To Cut or Not To Cut
Can Surgery Provide a Better Solution?

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Obese Patients Need More GP Consultations

Obese individuals consult GPs more frequently

They require more health resources – investigations, medications, physiotherapy, dieticians, nurses

Obese individuals have poorer quality of life in all measures.

Obese Die Early - After Long Drain on Resources!

Obesity Associated Co-morbidities

- Pulmonary Disease
  - Abnormal Function
  - Obstructive Sleep Apnea
  - Hypoventilation Syndrome
  - Asthma

- Nonalcoholic Fatty Liver Disease
  - Steatosis
  - Steatohepatitis
  - Cirrhosis

- Coronary Heart Disease
  - Diabetes
  - Dyslipidemia
  - Hypertension

- Obstructive Sleep Apnea

- Hypoventilation Syndrome

- Asthma

- Nonalcoholic Fatty Liver Disease
  - Steatosis
  - Steatohepatitis
  - Cirrhosis

- Gall Bladder Disease

- Gynecologic Abnormalities
  - Abnormal Menses
  - Infertility
  - Polycystic Ovarian Syndrome

- Osteoarthritis

- Skin

- Gout

- Idiopathic Intracranial Hypertension

- Stroke

- Cataracts

- Cancer
  - Breast, Uterus, Cervix
  - Colon, Esophagus, Pancreas
  - Kidney, Prostate

- Phlebitis
  - Venous stasis
  - Leg ulcers

Worsening Prevalence of Co-morbidities at NLOSS

- Obese individuals develop more co-morbidities
- These co-morbidities require more health resources and are expensive to manage in the community and in the hospital

Sufi et al, 2009
Cost of Obesity-related Disease

- 18 million lost working days and 30,000 premature deaths in 1998
- Direct cost £480m (1.5% of the total NHS expenditure) and indirect cost £2 billion in 2001
- Estimated economic cost £7.5 billion in 2005
  Foresight report (2007) - estimates for 2050
  - Cost to NHS: £6.5bn
  - Cost to UK economy: £49.9bn (7x greater)

http://www.foresight.gov.uk/Obesity/Obesity.html
http://www.obesityinamerica.org/PDF/economicimpact.pdf
Diabetes Consumed 10% of NHS Budget in 2009

- In **2006**, 28.4 million items to treat diabetes were prescribed at a cost of £561.4 million.
- In **2009**, diabetes prescribing accounted for 7% of all prescription costs (£9 billion).

Or:
- £173 million a week
- £25 million a day
- £1 million an hour
- £17,000 a minute
- £286 a second!

Diabetes is Increasingly Cause of Death & Morbidity

- 5th most common cause of death in the world.
- Among 20 to 79-year-olds in England:
  - 11.6% deaths in 2009.
  - 12.2% deaths attributable by 2010.
- Life expectancy is reduced, on average, by:
  - more than 20 years in people with Type 1 diabetes
  - up to 10 years in people with Type 2 diabetes alone.
- One in ten people admitted to hospital has diabetes. In some age groups, it is as many as one in five. This could be one in three coronary care admissions.
- Complications of diabetes make up around one in five of all CHD, foot and renal admissions - management of these consume scarce health resources.

Complications of Diabetes - Expensive and Debilitating

- **Macrovacular**
  - cardiovascular and
  - cerebrovascular disease

- **Microvascular**
  - diabetic retinopathy
  - nephropathy and
  - neuropathy

CODE2 - Effect of Complications on Hospitalization Costs

Williams R Eur Heart J Suppl 2005;7:D14-D17

- Treatment of these are expensive
- Increasing cost of social services to deal with consequences

© The European Society of Cardiology 2005.
Traditional Management Paradigm for Diabetes

A chronic disease
- invariably associated with development of long-term complications
- high morbidity and mortality
- important effects on patient’s quality of life
- socio-economic implications

Lifelong management through
- Education
- Controlled diet
- Physical exercise
- Pharmacological interventions

- Treatment of diabetes and its complications are expensive!
- There is an increasing burden on health and social services to deal with consequences like amputations, heart attack and strokes
Who will benefit from Bariatric Surgery?

