



HARVARD
MEDICAL SCHOOL

Skeletal Health after Bariatric Surgery

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Financial Disclosures

- Investigator-initiated research grants from Amgen Inc, Seres Therapeutics
- UpToDate, royalties for Osteoporosis screening, Osteoporosis in men
- I have no personal financial relationships with any relevant pharmaceutical companies

Objectives

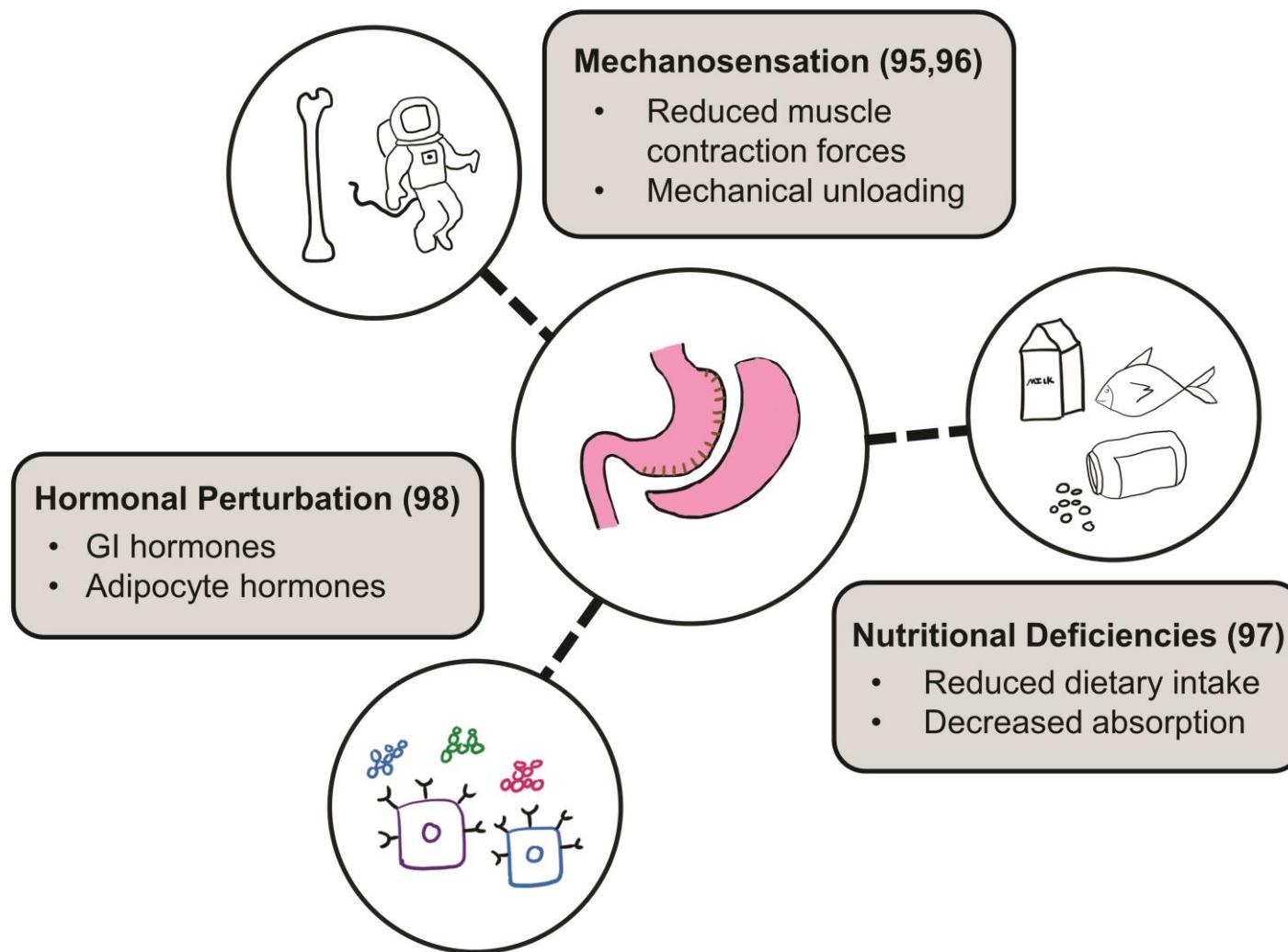
- Describe the variable impact of different bariatric procedures on bone metabolism
- Define fracture risk after bariatric surgery
- Review clinical recommendations for management of skeletal health after bariatric surgery

Case Presentation

- 47 year old postmenopausal woman with right femoral neck fracture s/p fall from standing
 - » Prior Roux-en-Y gastric bypass (RYGB) 7 years ago (lost 130 lbs)
 - » Calcium carbonate 600mg QD + Vitamin D 1000 IU QD
- Labs: normal calcium, 25OHD, PTH
- DXA: T -3.0 at PA spine, T -3.3 at femoral neck

Did her previous RYGB surgery contribute to her current osteoporosis and hip fracture?

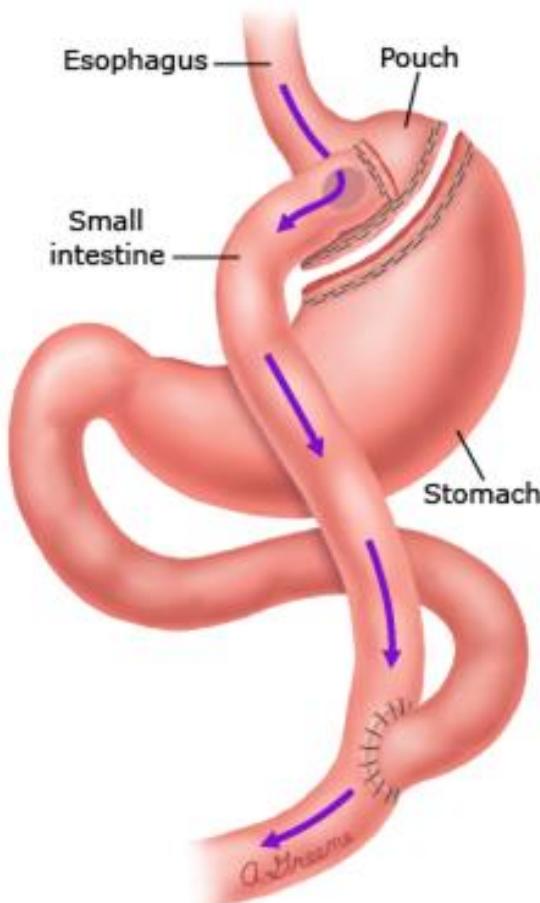
Why might bariatric surgery be bad for bone?



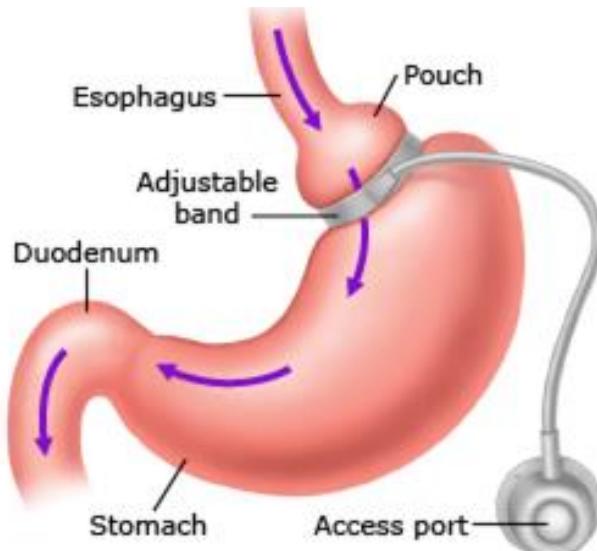
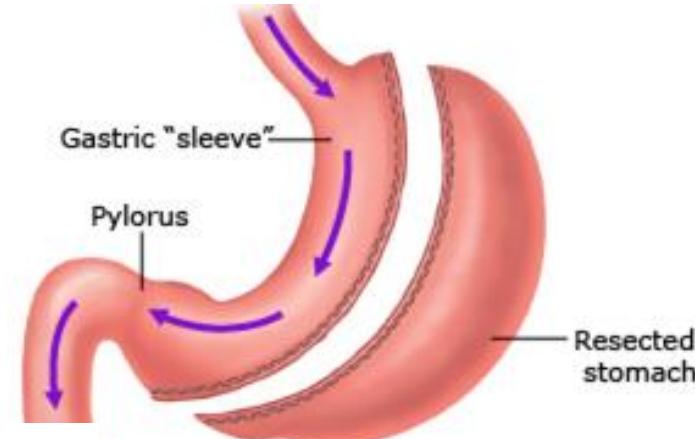
Roux-en-Y gastric bypass (RYGB)

