Challenges of managing obese patients with type 2 diabetes

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Outline of lecture

• Introduction

• Beneficial effects of modest and major weight reduction in patients with type 2 DM

• Barriers to effective treatment, including weight gain in treatment of hyperglycemia

• New treatments for obese patients with type 2 DM (GLP-1 agonists and SGLT-2 inhibitors)

• The role of bariatric surgery in the treatment of type 2 DM

• Conclusions
The prevalence of obesity is increasing

Data are self reported or through health examinations. OECD data represents the mean of the member countries.

OECD, Organisation for Economic Co-operation and Development

Obesity is associated with multiple chronic comorbid conditions

**Obesity related comorbidities**

- Cancer (various)
- Asthma
- Pulmonary embolism
- Back pain
- Osteoarthritis
- Stroke
- Hypertension
- Coronary artery disease
- Congestive heart failure
- Type 2 diabetes
- Gallbladder disease

**Increased risk of comorbidities with obesity**

<table>
<thead>
<tr>
<th>Comorbidity</th>
<th>RR [95% CI] Male</th>
<th>RR [95% CI] Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 2 diabetes</td>
<td>6.7 [5.6–8.2]</td>
<td>12.4 [9.0–17.1]</td>
</tr>
<tr>
<td>Coronary artery disease</td>
<td>1.7 [1.5–2.0]</td>
<td>3.1 [2.8–3.4]</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>1.8 [1.2–2.6]</td>
<td>1.8 [1.1–3.0]</td>
</tr>
<tr>
<td>Hypertension</td>
<td>1.8 [1.5–2.2]</td>
<td>2.4 [1.6–3.7]</td>
</tr>
<tr>
<td>Stroke</td>
<td>1.5 [1.3–1.7]</td>
<td>1.5 [1.3–1.7]</td>
</tr>
<tr>
<td>Osteoarthritis</td>
<td>4.2 [2.7–6.4]</td>
<td>2.0 [1.9–2.0]</td>
</tr>
<tr>
<td>Gallbladder disease</td>
<td>1.4 [1.0–2.0]</td>
<td>2.3 [1.2–4.6]</td>
</tr>
</tbody>
</table>

RR = relative risk

The prevalence of type 2 diabetes (T2D) increases with BMI.

Diabetes epidemic: IDF

- 285 million people with diabetes worldwide
- 438 million by 2030
- Further half a billion at risk

“Diabetes is looming as one of the greatest public health threats of the 21st century”
The vast majority of people with type 2 diabetes are overweight or obese

Individuals with type 2 diabetes

- **Overweight/obese**: 90%
- **Normal**: 10%

It is estimated that 20-25% of the world’s adult population has the metabolic syndrome

Beneficial effects of modest and major weight reduction in patients with T2DM
Weight loss reverses type 2 diabetes

11 people with T2DM < 4 yrs
BMI 33.6
8 weeks of 600 kcal diet

After 1 week of restricted energy intake, fasting plasma glucose normalised in the diabetic group (from 9.2±0.4 to 5.9±0.4 mmol/l; p=0.003)

BMI 28.7 week 8.

Lim et al 2011, Diabetologia 54:2506-2514
In patients with Type 2 diabetes, weight loss provides multiple benefits

The Look AHEAD study

- A modest weight loss from 5% to <10% was associated with a significant improvement in cardiovascular risk factors at 1 year

<table>
<thead>
<tr>
<th>Predefined criteria</th>
<th>Odds ratio</th>
<th>95% CI</th>
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</thead>
<tbody>
<tr>
<td>HbA₁c ↓ 0.5%</td>
<td>3.52</td>
<td>2.81–4.40</td>
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<tr>
<td>Systolic blood pressure ↓ 5 mmHg</td>
<td>1.56</td>
<td>1.27–1.91</td>
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<tr>
<td>Diastolic blood pressure ↓ 5 mmHg</td>
<td>1.48</td>
<td>1.20–1.82</td>
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<tr>
<td>HDL cholesterol ↑ 0.1 mmol/L</td>
<td>1.69</td>
<td>1.37–2.07</td>
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<tr>
<td>Triglycerides ↓ 0.45 mmol/L</td>
<td>2.20</td>
<td>1.71–2.83</td>
</tr>
</tbody>
</table>

This study was an observational analysis of participants in the Look AHEAD study conducted at 16 US sites in 5,145 participants (40.5% male, 37% from ethnic/racial minorities).

