# Effect of gastric bypass versus sleeve gastrectomy on the remission of type 2 diabetes, weight loss, and cardiovascular risk factors at 5 years (Oseberg): secondary outcomes of a single-centre, triple-blind, randomised controlled trial

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## Summary

**Background** For individuals with obesity and type 2 diabetes, weight loss improves insulin sensitivity and β-cell function and can induce remission of diabetes. However, the long-term comparative effectiveness of standard gastric bypass and sleeve gastrectomy on remission of type 2 diabetes remains unclear. We aimed to compare the effects of gastric bypass and sleeve gastrectomy on type 2 diabetes remission, weight loss, and cardiovascular risk factors 5 years after surgery.

**Methods** We present a secondary analysis of a two-armed, single-centre, triple-blind, randomised controlled trial conducted at a public tertiary obesity centre in Norway. Adults (ie, age ≥18 years) with type 2 diabetes and obesity were randomly assigned (1:1) by a computerised random number generator to laparoscopic gastric bypass or sleeve gastrectomy, with balanced block sizes of ten. Study personnel, participants, and the primary-outcome assessor were all masked to the allocation until 1 year after surgery, after which further follow-up was open label. Changes in key secondary outcomes, including type 2 diabetes remission, weight loss, and cardiovascular risk factors, were assessed 5 years after surgery. The trial procedure estimand assessed treatment effects in all randomised participants, with data collected after conversional surgery removed from analyses. The trial was registered with ClinicalTrials.gov (NCT01778738) and was completed in December, 2022.

**Findings** Between Oct 15, 2012, and Sept 1, 2017, 319 patients were assessed for eligibility, resulting in 109 participants who were randomly assigned to gastric bypass (n=54) or sleeve gastrectomy (n=55). The baseline mean age was 47·7 years (SD 9·6), mean BMI 42·3 kg/m² (SD 5·3), 72 (66%) were women, and 37 (34%) were men. 93 (85%) participants completed 5-year follow-up (47 [85%] in the sleeve gastrectomy group and 46 [85%] in the gastric bypass group). The proportions with remission of type 2 diabetes were higher after gastric bypass than after sleeve gastrectomy ($HbA_{1c}$ ≤6·0% 23 [50%] of 46 *vs* nine [20%] of 44, risk difference 29·5% [95% CI 10·8 to 48·3]; $HbA_{1c}$ <6·5% 29 [63%] *vs* 13 [30%], risk difference 33·5% [14·1 to 52·9]). Gastric bypass provided greater loss in bodyweight (mean 22·2% [95% CI 20·3 to 24·1] *vs* 17·2% [15·3 to 19·1], treatment difference 5·0% [2·4 to 7·7]) and lower LDL-cholesterol (treatment difference –0·5 mmol/L [–0·8 to –0·1]). The prevalence of erosive oesophagitis and Barrett's oesophagus was similar between groups, whereas pathological acid reflux occurred more frequently after sleeve gastrectomy (risk difference 51·1% [28·0 to 74·2]). More participants had symptomatic postprandial hypoglycaemia after gastric bypass than after sleeve gastrectomy (15 [28%] *vs* one [2%]).

**Interpretation** Gastric bypass was superior to sleeve gastrectomy regarding long-term remission of type 2 diabetes, weight loss, and LDL cholesterol concentrations, at the expense of a higher frequency of symptomatic postprandial hypoglycaemia. These findings could inform clinical practice and future guidelines regarding the preferred surgical procedure in patients with type 2 diabetes.

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For the Norwegian translation of the abstract see **Online** for appendix 1

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## Introduction

Metabolic bariatric surgery provides substantial health benefits for people living with type 2 diabetes, including the remission of diabetes,[1,2] weight loss,[3] improved serum lipid profile,[4] lower blood pressure,[5] lower cardiovascular morbidity and mortality,[6] and improved health-related

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## Research in context

### Evidence before this study

From the initiation of the Oseberg trial on January 28, 2013 until May 10, 2024, we searched PubMed regularly for new long-term clinical trials (ie, ≥5 years) comparing the effects of gastric bypass and sleeve gastrectomy on diabetes remission as a primary, secondary, or exploratory outcome, using the search terms "sleeve gastrectomy" and "gastric bypass" and "diabetes". An updated search was done upon completion of the trial using the same search terms, but restricted to article type "clinical trial", including trials published in English from database inception until May 10, 2024. All results were systematically assessed for relevance and cross-checked with ClinicalTrials.gov when appropriate.

First, the searches identified only one long-term (5-year) high-quality randomised clinical trial, the STAMPEDE trial, which showed that bariatric surgery (standard gastric bypass or sleeve gastrectomy) plus intensive medical therapy was superior to intensive medical therapy alone in reaching the primary endpoint of $HbA_{1c}$ less than or equal to 6% (with or without the use of diabetes medication) in patients with type 2 diabetes ($HbA_{1c}$ ≥7·1%) and BMI 27–43 kg/m². By contrast, the 5-year diabetes remission rates ($HbA_{1c}$ ≤6% without the use of diabetes medication, a secondary endpoint) were similar between standard gastric bypass (22%) and sleeve gastrectomy (15%). Second, another high-quality randomised clinical trial compared the 5-year effects of a modified banded (ie, silastic ring) gastric bypass and sleeve gastrectomy on the primary outcome remission of type 2 diabetes. This randomised trial showed that a silastic ring gastric bypass was superior to sleeve gastrectomy on remission of type 2 diabetes ($HbA_{1c}$ <6·0 %): 48% of patients had remission of diabetes after a silastic ring gastric bypass versus 31% after sleeve gastrectomy. In addition, three relatively large long-term randomised clinical trials comparing standard gastric bypass with sleeve gastrectomy, with long-term diabetes remission as secondary or exploratory outcomes and samples of which 25%, 42%, and 18% of patients had type 2 diabetes, showed no significant differences between the procedures.

### Added value of this study

To our knowledge, this is the first long-term (ie, ≥5 years) randomised clinical trial showing standard gastric bypass to be superior in providing remission of type 2 diabetes when compared with sleeve gastrectomy. In addition, gastric bypass provided a greater loss of bodyweight and had a greater long-term effect on cardiovascular risk factors and weight-specific quality of life than sleeve gastrectomy.

### Implications of all the available evidence

The 5-year results of the Oseberg trial provide data to the existing body of evidence, suggesting that gastric bypass is more than twice as likely to provide remission of type 2 diabetes compared with sleeve gastrectomy in the long term. These findings have the potential to change clinical practice regarding the preferred surgical procedure in people with type 2 diabetes and obesity, and they should be considered in the shared decision-making process before surgery.

quality of life (HRQOL).[7,8] However, bariatric surgery is also associated with a risk of various surgical, medical, and nutritional complications.[9,10]

International guidelines recommend bariatric surgery as an appropriate treatment option for individuals with type 2 diabetes and a BMI of 35 kg/m² or higher.[11,12] However, these guidelines do not specify a preferred surgical procedure in eligible individuals. Standard Roux-en-Y gastric bypass, generally referred to as a gastric bypass, and sleeve gastrectomy are the two most established and commonly performed bariatric procedures globally, constituting 90% of all bariatric procedures annually.[13]

Only one high-quality randomised clinical trial, the STAMPEDE trial, which was designed to compare bariatric surgery with intensive lifestyle intervention, has compared the long-term (ie, 5-year) treatment effects of gastric bypass with sleeve gastrectomy in people with type 2 diabetes.[2] Although underpowered to detect differences between the surgical procedures, this landmark study showed that gastric bypass was associated with greater 5-year weight loss compared with sleeve gastrectomy, whereas diabetes remission rates and changes in cardiovascular risk factors and generic HRQOL were similar. By contrast, a randomised controlled trial from New Zealand[1] comparing silastic ring gastric bypass with sleeve gastrectomy found the modified gastric bypass to provide greater diabetes remission rates and weight loss, greater improvement in HDL cholesterol, and better physical functioning 5 years after surgery. In addition, three long-term (ie, 5-year) clinical trials, including subpopulations with type 2 diabetes, have compared gastric bypass with sleeve gastrectomy,[14–17] all reporting similar diabetes remission rates after the different procedures. Finally, the 3-year results from the Oseberg trial[8] showed that gastric bypass, as compared with sleeve gastrectomy, provided greater diabetes remission rates, weight loss, and weight-related quality of life.

