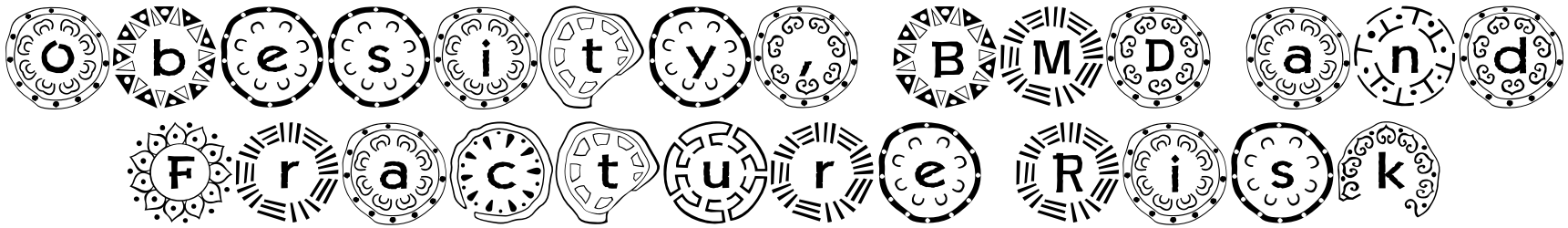
여성 비만 환자에서의 뼈 건강과 골다공증 약물치료

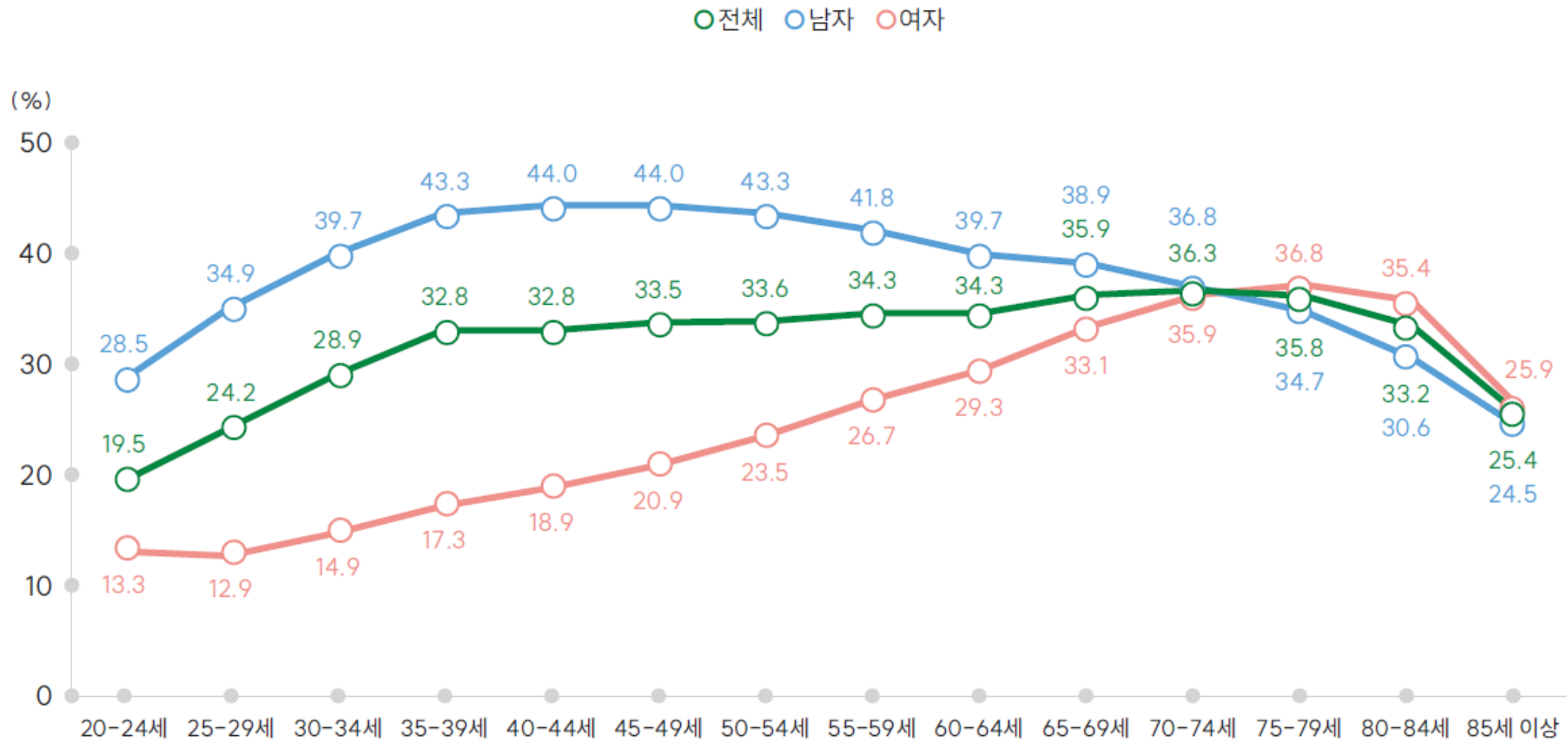
아주의대 가정의학교실

김범택

Contents

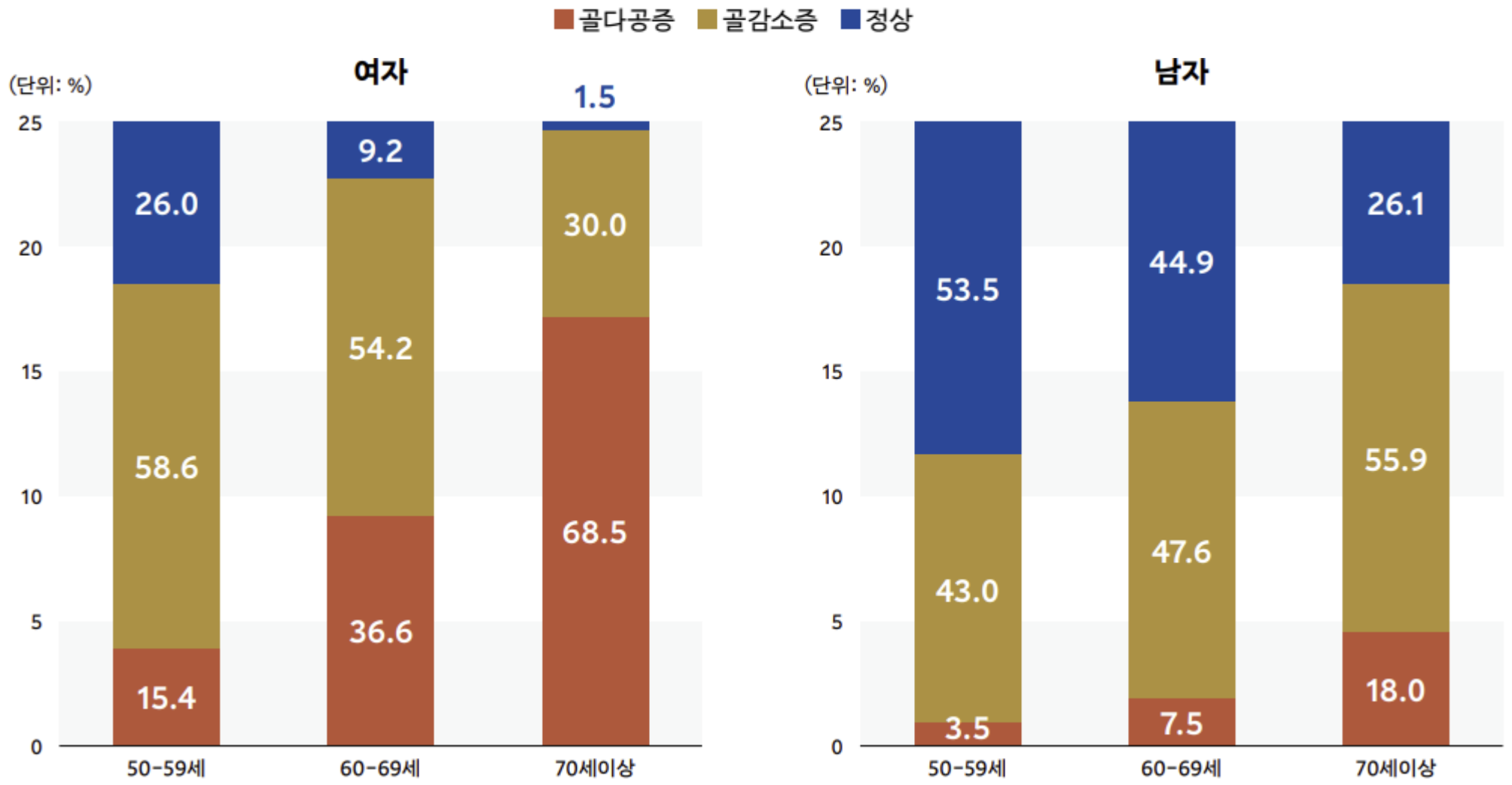

Obesity, BMD and
Fracture Risk

비만의 연령별 유병률



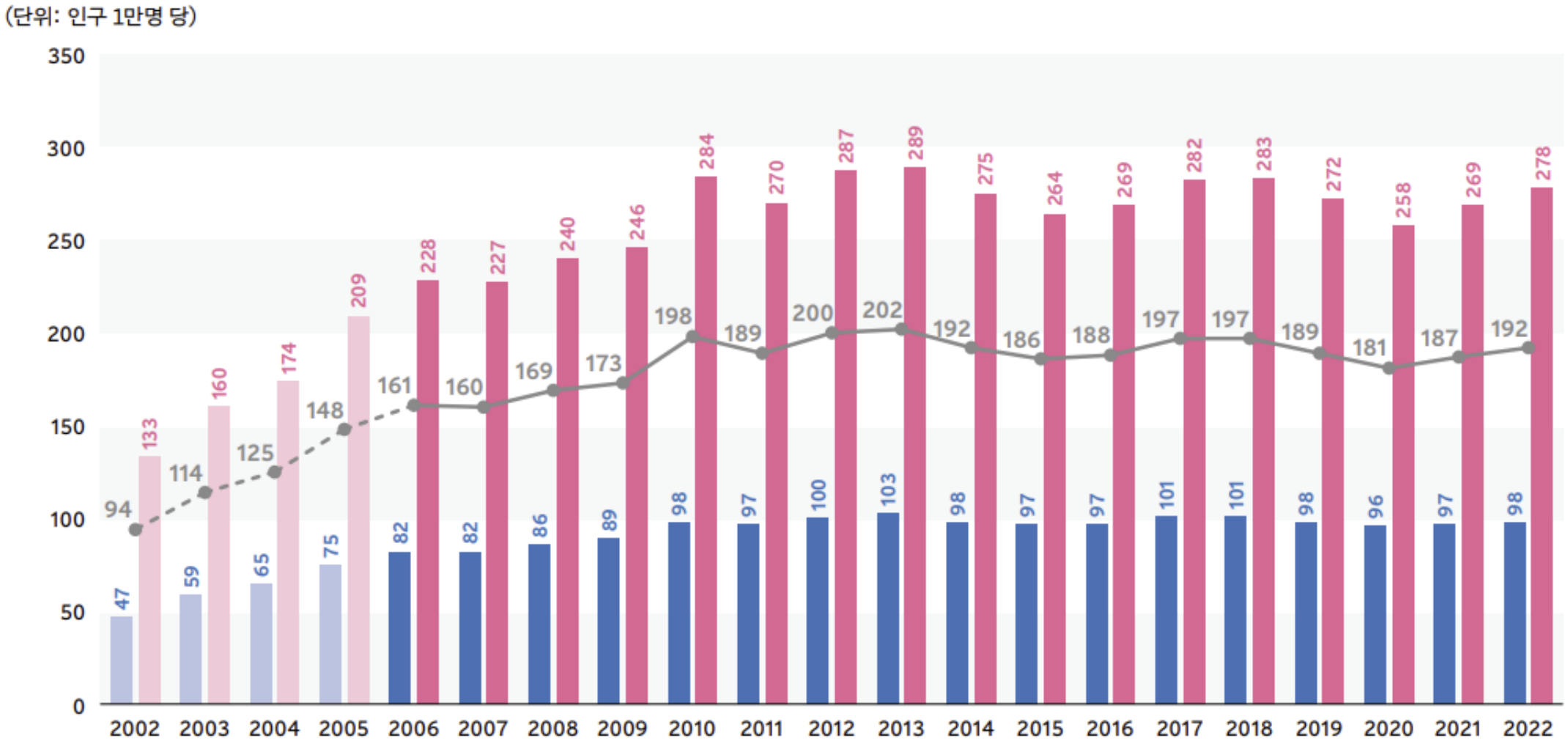
Obesity Factsheets Korea 2024

연령별 한국의 골다공증 유병률 (50세 이상)

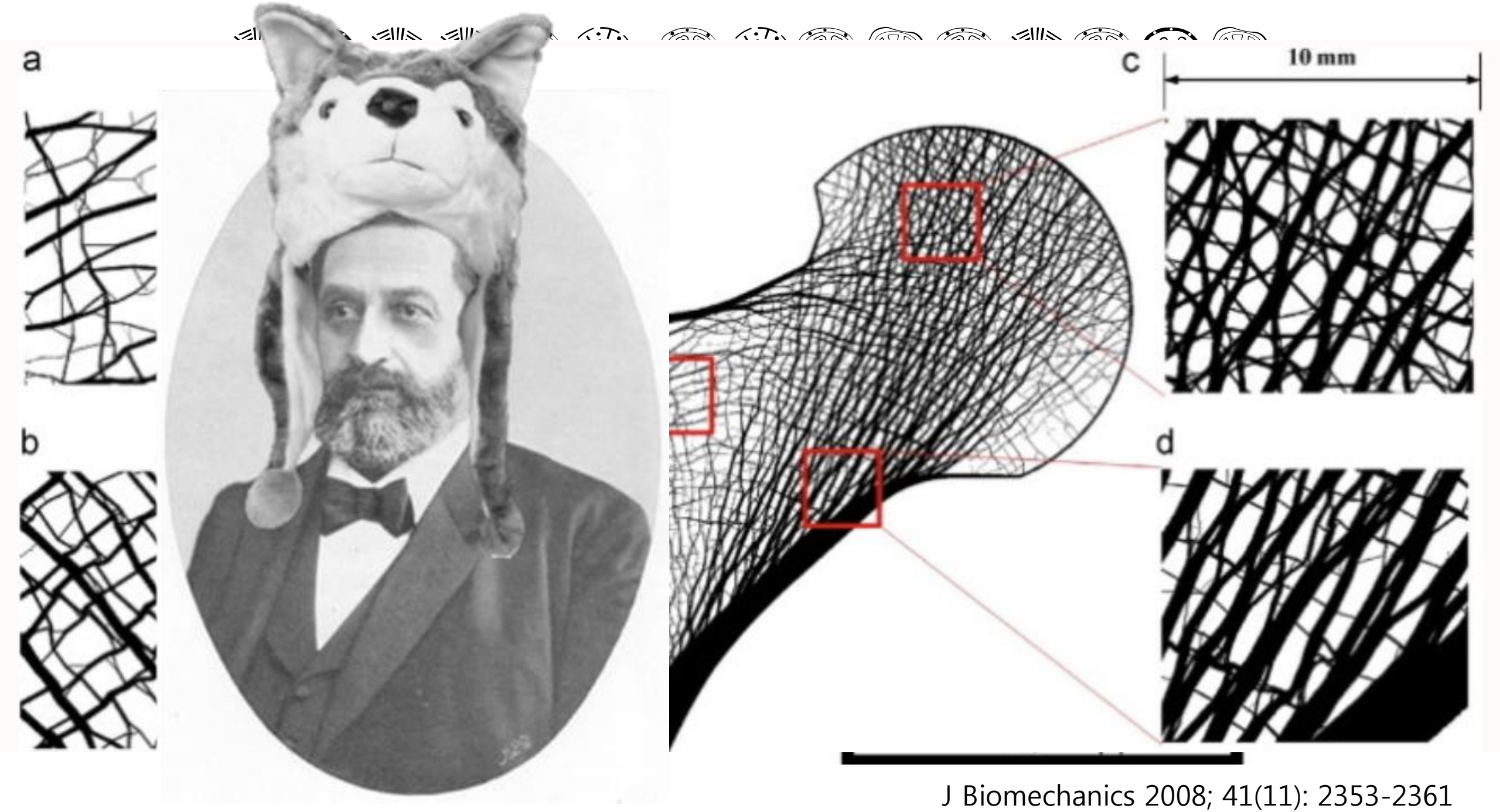


4기 국민건강영양조사, 2009-2011

최근 골다공증 골절의 발생 추이

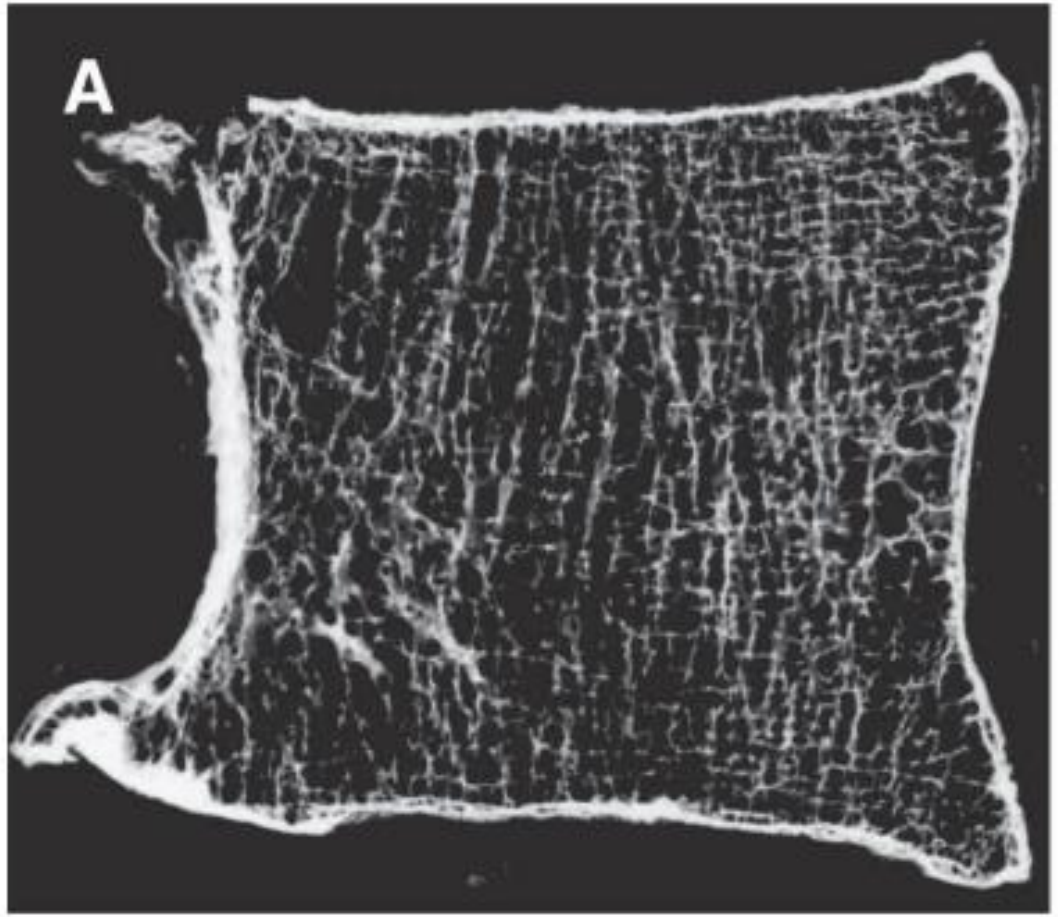


2002-2022 건강보험공단 자료



J Biomechanics 2008; 41(11): 2353-2361

Spared Vertical Trabecular in OPS

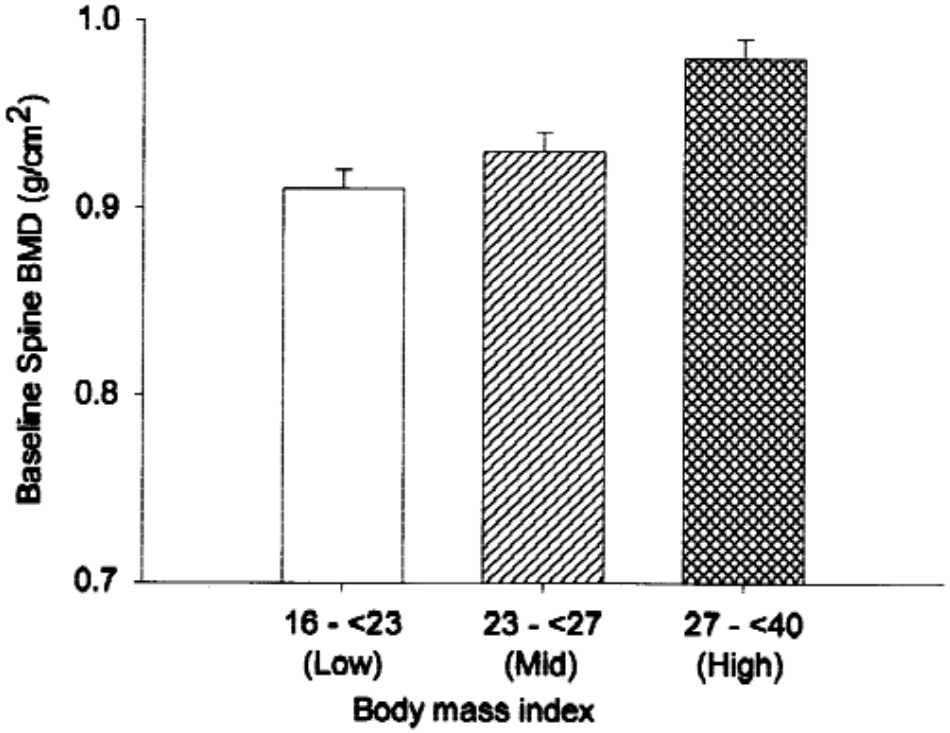


J Bone Miner Res 2006 ;21(9):1409-16

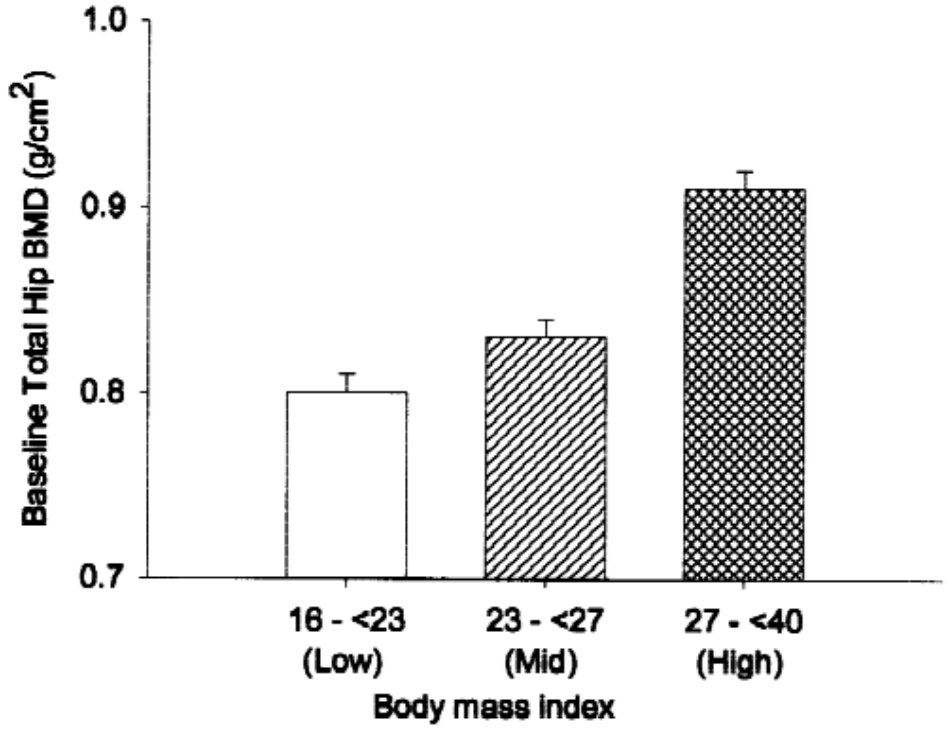
BMI와 골밀도의 관계

EPIC study

Spine BMD



Hip BMD



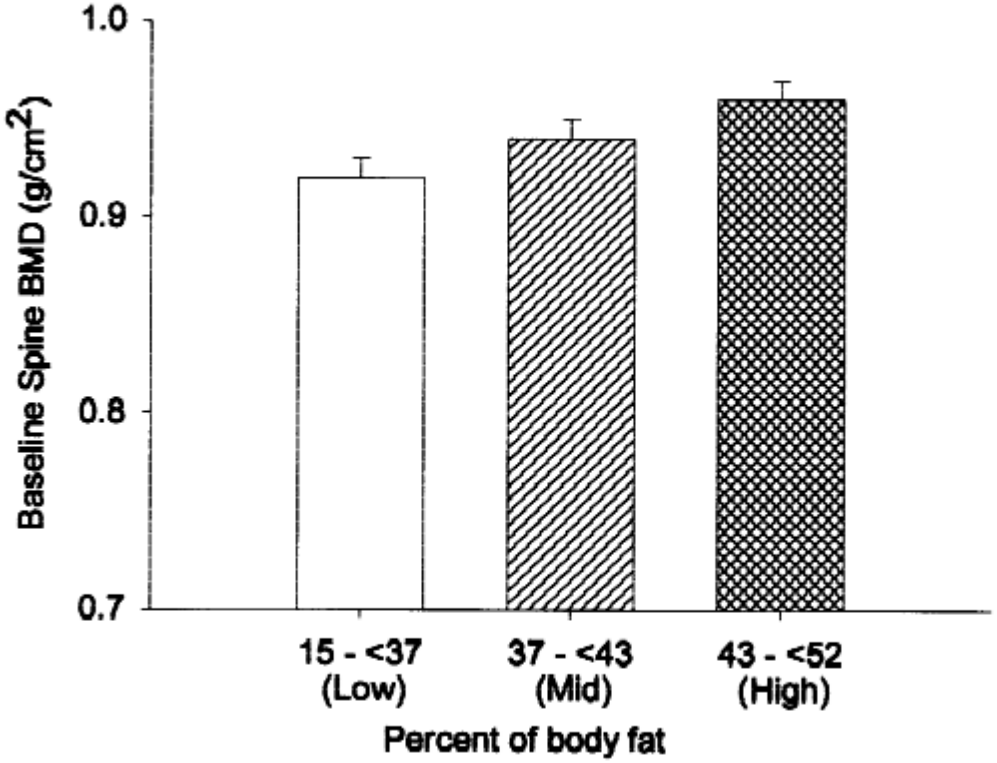
Early Postmenopausal Intervention Cohort (EPIC) Study