DIFFERENTIAL EFFECTS ON BONE

Sleeve gastrectomy (SG)



Adjustable gastric banding (AGB)

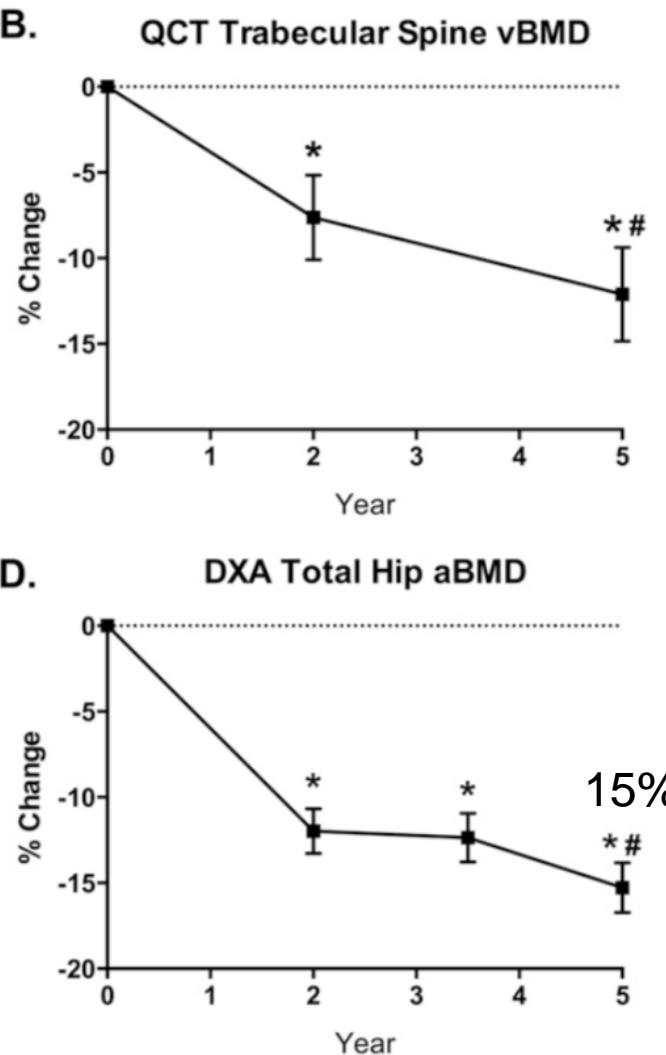
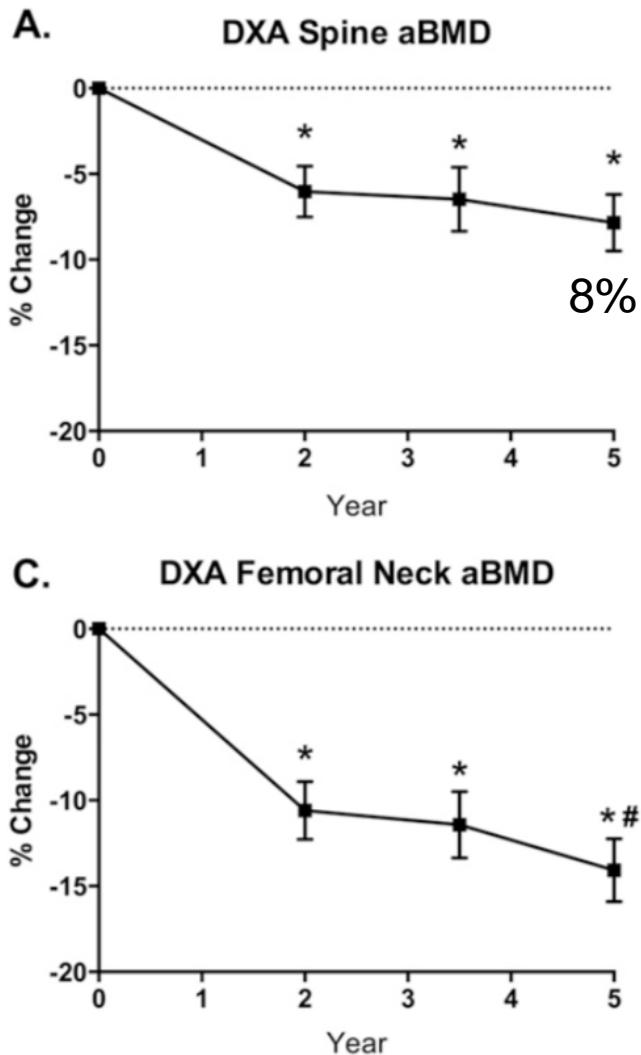