As such, an uncertainty remains as to whether one of the surgical procedures is preferrable with regards to several clinically important long-term outcomes in people with type 2 diabetes. In this Article we present prespecified secondary analyses of the Oseberg trial.[18] We hypothesised that gastric bypass would be superior to sleeve gastrectomy for remission of type 2 diabetes, weight loss, and improvement of cardiovascular risk factors, including lipid concentrations and blood pressure, and HRQOL. In addition, we expected that gastric bypass would lead to an increased incidence of symptomatic postprandial hypoglycaemia compared with sleeve gastrectomy.

## Methods

### Study design

The Oseberg trial was a two-armed, single-centre, triple-blind randomised clinical trial in a public tertiary care obesity centre at the Vestfold Hospital Trust, Tønsberg, Norway. The study protocol was approved by the Regional Committees for Medical and Health Research Ethics in Norway (2012/1427/REK sør-øst B) and has previously been published (appendix 2).[18] The trial is registered at ClinicalTrials.gov (NCT01778738).

### Participants

The inclusion criteria for the Oseberg trial were age 18 years or older, type 2 diabetes ($HbA_{1c}$ ≥6·5% or use of antidiabetic medications with $HbA_{1c}$ ≥6·1%), a previously verified BMI of at least 35·0 kg/m², and a current BMI of at least 33·0 kg/m². Patients scheduled for bariatric surgery who met the inclusion criteria were contacted by telephone and offered to participate in a screening consultation. Key exclusion criteria included previous major abdominal surgery, severe medical conditions with markedly increased risk of complications, pregnancy, severe gastro-oesophageal reflux, and drug or alcohol addiction. Sex was self-reported by participants as either male or female. All participants provided written informed consent.

### Randomisation and masking

Participants were randomly allocated (1:1) by use of a computerised random number generator, with balanced block sizes of ten, to receive either a sleeve gastrectomy or a gastric bypass. Author MS generated the randomisation sequence and was not involved in participant follow-up. The allocation was revealed to the surgical staff only on the day of surgery, after which an opaque envelope was resealed. The surgical staff were not involved in participant follow-up. Study personnel, participants, and the primary-outcome assessor were all masked to the allocation until blinding was broken at 1 year after surgery, after which further follow-up was open label.

### Procedures

Identical preoperative and postoperative care were given to both groups, including a low-calorie diet (ie, <1200 kcal/day) for the 2 weeks preceding surgery. Sleeve gastrectomy (with a 35 Fr bougie) and Roux-en-Y gastric bypass (with a 25 mL pouch, a 120 cm Roux limb, and a 60 cm biliopancreatic limb) were done laparoscopically, with similar skin incisions. Postoperative assessments were made at 5 weeks, 16 weeks, 34 weeks, 1 year, and then annually until completion of the trial at 5 years. Predefined algorithms concerning medication adjustments and vitamin supplements were specified in the protocol (appendix 2 pp 54–55).[18]

### Outcomes

The primary clinical outcome of the Oseberg trial was remission of type 2 diabetes 1 year after surgery.[18] This Article is a secondary analysis of predefined key secondary outcomes at 5 years, encompassing remission of type 2 diabetes, glycaemic control, medication use, changes in bodyweight and composition, changes in cardiovascular risk factors, and participant-reported outcomes.[18] In addition, the prevalence of gastro-oesophageal reflux disease (GERD) and all adverse events (≥6 weeks after surgery) are reported. Prespecified outcomes not addressed in this paper will be reported separately.

See Online for appendix 2

To better inform the reader, and to ensure comparability with previous and future studies, remission of type 2 diabetes was defined with two diagnostic cutoffs (ie, $HbA_{1c}$ ≤6·0% [42 mmol/mol] or $HbA_{1c}$ <6·5% [48 mmol/mol]), with no use of antidiabetic medication being a prerequisite for both definitions. At all post-operative follow-ups, participants underwent a clinical examination, blood tests, and a thorough medication review.[17] Urine samples were analysed for albuminuria. Bodyweight and composition were measured while participants wore light clothing and by use of a bioelectrical impedance analysis (InBody 720 body composition analyser, BioSpace, South Korea).

The patient-reported outcome measures reported in this analysis include generic HRQOL (36-item Short-Form Health Survey [SF-36]), weight-related quality of life (Impact of Weight on Quality of Life-Lite [IWQOL-Lite]), weight-related symptoms (Weight-related Symptom Measure), and depression (Beck's Depression Inventory). A detailed description of each measure is available in a previous publication.[8]

Methods for assessing GERD, dumping symptoms, postprandial hypoglycaemia, and adverse events are detailed in the appendix 3 (pp 2–3), and have been published previously.[8,18–23] Additionally, a post-hoc analysis of the number of individuals reaching an American Diabetes Association composite treatment goal[24] (ie, $HbA_{1c}$ <7·0%, LDL cholesterol <2·6 mmol/L, and systolic blood pressure <130 mm Hg, irrespective of medication) was conducted.

See Online for appendix 3

### Statistical analysis

The Oseberg trial was designed with a two-sided significance level of 5% and 80% power to detect differences in diabetes remission 1 year after surgery, requiring 55 participants in each group.[18] In accordance with the CONSORT guidelines, we did not perform any sample size calculation for secondary outcomes.

To compare the 5-year specific treatment effects of gastric bypass and sleeve gastrectomy, we analysed the data within the estimand framework.[25] Given that we aimed to compare the long-term effects of the two surgical procedures, we chose a hypothetical strategy by defining a trial procedure estimand (ie, the surgical treatment

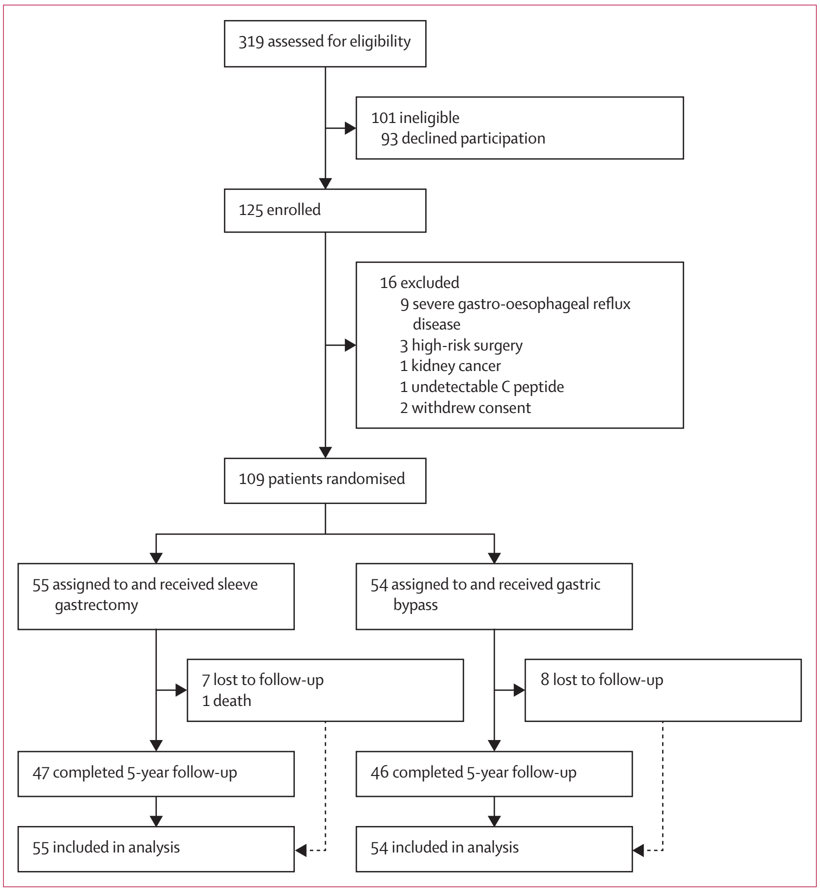


***Figure 1:*** **Trial profile**

effects that would occur if no conversional surgery had been performed during follow-up) for all analyses. All randomised participants were included in the analysis, but any participant data collected after conversional surgery from sleeve gastrectomy to gastric bypass were removed from the analyses. Missing data were not imputed, and mixed models for repeated measures were applied as detailed. Key secondary continuous outcomes (ie, $HbA_{1c}$ values, bodyweight, LDL cholesterol, and systolic blood pressure) were analysed in three different sensitivity analyses (appendix 3 p 11).

