

OHIO STATE UNIVERSITY HEALTH SCIENCES CENTER

The Metabolic Impact of Bariatric Surgery

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It is predicted that over the course of the next 20 years obesity will be the #1 health problem throughout the world

Percentage of population with BMI ≥ 30 kg/m²

USA, England, Australia, Brazil

1950, 1970, 1990, 2010, 2020

Obesity and Diabetes Trends Among U.S. Adults

Obesity: No Data, <10%, 10%–14, 15%–19%, 20%–24%, 25%–29%, ≥30%

Diabetes: No Data, <4%, 4%–6%, 6%–8%, 8%–10%, >10%

Source: CDC Behavioral Risk Factor Surveillance System.

Source: Mokdad et al., Diabetes Care 2000;23:1278-83.

Mortality and Obesity

- Risk of premature death doubles when BMI >35
- Sudden unexplained death is 13 times more likely in morbidly obese women
- Overweight men participating in the Framingham study had a mortality rate 3.9 times greater than the normal weight group.
 - 25-34 years old 12X mortality
 - 35-44 years old 6X mortality
- Risks are proportional to duration of obesity

JAMA, 243: 443-445, 1980
 Ann Int Med, 106:1006-9, 1985

A Life-Threatening Disease

- When BMI > 45
 - White men could lose up to 13 years of life
 - White women up to 8 years of life.
 - African American men up to 20 years of life
 - African American women up to 5 years of life

Swedish Obese Subjects study

- The prospective involving 4047 obese subjects.
 - 2010 underwent bariatric surgery
 - 2037 received conventional treatment
- Average follow-up of 10.9 years. (follow-up rate, 99.9%)
- Overall Mortality
 - 129 in control
 - 101 in surgery group
- Average weight loss
 - ±2% change in weight in control
 - 25%, 16%, and 14% weight losses (based on surgical procedure) from baseline in the surgery groups.

The New England Journal Of Medicine, 1533-4406, 2007 Aug 23, Vol. 357, Issue 8

Relative Risks with BMI>40

Co-morbidities	Men	Women
Type 2 DM	10.65	19.89
CAD	13.97	19.22
HTN	64.53	63.16
OSA	10.04	17.19

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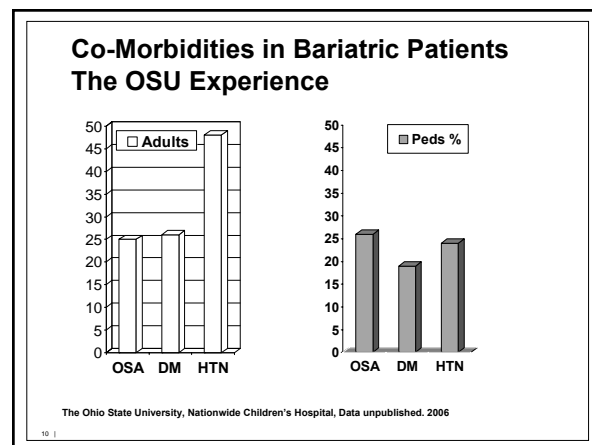
Relative Risks with BMI>40

Co-morbidities	Men	Women
Breast CA		1.70
Colon CA	1.84	1.36
Kidney CA	1.70	1.70
Liver CA	4.52	1.68

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Allison et.al. JAMA 1999;282:1530-1538, Calle et.al. N Engl J Med 1999;341:1097-1141, Manson et.al. N Engl J Med 1998;333:677-685.

