Table of Contents

| Item | Description |
|------------|--|
| eMethods | Very low / low calorie diets (VLCD/LCD) in the intensive lifestyle program |
| | Indications & follow-up after bariatric surgery in Sweden |
| | |
| eTable 1 | Psychosocial variables and personality traits used in the matching algorithm |
| eTable 2 | International Classification of Diseases (ICD) codes and Anatomical Therapeutic Chemical (ATC) classification system codes used |
| eTable 3 | Description of deaths by suicide |
| eTable 4 | Description of nonfatal self-harm events (excluding individuals dying by suicide who did not have a nonfatal self-harm event after intervention) |
| eTable 5 | Baseline characteristics in participants with history of psychiatric disorder or nonfatal self-harm |
| eTable 6 | Evidence table of studies on bariatric surgery and suicide |
| eTable 7 | Distribution by BMI category in the SOReg/Itrim study |
| | |
| eFigure 1 | Flow chart for the Swedish Obese Subjects (SOS) study |
| eFigure 2 | Flow chart for the SOReg/Itrim study of gastric bypass and low/very low calorie diet treated individuals (intervention years: 2006-2013) |
| | |
| References | |

eMethods

Very Low / Low Calorie Diets (VLCD/LCD) in the Intensive Lifestyle Program

- VLCD: Liquid-based formula diet of 500kcal/day for 3-10 weeks (125kcal/sachet, 4 sachets/day, approved as sole source VLCD by the Swedish National Food Agency) followed by 2-8 weeks gradual introduction of normal food. Early introduction of normal food occurred if patients were satisfied with the achieved weight loss or reached BMI<25kg/m². In June, 2009, the program was changed to 600 kcal/day for 3 weeks followed by 800kcal/day for up to 9 weeks.
- LCD: 2 calorie-restricted normal food meals and 2 formula-diet meal replacement sachets per day providing a total caloric intake of about 1200-1500kcal.

Indications & Follow-Up After Bariatric Surgery in Sweden

In the SOS study, patients underwent surgery between 1987 and 2001 at 25 surgical departments. During this time there were no uniform national guidelines for follow-up after bariatric surgery. Most follow-up visits were done by the bariatric surgeons and were focused on surgical and medical complications as well as nutritional and gastrointestinal problems. However, Sweden has a tax funded universally accessible health care system including access to psychologists and psychiatrists as well as internists, surgeons, primary care physicians, and dietitians. There has never been general use of psychological behavioural treatment or counselling before or after bariatric surgery in Sweden but if needed this was solved on an individual basis.

With growing numbers of operations in Sweden, specialist nurses were trained to handle much of the follow-up, and when SOReg started in 2007 this system for follow-up was fully developed. Certified nurses in Sweden have an academic education and work more independently than nurses in many other European countries and the US. If physical or psychological problems are identified patients can be referred to psychologists, psychiatrists, surgeons and dietitians associated with the surgical department. SOReg has implemented follow-up visits at 6 weeks (95% of patients covered), 1 year (87% covered), 2 years (65% covered), and recently also follow-up at 5 and 10 years.

The general recommendations regarding preoperative assessment include a psychiatric evaluation in individuals with psychiatric problems or eating disorders. Psychiatric disorders are relative contraindications and patients with such disorders may be accepted for surgery after psychiatric evaluation. Candidates for surgery are also required to have a stable psychosocial situation. Ongoing alcohol or substance abuse constitute absolute contraindications. Previous alcohol or substance abuse without documented abstinence for at least 2 years also constitute absolute contraindications. Previous alcohol or substance abuse more than 2 years back constitute relative contraindications.