A treatment policy strategy including all participants and with all collected data, regardless of conversional surgery being performed, was implemented for sensitivity analysis for the outcome remission of diabetes. Missing data for $HbA_{1c}$ and usage of diabetes medication were imputed by the use of chained multiple imputation (Stata version 17.0) with sex, diabetes duration, age, weight, $HbA_{1c}$ values, and diabetes medication at baseline as possible outcome predictors. Analyses in this Article are for the trial procedure estimand, unless otherwise specified.

Binary outcomes are reported as counts and percentages and are analysed with generalised linear models for the binomial family (identity link), including time (discrete), treatment, and their interaction as covariates. Results are reported as risk differences with 95% CIs. The continuous outcomes are analysed with mixed models for repeated measures with time (discrete), treatment, and time×treatment interaction entered as a fixed effect. Each participant was modelled with random intercept to capture within-participant variation. Between-participant variation was modelled with an unstructured covariance matrix. The normality assumption underlying linear mixed models was assessed by visual inspection of Q-Q plots and histograms of the residuals. Using the described mixed effects models, we calculated point estimates (with associated 95% CIs) for mean values of the outcome for all timepoints, change from baseline to 5 years, and the estimated difference in change between groups. All repeated measures analyses were started from baseline (coded as zero), and the models included all follow-up visits (ie, all consecutive assessment timepoints). None of the repeated measures models in the main analysis were adjusted for any confounders.

The number of late adverse events (ie, occurring ≥6 weeks after surgery), participants experiencing dumping symptoms, and participants with symptomatic postprandial hypoglycaemia are summarised throughout the trial period. Participant event proportions were compared with the $\chi^2$ test or Fisher's exact test as appropriate.

Cronbach's α was used to measure the internal consistency for the patient-reported outcome measures, with values of 0·7 or higher deemed acceptable and values of 0·8 or higher considered good. All tests were two-sided and significance level was set to 0·05. We did no correction for multiple testing. All statistical analyses were done using Stata versions 17.0 and 18.0.

### Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or the writing of the report.

## Results

Between Oct 15, 2012, and Sept 1, 2017, 319 consecutive participants with type 2 diabetes scheduled for bariatric surgery were assessed for eligibility, of whom 109 participants were randomly assigned to either sleeve gastrectomy (n=55) or gastric bypass (n=54; figure 1). At 5 years, eight participants were lost to follow up in both groups. A total of 93 (85%) participants completed the 5-year follow-up, of whom three had a simplified follow-up via telephone due to either the COVID-19 pandemic or personal refusal of a comprehensive follow-up. $HbA_{1c}$ (analysed in external laboratories) and the history of medication usage were collected from all three participants. Three participants underwent conversion from sleeve gastrectomy to gastric bypass during the trial period (one at 2 years and two at 3 years).

At baseline, the participants had a combined mean age of 47·7 years (SD 9·6) and a mean BMI of 42·3 kg/m² (5·3); 72 (66%) were women and 107 (98%) were White. Both groups had similar demographic characteristics (table 1). There were no significant differences in baseline demographic characteristics between those who completed the study and those lost to follow-up (appendix 3 p 4). The patient-reported outcome measures showed a good internal consistency, as indicated by a Cronbach's α of 0·8 or higher for most scores and 0·7 or higher for two subscales (general health and vitality) in the SF-36 and one subscale (work) in the IWQOL-Lite.

The proportion of participants with remission of type 2 diabetes at 5 years, independent of $HbA_{1c}$ cutoffs, was significantly higher after gastric bypass than after sleeve gastrectomy: $HbA_{1c}$ less than or equal to 6·0% for 23 (50%) of 46 participants in the gastric bypass group versus nine (20%) of 44 in the sleeve gastrectomy group (risk difference 29·5% [95% CI 10·8 to 48·3]) and $HbA_{1c}$ less than 6·5% for 29 (63%) of 46 in the gastric bypass group versus 13 (30%) of 44 in the sleeve gastrectomy group (risk difference 33·5% [14·1 to 52·9]; table 2; figure 2A). None of the three participants who were converted from sleeve gastrectomy to gastric bypass were in remission at the time of conversion, whereas all three were in remission ($HbA_{1c}$ ≤6·0%) at the 5-year follow-up. Analyses based on the treatment policy estimand confirmed the superiority of gastric bypass versus sleeve gastrectomy on remission of type 2 diabetes ($HbA_{1c}$ ≤6·0%: risk difference 20·9% [95% CI 2·9–38·8]; $HbA_{1c}$ <6·5%: risk difference 24·5% [5·7–43·4]). Both $HbA_{1c}$ and fasting glucose decreased significantly during the trial, with no significant difference between the groups (table 2; figure 2B; appendix 3 p 12). The proportions of participants using antidiabetic medication at the 5-year follow-up was significantly lower in the gastric bypass group than in the sleeve gastrectomy group, with a risk difference of 33·1% (95% CI 13·7–52·5), whereas the proportion of participants using insulin did not differ significantly between groups (table 2; figure 2C)

The mean 5-year change in BMI was –9·4 kg/m² (95% CI –10·2 to –8·6) after gastric bypass versus –7·3 kg/m² (–8·1 to –6·5) after sleeve gastrectomy (treatment difference –2·1 kg/m² [95% CI –3·3 to –0·9]; table 2). Bodyweight decreased in both groups, but decreased significantly more after gastric bypass than after sleeve gastrectomy (table 2; figure 2D). The mean 5-year total loss of bodyweight was 22·2% (95% CI 20·3 to 24·1) after gastric bypass versus 17·2% (15·3 to 19·1) after sleeve gastrectomy (between-group difference 5·0% [2·4 to 7·7]; table 2; appendix 3 p 13). Fat mass loss at 5 years was greater after gastric bypass (36·7% [33·1 to 40·2] reduction from baseline) than after sleeve gastrectomy (27·2% [23·6 to 30·8]), whereas fat-free mass decreased similarly after both procedures (9·0% [7·6 to 10·4] reduction from baseline for gastric bypass *vs* 8·4% [7·0 to 9·8] reduction for sleeve gastrectomy; table 2; appendix 3 p 14).

| | Sleeve gastrectomy (n=55) | Gastric bypass (n=54) |
|---|---|---|
| Age, years | 47·1 (10·2) | 48·2 (8·9) |
| Sex | | |
| Female | 32 (58%) | 40 (74%) |
| Male | 23 (42%) | 14 (26%) |
| Ethnicity | | |
| White | 54 (98%) | 53 (98%) |
| Other | 1 (2%) | 1 (2%) |
| Employed | 33 (60%) | 32 (59%) |
| Level of education* | | |
| Primary school | 7 (13%) | 13 (24%) |
| High school | 32 (58%) | 26 (48%) |
| Higher education | 15 (27%) | 15 (28%) |
| Current smoker | 4 (7%) | 7 (13%) |
| Bodyweight, kg | 126·7 (21·4) | 124·4 (23·2) |
| BMI, kg/m² | 42·1 (5·3) | 42·4 (5·4) |
| Waist circumference, cm | 128 (12) | 127 (12) |
| Diabetes duration, years | 5·0 (2·0–9·0) | 4·0 (2·0–10·0) |
| $HbA_{1c}$ | 7·9% (6·9–9·9) | 7·6% (6·8–8·5) |
| $HbA_{1c}$, mmol/mol | 63 (52–85) | 60 (51–70) |
| Systolic blood pressure, mm Hg | 131·9 (16·7) | 131·4 (13·4) |
| Diabetes medication | 50 (91%) | 46 (85%) |
| Insulin | 12 (22%) | 11 (20%) |
| Antihypertensive medication | 36 (66%) | 37 (69%) |
| LDL cholesterol, mmol/L | 2·6 (0·8) | 2·5 (0·8) |
| Lipid-lowering medication | 28 (51%) | 22 (41%) |
| Coronary artery disease | 2 (4%) | 6 (11%) |
| GSRS-R score | 1 (1–2) | 1 (1–2) |
| GERD-Q score | 6·5 (2·0) | 6·0 (1·4) |
| Acid exposure time | 4·1% (1·6–8·1) | 4·3% (1·7–10·4) |
| Erosive oesophagitis† | 31/53 (58%) | 30/53 (57%) |
| Antireflux medication | 11 (20%) | 17/54 (31%) |
| Early dumping symptoms | 22 (40%) | 26 (48%) |
| Late dumping symptoms | 15 (27%) | 15 (28%) |

Data are n (%), mean (SD) if normally distributed, or median (IQR) if skewed. GERD-Q=Gastro-oesophageal Reflux Disease Questionnaire. GSRS-R=Gastrointestinal Symptom Rating Scale-Reflux. *Data missing for one patient in the sleeve gastrectomy group. †Three participants did not have a gastroscopy at baseline.

