Bone Loss After Bariatric Surgery

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Disclosures

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Case presentation

61 y.o. man with obesity, type 2 diabetes

- 423→375 lbs (BMI 54→48 kg/m^2)
- Roux-en-Y gastric bypass surgery
  - ✓ 240 lbs (BMI 31)
  - ✓ Insulin discontinued
- New low back pain

  Why did he fracture?

Overview

- Obesity, weight loss, and bone health
- Skeletal effects of bariatric surgery
  - What happens?
  - Who is at risk?
  - Potential mechanisms
- Implications for clinical practice

Obesity and fracture risk

- High BMI is associated with high bone mineral density (BMD)[1] and protection against fracture[2]
- However, the protective effect of higher BMI may disappear in frank obesity[3]
- Meta-analysis: After adjustment for their higher BMD, obese women fractured *more*[4]

[1]Felson, JBMR 1993; [2]Cummings, N Engl J Med 1995; [3]Compston, Am J Med 2011; [4]Johansson, JBMR 2014

Potential skeletal effects of obesity

Positive	*Negative*
↑ Mechanical loading	↑ Impact with falling
Soft tissue padding	Vitamin D deficiency
↑ Aromatase → Estradiol	Hypogonadism
↑ Leptin (peripheral)[1]	Hyperglycemia
↓ Adiponectin[2]	↑ Inflammation

[1]Cornish, J Endocrinol 2002; [2]Biver, J Clin Endocrinol Metab 2011

Weight loss, BMD, and fracture risk

- Weight loss (even voluntary) is associated with ***loss*** of bone mass and ***increased*** fracture risk
  - Older women: 2-fold higher risk of hip fracture compared to stable weight

Ensrud, Arch Int Med 1997; Ensrud, J Clin Endocrinol Metab 2003

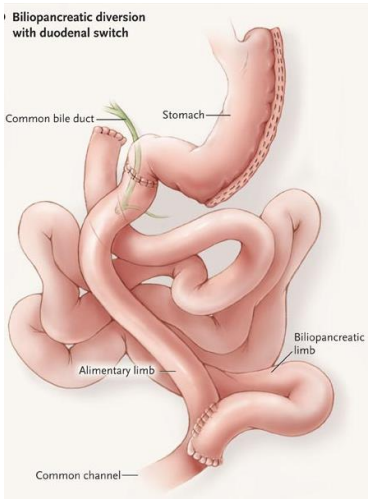
Bone loss during weight loss: Potential mechanisms

- Decreased mechanical loading
- Nutritional factors
  - ↓ vitamin D and Ca intake
  - ↓ Ca absorption[1,2]
- Change in adipokines
  - ↓ estradiol
  - ↑ adiponectin
- Loss of muscle mass
- Marrow fat changes

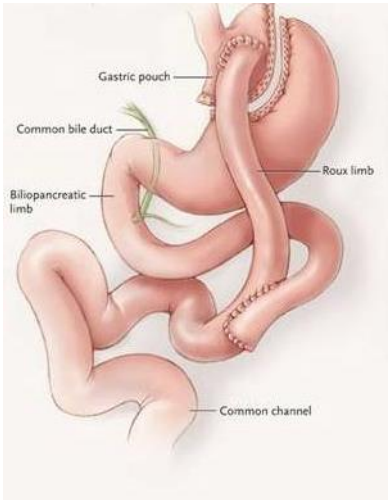
[1]Cifuentes, Am J Clin Nutr 2004; [2]Shapses, Am J Clin Nutr 2013

Growing demand for bariatric surgery

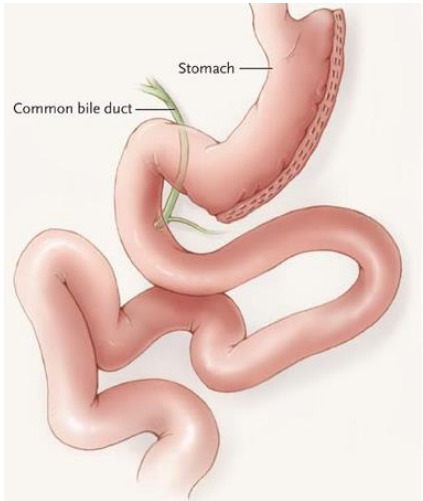
- US: 42% obese, 9% with BMI ≥40 kg/m^2 [1]
- Marked and durable weight loss[2]
- Comorbidities improve, mortality rates decline[2-3]



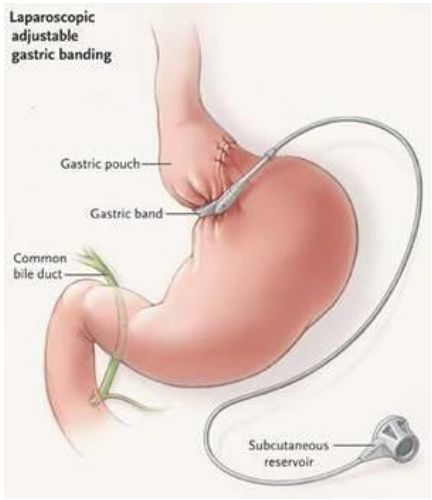
Biliopancreatic diversion w/ duodenal switch



Roux-en-Y gastric bypass



Sleeve gastrectomy



Adjustable gastric band

[1]NCHS 2020; [2]Sjostrom, NEJM 2007; [3]Arterburn, JAMA 2015

Bone loss during weight loss: Potential mechanisms

DRAMATIC! RAPID!

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- Nutritional factors **+ MALABSORPTION**
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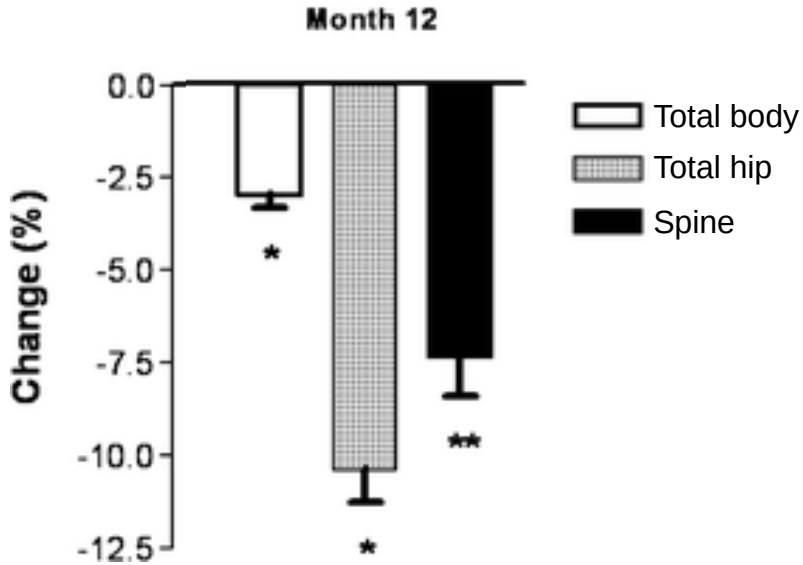
+ SURGERY-INDUCED NEUROHORMONAL EFFECTS

Δ GUT MICROBES

[1]Cifuentes, Am J Clin Nutr 2004; [2]Shapses, Am J Clin Nutr 2013

Early studies: bariatric surgery negatively affects the skeleton

- Increases in bone turnover
- Decreases in BMD[1-3]



[1]Coates, J Clin Endocrinol Metab 2004; [2]Fleischer, J Clin Endocrinol Metab 2008; [3]Carrasco, Obes Surg 2009

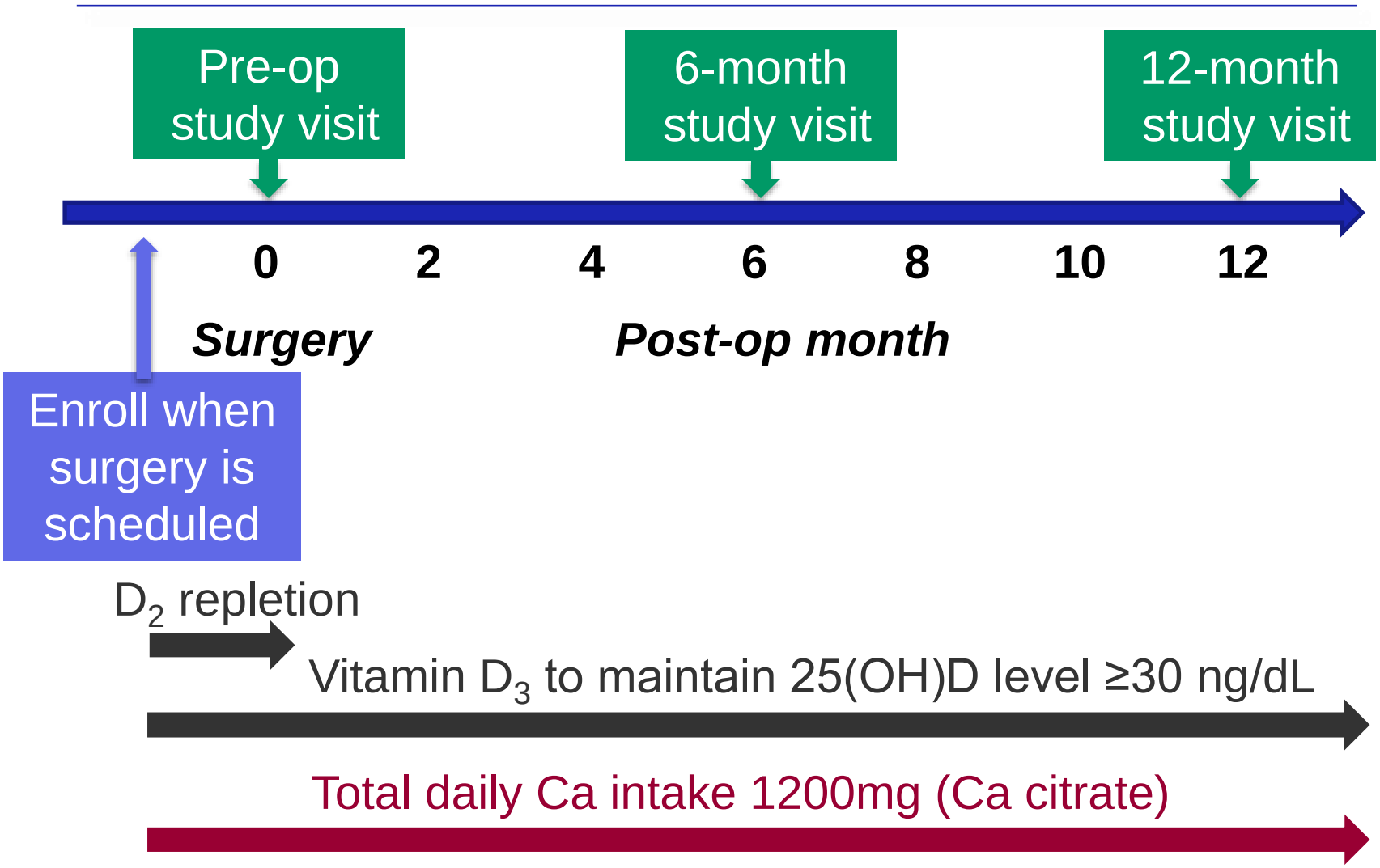
Concern for early fracture-related morbidity and mortality among bariatric surgery patients

What skeletal changes occur?
Who is at risk?
Why?