Rapid increase in utilization of bariatric surgery

<1% of eligible patients receive bariatric surgery

BONE DENSITY AND BARIATRIC SURGERY

Bone loss in the 5 years after RYGB

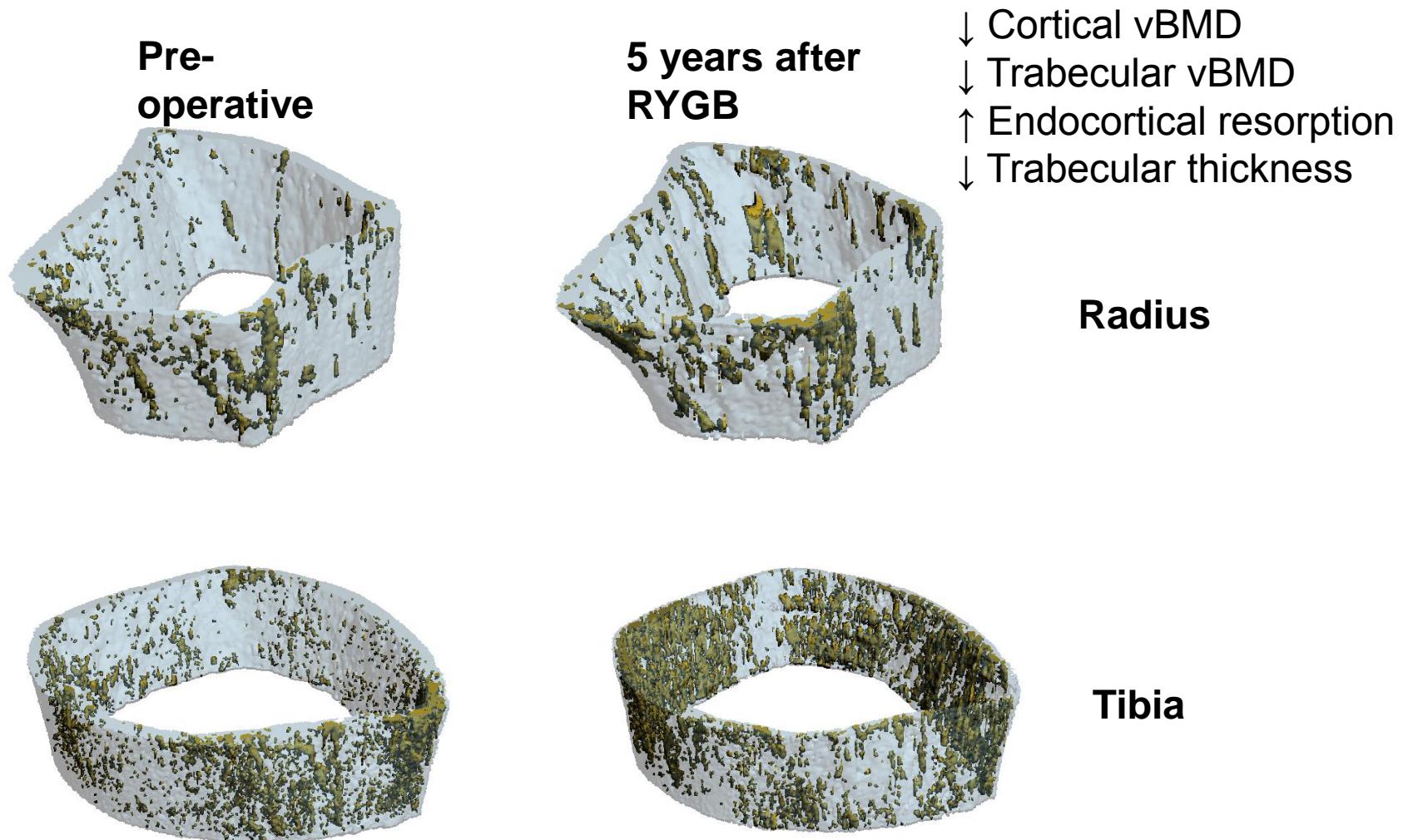


Despite aggressive Ca/D supplementation and stable serum calcium, 25OHD, and PTH

Postmenopausal women may be particularly susceptible to bone loss

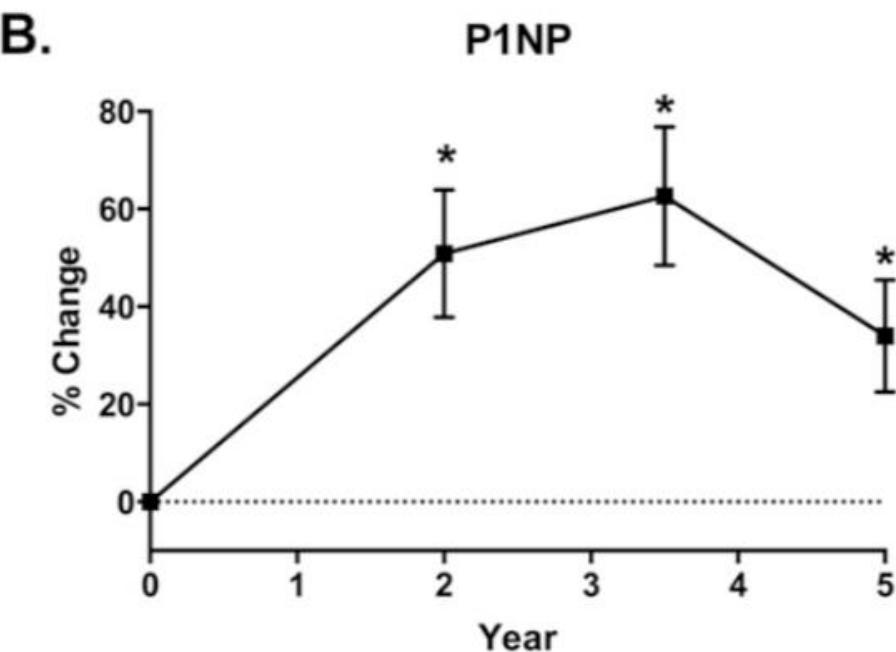
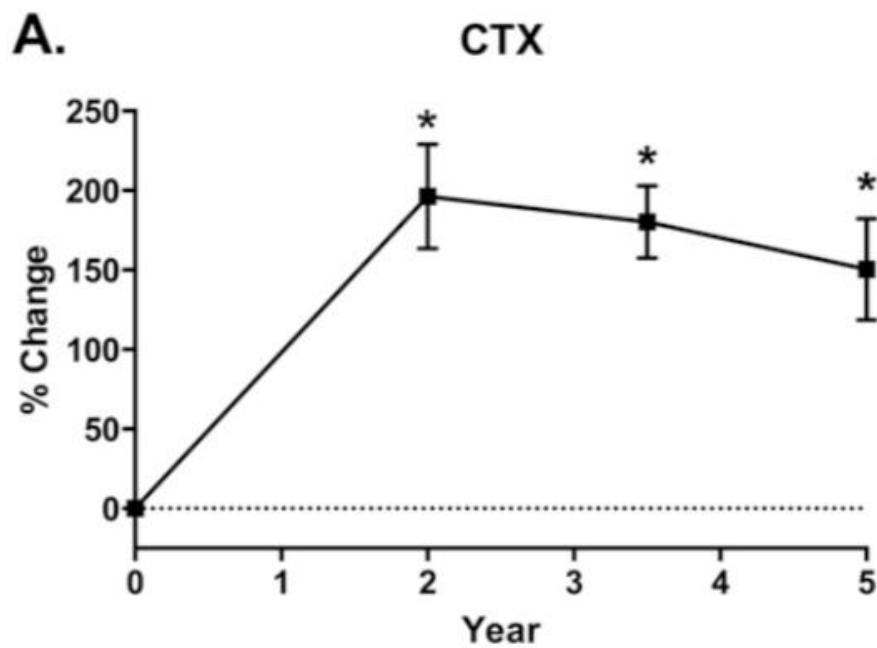
Schafer et al JBMR 2018

Increase in cortical porosity after RYGB

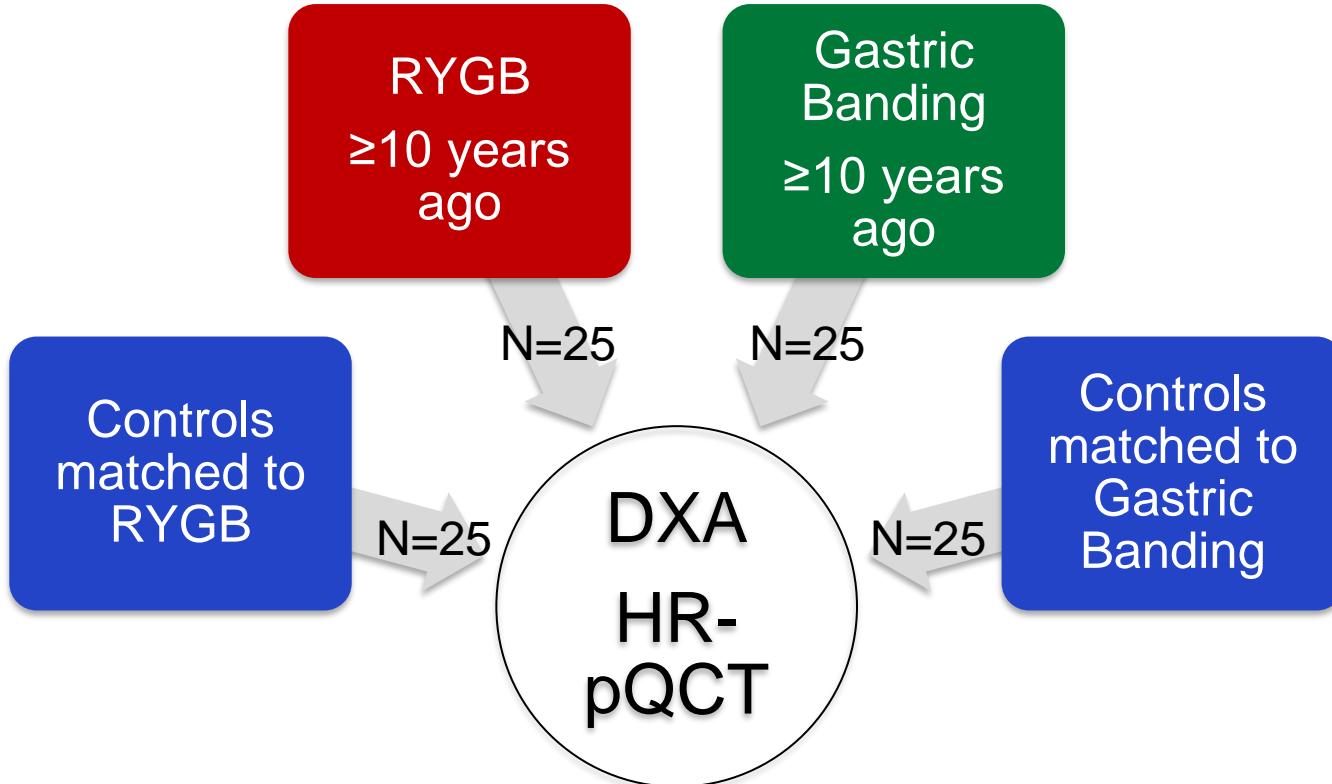


Increase in bone turnover after RYGB

Bone resorption increases within the first week of surgery, even prior to weight loss Yu et al JCEM 2016