***Table 1:* Baseline characteristics**

Total cholesterol concentrations were reduced 5 years after gastric bypass, but unchanged after sleeve gastrectomy (between-group difference –0·4 mmol/L [95% CI –0·8 to –0·02]; table 2; appendix 3 p 15). LDL cholesterol concentrations remained unchanged after gastric bypass, but increased after sleeve gastrectomy (between-group difference –0·5 mmol/L [–0·8 to –0·1]). Both triglycerides and HDL cholesterol concentrations improved similarly in both groups, whereas the

| | Sleeve gastrectomy (n=55) | Gastric bypass (n=54) | Risk difference (%) or between-group difference (95% CI) | p value |
|---|---|---|---|---|
| **Diabetes remission at 5 years*** | | | | |
| $HbA_{1c}$ ≤6·0% (42 mmol/mol) without antidiabetic drugs | 9/44 (20%) | 23/46 (50%) | 29·5 (10·8 to 48·3) | 0·0020 |
| $HbA_{1c}$ <6·5% (48 mmol/mol) without antidiabetic drugs | 13/44 (30%) | 29/46 (63%) | 33·5 (14·1 to 52·9) | 0·0007 |
| **Glucose homoeostasis** | | | | |
| $HbA_{1c}$ | | | | |
| Baseline | 8·4% (8·1 to 8·7) | 7·9% (7·6 to 8·2) | .. | .. |
| 5 year | 6·8% (6·5 to 7·1) | 6·2% (5·9 to 6·6) | –0·5 (–1·0 to –0·1) | 0·017 |
| Change from baseline | –1·6% (–1·9 to –1·3) | –1·7 (–1·9 to –1·4) | –0·1 (–0·4 to 0·3) | 0·77 |
| $HbA_{1c}$, mmol/mol | | | | |
| Baseline | 68·2 (64·8 to 71·5) | 62·8 (59·5 to 66·2) | .. | .. |
| 5 year | 50·6 (47·1 to 54·1) | 44·6 (41·2 to 48·1) | –6·0 (–10·9 to –1·1) | 0·017 |
| Change from baseline | –17·6 (–20·5 to –14·6) | –18·2 (–21·1 to –15·2) | –0·6 (–4·8 to 3·6) | 0·77 |
| Fasting glucose, mmol/L | | | | |
| Baseline | 12·1 (11·2 to 13·0) | 11·7 (10·8 to 12·6) | .. | .. |
| 5 year | 8·3 (7·3 to 9·2) | 7·2 (6·2 to 8·1) | –1·1 (–2·5 to 0·2) | 0·097 |
| Change from baseline | –3·8 (–4·7 to –3·0) | –4·6 (–5·4 to –3·7) | –0·7 (–1·9 to 0·5) | 0·23 |
| Antidiabetic drugs | | | | |
| Baseline | 50 (91%) | 46 (85%) | .. | .. |
| 5 year* | 27/44 (61%) | 13/46 (28%) | 33·1 (13·7 to 52·5) | 0·0008 |
| Use of insulin | | | | |
| Baseline | 12 (22%) | 11 (20%) | .. | .. |
| 5 year* | 6/44 (14%) | 4/46 (9%) | 4·9 (–17·9 to 8·1) | 0·46 |
| **Bodyweight and composition** | | | | |
| BMI, kg/m² | | | | |
| Baseline | 42·1 (40·7 to 43·5) | 42·4 (41·0 to 43·8) | .. | .. |
| 5 year | 34·8 (33·4 to 36·2) | 33·0 (31·6 to34·5) | –1·7 (–3·8 to 0·3) | 0·090 |
| Change from baseline | –7·3 (–8·1 to –6·5) | –9·4 (–10·2 to –8·6) | –2·1 (–3·3 to –0·9) | 0·0005 |
| Bodyweight, kg | | | | |
| Baseline | 126·7 (121·3 to 132·0) | 124·4 (119·0 to 129·7) | .. | .. |
| 5 year | 104·8 (99·4 to 110·2) | 96·7 (91·3 to 102·1) | –8·1 (–15·8 to –0·5) | 0·038 |
| Change from baseline | –21·8 (–24·4 to –19·3) | –27·7 (–30·2 to –25·1) | –5·8 (–9·4 to –2·2) | 0·0015 |
| Total bodyweight loss | 17·2% (15·3 to 19·1) | 22·2% (20·3 to 24·1) | 5·0 (2·4 to 7·7) | 0·0002 |
| Fat mass, kg | | | | |
| Baseline | 58·4 (55·1 to 61·7) | 59·9 (56·6 to 63·2) | .. | .. |
| 5 year | 42·3 (38·9 to 45·7) | 38·1 (34·7 to 41·5) | –4·2 (–9·0 to 0·6) | 0·085 |
| Change from baseline | –16·1 (–18·3 to –13·9) | –21·8 (–24·0 to –19·6) | –5·7 (–8·8 to –2·6) | 0·0003 |
| Reduction from baseline | 27·2% (23·6 to 30·8) | 36·7% (33·1 to 40·2) | 9·5 (4·5 to 14·6) | 0·0002 |
| Fat-free mass, kg | | | | |
| Baseline | 68·2 (64·7 to 71·8) | 64·5 (60·9 to 68·1) | .. | .. |
| 5 year | 62·6 (59·0 to 66·1) | 58·6 (55·1 to 62·2) | –3·9 (–9·0 to 1·1 | 0·13 |
| Change from baseline | –5·7 (–6·6 to –4·7) | –5·8 (–6·8 to –4·9) | –0·2 (–1·5 to 1·1) | 0·79 |
| Reduction from baseline | 8·4% (7·0 to 9·8) | 9·0% (7·6 to 10·4) | 0·5 (–1·4 to 2·5) | 0·59 |
| Waist circumference, cm | | | | |
| Baseline | 128·3 (124·7 to 131·8) | 127·2 (123·7 to 130·8) | .. | .. |
| 5 year | 114·9 (111·3 to 118·6) | 108·3 (104·6 to 111·9) | –6·7 (–11·8 to –1·5) | 0·012 |
| Change from baseline | –13·3 (–15·7 to –11·0) | –19·0 (–21·3 to 16·6) | –5·6 (–9·0 to –2·3) | 0·0006 |

(Table 2 continues on next page)