- 90% - 95% of BMI of $\geq 35 \text{ kg/m}^2$ with co-morbidities or BMI $\geq 40 \text{ kg/m}^2$ unlikely to achieve or maintain clinically beneficial weight loss through non-surgical means.
- For Asian ethnicity, the referral criteria should be 3 BMI points less!
- In England, 390,000 people (0.8%), have BMI 35-39.9 kg/m$^2$ with at least one co-morbidity:
  - Type II diabetes mellitus
  - Hypertension, Cardiomyopathy, Coronary heart disease
  - Obstructive sleep apnoea, Pulmonary hypertension
  - Osteoarthritis
  - Ischaemia and CVA
- Failure of conservative measures beyond 6 months.

http://www.nice.org.uk/usingguidance/commissioningguides/bariatric/determininglocalservicelevels/Assumptions.jsp
Blood-glucose-lowering therapy

- If HbA₁c ≥ 6.5% after trial of lifestyle interventions:
  - Consider sulphonylurea\(^{2}\)
    - See page 10
  - Metformin\(^{3}\)
    - See page 10
- If HbA₁c ≥ 6.5% and Metformin* Monitor for deterioration
  - Metformin + sulphonylurea\(^{4}\)
    - See page 10
- If HbA₁c ≥ 7.5%:
  - Monitor for deterioration
  - Add insulin\(^{2,8}\) (See page 11), particularly if the person is markedly hyperglycaemic
    - Insulin + metformin + sulphonylurea\(^{4}\)
      - See page 10
  - Increase insulin dose and intensify regimen over time (see page 11). Consider pioglitazone with insulin if:
    - Thiazolidinedione has previously had a marked glucose-lowering effect, or
    - Blood glucose control is inadequate with high-dose insulin

**Surgery?**

- Consider a rapid-acting insulin in someone who is overweight or has an elevated risk of complications.
- Consider substituting a DPP-4 inhibitor\(^{1,9}\) or a thiazolidinedione\(^{1,10}\) for the sulphonylurea if there is a significant risk of hypoglycaemia (or its consequences) or if the sulphonylurea is contraindicated or not tolerated.
- Consider adding sitagliptin or a thiazolidinedione instead of insulin if insulin is unacceptable (because of employment, social, recreational or other personal issues, or obesity).
- Consider adding exenatide\(^{6}\) to metformin and a sulphonylurea if:
  - BMI ≥ 35 kg/m² in people of European descent and there are problems associated with high weight, or
  - BMI < 35 kg/m² and insulin is unacceptable because of occupational implications or weight loss would benefit other comorbidities.
- Consider adding a DPP-4 inhibitor or a thiazolidinedione if there is a high risk of hypoglycaemia.

**Surgery?**

- Consider adding a DPP-4 inhibitor\(^{5}\) or a thiazolidinedione\(^{5,10}\) if metformin is contraindicated or not tolerated.
Weight Gain Increases Risk of Developing Diabetes

Relative Risk

Weight Change (kg)

Men

Women

Type 2 Diabetes

Relationship between BMI and Type 2 Diabetes

0 25 50 75 100

Age-Adjusted Relative Risk

## Benefits of Weight Loss (10%)

| diabetes | 30-50% decrease in fasting glucose  
50% decrease in risk of developing diabetes  
15% decrease in levels of HbA1c |
<table>
<thead>
<tr>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Blood pressure</td>
<td>decrease of 10mm Hg systolic and 20mm Hg diastolic pressure</td>
</tr>
</tbody>
</table>
| lipids | 10% decrease in total cholesterol  
15% decrease in LDL  
30% decrease in triglycerides  
8% increase in HDL |
| mortality | >20% decrease in total mortality  
>30% decrease in diabetes related deaths  
>40% decrease in obesity related cancers |

(Source: Jung 1997 and Stanford University Medical Centre 2004)
Insulin Sensitivity Improves with Weight Loss in Patients With Type 2 Diabetes

Compare Effect of Diet and Surgery on Weight

- Are we refusing to acknowledge the obvious?
- Diet & exercise effective only up to 6m
  - 60% failure at 1 yr
  - 80% failure at 2 yrs
  - 100% failure at 5 yrs
- Conservative measures fail due to complex homeostatic mechanisms leading to obligatory defence of weight!
- Only surgery is effective long-term (80%)

Changes In Energy Expenditure Resulting From Altered Body Weight
http://content.nejm.org/cgi/reprint/332/10/621.pdf

Is the Energy Homeostasis System Inherently Biased Toward Weight Gain
http://diabetes.diabetesjournals.org/content/52/2/232.full.pdf+html

