

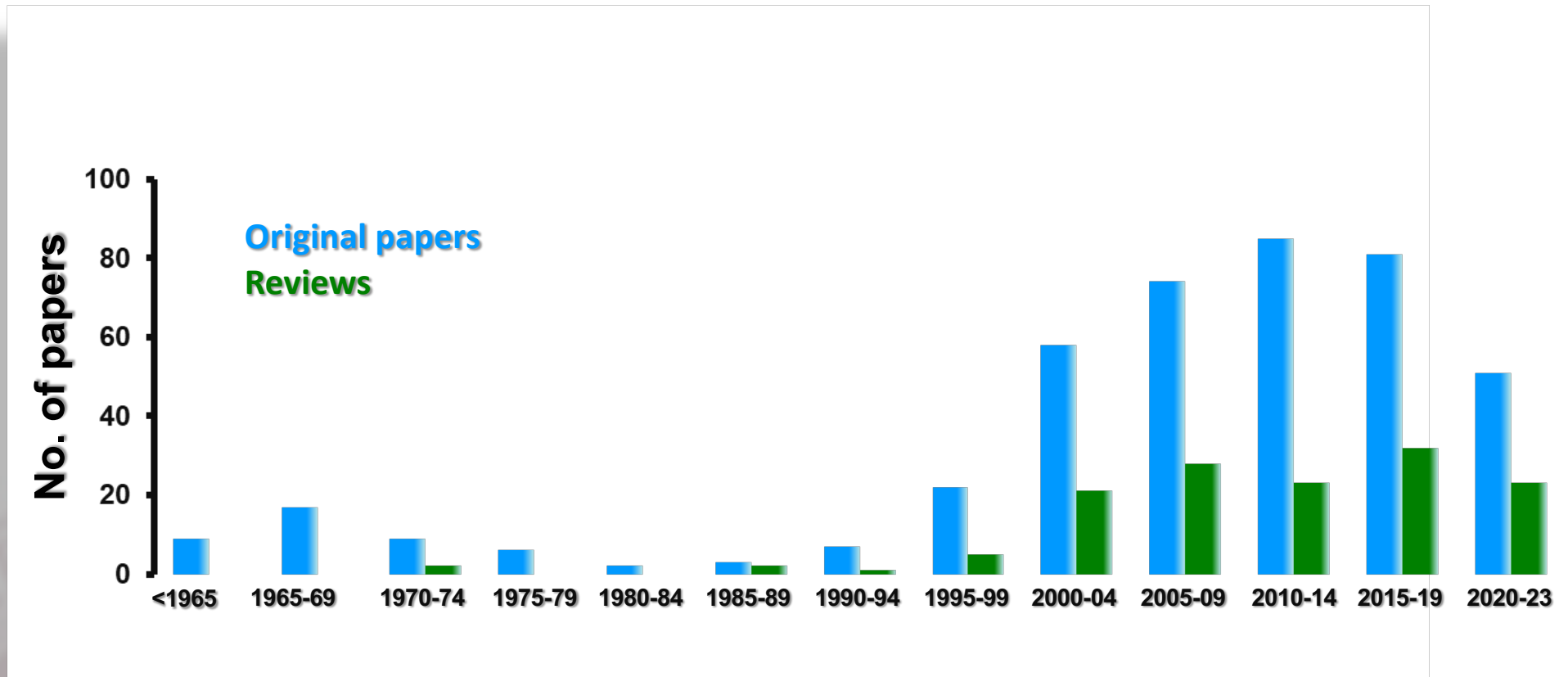


METABOLISMO OSTEO-MINERALE E MALATTIA CELIACA



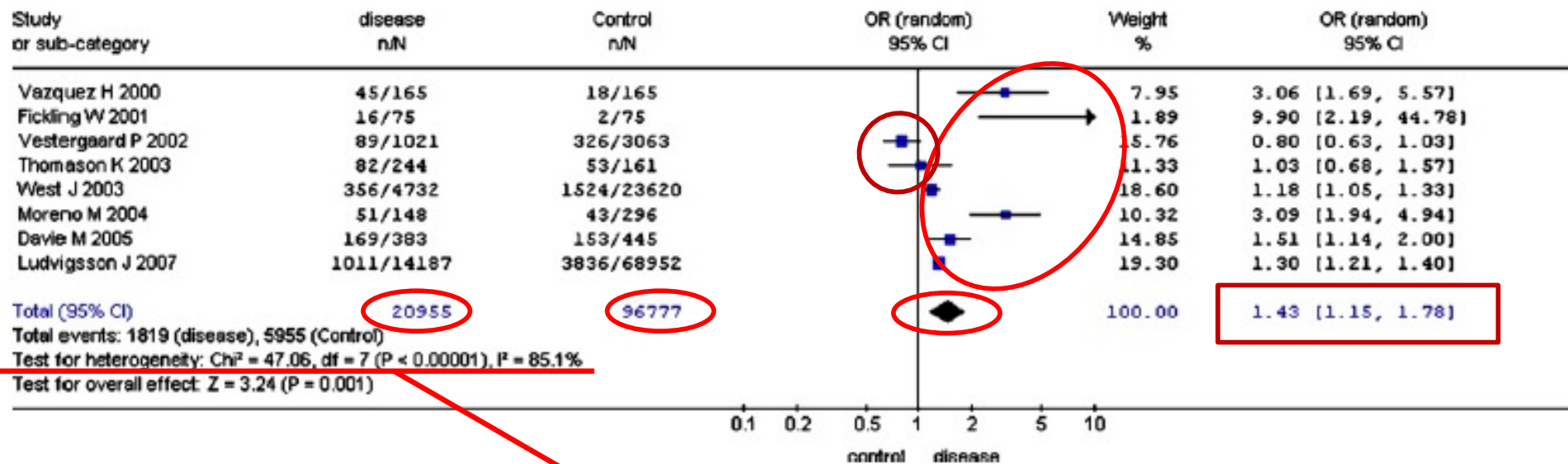
Michele Di Stefano
UOC Medicina Interna 1
IRCCS "S.Matteo" Hospital Foundation
Pavia