| | Sleeve gastrectomy (n=55) | Gastric bypass (n=54) | Risk difference (%) or between-group difference (95% CI) | p value |
|---|---|---|---|---|
| (Continued from previous page) | | | | |
| **Cardiovascular risk factors** | | | | |
| Total cholesterol, mmol/L | | | | |
| Baseline | 4·6 (4·3 to 4·8) | 4·4 (4·2 to 4·7) | .. | .. |
| 5 year | 4·6 (4·4 to 4·9) | 4·1 (3·9 to 4·4) | –0·5 (–0·9 to –0·2) | 0·0051 |
| Change from baseline | 0·1 (–0·2 to 0·3) | –0·3 (–0·6 to –0·1) | –0·4 (–0·8 to –0·0) | 0·039 |
| LDL cholesterol, mmol/L | | | | |
| Baseline | 2·6 (2·4 to 2·8) | 2·5 (2·3 to 2·7) | .. | .. |
| 5 year | 3·0 (2·7 to 3·2) | 2·5 (2·2 to 2·7) | –0·5 (–0·8 to –0·2) | 0·0018 |
| Change from baseline | 0·4 (0·1 to 0·6) | –0·1 (–0·3 to 0·2) | –0·5 (–0·8 to –0·1) | 0·0085 |
| HDL cholesterol, mmol/L | | | | |
| Baseline | 1·0 (1·0 to 1·1) | 1·0 (0·9 to 1·1) | .. | .. |
| 5 year | 1·3 (1·2 to 1·3) | 1·3 (1·2 to 1·4) | 0·0 (–0·1 to 0·1) | 0·66 |
| Change from baseline | 0·2 (0·2 to 0·3) | 0·3 (0·2 to 0·3) | 0·0 (–0·0 to 0·1) | 0·31 |
| Triglycerides, mmol/L | | | | |
| Baseline | 2·2 (2·0 to 2·4) | 2·2 (2·0 to 2·5) | .. | .. |
| 5 year | 1·6 (1·3 to 1·9) | 1·4 (1·1 to 1·6) | –0·3 (–0·6 to 0·1) | 0·21 |
| Change from baseline | –0·6 (–0·9 to –0·3) | –0·9 (–1·2 to –0·6 | –0·3 (–0·7 to 0·2) | 0·20 |
| Lipid-lowering medication | | | | |
| Baseline | 28 (51%) | 22 (41%) | .. | .. |
| 5 year* | 21/44 (48%) | 15/46 (33%) | 15·1 (–4·9 to 35·2) | 0·14 |
| Systolic blood pressure, mm Hg | | | | |
| Baseline | 132·0 (128·0 to 136·0) | 131·0 (127·0 to 136·0) | .. | .. |
| 5 year | 131·0 (127·0 to 136·0) | 130·0 (125·0 to 134·0) | 1·9 (–8·1 to 4·4) | 0·56 |
| Change from baseline | –0·5 (–5·5 to 4·5) | –1·9 (–6·8 to 3·1) | –1·4 (–8·4 to 5·6) | 0·70 |
| Diastolic blood pressure, mm Hg | | | | |
| Baseline | 84·0 (82·0 to 86·0) | 84·0 (82·0 to 86·0) | .. | .. |
| 5 year | 83·0 (81·0 to 85·0) | 79 (77·0 to 82·0) | –3·6 (–6·7 to –0·5) | 0·023 |
| Change from baseline | –1·3 ( –3·8 to 1·1) | –4·8 (–7·2 to –2·4) | –3·5 (–6·9 to –0·0) | 0·047 |
| Antihypertensive medication | | | | |
| Baseline | 36 (65%) | 37 (69%) | .. | .. |
| 5 year* | 20/43 (47%) | 23/46 (50%) | 3·5 (–24·2 to 17·3) | 0·74 |
| C-reactive protein, mg/L | | | | |
| Baseline | 10·0 (8·4 to 11·6) | 9·6 (8·0 to 11·2) | .. | .. |
| 5 year | 3·9 (2·2 to 5·6) | 2·2 (0·5 to 3·9) | –1·7 (–4·1 to 0·7) | 0·16 |
| Change from baseline | –6·1 (–7·9 to 4·3) | –7·4 (–9·2 to –5·6) | –1·3 (3·8 to 1·2) | 0·31 |
| Albuminuria (ACR >3 mg/mmol) | | | | |
| Baseline† | 5/53 (9%) | 12 (22%) | .. | .. |
| 5 year* | 1/37 (3%) | 5/39 (13%) | 10·1 (–21·8 to 1·6) | 0·091 |

Outcome variables are reported as mean (95% CI) and between-group differences (95% CI) for continuous variables (ie, linear mixed models) and n (%) and risk difference (95% CI) for categorical variables (ie, generalised linear models for the binomial family by use of identity link). ACR=albumin–creatinine ratio. *Denominators for percentage of participants at 5 years are the numbers of participants for whom data were available at the 5-year visit. †Data missing for two participants at baseline.

*Table 2:* **Diabetes remission, weight loss, and cardiovascular risk factors**

proportions of participants using lipid-lowering medication did not differ between the groups (table 2; appendix 3 p 15).

Diastolic blood pressure declined slightly after gastric bypass, but remained almost unchanged after sleeve gastrectomy (between-group difference –3·5 mm Hg [95% CI –6·9 to –0·04]). Systolic blood pressure did not change in either group, and the proportions of participants using antihypertensive medication did not differ between the groups (table 2; appendix 3 p 15). Both C-reactive protein concentrations and the proportions of participants with albuminuria were reduced during follow-up, with no difference between the groups at 5 years (table 2).

The proportion of participants achieving the American Diabetes Association's composite triple endpoint was

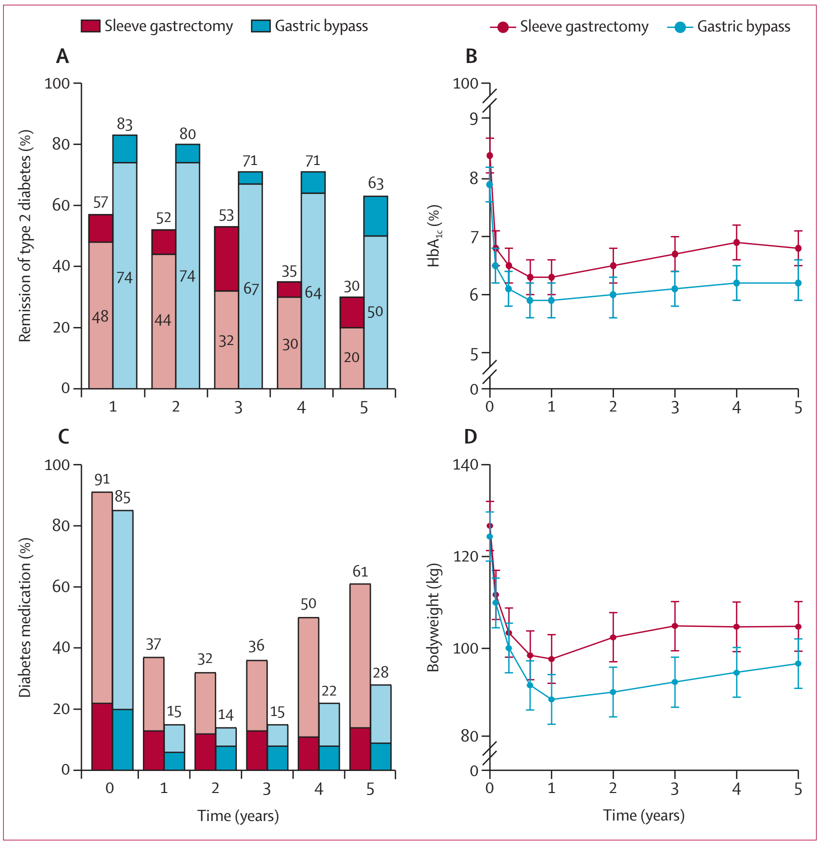


*Figure 2:* **Remission of diabetes, change in $HbA_{1c}$, diabetes medication, and weight loss during 5 years of follow-up**

Error bars indicate 95% CI. (A) Proportions of participants with remission of type 2 diabetes, defined as either $HbA_{1c}$ ≤6·0% (42 mmol/mol; lighter shade) or $HbA_{1c}$ <6·5% (48 mmol/mol; entire bar), both without diabetes medication. (B) Change in $HbA_{1c}$. (C) Proportions of participants using one or more diabetes medication. Darker shades indicate insulin use; the entire bar indicates those who had one or more diabetes medications, including insulin. (D) Bodyweight loss.

significantly higher after gastric bypass (14 [32%] of 44) than after sleeve gastrectomy (four [9%] of 43; risk difference 23% [95% CI 6–39]; appendix 3 p 5).

Sensitivity analyses of changes in bodyweight, LDL cholesterol, and systolic blood pressure were consistent with the main analysis (appendix 3 p 11). However, adjustment for baseline $HbA_{1c}$ in the model starting from the first follow-up visit showed a significant between-group difference in favour of gastric bypass (–0·39% [95% CI –0·74 to –0·04]; appendix 3 p 11).

In the sleeve gastrectomy group, 32 (68%) of the 47 participants who completed the 5-year follow-up underwent upper endoscopy and 24 (51%) had pH measurements. In the gastric bypass group, 30 (65%) of 46 who completed the 5-year follow-up underwent upper endoscopy and 25 (54%) had pH measurements. 42 (89%) in the sleeve gastrectomy group and 42 (91%) in the gastric bypass group completed the patient-reported outcome measures. The SF-36 physical component summary improved similarly in both groups (by a mean of 6·7 points [95% CI 4·4 to 8·9] after gastric bypass *vs* 7·4 points [5·1 to 9·6] after sleeve gastrectomy; between-group difference –0·7 [–3·9 to 2·5]), whereas the SF-36 mental component summary improved in the sleeve gastrectomy group only (by 5·0 points [2·6–7·5]; between-group difference –3·0 [–6·5 to 0·4]; appendix 3 pp 6–7, 16). There were similar improvements in most subcategories for both groups, whereas role emotional and mental health improved after sleeve gastrectomy only, with treatment differences of –8·1 points (–17·8 to 1·7) for role emotional and –5·6 (–12·4 to 1·2) for mental health. (appendix 3 pp 6–7, 16). A meaningful change in IWQOL-Lite total score (defined as 12 points or more) from baseline was reached by 37 (88%) of 42 participants after gastric bypass versus 34 (81%) of 42 participants after sleeve gastrectomy. The mean IWQOL-Lite total score increased more after gastric bypass than after sleeve gastrectomy (33·8 points [95% CI 29·4–38·2] *vs* 27·5 points [23·2–31·9]; between-group difference 6·2 points [95% CI 0·0–12·5]; appendix 3 pp 6–7,16). The subcategory of self-esteem score improved significantly more after gastric bypass than after sleeve gastrectomy (between-group difference 11·7 points [95% CI 2·4–21·0]), whereas the other subcategory scores improved similarly in both groups (appendix 3 pp 6–7, 16). Both the number of weight-related symptoms and the weight-related symptom bothersomeness score improved during the trial period, with no differences between the groups (appendix 3 pp 6–7). The Beck Depression Inventory symptom scores were similarly reduced in both groups with no differences between the groups (appendix 3 pp 6–7).

