Gastric Bypass:

The Future of Type II Diabetes Treatment

James Cromie

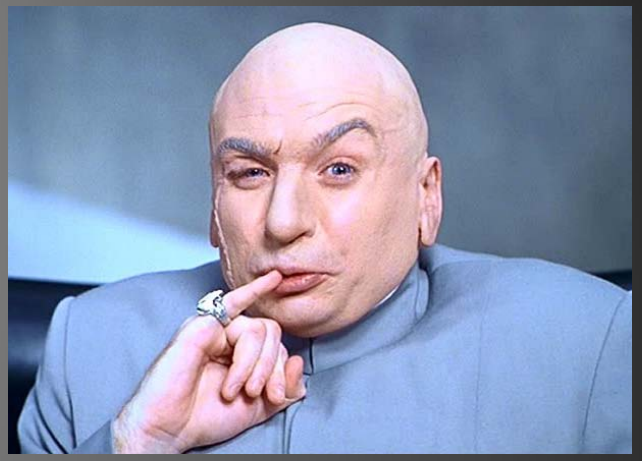
Surgery Not just for the morbidly obese

The Arguments:

- T2DM - tremendous economic burden globally
- Lifestyle / Pharm Rx:
  - INEFFECTIVE and UNSUSTAINED
- Bariatric surgery is an **Effective** and **Durable** treatment option
  - Well established for BMI > 35
  - Effective for BMI > 25
- Surgery is a **Cost Effective** and **Safe** option

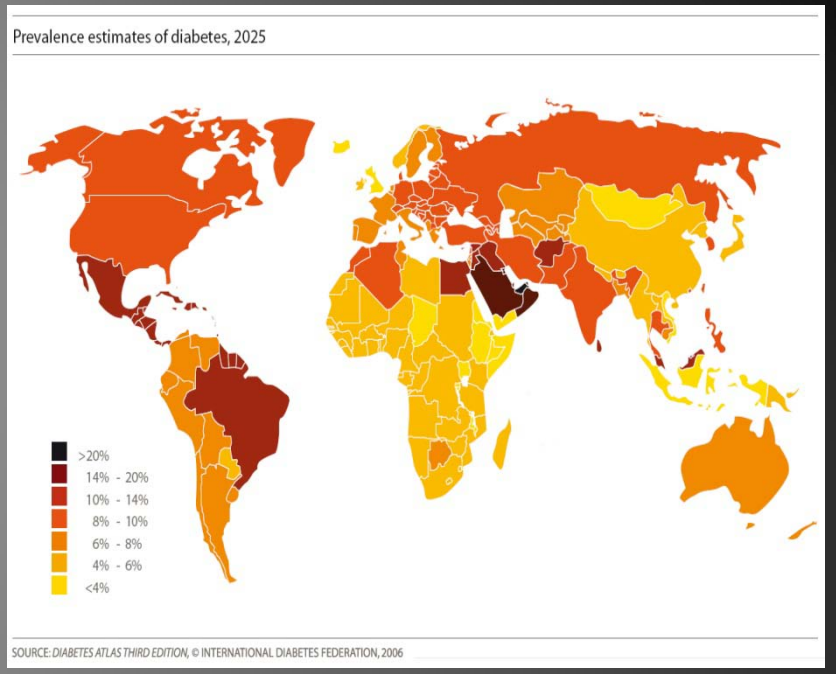
Epidemic of obesity and DM

- > 30% of American population obese (BMI > 30)
  - **By 2030**
    - 90% of adult Americans projected to be overweight / obese (> 50% obese)
    - US Obesity-related medical spending: $956 billion dollars



- 8.3% of Americans have type II DM
  - BMI > 40: 7X more likely to develop T2DM than nml BMI
- 285 million people worldwide with T2DM
  - 438 million projected for 2030 (WHO)

Surg Clin North Am. 2011; 91: 1163-1172



- 2010: US spent $198 billion on DM treatment
  - $9677 per patient diagnosed
  - $58 billion in lost earnings / decreased productivity
- By 2030: Global expenditure for DM treatment and prevention will be $490 billion
  - 12% of worldwide healthcare expenditure spent for DM

Surg Clin North Am. 2011; 91: 1163-1172

ADA recommendations:

Table I. The ABCs of diabetes care: treatment targets as recommended by the American Diabetes Association.[3]

HbA_{1c}

<7.0% in general; <6.0% in selected individuals

Blood pressure

<130/80 mm Hg

Cholesterol

LDL-C: <100 mg/dL (<70 mg/dL in very high-risk patients)

