least one parent who had undergone bariatric surgery. Our impression was that this made patients and parents more confident in agreeing to participate in the trial. There was a tendency that the younger the patient, the more common it was to have a parent who had undergone surgery.

Another observation is that 39/89 (43.8%) of patients eligible for inclusion declined participation. The most common reason was that the patient and families were not "interested", which we, in most cases, interpreted as not interested in being randomized to surgery. A sub-group expressed that they considered surgery appearing too drastic. We lack further details of the reasoning as we base our analysis on the documentation from the clinical records. However, the relatively low acceptance rate of participation appears important as some may argue that bariatric surgery is an "easy way" or a "magic bullet" and a tempting option for adolescents with severe obesity. Instead, we believe that those accepting inclusion in this randomized trial had carefully considered participation and were prepared for both treatments.

We presented the two study-arms as having clinical equipoise, with both of them having possible benefits as well as drawbacks. We also tried to evaluate the young person's ability to encompass the remaining issues of long-term beneficial lifestyle modifications and long-term aspects of living with bariatric surgery. A qualitative study

by Doyle et al. have investigated the decision making from the patients' perspective, with semi-structured interviews of nine patients opting for bariatric surgery. They identified a range of motivations for choosing surgery, including a desire for a better future, to be confident, healthy, and "normal" [26].

We noted an interesting sex difference where the acceptance for participation was higher among girls despite a slight majority of screened patients were male. The reasons for these differences deserve further exploration, preferably in qualitative research. A possible reason might be that severe obesity is a more substantial psychosocial burden for adolescent girls in comparison to boys, making girls more prone to accept an invasive treatment as surgery. Another reason may be sex-differences in the patients' experiences of the effect of previous treatments.

The older age span (16 years) constituted almost half of the included patients, and patients accepting inclusion were significantly older than those who declined. These observations again illustrate that bariatric surgery is just emerging and beginning to be accepted as a treatment alternative for the youngest adolescents. Issues regarding the individual's autonomy and legal aspects must be considered when treating adolescents. At the same time, the young person may need a robust environment to reflect and evaluate long-term aspects of treatment options. A very relevant point for young female patients is bariatric surgery in relation to fertility and pregnancy outcomes. In a recent in-depth and comprehensive analysis of all deaths during pregnancy and 42 days after delivery in Sweden in 2007–2017, 15/67 of deceased women had BMI > 30 kg/m<sup>2</sup>, and 4/67 had BMI > 45 kg/m<sup>2</sup> [27]. Also, large register-based studies from Sweden show improved outcomes for the children born by mothers after bariatric surgery compared to weight-matched controls with obesity [28,29]. Collectively, these results suggest that bariatric surgery before pregnancy appears beneficial for the mother as well as for the child.

Bariatric surgery has become standard practice in the treatment of adolescents with severe obesity in the United States over the last decade, where guidelines state that bariatric surgery should be considered in adolescents having a BMI > 35 kg/m<sup>2</sup> and a co-morbidity or with BMI > 40 kg/m<sup>2</sup> [30]. In contrast, in the UK, the National Institute of Clinical Excellence states that bariatric surgery may be considered for adolescents with severe obesity in "exceptional circumstances" [31]. Similarly, when discussing the role of bariatric surgery in adolescents with non-alcoholic steatohepatitis, the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition in 2016 stated that "Future studies and a long-term risk analysis of patients with obesity associated liver disease are much needed to clarify the exact indications for bariatric surgery in adolescents" [32]. In Sweden, the current guidelines with an age limit of 18 years have been increasingly questioned in light of the ongoing AMOS projects [33]. Also, randomized studies are ongoing in adults to compare different surgical techniques, and these results will likely benefit also the younger patients where the long-term results of surgery will be even more critical [34,35].

Still, data underpinning a surgical strategy are relatively scarce, and randomized clinical trials are lacking. Despite the need for controlled studies - that we hope to address with AMOS2 - the risks of *not* performing bariatric surgery need to be considered when comparing risks and benefits in treating severe obesity in adolescents. Studies demonstrate a high risk of aggravated medical and psychosocial complications, along with substantial further weight gain without intervention. Increased awareness about bariatric surgery as a treatment option leads to more requests from patients and parents. Concerns regarding the long-term effects of bariatric surgery, such as bone health and risk for substance abuse, are especially valid for younger patients. The timing of surgery, if performed, becomes a highly relevant issue.

## 5. Conclusions

AMOS2 is a randomized clinical trial comparing bariatric surgery (Roux-en-Y gastric bypass or gastric sleeve) and intensive non-surgical treatment in adolescents with severe obesity. We included 50 patients in AMOS2, and there were no significant differences between the two study groups at inclusion. The main scientific question addresses whether it is beneficial to undergo bariatric surgery during adolescence or whether an intensive non-surgical program can be a better option.

### 5.1. Limitations

All participants had to be prepared to accept the two alternatives (intense treatment with LCD and bariatric surgery) before inclusion. This design may have made patients desiring surgical treatment more likely to take part as surgery was not an option outside controlled studies in Sweden. However, great efforts were invested in presenting both treatments as attractive, and both groups had a higher intensity in treatment than standard care. Patients were informed before randomization that they could be assessed for surgery after the study period if randomized to non-surgical treatment.

Eligible adolescents with severe obesity who had severe metabolic complications, such as type 2 diabetes, were offered bariatric surgery on a clinical indication ( $n = 13$ ) during the period of inclusion.

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