Few participants had GERD symptoms (ie, a GERD questionnaire score ≥8) 5 years after surgery, with a slightly lower prevalence after gastric bypass (one [2%] of 42) than after sleeve gastrectomy (six [14%] of 42; risk difference –11·9% [95% CI –23·4 to –0·4]; table 3). Further, the prevalence of both erosive oesophagitis (13 [41%] of 32 in the gastric bypass group *vs* 11 [38%] of 29 in the sleeve gastrectomy group) and Barrett's oesophagus (one [3%] *vs* one [3%]) was similar after gastric bypass and sleeve gastrectomy. Finally, the acid exposure time decreased after gastric bypass, whereas it nearly doubled after sleeve gastrectomy, with the proportions of participants with acid exposure time greater than 6% differing substantially between groups (two [8%] of 25 for gastric bypass *vs* 13 [59%] of 22 for sleeve gastrectomy; risk difference –51·1% [95% CI –74·2 to –28·0]).

45 (83%) of 54 participants in the gastric bypass group reported symptoms of early dumping (Arts' questionnaire) on at least one of the annual follow-ups versus 37 (67%) of 55 in the sleeve gastrectomy group. For reports of late dumping symptoms, these values were 32 (59%) participants after gastric bypass versus 26 (47%) after sleeve gastrectomy on at least one of the annual follow-ups. Sweating, flushing, and nausea were reported more frequently after gastric bypass than after sleeve

| | Sleeve gastrectomy (n=55) | Gastric bypass (n=54) | Risk difference (%) or between-group difference (95% CI) | p value |
|---|---|---|---|---|
| **GERD symptoms** | | | | |
| GSRS-R score | | | | |
| Baseline | 1·57 (1·34 to 1·80) | 1·63 (1·40 to 1·86) | .. | .. |
| 5 year | 1·50 (1·25 to 1·76) | 1·32 (1·07 to 1·58) | –0·2 (–0·5 to 0·2) | 0·33 |
| Change from baseline | –0·07 (–0·34 to 0·20) | –0·31 (–0·58 to –0·04) | –0·2 (–0·6 to 0·1) | 0·22 |
| GERD-Q score | | | | |
| Baseline | 6·5 (6·1 to 6·9) | 6·0 (5·6 to 6·4) | .. | .. |
| 5 year | 6·1 (5·6 to 6·6) | 5·4 (5·0 to 5·9) | –0·7 (–1·3 to –0·0) | 0·047 |
| Change from baseline | –0·4 (–1·0 to 0·2) | –0·6 (–1·2 to –0·02) | –0·2 (–1·0 to 0·6) | 0·62 |
| GERD-Q score ≥8 at baseline | 7/55 (13%) | 5/54 (9%) | .. | .. |
| GERD-Q score ≥8 at 5 years | 6/42 (14%) | 1/42 (2%) | –11·9% (–23·4 to –0·4) | 0·043 |
| **Erosive oesophagitis** | | | | |
| Total | | | | |
| Baseline* | 31/53 (58%) | 30/53 (57%) | .. | .. |
| 5 year† | 11/29 (38%) | 13/32 (41%) | 2·7% (–21·8 to 27·2) | 0·83 |
| Los Angeles grade A | | | | |
| Baseline* | 19/53 (36%) | 21/53 (40%) | .. | .. |
| 5 year† | 8/29 (28%) | 10/32 (31%) | 3·7% (–19·2 to 26·5) | 0·75 |
| Los Angeles grade B | | | | |
| Baseline* | 12/53 (23%) | 9/53 (17%) | .. | .. |
| 5 year† | 2/29 (7%) | 2/32 (6%) | 0·6% (–13·1 to 11·8) | 0·92 |
| Barrett's oesophagus | | | | |
| Baseline | .. | .. | .. | .. |
| 5 year† | 1/29 (3%) | 1/32 (3%) | 0·3% (–9·3 to 8·6) | 0·94 |
| **Acid reflux** | | | | |
| Acid exposure time (pH <4 per 24 h of monitoring) | | | | |
| Baseline | 5·4% (3·9 to 6·9) | 6·3% (4·9 to 7·8) | .. | .. |
| 5 year | 10·2% (8·0 to 12·4) | 1·5% (–0·5 to 3·6) | –8·6% (–11·6 to –5·6) | <0·0001 |
| Change from baseline | 4·8% (2·3 to 7·3) | –4·8% (–7·1 to –2·4) | –9·6% (–13·0 to –6·1) | <0·0001 |
| Acid exposure time >6% at 5 years | 13/22 (59%) | 2/25 (8%) | –51·1% (–74·2 to –28·0) | <0·0001 |
| DeMeester score | | | | |
| Baseline | 20·5 (14·4 to 26·5) | 24·3 (18·4 to 30·2) | .. | .. |
| 5 year | 39·4 (30·6 to 48·2) | 7·2 (–1·0 to 15·5) | –32·2 (–44·3 to 20·2) | <0·0001 |
| Change from baseline | 19·0 (9·0 to 28·9) | –17·1 (–26·5 to –7·7) | –36·1 (–49·8 to –22·4) | <0·0001 |
| Pathological acid reflux at 5 years‡ | 17/22 (77%) | 3/25 (12%) | –65·3% (–86·9 to –43·6) | <0·0001 |
| Conclusive evidence of pathological reflux§ | 15/22 (68%) | 5/26 (19%) | –49·0% (–73·6 to –24·3) | 0·0001 |
| Number of acid reflux episodes¶ | | | | |
| Baseline | 86 (68 to 104) | 90 (73 to 108) | .. | .. |
| 5 year | 114 (87 to 140) | 37 (12 to 62) | –76·7 (–112·9 to –40·5) | <0·0001 |
| Change from baseline | 28 (–2 to 58) | –53 (–82 to –25) | –81·1 (–122·6 to –39·6) | 0·0001 |
| Antireflux medication | | | | |
| Baseline | 11/55 (20%) | 17/54 (31%) | .. | .. |
| 5 year | 13/44 (30%) | 10/46 (22%) | –7·8% (–25·8 to 10·2) | 0·40 |

Outcome variables are reported as mean (95% CI) with between-group differences (95% CI) for continuous variables (linear mixed models), and n (%) with risk difference (95% CI) for categorical variables (generalised linear models for the binomial family by use of identity link). GERD=gastro-oesophageal reflux disease. GERD-Q=Gastro-oesophageal Reflux Disease Questionnaire. GSRS-R=Gastrointestinal Symptom Rating Scale-Reflux. *The three participants missing upper endoscopy at baseline declined to undergo the procedure. †Denominators for percentage of participants at 5 years are the numbers of participants for whom data were available at 5-year visit. ‡DeMeester score ≥14·72. §Conclusive evidence of pathological reflux (ie, Lyon 2.0 criteria): either erosive oesophagitis Los Angeles grade B, C, or D, or Barrett's oesophagus, or increased total acid exposure time (>6%). ¶Acid reflux episode defined as pH<4 and duration ≥5 s.

*Table 3:* **GERD symptoms, erosive oesophagitis, and acid reflux**

gastrectomy (appendix 3 p 8). A total of 15 (28%) participants in the gastric bypass group versus one (2%) patient in the sleeve gastrectomy group reported episodes of symptomatic postprandial hypoglycaemia on at least one of the annual follow-ups (appendix 3 p 8).