HDL-C: >40 mg/dL in men; >50 mg/dL in women

Non–HDL-C: <130 mg/dL (<100 mg/dL in high-risk patients)

Triglycerides: <150 mg/dL

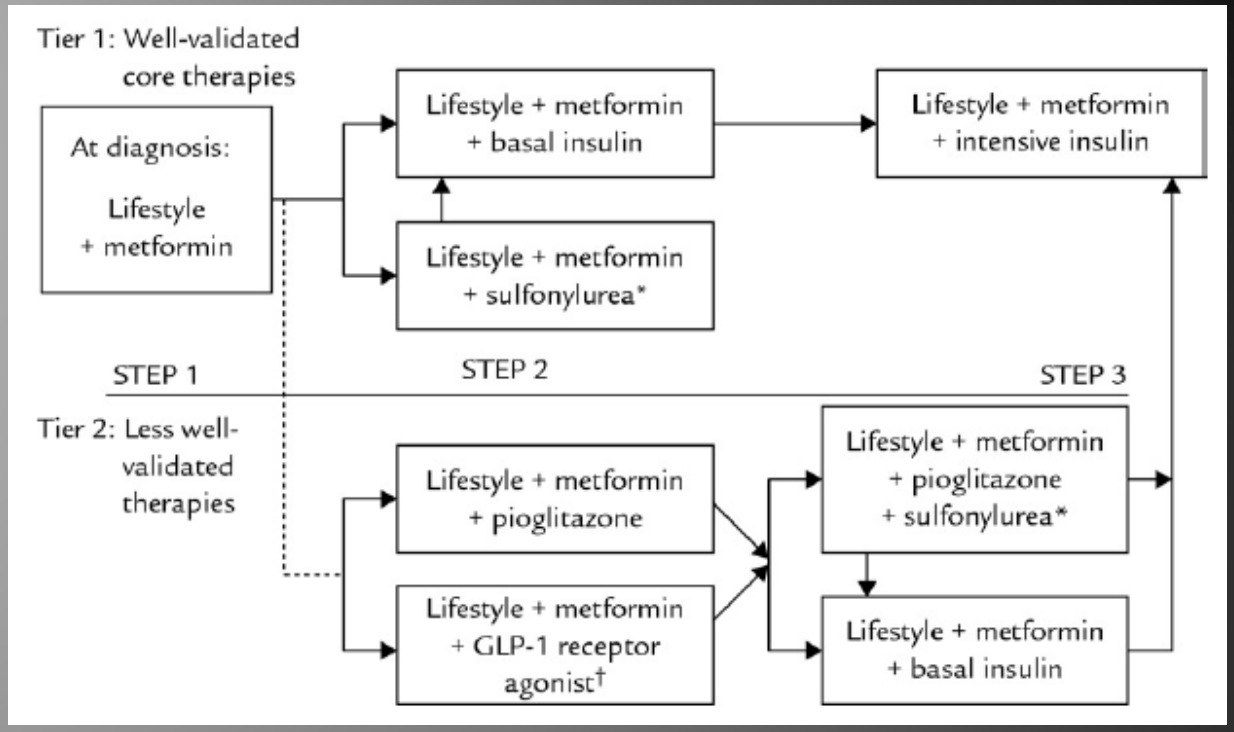
HbA_{1c} = glycosylated hemoglobin.

How good is lifestyle / medical management?

- National Health and Nutrition Examination Survey (NHANES); 2006
  - 88% fail to achieve all 3 ADA standards
  - 44% fail to achieve HbA1C < 7%
- Complete remission of hyperglycemia and metabolic consequences is rare
  - Metformin / sulfonylureas → progressive loss of β-cell function.

Am J Med. 2006; 122:443-453

The "ADA Way"



Follow up (yrs)	% Failing Monotherapy
3	50%
9	75%

UKPDS. JAMA. 1999; 281:2005-2012

Who Would Have Thought It?

An Operation Proves to Be the Most Effective Therapy for Adult-Onset Diabetes Mellitus

Walter J. Pories, M.D., Melvin S. Swanson, Ph.D., Kenneth G. MacDonald, M.D., Stuart B. Long, B.S., Patricia G. Morris, B.S.N., Brenda M. Brown, M.R.A., Hisham A. Barakat, Ph.D., Richard A. deRamon, M.D., Gay Israel, Ed.D., Jeanette M. Dolezal, Ph.D., and Lynis Dohm, Ph.D.