AHEAD, Action for Health Diabetes; CI, confidence interval; HDL, high-density lipoprotein.

Adapted from Wing RG et al. Diabetes Care 2011;34:1481–1486.
A Trial Assessing the Impact of a Low Calorie Diet on Weight Loss in Obese Patients with Type 2 Diabetes Mellitus Treated with Insulin

Adrian Brown
PhD Student Imperial College London
Specialist Dietitian
Intervention - 0-6 Months

**Step 1**
- 800kcal
- 4 x Total Diet Replacement

**Step 2**
- 1000kcal
- 3 x + 400kcal protein rich foods, skimmed milk
- OR 2 x + 600kcal protein rich food, skimmed milk and fruit

**Step 3**
- 1200kcal
- 2 x + 800kcal breakfast, lunch and dinner, skimmed milk and fruit

**Step 4**
- 1500kcal
- 2 x + 1100kcal breakfast, lunch and dinner, skimmed milk and fruit
- OR 1 x + 1300kcal food options

**Step 5**
- My Life
  - A healthy diet with an option to include formula meal replacements once or twice a day

12 weeks  | 6 weeks  | 6 weeks  | As required  | Time
Preliminary Weight Loss Outcome – 12 weeks

Mean Weight Loss (kg)

GSC

LED

***

***
Preliminary HbA1c Change – 12 Weeks

HbA1c change (mmol/mol)

**

GSC

LED

0 5 10 15 20 25

**
Assessment of obese patient
<table>
<thead>
<tr>
<th></th>
<th>Stage 0</th>
<th>Stage 1</th>
<th>Stage 2</th>
<th>Stage 3</th>
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</thead>
<tbody>
<tr>
<td><strong>Obesity Staging Score</strong></td>
<td>&quot;Normal health&quot;</td>
<td>&quot;At risk&quot;</td>
<td>&quot;Established disease&quot;</td>
<td>&quot;Advanced disease&quot;</td>
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<tr>
<td>Airways</td>
<td>Normal</td>
<td>Snoring</td>
<td>Require CPAP</td>
<td>Cor pulmonale</td>
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<tr>
<td>Body mass index</td>
<td>&lt;35</td>
<td>35-40</td>
<td>40-60</td>
<td>&gt;60</td>
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<tr>
<td>Cardiovascular</td>
<td>&lt;10% risk</td>
<td>10-20% risk</td>
<td>Heart disease</td>
<td>Heart failure</td>
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<tr>
<td>Diabetes</td>
<td>Normal</td>
<td>Impaired fasting glycaemia</td>
<td>Type 2 diabetes</td>
<td>Uncontrolled type 2 diabetes</td>
</tr>
<tr>
<td>Economic</td>
<td>Normal</td>
<td>Expensive travel/clothes</td>
<td>Workplace discrimination</td>
<td>Unemployed due to obesity</td>
</tr>
<tr>
<td>Functional</td>
<td>Can manage 3 flights of stairs</td>
<td>Manages 1 or 2 flights of stairs</td>
<td>Requires walking aids or wheelchair</td>
<td>House bound</td>
</tr>
<tr>
<td>Gonadal</td>
<td>Normal</td>
<td>PCOS</td>
<td>Infertility</td>
<td>Sexual dysfunction</td>
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<tr>
<td>Health perceived</td>
<td>Normal</td>
<td>Low mood or QoL</td>
<td>Depression or poor QoL</td>
<td>Severe depression</td>
</tr>
<tr>
<td>body Image</td>
<td>Normal</td>
<td>Dislikes body</td>
<td>Body image dysphoria</td>
<td>Eating disorder</td>
</tr>
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</table>
What anti-obesity treatments are available?
Treatment options

- Lifestyle modification
  - Diet, exercise and behavioural modification

- Pharmacotherapy
  - Orlistat (lipase inhibitor)
    - Sibutramine
    - Rimonabant
    - Phen-Fen
  - Bariatric surgery
Orlistat: structure and mode of action