MEDLINE SEARCH FOR COELIAC DISEASE AND BONE LOSS



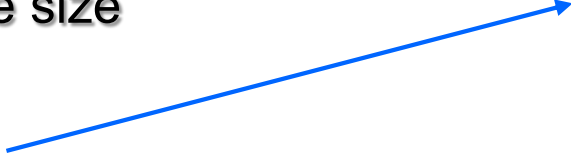
PubMed.gov, November 2023

SYSTEMATIC REVIEW AND META-ANALYSIS OF OBSERVATIONAL STUDIES ON THE PREVALENCE OF FRACTURES IN COELIAC DISEASE

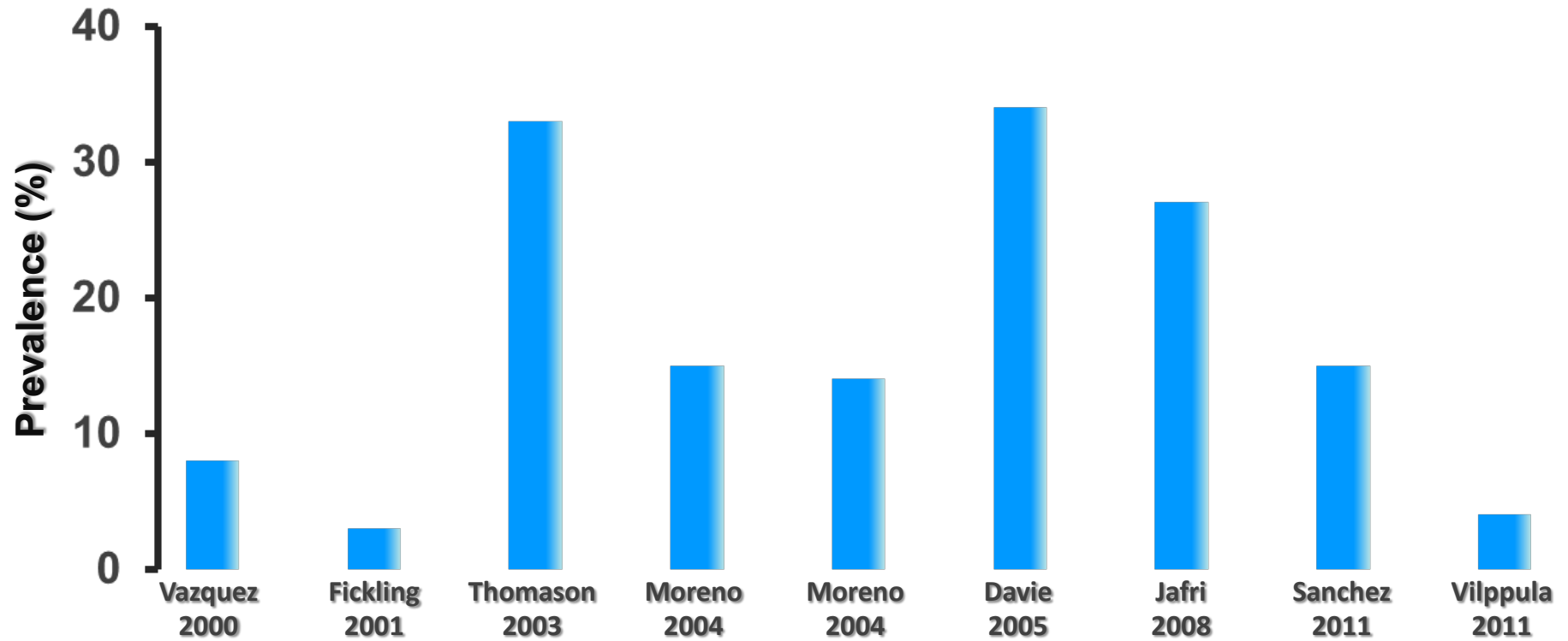


Test for heterogeneity: $\text{Chi}^2 = 47.06$, $\text{df} = 7$ ($P < 0.00001$), $I^2 = 85.1\%$

CAUSES OF HETEROGENEITY OF STUDIES ON THE PREVALENCE OF FRACTURES IN COELIAC DISEASE

- study design