eTable 1 Psychosocial variables and personality traits used in the matching algorithm

| | Swedish Obese Subjects Recruitment: 1987-2001 | | |
|---|--|----------------------|--------|
| Mean (SD) | Bariatric Surgery (n=2010) | Controls (n=2037) | Р |
| Current Health Score (9-36, higher better) | 21.4 (6.1) | 22.7 (6.2) | <0.001 |
| Monotony Avoidance Score ^a (10-40) | 22.5 (5.1) | 22.6 (5.0) | 0.525 |
| Psychasthenia Score ^b (10-40) | 23.9 (5.2) | 23·2 (5·3) | <0.001 |
| Quantity of Social Support (0-12) | 6.0 (2.4) | 6.1 (2.5) | 0.483 |
| Quality of Social Support (0-5) | 4.3 (1.3) | 4.3 (1.3) | 0.551 |
| Stressful Life Events (0-8) | 2.5 (1.3) | 2.4 (1.3) | 0.091 |

eTable 2 International Classification of Diseases (ICD) codes and Anatomical Therapeutic Chemical (ATC) classification system codes used

| Condition | ICD-10 | ICD-9 | ICD-8 | ATC Code |
|--|--------------|------------|-------------|----------|
| Substance Abuse | F10-19 | 291-292, | 291; 294,3; | NO7BB, |
| Substance Abuse | F10-19 | 303-305 | 303-304 | N07BC |
| Attempted Suicide/Self-Harm | X60-84 | E950-959 | E950-959 | |
| Attempted Suicide/Sell-Harili | Y10-34, Y870 | E980-989 | E980-989 | |
| Suicide – Undetermined Intent | Y10-34, Y870 | E980-989 | E980-989 | |
| Suicida Daisanina | X60-X69 | E950-E952, | E950-E952, | |
| Suicide - Poisoning | Y10-Y19 | E980-E982 | E980-E982 | |
| Psychiatric Care or Any Psychiatric Drug | Chapter F | 290-319 | 290-315 | N05, N06 |
| Antidepressants | | | | N06A |
| Antidiabetic Drugs | | | | A10 |
| Anxiolytic Drugs | | | | N05B |
| Hypnotic or Sedative Drugs | | | | N05C |
| Cardiovascular Disease | Chapter I | 390-459 | 390-458 | |

Events of undetermined intent are usually included in Swedish suicide research. Several studies have reported a large fraction of definite suicides when re-evaluating such events.(1, 2)

^a Monotony avoidance is a personality trait characterised by abnormal attempts to avoid routine and to seek change and action (i.e., thrill- or sensation-seeking behaviour)

^b Psychasthenia is characterised by tiredness, concentration and memory difficulties, and various sensations including palpitations

eTable 3 Description of deaths by suicide

| | Swedish Obese Subjects Recruitment: 1987-2001 | | SOReg/Itrim Recruitment: 2006-2013 | |
|-----------------------------|--|-------------------|---------------------------------------|------------------------------|
| | Bariatric Surgery (n=9) | Controls (n=3) | Gastric Bypass (n=33) | Intensive Lifestyle (n=5) |
| Suicide | 9 (100%) | 3 (100%) | 33 (100%) | 5 (100%) |
| - Undetermined Intent | 2 (22%) | 1 (33%) | 10 (30%) | 3 (60%) |
| Mode of Suicide | | | | |
| - Poisoning | 7 (78%) | 3 (100%) | 26 (79%) | 4 (80%) |
| - Other | 2 (22%) | 0 (0%) | 7 (21%) | 1 (20%) |
| Non-Fatal Self-Harm Event | | | | |
| - Before Baseline | 2 (22%) | 0 (0%) | 7 (21%) | 1 (20%) |
| - After Intervention | 3 (33%) | 1 (33%) | 8 (24%) | 1 (20%) |
| Previous Substance Abuse | | | | |
| - Before Baseline | 2 (22%) | 0 (0%) | 5 (15%) | 2 (40%) |
| - After Intervention | 2 (22%) | 0 (0%) | 10 (30%) | 1 (20%) |
| Season ^c | | | | |
| Spring (March-May) | 1 (11%) | 0 (0%) | 7 (21%) | 0 (0%) |
| Summer (June-August) | 1 (11%) | 0 (0%) | 7 (21%) | 3 (60%) |
| Fall (September-November) | 3 (33%) | 0 (0%) | 12 (36%) | 1 (20%) |
| Winter (December-February) | 4 (44%) | 3 (100%) | 7 (21%) | 1 (20%) |
| Primary Bariatric Procedure | | | | |
| Gastric Bypass | 2 (22%) | - | 33 (100%) | - |
| Gastric Banding | 2 (22%) | - | - | - |
| VBG ^d | 5 (56%) | - | - | - |
| Revision Surgery | | | | |
| VBG to Gastric Bypass | 2 (22%) | - | - | - |
| Banding to Gastric Bypass | 1 (11%) | ı | - | - |