Pyruvate and Satiety: Can We Fool the Brain?
http://endo.endojournals.org/cgi/reprint/146/1/1.pdf

Figure 1. Weight Changes among Subjects in the SOS study over a 10-Year Period. All data are for subjects who completed 10 years of the study. The average weight change in the entire group of surgically treated subjects was almost identical to that in the subgroup of subjects who underwent vertical banded gastroplasty. The 1 bars represent the 95 percent confidence intervals.
Human Body Vigorously Defends Its Weight - Neuro-Endocrine Energy Homeostasis:

- Energy balance is complex
- The body vigorously defends status quo (final weight)
- Hence diet and conservative measures fail

Gut hormones and the regulation of energy homeostasis Kevin G. Murphy and Stephen R. Bloom Nature 444, 854-859 (14 December 2006); doi:10.1038/nature05484
Weight Loss is Beneficial for Glycaemic Control

- Surgery changes the homeostatic mechanism and effectively -
  - Controls hyperglycaemia in the long-term (80% average)
  - Arrests progression of co-morbidities
  - Frees up health resources to deal with other conditions
  - Is economically less expensive in the medium to long term
Metabolic Syndrome

- Central obesity (defined as waist circumference $\geq 94$cm for Europid men and $\geq 80$cm for Europid women, with ethnicity specific values for other groups)
- plus any two of the following four factors:
  - raised TG level: $\geq 150$ mg/dL (1.7 mmol/L), or specific treatment for this lipid abnormality
  - reduced HDL cholesterol: $< 40$ mg/dL (1.03 mmol/L*) in males and $< 50$ mg/dL (1.29 mmol/L*) in females, or specific treatment for this lipid abnormality
  - raised blood pressure: systolic BP $\geq 130$ or diastolic BP $\geq 85$ mm Hg, or treatment of previously diagnosed hypertension
  - raised fasting plasma glucose (FPG) $\geq 100$ mg/dL (5.6 mmol/L), or previously diagnosed type 2 diabetes
Metabolic Surgery

- Treatment of metabolic derangements (metabolic syndrome) with alterations of the gut anatomy
- Emphasis of weight loss and on the improvement of metabolic conditions resulting from these interventions, particularly the remission of diabetes
- A range of procedures
  - **Restrictive**
    - Decreases the size of the stomach
    - Patients are sated with smaller volumes of food
  - **Malabsorptive**
    - Segments of the bowel are bypassed
    - Patients are less able to absorb nutrients
  - **Combined restrictive/malabsorptive or diversionary procedures**
    - Includes some element of both restrictive and malabsorptive procedures

- Energy balance is complex
- The body vigorously defends status quo (final weight)
- Surgery resets the balance
Gastric bypass has a complex mechanism of action:
1. Restriction due to a small gastric pouch
2. Malabsorption – due to diversion of gastric and bilo-pancreatic juice about 100cms from GOJ.
3. Duodenal bypass – leads to:
   a. Increased Incretin levels e.g. GLP-1, PPY etc
   b. Reduced levels of Leptin (satiety hormone) and Ghrelin (hunger hormone)
4. Altered neuronal and vagal stimulation
5. Change of bacterial flora of gut
ADA - Standards of Medical Care in Diabetes—2009
Bariatric surgery should be considered for adults with BMI 35 kg/m² and type 2 diabetes, especially if the diabetes is difficult to control with lifestyle and pharmacologic therapy. (B)

International Conference on Gastrointestinal Surgery to Treat Type 2 Diabetes—2009 (DSS)
GI surgery (i.e., RYGB, LAGB, or BPD) should be considered for the treatment of T2DM in acceptable surgical candidates with BMI 35 kg/m² who are inadequately controlled by lifestyle and medical therapy (A).*
A surgical approach may also be appropriate as a non-primary alternative to treat inadequately controlled T2DM in suitable surgical candidates with mild-to-moderate obesity (BMI 30-35 kg/m²) (B). RYGB may be an appropriate surgical option for diabetes treatment in this patient population (C).

Metabolic Surgery - Cost-Effective & Saves Money!