J Bone Miner Res. 1999;14(9):1622-7

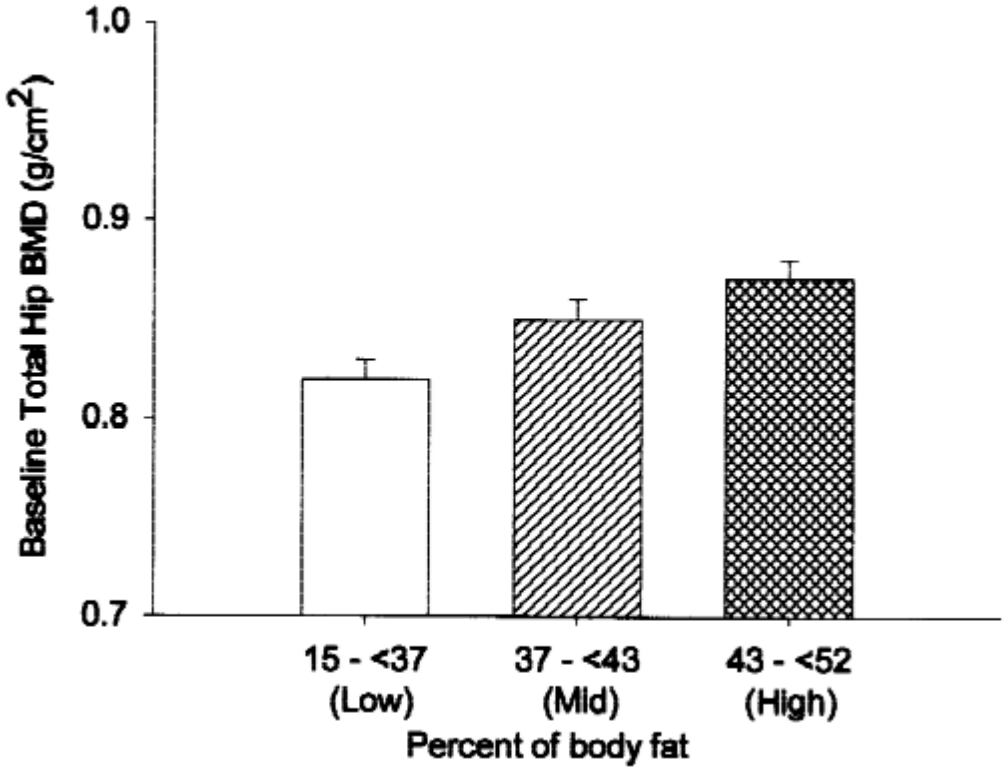
Body fat %와 골밀도의 관계

EPIC study

Spine BMD



Hip BMD

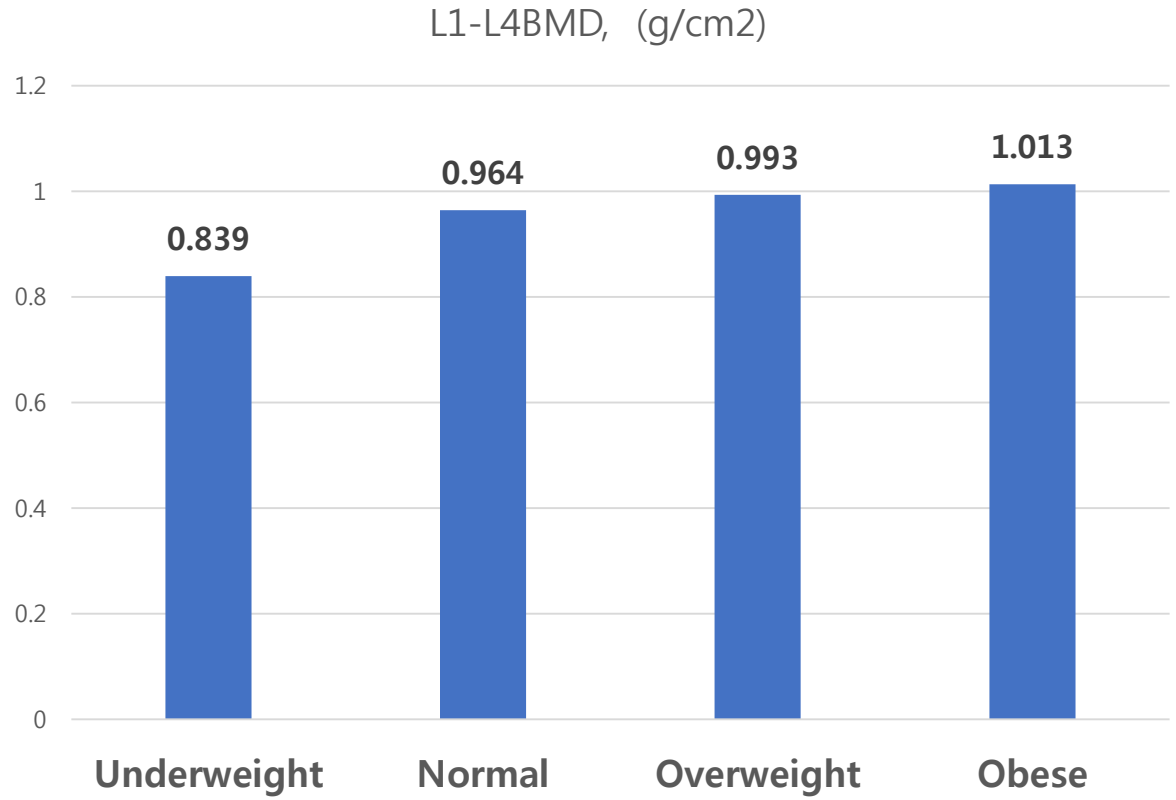


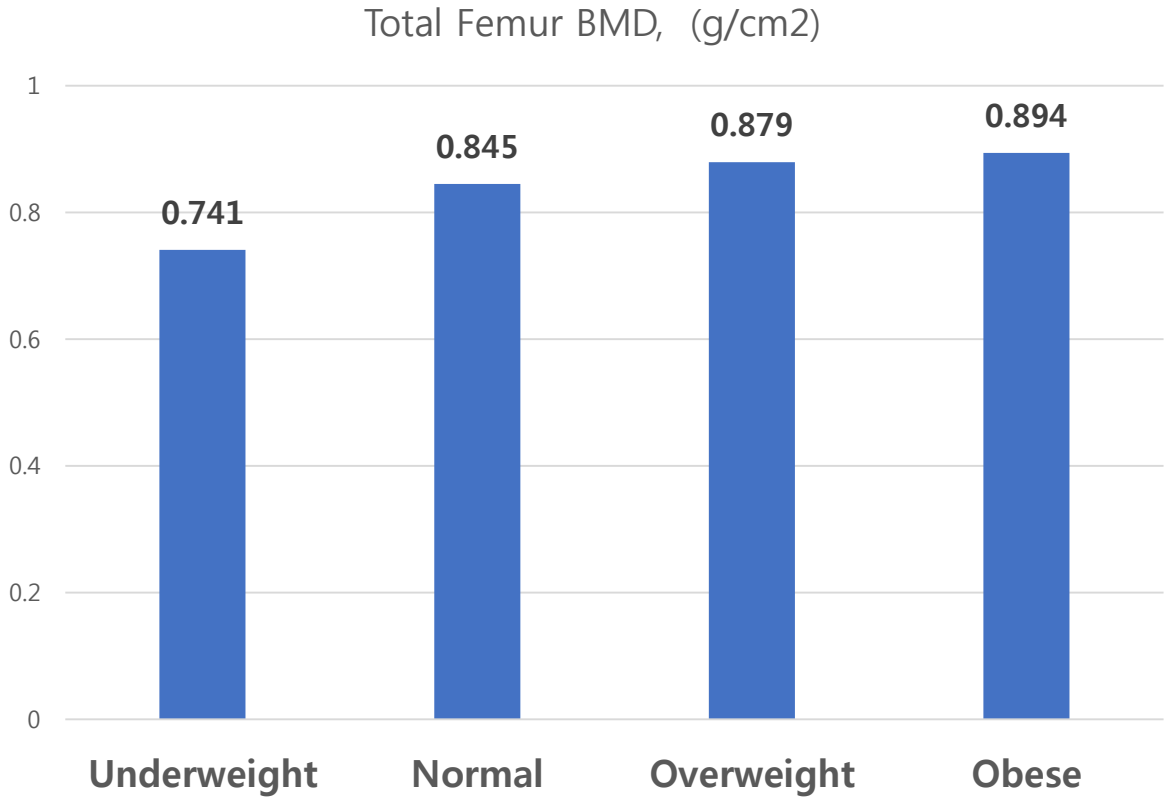
Early Postmenopausal Intervention Cohort (EPIC) Study

J Bone Miner Res. 1999;14(9):1622-7

Obesity and Bone Mineral Density

Ajou Bone Love Data (ABLD) study
N = 18,151





Osteoporos Sarcopenia. 2025;11(2):65-68

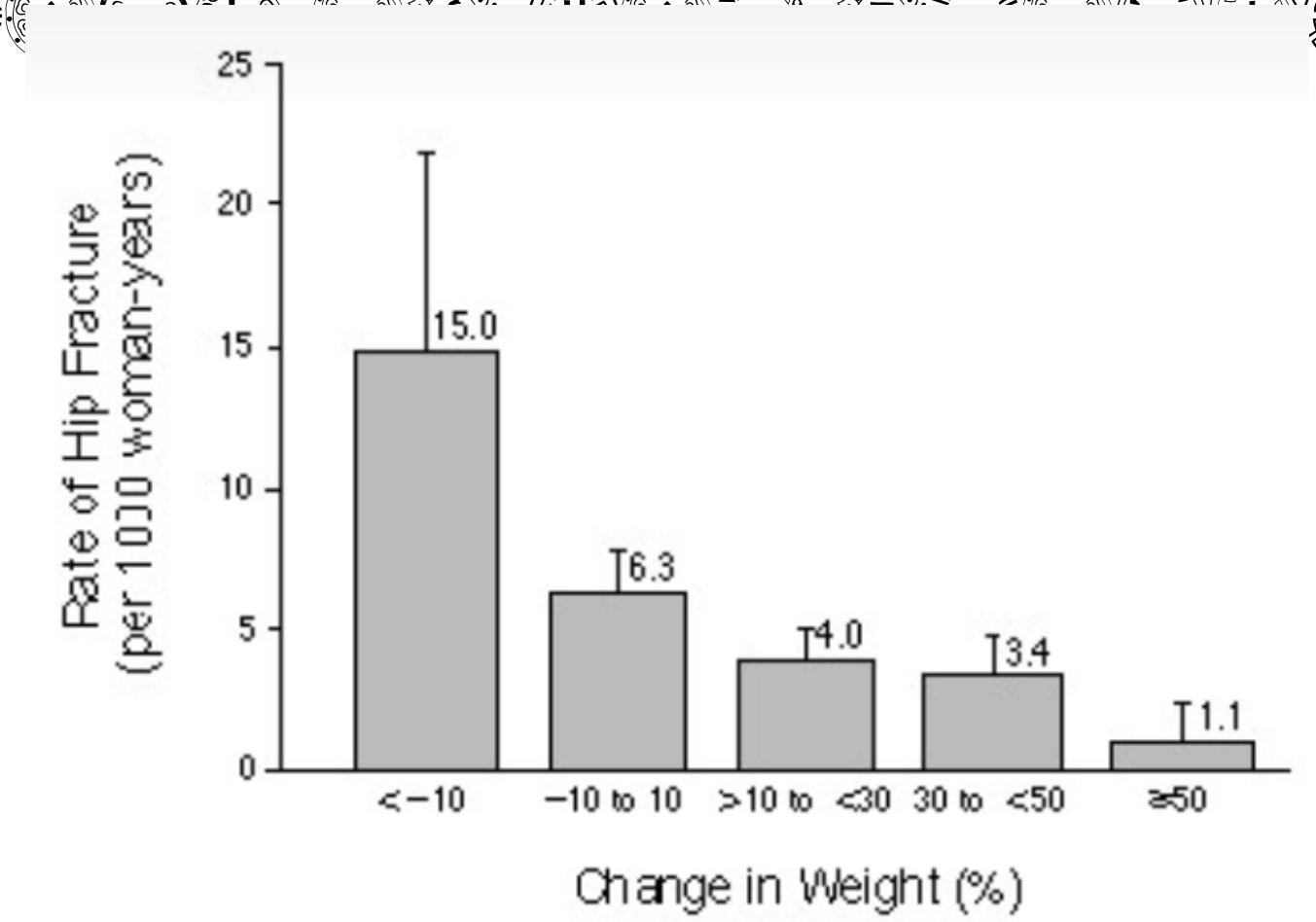
obesity and the Risk of Hip Fracture

Body Mass Index ($kg/m^{1.5}$)	Hip Fractures	Crude Risk	Crude Rate	Age-adjusted Rate
≤ 28.7	17	0.029	32.5	35.8
28.8 - 32.3	18	0.031	34.0	37.8
32.4 - 37.0	14	0.025	26.2	28.9
> 37.0	6	0.011	11.5	11.9

* Based on quartiles of its distribution.

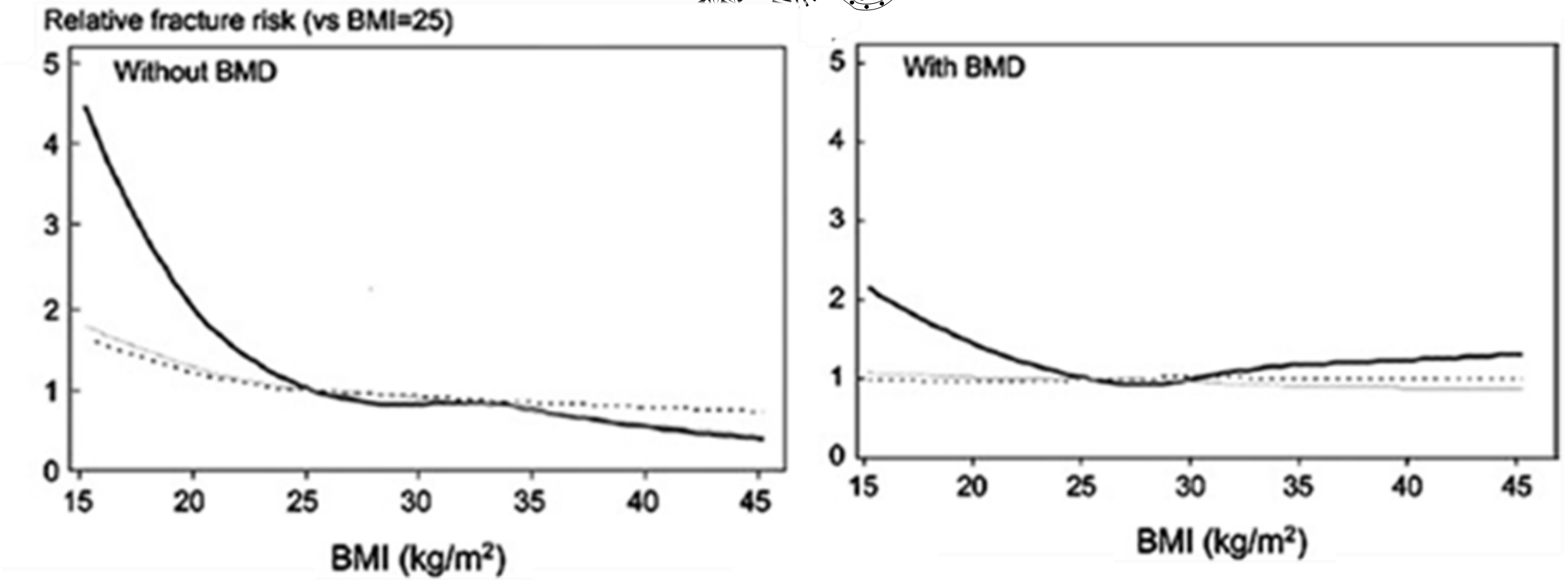
Obes Res. 1993 Sep;1(5):357-63

Association between the Change in Body Weight after the Age of 25 and the Rate of



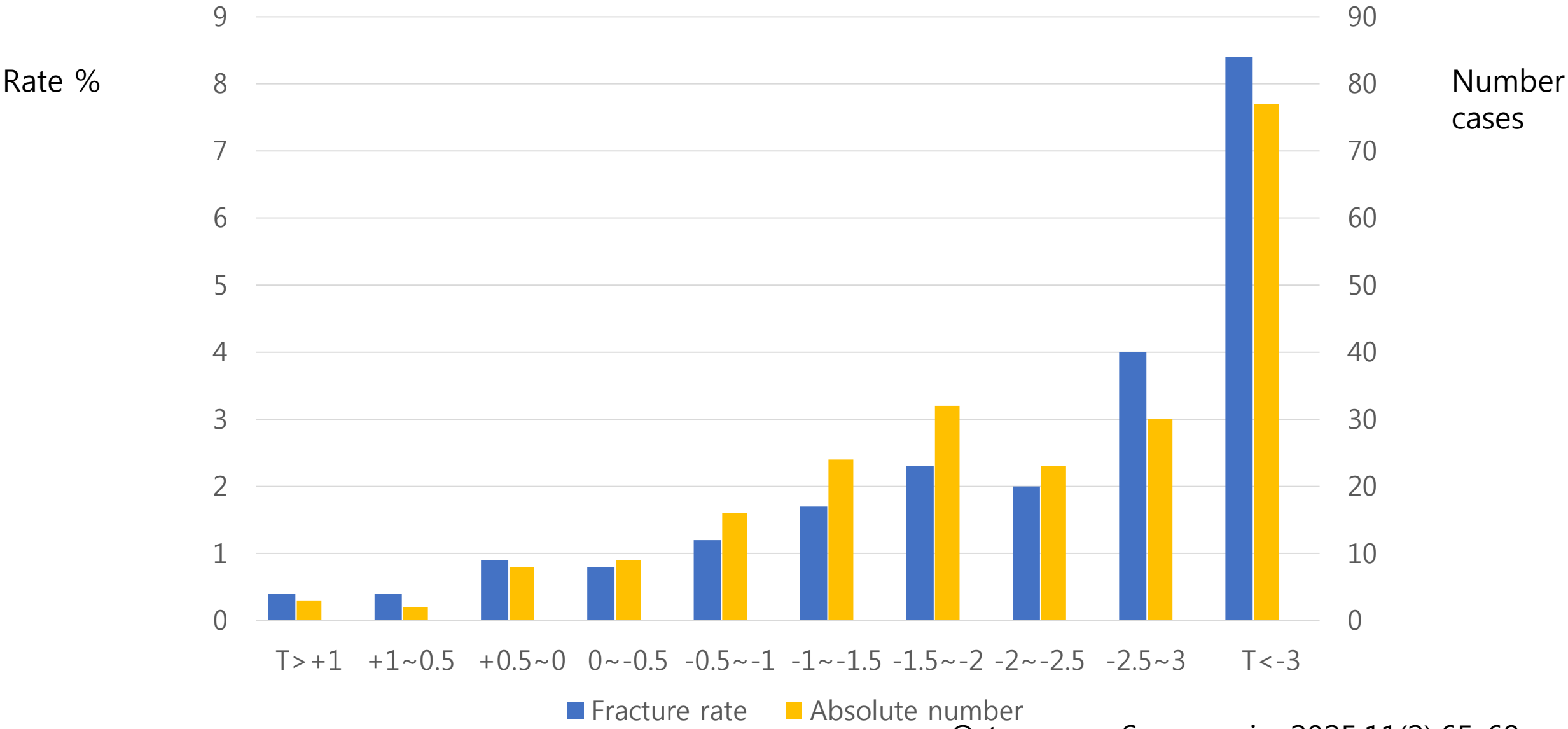
N. Engl. J. Med. 1995;332:767–773

Fracture Risk Associations with BMI



Osteoporos Int. 2005;16:1330–1338

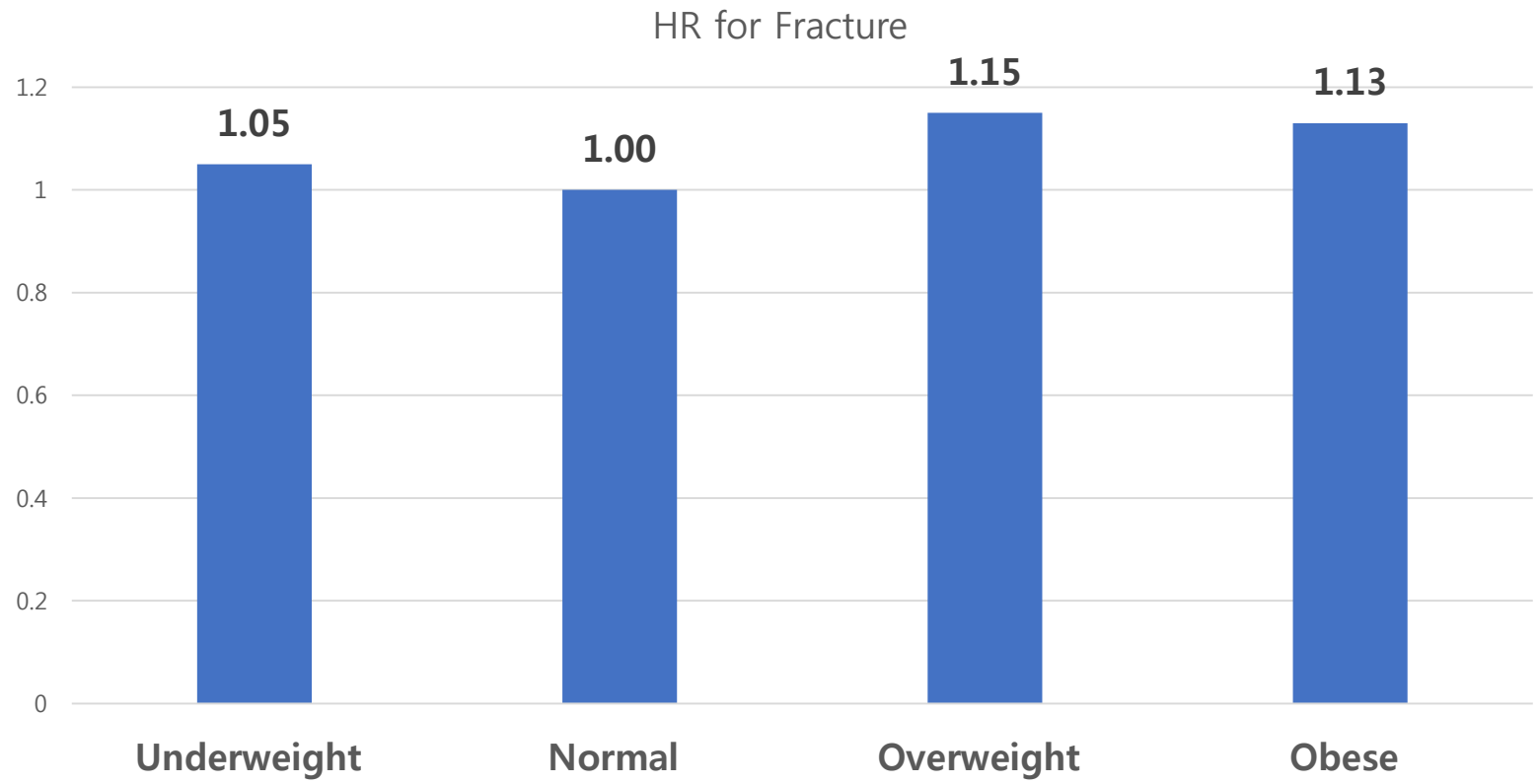
Fracture rate and absolute numbers of New vertebral Fractures in Postmenopausal women