^c Calendar definition (source: Swedish Meteorological and Hydrological Institute [SMHI]); https://www.smhi.se/kunskapsbanken/meteorologi/arstider-1.1082)

d Vertical-banded gastroplasty

eTable 4 Description of nonfatal self-harm events (excluding individuals dying by suicide who did not have a nonfatal self-harm event after intervention)

| | Swedish Obese Subjects Recruitment: 1987-2001 | | SOReg/Itrim Recruitment: 2006-2013 | | |
|-----------------------------|--|-----------|---------------------------------------|---------------------|--|
| | Bariatric Surgery | Controls | Gastric Bypass | Intensive Lifestyle | |
| | (n=81) | (n=47) | (n=316) | (n=80) | |
| Nonfatal Self-Harm Events | 81 (100%) | 47 (100%) | 316 (100%) | 80 (100%) | |
| - Undetermined Intent | 32 (40%) | 20 (43%) | 85 (27%) | 33 (41%) | |
| Mode of Self-Harm | | | | | |
| - Poisoning | 57 (70%) | 25 (53%) | 214 (68%) | 47 (59%) | |
| - Other | 24 (30%) | 22 (47%) | 102 (32%) | 33 (41%) | |
| Baseline Nonfatal Self-Harm | 17 (21%) | 4 (9%) | 41 (13%) | 13 (16%) | |
| Substance Abuse | | | | | |
| - Before Baseline | 11 (14%) | 3 (6%) | 35 (11%) | 13 (16%) | |
| - After Intervention | 39 (48%) | 13 (28%) | 162 (51%) | 23 (29%) | |
| Seasone | | | | | |
| Spring (March-May) | 21 (26%) | 13 (28%) | 64 (20%) | 19 (24%) | |
| Summer (June-August) | 16 (20%) | 11 (23%) | 80 (25%) | 18 (23%) | |
| Fall (September-November) | 17 (21%) | 14 (30%) | 93 (29%) | 24 (30%) | |
| Winter (December-February) | 27 (33%) | 9 (19%) | 79 (25%) | 19 (24%) | |
| Primary Bariatric Procedure | | | | | |
| Gastric Bypass | 16 (20%) | - | 316 (100%) | - | |
| Gastric Banding | 14 (17%) | - | - | - | |
| VBG ^f | 51 (63%) | - | - | - | |
| Revision Surgery | | | | | |
| VBG to Gastric Bypass | 10 (12%) | - | | | |
| Banding to Gastric Bypass | 3 (4%) | - | | | |

 $^{^{\}rm e} \ {\sf Calendar} \ {\sf definition} \ ({\sf source: Swedish \ Meteorological \ and \ Hydrological \ Institute \ [SMHI]); \\ \underline{\sf https://www.smhi.se/kunskapsbanken/meteorologi/arstider-1.1082})$

f Vertical-banded gastroplasty

eTable 5 Baseline characteristics in participants with history of psychiatric disorder or nonfatal self-harm