- ### Medical Sequelae of Obesity
- | | |
|---|--|
| <ul style="list-style-type: none"> Hypertension Lipid disorders Diabetes Ischaemic heart disease Cardiomyopathy Pulmonary hypertension Asthma Obstructive sleep apnea Gallstones NASH (Non-alcoholic steatohepatitis) Urinary incontinence | <ul style="list-style-type: none"> GERD Arthritis/back pain Infertility/menstrual problems Obstetric complications DVT and thromboembolism Depression Immobility Breast/bowel/prostate/endo-metrial cancer Venous stasis ulcers Intertrigo Accident prone |
|---|--|
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- ### Economic Cost of Diabetes
- **\$174 Billion in 2007**
 - \$116 billion in excess medical expenditures
 - \$27 billion for care to directly treat diabetes (including \$21 billion for medication and supplies)
 - \$58 billion to treat chronic complications that are attributed to diabetes
 - \$31 billion in excess general medical costs.
 - \$58 billion in reduced national productivity.
 - \$2.6 billion due to increased absenteeism
 - \$20.0 billion for reduced productivity while at work
 - \$0.8 billion for reduced productivity for those not in the labor force
 - \$7.9 billion due to unemployment from disease-related disability
 - \$26.9 billion due to lost productive capacity due to early mortality
 - People with diagnosed diabetes cost an average \$11,744 per year \$6,649 is attributed to diabetes (2.3 times higher than without diabetes)
 - 1 in 10 health care dollars in the U.S. is spent attributed to diabetes
- ADA Diabetes Care 31:596-615, 2008
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- ### Predisposition to Morbid Obesity
- Despite recognition that obesity is not healthy, we do not fully understand why
 - Nor do we understand how some individuals gain large amounts of weight while others do not
 - Because of this lack of understanding, there is also a lack of effective treatments
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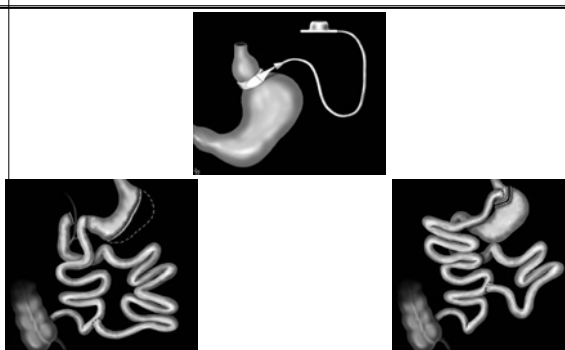
WEIGHT REDUCTION STRATEGIES



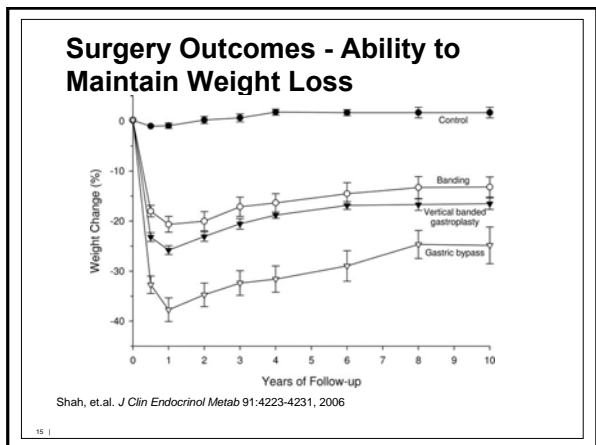
- Diet
- Exercise
- Comp wt management
- Medications
- Bariatric surgery

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CURRENT BARIATRIC SURGERY



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Weight Regain/Failure – Surgery Outcomes

- Weight regain at 10 years post-op
 - There was a significant increase in BMI in both morbidly obese (BMI <50) and super obese patients (BMI > 50) from the nadir to 5 years & from 5 to 10 years.
 - There was an increase in failures and decrease in excellent results at 10 years vs. 5 years.
 - The failure rate when all patients are followed for at least 10 years was 20.4% for morbidly obese patients and 34.9% for super obese patients.

Nicolas V. Christou, MD, Annals of Surgery, 11/2006

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Metabolic Surgery – What are the Metabolic Consequences?



L'OBESITE EST UNE MALADIE GRAVE
 QUI TUE 85 000 PERSONNES PAR AN EN FRANCE.
 CE N'EST NI UNE FAUTE, NI UNE FATALITE,
 ENCORE MOINS UNE PLAISANTERIE.

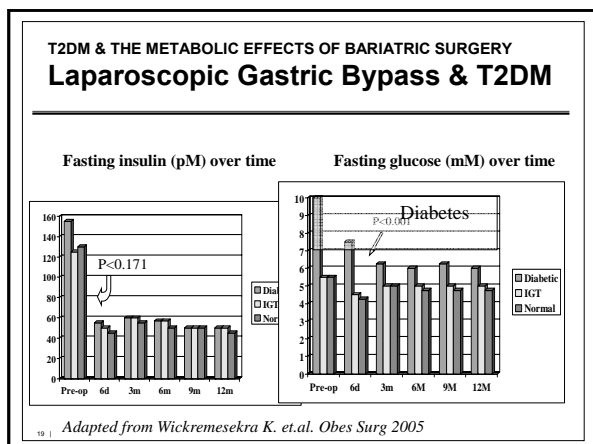
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T2DM & THE METABOLIC EFFECTS OF BARIATRIC SURGERY