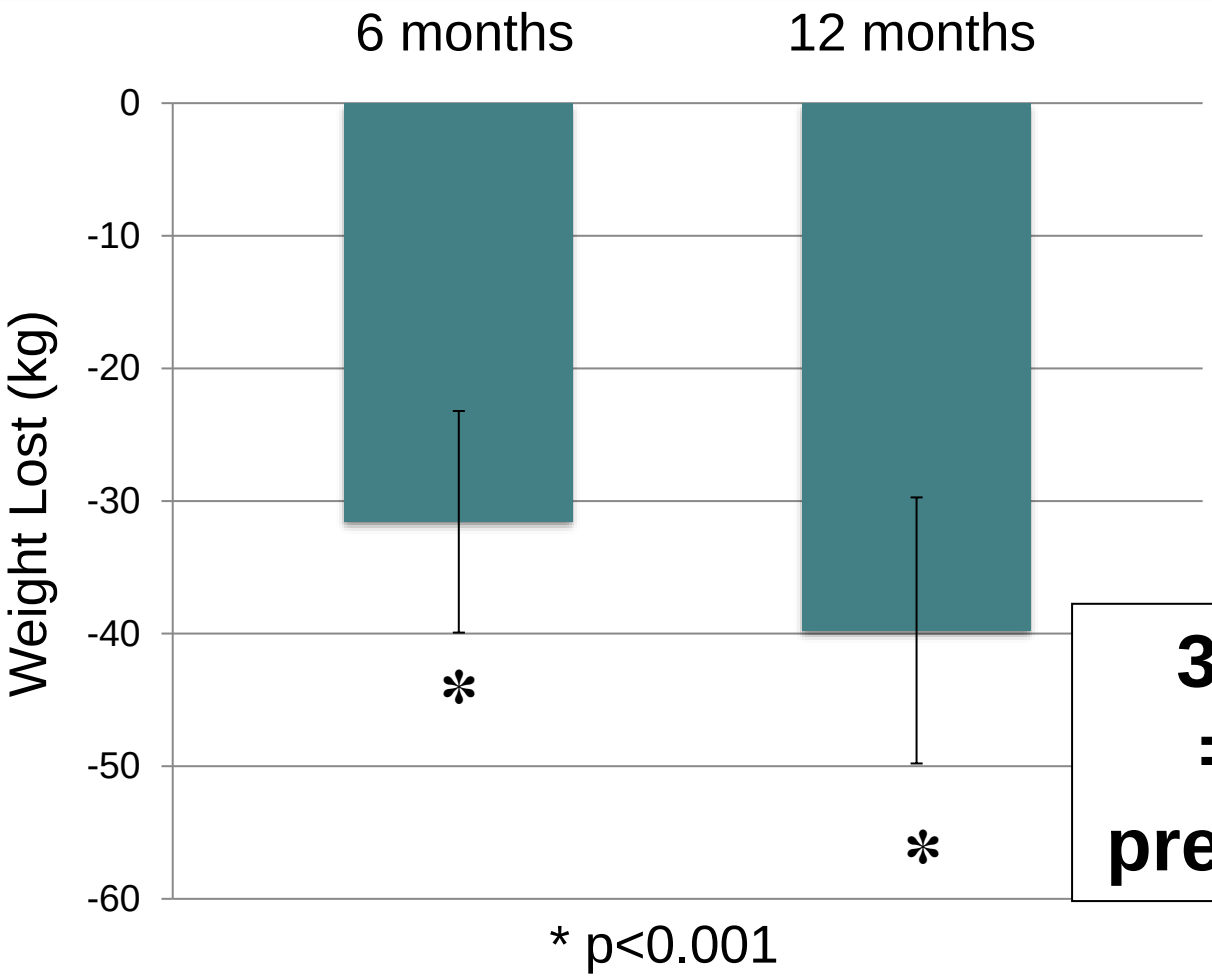
Gastric bypass cohort design

- Prospective, pre-post cohort (N=54)
- Obese men and women scheduled for gastric bypass
- University and VA hospitals