| | Swedish Obese Subjects Recruitment: 1987-2001 | | | SOReg/Itrim Recruitment: 2006-2013 | | |
|--|--|---------------------|---------|---------------------------------------|---------------------------------|---------|
| | Bariatric Surgery (n=379) | Controls (n=334) | Р | Gastric Bypass (n=7639) | Intensive Lifestyle (n=4270) | P |
| Women, n (%) | 289 (76·3%) | 240 (71.9%) | 0.181 | 6917 (90·5%) | 3866 (90·5%) | 1.0 |
| Age (Years), Mean (SD) | 48·1 (6·0) | 49·3 (6·5) | 0.0092 | 42.0 (10.0) | 42·2 (10·3) | 0.501 |
| Body Mass Index (kg/m²), Mean (SD) | 42.0 (4.4) | 40·1 (4·8) | <0.0001 | 40.4 (3.7) | 39.8 (3.9) | <0.0001 |
| University Education, n (%) | 44 (11.6%) | 56 (16·8%) | 0.048 | 1795 (23.5%) | 1003 (23·5%) | 1.0 |
| Married, n (%) | - | - | - | 3348 (43.8%) | 1777 (41-6%) | 0.019 |
| Income (1000 €), Mean (SD) | - | - | - | 21.7 (12.1) | 26·2 (15·5) | <0.0001 |
| Disability Pension, n (%) | - | - | - | 1617 (21·2%) | 525 (12·3%) | <0.0001 |
| Unemployment, n (%) | - | - | - | 769 (10·1%) | 314 (7·4%) | <0.0001 |
| History of Psychiatric Illness, n (%) | | | | | | |
| Self-Harm | 69 (18·2%) | 38 (11·4%) | 0.011 | 403 (5·3%) | 225 (5·3%) | 1.0 |
| Substance Abuse | 58 (15·3%) | 49 (14·7%) | 0.813 | 294 (3·8%) | 164 (3.8%) | 1.0 |
| Psychiatric Hospital Visits ⁷ | 200 (52·8%) | 175 (52·4%) | 0.920 | 3083 (40-4%) | 1723 (40·4%) | 1.0 |
| Use of Antidepressants | 133 (35·1%) | 114 (34·1%) | 0.788 | 6108 (80.0%) | 3414 (80.0%) | 1.0 |
| Use of Anxiolytics | 98 (25·9%) | 88 (26·3%) | 0.882 | 3446 (45·1%) | 1926 (45·1%) | 1.0 |
| Use of Hypnotics & Sedatives | 74 (19·5%) | 59 (17·7%) | 0.525 | 3316 (43.4%) | 1632 (38·2%) | <0.0001 |
| Physical Health Status, n (%) | | | | | | |
| Diabetes | 76 (20·1%) | 49 (14·7%) | 0.059 | 434 (5·7%) | 243 (5·7%) | 1.0 |
| Cardiovascular Disease | 90 (23·7%) | 59 (17·7%) | 0.046 | 1521 (19.9%) | 850 (19·9%) | 1.0 |

⁷ SOS: Inpatient care only; SOReg/Itrim: Inpatient care (17·8% surgery versus 17·2% intensive lifestyle; P=0·460) and outpatient care (32·8% versus 32·5%; P=0·739)