Late adverse events (ie, ≥6 weeks after surgery) occurred in 37 (69%) of 54 participants (86 events) after gastric bypass, and in 40 (73%) of 55 participants (93 events) after sleeve gastrectomy (table 4). The most prevalent categories of adverse events were infectious, gastroenterological, musculoskeletal, and cardiovascular complications, with similar rates of events in both groups. Three participants underwent conversion from sleeve gastrectomy to gastric bypass during the trial period, with one patient opting to undergo the procedure after 2 years, and two participants after 3 years. The decision to convert was made due to their dissatisfaction with the amount of weight loss after a shared decision-making process with the staff at the obesity centre. One patient in the gastric bypass group received an operation for a small bowel obstruction. One patient in the sleeve gastrectomy group died from a lower gastrointestinal tract malignancy.

| | Sleeve gastrectomy (n=55) | Gastric bypass (n=54) |
|---|---|---|
| Number of patients with complications* | 40 (73%) | 37 (69%) |
| Total number of late adverse events | 93 | 86 |
| Cardiovascular complications | 11/93 (12%) | 12/86 (14%) |
| Chest pain of unknown cause | 4/93 (4%) | 3/86 (3%) |
| Other benign cardiac inquiries | 1/93 (1%) | 2/86 (2%) |
| Coronary heart disease | 2/93 (2%) | 2/86 (2%) |
| Tachyarrhythmia | 2/93 (2%) | 1/86 (1%) |
| Peripheral artery disease | 0/93 | 1/86 (1%) |
| Venous thromboembolism | 0/93 | 2/86 (2%) |
| Chronic leg ulcer | 1/93 (1%) | 1/86 (1%) |
| Aortic valve repair | 1/93 (1%) | 0/86 |
| Neurological complications | 5/93 (5%) | 6/86 (7%) |
| Cerebrovascular disease | 2/93 (2%) | 1/86 (1%) |
| Lumbar radiculopathy | 2/93 (2%) | 2/86 (2%) |
| Carpal tunnel syndrome | 0/93 | 2/86 (2%) |
| Peripheral neuropathy | 1/93 (1%) | 1/86 (1%) |
| Benign and malignant complications | 2/93 (2%) | 6/86 (7%) |
| Benign ovarian lesion | 0/93 | 2/86 (2%) |
| Premalignant lesions | 2/93 (2%) | 2/86 (2%) |
| Ovarian cancer | 0/93 | 1/86 (1%) |
| Skin cancer | 0/93 | 1/86 (1%) |
| Infectious complications | 17/93 (18%) | 15/86 (17%) |
| Urinary tract infection (including recurring) | 7/93 (8%) | 6/86 (7%) |
| Respiratory tract infection (including recurring) | 4/93 (4%) | 4/86 (5%) |
| Skin infection (including recurring) | 2/93 (2%) | 2/86 (2%) |
| Upper airway infection | 2/93 (2%) | 1/86 (1%) |
| Gastroenteritis | 1/93 (1%) | 2/86 (2%) |
| Colonic diverticulitis | 1/93 (1%) | 0/86 |
| Psychiatric and psychosomatic complications | 7/93 (8%) | 5/86 (6%) |
| Depression | 3/93 (3%) | 3/86 (3%) |
| Anxiety | 1/93 (1%) | 1/86 (1%) |
| Bipolar disease | 0/93 | 1/86 (1%) |
| Asthenia | 3/93 (3%) | 0/86 |
| Genitourinary complications | 1/93 (1%) | 5/86 (6%) |
| Urolithiasis | 1/93 (1%) | 1/86 (1%) |
| Pelvic organ prolapse | 0/93 | 2/86 (2%) |
| Urinary incontinence | 0/93 | 1/86 (1%) |
| Metrorrhagia | 0/93 | 1/86 (1%) |
| (Continued from previous column) | | |
| Gastroenterological complications | 19/93 (20%) | 14/86 (16%) |
| Abdominal pain of unknown cause | 6/93 (6%) | 5/86 (6%) |
| Cholelithiasis | 4/93 (4%) | 3/86 (3%) |
| Appendicitis | 1/93 (1%) | 1/86 (1%) |
| Abdominal wall hernia | 2/93 (2%) | 2/86 (2%) |
| Small bowel obstruction | 0/93 | 1/86 (1%) |
| Fecaloma | 1/93 (1%) | 0/86 |
| Diarrhoea | 0/93 | 2/86 (2%) |
| Dyspepsia (requiring proton pump inhibitor) | 5/93 (5%) | 0/86 |
| Musculoskeletal complications | 18/93 (19%) | 17/86 (20%) |
| Minor traumatic musculoskeletal injuries | 9/93 (10%) | 7/86 (8%) |
| Minor non-traumatic musculoskeletal injuries | 6/93 (6%) | 8/86 (9%) |
| Arthrosis | 2/93 (2%) | 2/86 (2%) |
| Fibromyalgia | 1/93 (1%) | 0/86 |
| Miscellaneous | 9/93 (10%) | 6/86 (7%) |
| Cosmetic surgery (including abdominoplasty) | 3/93 (3%) | 4/86 (5%) |
| Cataract | 2/93 (2%) | 0/86 |
| Other minor adverse events† | 2/93 (2%) | 1/86 (1%) |
| Anaemia (including iron deficiency) | 2/93 (2%) | 0/86 |
| Ketoacidosis (SGLT2 inhibitor) | 0/93 | 1/86 (1%) |
| Number of adverse events requiring surgical procedures | 16/93 (17%) | 19/86 (22%) |
| Converted surgery (sleeve gastrectomy to gastric bypass) | 3/93 (3%) | .. |
| Death (lower gastrointestinal tract malignancy) | 1/93 (1%) | 0/86 |

(Table 4 continues in next column)

*p=0·44 ($\chi^2$ test). †Includes allergic reaction (one [1%] in the gastric bypass group), transient thyroiditis (one [1%] in the gastric bypass group), and genital herpes (one [1%] in the sleeve gastrectomy group).

*Table 4:* **Adverse events from 6 weeks up to 5 years after surgery**

## Discussion

This prespecified secondary analysis of the Oseberg trial demonstrated that participants with type 2 diabetes who underwent standard gastric bypass were more than twice as likely to have long-term (ie, 5-year) remission of diabetes (without antidiabetic medication) than those who underwent sleeve gastrectomy. To the best of our knowledge, these findings are the first to support the generally accepted notion that patients with type 2 diabetes who undergo gastric bypass have a substantially higher likelihood of long-term remission of diabetes compared with patients who undergo sleeve gastrectomy, whether defined as $HbA_{1c}$ less than or equal to 6·0% or $HbA_{1c}$ less than 6·5%, without the use of antidiabetic medication. This effect might translate into a lower risk of future cardiovascular and microvascular complications in patients who receive gastric bypass than those who receive sleeve gastrectomy.[6]

Other clinically important beneficial treatment effects of gastric bypass versus sleeve gastrectomy included a greater bodyweight loss of 5.0 percentage points (95% CI 2·4 to 7·7) and significantly lower LDL cholesterol concentrations (treatment difference –0·5 mmol/L [–0·8 to –0·1]). However, the number of patients with symptomatic postprandial hypoglycaemia was markedly higher after gastric bypass than after sleeve gastrectomy (15 *vs* one). Further, the prevalence of erosive oesophagitis and Barrett's oesophagus and the number of adverse events were similar between groups. These findings are largely sustained from the 1-year and 3-year results from the Oseberg trial.[8,18]

Weight loss by non-invasive means has been shown to resolve hyperglycaemia with remission of type 2 diabetes.[26] However, our previously published 1-year results of the Oseberg trial suggest that the higher likelihood of diabetes remission after gastric bypass could be partly explained by higher postprandial GLP-1 concentrations and higher β-cell glucose sensitivity after gastric bypass than after sleeve gastrectomy,[27] suggesting that gastric bypass might have specific mechanisms beyond weight loss that contribute to its effects. Some evidence indicates that these beneficial effects could be sustained long-term.[28] Moreover, these mechanisms might partly explain the increased occurrence of postprandial hypoglycaemia after gastric bypass.