Osteoporos Sarcopenia. 2025;11(2):65-68

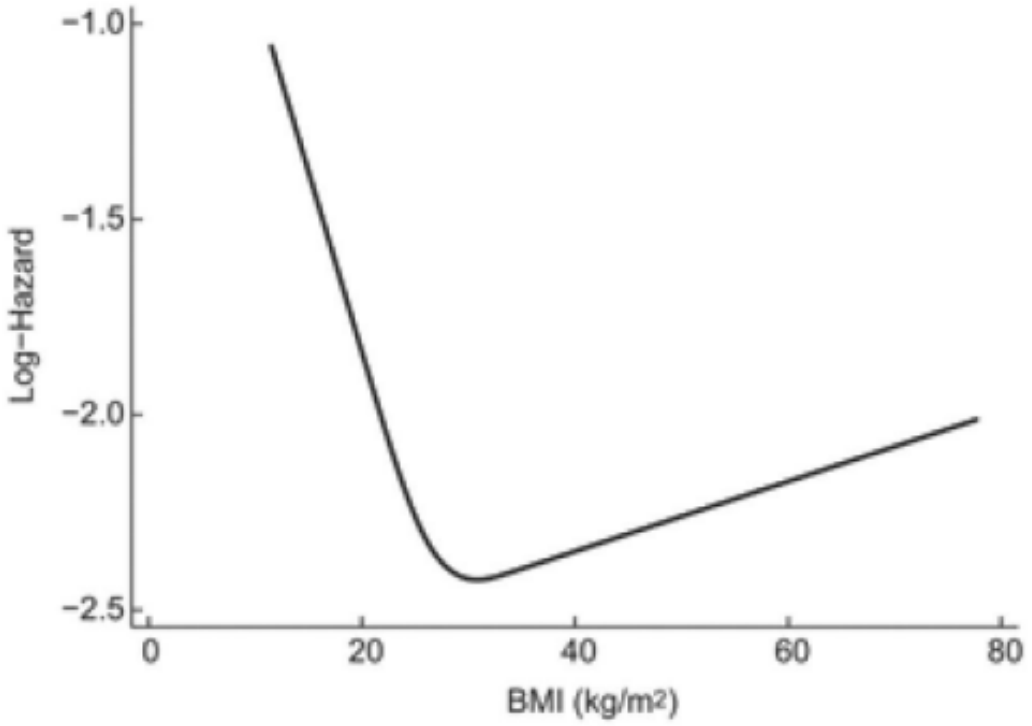
obesity and Fracture rate

Ajou Bone Love Data (ABLD) study
N = 18,151



Osteoporos Sarcopenia. 2025;11(2):65-68

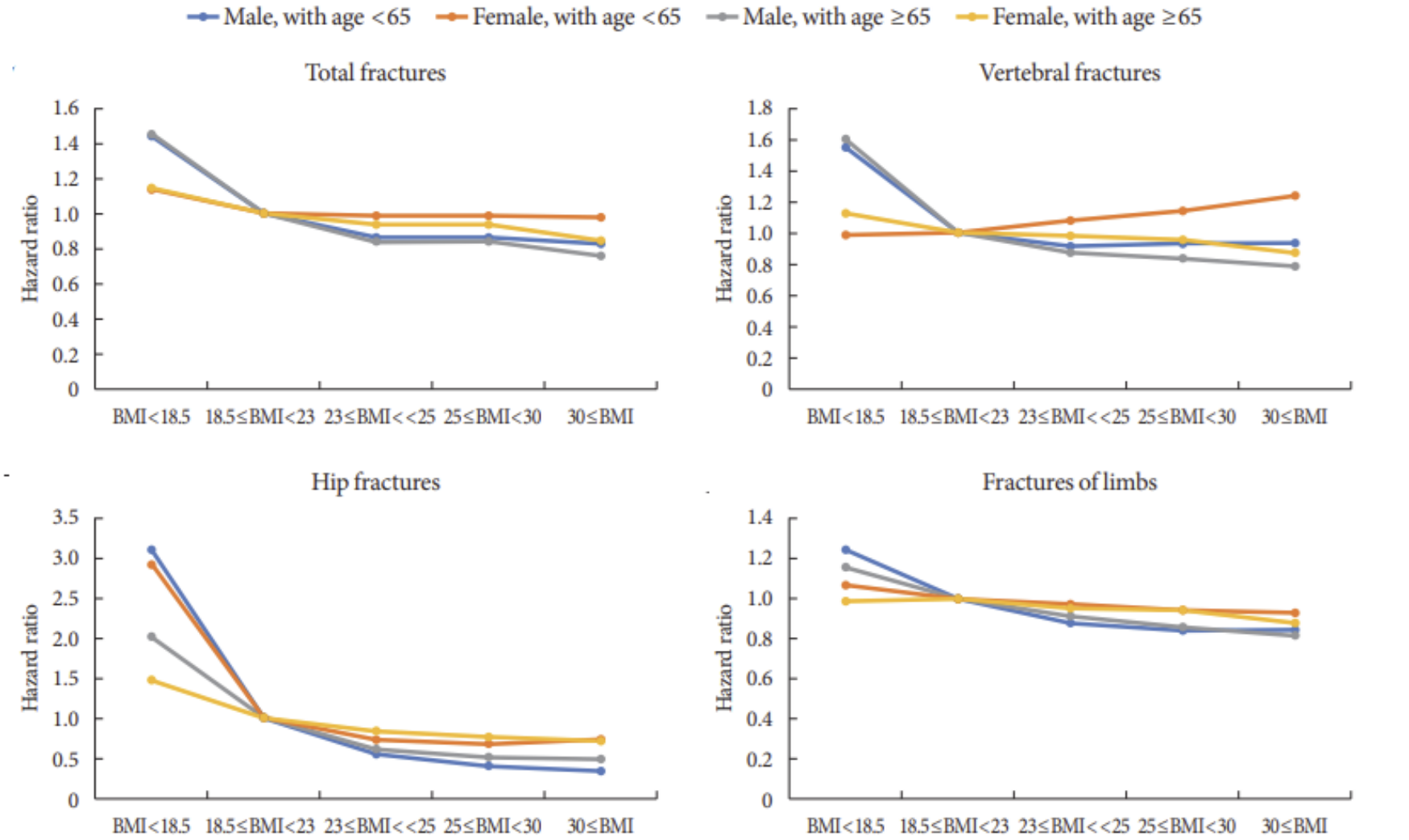
BMI와 골절 발생의 관계



Fracture site	Best form of BMI/weight/ height	Adjusted HR (95% CI)	χ^2	*p*	Next best model with different covariate	χ^2	*p*
Hip[a] (*n* = 309)	Linear BMI (per 5 kg/m^2)	0.80 (0.71–0.90)	14.3	<0.001	Linear weight	12.9	<0.001
Spine[b] (*n* = 442)	Linear BMI (per 5 kg/m^2)	0.83 (0.76–0.92)	14.5	0.0001	Linear weight	6.9	<0.01
Wrist[c] (*n* = 923)	Linear BMI (per 5 kg/m^2)	0.88 (0.83–0.94)	16.3	<0.0001	Linear weight	13.4	<0.001
Ankle[d] (*n* = 550)	Linear weight (per 5 kg)	1.05 (1.02–1.07)	13.9	<0.001	Linear BMI	11.4	<0.001

J Bone Miner Res. 2014 ; 29(2): 487–493

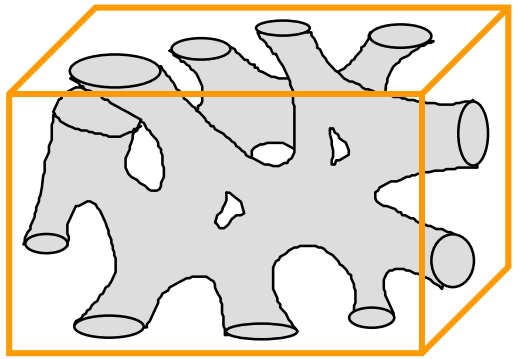
obesity with T2DM and Fracture Risk



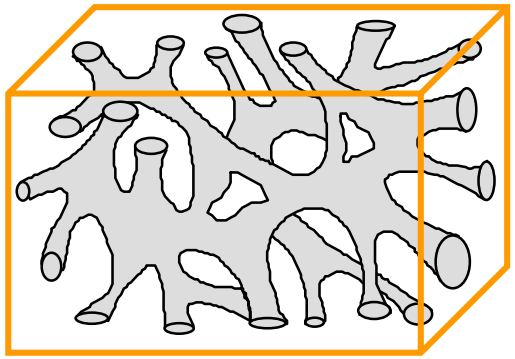
Diabetes Metab J 2023;47(2):242-254.

Paradoxical Effects of Excessive Body Weight on Bone Health

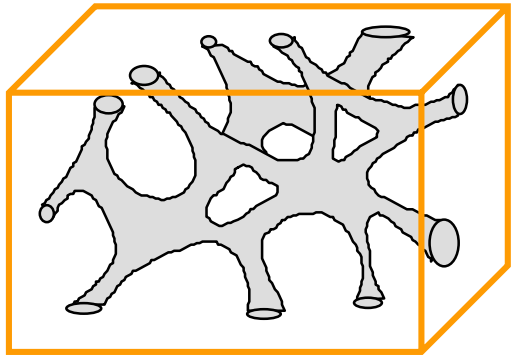
High Bone Mineral Density?



Thickness ↑

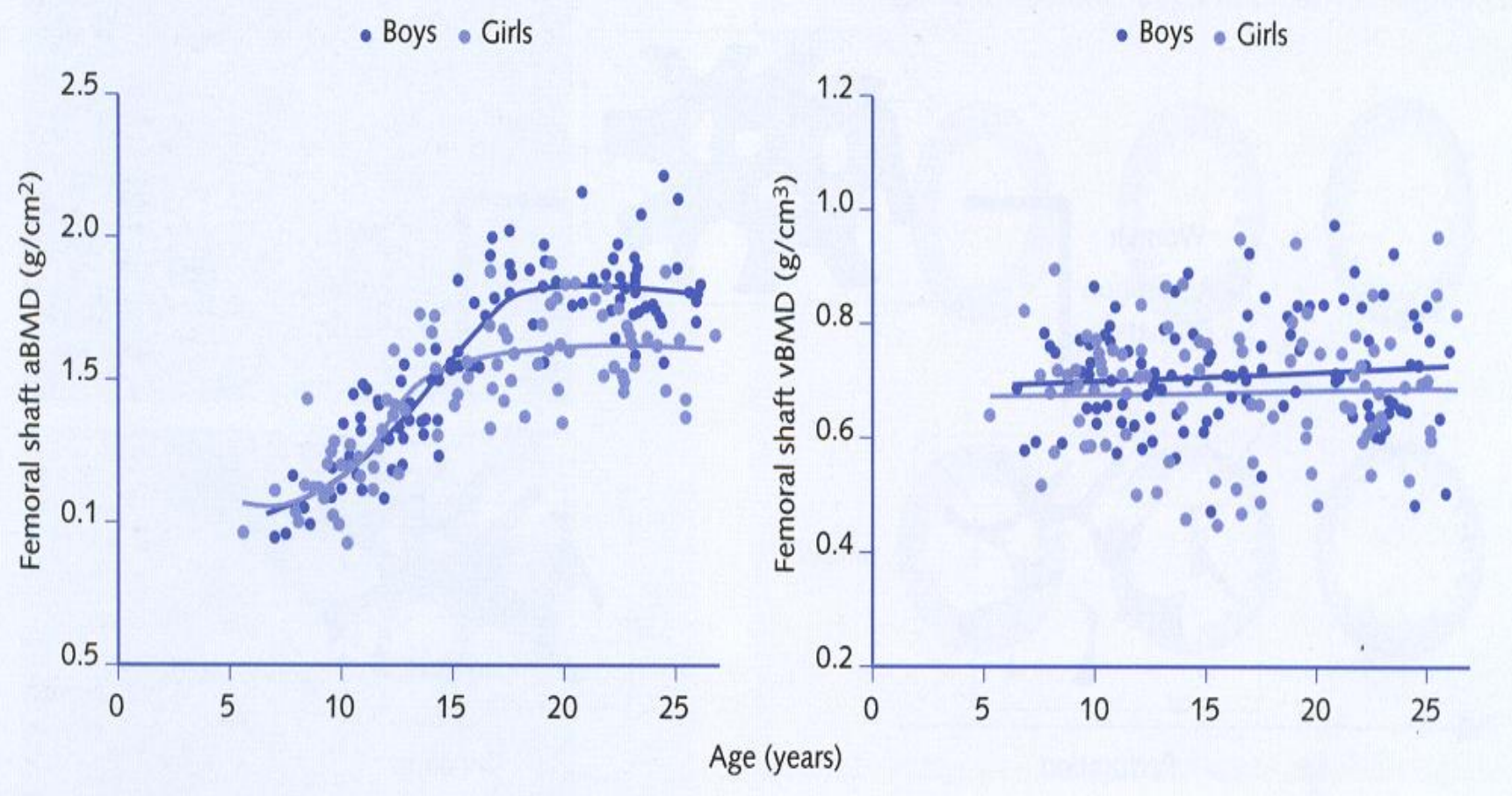


Number ↑



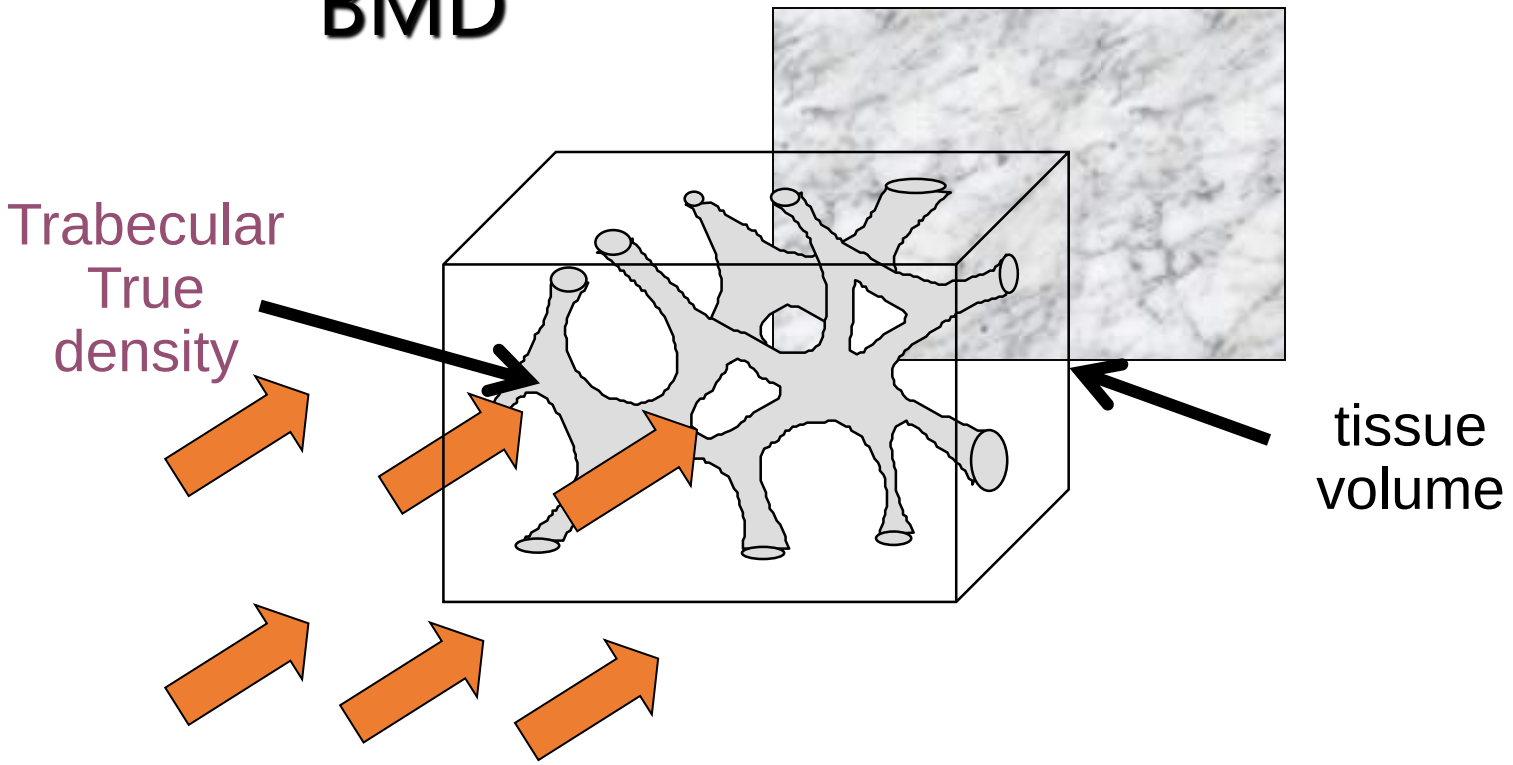
True density ↑

Gender Difference in BMD?