Study schema



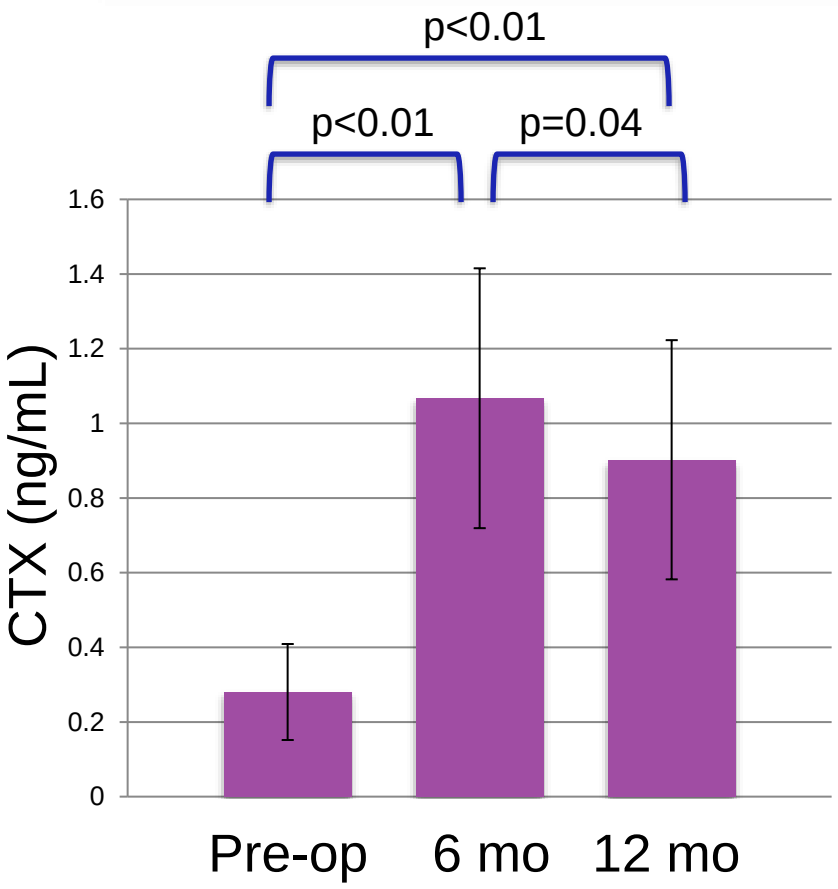
Weight loss is dramatic

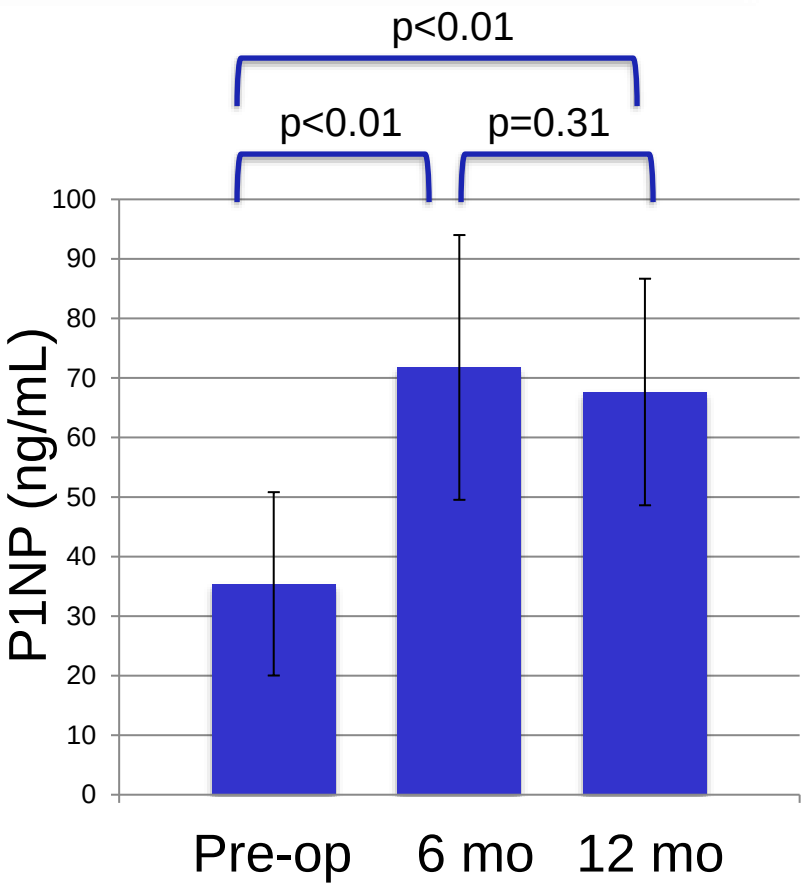


39 ± 8 kg = 32% of pre-op weight

Schafer, JBMR 2018

Bone turnover increases early



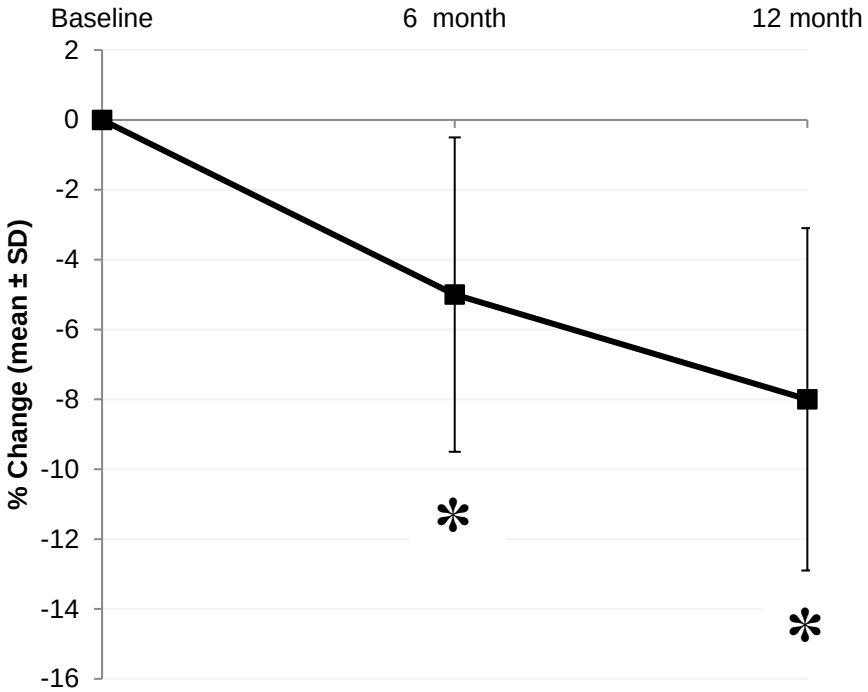


Mean ±1 SD

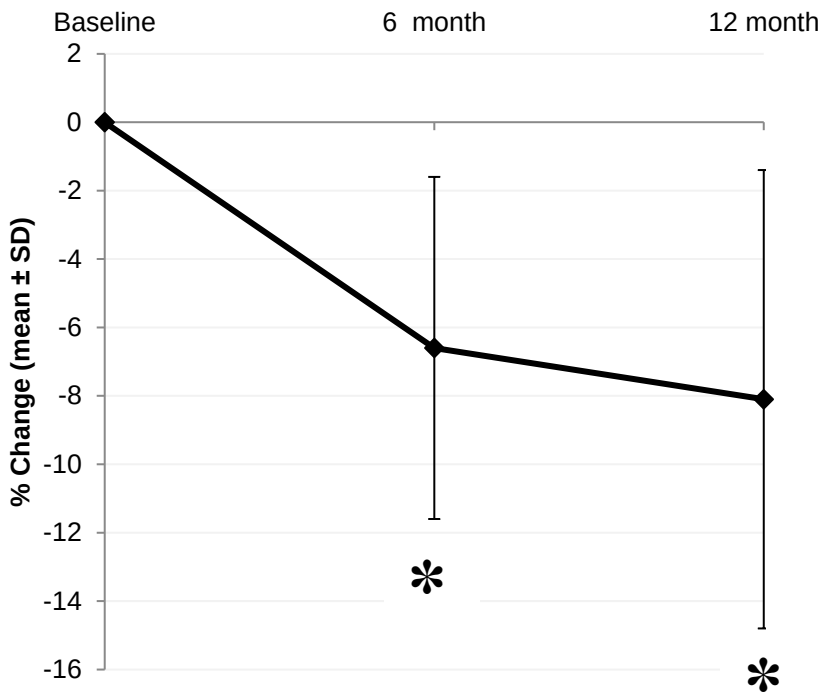
Schafer, JBMR 2018

BMD decreases substantially by both DXA and QCT

Femoral neck aBMD (DXA)



Spine vBMD (QCT)



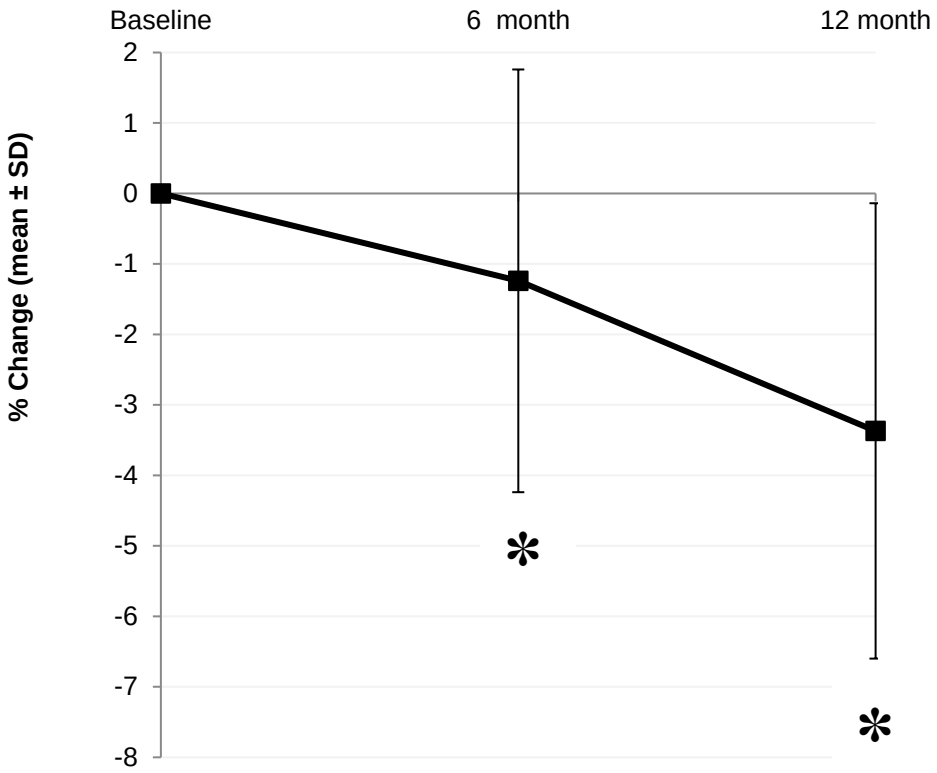
* p<0.05

Mean ±1 SD

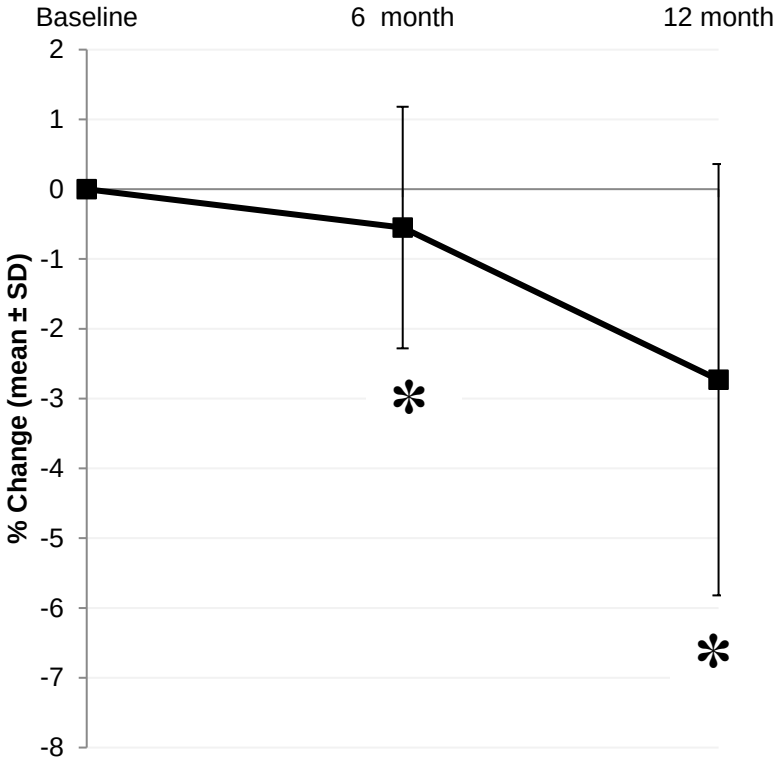
Schafer, JBMR 2018

BMD declines at non-weight-bearing radius and weight-bearing tibia

Radius total vBMD (HR-pQCT)



Tibia total vBMD (HR-pQCT)