 - inadequate sample size
 - selection of cases 
 - selection of controls 
 - failure to define the duration of CD
 - method used to ascertain fractures 
- ▶ clinical presentation
 - ▶ adherence to GFD
 - ▶ age
 - ▶ comorbidities
 - ▶ drug use
- ▶ general population
 - ▶ functional GI disorders
- ▶ interviews
 - ▶ questionnaires
 - ▶ discharge registers
 - ▶ GP database
 - ▶ x-ray studies

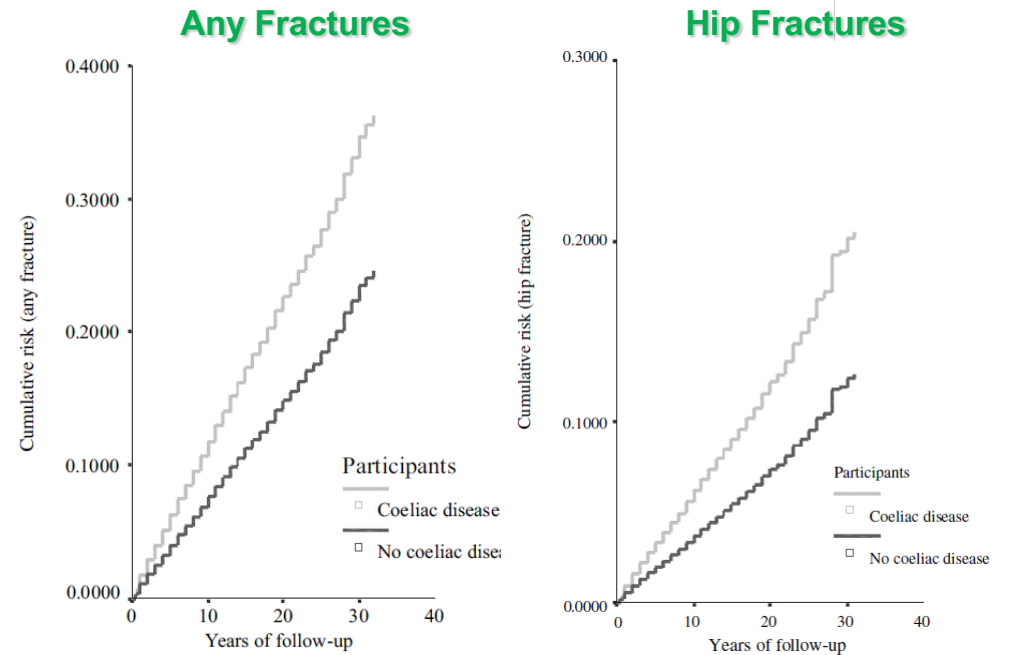
RISK OF FRACTURES IN CD: PREVALENCE OF FRACTURES IN CONTROLS