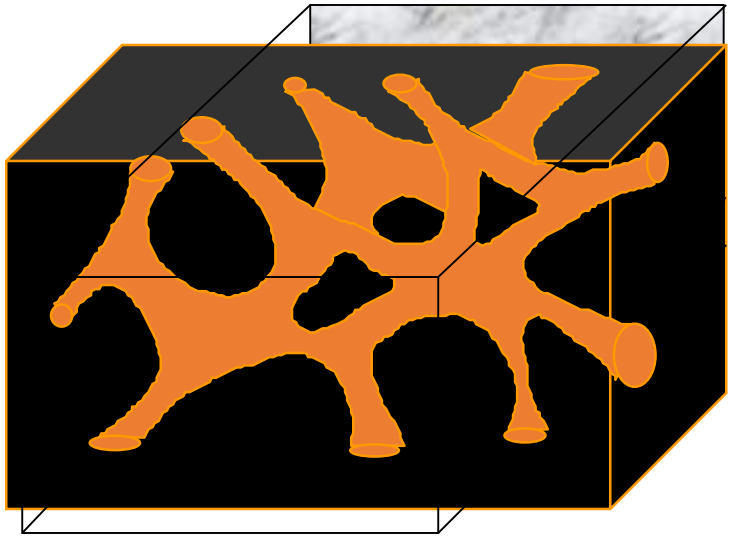


Back to the principle of DEXA

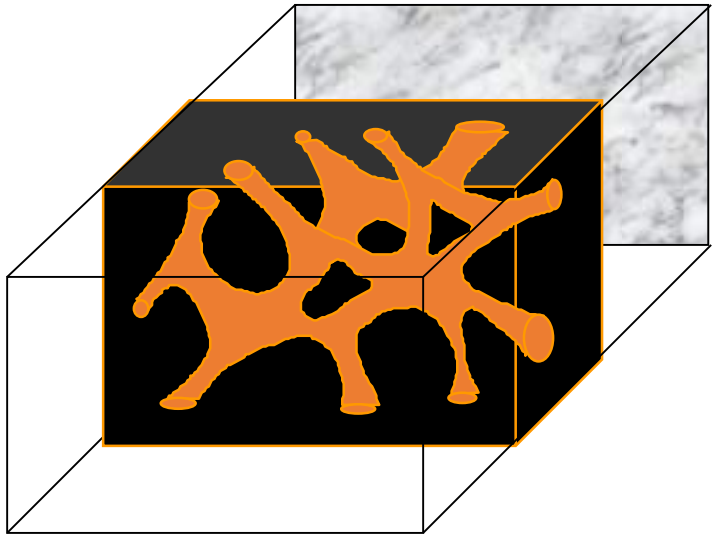
Areal BMD



Same Number
Same Thickness
Same Density



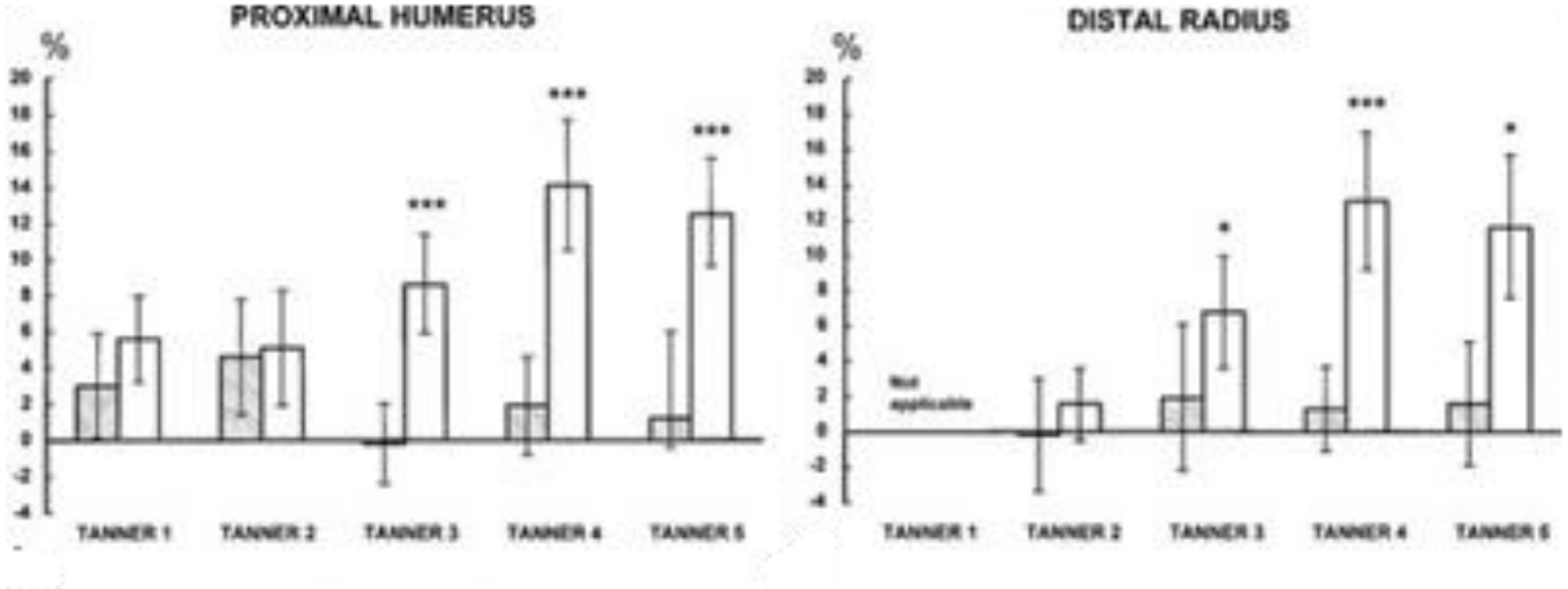
BUT



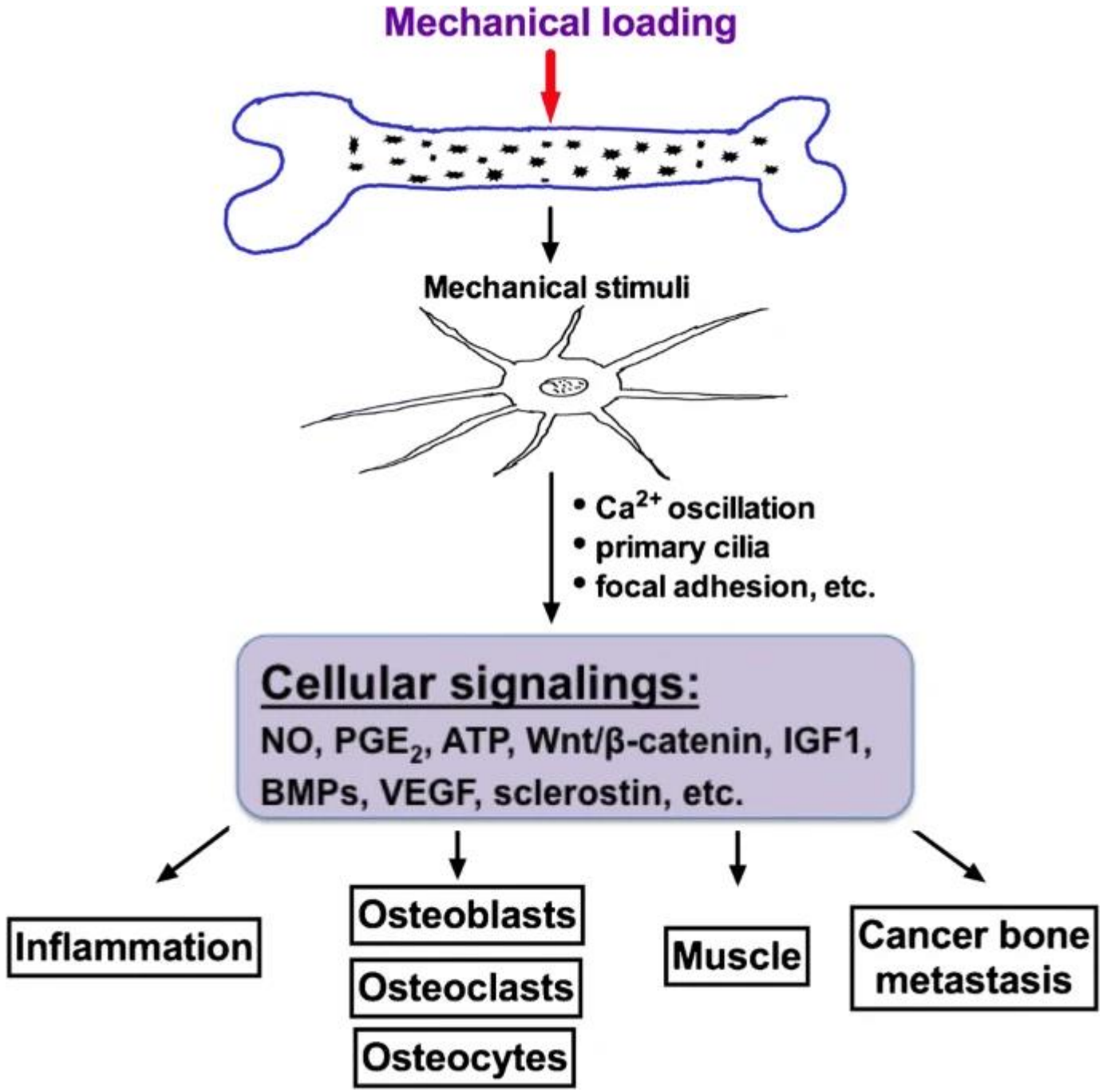
Different BMD

Comparison of both Arm BMDs in controls and tennis players

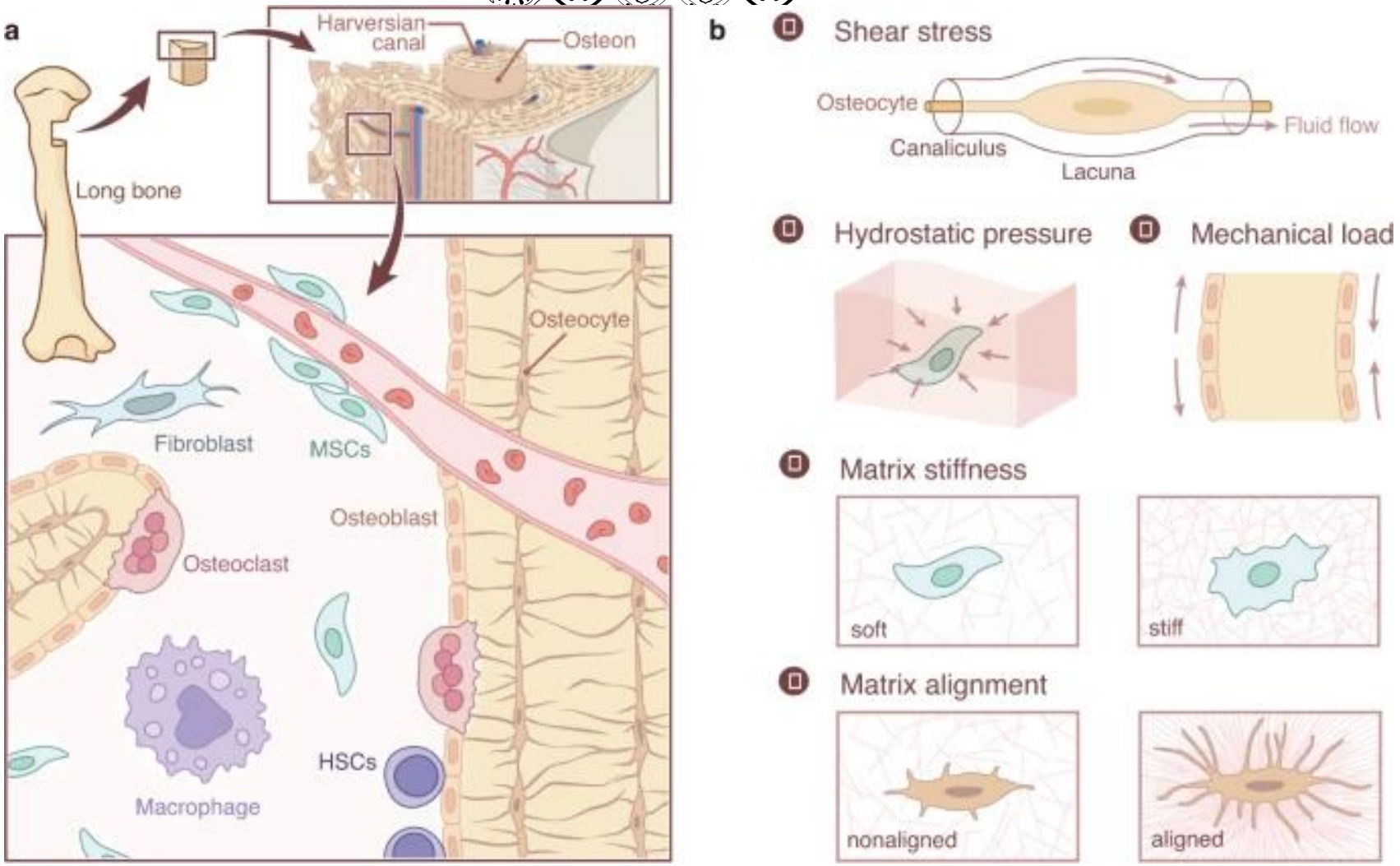
Controls (shaded bars) Tennis players (open bars)



J Bone Miner Res. 1998;13(2):310-9

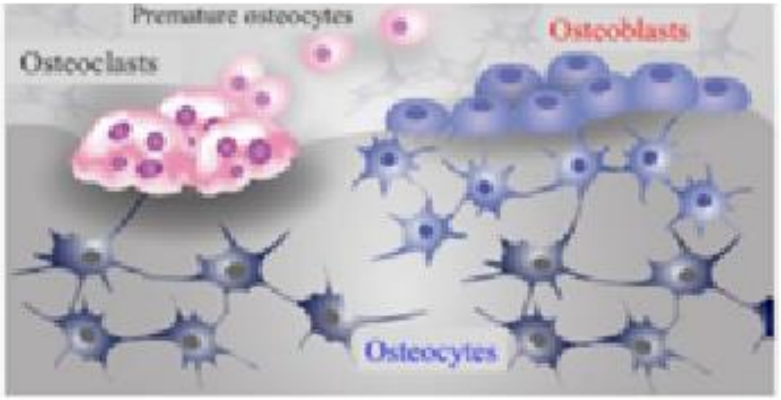

Mechanical loading
Mechanical stimuli
• Ca^{2+} oscillation
• primary cilia
• focal adhesion, etc.
Cellular signalings:
NO, PGE_2, ATP, Wnt/β-catenin, IGF1,
BMPs, VEGF, sclerostin, etc.
Inflammation
Osteoblasts
Osteoclasts
Osteocytes
Muscle
Cancer bone metastasis

The structural basis of mechanical stress in skeletal cells



Bone Res. 2022;10(1):16.

Mechanotransduction
From mechanical Stimuli To Bone formation



Mechanical stress

⇩

Suppression of **sclerostin** in **osteocytes**

⇩

Activation of **Wnt/beta-catenin** signaling in **osteocytes**

⇩

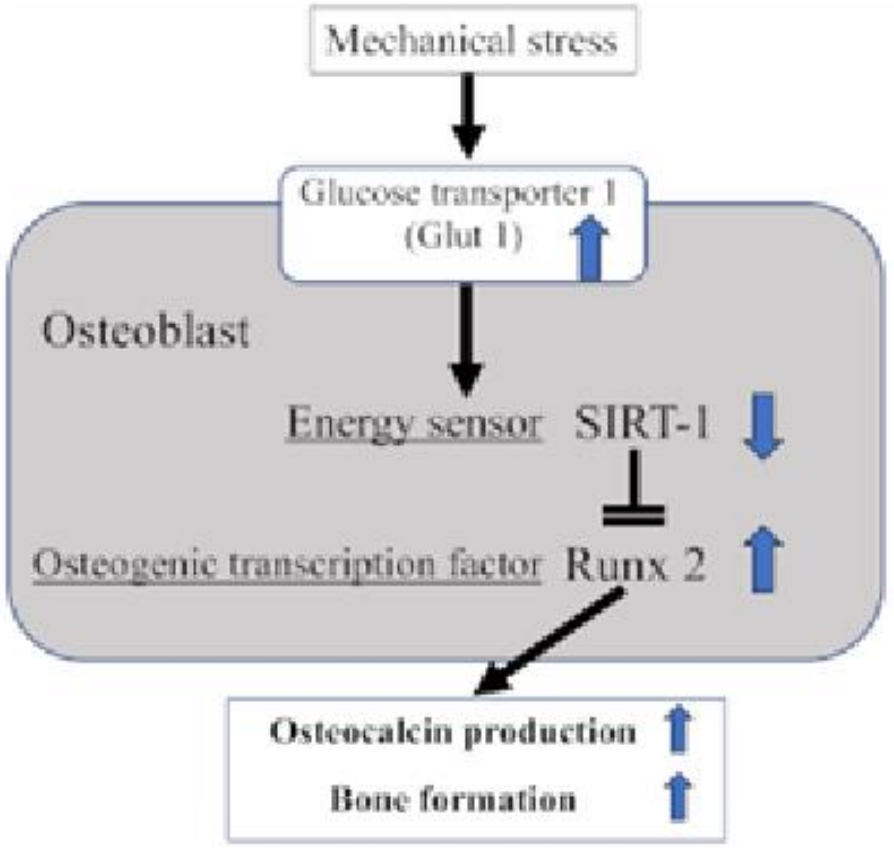
Activation of Wnt signaling in **osteoblasts**

⇩

Osteoblast differentiation

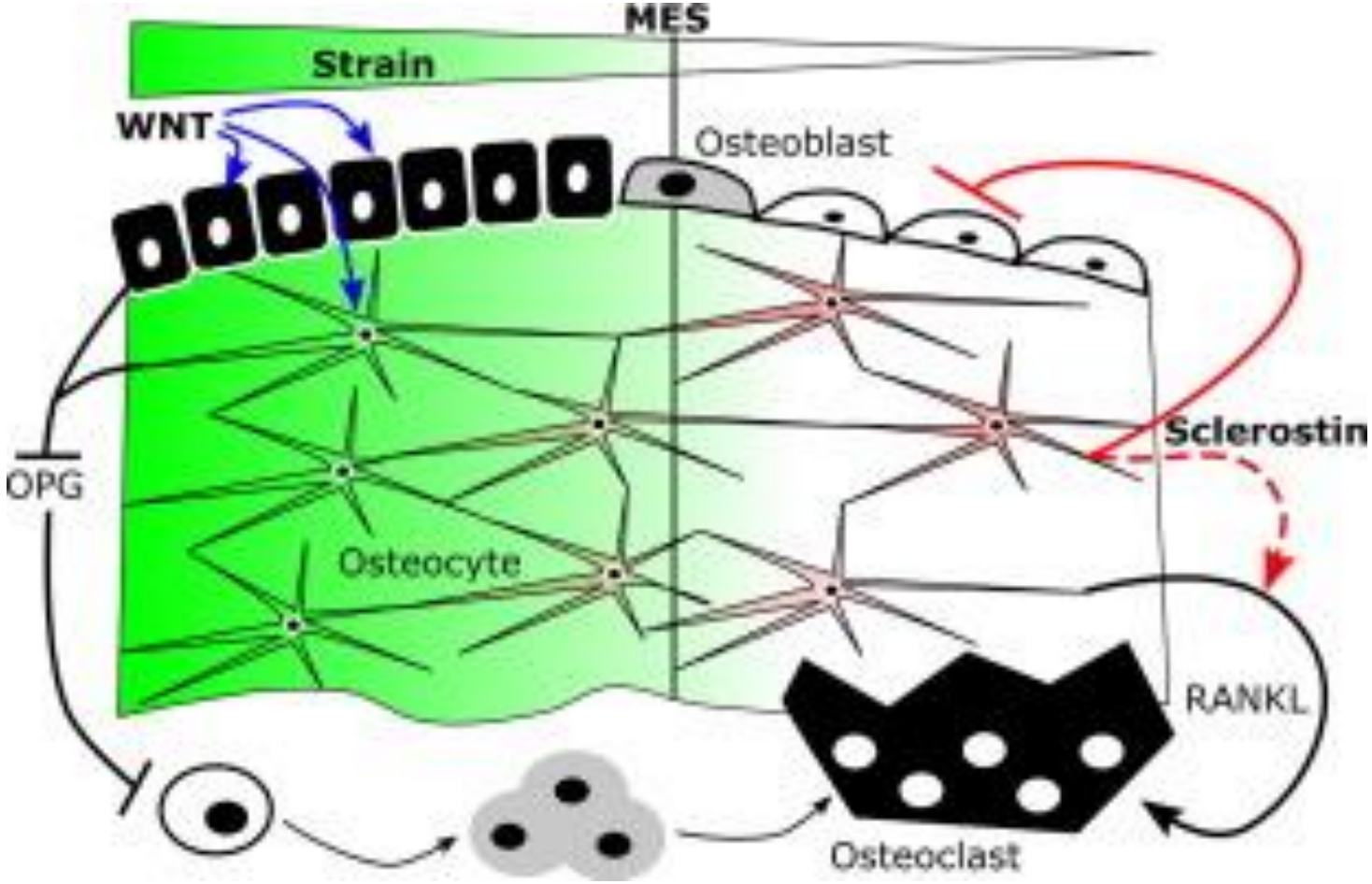
⇩

Bone formation



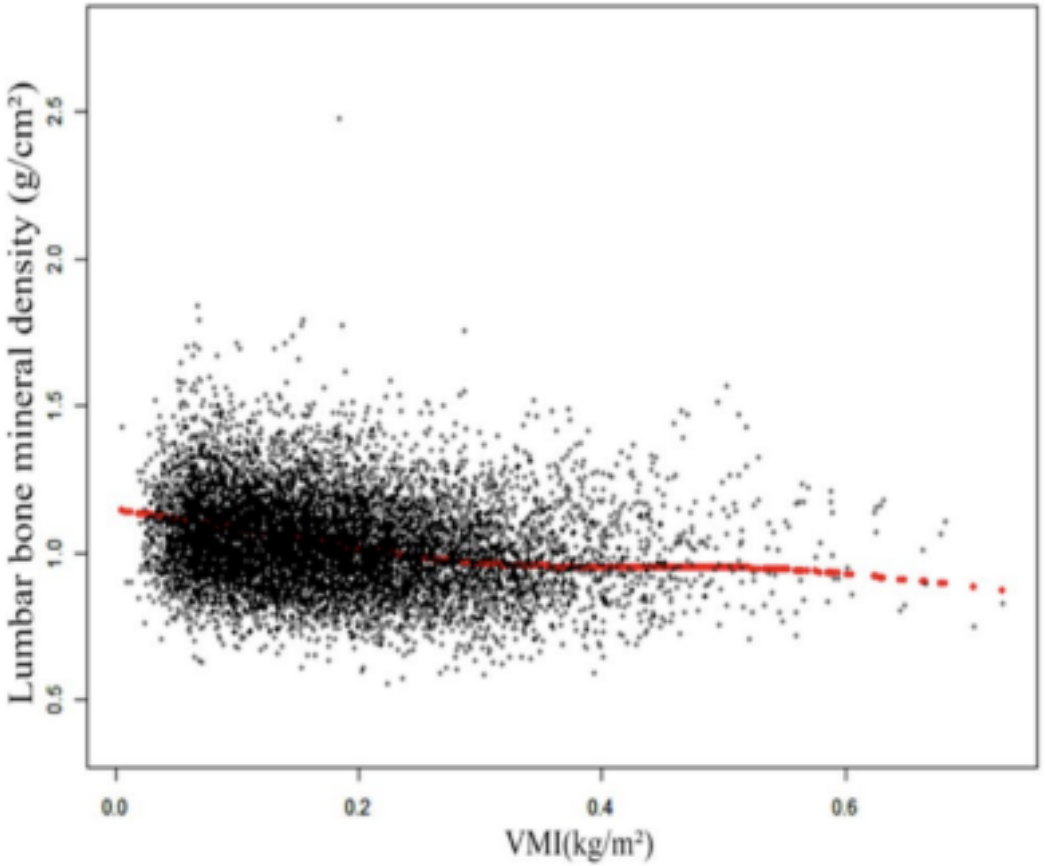
Int. J. Mol. Sci. 2021, 22(16), 9070;

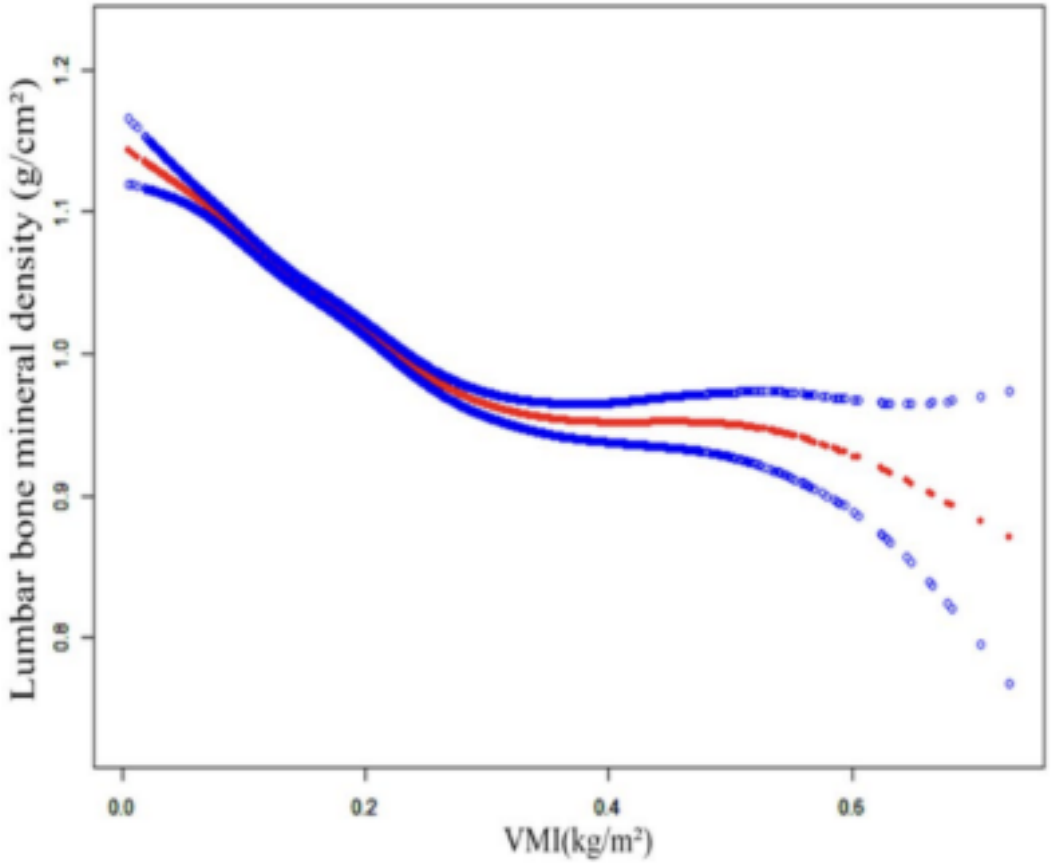
Osteocyte-Mediated Translation of Mechanical Stimuli to Cellular Signaling



Curr Osteoporos Rep 2020 Feb;18(1):67-80

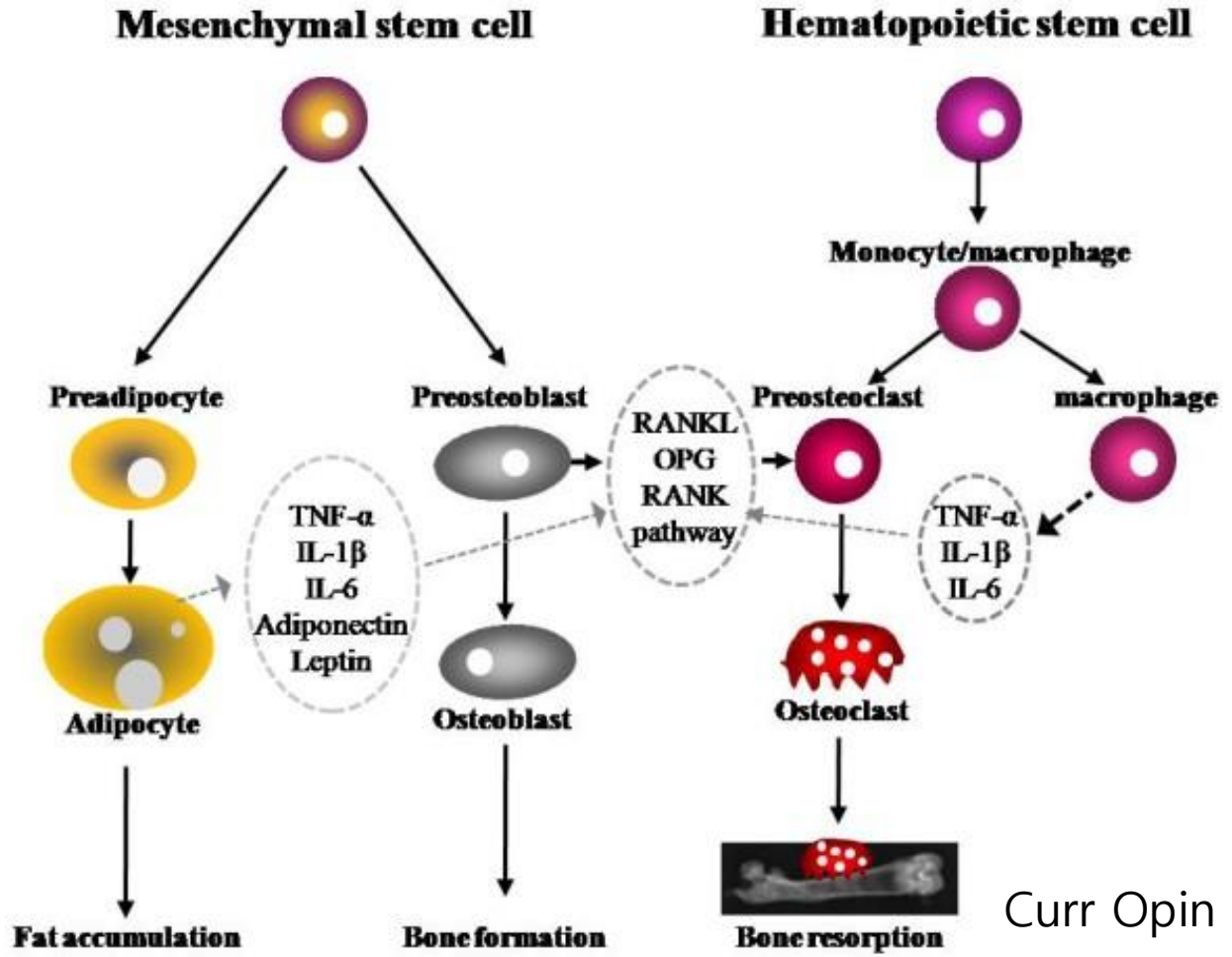
between visceral fat mass index (VMI) and lumbar bone mineral density





Sci Rep. 2023 ;13(1):10682

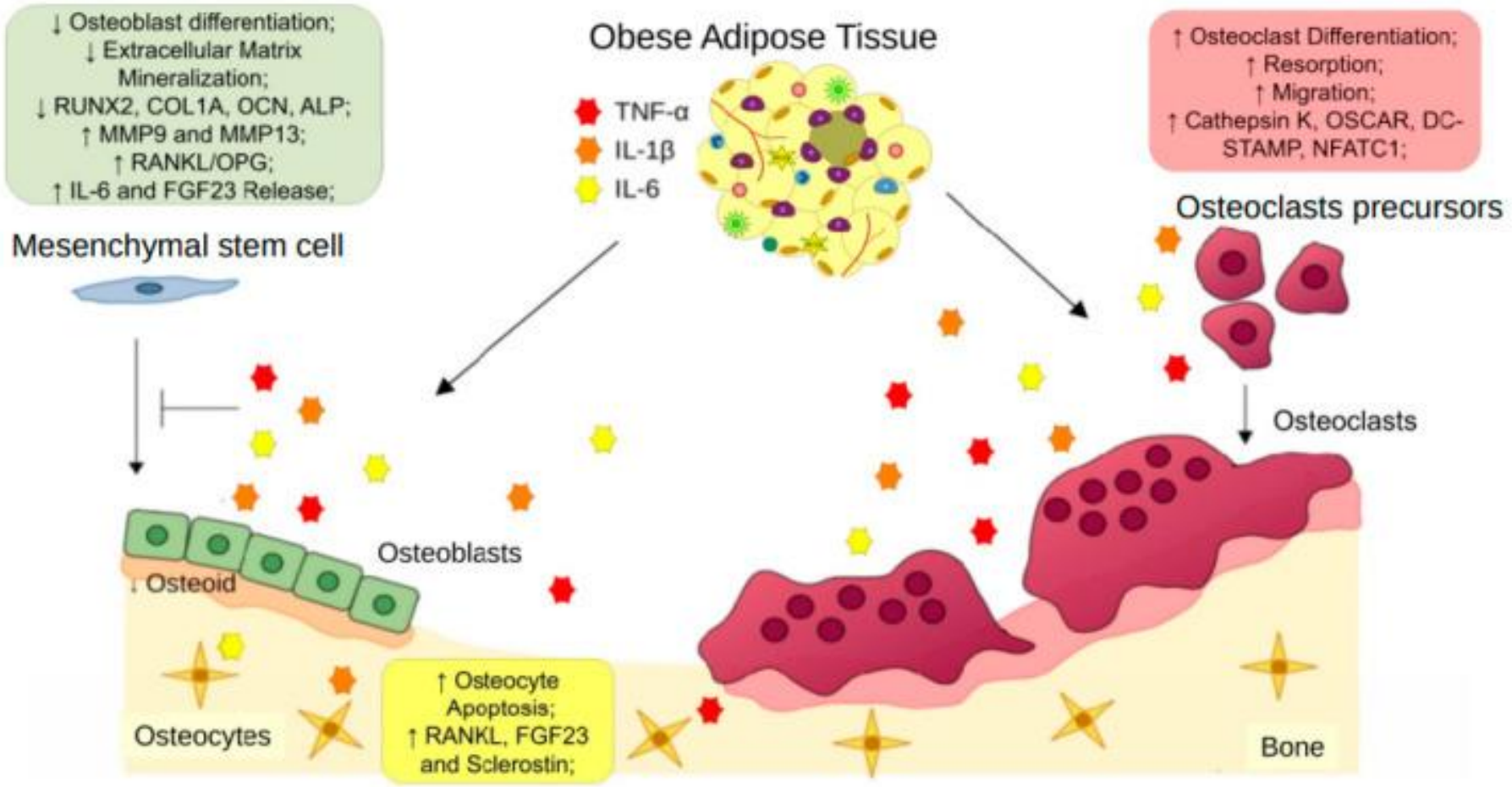
Bone metabolism regulated by adipocytes



Curr Opin Pharmacol. 2004;4(3):290-4.

