

36-year-old woman with DM1 undergoing bariatric surgery

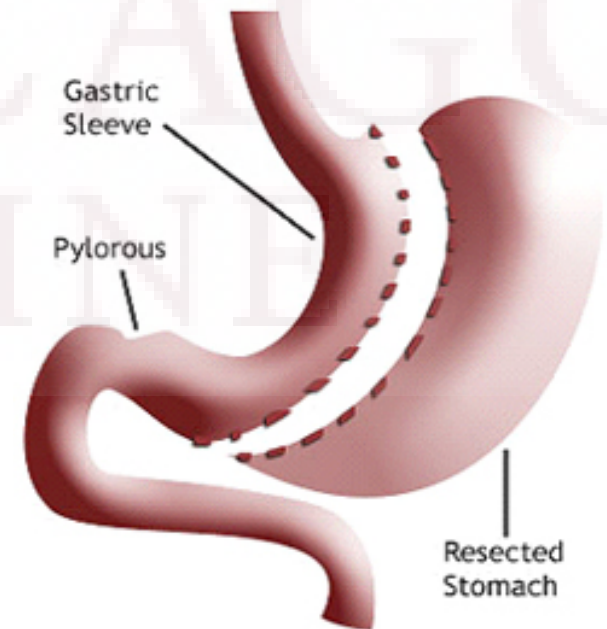
Sharon H. Chou, MD

Endorama

11/21/13

History of Present Illness

- 36 yo female nurse with DM1 x 24 years was admitted for sleeve gastrectomy and laparoscopic cholecystectomy.



Past Medical History

- Diabetes mellitus type 1:

- Insulin pump x 3 months
 - Basal rate: 0.8 units/hr
 - I:C ratio 1:10
 - ISF 50 with goal of 120
- Reports fasting glucose of ~120, before lunch and dinner in the 130s.
- Mild hypoglycemic episodes <1x/wk, usually in the morning since starting the preop diet.
- Peripheral neuropathy symptoms; no known retinopathy; no microalbuminuria.
- Previously tried Bydureon and metformin in the past.

Past Medical History

- Obesity (BMI 36.5)
- Osteoarthritis of both hips
- Obstructive sleep apnea
- Hypothyroidism
- Anxiety/Depression
- Medications:
 - Novolog
 - Levothyroxine 175 mcg daily
 - Paroxetine 20 mg daily
 - Multivitamin
 - Vitamin B complex
 - Calcium and vitamin D supplement

History cont.

- Social history:

- RN here.
- 5 children.
- No tobacco use.

- Family history:

- Daughter with DM1.
- Mother with hypothyroidism.
- 2 sons with ADHD

- Review of Systems:

- Weight loss of 10 lbs on preop diet
- + nausea, no vomiting, abdominal pain controlled
- + peripheral neuropathy
- +anxiety

Physical Exam

- BP 106/58 | Pulse 103 | Temp 96.8 °F (Tympanic) | Resp 16 | Ht 154.9 cm (5' 1") | Wt 87.635 kg (193 lb 3.2 oz) | BMI 36.50 kg/m² | SpO₂ 99%
- Constitutional: Patient appears well-developed, well-nourished, in no acute distress.
- Eyes: Conjunctivae are not injected. Sclerae anicteric. Pupils are equal, round, and reactive to light. Extraocular movements are intact.
- ENT: Mucous membranes moist.
- Neck: Supple. No thyromegaly or nodules palpated.
- Cardiovascular: Regular rhythm and rate. No murmurs appreciated. Intact distal pulses.
- Respiratory/Chest: Normal respiratory effort. No wheezes or crackles.
- Gastrointestinal/Abdomen: + bowel sounds. Soft, diffusely tender, nondistended.
- Musculoskeletal/extremities: No peripheral edema.
- Neurological: Alert and oriented to person, place, and date. Normal deep tendon reflexes.
- Skin: Skin is warm and dry. No acanthosis.
- Psychiatric: Normal mood and affect.