Bariatric Surgery Efficacy

Author	Procedure	Resolution
Porjes et al 1995	Gastric Bypass	89%
Torquati et al 2005	Gastric Bypass	74%
Schauer et al 2003	Gastric Bypass	82%
Sugerman et al 2003	Gastric Bypass	86%
Dixon et al 2003	Lap Band	64%
Gagner (unpublished)	Sleeve Gastrectomy	65%

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T2DM & THE METABOLIC EFFECTS OF BARIATRIC SURGERY Gastric Banding & T2DM

Lap-Band® vs. Intensive Medical Management

– Results

- Weight Change
 - 87.2% excess weight loss (surgical)
 - 21 % excess weight loss (nonsurgical)
- Metabolic Syndrome (in 38% each group at start)
 - 24% nonsurgical group with residual
 - 3% surgical group with residual (p<0.002)

Dixon et.al. Ann Int Med, 2006

T2DM & THE METABOLIC EFFECTS OF BARIATRIC SURGERY Bariatric Surgery Efficacy

Author	Intervention	Resolution	“Failure” more likely with....
Pories et.al. 1995	Gastric Bypass	89%	Older patients; long standing disease
Dixon et.al 2003	Lap Band	64%	Less weight loss; long standing disease
Schauer et.al. 2003	Gastric Bypass	82%	Long standing disease; disease severity; insulin usage

Diabetes Surgery Symposium – Rome, Italy (March 29-31, 2007)

- International multidisciplinary voting panel of experts made up of Surgeons (1/3 of the panel), Endocrinologists, Basic Scientists
- Major points of consensus
 - Anatomic modification of various regions of the GI tract likely contribute to the amelioration of T2DM through distinct physiological mechanisms.
 - Gastrointestinal bypass procedures can improve diabetes by mechanisms beyond changes in food intake and body weight.
 - Gastrointestinal surgery may be appropriate for the treatment of T2DM in patients who are appropriate surgical candidates with BMI of 30 to 35 who are inadequately controlled by lifestyle and medical therapy

Resolution of Co-Morbidities: Hypertension

- All forms of weight loss results in reduction in BP
 - *Resolution 62% with significant improvement 78.8%
 - **In DM subset, 69% resolution at 1yr., 66% at 7yr.
 - Gastric bypass is more effective than vertical banding in resolution of HTN

*Buchwald, et.al. JAMA 2004, **Sugarman, et.al. Ann Surg 2003

Resolution of Co-Morbidities: Dyslipidemia

- Significant improvement in lipids in 70%
 - Gastric by-pass better than vertical bands
 - HDL improve significantly with vertical bands
- Swedish Obesity Study
 - 2 & 10 yrs, improvement in HDL & triglycerides
 - Total cholesterol was not changed

Buchwald, et.al. JAMA 2004, Sjostrom, et.al. NEJM 2008

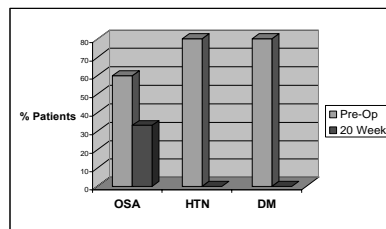
Resolution of Other Co-Morbidities OSA, NASH, Pseudotumor Cerebri

- NASH – decrease in severity
- OSA - 85.7-93% resolution
- Pseudotumor Cerebri – success rates are higher than results of shunt placement

No long term studies examining recurrence

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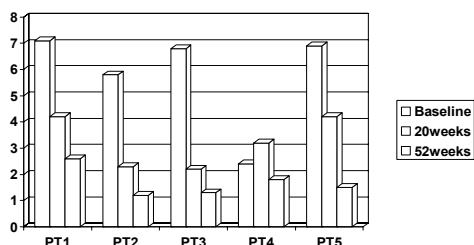
Resolution of Obesity-Related Co-morbidities 20 wks after Pediatric RYGB



Unpublished, The Ohio State University, Columbus Children's Hospital 2006

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Improvement in HOMA-IR Post-RYGB in Pediatric Population



Unpublished, The Ohio State University, Columbus Children's Hospital 2006

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Psychological Disorders After Weight Loss Surgery

- Does mental health improve?
 - Balsiger, et.al. 2000 93% followed for 3yrs. reported improvement
 - Maddi, et.al. 2001 improvement in MMPI-2
 - Waters, et.al. 1991 found improvement in psychological fx, but lack of difference by 3 yrs.