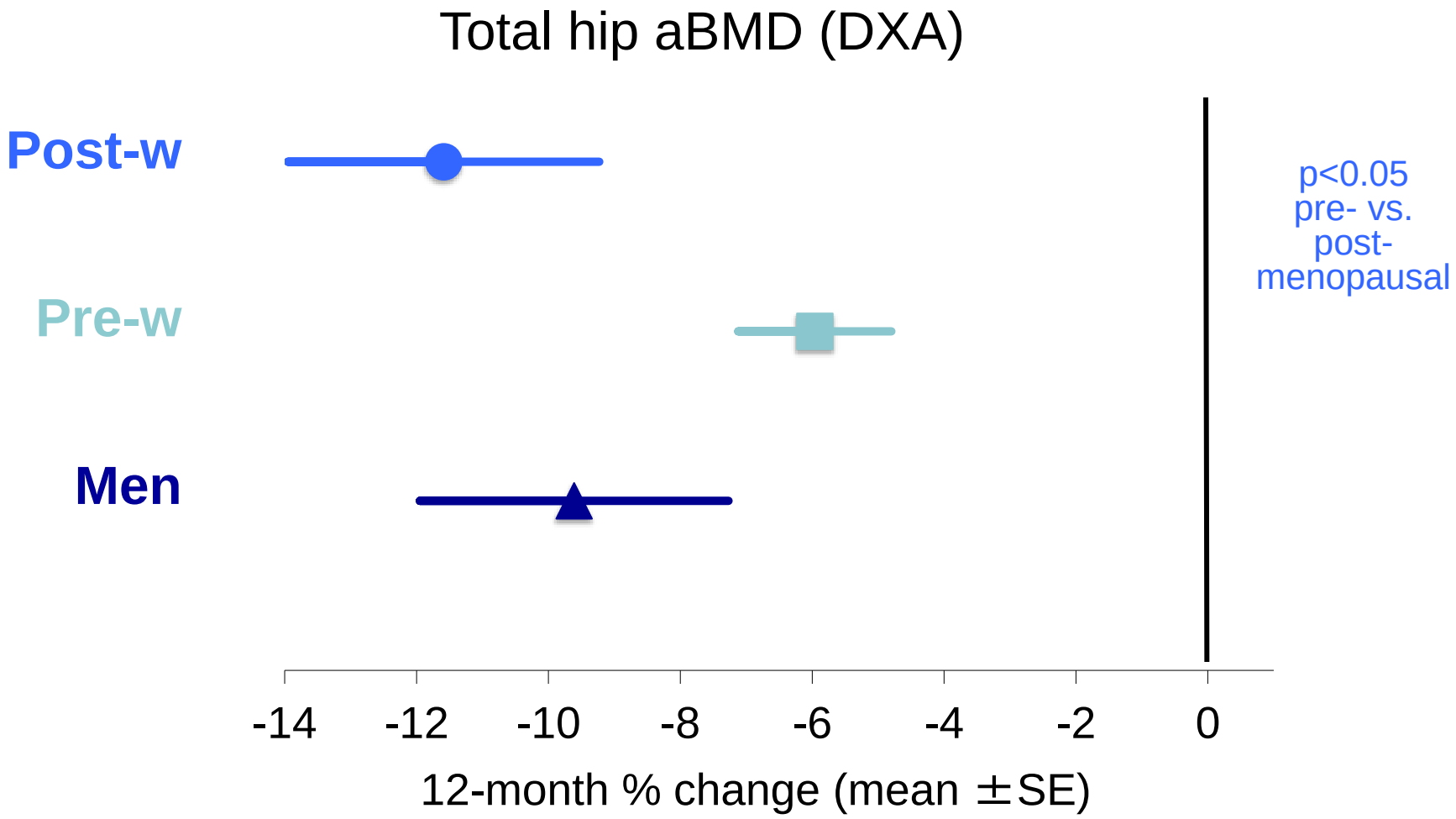


* p<0.05

Mean ±1 SD

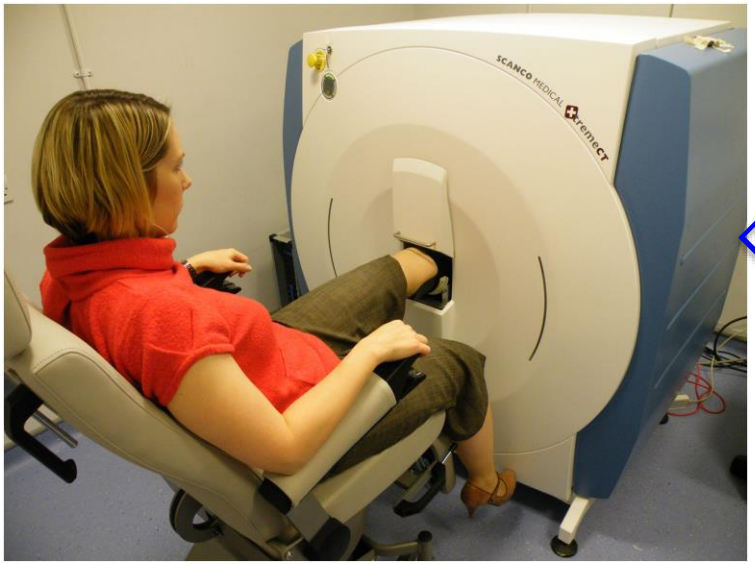
Schafer, JBMR 2018

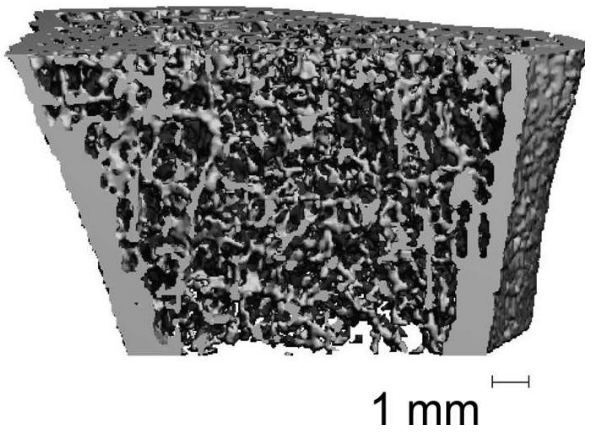
Postmenopausal women experience worst BMD declines

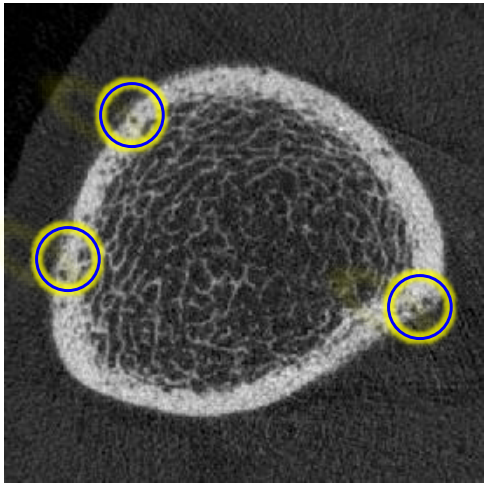


Schafer, JBMR 2018

Detrimental effects on bone microstructure and estimated strength

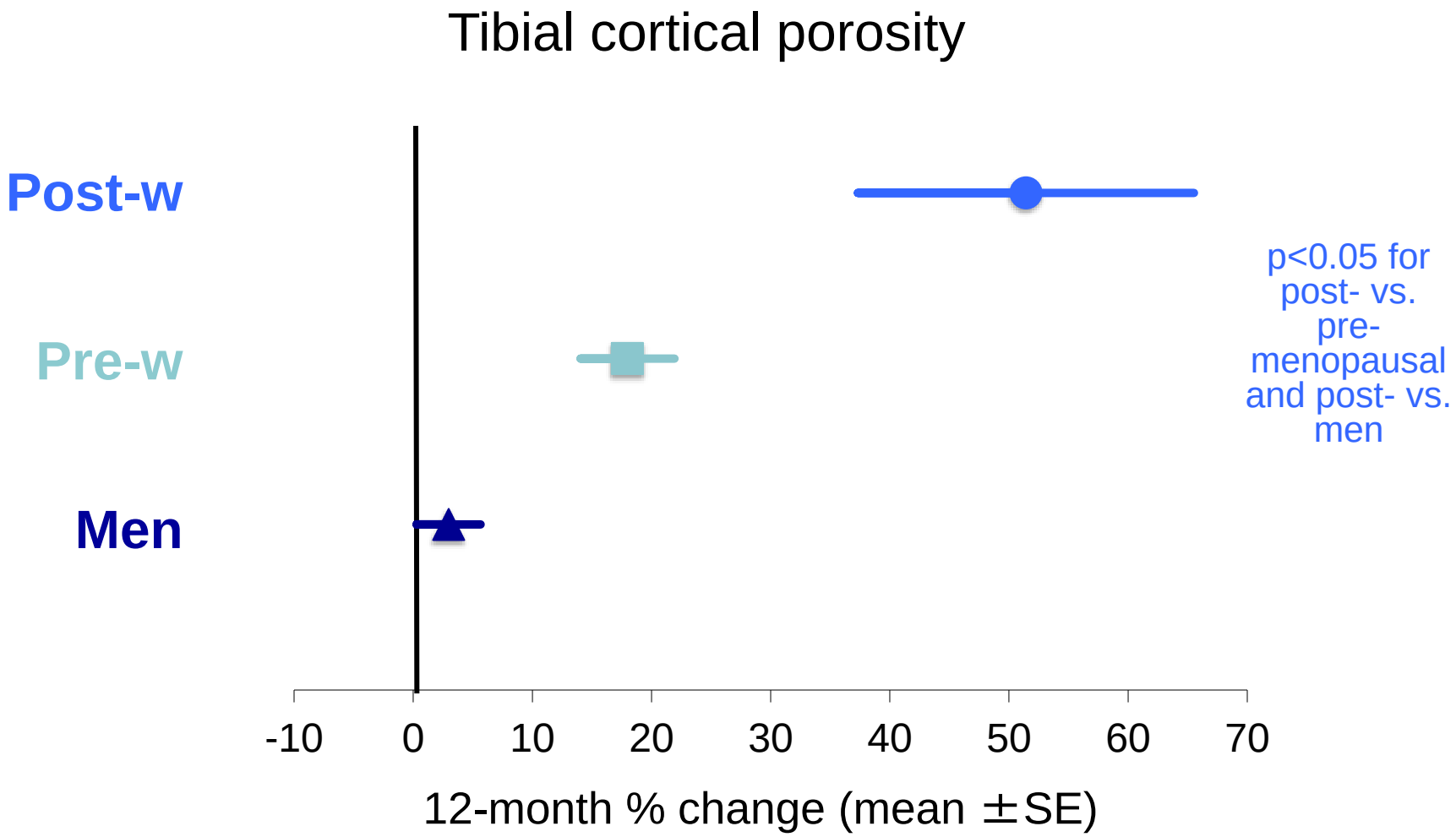






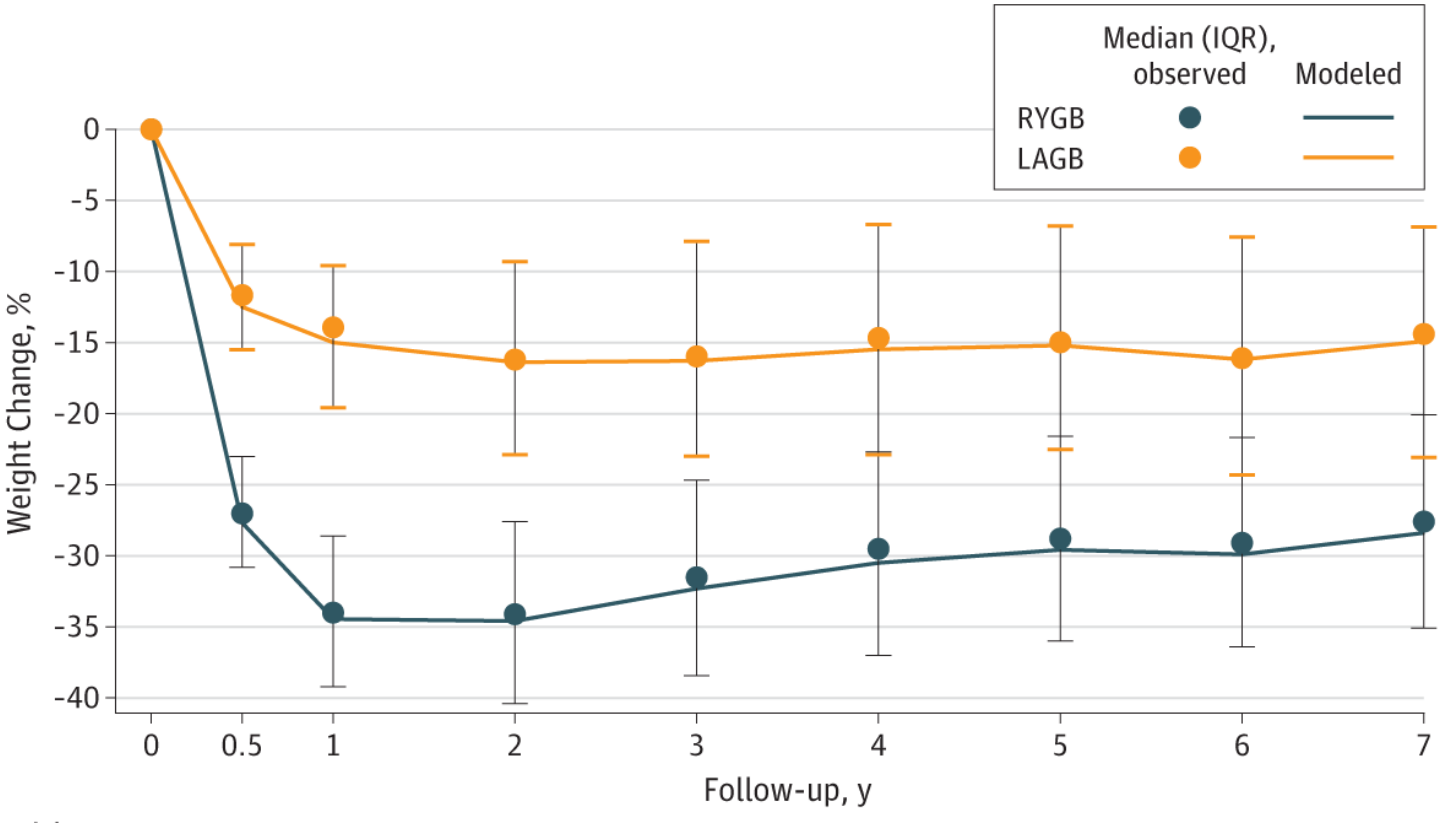
- Trabecular deterioration tibia
- Decreased strength radius and tibia (FEA)