- 608 patients, using current NIH inclusion criteria
  - RYGB
  - 14 yr Follow up
- 82.9% DM resolution in those with T2DM dx.
- 98.7% normalization in those with pre-diabetes

Annals of Surg. 1995; 222:339-352

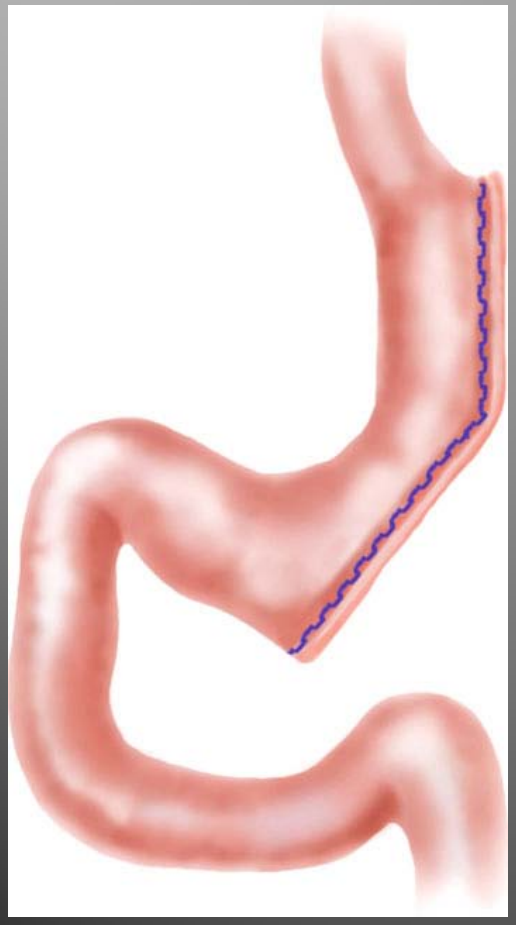
General observations

- Correction of T2DM occurs within days of the operation before weight loss occurs
- Effects are maintained long-term, though patients remain overweight / obese
- DM "cure" less likely for older patients or those with DM for > 5 – 10 years (due to lower B-cell reserve)