J Orthop Surg Res. 2011;6:30.

obese adipose tissue-derived proinflammatory cytokines on bone

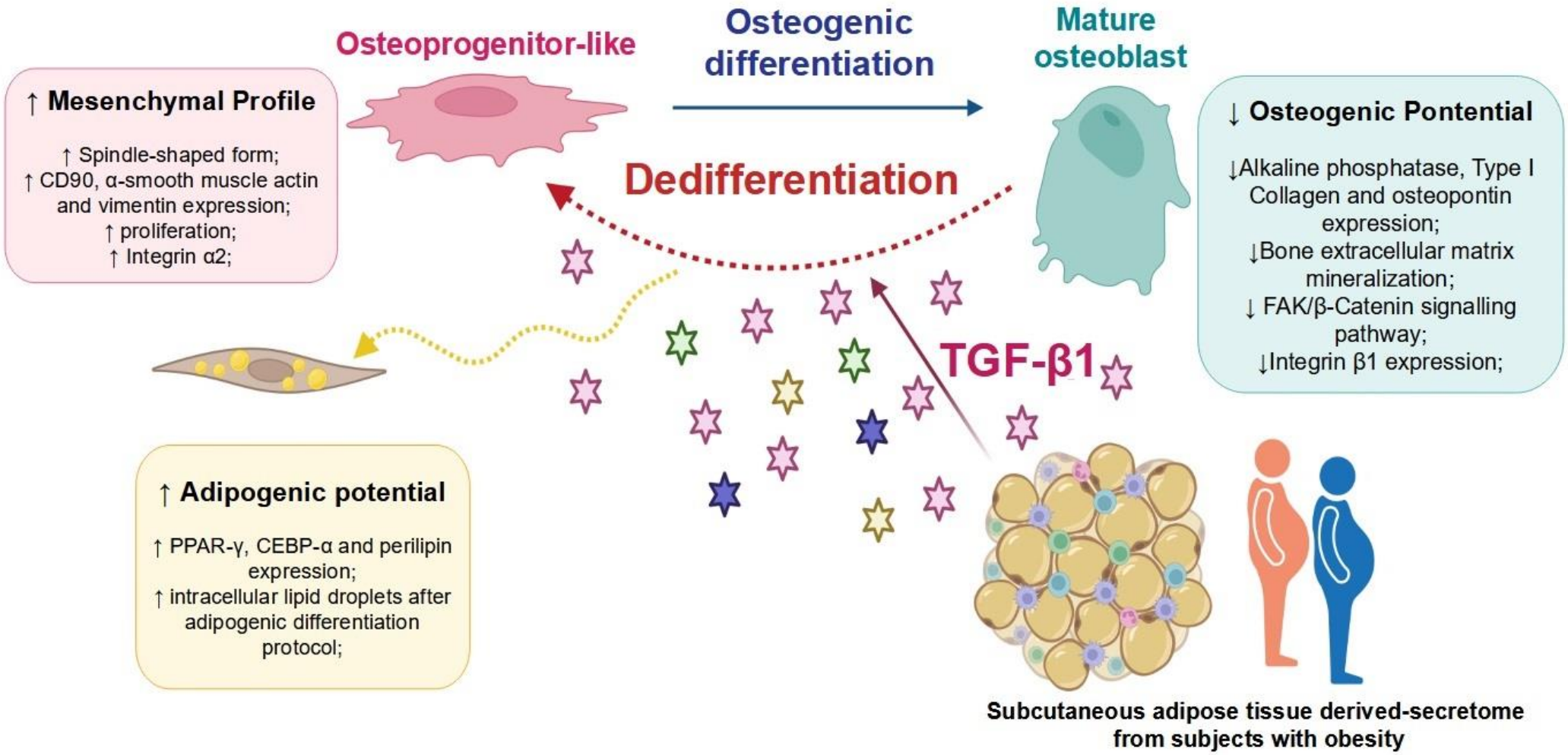


Cells. 2023 ;12(4):521.

of maturer

osteoblast

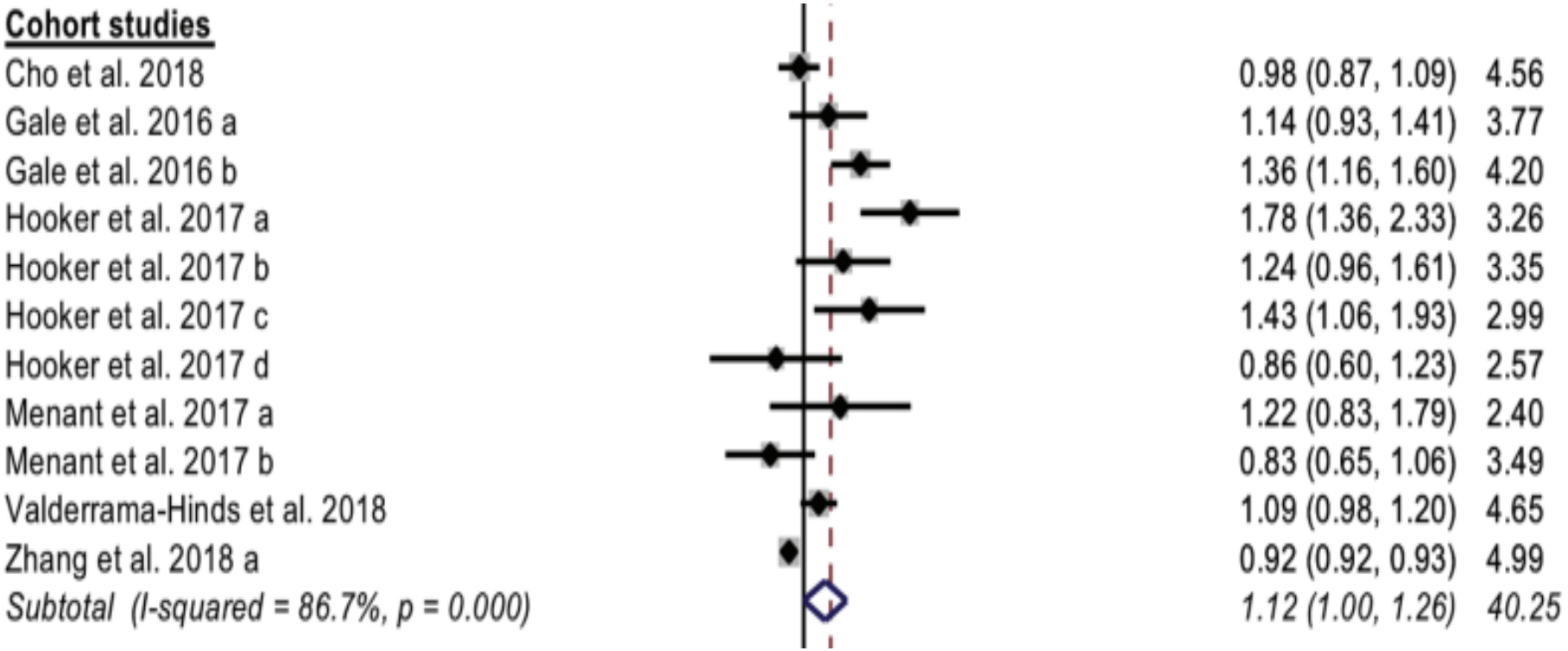
by adipose tissue



Cells 2024, 13(17), 1418

Obesity increases Fall Risk

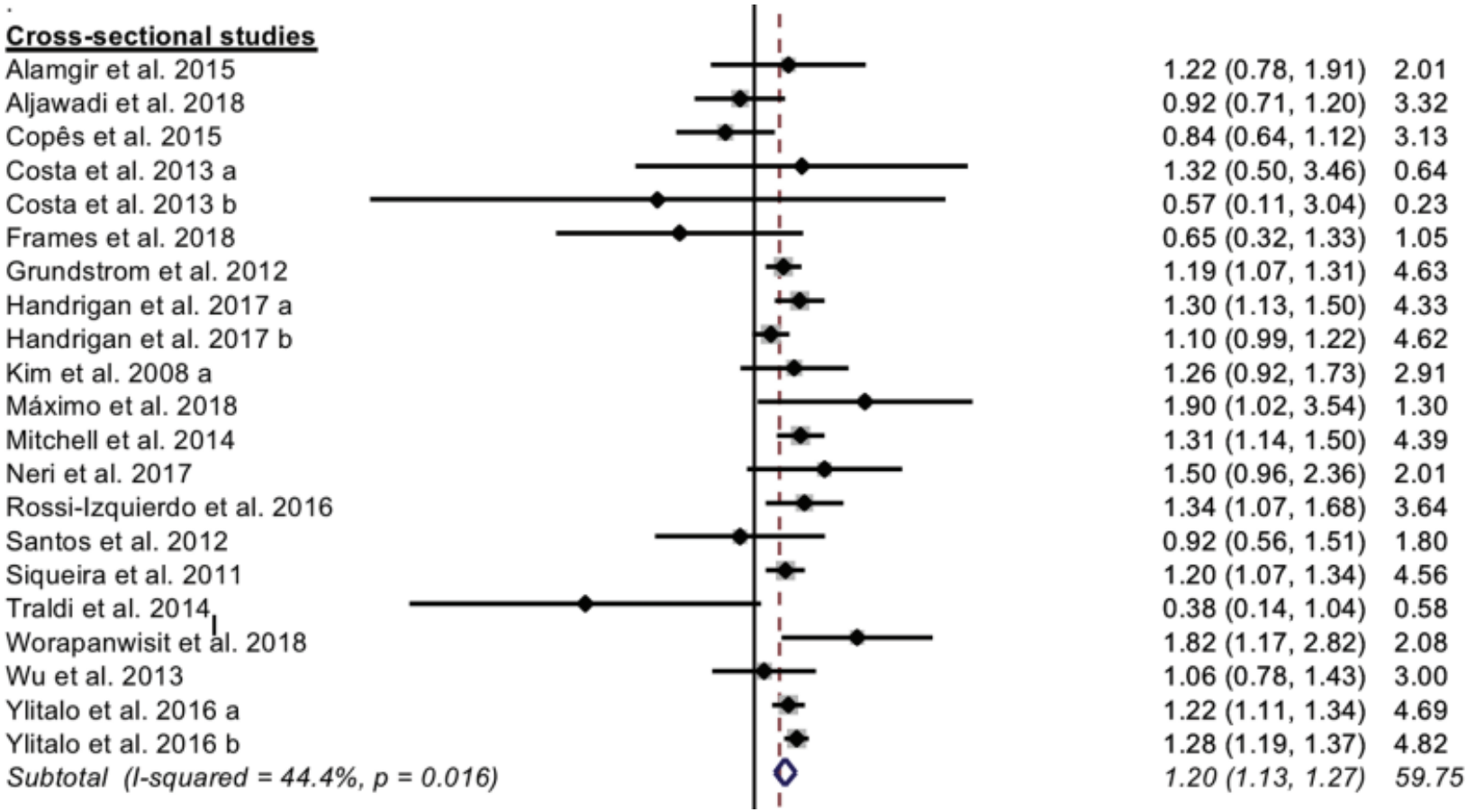
A Systematic Review and Meta-analysis of Observational Studies



J Gerontol A Biol Sci Med Sci. 2020;75(5):952-960.

Obesity increases Fall Risk

A Systematic Review and Meta-analysis of Observational Studies



J Gerontol A Biol Sci Med Sci. 2020;75(5):952-960.

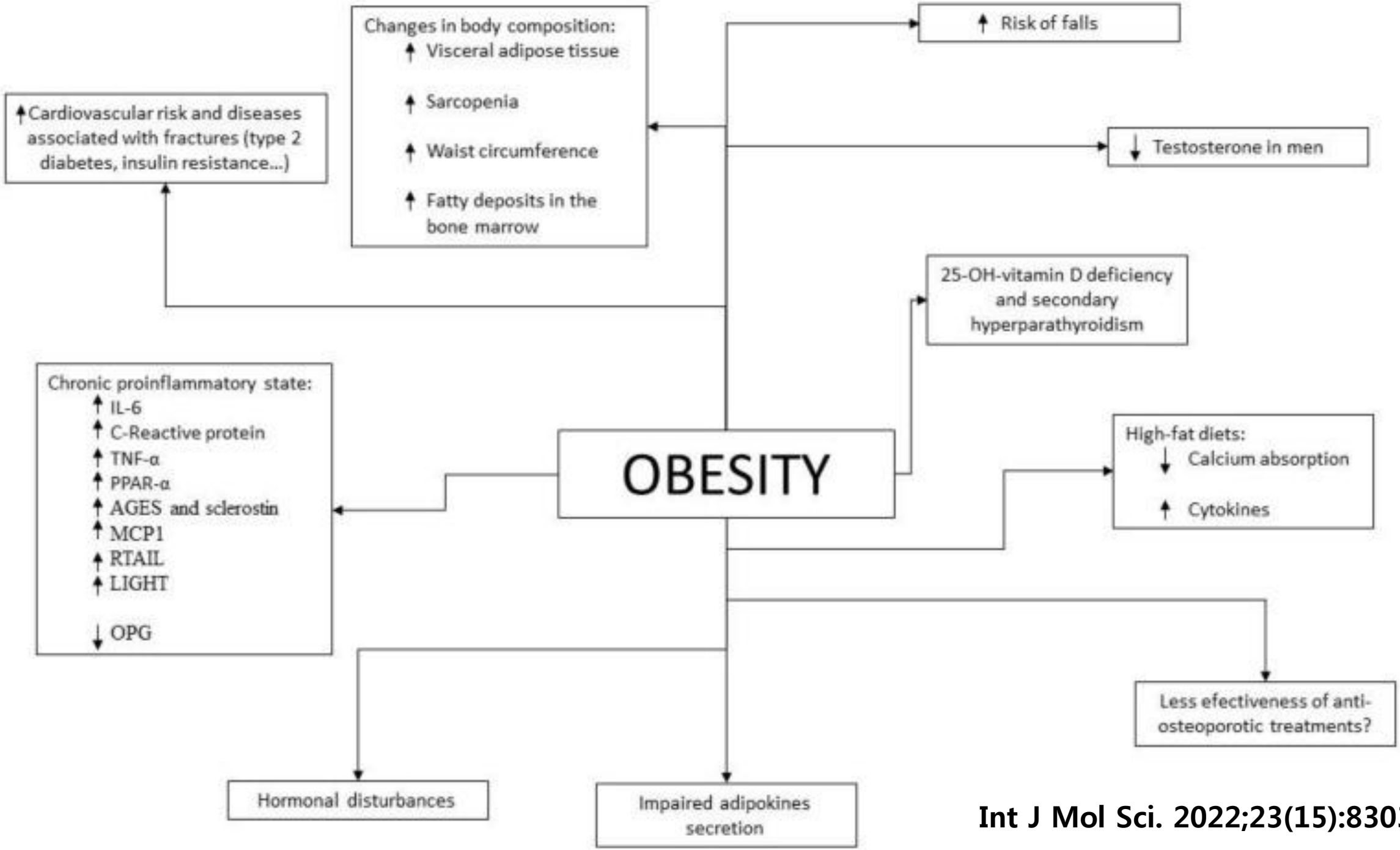
Paradoxical Effects of Excessive Body Weight on Bone health

Positive signals (↑ BMD)

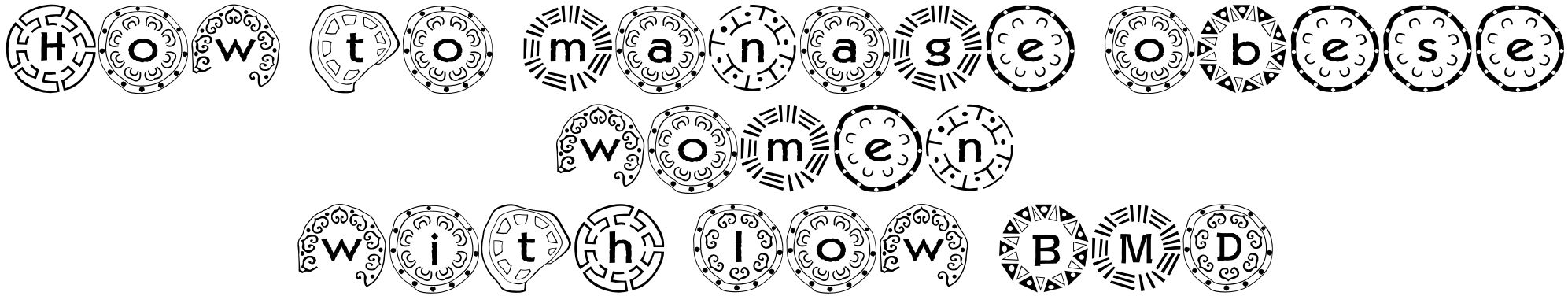
- Increased bone size
- Mechanical load
- Conversion of androgen to estrogen
- Increased levels of free sex-hormones
- Secretion of insulin and amylin by β-cells
- Increased glucagon-like peptide-2
- Leptin (?)
- Adiponectin (?)

Negative signals (↓ BMD)

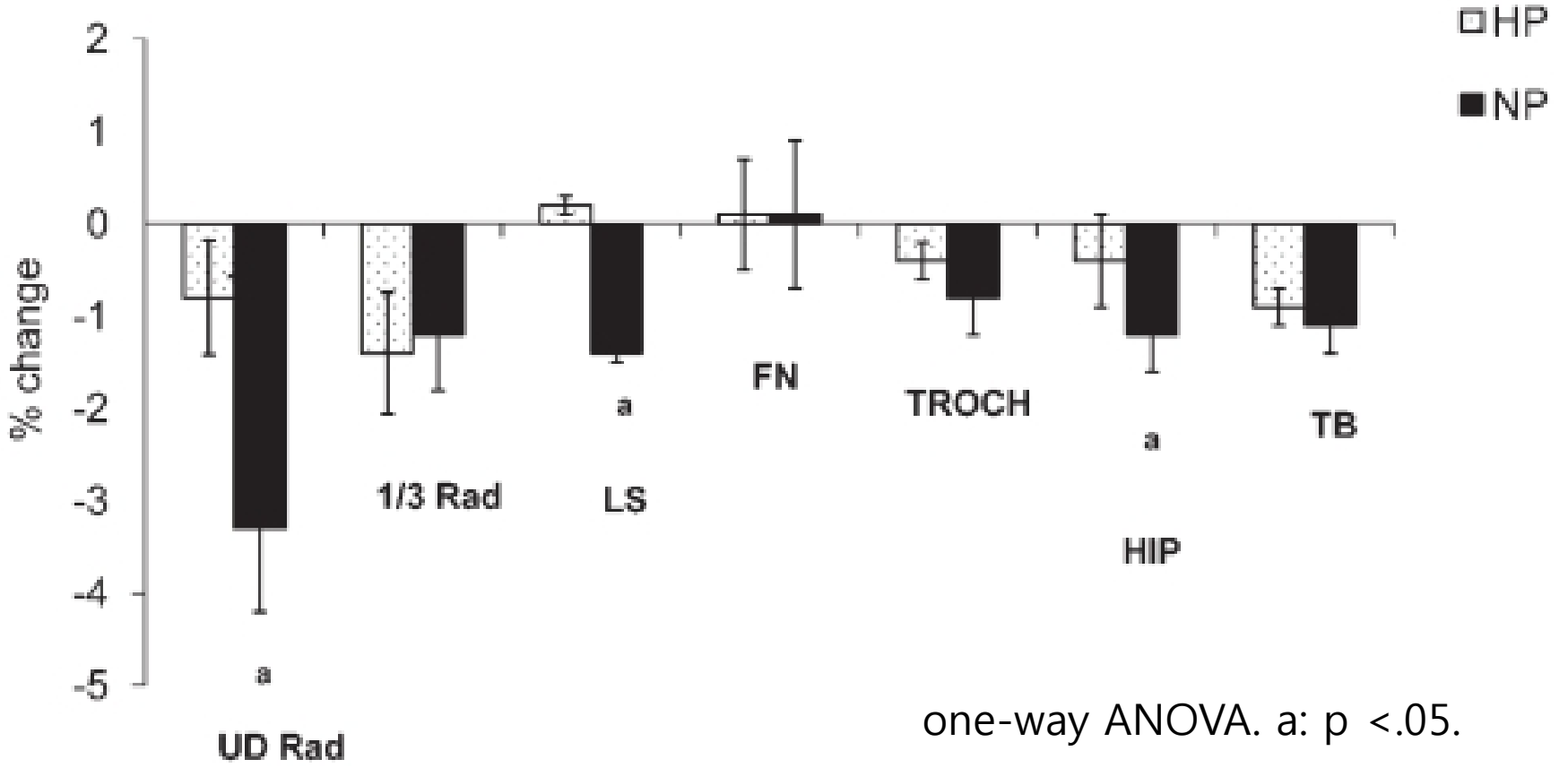
- Reactive oxygen Species
- Proinflammatory cytokines (IL-6, TNF-α)
- Leptin (?)
- Adiponectin (?)
- Reduced 25OH-D levels
- Increased PTH levels
- Increased Fall Risk
- Increased T2DM



Int J Mol Sci. 2022;23(15):8303


How to manage obese
women
with low BMD

The % change in BMD after weight reduction with High protein diet



one-way ANOVA. a: p <.05.