Cortical porosity increases most in postmenopausal women



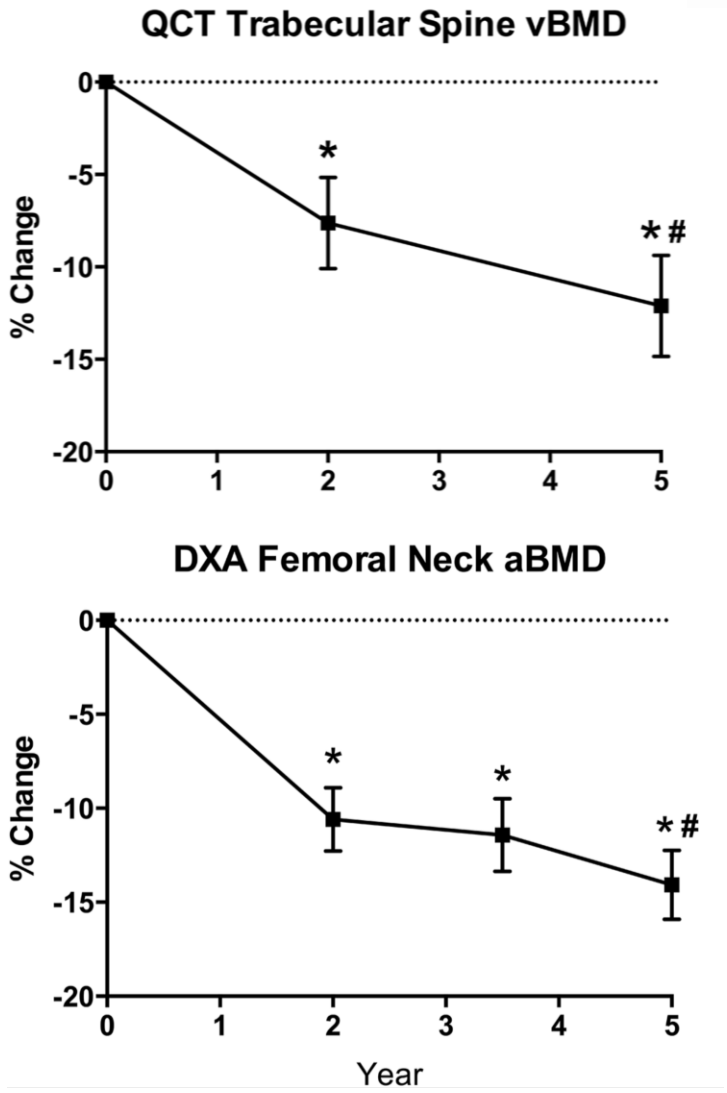
Schafer, JBMR 2018

Do detrimental skeletal changes persist after weight stabilizes?



Courcoulas, JAMA Surg 2018

Bone loss persists 5 years after gastric bypass

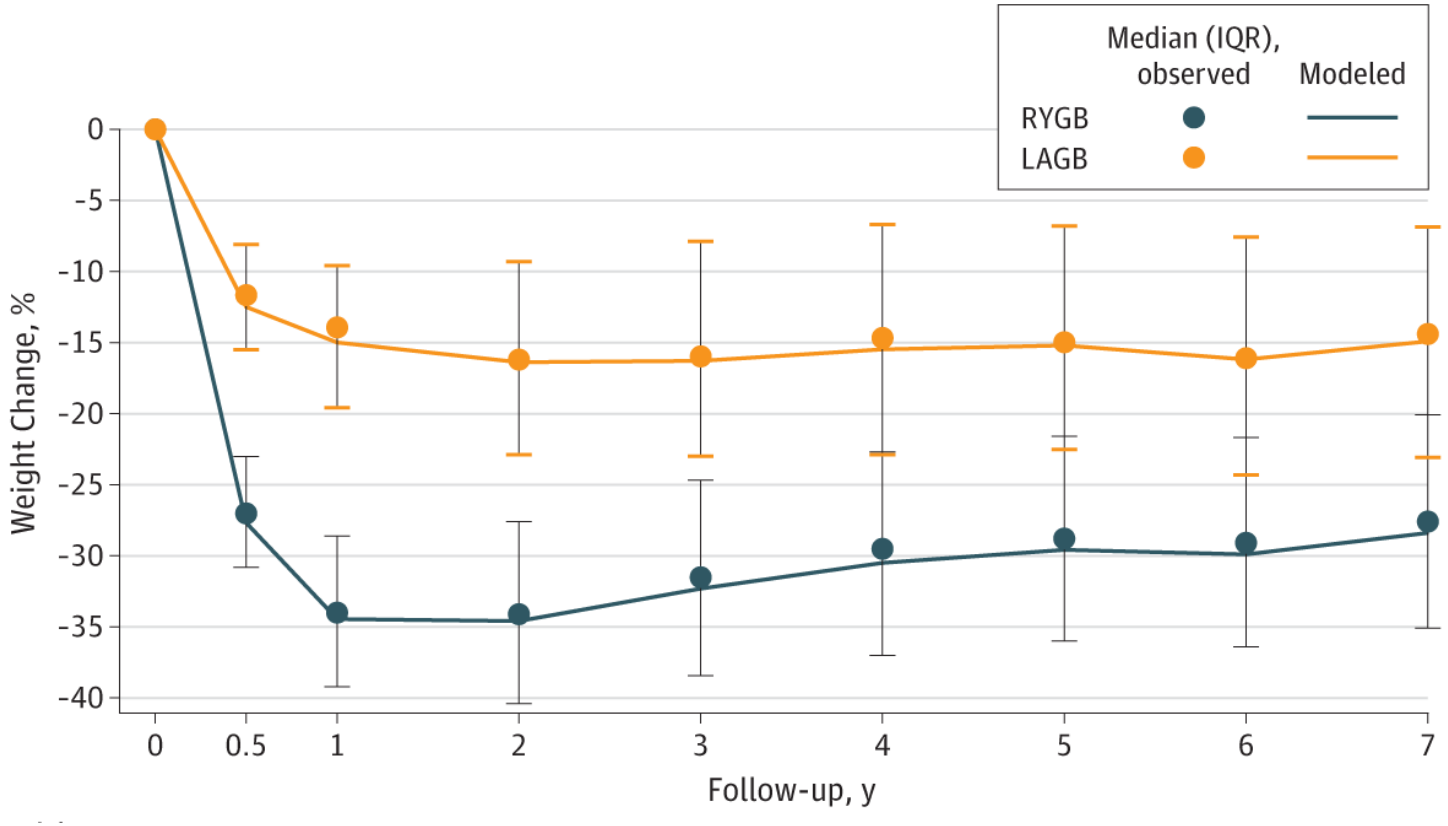


BTMs still above pre-op baseline:

- *CTX by 150%*
- *P1NP by 34%*

Lindeman, JCEM 2018; Crawford, Endocr Pract 2018

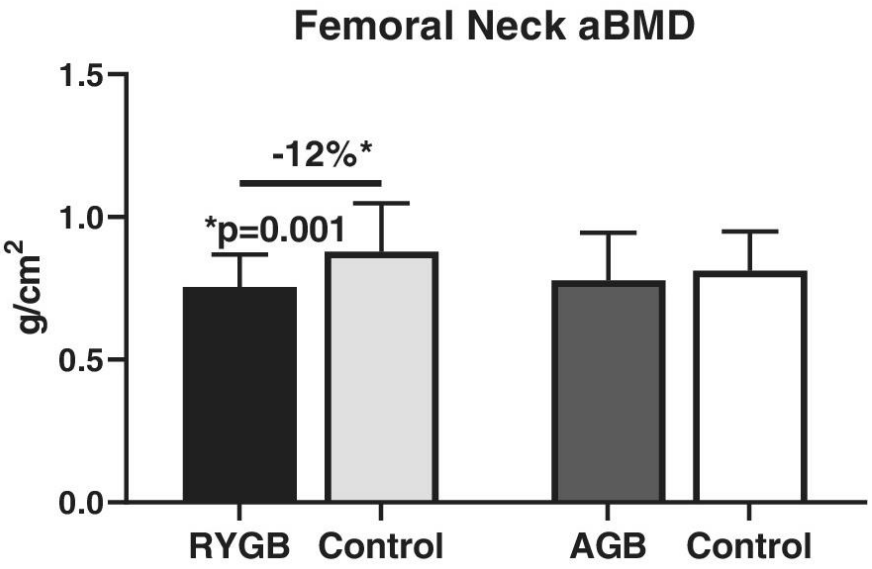
Is bone loss simply the expected physiologic adaptation to the new lower weight?