- Orlistat is a lipase inhibitor that acts by reducing absorption of dietary fats:
  - Gastric and pancreatic lipases digest TG into absorbable MG and FFA
  - Orlistat covalently binds to lipases at serine residues in their active sites, preventing hydrolytic cleavage
  - Undigested TG cannot be absorbed – the resulting caloric deficit can lead to weight loss
  - Orlistat 120 mg inhibits dietary fat absorption by approximately 30%\(^1\)

1. Roche. Xenical® Packet Insert. 2011
Orlistat: body weight loss over 1 year and prevention of weight regain over 2 years

- At the end of year 1, subjects on orlistat 120 mg TID lost more body weight than those in the placebo group (10.3 kg vs. 6.1 kg; \( p < 0.001 \))
- During year 2, patients who continued with orlistat regained half as much weight as those patients switched to placebo (2.4 kg mean difference; \( p < 0.001 \))

Type 2 diabetes incidence with orlistat

XENDOS: 4 year data

Cumulative incidence of diabetes (%)

- Placebo + lifestyle – IGT patients
- Placebo + lifestyle – All patients
- Orlistat + lifestyle – IGT patients
- Orlistat + lifestyle – All patients

-45.0%
-37.3%
p=0.0024
p=0.0032

Weeks
0 26 52 78 10 13 15 18 20

Orlistat: GI tolerability

- In trials with obese and overweight adults, several AEs occurred with orlistat, at rates of 15–30%:\(^1\)
  - Fatty/oily stool
  - Faecal incontinence/urgency
  - Oily spotting

- Over 80% of orlistat-treated subjects had at least one GI AE\(^1\)

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*Faecal incontinence reported as a separate endpoint in three trials only

AE, adverse event; GI, gastrointestinal

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Change in body weight (%)

Baseline weight: **106 kg**

- **Liraglutide 3.0 mg**
  - Observed mean LOCF

- **Placebo**
  - Observed mean LOCF

**Graph:**
- Week 0: Baseline weight
- Week 56: Change in weight (%)
- **Liraglutide 3.0 mg:** -8.0% change, **Placebo:** -2.6% change

**Notes:**
- FAS, fasting visit data only. Line graphs are observed means (±SE). Circles are observed means LOCF.
- FAS, full analysis set; LOCF, last observation carried forward; SE, standard error. *Statistical analysis is ANCOVA.
- Test for no treatment by prediabetes interaction *p*=0.5907
- Pi-Sunyer et al. AACE 2014. Abstract 700.

**Statistical Significance:**
- **Liraglutide 3.0 mg** vs **Placebo**: *p*<0.0001*
Body weight reduction from baseline in obese patients without diabetes (20 weeks)

- Placebo: -2.8 kg
- Liraglutide 1.2 mg, OD: -4.8 kg
- Liraglutide 1.8 mg, OD: -5.5 kg
- Liraglutide 2.4 mg, OD: -6.3 kg
- Liraglutide 3.0 mg, OD: -7.2 kg
- Orlistat 120 mg T.I.D: -4.1 kg

**p<0.01, ***p<0.0001 vs. placebo
††p<0.01, †††p<0.0001 vs. orlistat 120 mg T.I.D

3mg:
76% > 5%
28% > 10%

Subjects achieving ≥5% and >10% weight loss

<table>
<thead>
<tr>
<th>Weight Loss</th>
<th>Liraglutide 3.0 mg</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>≥5% weight loss</td>
<td>63.2</td>
<td>27.1</td>
</tr>
<tr>
<td>&gt;10% weight loss</td>
<td>33.1</td>
<td>10.6</td>
</tr>
</tbody>
</table>

FAS-LOCF. Data are observed proportions.
*Statistical analysis is logistic regression. FAS, full analysis set; LOCF, last observation carried forward

Pi-Sunyer et al. AACE 2014. Abstract 700.
Bupropion/naltrexone (Mysimba EU, Contrave USA)

• Combination of anti-depressant (bupropion) and non-selective opioid receptor blocker (naltrexone, treats alcoholism and opiate addiction)