J Bone Miner Res. 2010;26(6):1339–1348

turnover markers after weight

	Weight maintenance, *n* = 17	Moderate weight loss, *n* = 39	Severe weight loss, *n* = 17	*P*-value[1]
Body weight (kg)	0.3±1.3[a]	−5.6±2.7[b]	−37.4±9.3[c]	<0.0001
Serum Osteocalcin (ng/ml)	0.3±2.2[a]	−0.4±1.2[a]	3.7±2.5[b]	<0.0001
Serum NTx (nM BCE)	−1.0±3.9[a]	−0.8±4.7[a]	9.8±4.4[b]	<0.0001
Urinary PYD (nM/day)	−8.2±77.3[a]	−13.7±122.9[a]	351.1±212.9[b]	<0.0001
Urinary DPD (nM/day)	−4.5±44.4[a]	−1.3±48.6[a]	72.1±63.3[b]	<0.0001
Urinary calcium (mg/day)	−4.6±58.3[a]	−16.9±77.5[a]	−83.0±88.3[b]	0.0070

J Expo Sci Environ Epidemiol. 2008;19(1):90–96.

turnover markers after bariatric

Bone variables						
vBMD, mg/cm^3[a]	n/a	189.8 (36.7)	–	187.7 (47.6)	191.0 (32.0)	0.92
VBM fat, %[a]	n/a	37.8 (20.8)	–	39.5 (21.5)	36.8 (21.1)	0.86
CTX, ng/mL	0.52 (0.37)	0.32 (0.18)	**0.005**	0.31 (0.24)	0.32 (0.13)	0.28
PINP, ng/mL	54.1 (39.7)	38.2 (15.1)	**0.027**	39.2 (19.1)	37.5 (11.3)	0.63
TRAcP5b, U/L	2.6 (0.9)	2.4 (0.6)	0.65	2.5 (0.7)	2.4 (0.6)	1.00
TRAcP5a, U/L	2.2 (0.6)	2.2 (0.5)	0.84	2.3 (0.6)	2.1 (0.4)	0.54
TotalOC, ng/mL	8.4 (3.7)	5.2 (1.9)	**<0.001**	5.0 (2.2)	5.4 (1.7)	0.54
ucOC, ng/mL	2.4 (1.9)	1.7 (1.1)	0.37	1.7 (1.2)	1.6 (1.1)	0.67
CTX/TRAcP5b ratio	0.19 (0.08)	0.13 (0.07)	**<0.001**	0.12 (0.08)	0.14 (0.06)	0.14
PINP/CTX, ratio	112 (33)	143 (58)	**0.018**	164 (74)	127 (37)	0.10
fS-Ca-ion, mmol/L	1.22 (0.03)	1.22 (0.05)	0.27	1.21 (0.06)	1.22 (0.03)	0.27
S-Phosphate, mmol/L	1.03 (0.13)	0.98 (0.15)	0.16	0.96 (0.18)	0.99 (0.12)	0.71
S-25(OH)D, nmol/L[b]	66 (17)	59 (18)	0.13	53 (13)	62 (19)	0.30

Bone. 2017:95:47-54

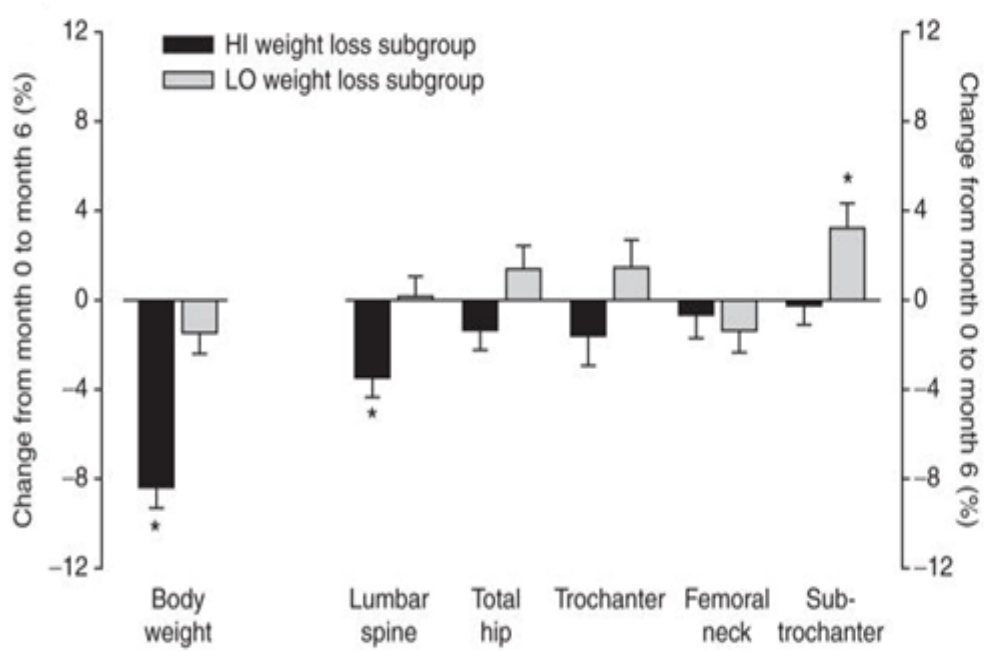
BMD change and prevalence of osteoporosis 30 years after weight change

Weight change category	BMD* (g/cm^2)†		BMD (g/cm^2)‡		Osteoporosis‡ (%)
	Mean	95% CI*	Mean	95% CI	
Loss of ≥10%	0.899	0.870, 0.927	0.908	0.880, 0.937	15.1
Loss of 5–<10%	0.927	0.905, 0.949	0.930	0.908, 0.952	14.1
Loss or gain of <5%	0.963	0.953, 0.973	0.963	0.953, 0.973	6.2
Gain of 5–<10%	0.999	0.985, 1.013	0.997	0.983, 1.012	2.6
Gain of ≥10%	1.009	0.996, 1.021	1.007	0.995, 1.019	0.6

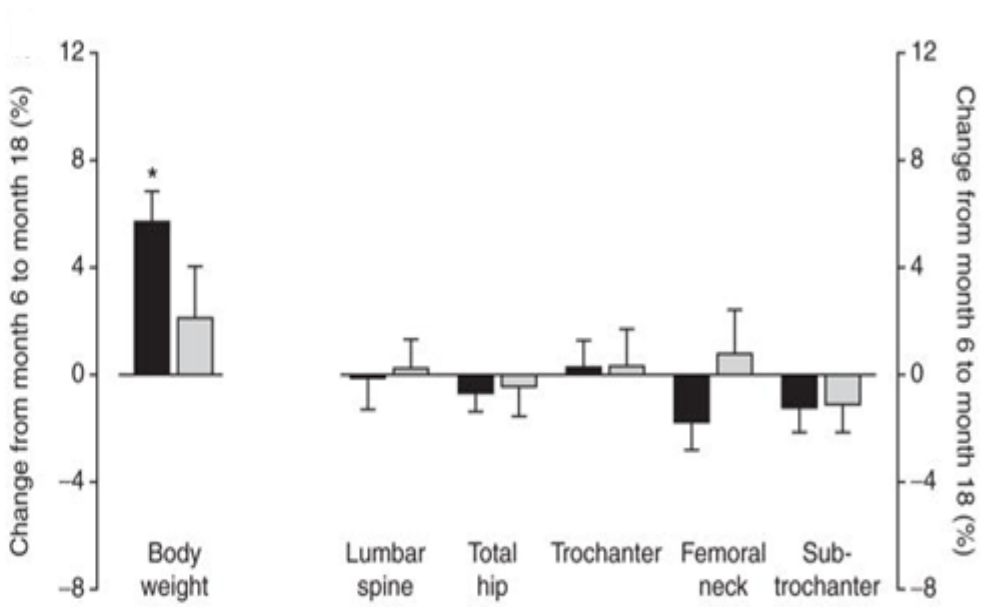
Am J Epidemiol. 2008 ;168(4):454-60

Weight regain and BMD change

0 to 6 Months Since weight loss



6 to 18 Months Since weight loss



Obesity (Silver Spring) 2011;19:2345–50

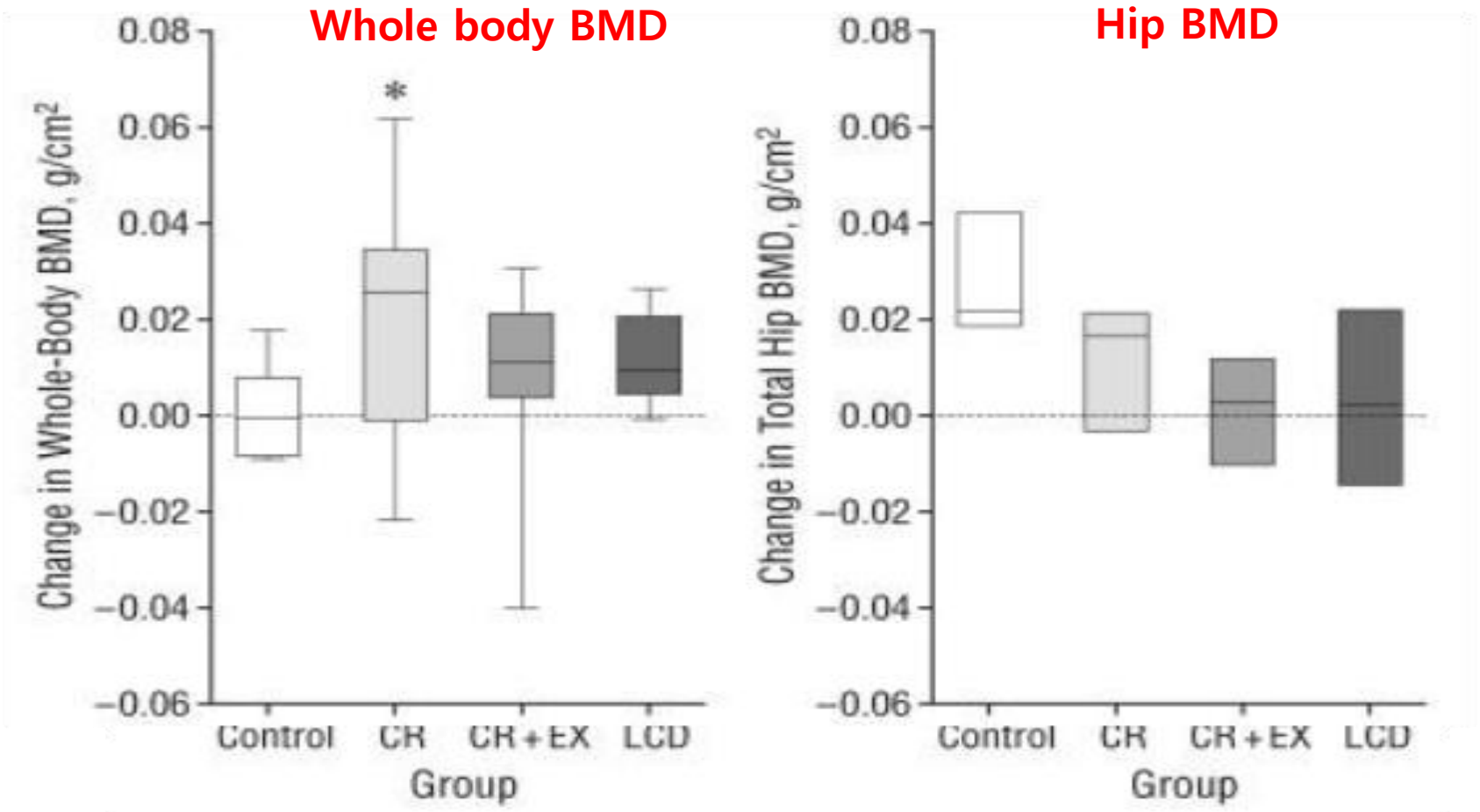
Incidence and adjusted relative risks of hip fracture among white women aged 50—74 years (y) (e) a r (s)

NHANES I Epidemiologic Follow-up Study (NHEFS),

Weight change from maximum	Age at baseline (yrs)									
	Aged 50–64 years (n = 853)					Aged 65–74 years (n = 1327)				
	Mean (SD) weight loss, lb	Hip fractures	Person-years	Incidence rate[a]	RR (95% CI)[b]	Mean (SD) weight loss, lb	Hip fractures	Person-years	Incidence rate[a]	RR (95% CI)[b]
Loss <5%[a]	1.6 (1.6)	9	6691	1.34	1.0	1.7 (1.7)	38	7087	5.36	1.0
Loss 5–<10%	7.6 (1.5)	5	3670	1.36	0.96 (0.32–2.93)	7.5 (1.4)	30	3903	7.69	1.50 (0.93-2.43)
Loss ⩾10%	18.2 (6.9)	16	4655	3.44	2.54 (1.10-5.86)	18.3 (7.0)	73	7168	10.18	2.04 (1.37-3.04)
Total		30	15016	2.00	–		141	18158	7.76	–

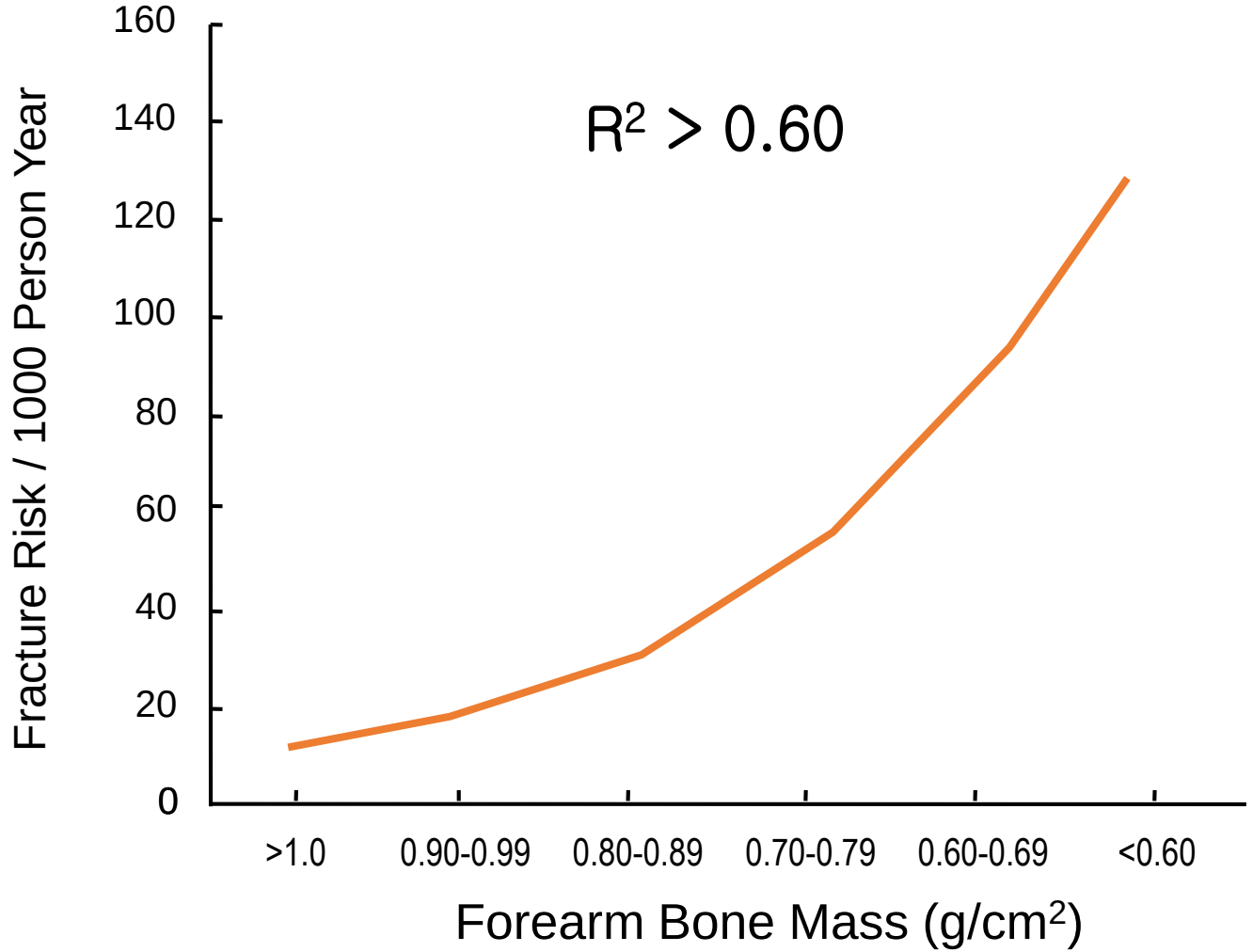
Osteoporos Int. 2001;12(9):763-8.

BMD changes after weight reduction in young women



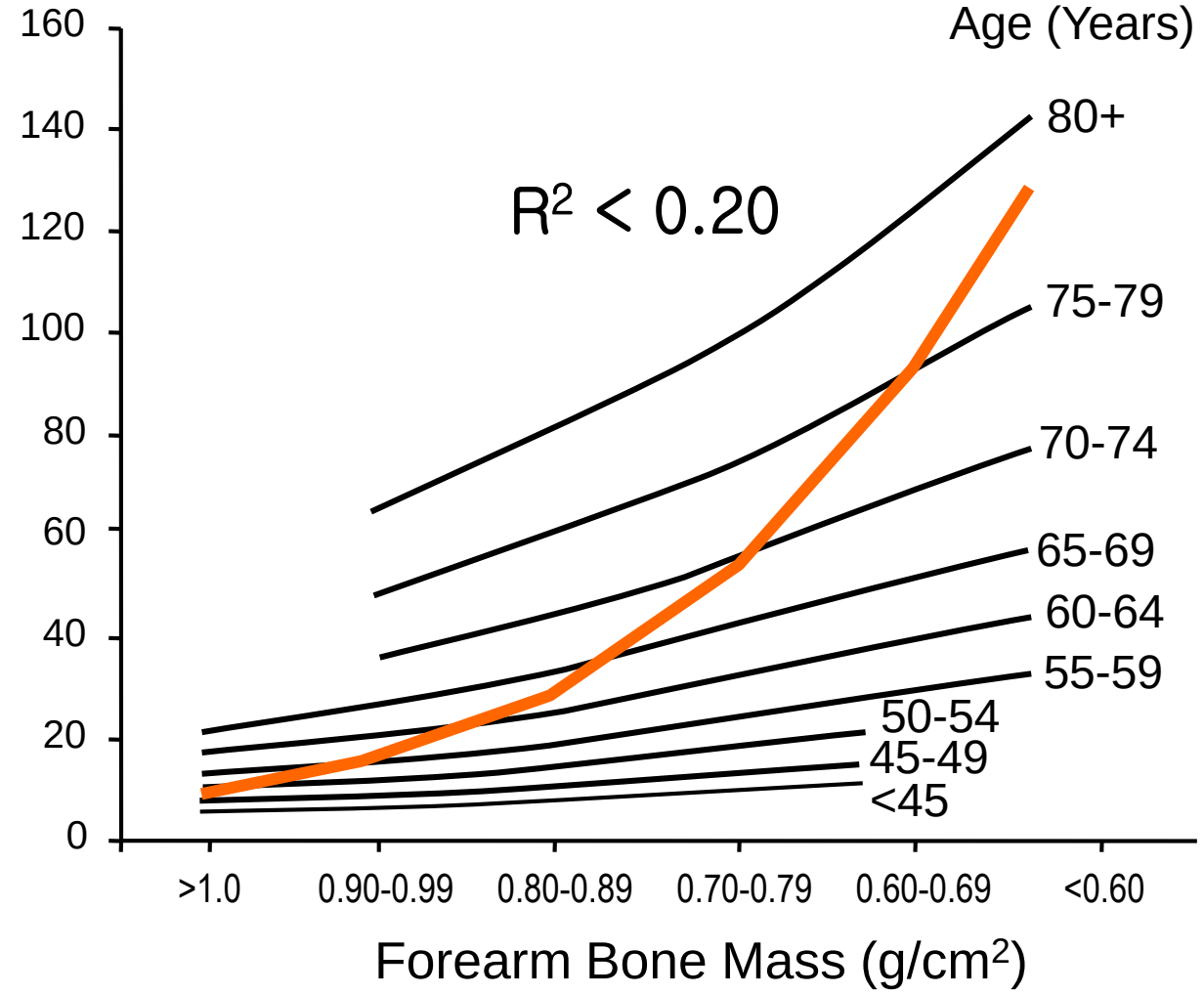
Arch Intern Med. 2008;168(17):1859–1866

Bone Mass and Fracture Rate



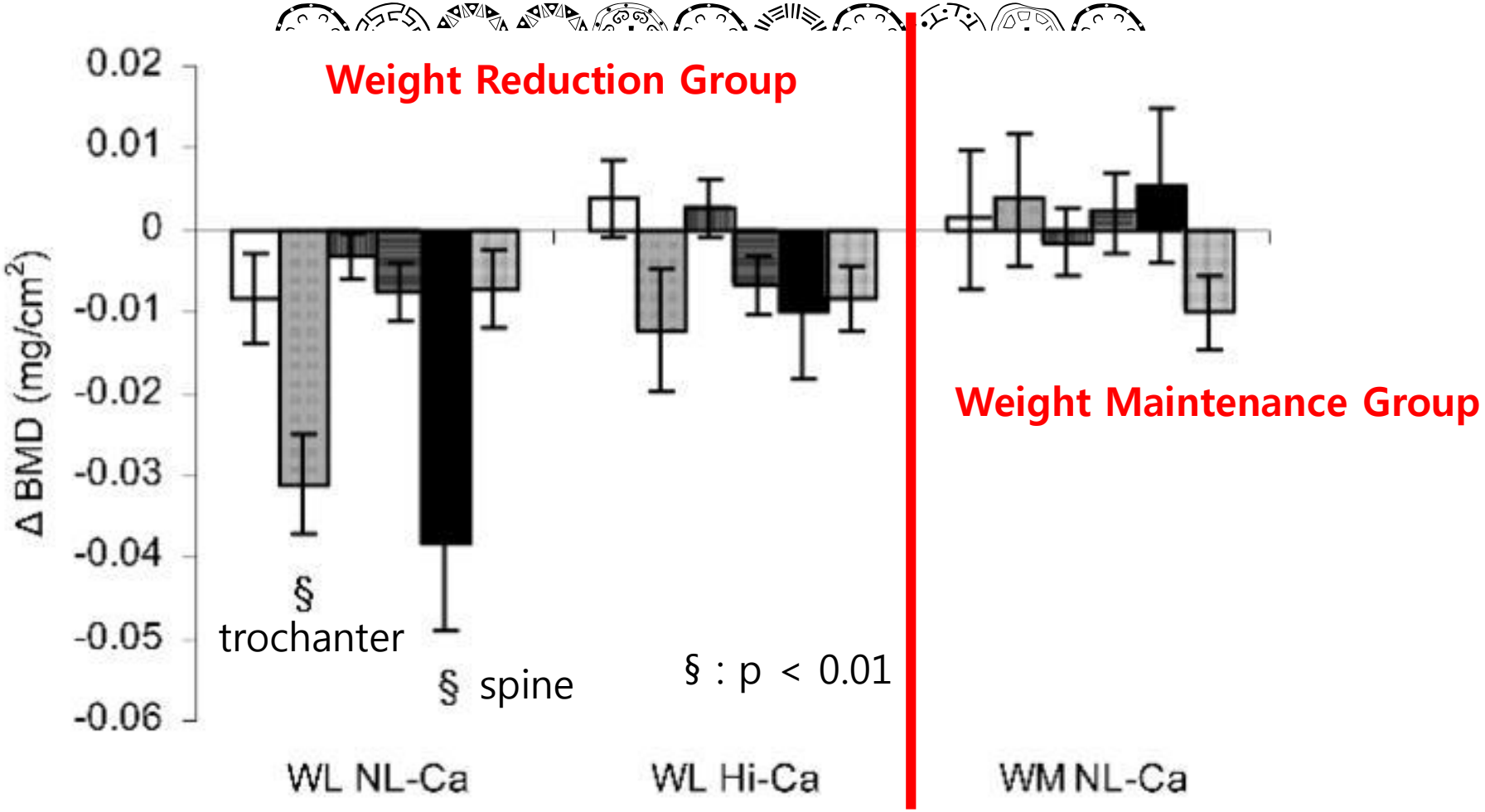
Hui SL et al. *J Clin Invest* 81:1804-1809; 1988

In young Age, BMD does not predict Fracture Risk



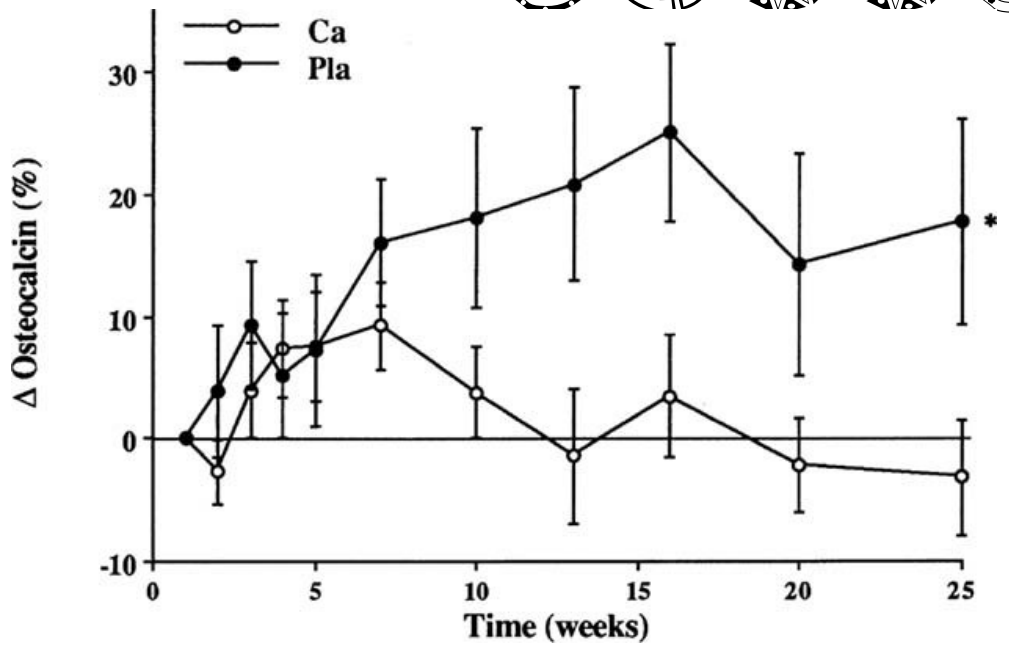
Hui SL et al. *J Clin Invest* 81:1804-1809; 1988

