

Diabetes Digest

Diabetes Digest summarises recent key papers published in the area of coexistent diabetes and obesity – diabetes. To compile the digest a PubMed search was performed for the 3 months ending May 2014 using a range of search terms relating to type 2 diabetes, obesity and diabetes. Articles have been chosen on the basis of their potential interest to healthcare professionals involved in the care of people with diabetes. The articles were rated according to readability, applicability to practice, and originality.



Should bariatric surgery be used for people with diabetes and a BMI of <35 kg/m²?

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NICE have been considering the role of bariatric surgery for the treatment of diabetes among people with BMI under 35 kg/m²; specifically, in cases of early onset insulin resistance, and in cases that are severe and complex. The paper by Boza et al (summarised alongside) is, therefore, timely.

Physicians often react with wonder, after having pharmacotherapy withdrawn or non-authorised on dubious grounds, to find that a surgeon can wake up one morning having dreamt up a new procedure and perform it the next day. Thus, this is a retrospective analysis of operations performed since 2002 in contravention of most international guidelines.

Bariatric surgery is successful in alleviating obesity and diabetes, but not for the reasons the surgeons anticipated. The efficacy of the restrictive element of Roux-en-Y gastric bypass (RYGB) is clear: after RYGB, one channel of the “Y” contains food and the other contains gastric juices; only when the two merge in the common channel does digestion commence. This is thought to be a factor in the degree of weight loss. Theories around alterations in bile metabolism are also convincing (Kohli et al, 2013).

However, what the pioneers of RYGB could not anticipate was the regulation of gut peptides induced by mechanical interference to the gut itself. The influence of the incretin system emanating from the L cells of the intestine, which produce glucagon-like peptide-1 among other peptides, on diabetes control is now widely accepted.

The resolution of diabetes in obese individuals is an important and unique challenge. The paper by Boza et al provides some important answers (primarily that surgery can reverse type 2 diabetes in individuals with BMI <35 kg/m²) and poses some equally important questions. It seems likely,

as confirmed by previous papers (Ricci et al, 2014; Zhang et al, 2014), that RYGB is a viable option in people with type 2 diabetes. In this study, excess weight loss percentage (EWLp) for individuals with BMI <35 kg/m² was 93%, which does not suggest that they lost more weight than people with BMI >35 kg/m² who have had surgery, just that EWLp is grossly misleading. If a person is an ounce overweight and they lose an ounce, EWLp is 100%, so the lower a person’s excess weight to begin with, the higher EWLp will be for any given weight loss.

Another anomaly in the methods of this analysis is the use of remission rate for diabetes, quoted as 53.2% for complete remission (defined as HbA_{1c} <42.1 mmol/mol [<6%] and off medication) and 9.6% partial remission (defined as HbA_{1c} <47.5 mmol/mol [<6.5%] and off medication). Most bariatric physicians now consider it a mistake to prematurely stop glucose-lowering drugs when HbA_{1c} returns towards normal. Individuals should ideally remain on diabetes registers and drug treatments that are effective and do not cause hypoglycaemic episodes in order to reap the long-term benefits of ongoing screening and reduced chance of recurrence. It is interesting to note that participants in this analysis were diagnosed with type 2 diabetes at a median of only 4 years preoperatively, and that remission occurred exclusively in those not taking insulin prior to surgery.

The paper concludes: “These findings suggest that surgery should be offered earlier to diabetic patients and not when there is an impaired pancreatic function with little chance of recovery”. NICE take note. ■

Kohli R et al (2013) *J Clin Endocrinol Metab* **98**: E708–12
Ricci C et al (2014) *Obes Surg* **24**: 522–8
Zhang C (2014) *Obes Surg* **24**: 1528–35

Obesity Surgery

Diabetes remission after bariatric surgery in people with BMI <35 kg/m²

Readability	////
Applicability to practice	////
Originality	////

1. Roux-en-Y gastric bypass (RYGB) is effective in the remission of T2D among people with BMI >35 kg/m². The authors carried out a retrospective analysis of RYGB for its effectiveness in T2D remission among people with BMI <35 kg/m².
2. Between 2002 and 2010, 100 people with T2D and BMI <35 kg/m² (mean 32.7 kg/m²) underwent RYGB. Preoperative T2D duration was 4 years and median age of participants was 48 years. In total, 60% were women.
3. The authors analysed the variables associated with remission: participant demographics, comorbidities, BMI, excess weight loss percentage (EWLp), complications and metabolic results at 3 years.
4. Median EWLp after 3 years was 93%. The highest median EWLp was 99% after 1 year, but participants experienced some weight regain in the following years. After 3 years the median BMI was 25.4 kg/m².
5. At 3-year follow-up, 53.2% of participants achieved complete remission of T2D (defined as HbA_{1c} <42.1 mmol/mol [<6%] and off medication), 9.6% achieved partial remission (defined as HbA_{1c} <47.5 mmol/mol [<6.5%] and off medication), and 11.7% showed no improvement.
6. In multivariate analysis, the only variable associated with T2D remission after RYGB was non-insulin use prior to surgery (odds ratio=15.1 [95% confidence interval, 2.8–81.2], P=0.002).