• Weight loss between 5-10%

• Nausea main side effect, slight increase in pulse rate and BP
Lorcaserin (Belviq)

• 5HT2C serotonin agonist (x15 vs 5HT2A, X100 vs 5HT2B)

• 5HT2C almost exclusively in the brain

• Valvulopathy thought to occur via 5HT2B (fenfluramine and dexfenfluramine)

• Weight loss 5.8 Kg at one year vs 2.2 kg placebo

• Lowest discontinuation rate vs any obesity drug in phase III but CANCER IN RATS (mammary gland, nerve tissue, skin)

• Affects cognitive abilities, depression, suicidal thoughts
Qsymia

- Qsymia- phentermine (Phen half of Fen-Phen, noradrenergic) plus topiramate (via GABA)

- Combination of amphetamine and anti-convulsant

- Weight loss between 5-14% at one year

- Concerns re cardiovascular (increase in HR) and psychiatric effects (depression, altered mood)
Hyperglycemia: the challenges of weight gain as a consequence of treatment
Glucose-lowering medications and weight profile

Range of weight change (kg) in response to diabetes medications

- Sulphonylureas
- Glinides
- Thiazolidinediones
- Insulin
- DPP-4 inhibitor (sitagliptin)
- Metformin
- GLP-1 receptor agonists
- SGLT-2 inhibitors

Role of GLP-1 receptor agonists in management of type 2 diabetes
GLP-1 regulates appetite

- Two potentially complementary mechanisms for the effect of GLP-1 on appetite:
  - (A) **indirect effects** on fullness and satiety through *delayed gastric emptying* and *distension of the stomach*
  - (B) **direct effects** on GLP-1 receptors in the central nervous system (CNS)

GLP-1 is released in response to food intake

GLP-1 activates brain areas in humans that regulate food intake

GLP-1, glucagon-like peptide-1; PET, positron emission tomography

GLP-1 response after bariatric surgery

Nausea is a side-effect

Figure 3: Proportion of patients with an episode of nausea between baseline and week 26.
SGLT-2 inhibitors in the management of T2DM
Renal glucose handling in the nephron of the healthy individual

- **Plasma glucose concentration**: 5–5.5 mmol/L
- **Plasma filtered**: 180 L/day
- **Glucose filtered**: 160–180 g/day
- **Glucose reabsorbed**: 160–180 g/day
- **Glucose excreted**: Minimal

*SGLT*=sodium–glucose co-transporter

Figure adapted from Bailey CJ (2011) *Trends Pharmacol Sci* **32**: 63–71
SGLT2 inhibition lowers the inappropriately elevated renal threshold for glucose in type 2 diabetes

- Plasma glucose concentration: 10 mmol/L
- Plasma filtered: 180 L/day
- Glucose filtered: ~320 g/day
- Glucose reabsorbed (assuming 20–25% inhibition of reabsorption): ~240–255 g/day
- Glucose excreted: ~65–80 g/day (equivalent to ~260–320 kcal/day)

SGLT=sodium–glucose co-transporter

Figure adapted from Bailey CJ (2011) *Trends Pharmacol Sci* 32: 63–71
Dual therapy add-on to metformin: Weight changes* with canagliflozin versus sitagliptin over 52 weeks (LOCF)

Canagliflozin is not indicated for weight loss. *Pre-specified secondary endpoint.

CI=confidence interval; LOCF=last observation carried forward; LS=least squares.


Baseline weight (kg) | n at baseline
---|---
Sitagliptin 100 mg | 87.7 | 366
Canagliflozin 100 mg | 88.8 | 368
Canagliflozin 300 mg | 85.4 | 367

**Time point (week)**

**LS mean change in body weight from baseline (%)**

-1.3% (-1.2 kg) for Canagliflozin 100 mg
-3.8% (-3.3 kg) for Canagliflozin 300 mg

Difference from sitagliptin:

-2.1 kg (-2.4%) \( P<0.001 \)
-2.5 kg (-2.9%) \( P<0.001 \)
Add-on to insulin ± OADs: Weight changes* with canagliflozin versus placebo over 18 weeks (LOCF)

Canagliflozin is not indicated for weight loss. *Pre-specified secondary endpoint.