Laboratory Results

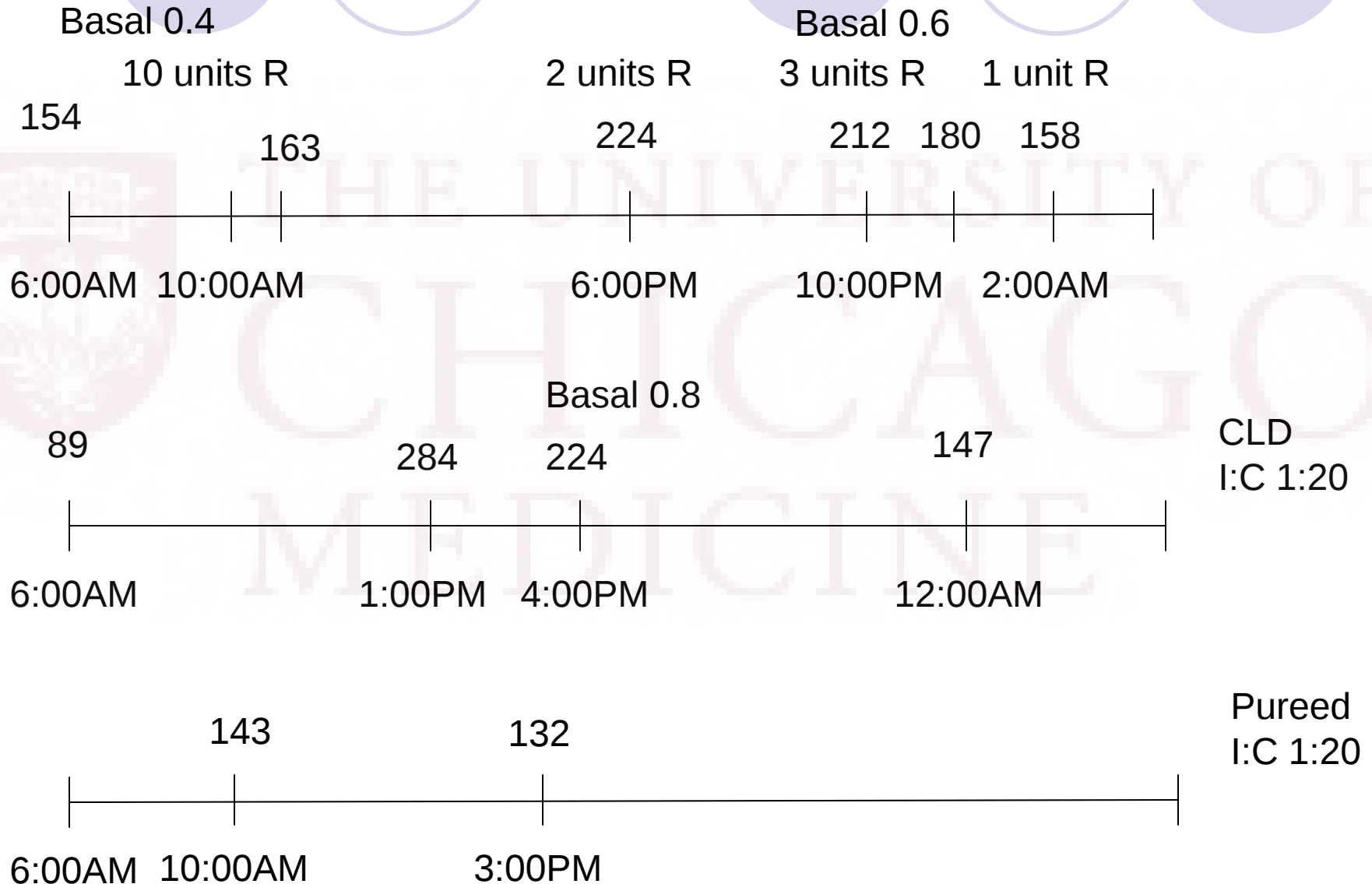
135	100	14	256
4.4	25	0.7	

5.4	13.7	261
	40.0	

Total protein 6.8, Alb
4.3, total bili 0.3, alk
phos 71, AST 13, ALT
11

A1c 8.9%

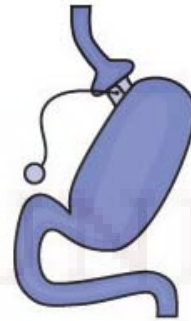
Blood glucose



Questions:

- What are the mechanisms behind the immediate effects of bariatric surgery on type 2 diabetes?
- Is there any suggestion that these immediate effects would apply to type 1 diabetes?