Long-term outcomes ≥ 10 years



Matching criteria

BMI $\pm 4 \text{ kg/m}^2$

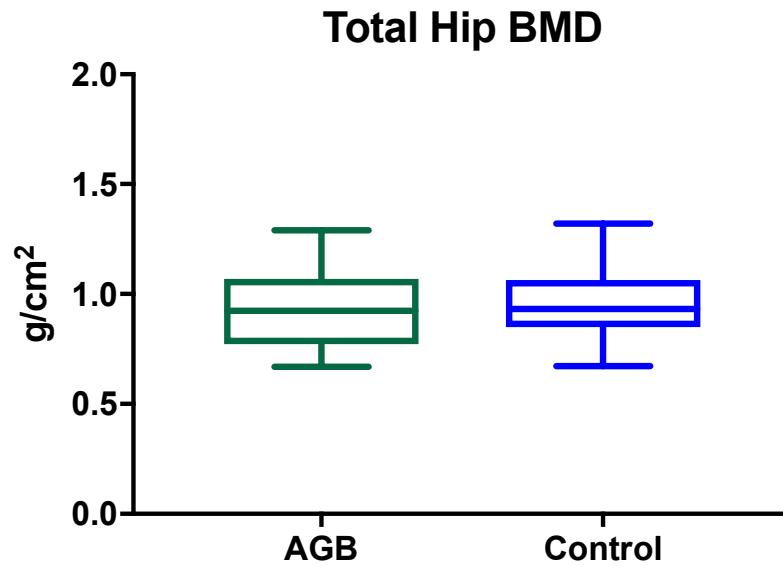
Age ± 5 years

Sex / Menopause status

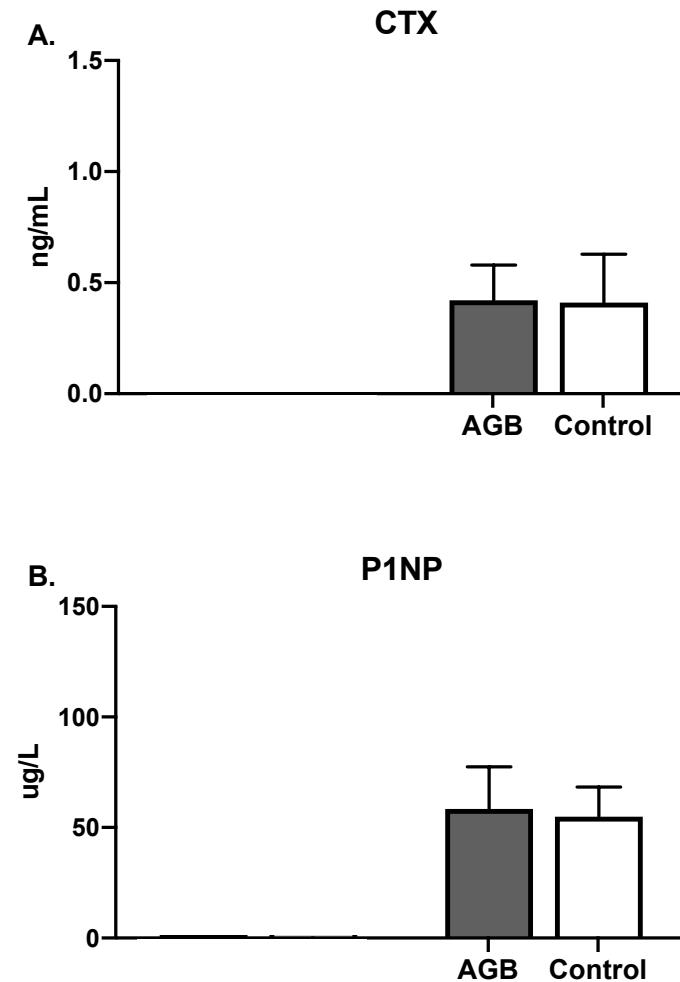
Race / Ethnicity

Is amount of bone loss
physiologically appropriate for
the patient's new lower weight?

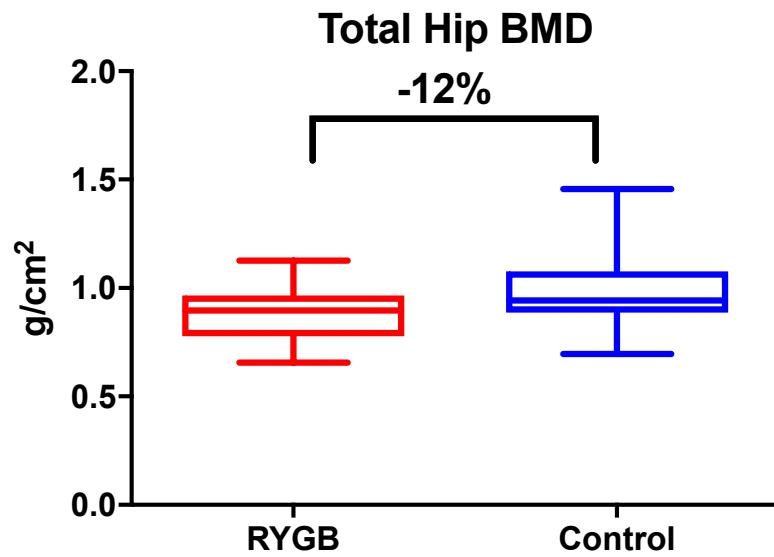
Adjustable Gastric Banding patients have similar hip BMD as matched controls



Similar BMD results at femoral neck and spine



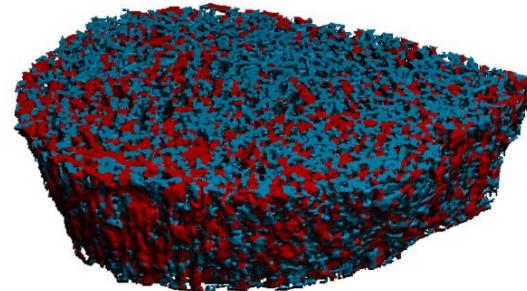
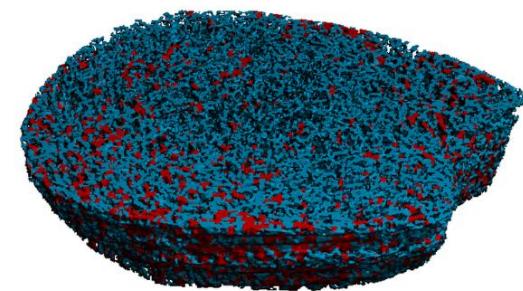
Lower hip BMD and altered microarchitecture in RYGB patients than matched controls



RYGB

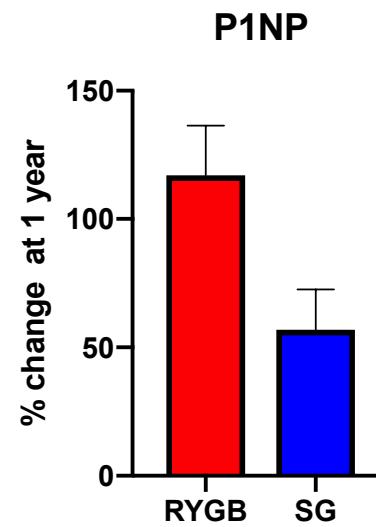
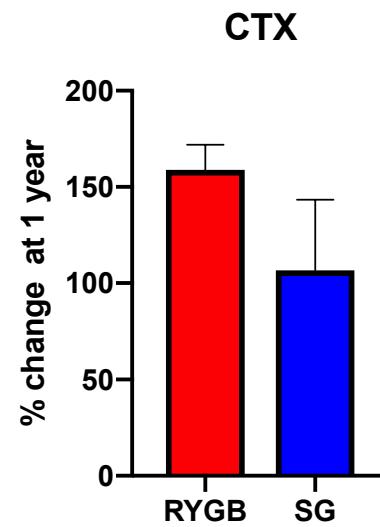
Control

Trabecular Rod
Trabecular Plate



Unlike gastric banding, bone deterioration after RYGB exceeds the physiologic expectations of post-surgical weight

Sleeve gastrectomy (SG) increases bone markers, although less than RYGB

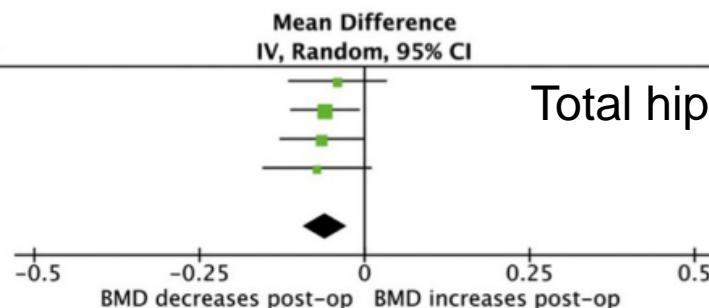


6-12 month
f/u for most
studies

Sleeve Gastrectomy and Bone Density

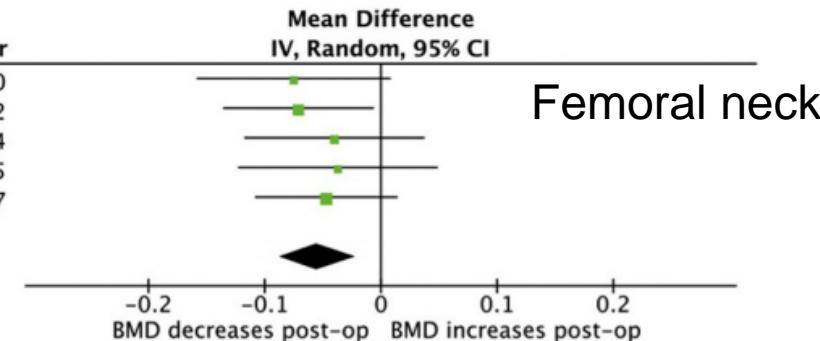
A

Study or Subgroup	Mean Difference IV, Random, 95% CI	Year
Pluskiewicz et al.	-0.04 [-0.12, 0.03]	2012
Hsin et al.	-0.06 [-0.11, -0.01]	2015
Adamczyk et al.	-0.06 [-0.13, -0.00]	2015
Bredella et al.	-0.07 [-0.15, 0.01]	2017
Total (95% CI)	-0.06 [-0.09, -0.03]	
Heterogeneity: $\tau^2 =$		g/cm^2
Test for overall effect:		