No standards exist

Severity rather than nature of symptoms was predictive of success

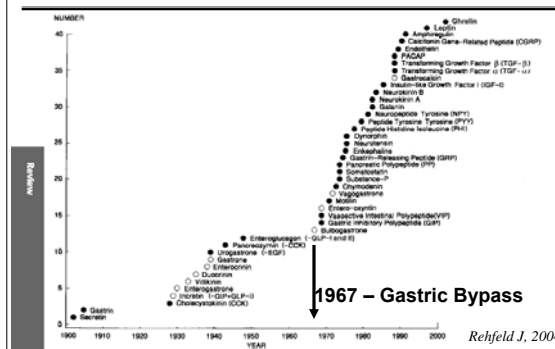
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Obesity Surgery and Reduction in Long-Term Mortality

- Flum&Dellinger *J Am Coll Surg* 199:543-551, 2004. Surgical pts. had a 59% greater chance at 5yr survival than nonsurg obese pts.
- Christou, et.al. *Advances in surgery* vol. 39, (2005): 165-79. Reported mortality rate of 0.67% vs. 6.17% in surg vs. nonsurg
- MacLean, Lloyd D MacDonald, et.al. *J Gastrointest Surg* 1:213-220, 1997. The 6-9yr mortality 1% vs. 4.5% in surg vs. nonsurg
- Sjostrom, et.al. *NEJM* 357(8):741-52, 2007. Gastric bypass reduced all cause mortality by 40%
- Adams, T.D. et al. *NEJM* 357(8):753-761. 92% reduction in death due to diabetes

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T2DM & THE METABOLIC EFFECTS OF BARIATRIC SURGERY The Entero-insular Axis



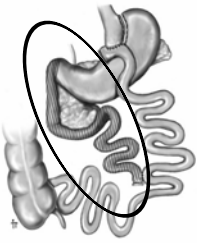
Rehfeld J, 2004

T2DM & THE METABOLIC EFFECTS OF BARIATRIC SURGERY

The Entero-insular Axis

The Foregut Theory

- Exclusion of the duodenum results in inhibition of a "putative" signal that is responsible for insulin resistance and/or abnormal glycemic control (T2DM)



Rubino et.al, Ann Surg, 2006

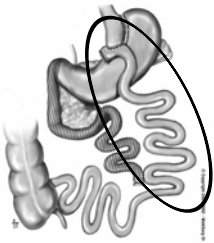
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T2DM & THE METABOLIC EFFECTS OF BARIATRIC SURGERY

The Entero-insular Axis

The Hindgut Theory

- The more rapid delivery of undigested nutrients to the distal bowel upregulates the production of L-cell derivatives like GLP-1



Mason E. Obes Surg 2005 15, 459-461
Rubino et.al, Ann Surg, 2006

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T2DM & THE METABOLIC EFFECTS OF BARIATRIC SURGERY

The Adipo-insular Axis

- Epidemiologic/scientific evidence supports the association of visceral adiposity and insulin resistance/diabetes and mortality
- Moderate debate about significance of visceral versus subcutaneous adiposity
- "Theoretical" mechanisms of action
 - Increased release of free fatty acids into portal circulation
 - Abnormal expression of fat-derived peptides

Gabriely I. Diabetes 2002
Nielsen S. J Clin Invest, 2004

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T2DM & THE METABOLIC EFFECTS OF BARIATRIC SURGERY

The Adipo-insular Axis

Free fatty acids and insulin resistance – Theories

- Impaired insulin signaling (muscle) / glucose transport
- Increased oxidative stress (reactive oxygen species)
- Inhibition of insulin suppression of glycogenolysis in liver
- Direct endothelial damage
- Impairment of beta cell function
- Alterations in blood pressure

Boden G. Diabetes Care, 2004
Miles J. Diabetes Care, 2005

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T2DM & THE METABOLIC EFFECTS OF BARIATRIC SURGERY

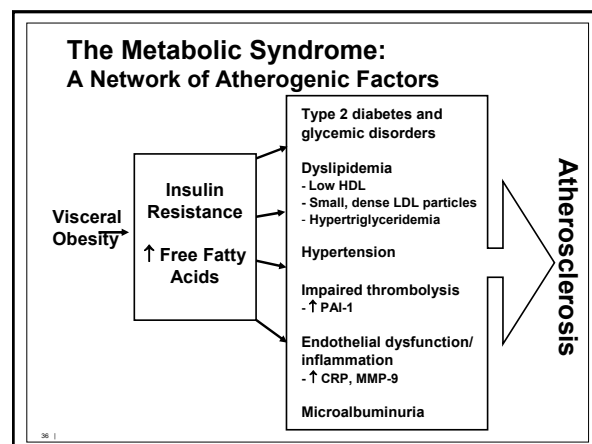
The Adipo-insular Axis

Fat-derived peptides – "Adipokines"