Rates of DM2 Improvement after Bariatric Surgery



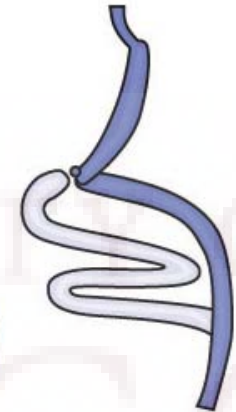
Adjustable
Gastric Band
(AGB)



Roux-en-Y
Gastric Bypass
(RYGB)



Vertical Sleeve
Gastrectomy
(VSG)



Biliopancreatic
Diversion With a
Duodenal Switch
(BPD-DS)

- Restrictive

- AGB: 44%

- VSG: 55%

- Restrictive & Malabsorptive

- RYGB: 83%

- BPD-DS: 94%

Hutter et al. [Ann Surg.](#) 2011 Sep;254(3):410-20.

Vage et al. [Obes Surg.](#) 2013 Jan;23(1):80-6.

Hypotheses for immediate glycemic effects

- Caloric restriction hypothesis

- Fails to explain why improvements in glycemia control occur much faster after RYGB than AGB.

- Malabsorption hypothesis

- Only fat absorption decreased after RYGB and malabsorption accounted for only 6% of the total reduction in energy absorption at 5 months.

Hypotheses for immediate glycemic effects

- Ghrelin hypothesis:
 - Ghrelin is produced by the fundus of the stomach and stimulates appetite/food intake and suppresses glucose-induced insulin secretion.
 - Preprandial ghrelin levels are low after bariatric surgery.
- Hindgut hypothesis:
 - Expedited delivery of nutrients to the lower bowel increases GLP-1 release from intestinal cells.
 - Up to 10-fold increase in area-under-curve value for GLP-1 has been reported 1 week after RYGB.
- Foregut hypothesis:
 - Exclusion of duodenal contact with ingested nutrients has a direct effect (unknown mechanism).