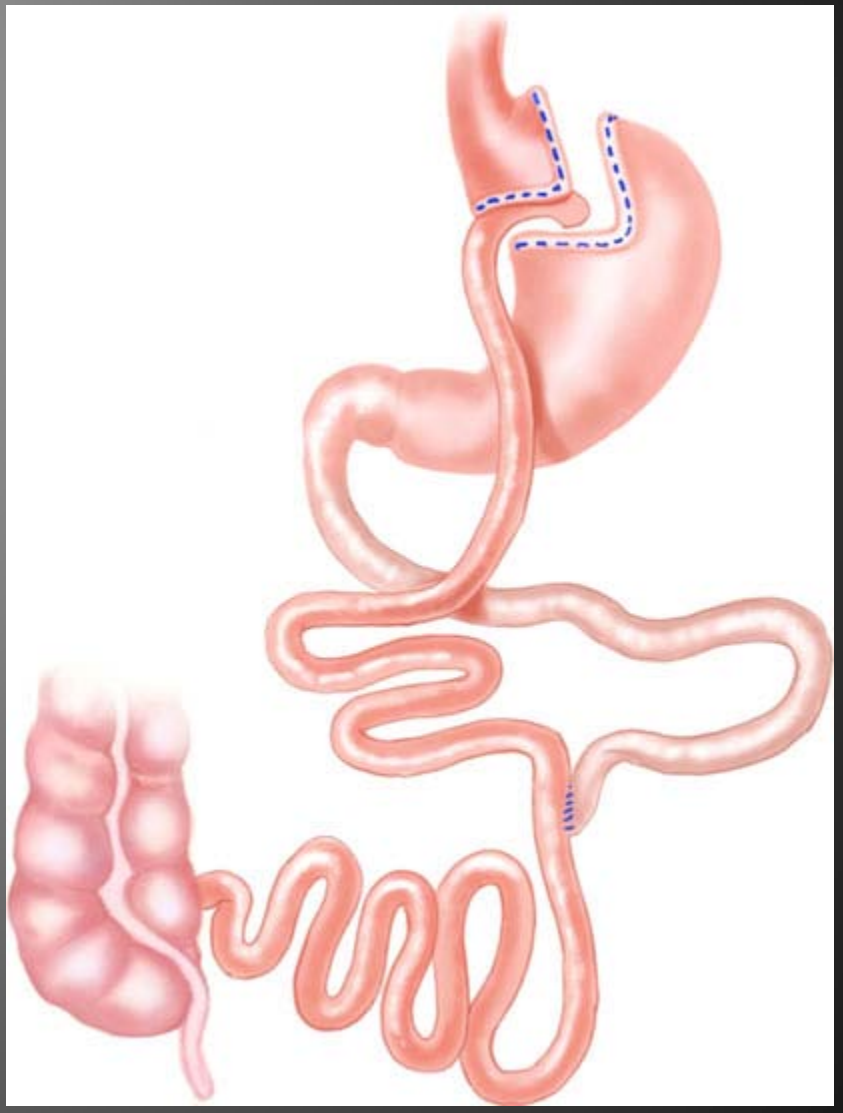
Bariatric Surgery for T2DM

- Utility of bariatric surgery well established for DM in morbidly obese patients (BMI >35)
  - **92% DM-related mortality reduction**
  - compared to medical management
- In 2000: NIH recommendation:
  - BMI > 40
    - Or,
  - BMI > 35 AND:
    - DM, HTN, OSA, GERD, etc.
- In 2009, centers for Medicare and Medicaid services provided coverage for bariatric surgery for above indications

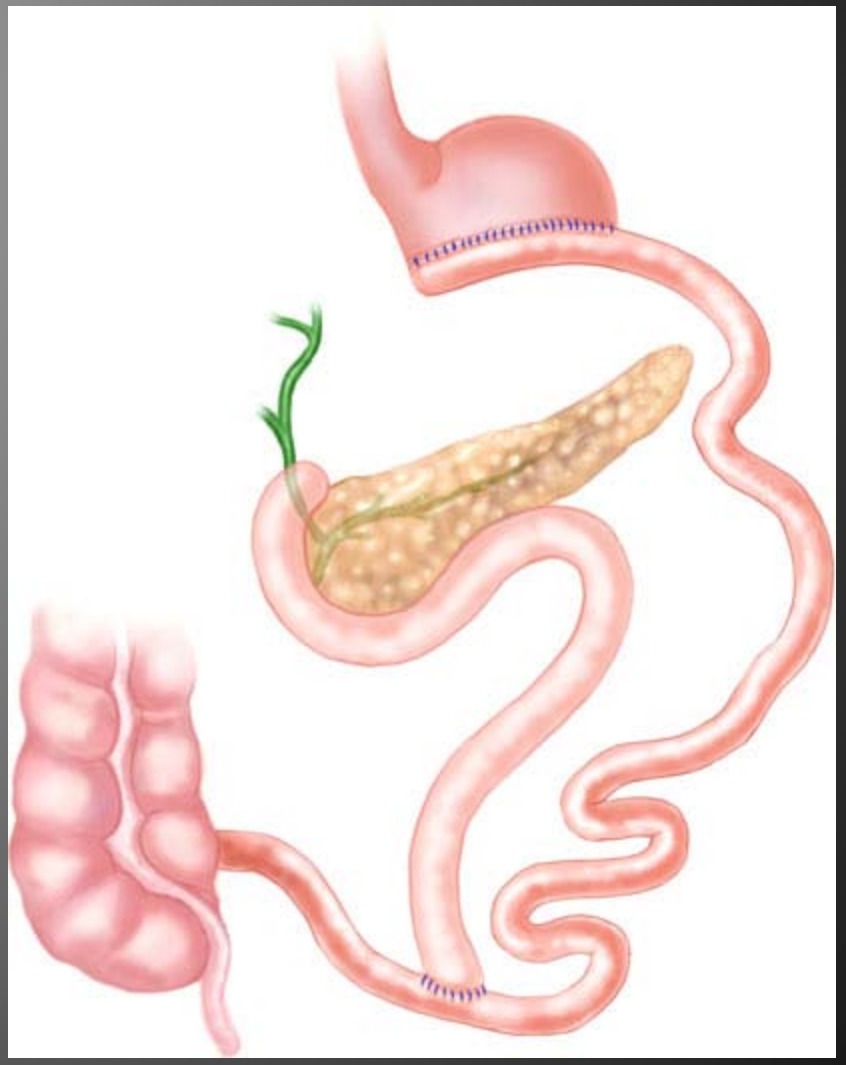
- Lap adjustable gastric band
- Sleeve gastrectomy



- Roux-en-Y gastric bypass
  - Restrictive-Malabsorptive
  - Most common technique
  - 30cc gastric pouch
  - 100 – 150cm roux limb



- Biliopancreatic diversion
  - Restrictive-malabsorptive
  - 200-500cc gastric pouch
  - 50cm common limb