RISK OF FRACTURES IN COELIAC DISEASE: RESULTS OF STUDIES ON LARGE COHORTS

Variable	Overall				
	n ^a	No. fractures	Rate per 10,000 person-years	Hazard ratio	95% CI
Any fracture					
Control cohort ^c	23,616	1524	105.9	1	
Celiac disease cohort	4732	356	137.9	1.30	1.16–1.46
Hip fracture					
Control cohort ^c	23,620	71	4.7	1	
Celiac disease cohort	4732	24	8.9	1.90	1.20–3.02
Ulna/radius fracture					
Control cohort ^c	23,619	210	14.1	1	
Celiac disease cohort	4732	67	24.9	1.77	1.35–2.34

West J, et al. *Gastroenterology* 2003



Ludvigsson JF, et al. *APT* 2007

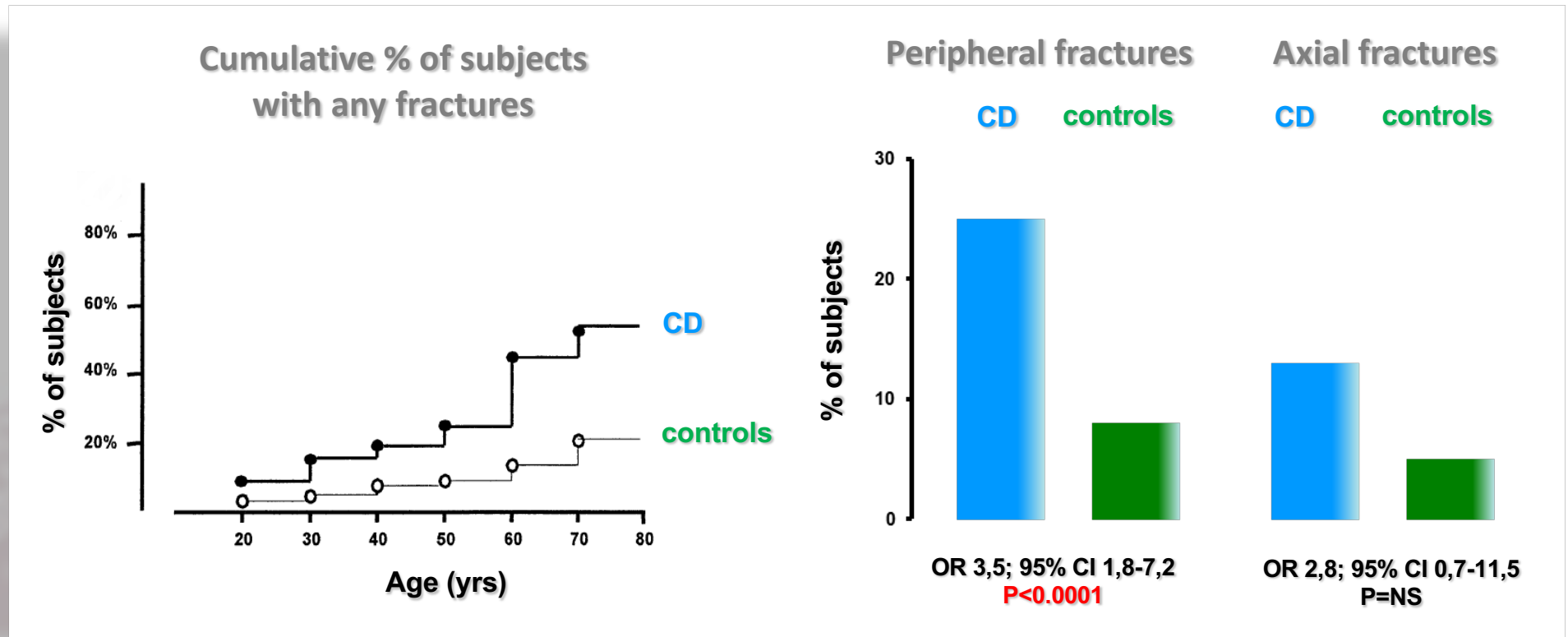
OSTEOPOROSIS AND BONE FRACTURES IN CD: A NATIONWIDE REGISTRY-BASED, DANISH STUDY

	No. of events	Crude HR 95 % CI	Adjusted HR 95 % CI
Osteoporosis			
CD patients	660	5.39 (4.89, 5.95)	5.30 (4.80, 5.85)
Reference population	1861	1.00 (ref)	1.00 (ref)
Major osteoporotic fractures			
CD patients	530	1.37 (1.25, 1.51)	1.38 (1.26, 1.52)
Reference population	4117	1.00 (ref)	1.00 (ref)
Any fracture			
CD patients	923	1.27 (1.18, 1.36)	1.28 (1.19, 1.37)
Reference population	7828	1.00 (ref)	1.00 (ref)