Hypotheses for immediate glycemic effects

- Gut microbiota hypothesis
- Branched-chain amino acids hypothesis

Immediate Effects in Sleeve Gastrectomy

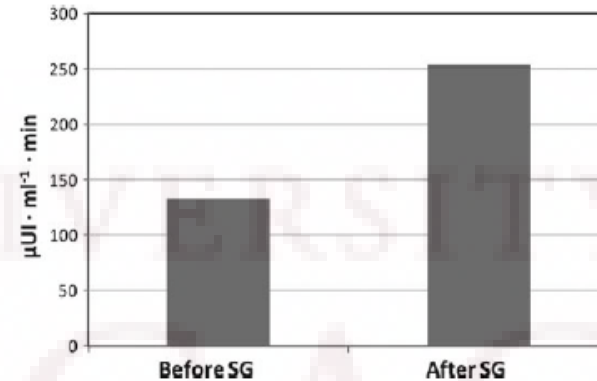
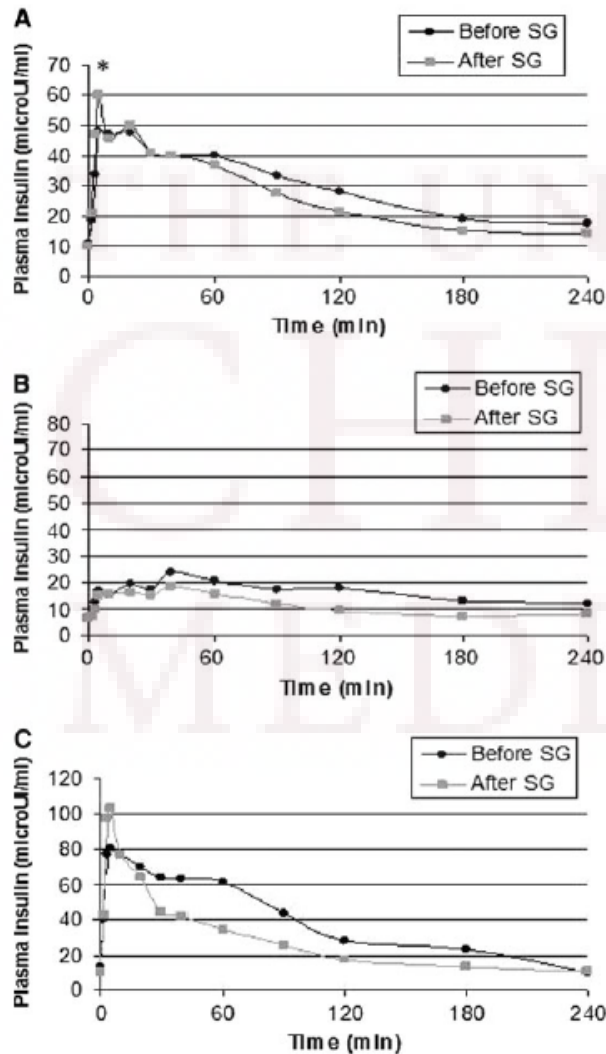


Fig. 3 Early insulin AUC in group A before and after SG; $P = 0.012$

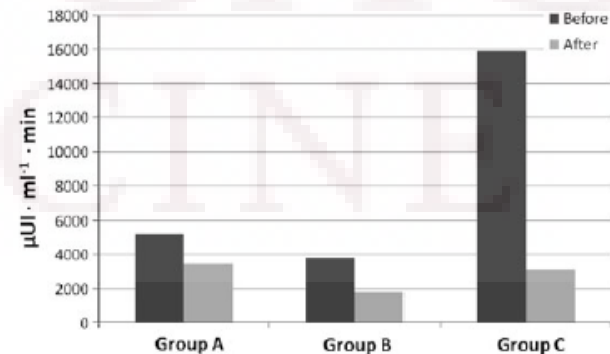
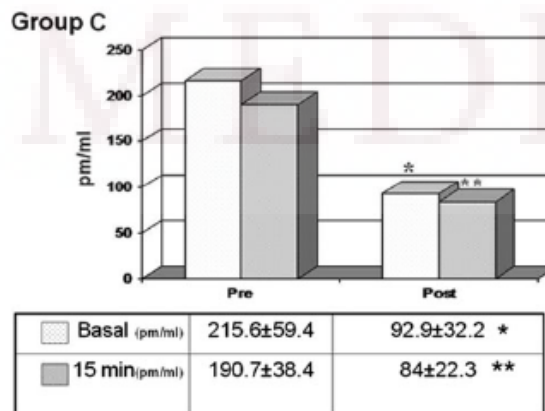
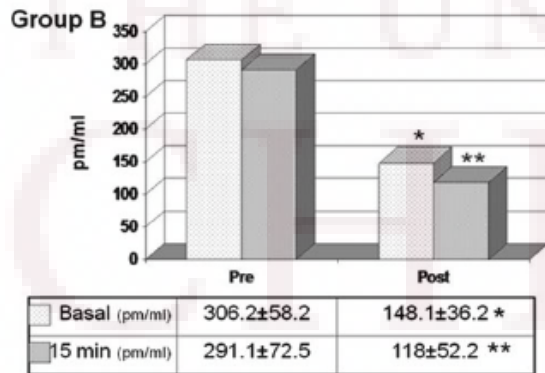
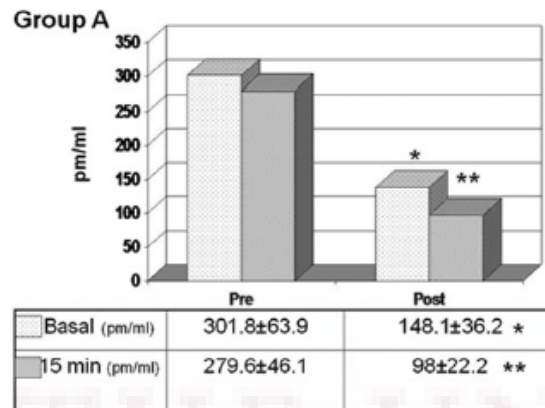