<table>
<thead>
<tr>
<th>Recommendations with a significant resource impact</th>
<th>Yr 10 cost (£000s)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Recurrent costs</strong></td>
<td></td>
</tr>
<tr>
<td>Treatment of overweight/obese children with comorbidities</td>
<td>9,632</td>
</tr>
<tr>
<td>Bariatric surgery for obese adults with a BMI above 50 kg/m²</td>
<td>25,878</td>
</tr>
<tr>
<td><strong>Total estimated costs</strong></td>
<td>35,510</td>
</tr>
<tr>
<td><strong>Cash-releasing savings</strong></td>
<td></td>
</tr>
<tr>
<td>Reduced prescription costs in primary care</td>
<td>-13,992</td>
</tr>
<tr>
<td><strong>Opportunity savings</strong></td>
<td></td>
</tr>
<tr>
<td>Reduced GP contacts</td>
<td>-41,636</td>
</tr>
<tr>
<td><strong>Total estimated savings</strong></td>
<td>-55,628</td>
</tr>
</tbody>
</table>

NICE Guideline CG43 - Cost Report

- In the USA, after taking into account age, sex, and comorbidities, the initial investment is returned within 4 years for patients who undergo open surgery and within 2 years for patients who undergo laparoscopic surgery.
- Even ignoring potential quality-of-life and length-of-life benefits, as well as disability and work loss, third-party payers can rely on bariatric surgery paying for itself through decreased comorbidities within 2 to 4 years.

Crémieux PY et al A Study on the Economic Impact of Bariatric Surgery
Economic Impact of Metabolic Surgery

Dixon et al. Cost-Effectiveness of Surgically Induced Weight Loss for the Management of Type 2 Diabetes: Modelled Lifetime Analysis
### Economic Impact of Metabolic Surgery - Cost-effective

<table>
<thead>
<tr>
<th>Model results (lifetime means per patient)</th>
<th>Surgical</th>
<th>Conventional</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Undiscounted</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Years in diabetes remission</td>
<td>11.4</td>
<td>2.1</td>
<td>9.4</td>
</tr>
<tr>
<td>Total life-years</td>
<td>32.1</td>
<td>30.5</td>
<td>1.6</td>
</tr>
<tr>
<td>QALYs</td>
<td>24.9</td>
<td>22.6</td>
<td>2.3</td>
</tr>
<tr>
<td><strong>Discounted at 3% for both costs and benefits</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Costs (AUD)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2-year RCT intervention</td>
<td>13,383</td>
<td>3,397</td>
<td>9,987</td>
</tr>
<tr>
<td>Surgical intervention maintenance</td>
<td>6,477</td>
<td></td>
<td>6,477</td>
</tr>
<tr>
<td>Surgical intervention complications</td>
<td>1,768</td>
<td></td>
<td>1,768</td>
</tr>
<tr>
<td>Type 2 diabetes remission—monitoring costs</td>
<td>16,479</td>
<td>2,874</td>
<td>13,605</td>
</tr>
<tr>
<td>Health care costs to treat type 2 diabetes</td>
<td>60,824</td>
<td>95,105</td>
<td>-34,281</td>
</tr>
<tr>
<td>Total cost</td>
<td>98,931</td>
<td>101,376</td>
<td>-2,444</td>
</tr>
<tr>
<td><strong>Effectiveness</strong></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Total life-years</td>
<td>20</td>
<td>19.2</td>
<td>0.7</td>
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<tr>
<td>QALYs</td>
<td>15.7</td>
<td>14.5</td>
<td>1.2</td>
</tr>
<tr>
<td><strong>Cost-effectiveness</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cost per life-year gained</td>
<td>Dominant</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cost per QALY</td>
<td>Dominant</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Probability of dominance</td>
<td></td>
<td></td>
<td>57%</td>
</tr>
<tr>
<td>Probability of cost-effectiveness at willingness-to-pay threshold</td>
<td></td>
<td></td>
<td>98%</td>
</tr>
</tbody>
</table>

Dominant: generates health care savings and health benefits. Willingness-to-pay threshold, 50,000 AUD per QALY.

Dixon et al. Cost-Effectiveness of Surgically Induced Weight Loss for the Management of Type 2 Diabetes: Modelled Lifetime Analysis
A Stitch in Time Saves Nine!

**Choices –**

• Invest now to save within 2 years!

OR

• Continue to spend increasing resources and money on management of obesity and its complications - diabetes, stroke, cardiovascular diseases, arthritis and many more!
Why is Metabolic Surgery Not Mentioned?

I.V. League

I did not know!!!!