Bariatric surgery for BMI > 35

- International meta-analysis.
  - 22, 094 patients with T2DM in 136 studies:
  - 84% remission rate overall, 2 yr f/u
    - BPD / DS : 95.1%
    - RYGB: 80.3%
    - Gastroplasty: 79.7
    - LAGB: 56.7%
- Effect of DM duration:
  - 95% remission when DM < 5 years
  - 54% remission if DM > 10 yrs
- Modest weight loss can result in 20% reduction in all-cause mortality

Buchwald et al. Am J Med. 2009; 122(3): 248-56

Long term results: gastric bypass for BMI > 35

- 312 patients with T2DM
  - BMI 50 +/- 9
  - 10 year follow up. None on antidiabetic Rx.

	Prior to BPD	At 1 year	At 2 years	At 3 years	At 5 years	At 10 years
n	312	305	300	290	272	243
Body weight (kg)	135.4 ± 25.6	88.9 ± 20.9	84.3 ± 16.5	88.2 ± 18.3	85.8 ± 18.3	86.6 ± 18.5
BMI (kg/m^2)	50.1 ± 9.0	32.8 ± 7.4	31.1 ± 6.5	32.1 ± 7.0	31.6 ± 6.4	32.0 ± 6.7
GL (mg/dl)	178 ± 61	84 ± 15	85 ± 18	84 ± 14	86 ± 18	89 ± 24
TG (mg/dl)	220 ± 155	120 ± 55	124 ± 107	96 ± 61	83 ± 36	82 ± 35
CHOL (mg/dl)	222 ± 75	136 ± 34	133 ± 33	126 ± 32	126 ± 31	113 ± 29

	Hyperglycemia	Hypertriglyceridemia	Hypercholesterolemia	Arterial hypertension
Prior to BPD	312/312 (100)	119/311 (38)	197/312 (63)	268/312 (86)
At 1 year	2/305 (0.7)	24/305 (8)	1/305 (0.3)	152/305 (50)
At 2 years	2/300 (0.7)	20/300 (7)	0/300 (0)	129/300 (43)
At 3 years	3/290 (1)	5/288 (2)	0/290 (0)	128/290 (44)
At 5 years	6/247 (2)	2/245 (1)	0/242 (0)	59/163 (36)
At 10 years	6/195 (3)	2/193 (1)	0/192 (0)	31/121 (26)

Scopinaro, et al. Diabetes Care. 2005; 28: 2406-11

Bariatric surgery for BMI < 35

- Growing evidence base for similar benefits for BMI 25 – 35
- Sporadic case reports of gastric resection in non-obese diabetic patients resulting in T2DM remission
- 1998: Noya et al.
  - First clinical report of Biliopancreatic diversion in BMI 24 - 38
  - 10 patients with uncontrolled T2DM and hypercholesterolemia
  - 18 month follow up
  - 9/10 achieved normoglycemia
  - 100% normalized cholesterol / triglycerides
  - 100% normalized BP