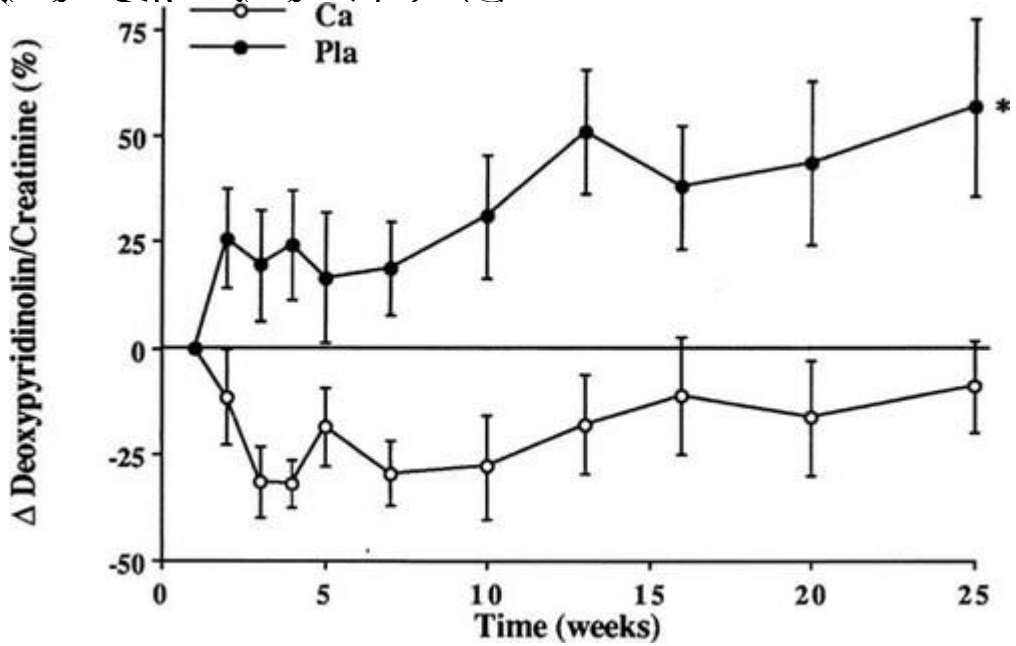
BMD change after 6 Month weight Reduction with increased calcium



J Bone Miner Res. 2004;20(3):455–463

change during weight reduction with calcium supplement

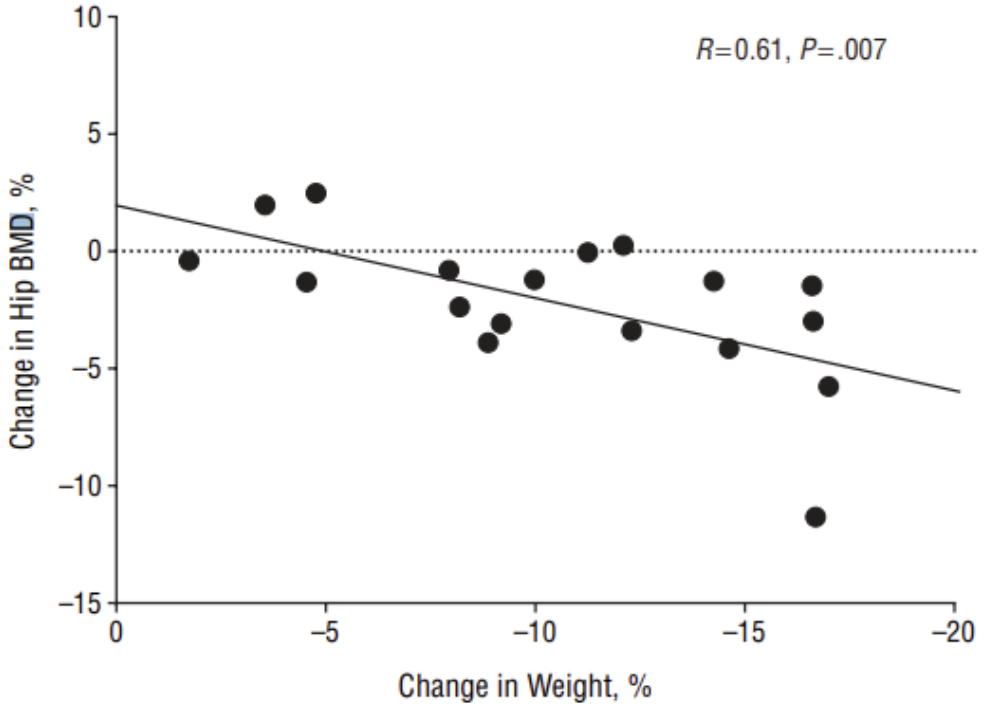




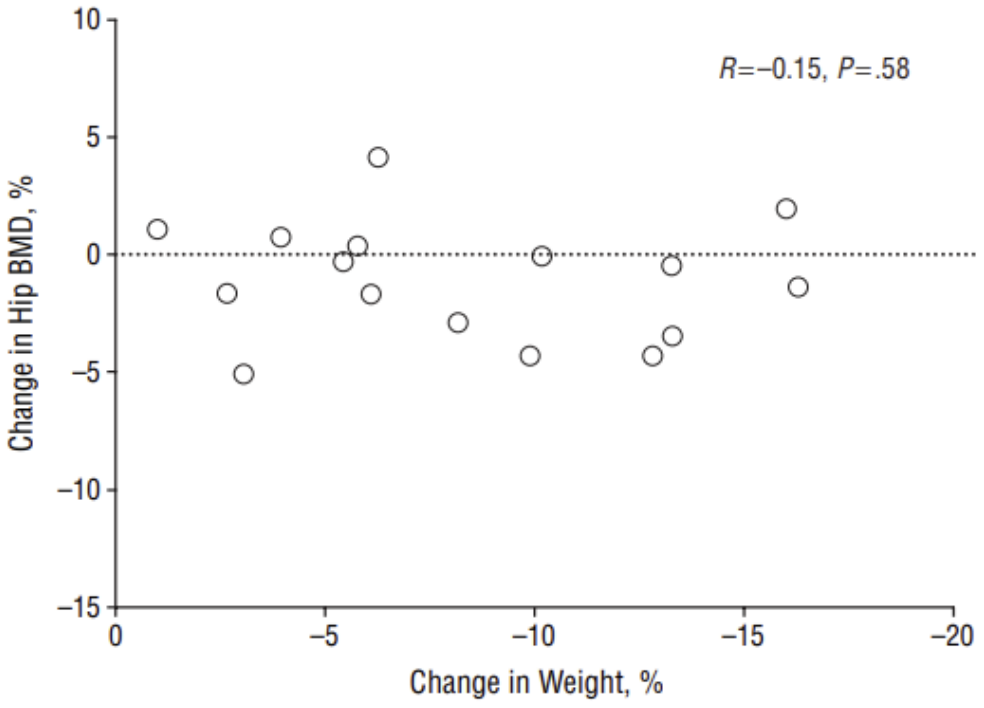
J Bone Miner Res. 1998 Jun;13(6):1045-50

BMD change after weight reduction with or without exercise

Caloric restriction-induced weight loss



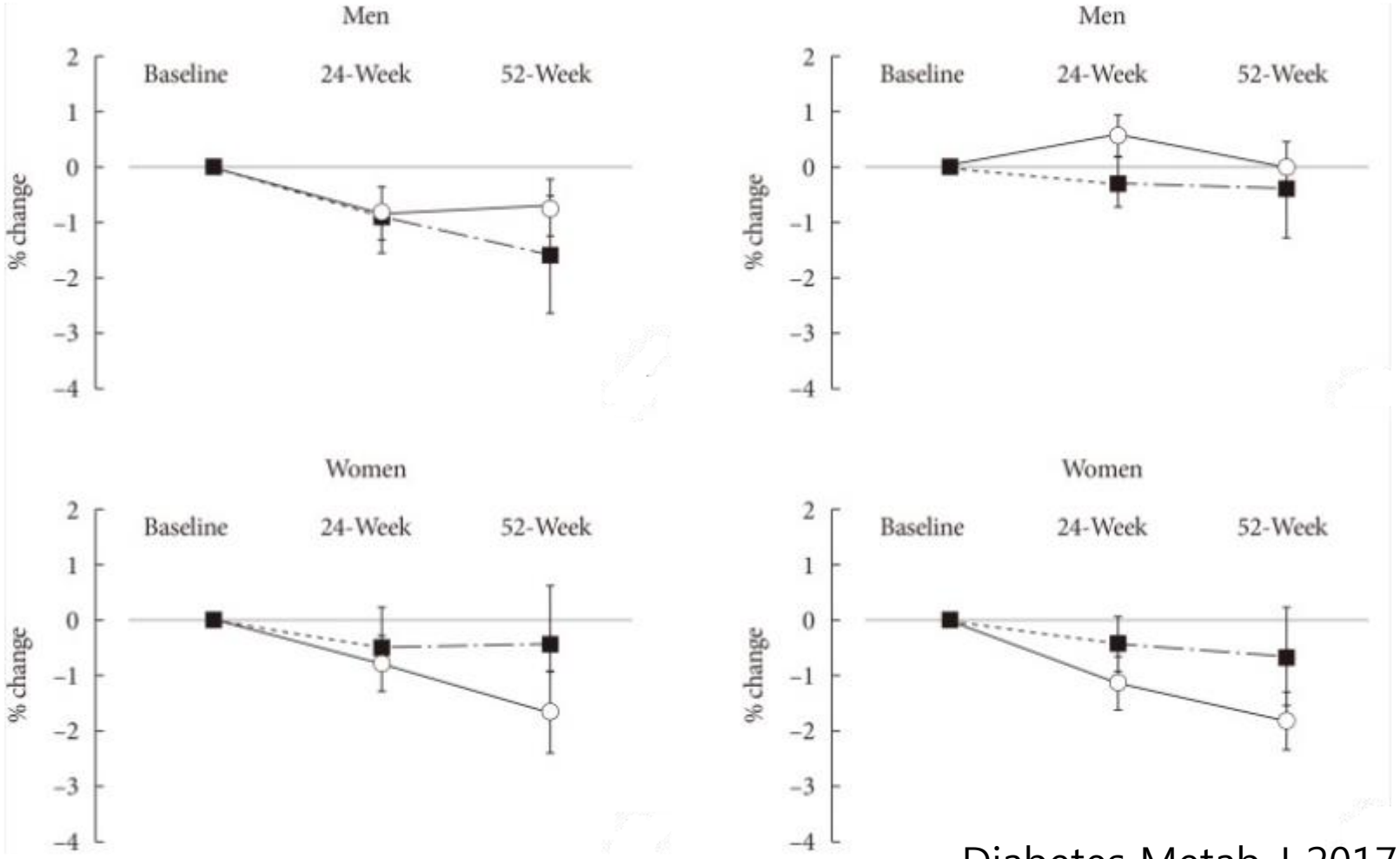
Exercise-induced weight loss



Arch Intern Med. 2006;166(22):2502-10

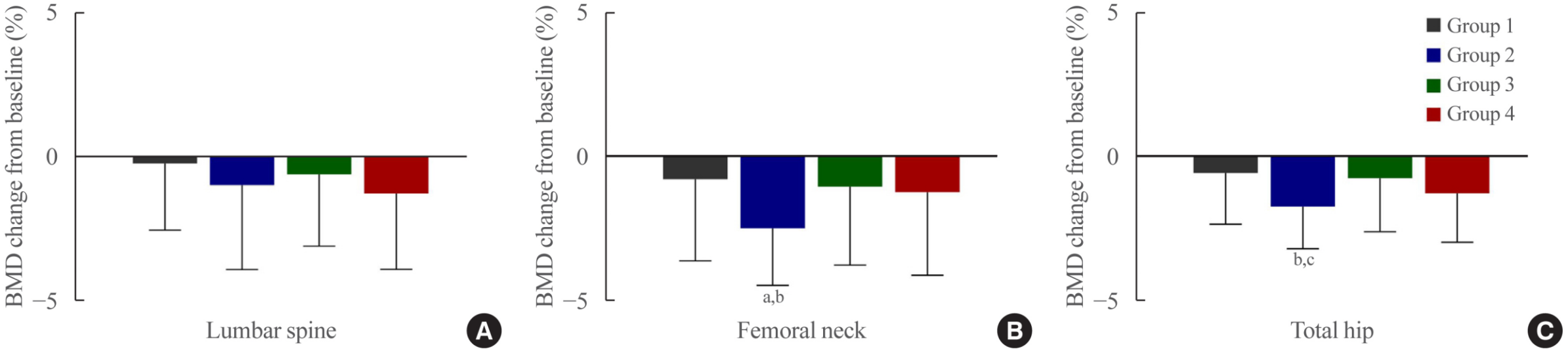
Thiazolidinedione and bone loss

Lobeglitazone



Diabetes Metab J 2017;41(5):377-385

12 months administration of different antidiabetic drugs

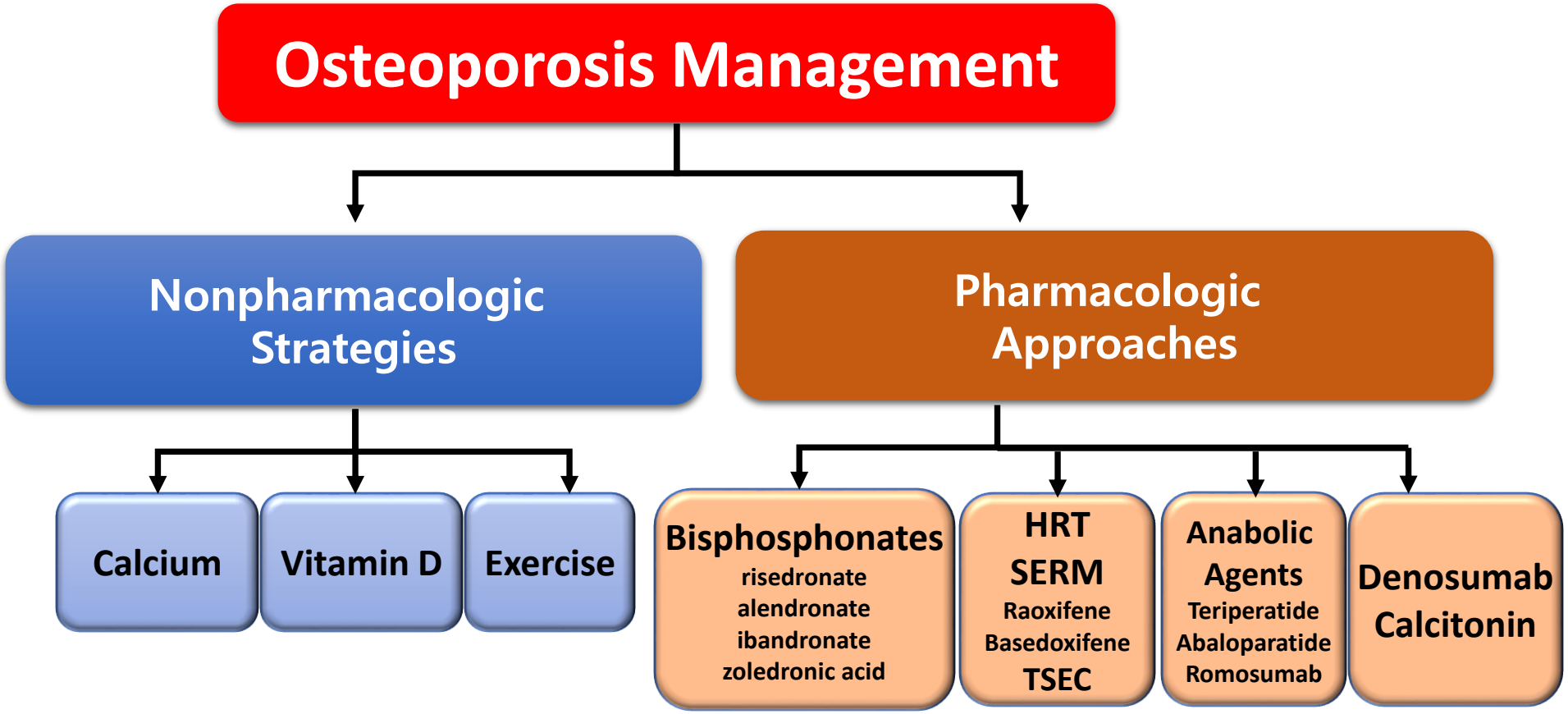


Group 1, metformin or metformin + sulfonylurea
Group 2, **TZD** + metformin +/- sulfonylurea
Group 3, DPP4 i + metformin +/- sulfonylurea
Group 4, **SGLT2i** + metformin +/- sulfonylurea

a : P<0.05 compared with Group 1, 3, and 4;
b : P<0.05 compared with baseline
c : P<0.05 compared with Group 1 and 3.

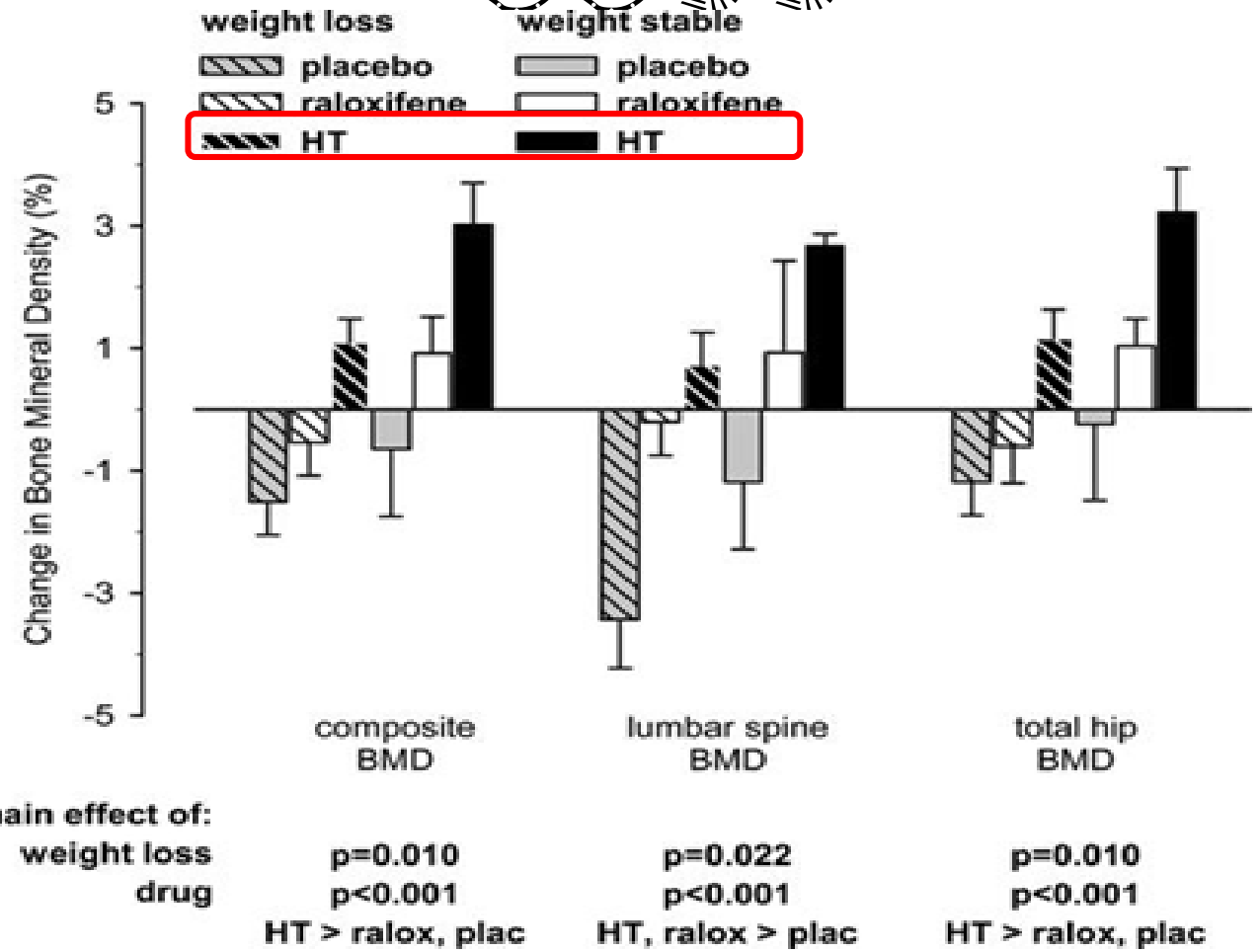
Endocrinol Metab 2021;36(4):895-903

Strategies for Osteoporosis Management



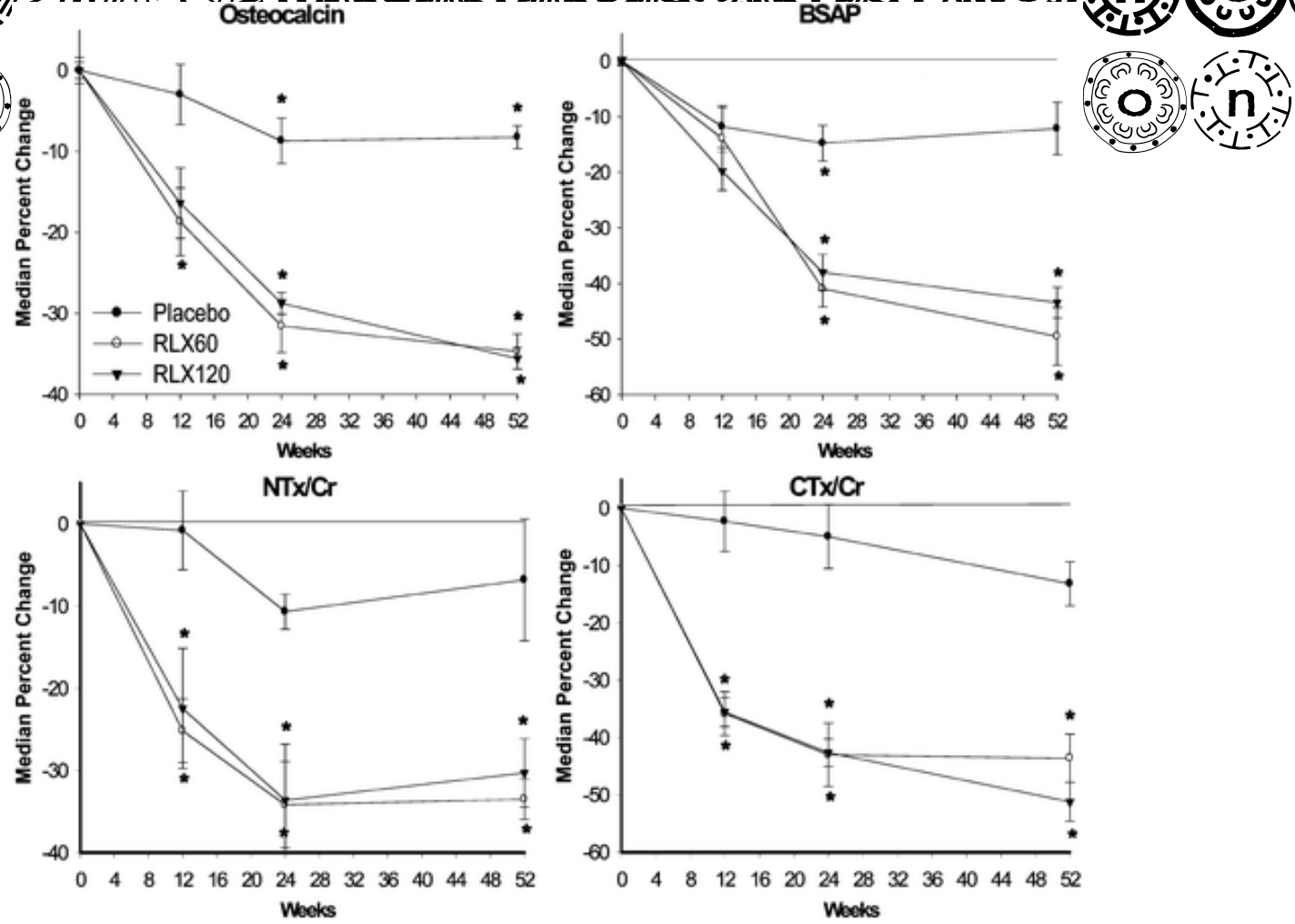
1. NIH. *JAMA*. 2001;285:785-795.
2. AACE. *Endocr Pract.* 2003;9:544-564.
3. NOF. *Clinician's Guide to Prevention and Treatment of Osteoporosis.* NOF; 2010.
4. US DHHS. *Bone Health and Osteoporosis: A Report of the Surgeon General.* Office of the Surgeon General; 2004.

changes in BMD after 12 months administration of HRT or SERM



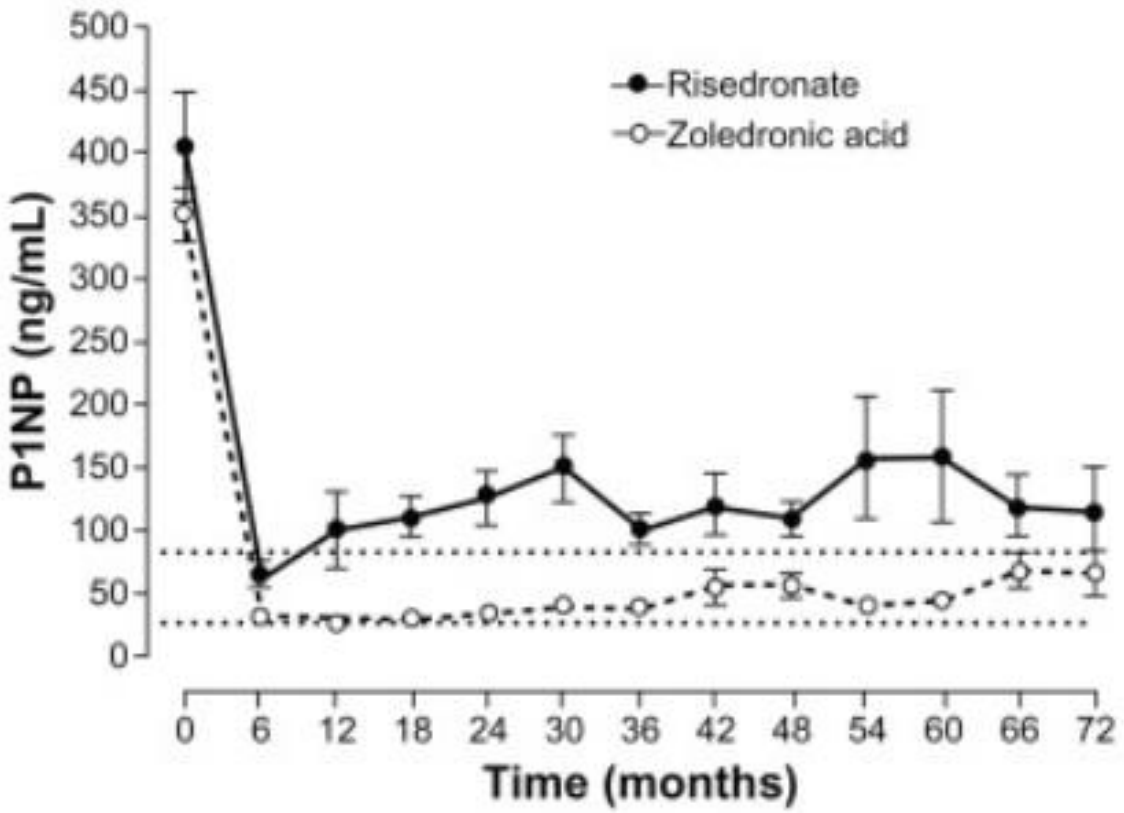
J Clin Endocrinol Metab. 2005;90(1):52-9.