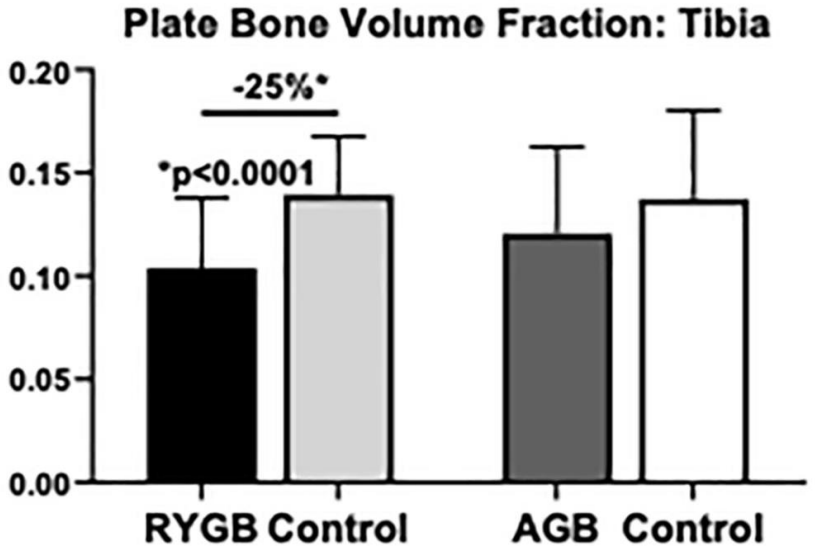


Courcoulas, JAMA Surg 2018

Gastric bypass→ lower bone mass than controls with same post-op BMI

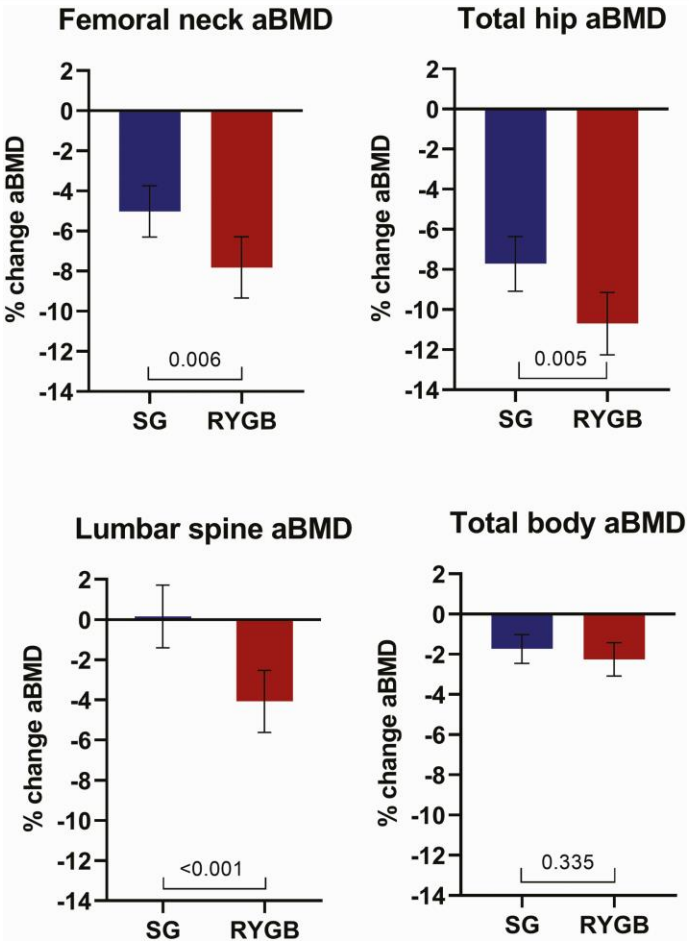
- Adults 10+ yrs s/p gastric bypass and band
- Nonsurgical controls matched for age, sex, <u>current BMI</u>