The STAMPEDE trial[2] reported a greater total bodyweight loss after gastric bypass than after sleeve gastrectomy (22% *vs* 19%), which aligns with our findings (22% *vs* 17%). However, unlike our findings, STAMPEDE showed no significant difference in the proportions of patients reaching $HbA_{1c}$ less than or equal to 6·0% without diabetes medication 5 years after surgery (22% after gastric bypass *vs* 15% after sleeve gastrectomy). This discrepancy could be partly explained by a higher baseline $HbA_{1c}$, a longer duration of diabetes, a lower mean BMI, and a higher proportion of patients using insulin in STAMPEDE as compared with the Oseberg trial.[29]

By contrast, similar to our findings, Murphy and colleagues[1] showed significantly higher diabetes remission ($HbA_{1c}$ <6·0% without diabetes medication) rates after silastic ring gastric bypass (48%) than after sleeve gastrectomy (31%) with corresponding weight losses of 27% versus 16%. The addition of a silastic ring might partly explain the higher weight loss after gastric bypass compared with the Oseberg trial, yet the similar remission rates suggest that pouch dilation might not affect long-term remission. Although weight loss 5 years after sleeve gastrectomy in this previous study was similar to the results from the Oseberg trial, the diabetes remission rates were notably higher. The reason for this discrepancy remains unclear.

Additionally, three randomised clinical trials (SleeveBypass,[14] SM-BOSS,[15,17] and SLEEVEPASS[16,17]), primarily comparing the long-term (ie, 5-year) weight loss of gastric bypass with sleeve gastrectomy, included subpopulations with type 2 diabetes. Compared with the Oseberg trial, these three trials used similar surgical procedures and definitions of diabetes remission, but they did not find any significant differences in diabetes remission rates between the procedures. However, the inclusion of patients without type 2 diabetes and the absence of standardised treatment algorithms in these trials limit the comparability with our results.

The mean LDL cholesterol concentrations 5 years after gastric bypass (2·4 mmol/L) and sleeve gastrectomy (3·0 mmol/L) in the STAMPEDE trial[2] were strikingly similar to our results (2·5 mmol/L *vs* 3·0 mmol/L). Although the absolute changes in LDL cholesterol must be interpreted within the context of the lipid-lowering treatment algorithm (both the Oseberg and STAMPEDE trials targeted an LDL cholesterol of ≤2·6 mmol/L), evidence from a 2024 trial indicates that gastric bypass might have a specific LDL-cholesterol lowering effect beyond weight loss.[30]

Our blood pressure findings were largely in line with those from the STAMPEDE trial,[2] which showed a well regulated similar blood pressure and equal reductions in antihypertensive medication in both groups 5 years after both procedures. Of note, the STAMPEDE and Oseberg trials used similar blood pressure treatment algorithms.

A post-hoc analysis of our data showed that gastric bypass was associated with a higher likelihood of reaching the American Diabetes Association composite treatment goal[24] than sleeve gastrectomy, indicating a more favourable cardiovascular risk profile. Conversely, both groups had similar reductions in C-reactive protein concentrations, possibly reflecting a similar decrease in chronic inflammation.[31]

Our findings of similarly improved generic HRQOL scores (with the SF-36) in both surgical groups support previous findings from the STAMPEDE trial[2] and Murphy and colleagues[1] (with the RAND-36 health survey). Further, in line with Murphy and colleagues,[1] we found that both procedures were associated with a reduction of depressive symptoms after 5 years. Consistent with our 3-year analysis,[8] gastric bypass was associated with a greater IWQOL-Lite score than sleeve gastrectomy. Of note, similar proportions of participants reached a meaningful change in weight-related quality of life after the two procedures.

Our findings of similar rates of erosive oesophagitis and Barrett's oesophagus between the two surgical procedures after 5 years differ from the results of a 2024 meta-analysis,[32] which reported an increased risk of erosive oesophagitis and Barrett's oesophagus 2–126 months after sleeve gastrectomy while showing a reduced risk for both outcomes 6–60 months after gastric bypass. This discrepancy might have several explanations, but the relatively small sample size and low numbers of upper endoscopies at the 5-year follow-up have clearly reduced the power to detect a true difference between the surgical procedures in our study. However, in line with our results, the meta-analysis showed a significantly higher acid exposure time after sleeve gastrectomy and reduced acid exposure time after gastric bypass.

The number of patients reporting early and late dumping symptoms was similar between groups, whereas early dumping symptoms of sweating, flushing, and nausea were more frequent in the gastric bypass group.

During the 5-year follow-up, a total of 15 participants in the gastric bypass group reported episodes of symptomatic postprandial hypoglycaemia, compared with only one participant in the sleeve gastrectomy group. These findings contrast with a 2022 meta-analysis[33] indicating that postbariatric hypoglycaemia is equally prevalent after both procedures. However, the meta-analysis reported a higher glucose variability after gastric bypass compared with sleeve gastrectomy and exclusively included trials that used continuous glucose monitors to assess hypoglycaemia. In our trial, the findings were based exclusively on self-reported capillary blood glucose measures.

There are several limitations to our trial. First, the single-centre design and the inclusion of mainly White participants might limit the generalisability of the results. Second, we cannot exclude a potential measurement bias (eg, the blinding of group allocation was lifted at 1-year and adverse events and dumping symptoms were self-reported). Third, no correction for multiple testing was done, and as the number of analyses was high, we cannot exclude the risk of type 1 error (ie, false-positive results). Fourth, our main analysis was not adjusted for potential baseline confounding. However, sensitivity analyses on key secondary outcomes, including baseline adjustments, showed consistent or even more favourable results for gastric bypass compared with the main analysis. Fifth, a small proportion of participants dropped out, possibly introducing selection bias, increasing the risk of type 2 error (ie, false-negative results), and limiting the generalisability of the results. Sixth, postprandial hypoglycaemia was based on self-measured capillary blood glucose measures. Seventh, given that this study is a secondary analysis of prespecified outcomes, the findings should be interpreted with caution and need confirmation in future studies. Eighth, some prespecified secondary outcomes (appendix 3 p 9) are not included in this paper but will be reported separately. Finally, a major limitation is the low number of participants undergoing oesophagogastroduodenoscopy and ambulatory 24-h pH monitoring, markedly limiting the power of outcomes related to these procedures (figure 1; appendix 3 p 4). By contrast, our trial has some important strengths, including the randomised design, a fairly low attrition rate, prespecified secondary outcomes, and predefined treatment algorithms for medication adjustment, increasing the reliability of the results.

Additional research is needed to better understand the long-term, weight-independent effects of gastric bypass on diabetes remission, LDL reduction, and the mechanisms of postprandial hypoglycaemia. Moreover, future research assessing postbariatric hypoglycaemia should include continuous glucose monitoring for registration of daily glucose fluctuations. Finally, with the increasing use of effective incretin-based therapies targeting both obesity and type 2 diabetes,[34] future research assessing when bariatric surgery should be an alternative or a complementary option in selected individuals is warranted.

In conclusion, 5 years after surgery, gastric bypass, as compared with sleeve gastrectomy, was associated with a higher likelihood of diabetes remission, superior weight loss, and lower LDL cholesterol, but also increased the risk of symptomatic postprandial hypoglycaemia. The rate of pathological acid reflux was higher after sleeve gastrectomy. However, the rates of erosive oesophagitis and adverse events were similar. Therefore, we hypothesise that selecting gastric bypass over sleeve gastrectomy in individuals with type 2 diabetes could improve patient care and decrease long-term cardiovascular risk. This novel evidence has the potential to change clinical practice regarding the preferred surgical procedure in patients with type 2 diabetes and obesity, and should be addressed in the shared decision-making process before surgery.

**Contributors**

DH and JH conceived the study and are the principal investigators. HB, MS, LKJ, HLG, KIB, JKH, RLK, RS, TGV, ML, JL, BS, DH, and JH contributed to the design of the study. HB, MS, LKJ, HLG, KIB, JKH, RLK, RS, TGV, ML, JWH, JL, BS, MH, DH, and JH supervised the study. JWH, HB, and MH did the statistical analyses. JWH, HB, DH, and JH wrote the original draft manuscript. All authors contributed to writing the manuscript, critically participated in the interpretation of the data, reviewed the manuscript for intellectual content, and approved the final version of the manuscript. All authors had full access to the data and all authors verified data completeness and accuracy and the fidelity of the trial protocol. All authors had the final responsibility for the decision to submit for publication.

**Declaration of interests**

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**Data sharing**

Access to data collected from this study, including de-identified, individual-participant data, will be made available following publication

upon email request to the corresponding author. After approval of a proposal, data will be shared with investigators whose proposed use of the data has been approved by the Oseberg trial steering committee, according to the consent given by the participants and Norwegian laws and legislations.

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