eTable 6 Evidence table of studies on bariatric surgery and suicide

| Author | Intervention | Comparator | Suicide/self-harm |
|---------------------------|--|--|--|
| Journal, Year | Intervention years | | |
| Country | Follow-up | | |
| Vs Obese Comparators | | | |
| Adams et al (3) | Gastric bypass (n=9949) | Severely obese individuals applying for driver's | 15 vs 5 suicides (2·6 vs 0·9 per 10,000 pyrs) |
| NEJM, 2007 | 1984-2002 | licenses (n=7925) | Adjusted HR: 2·03 (95%CI 0·66-6·27), P=0·22 |
| USA | Mean follow-up 7·1y | | |
| Adams et al (4) | Gastric bypass (n=418) | Severely obese individuals seeking but not receiving | 4 vs 0 suicides (difference not statistically significant) |
| JAMA, 2012 | 2000-2011 | surgery (n=417) | |
| USA | Median follow-up: 5-8y | Severely obese individuals drawn at random from the | 4 vs 0 suicides (difference not statistically significant) |
| | | Utah Health Family Tree Program database (n=321) | |
| | | Both control groups combined | 4 vs 0 suicides |
| | | | Odds ratio 18 (95%Cl 1-385), P=0·02 |
| Kovacz et al (5) | KJDF00-KJDF98 (n=9641) ⁸ | Individuals with a hospital diagnosis of obesity | HR for suicide (adjusted for sex and age): |
| Acta Psych, 2017 | 1997-2013 | (n=7973) | 1·35 (95%CI 0·36-5·07), P=0·658 |
| Denmark | Mean follow-up: 4·0y | | HR for intentional self-harm: |
| | | | 3·23 (95%Cl 1·93-5·40), P<0·001 |
| Vs General Population | | | |
| Backman et al (6) | Gastric bypass (n=16,755) | Age-sex-matched general population (n=167,550) | 21·2 vs 10·6 suicide attempts per 10,000 pyrs |
| BJS, 2016 | 2001-2010 | | Adjusted HR: 2·85 (95%CI 2·40-3·39) |
| Sweden | Follow-up: 4y | | 10/4 ::: / |
| Trolle-Lagerros et al (7) | Gastric bypass (n=22,539) 2008-2012 | General population via estimation of standardised | 13/4 suicides in women/men |
| Ann Surg, 2017 | | mortality ratios (SMRs) | SMR women: 4·50 (95%CI 2·50-7·50) |
| Sweden Tindle et al (8) | Follow-up: 2y | Constant and Jaking (25 CA) | SMR men: 1·71 (95%CI 0·54-4·12) 31 suicides after bariatric surgery |
| Am J Med, 2010 | Bariatric surgery (n=16,683) 1995-2004 | General population (35-64y) | Incidence per 10,000pyrs (women/men): |
| USA | Follow-up: Until December 2006 | | Bariatric surgery: 13·7 / 5·2 |
| USA | Tollow-up. Ontil December 2000 | | United States general population: 2·4 / 5·7 |
| Morgan & Ho (9) | Gastric banding, gastric bypass, sleeve gastrectomies, ileo- | General population | Higher rate of hospitalisations due to deliberate self-harm for |
| Ann Surg, 2017 | pancreatic diversions (n=12,062) | General population | bariatric surgery patients than the general population: |
| Australia | 2007-2011 | | IRR 1·47 (95%CI 1·11–1·94), P=0·005 |
| | Follow-up: 40·6 months | | (22,13, 222 23.)). |
| Gribsholt et al (10) | Gastric bypass (n=9895) | Age-sex-matched general population (n=247,366) | Mortality rate ratio for suicide: |
| SOARD, 2017 | 2006-2010 | 5 | 2·78 (95%CI 1·44-5·33) |
| Denmark | Follow-up: Until end of 2013 | | , |

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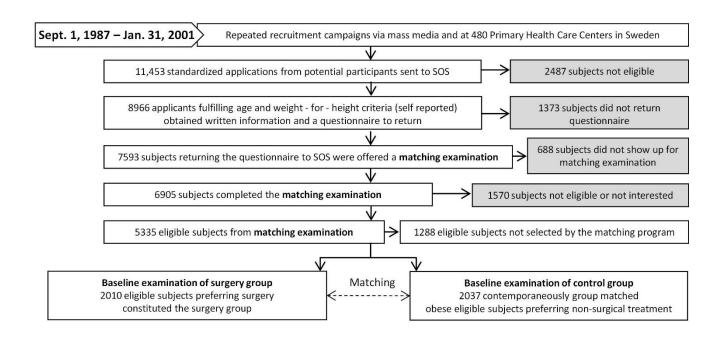
⁸ Individuals with psychiatric contacts before surgery were excluded from the analysis of suicide after surgery (surgery group: 9487 women + 3125 men - 2971 with psychiatric contact; comparator group: 8598 women + 1241 men – 1866 with psychiatric contact)

eTable 6 Evidence table of studies on bariatric surgery and suicide (continued)