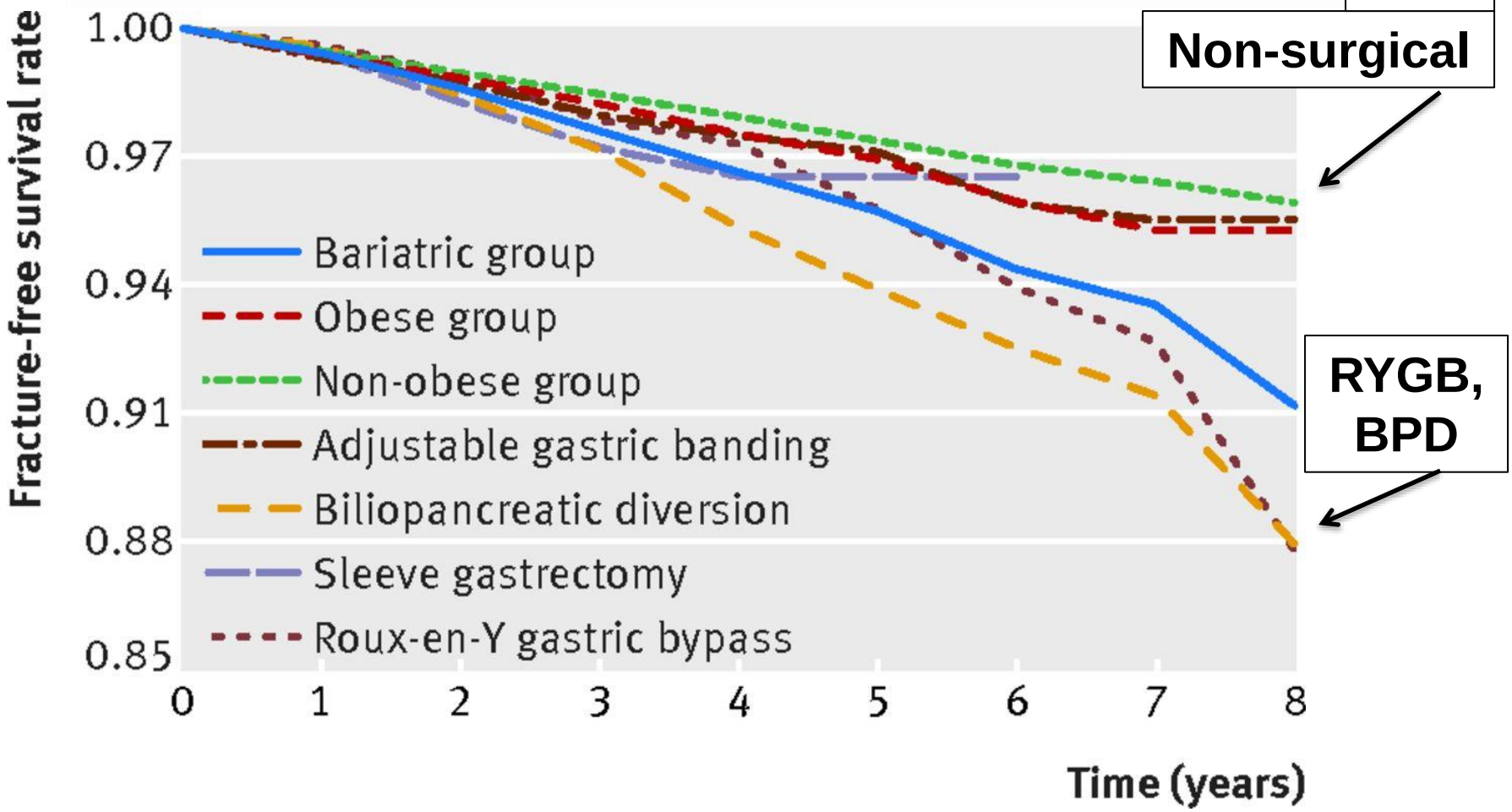
Lindeman, JBMR 2020

aBMD decline appears greater after gastric bypass than sleeve



Hofsø, J Clin Endocrinol Metab 2021; Guerrero-Pérez, Obes Surg 2020

Fracture risk increases after bariatric surgery



Rousseau, BMJ 2016

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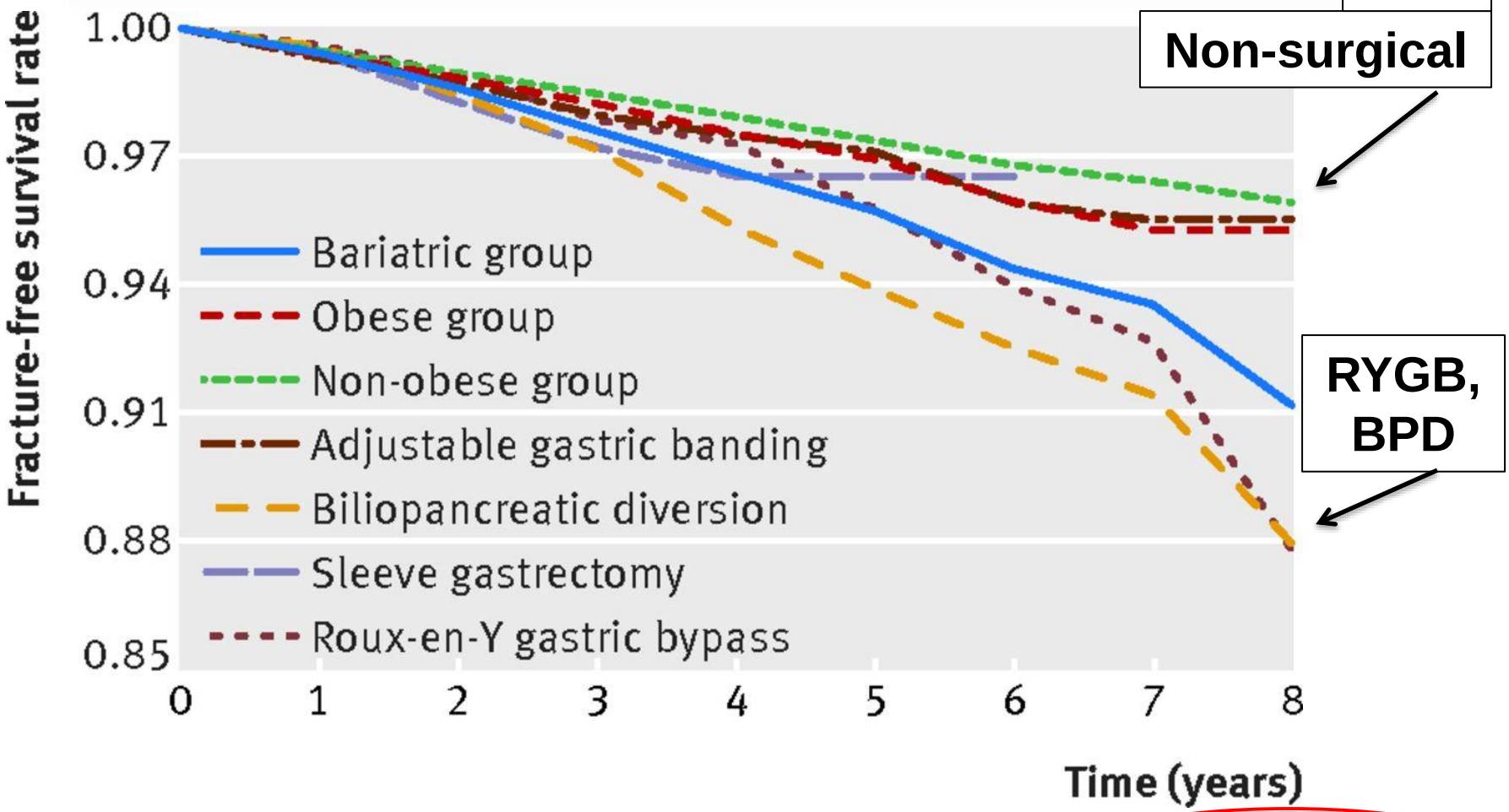
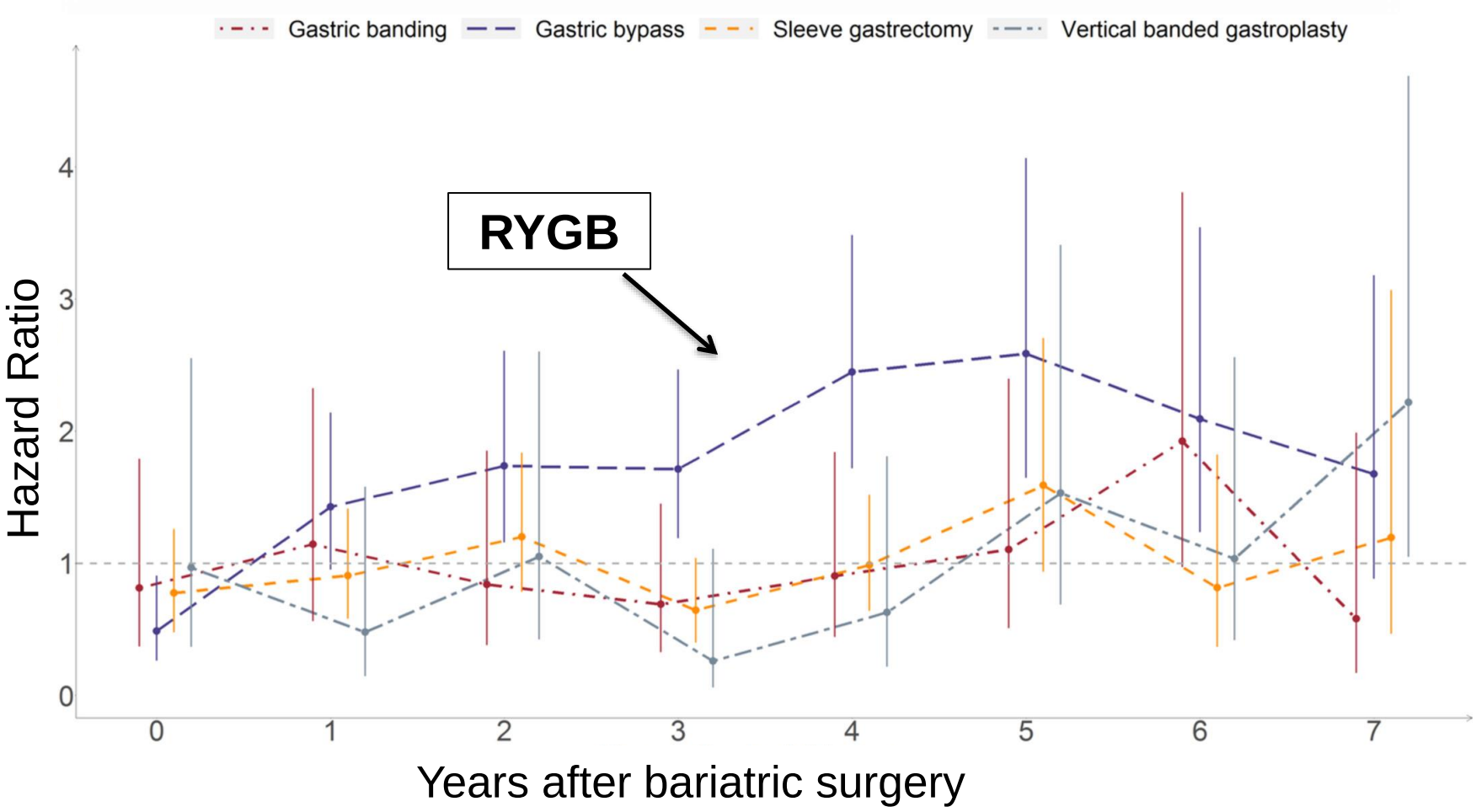


Rousseau, BMJ 2016; Nakamura, Osteo Int 2014; Lu, Medicine 2015; Paccou, JBMR 2020; Axelsson, JBMR 2018; Fashandi, Surg Endosc 2018; Yu, JBMR 2017; Yu, JAMA Surg 2019

Fracture risk increases after bariatric surgery



Paccou, JBMR 2020

Fracture risk increases after bariatric surgery

- Increased risk after gastric bypass
  - –Compared to gastric band
  - –Regardless of diabetes status
- Possibly not after sleeve gastrectomy
- Studies vary substantially in control group, follow-up time

Bone loss during weight loss: Potential mechanisms

DRAMATIC! RAPID!

- Decreased mechanical loading
- Nutritional factors **+ MALABSORPTION**
  - ↓ vitamin D and Ca intake
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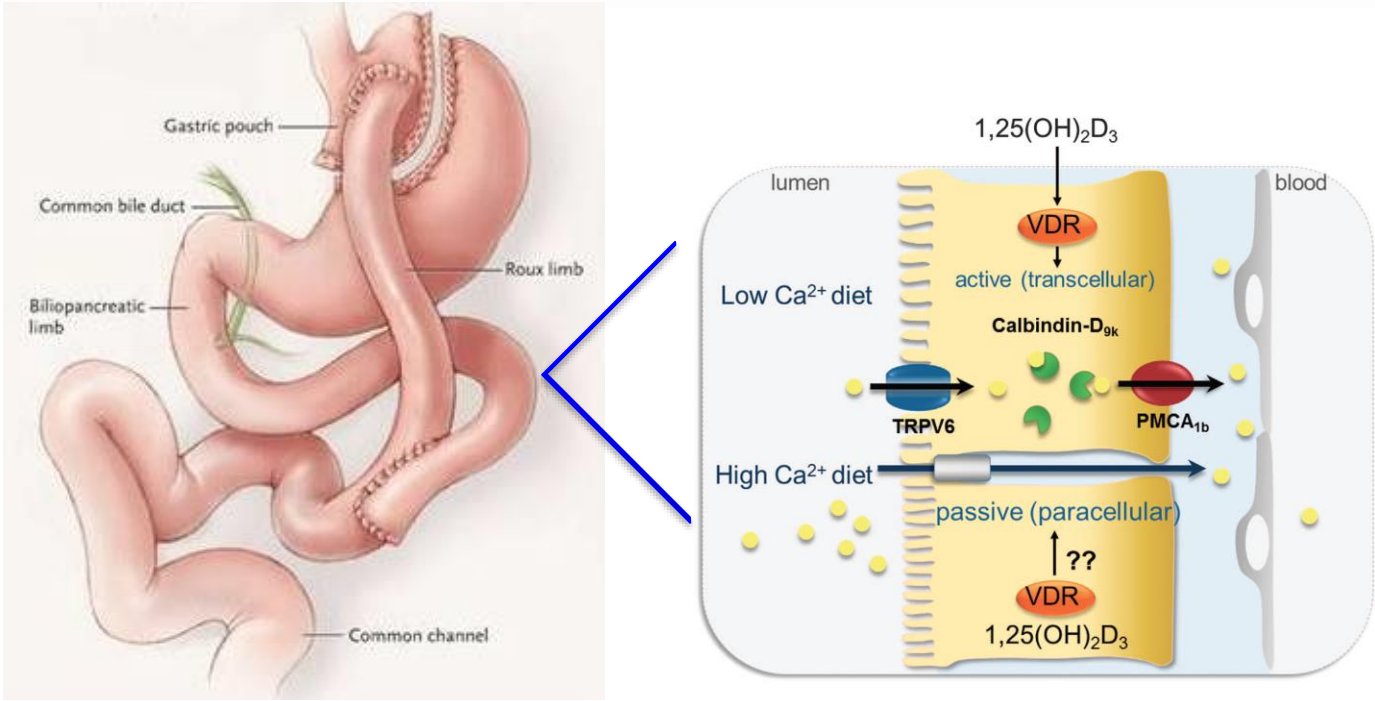
Intestinal calcium absorption

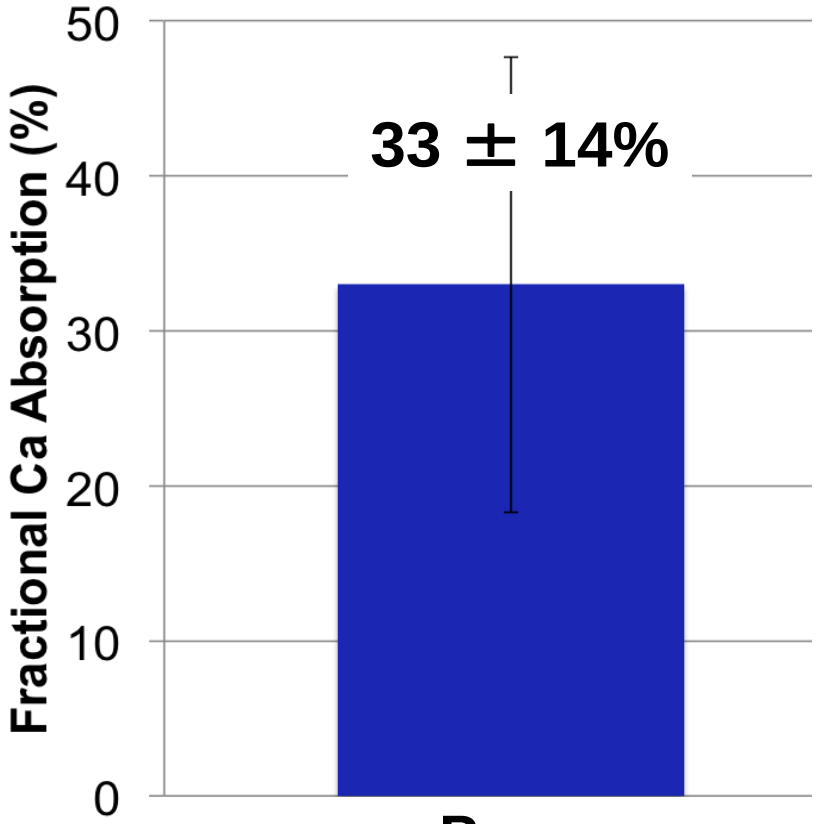


What are RYGB's effects on fractional calcium absorption?