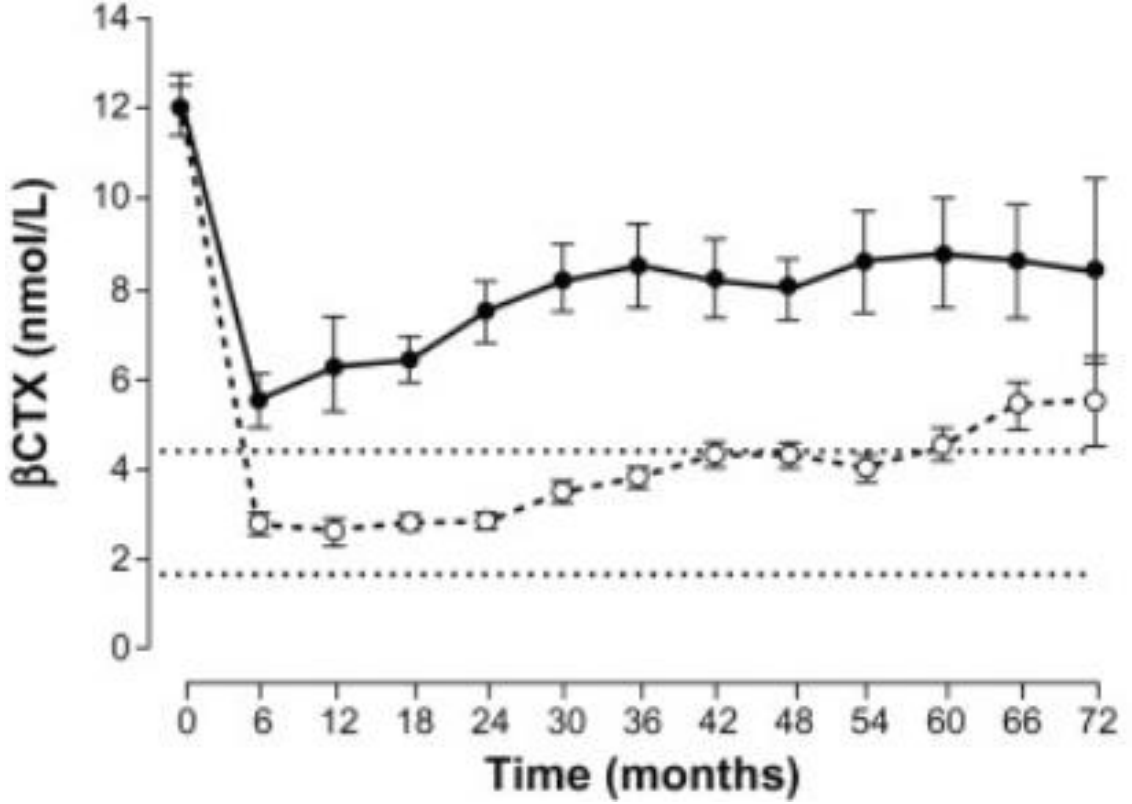
turnover markers after SERM (Raloxifene) add on



Osteoporos Int. 2003 Oct;14(10):793-800.

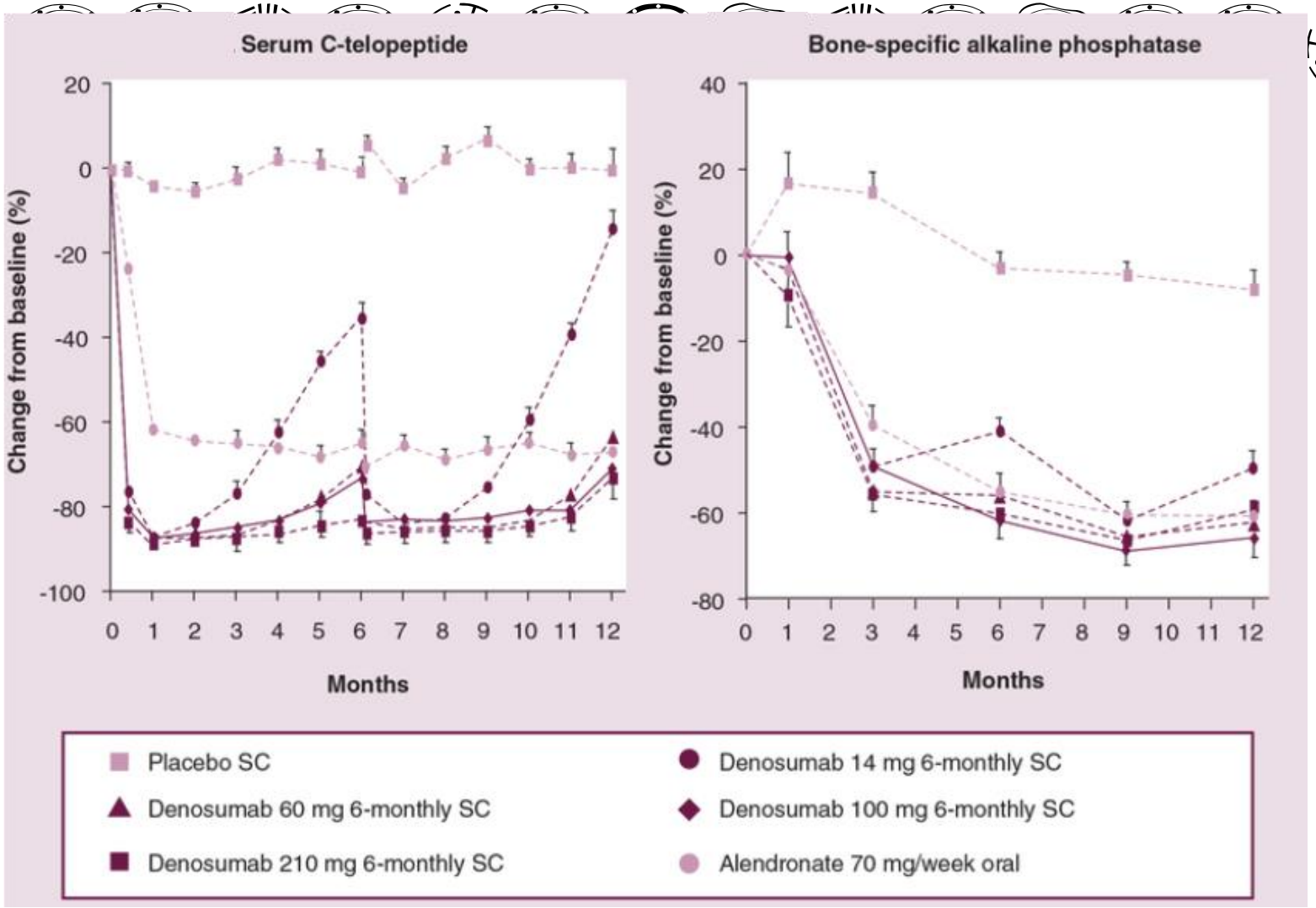
turnover markers after bisphosphonate treatment





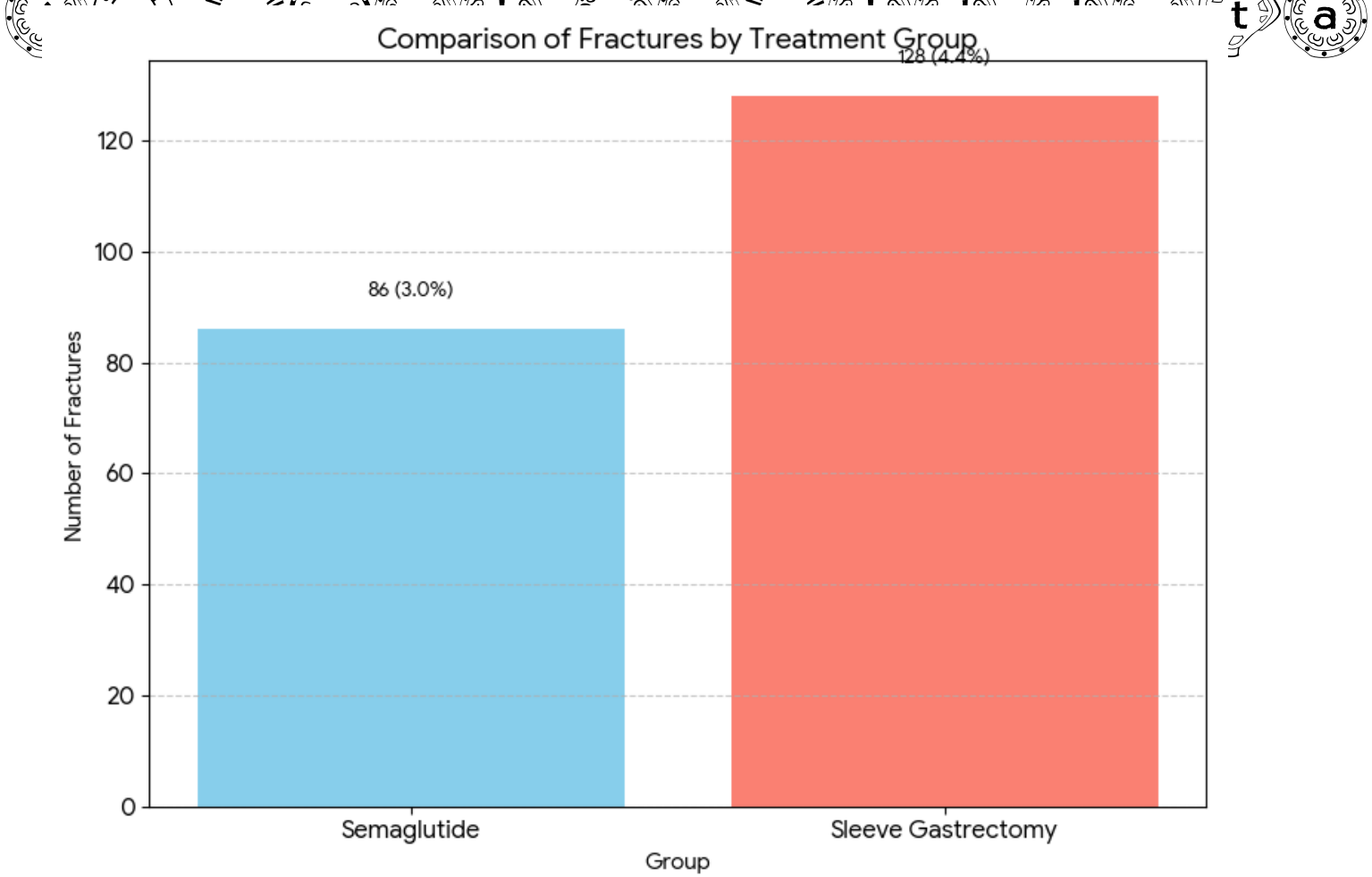
Int J Womens Health. 2012 Sep 3;4:455–469

Changes of Bone turnover markers after Denosumab

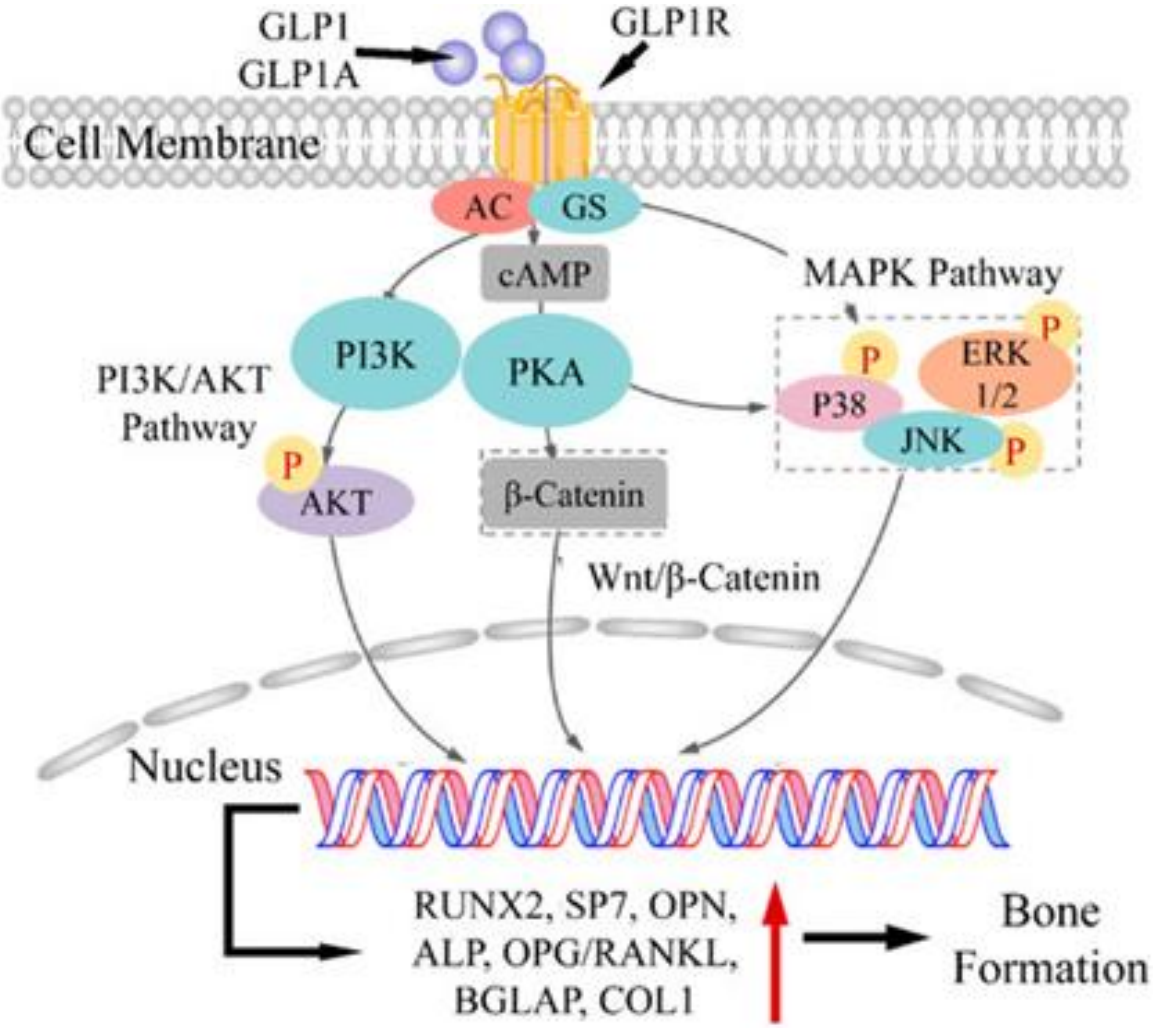


Womens Health (Lond) 2006;2(4):517-25.

Fracture risk after semaglutide use for 3 years



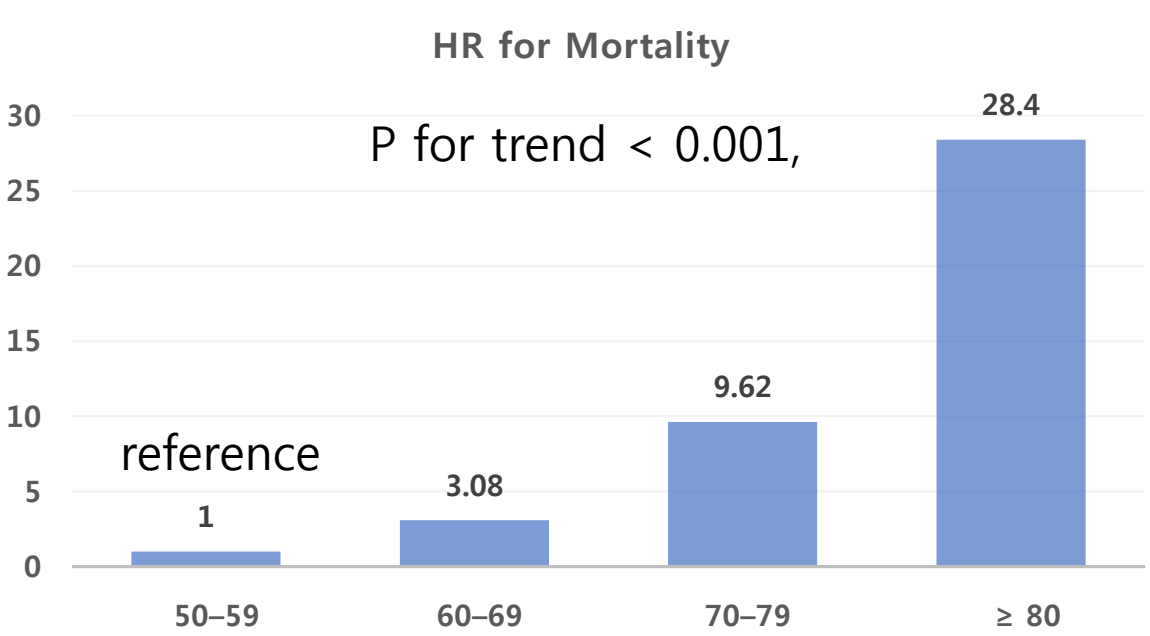
The Impact of GLP1 Agonists on Bone Metabolism



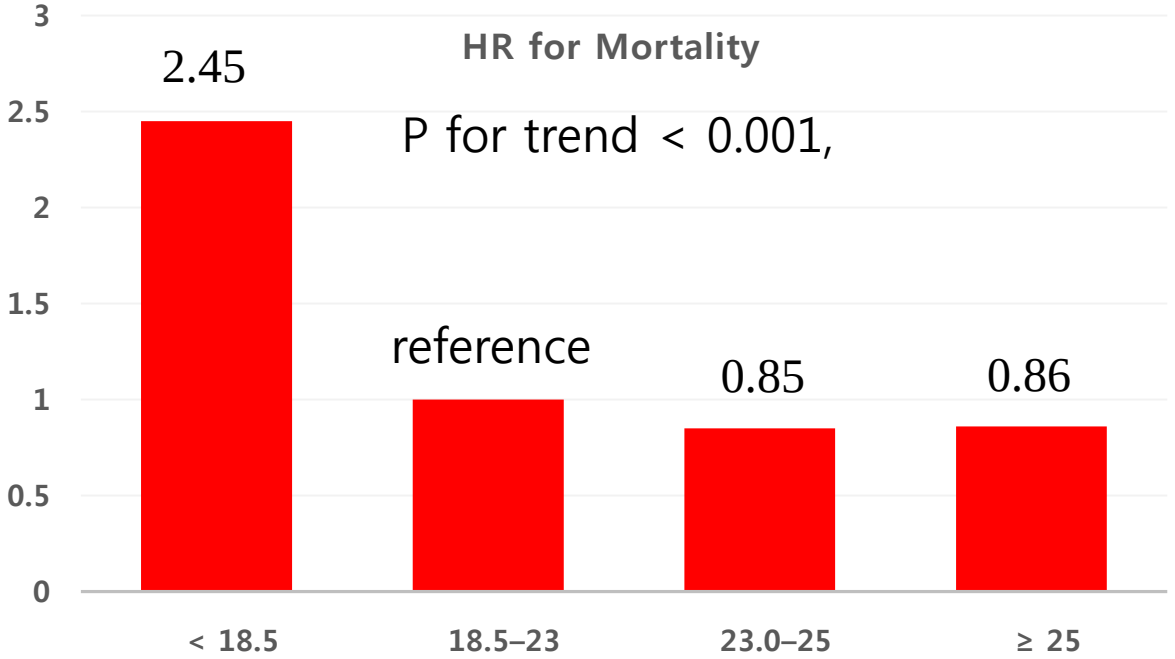
Medicina 2022, 58(2), 224

폐경 후 여성에서 사망률

국민건강보험 공단 데이터



Age, years



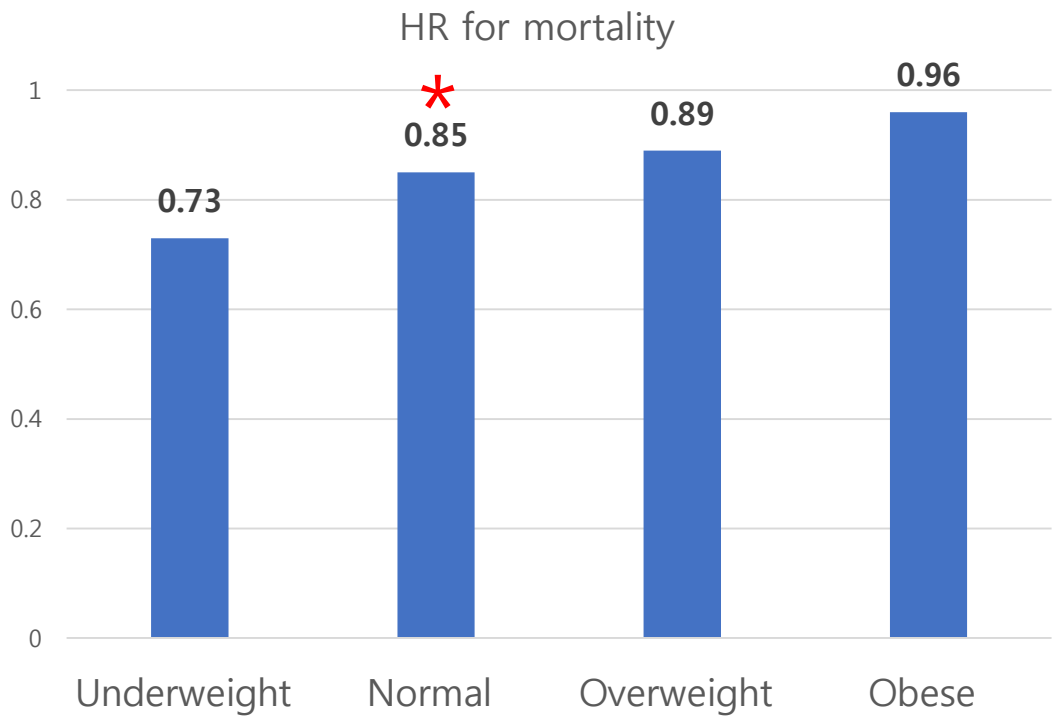
BMI (kg/m^2)

Park JM, Kim BT, unpublished data

Hazard Ratios for Death Events by Bisphosphonate Prescription Based on Cox Regression Analysis

국민건강보험 공단 데이터

	Hazard ratio	95% confidence interval
Model 1	0.91	0.82–0.99
Model 2	0.90	0.82–0.99
Model 3	0.89	0.81–0.98



Model 1: adjusted for age.
Model 2: adjusted for age and comorbidities (hypertension, diabetes, and dyslipidemia)
Model 3: adjusted for age, BMI, comorbidities (hypertension, diabetes, and dyslipidemia), and smoking, alcohol consumption, exercise, household income.

* P < 0.001

Park JM, Kim BT, unpublished data

Take Home Messages

1. 비만은 비록 골밀도는 증가시키지만, 골절의 위험은 증가시킨다.

2. 늙어난 체중은 뼈에 부하를 증가시켜 골형성을 촉진하지만, 늙어난 지방세포는 조골세포의 형성을 억제하고, 염증유발 cytokines을 방출하여, 파골세포의 활동을 촉진한다.

3. 급격한 체중 감량은 골에 가해지는 부하를 감소시켜 급격한 골소실을 일으킬 수 있다.

4. 따라서 폐경 후 골다공증이 있는 비만 환자에서 무분별한 체중 감량은 오히려 골절의 위험을 증가시킬 수 있으므로 칼슘 섭취와 운동을 추천하고, 골흡수를 강력하게 추천하는 Denosumab 이나 BP를 체중 감량 전 우선 투여한다.