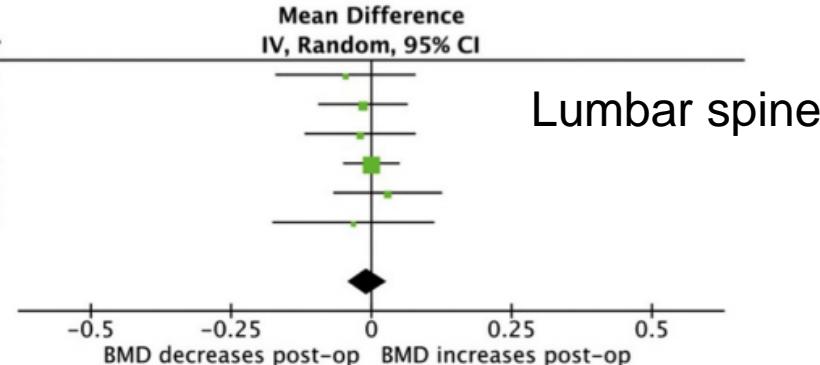
B

Study or Subgroup	Mean Difference IV, Random, 95% CI	Year
Nogues et al.	-0.07 [-0.16, 0.01]	2010
Pluskiewicz et al.	-0.07 [-0.14, -0.01]	2012
Carrasco et al.	-0.04 [-0.12, 0.04]	2014
Adamczyk et al.	-0.04 [-0.12, 0.05]	2015
Bredella et al.	-0.05 [-0.11, 0.01]	2017
Total (95% CI)	-0.05 [-0.09, -0.02]	
Heterogeneity: $\tau^2 =$		g/cm^2
Test for overall effect:		



C

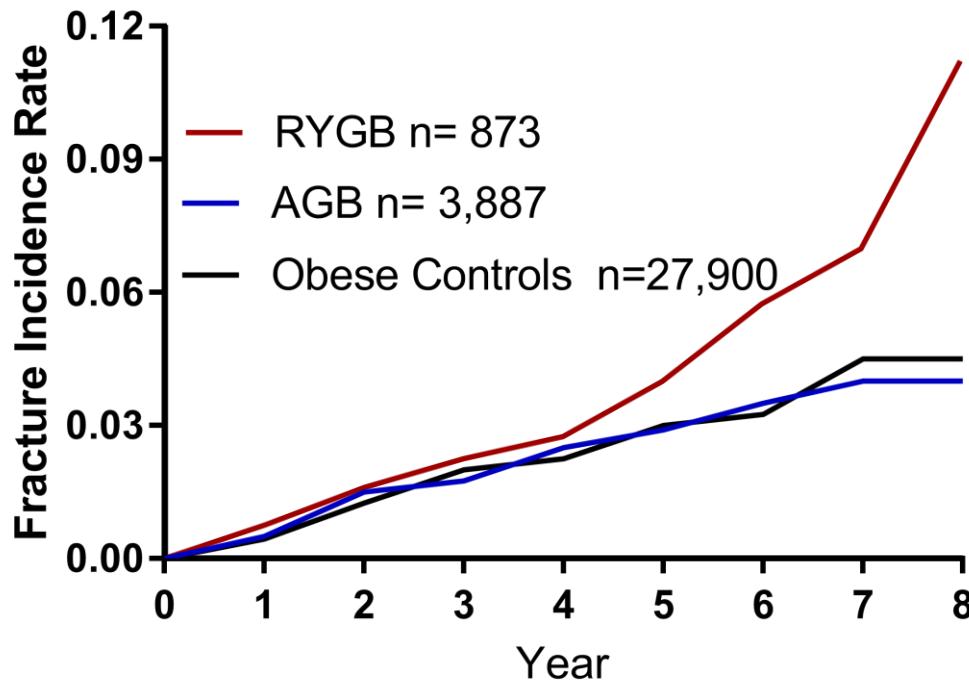
Study or Subgroup	Mean Difference IV, Random, 95% CI	Year
Nogues et al.	-0.05 [-0.17, 0.08]	2010
Pluskiewicz et al.	-0.02 [-0.09, 0.06]	2012
Carrasco et al.	-0.02 [-0.12, 0.08]	2014
Hsin et al.	0.00 [-0.05, 0.05]	2015
Adamczyk et al.	0.03 [-0.07, 0.13]	2015
Bredella et al.	-0.03 [-0.18, 0.11]	2017
Total (95% CI)	-0.01 [-0.04, 0.03]	
Heterogeneity: $\tau^2 =$		g/cm^2
Test for overall effect:		