- *25(OH)D ≥30 ng/mL*
- *Ca intake 1200 mg/day*

DeMaria, N Engl J Med 2007; Christakos, Bonekey Rep 2014

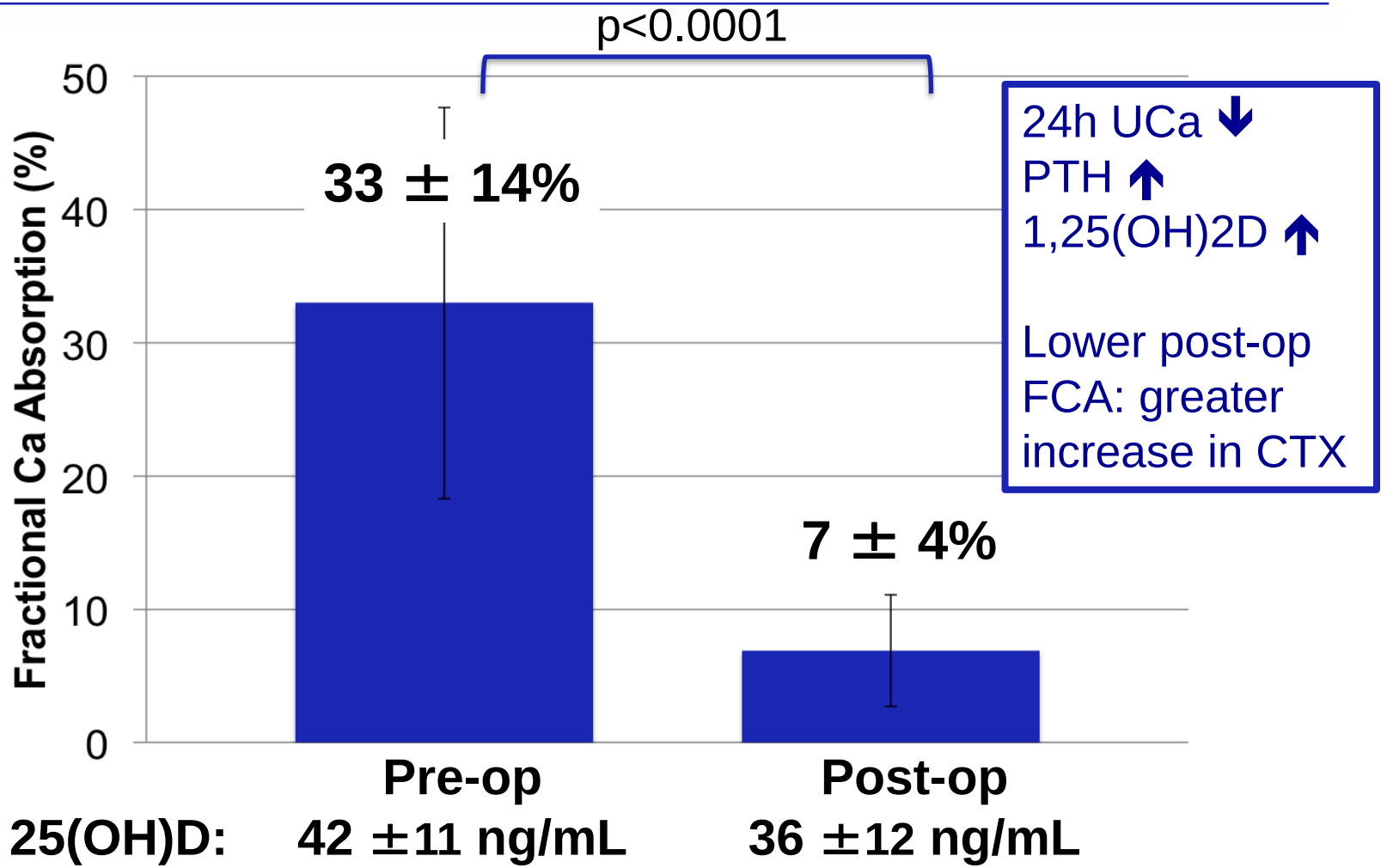
Pre-op FCA was normal



25(OH)D: 42 ±11 ng/mL

Schafer, JBMR 2018

FCA decreased precipitously



Schafer, JBMR 2018

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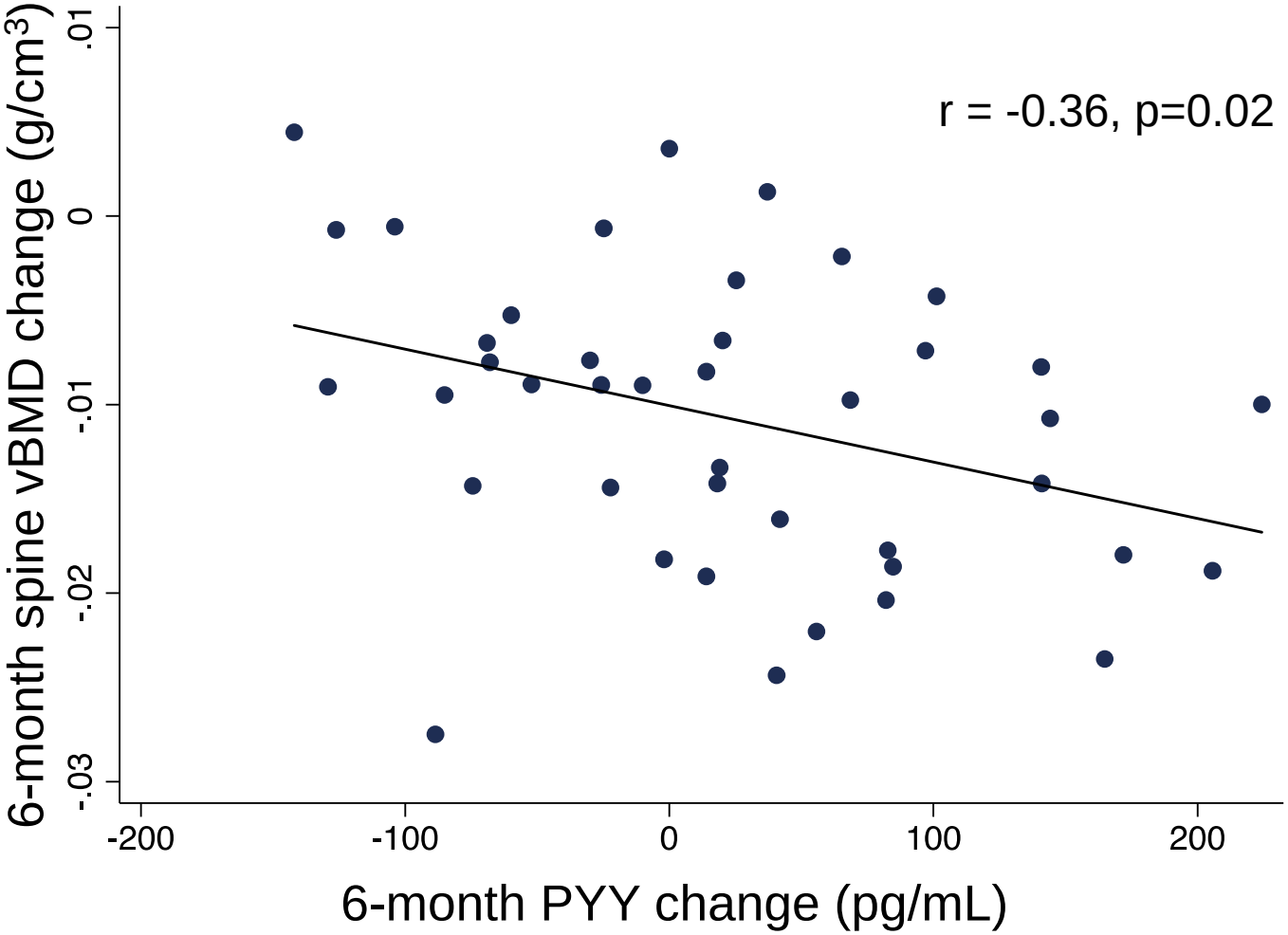
Post-op increases in PYY are associated with greater declines in spinal vBMD



Kim, Bone 2020

Also after bariatric surgery . . .

- Those with post-op increases in bone marrow adiposity have more BMD loss[1]
- "Uncoupling" of bone turnover correlates with BMD loss[2]
- Post-op increases in gut microbial diversity might be protective against BMD decline

[1]Kim, JBMR 2017; [2]Kim, Bone 2020

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- Roux-en-Y gastric bypass surgery
  - ✓ 240 lbs (BMI 31)
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  Why did he fracture?

- Not taking Ca or vitamin D supplements
- DXA: Total hip T-score -1.8

Ca (8.5-10.5)	Alb (3.3-5.2)	Phos (2.5-4.5)	Cr (0.6-1.3)	25OH D (30-50)	PTH (12-65)	24h Uca (100-250)
8.4	3.6	2.5	1.1	17		

- Vitamin D repletion course, daily Ca carbonate and vitamin D maintenance

8.5	3.5	3.0	1.1	28	80	58
8.4	3.7	2.8	1.3	34	144	

- Increased Ca intake and switched to citrate

Implications for patient care

- ✓Check and replete 25(OH)D pre-op
- ✓Universal post-op supplementation
  - Multivitamin
  - Calcium (as citrate) *(1200mg-1500mg daily)*
  - Vitamin D *(3000 IU daily – often in MVI)*
- ✓Labs q 6 mo x 2 yrs then annually
  - Ca, albumin, Cr, 25(OH)D, PTH
  - 24h urinary Ca if additional data needed

Kim, SOARD 2015; Mechanick (AACE/TOS/ASMBS), SOARD 2013

Implications for patient care

✓Protein intake 60-75 g/day

✓Post-op exercise/resistance training[1]

RYGB or SG

- Ca + D + protein + exercise
- no supplements, no obligatory exercise

Attenuated *increases in BTMs and decreases in aBMD, lean mass*[2]

✓DXA or QCT when indicated; higher-risk pts

[1]*Diniz-Sousa, J Bone Miner Res 2016;* [2]*Muschitz, J Bone Miner Res 2021*

Pharmacologic therapy?

? High-risk pts as they undergo surgery

- ✓Dramatic high bone turnover state → antiresorptive agent
  - ✓Parenteral (ZOL, DMAB)
  - ✓**Only** when Ca, vit D status adequate

Conclusions

- Gastric bypass negatively impacts axial and appendicular BMD and bone microstructure
  - Weight-bearing and non-weight-bearing sites
  - Bone loss continues after weight loss complete
  - Postmenopausal women particularly affected
- Sleeve gastrectomy may be less detrimental, but more data needed
- Mechanical unloading and Ca malabsorption contribute, but other mechanisms also at play

Acknowledgments

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