Fig. 4 Late insulin AUC before and after SG in group A ($P = 0.04$), group B ($P = 0.04$), and group C ($P = 0.028$)

Ghrelin



GLP-1

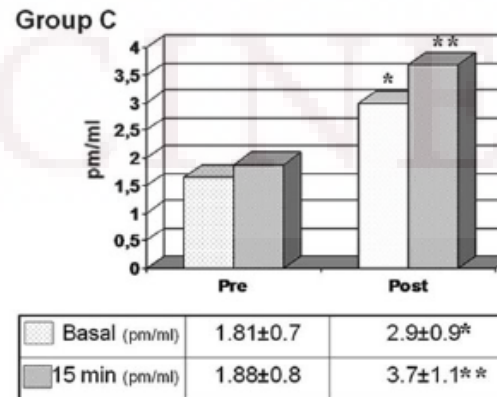
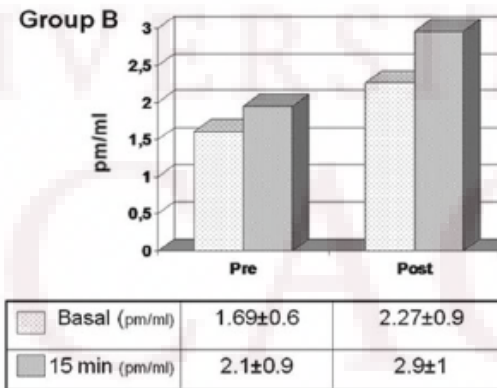
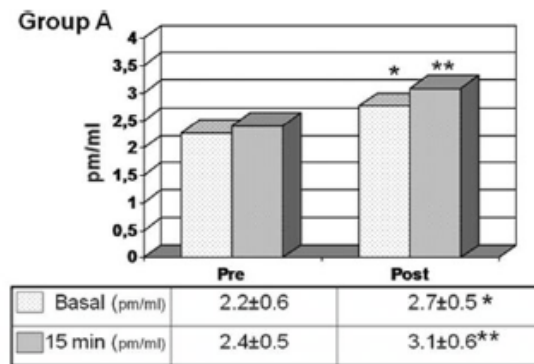


Fig. 6 GLP-1 values in basal conditions and at 15 min. During

Case report for Type 1 Diabetes

Table II

Patient A development of insulin requirements the first days after surgery

<i>Patient A with CSII</i>	<i>Amount of insulin during stay in hospital</i>
1 st day	50% of basal rate (basal rate = 24.2 IU)
2 nd day – surgery in the morning	During surgery CSII was stopped
3 rd day	40% of basal rate (11 am CSII was started again)
4 th day	30-40% basal rate
5 th day	40 % basal rate
6 th day	During the night 40%, during the morning 30% due to more physical activity, in the afternoon 50%

Pt	Years of DM1	Operation	BMI	A1c	Insulin u/kg
Pt A	18	RYGB	43.9	6.7	0.54
33F		4 wks	38.0		0.22
Pt B	19	SG	37.3	7.4	0.72
38F		4 wks	33.3	6.5	0.41

GLP-1 Use in Type 1 Diabetes

- Acute Effects:

- Decreased glucose excursion by 33% during mixed meal test.
- Suppresses glucagon levels.
- Delays gastric emptying.
- Does not change insulin secretion rate.