FRACTURES AND BARIATRIC SURGERY

Canada study

ADJUSTABLE GASTRIC BANDING (AGB) DOES NOT AFFECT FRACTURE RISK

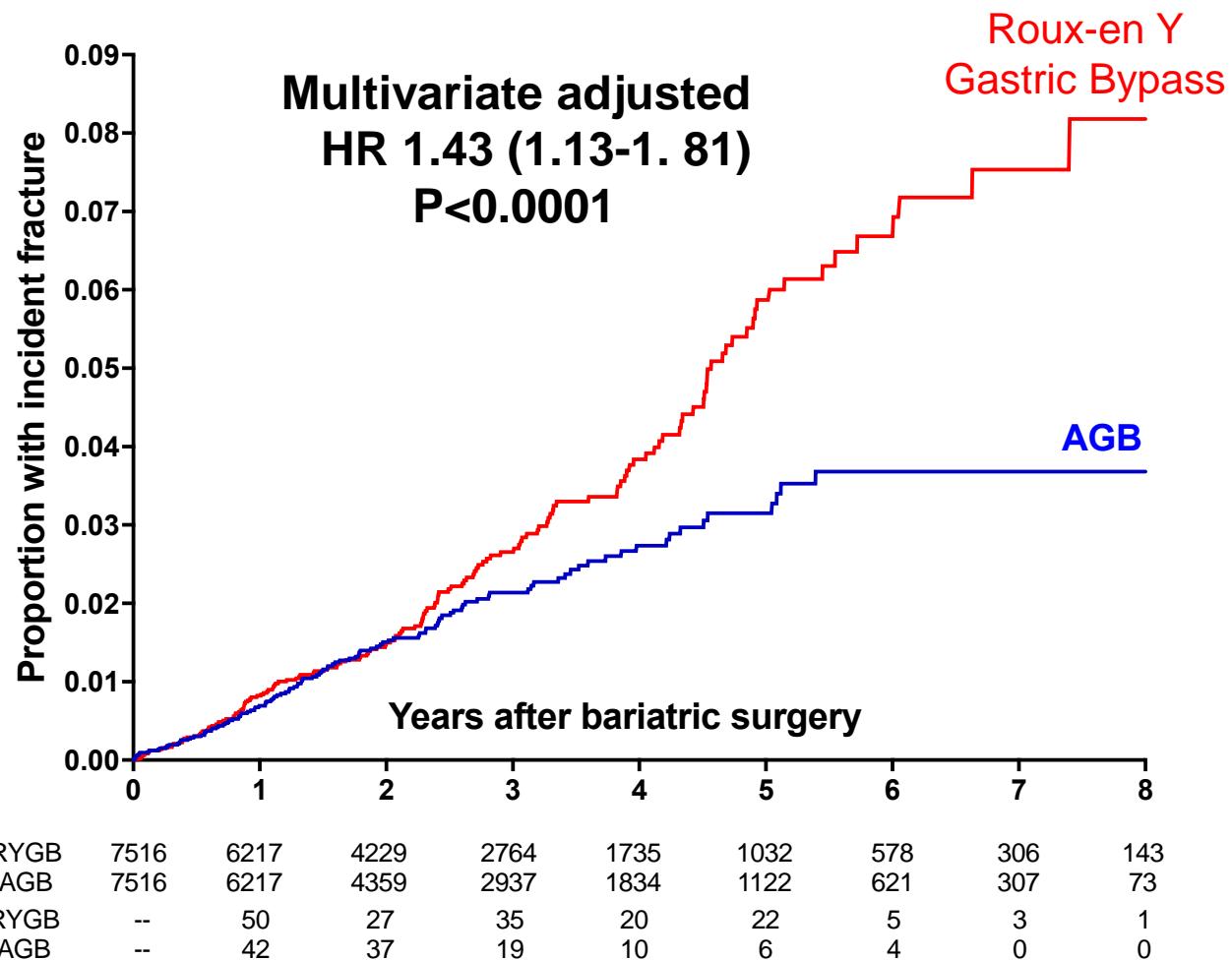


RYGB increases non-vertebral fracture risk

Propensity-score matched cohort
N= 15,032 adults

Administrative claims database

Increase in hip, pelvis, and wrist fractures



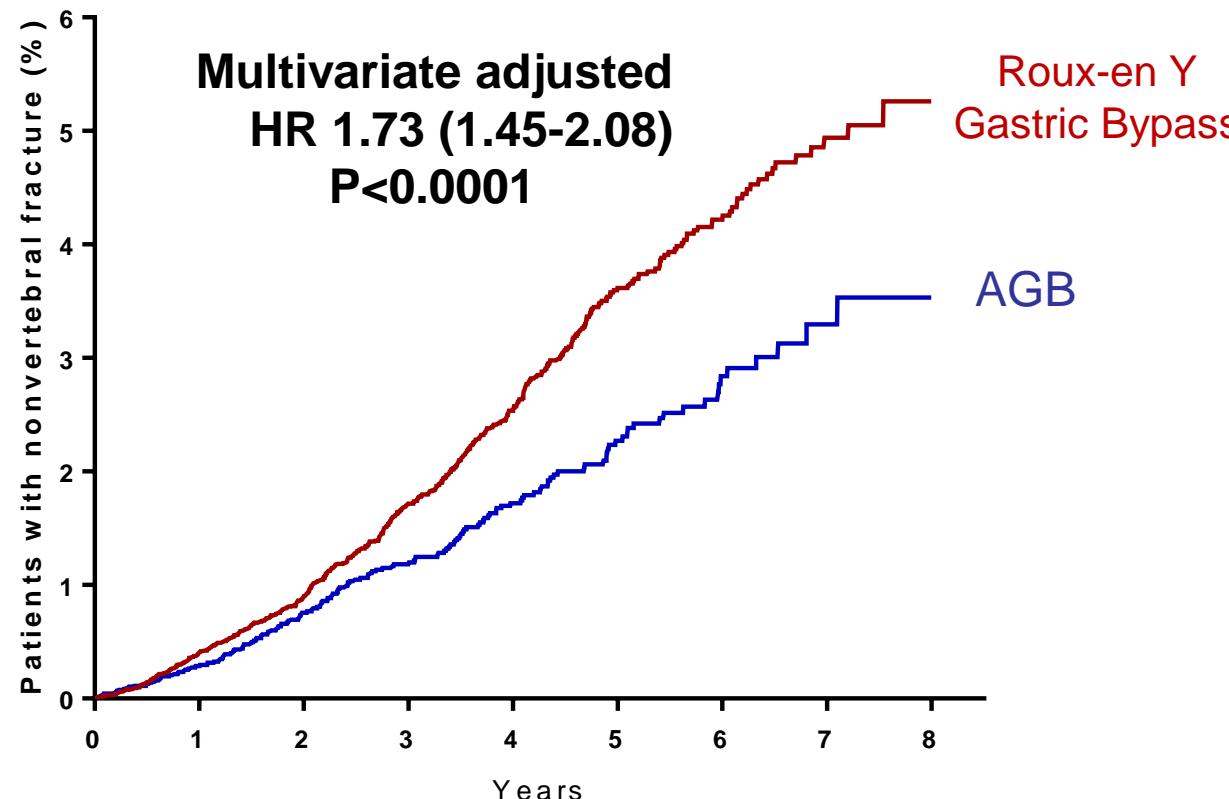
Number at risk	RYGB	7516	6217	4229	2764	1735	1032	578	306	143
Events	RYGB	--	50	27	35	20	22	5	3	1
	AGB	--	42	37	19	10	6	4	0	0

Only 6% of cohort >60y

RYGB increases non-vertebral fracture risk

Medicare Recipients
N=42,345

Fracture site	HR	95% CI
Hip	2.81	1.82-4.49
Pelvis	1.48	1.08-2.07
Wrist	1.70	1.33-2.14



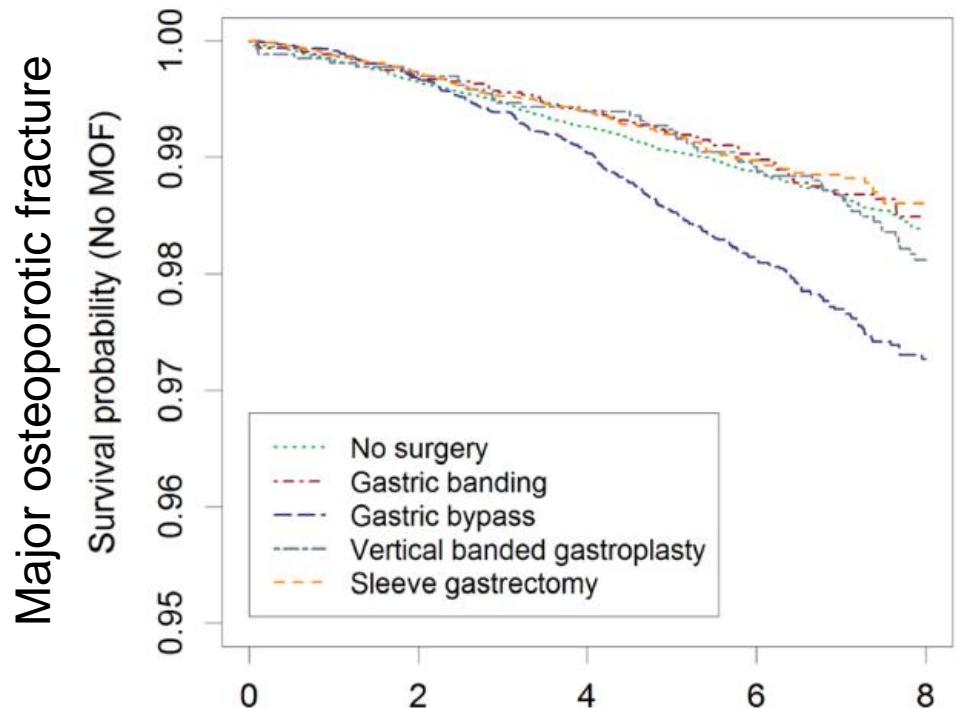
Number at risk:

RYGB	29624	21202	15997	11314	7737	4946	2731	1095
AGB	12721	9859	7985	6003	4300	2680	1371	448

Number of fractures:

RYGB	--	96	92	112	79	71	24	2
AGB	--	31	42	31	28	19	11	4

Sleeve gastrectomy and fracture risk



Sleeve gastrectomy, HR 0.95
Gastric banding, HR 0.95
Obese controls

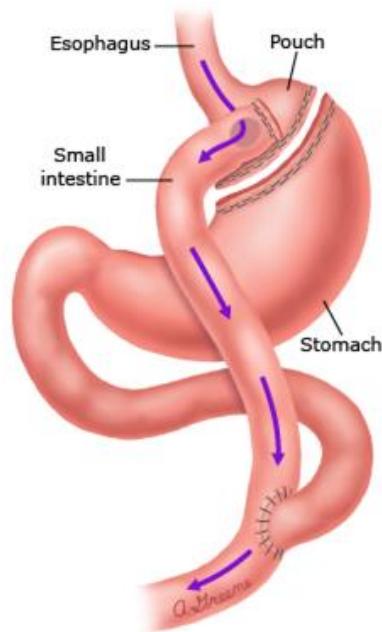
RYGB, HR 1.70 for MOF
HR 2.24 for Hip fx
HR 2.70 for Forearm fx

	Number at risk (number of events)				
No surgery	40992 (0)	35534 (134)	32680 (266)	16757 (365)	0 (416)
Gastric banding	5178 (0)	5153 (16)	5124 (31)	3775 (48)	0 (64)
Gastric bypass	14532 (0)	14439 (49)	14311 (140)	7871 (246)	0 (292)
Vertical banded gastroplasty	2647 (0)	2625 (8)	2606 (16)	2435 (28)	0 (46)
Sleeve gastrectomy	18635 (0)	18535 (52)	18438 (111)	7580 (169)	0 (183)