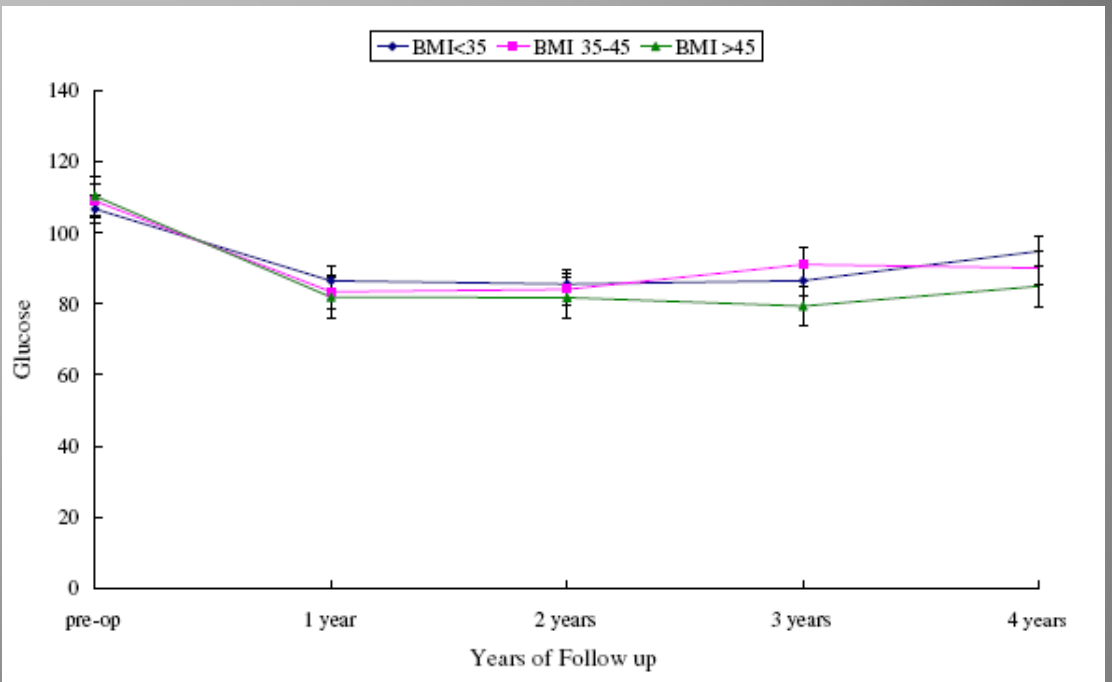
Obesity Surgery 1998; 8: 67 - 72

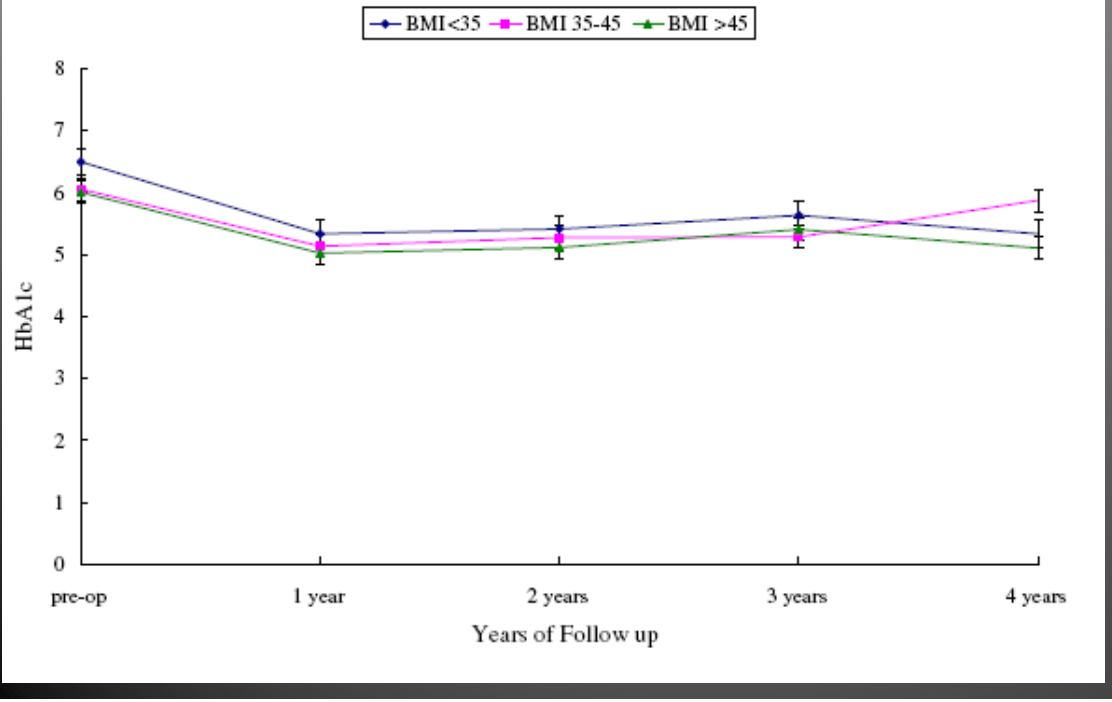
Effect of Laparoscopic Mini-Gastric Bypass for Type 2 Diabetes Mellitus: Comparison of BMI >35 and <35 kg/m^2

Wei-Jei Lee · Weu Wang · Yi-Chih Lee · Ming-Te Huang · Kong-Han Ser · Jung-Chien Chen

- 117 patients with DM, 84 patients with pre-diabetes
  - Lap mini-gastric bypass surgery
    - BMI > 35 vs < 35
- 5-yr follow up.
- 0.12% mortality, 2.2% complications
- Baseline:
  - Glucose: 158 mg/dl
  - Cholesterol: 200 mg/dl
  - LDL: 142 mg/dl
  - HbA1C: 7.2%