- TNF-alpha – impairs insulin signaling pathways / suppresses adipocyte differentiation
- Leptin – enhances insulin action / anorexigenic
- Resistin – Known to be elevated in obesity / IR – unknown action
- Adiponectin - enhances insulin action / glucose clearance / fatty acid oxidation
- IL-1/IL-6 – undefined activity

Pitombo C. Unpublished manuscript

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Early Surgical Complications

Gastric Bypass	Lap-band
<ul style="list-style-type: none"> • Enteric leak • Sepsis • DVT/PE • GI hemorrhage • Vomiting • Early Obstruction • Wound Infection • Rhabdomyolysis 	<ul style="list-style-type: none"> • Surgical injury • Early gastrointestinal leak • Intra-abdominal esophagus • Early surgical obstruction • DVT

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Late Surgical Complications

Gastric Bypass	Lap-band
<ul style="list-style-type: none"> • Vomiting • Abdominal Pain • Marginal Ulcer 2-5% • Incisional hernia 1-2% • Internal hernia 3.3% • Cholelithiasis (1%) • Nutritional deficiencies 	<ul style="list-style-type: none"> • Breakage of access port • Band slippage • Erosions through the gastric wall • Esophageal dilatation/pseudoachalasia • Access port infection

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Nutritional & Metabolic Complications

Complication	VBG	RYGB
Severe Malnutrition	Rare	Less common (4.7%)
Fat Malabsorption	None	Less common
Vitamin B12	None	Common (30%) 1-9
Iron deficiency	Rare	Common (20-49%)
Folate deficiency	None	Less common
Thiamine deficiency	Rare	Common
Fat-soluble vitamins	None	Less common (65%) 4
Calcium deficiency	Rare	Less common
Bone disease	Rare	Common
Cholelithiasis	Less common	Common

Majumowski, et.al., *Am J Med Sci* 2006;331(4):219-225.

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Post-operative RYGB* and Vertical Banding Follow up Recommendations

<ul style="list-style-type: none"> • Lifelong monitoring • Tests performed 3-6month intervals for first 2 years • Yearly thereafter 	<ul style="list-style-type: none"> • Complete blood count • Chem 10 • Albumin/pre-albumin • B₁₂, folate • PT/PTT • Fat soluble vitamins* • Uric Acid • PTH
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Prophylactic Nutritional Supplementation

Supplement	VBG	RYGB
Multivitamin with minerals	√	√
Vitamin B ₁₂ (350-500ug/d)		√
Calcium elemental (1200-1500)		√
Ferrous Sulfate (325-650mg/d)		√
Protein (40-100mg/d)		√

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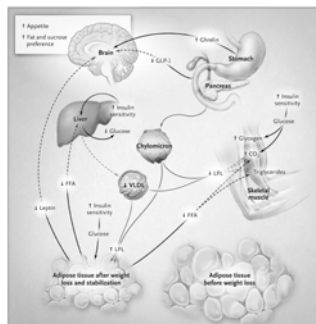
Toward the Rational and Equitable Use of Bariatric Surgery

Flum, David R. MD, MPH; Khan, Tipu V. BA, BS; Dellinger, E. Patchen MD *JAMA* 298(12), 26 September 2007, p 1442-1444

1. More than 5% of the USA population qualify for bariatric surgery but only small fraction is considered for it.
2. Demographics of individuals having bariatric surgery do not equate to the demographics of the morbidly obese population
 - 84% female (rates of morbid obesity 2.8M vs. 6.9%F)
 - >90% Caucasian
 - Most have higher income levels
3. Etiology unclear
 - Predictive scoring of obesity risk vs. surgical risk
 - Social and attitudinal behaviors
 - Lack of understanding of causes of obesity

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Weight Management is Lifelong!



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The OSU Team

- Surgeons
- Dietitians
- Psychologists
- Exercise Physiologists
- PCRM's and Nurse Practitioner
- Specialties
 - Endocrinology
 - Pulmonary
 - Gastroenterology
 - Plastic surgery
 - Genetics



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