LOCF=last observation carried forward; LS=least squares; OAD=other antidiabetes drug.

SGLT-2 inhibitors: Summary of common or very common adverse reactions

- Safety evaluated in >6,000 people with type 2 diabetes who received canagliflozin in nine double-blind, controlled phase 3 clinical studies
- Primary assessment of safety and tolerability was conducted in a pooled analysis (N=2,313) of four 26-week placebo-controlled clinical studies
- In this analysis, reactions classed as very common (≥10%) or common (≥1%) included:

**Very common**
- Hypoglycaemia when used in combination with insulin or sulphonylurea
- Vulvovaginal candidiasis (thrush)

**Common**
- Constipation, thirst, nausea
- Polyuria (increased urine volume) or pollakiuria (increased urine frequency)
- Urinary tract infection
- Balanitis or balanoposthitis
- Dyslipidaemia
- Increased haematocrit

1. Canagliflozin summary of product characteristics
SGLT2 inhibitors and cardiovascular risk: empagliflozin (sep 2014, NEJM)

• 7020 patients randomised to 10mg or 25 mg EMPA vs placebo

• Primary composite outcome was death from cardiovascular causes, nonfatal MI, or nonfatal stroke

• 12.5% in EMPA vs 12.1% placebo (p=0.04), median obs time 3.1 years

• Patients with T2DM at high risk for CVS who received empagliflozin, as compared to placebo, had a lower rate of the primary composite cardiovascular outcome
Role of SGLT-2s in management of type 2 diabetes

- Clear weight (and cardiovascular) benefit (lose calories!!)
- Oral therapy, once a day
- Caution in elderly- increased risk of urinary tract infections and genito-urinary infections
The role of Bariatric Surgery in obesity and T2DM

Adjustable Gastric Banding

Proximal Gastric Bypass

Sleeve Gastrectomy
Surgical treatment: adults

Consider surgery *if all* of the following conditions are met:

- the person has a BMI of 40 kg/m² or more, OR a BMI of 35 to 40 kg/m² plus other significant disease that could be improved with weight loss
- non-surgical measures have failed to achieve or maintain clinically beneficial weight loss for at least 6 months
- the person has been receiving or will receive intensive management in a specialist obesity service, such as psychological support

Consider surgery first line if BMI>50

NICE Guidance, 2006
Bariatric surgery for T2DM: update on NICE guidelines (2014)

• Offer an expedited assessment for bariatric surgery to people with BMI of 35 or over who have recent-onset T2DM as long as they are also receiving or will receive assessment in a Tier 3 service or equivalent

• Consider an assessment for bariatric surgery for people with a BMI of 30-34.9 who have recent-onset T2DM as long as they are also receiving or will receive assessment in a Tier 3 service or equivalent

• Consider an assessment for bariatric surgery for people of Asian family origin who have recent-onset T2DM at a lower BMI than other populations as long as they are also receiving or will receive assessment in Tier 3 service
# Resolution of co-morbidities

<table>
<thead>
<tr>
<th>Condition</th>
<th>Gastric bypass (n = 1104)</th>
<th>Adjustable gastric band (n = 84)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-op status</td>
<td>Post-op resolution</td>
</tr>
<tr>
<td>Type 2 diabetes</td>
<td>24.8%</td>
<td>80.5%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>51.3%</td>
<td>63.3%</td>
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<tr>
<td>Sleep apnea</td>
<td>45.1%</td>
<td>68.9%</td>
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<tr>
<td>GERD</td>
<td>57.9%</td>
<td>87.6%</td>
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<td>Venous insufficiency</td>
<td>54.1%</td>
<td>71.0%</td>
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<tr>
<td>Infertility</td>
<td>4.7%</td>
<td>6.0</td>
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<tr>
<td>Asthma</td>
<td>26.1%</td>
<td>66.0%</td>
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<td>Stress incontinence</td>
<td>55.0%</td>
<td>84.0%</td>
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<tr>
<td>Depression</td>
<td>18.9%</td>
<td>31.4%</td>
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<td>DJD</td>
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<td>Hyperlipidemia</td>
<td>47.8%</td>
<td>61.4%</td>
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<tr>
<td>Average medications</td>
<td>4.4</td>
<td>1.3</td>
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Pories et al., JCEM Nov 2008
Dieting vs. Bariatric Surgery