Wei-Jei, et al. J Gastrointest Surg (2008) 12:945-952





- Achieving ADA guidelines (1yr)
  - (A1C < 7%; LDL < 100 mg/dl; Triglyceride < 150 mg/dl)
  - BMI < 35: 76.5%
  - BMI 35-45: 88.9%
  - BMI > 45: 100%
  - Compare:
    - 12% of those medically managed, meeting ADA standards
    - (NHANES 2006)

- Asia-Pacific bariatric guidelines
  - BMI 27 definition of obesity in Taiwan
  - 90% of T2DM cases in Taiwan have BMI < 30
- Modified to include BMI > 32 with T2DM:

RYGB for BMI < 35

Gastrointestinal Metabolic Surgery for the Treatment of Diabetic Patients: A Multi-Institutional International Study

Wei-Jei Lee · Kyung Yul Hur · Muffazal Lakadawala · Kazunori Kasama · Simon K. H. Wong · Yi-Chih Lee

- 200 patients, BMI < 35
  - Lap RYGB: 86%
  - L AGB / SG: 14%
- 1 year follow-up
- 72.4% overall diabetes resolution
  - DM < 5 yrs: 90.3% remission
  - DM > 10 yrs: 62.5% remission
- 1% major complication (anastomotic leakage, requiring surgical revision)

Wei-Jei, et al. J Gastrointest Surg. 2012; 16:45-52

Long term results for BMI < 35

Long-Term Control of Type 2 Diabetes Mellitus and the Other Major Components of the Metabolic Syndrome after Biliopancreatic Diversion in Patients with BMI <35 kg/m^2

Nicola Scopinaro, MD; Francesco Papadia, MD; Giuseppe Marinari, MD; Giovanni Camerini, MD; Gianfranco Adami, MD

- Retrospective, 7 patients, on medication for DM
- BMI 32 – 34.6
- Mean follow up: 13 years (10 – 18 years)

Scopinaro, et al. Obesity Surg. 2007; 17: 185-192

10 year follow up

- ADA criteria
  - Triglycerides: 100%
  - BP control : 86%
    (No medications)
  - HbA1c not reported
    (Glucose < 126): 40%

*long term remission for those with DM < 4 yrs

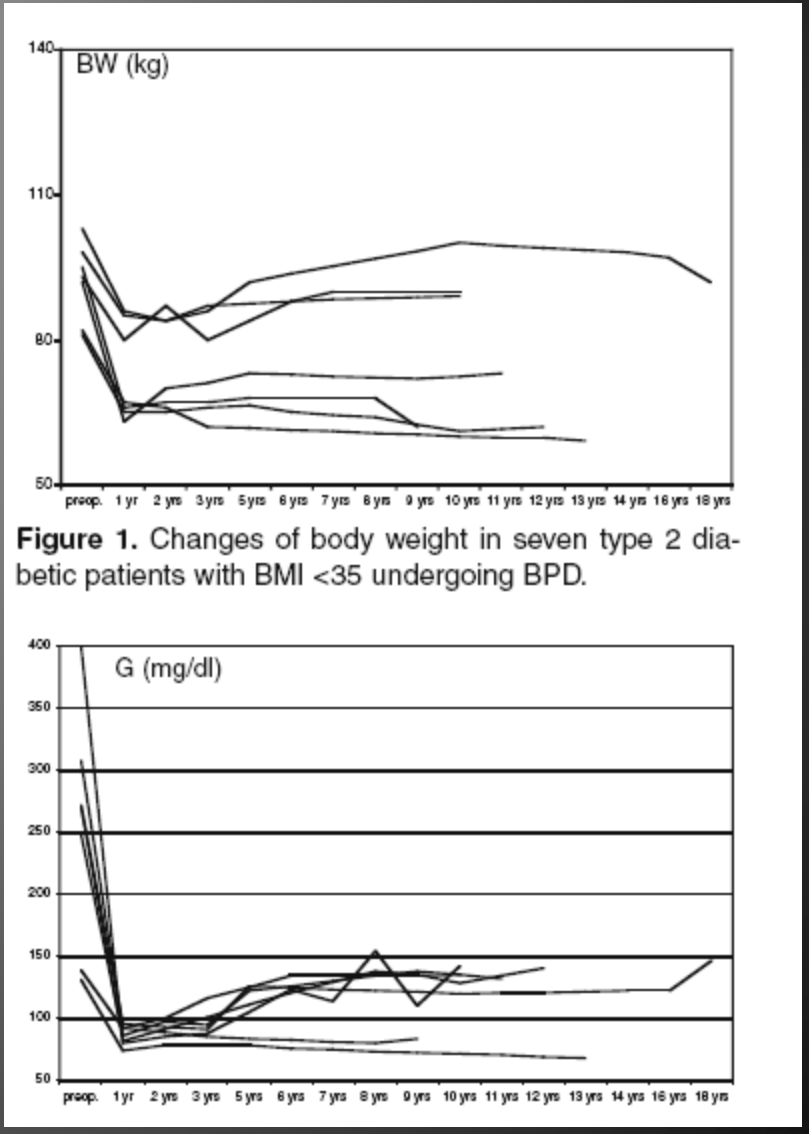


Figure 1. Changes of body weight in seven type 2 diabetic patients with BMI <35 undergoing BPD.