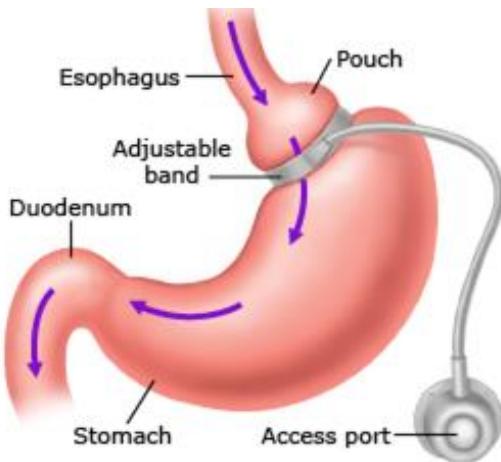


SUMMARY OF BONE OUTCOMES

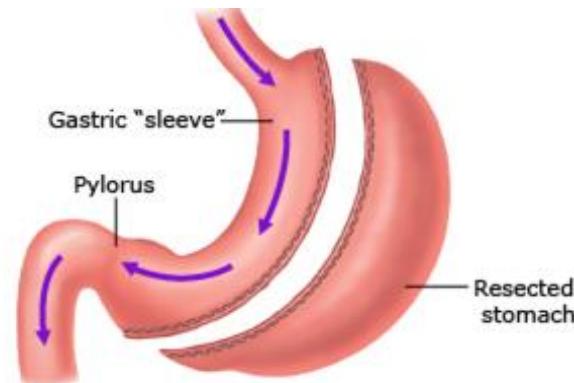
Roux-en-Y Gastric Bypass



Adjustable Gastric Band



Sleeve Gastrectomy



At 2 years post-op

5-7% spine bone loss
7-10% hip bone loss

No spine bone loss
2% hip bone loss

2-3% spine bone loss
5-7% hip bone loss

Fracture risk

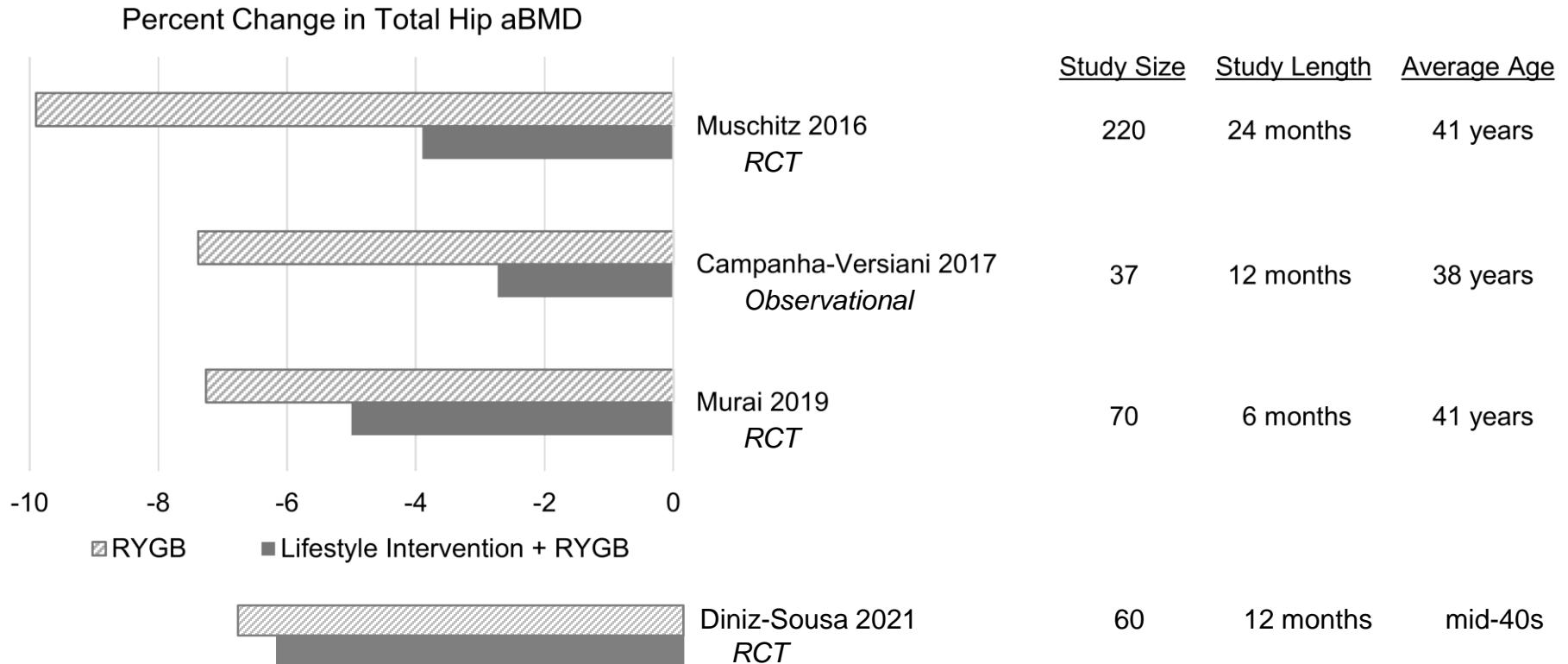
~70% increase any fx
2-fold increase hip fx

No change in fracture risk

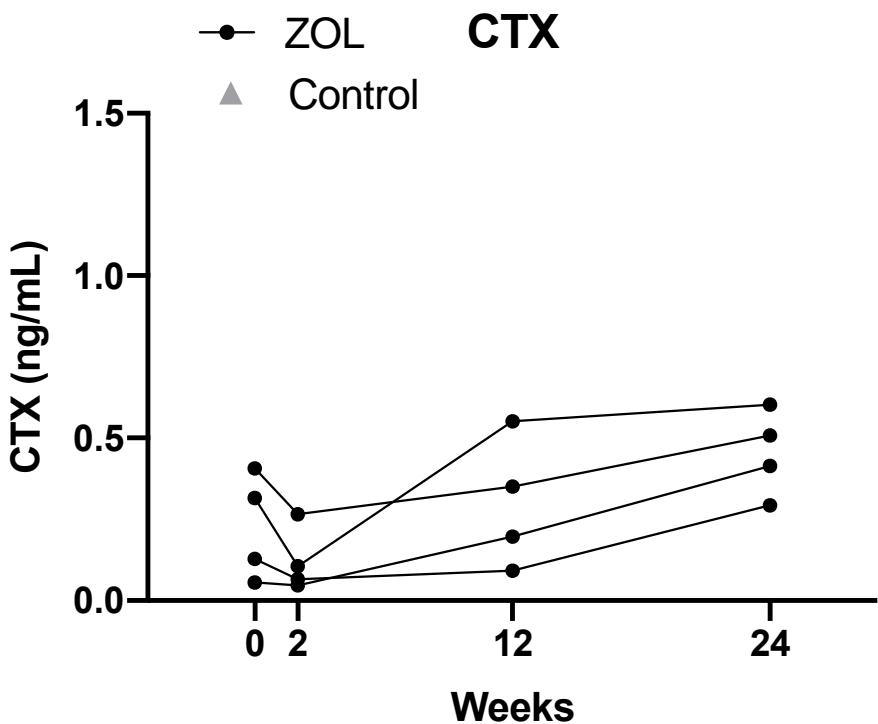
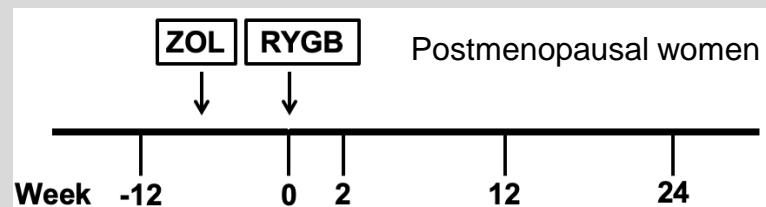
Possibly no change in fracture risk?