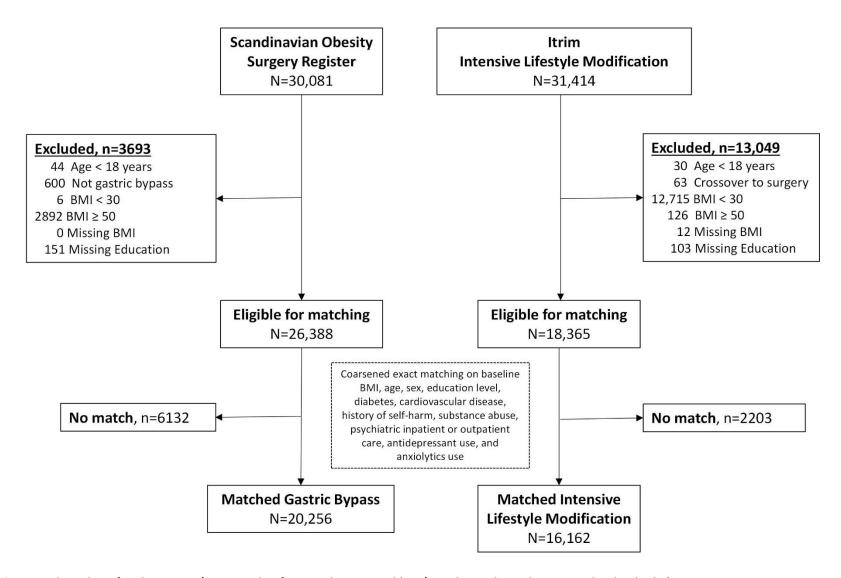
| Author | Intervention | Comparator | Suicide/self-harm |
|------------------------|--|------------|---|
| Journal, Year | Intervention years | | |
| Country | Follow-up | | |
| Before/After | | | |
| Bhatti et al (11) | Gastric bypass (n=8681), intestinal bypass (n=89), sleeve | - | Self-harm emergencies (per 1000pyrs) |
| JAMA Surg, 2015 | gastrectomy (n=45) | | 2·33 before vs 3·63 after surgery |
| Canada | 2006-2011 | | Rate ratio 1·54 (95%CI 1·03-2·30), P=0·007 |
| | Follow-up: 3y | | |
| Kovacz et al (5) | KJDF00-KJDF98 (n=12,612) | - | Intentional self-harm HRs: |
| Acta Psych Scand, 2017 | 1997-2013 | | 1y: 1·71 (95%Cl 1·14-2·55), P<0·01 |
| Denmark | Follow-up: 3, 5 and 7y | | 3y: 1·60 (95%Cl 1·09-2·33), P<0·05 |
| | | | 5y: 1·91 (95%Cl 1·24-2·93), P<0·01 |
| Morgan & Ho (9) | Gastric banding, gastric bypass, sleeve gastrectomies, ileo- | - | No statistically significant increase in deliberate self-harm |
| Ann Surg, 2017 | pancreatic diversions (n=12,062) | | hospitalisations after vs before surgery: IRR 0·79 (95%CI 0·54– |
| Australia | 2007-2011 | | 1·16), P=0·21) |
| | Follow-up: 40·6 months | | |

eTable 7 Distribution by BMI category in the SOReg/Itrim study

| | SOReg/Itrim Recruitment: 2006-2013 | | |
|----------------------|---------------------------------------|-----------------------------------|--|
| BMI Category (kg/m²) | Gastric Bypass (n=20 256) | Intensive Lifestyle (n=16 162) | |
| 30 to <35 | 888 (4.4%) | 709 (4.4%) | |
| 35 to <40 | 7519 (37.1%) | 5999 (37.1%) | |
| 40 to <45 | 8255 (40.8%) | 6587 (40.8%) | |
| 45 to <50 | 3594 (17.7%) | 2868 (17.7%) | |



eFigure 1 Flow chart for the Swedish Obese Subjects (SOS) study



eFigure 2 Flow chart for the SOReg/Itrim study of gastric bypass and low/very low calorie diet treated individuals (intervention years: 2006-2013)

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