Scopinaro, et al. Obesity Surg. 2007; 17: 185-192

Safety

- Bariatric Outcomes Longitudinal Database (BOLD)
  - 55,000 patients
  - All cause 30 day mortality: 0.09%
- Longitudinal Assessment of Bariatric Surgery (LABS) Consortium
  - 10 center prospective trial
  - 4776 morbidly obese patients
  - 0.3% 30-day post-op mortality
  - 4.3% complication rate (open & laparoscopic)
    - 3.1% Anastomotic leak (1.4% for laparoscopic)
    - 2.3% wound infection
    - 2.2% pulm. Events
    - 1.7% hemorrhage
- BMI < 35 bariatric surgery review:
  - 0.29% 30-day mortality
  - < 4% complication rate

Cost Effectiveness

- Modeling Assumptions:
  - Cost-effective QALY benchmark: $50,000
- Takes into account:
  - DM remission risk based on 2 and 10 year data
  - Reduced risk related to:
    - Reduced BP
    - DM remission
    - Reduced cholesterol
  - Costs of bariatric surgery
- Evaluated effect of BMI 30 – 34 and > 35

- Modeled for BMI > 35
  - BMI 30 – 34 approximately doubled cost-effectiveness ratios ($ / QALY)
- RYGB is cost-effective, but not cost-saving

	Total costs*	Remaining life-years	QALYs*	Cost-effectiveness ratio ($/QALY)†
Patients with newly diagnosed diabetes				
No surgery (standard care)	$71,130	21.62	9.55	
Bypass surgery	$86,665	23.34	11.76	
Incremental (vs. no surgery)	$15,536	1.72	2.21	$7,000
Banding surgery	$89,029	22.76	11.12	
Incremental (vs. no surgery)	$17,900	1.14	1.57	$11,000
Patients with established diabetes				
No surgery	$79,618	16.86	7.68	
Bypass surgery	$99,944	17.95	9.38	
Incremental (vs. no surgery)	$20,326	1.09	1.70	$12,000
Banding surgery	$96,921	17.80	9.02	
Incremental (vs. no surgery)	$17,304	0.94	1.34	$13,000

Diabetes care. 2010; 33(9):1933-1939

- $15,000 - 20,000 per capita *excess* cost compared to standard care
  - Remaining life years in cost-effectiveness model: 20 years
- If we consider…
  - $58 billion annual indirect costs related to DM
    - (lost earnings and decreased productivity)
  - → $2, 233/yr per American with DM
    - X 10 yrs
- >$22,000 per capita lost earnings related to DM over 10 years

Surg Clin North Am. 2011; 91:1163 - 1172

The Diabetes Surgery Summit Consensus Conference

Recommendations for the Evaluation and Use of Gastrointestinal Surgery to Treat Type 2 Diabetes Mellitus

Francesco Rubino, MD,† Lee M. Kaplan, MD, PhD,‡ Philip R. Schauer, MD,§ and David E. Cummings, MD,¶ on behalf of the Diabetes Surgery Summit Delegates*

- 2010: 50 international delegates, Rome, Italy
- Consensus Statement:

(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/m^2) (B). RYGB may be an appropriate surgical option for diabetes treatment in this patient population (C).

Annals of Surgery. 2010; 251: 405-399

- International Diabetes Federation
  - March 2011:
    - Bariartic surgery should be an accepted option in people who have T2DM and BMI > 35
    - Surgery should be considered for BMI 29 – 35 when DM poorly controlled
    - Asians: may reduce BMI threshold to 25

Conclusions

- Bariatric surgery results in complete and durable remission of T2DM in carefully selected patients with BMI 25 – 35
  - Best outcomes for :
    - Short duration of DM (<5yrs)
    - Insulin independent
    - Young
    - Evidence of adequate beta cell mass (C-peptide > 3 ng/ml)
- Will need better long term data
- Surgery, as compared to standard of care, is a safe and cost-effective treatment modality.

Thank You