- Longer Term Effects (4 weeks):

Treatment	C-peptide positive		C-peptide negative		C-peptide negative	
	Liraglutide + insulin		Liraglutide + insulin		Insulin only	
	Week 0	Week 4	Week 0	Week 4	Week 0	Week 4
Insulin dose (units/kg per day)	0.50 ± 0.06	0.31 ± 0.08*	0.72 ± 0.08	0.59 ± 0.06†	0.62 ± 0.04	0.64 ± 0.05 (NS)
Mean blood glucose (mmol/L)	6.0 ± 0.2	6.3 ± 0.3 (NS)	7.5 ± 0.4	7.7 ± 0.4 (NS)	7.5 ± 0.4	7.5 ± 0.6 (NS)
HbA _{1c} (%)	6.6 ± 0.3	6.4 ± 0.2†	7.5 ± 0.2	7.0 ± 0.1†	7.1 ± 0.3	6.9 ± 0.2 (NS)
C-peptide (pmol/L)‡	520 ± 106	457 ± 79 (NS)	—	—	—	—

Follow up

Surgery:

- 2 weeks
 - 202 lbs → 184 lbs
 - Meal size 10% of pre-op
 - Appetite decreased, increased satiety
 - Loose stools
- 2 months
 - 172 lbs
 - Meal size 20% of pre-op
 - Nausea req. Zofran

Endocrine:

- 2.5 months
 - A1c 8.0% (from 8.9%)
 - Frequent hypoglycemia in the last 2 weeks.
 - Decreased basal to 0.6, I:C 1:15.
- 3 months
 - 163 lbs
 - BMI: 30
 - Mild nausea

References

- Allen et al. [Theor Biol Med Model.](#) 2013 Jul 13;10:45.
- Basso et al. [Surg Endosc.](#) 2011 Nov;25(11):3540-50.
- Ghazi et al. [Diabetes Care.](#) 2013 Aug 12.
- Hutter et al. [Ann Surg.](#) 2011 Sep;254(3):410-20.
- Kielgast et al. [Diabetes Care.](#) 2011 Jul;34(7):1463-8.
- Raab et al. [Nutr Hosp.](#) 2013 Mar;28 Suppl 2:31-4.
- Vage et al. [Obes Surg.](#) 2013 Jan;23(1):80-6.

Ghrelin and Type 1 Diabetes

- Use of ghrelin agonists being studied for diabetic gastroparesis
- Shin et al: 10 patients with DM1, avg age of 46, avg BMI 24, avg duration of DM1 of 32 years, avg HgbA1c 9.1%.
 - Faster solid gastric emptying of 34 min.
 - Avg blood glucose at 120 min. were 248 v. 231, NS.

Case series

	Pt	Yrs of DM1	Surgery	BMI	A1c	Insulin IU/kg
Czupryniak et al. 2010	23F	8 yrs	RYGB 8 yrs	38.8 26.6	9.5% 6.9%	0.6 0.53
	28F	23 yrs	RYGB 6 yrs	46.3 39.7	10.4-11.8% 7.5%	0.95 0.83
	19M	4 yrs	RYGB 5 yrs	41.5 30.4	10.5% 6.8%	0.71 0.30
Mendez et al. 2010	29F	8 yrs	RYGB 12 mo	40.6 34.4%	8.2% 7.5%	0.57 0.6
	62F	53 yrs	RYGB 12 mo	43.9 29.8%	7.6% 7.8%	0.47 0.46
	36F	14 yrs	RYGB 12 mo	53.2 42.1%	8.1% 8.8%	1.08 0.5
Raab et al. 2013	38F	19 yrs	SG 12 mo	37.3 25.3	7.4% 7.2%	0.72 0.58
	43F	8 yrs	BPD-DS 12 mo	43 29	9.8% 6.4%	1.13 0.14
	46F	12 yrs	BPD-DS 12 mo	46 28.4	8.7% 5.7%	0.93 0.62
	42F	25 yrs	BPD-DS 12 mo	42 28.6	7.9% 8.5%	1.2 0.32