Boza C, Valderas P, Daroch DA et al (2014) Metabolic surgery: Roux-en-Y gastric bypass and variables associated with diabetes remission in patients with BMI <35. *Obes Surg* **24**: 1391–7

Diabetes Obes Metab

Mixed treatment comparison meta-analyses: The effect of antiobesity drugs on waist circumference

Readability	✓✓✓
Applicability to practice	✓✓✓
Originality	✓✓✓✓

1. No randomised controlled trials (at the time of writing) have taken place that directly compare the efficacy of orlistat and lorcaserin in weight loss among overweight and obese people.
2. The authors identified publications from electronic databases that compared orlistat or locaserin to lifestyle advice (standard care), placebo, sibutramine, rimonabant or metformin, and investigated the effect of orlistat and locaserin on changes to waist circumference and participant drug withdrawals due to adverse events.
3. In place of direct evidence, the authors carried out mixed treatment comparison meta-analyses to use indirect evidence from various sources and compare through a common comparator.
4. Orlistat was found to be significantly better than placebo and standard care at reducing waist circumference at 6 and 12 months (orlistat reduced waist circumference by -6.96 cm [95% credible interval -8.93 cm, -4.96 cm] compared to standard care at 6 months). Locaserin was shown to lead to a greater reduction in waist circumference than all other interventions at 12 months, but the differences were not statistically significant.
5. On average, 6.5% of people taking orlistat and 5.4% of those taking locaserin had discontinued their treatment due to adverse events at 12 months.
6. The paper concludes that orlistat should be considered as an addition to lifestyle interventions in the treatment of obesity. Lorcaserin has been launched in the US, and these findings suggest that it is similar in both efficacy and safety to orlistat.

Chilton M, Dunkley A, Carter P et al (2014) The effect of antiobesity drugs on waist circumference: a mixed treatment comparison. *Diabetes Obes Metab* 16: 237–47

Diabetes Technol Ther

Gastric banding: What are the effects on metabolic syndrome and insulin resistance?

Readability	✓✓✓✓
Applicability to practice	✓✓✓
Originality	✓✓✓

1. The authors investigated the impact of Roux-en-Y gastric bypass (RYGB) on metabolic syndrome (MetS), which is defined as a cluster of interconnected metabolic factors that increase the risk of coronary heart disease and T2D.
2. Ninety-six obese people with MetS underwent RYGB. All had T2D and the mean age and BMI of participants at surgery was 46 years and 44.3 ± 8.7 kg/m² respectively.
3. In the retrospective analysis, after a mean follow-up of 34 months post-surgery, 88.5% of people experienced MetS resolution, 90.6% experienced T2D resolution, 85.6% experienced hypertension resolution and 54.2% experienced dyslipidemias resolution.
4. There were significant decreases in fasting glucose, fasting insulin, HbA_{1c}, LDL-lipoprotein and triglyceride levels, and an increase in HDL-lipoprotein level after surgery.
5. A decrease in subsequent insulin resistance was confirmed by homeostasis model assessment (HOMA-IR).
6. Significant mean weight loss (29.9 ± 9.1 kg [$P < 0.0001$]) and a decrease to mean waist circumference (mean preoperative waist circumference = 128 ± 13.9 cm, mean postoperative waist circumference = 98 ± 14.3 cm; $P < 0.001$) were also observed.
7. RYGB contributes to improvements in MetS and its components by mechanisms including decreasing food intake and increasing hormonal incretin action in the gut.
8. There is a clear beneficial role for RYGB in obese people with MetS in lowering cardiovascular morbimortality and T2D complication risk.

Cazzo E, Gestic MA, Utrini MP et al (2013) Impact of Roux-en-Y gastric bypass on metabolic syndrome and insulin resistance parameters. *Diabetes Technol Ther* 16: 262–5

Diabetes Obes Metab

Differing diabetes risk: MetS components and response to lifestyle and metformin interventions

Readability	✓✓✓
Applicability to practice	✓✓✓✓
Originality	✓✓✓

1. The aim of the study was to determine the association of metabolic syndrome (MetS) and its components with diabetes risk in people with impaired glucose tolerance (IGT), and whether intervention-related changes in MetS lead to differences in diabetes incidence (i.e. placebo, metformin, lifestyle advice).
2. Using data from 3234 participants from the Diabetes Prevention Program who had IGT and with an average follow-up of 3.2 years, the authors investigated the baseline and intervention-related changes of MetS components to predict incident diabetes.
3. In an intention-to-treat analysis, the demographic-adjusted hazard ratios for diabetes in those with MetS (versus those without MetS) at baseline were 1.7 (95% confidence interval [CI], 1.3–2.3), 1.7 (95% CI, 1.2–2.3) and 2.0 (95% CI, 1.3–3.0) for placebo, metformin and lifestyle groups, respectively.
4. Higher levels of fasting plasma glucose and triglycerides at baseline were independently associated with increased risk of diabetes in this group of people.
5. Increased waist circumference was associated with higher risk of diabetes in placebo and lifestyle groups, but not in the metformin group.
6. The most predictive factors for T2D in people with MetS and IGT were baseline hyperglycaemia, followed by triglyceridaemia, and baseline and lifestyle-associated changes in waist circumference.
7. These factors should be targeted to help assess the benefits of interventions that reduce diabetes incidence.

Florez H, Temprosa MG, Orchard TJ et al (2014) Metabolic syndrome components and their response to lifestyle and metformin interventions are associated with differences in diabetes risk in persons with impaired glucose tolerance. *Diabetes Obes Metab* 16: 326–33

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