“But Doctor, if bariatric surgery is the most effective treatment for my diabetes, why didn’t you mention it?”
Diabetes Management - A Stitch in Time?

Blood-glucose-lowering therapy

1. HbA1c ≥ 6.5%1 after trial of lifestyle interventions.
   - Metformin2 (see page 10)
   - If HbA1c ≥ 6.5%
     - HbA1c < 6.5%
       - Consider Metabolic Surgery
     - HbA1c > 6.5%
       - Monitor for deterioration
   - Metformin + sulfonlurea4 (see page 10)
   - If HbA1c > 7.5%
     - Add insulin2,8 (see page 11), particularly if the person is markedly hyperglycemic.
       - Insulin + metformin + sulfonlurea4
   - If HbA1c < 7.5%
     - Monitor for deterioration
   - Consider adding sitagliptin or a thiazolidinedione10 instead of insulin if insulin is unacceptable because of employment, social, recreational or other personal issues, or obesity.
   - Consider adding exenatide6 to metformin and a sulfonylurea if:
     - BMI ≥ 35 kg/m² in people of European descent1 and there are problems associated with high weight, or
     - BMI < 35 kg/m² and insulin is unacceptable because of occupational implications or weight loss would benefit other considerations.
   - Increase insulin dose and intensify regimen over time (see page 11).
   - Consider pioglitazone with insulin if:
     - a thiazolidinedione has previously had a marked glucose-lowering effect, or
     - blood glucose control is inadequate with high-dose insulin.

Sulfonylurea4 (see page 10)

1. Or individually agreed target.
2. With active dose titration.
4. Other once-daily sulfonylureas if adherence is a problem.
5. Only continue DPP-4 inhibitor or thiazolidinedione if reduction in HbA1c of at least 0.5 percentage points in 6 months.
6. Only continue exenatide if reduction in HbA1c of at least 1 percentage point and weight loss of at least 3% of initial body weight in 6 months.
7. With adjustment for other ethnic groups.
8. Continue with metformin and sulfonylurea (and asaccharide, if used), but only continue other drugs that are licensed for use with insulin. Review the use of sulfonylurea if hyperglycemia occurs.
9. DPP-4 inhibitor refers to sitagliptin and vilaglitazone.
10. Thiazolidinedione refers to pioglitazone and rosiglitazone.
**Provocative - Who Knows What The Future Holds?**

<table>
<thead>
<tr>
<th>OR</th>
<th>Dx</th>
<th>Operation</th>
<th>Surgeon</th>
</tr>
</thead>
<tbody>
<tr>
<td>14</td>
<td>Diabetes</td>
<td>Gastric Bypass</td>
<td>Jones</td>
</tr>
<tr>
<td>14</td>
<td>Hypertension</td>
<td>Gastric Bypass</td>
<td>Jones</td>
</tr>
<tr>
<td>14</td>
<td>Cardio-pulmonary Failure</td>
<td>Gastric Bypass</td>
<td>Jones</td>
</tr>
<tr>
<td>11</td>
<td>Asthma</td>
<td>Gastric Bypass</td>
<td>Brown</td>
</tr>
<tr>
<td>11</td>
<td>Pseudotumor Cerebri</td>
<td>Gastric Bypass</td>
<td>Brown</td>
</tr>
<tr>
<td>11</td>
<td>Crippling Arthritis</td>
<td>Gastric Bypass</td>
<td>Brown</td>
</tr>
</tbody>
</table>
Conclusion

• Obesity and especially diabetes is a major cause of morbidity and mortality
• The number of obese and diabetics are increasingly rapidly
• Treatment of obesity and diabetes consumes an increasingly large proportion of health resources
• Lifestyle interventions and pharmacotherapy has limited impact on obesity and diabetes
• Apart from standard bariatric surgery, “Metabolic Surgery” has the potential to provide remission in a large proportion of diabetics and should be considered earlier in management of these patients.
• Early “Metabolic Surgery” will be cost-effective within 2 years and is already practised in many centres in USA, Europe and Asia!

Some trials investigating effects of metabolic surgery in diabetics:

- STAMPEDE, TRIABETES, SOLID, SLIMM-T2D, DIBASY, LABS-3, 01041768, 00641251, 00540462, 00428571, DIA-BPD 25-30, SLIDE, Teen-LABS, MIDAS, OBEDIAB, 01130207