PREVENTION OF BONE LOSS AFTER BARIATRIC SURGERY

Exercise can partly prevent RYGB-bone loss



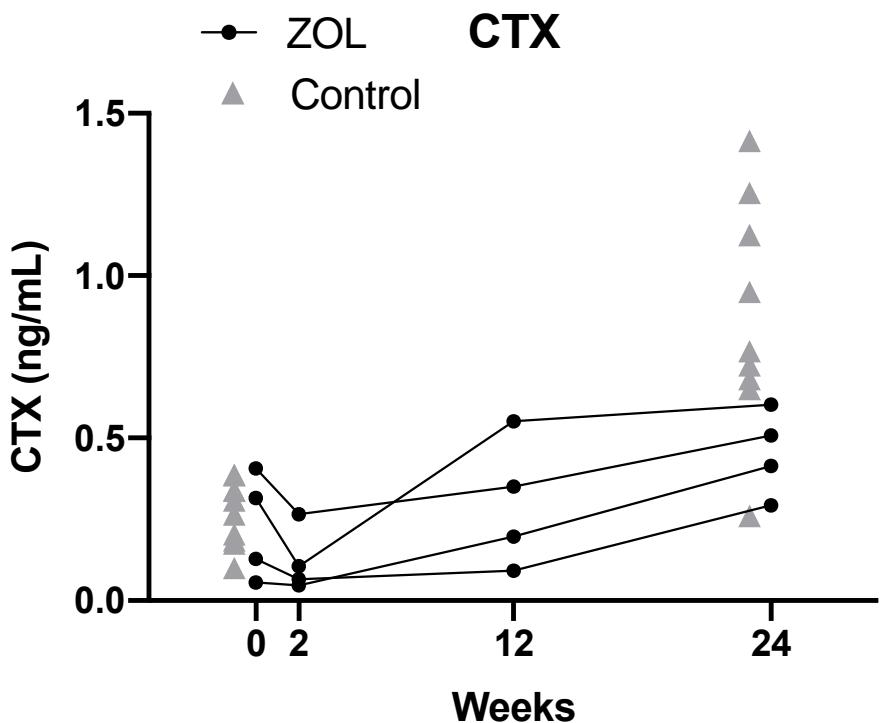
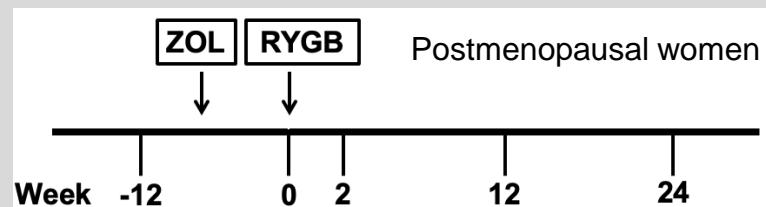
RYGB-Zoledronic acid pilot study



By 24 weeks:

- CTX levels above baseline despite ZOL ($p=0.030$)

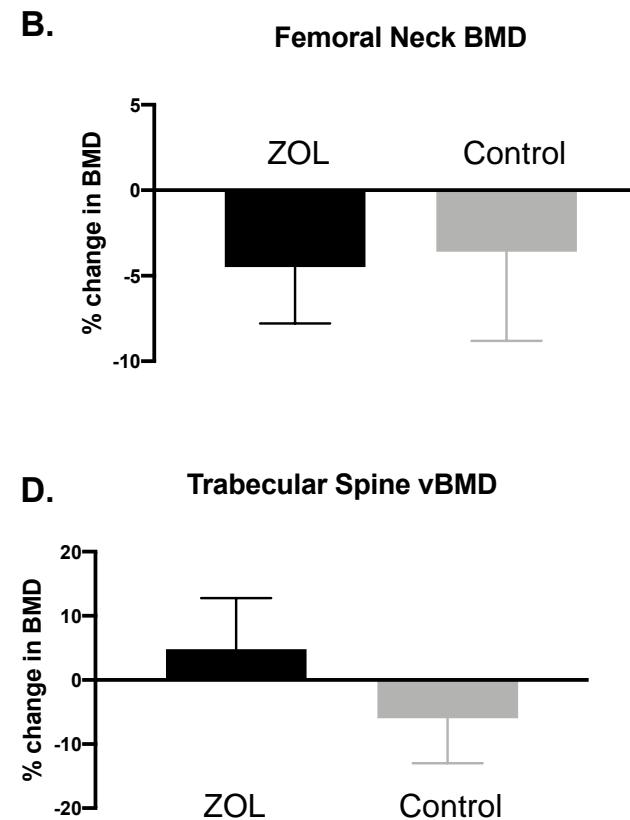
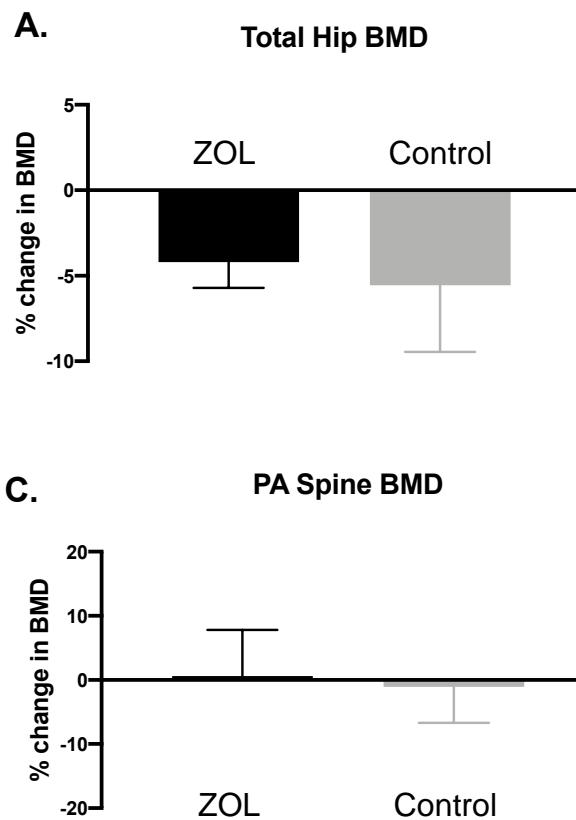
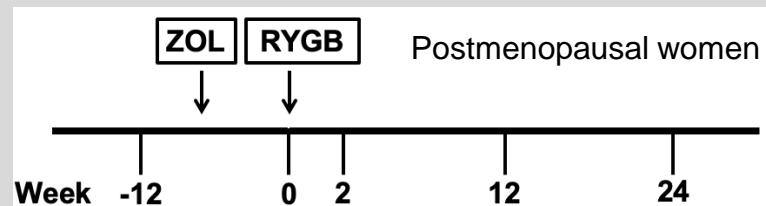
RYGB-Zoledronic acid pilot study



By 24 weeks:

- CTX levels above baseline despite ZOL ($p=0.030$)
- CTX levels in ZOL group lower than untreated controls ($p=0.042$)

RYGB-Zoledronic acid pilot study



ZOL may be insufficient to prevent bone loss after RYGB

Clinical considerations

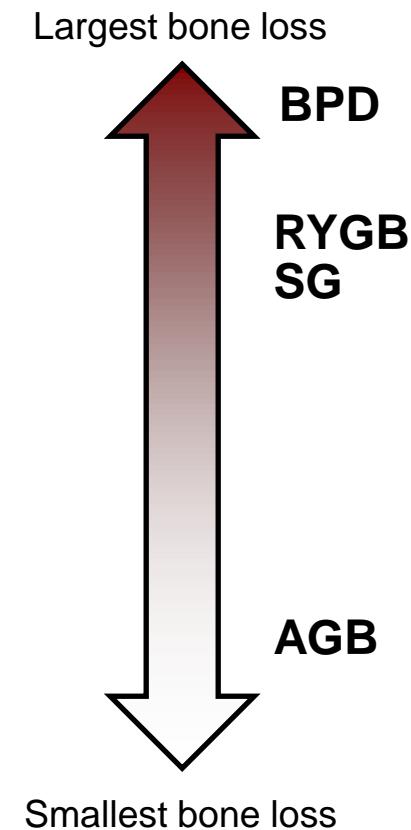
- Management guidelines for bariatric surgery patients
 - » Calcium citrate ~1500mg/day
 - » Vitamin D ~3000 IU/day
 - » Physical activity, maintenance of lean mass
 - » Bone density screening for high-risk patients prior to bariatric surgery, and all patients after bariatric surgery
- Discussion of potential negative skeletal impact for patients
- Additional trials are needed to determine whether osteoporosis medications can prevent bariatric surgery induced bone loss (caution with oral bisphosphonates)

Case Presentation

- 47 year old woman with h/o RYGB with a right femoral neck fragility fracture and osteoporosis by DXA
- Management:
 - » Switched from calcium carbonate to calcium citrate and increased dose to 2000 mg / day
 - » Switched to ergocalciferol 50,000 IU / week
 - » Recommended increased regular weight-bearing exercise
 - » Started zoledronic acid 5 mg IV

Conclusions

- Bariatric surgery is highly effective for treating obesity but has the unintended consequence of accelerated bone loss
 - » Magnitude of effect varies by procedure
- RYGB increases risk of fractures by 40-60%, particularly hip and wrist fractures
 - » DXA screening and therapies should be considered
- Future research is required to evaluate treatment options to minimize high-turnover bone loss



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