Swedish Obese Subjects Study: NEJM 2007

<table>
<thead>
<tr>
<th>Years</th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
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<tr>
<td>Control</td>
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<td>Banding</td>
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<td>Vertical-banded gastroplasty</td>
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<td>245</td>
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<td>211</td>
<td>209</td>
<td>166</td>
<td>92</td>
<td>58</td>
<td>10</td>
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</table>

Swedish Obese Subjects Study: NEJM 2007
LAGB induces T2D remission

Dixon et al. JAMA 2008; 299:316-323

- RR remission 5.5 in surgical group
- Remission of type 2 DM related to weight loss

LAGB vs pharmacotherapy and lifestyle (n=60)
BMI >30 and <40 with T2DM <2 yrs
Remission HbA1c <6.2% and no meds

Patients (%)

0 10 20 30 40 50 60 70 80

2 years

Control group

LAGB

13%

73%

p<0.001

Dixon et al 2008 JAMA 299:316-323
Bariatric Surgery versus Conventional Medical Therapy for Type 2 Diabetes

Geltrude Mingrone, M.D., Simona Panunzi, Ph.D., Andrea De Gaetano, M.D., Ph.D., Caterina Guidone, M.D., Amerigo Iaconelli, M.D., Laura Leccesi, M.D., Giuseppe Nanni, M.D., Alfons Pomp, M.D., Marco Castagneto, M.D., Giovanni Ghirlanda, M.D., and Francesco Rubino, M.D.
Bariatric surgery vs conventional medical therapy for T2DM
Bariatric-metabolic surgery versus conventional medical treatment in obese patients with type 2 diabetes: 5 year follow-up of an open-label, single-centre, randomised controlled trial

Geltrude Mingrone, Simona Panunzi, Andrea De Gaetano, Caterina Guidone, Amerigo Iaconelli, Giuseppe Nanni, Marco Castagneto, Stefan Bornstein, Francesco Rubino

<table>
<thead>
<tr>
<th>Medical treatment group (n=15)</th>
<th>Roux-en-Y gastric bypass group (n=19)</th>
<th>Biliopancreatic diversion group (n=19)</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADA partial remission at 2 years</td>
<td>0</td>
<td>15 (75%)</td>
<td>&lt;0.0001</td>
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<tr>
<td>ADA partial remission at 5 years</td>
<td>0</td>
<td>7 (37%)</td>
<td>0.0007</td>
</tr>
<tr>
<td>ADA complete remission at 5 years</td>
<td>0</td>
<td>0</td>
<td>..</td>
</tr>
<tr>
<td>HbA1c ≤6% (≤42.1 mmol/mol) and FPG ≤5.6 mmol/L without glucose-lowering drugs</td>
<td>0</td>
<td>1 (5%)</td>
<td>0.0039</td>
</tr>
<tr>
<td>HbA1c ≤6.5% (≤47.5 mmol/mol) without glucose-lowering drugs</td>
<td>0</td>
<td>8 (42%)</td>
<td>0.0003</td>
</tr>
<tr>
<td>HbA1c ≤6.5% (≤47.5 mmol/mol) with or without glucose-lowering drugs</td>
<td>4 (27%)</td>
<td>8 (42%)</td>
<td>0.0457</td>
</tr>
<tr>
<td>Relapse</td>
<td>..</td>
<td>8/15 (53%)</td>
<td>7/19 (37%)</td>
</tr>
<tr>
<td>ADA treatment goals†</td>
<td>0</td>
<td>2 (11%)</td>
<td>6 (32%)</td>
</tr>
</tbody>
</table>

Mean HbA1c 6.7% patients with relapse, 82% had mean HbA1c < 7% at 5 yrs with little or no use of glucose lowering drugs
The Surgical Treatment and Medications Potentially Eradicate Diabetes Efficiently (STAMPEDE)

Philip Schauer et al

150 pts with T2DM Randomised to medical tx, RYGB or sleeve

Primary end-point HbA1c ≤ 6%

Remission of 5% in medical group, vs 38% in RYGB and 24% in sleeve at 3 yrs
Nutritional deficiencies

- Commonest
  - Iron
  - B12 ~30%
  - Folate
  - Vitamin D ~ 60%
  - Calcium
  - Zinc
  - Magnesium

- Vitamin A (night blindness)
- Vitamin K
- B1 – thiamine
- Copper (haematological abnormalities and gait abnormalities)
- Niacin
- Zinc
- Selenium
Case study: Mrs MW

- 66 yrs
- Weight 161 Kg, height 151 cm, BMI 70.6 (May 2010)
- Type 2 DM (1996)
- Maculopathy and retinopathy (2005)
- Diabetic nephropathy (2005)
Case study: Mrs MW

- Hypertension (1999)
- Acute MI (1999)
- Hyperlipidemia (1999)
- COAD (2002)
- Obstructive sleep apnoea (2009)- started on CPAP
- Osteoarthritis
- Decreased mobility, walks with 2 sticks
MW: medication

- Novorapid 30 units tds
- Insulatard 40 units am, 60 units pm
- Metformin 500 bd
- Aspirin 75 mg
- Enalapril 15 mg
- Frusemide 80 mg bd
- Diltiazem 180 mg
- Doxazosin 4 mg od
- Thiamine 50 mg bd
- GTS spray
- Atorvastatin 20mg od
MW: visits to GSTT

116 visit since July 2002!!

Diabetes
Bariatric service
Cardiology
Sleep medicine
Eye Department
Chest Medicine
Gastroenterology
Knee Assessment
Lung Function
Dietetics
Anaesthetic
Physiotherapy
Mrs MW:
HbA1c and weight chart

Haemoglobin A1c (DCCT)

12%

6.6%

Bariatric surgery

Lower limit of normal range (4.4%)

Oral hypoglycemics
Insulin 88 units
Insulin 250 units
Insulin 50 units

Mrs MW: 161 kg

93 kg

116 kg
MW: Post-bariatric surgery (gastric sleeve)

- Required 2 nights in ITU
- Wound infection post-op
- Weight loss: 44 Kg (161 Kg down to 116 kg)
- BMI from 70 down to 55.5
- Insulin requirements down from >250 units to 50 units
- HbA1c 6.6%, fasting glucose of 5.7 mmol/L
MW: Post-bariatric surgery

- BP 105/60
- Off enalapril and doxazosin
- Stopped using CPAP
- Taking multivitamins, calcium and iron supplements
- Increased mobility
- Very grateful to all of us
Bariatric Surgery is Life-Changing
GLIDE
Gastric band and Liraglutide Intervention in Diabetes Evolution

A multicentre, prospective, double-blind placebo-controlled trial

Chief Investigator: Dr Barbara McGowan

James Crane
Clinical Research Fellow
Diabetes and Endocrinology

Guy’s and St Thomas’ NHS Foundation Trust
GLIDE: Hypothesis

The addition of liraglutide (1.8mg OD) to laparoscopic adjustable gastric banding will result in a favourable impact on glucose metabolism compared to laparoscopic adjustable gastric band alone.
GLIDE: Design

- Prospective, double-blind RCT
- Liraglutide 1.8mg OD vs placebo
- Multicentre
GLIDE: Inclusion

Inclusion

• Adult patients with T2DM
• Age 18-70 years
• HbA1c ≥6.5% and <11% at screening 6 weeks post-surgery
• BMI ≥35kg/m²
Summary

• Most people with T2DM are overweight or obese

• Orlistat is the only available anti-obesity agent in EU, but has limited efficacy and a poor side effect profile

• Treatment of T2DM in the obese remains a therapeutic challenge
Reasons include:

• Weight gain
• Poor adherence to therapy due to side effects of weight gain and hypoglycaemia

• GLP-1 receptor agonists and SGLT-2 inhibitors in management of T2D are beneficial due to their effects on body weight

• Bariatric surgery should be considered for obese patients with type 2DM