Hansen S, et al, *Bone* 2023

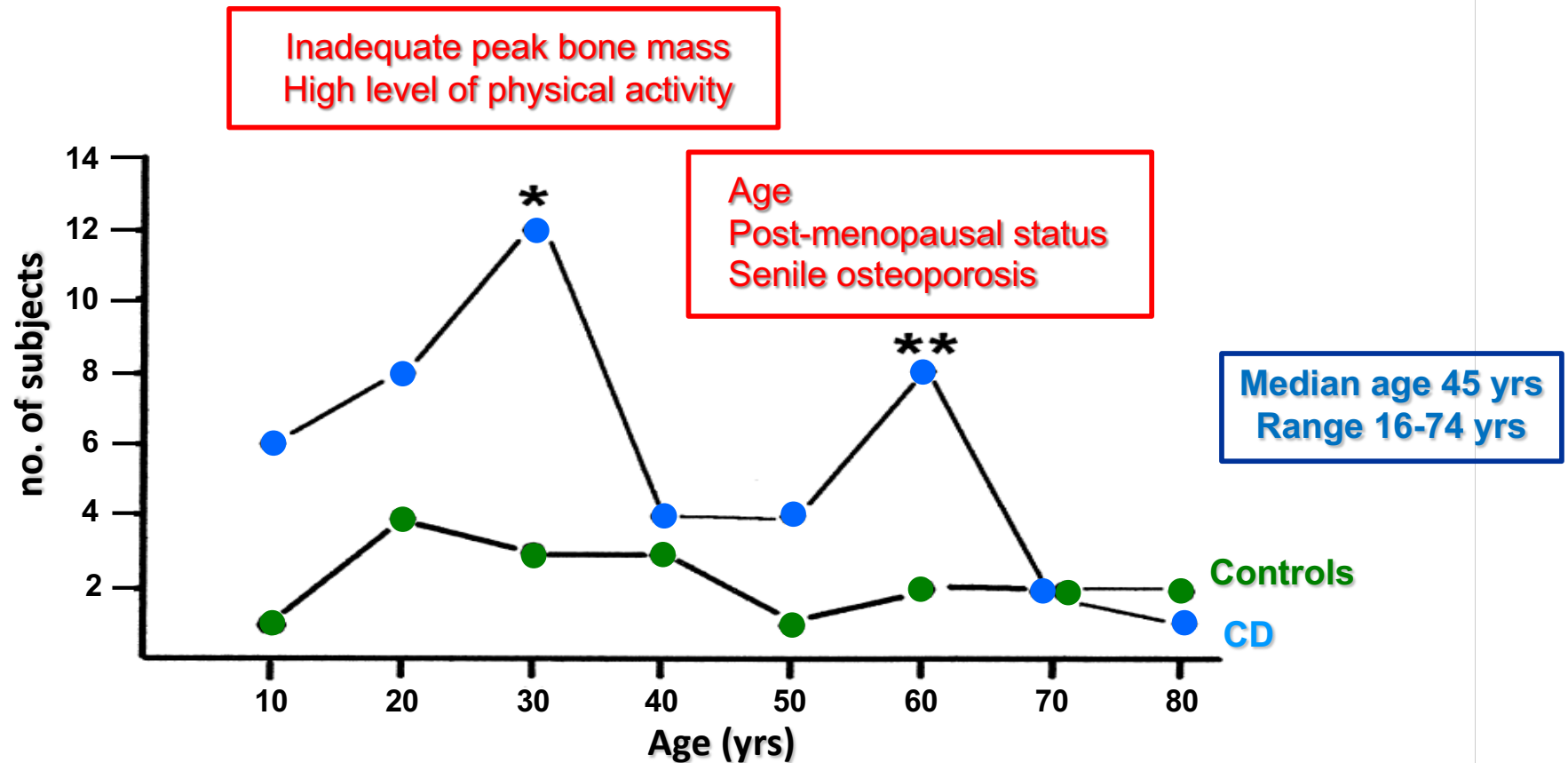
RISK OF FRACTURES IN CD: A CROSS-SECTIONAL, CASE-CONTROL STUDY

X-Ray studies in patients and controls

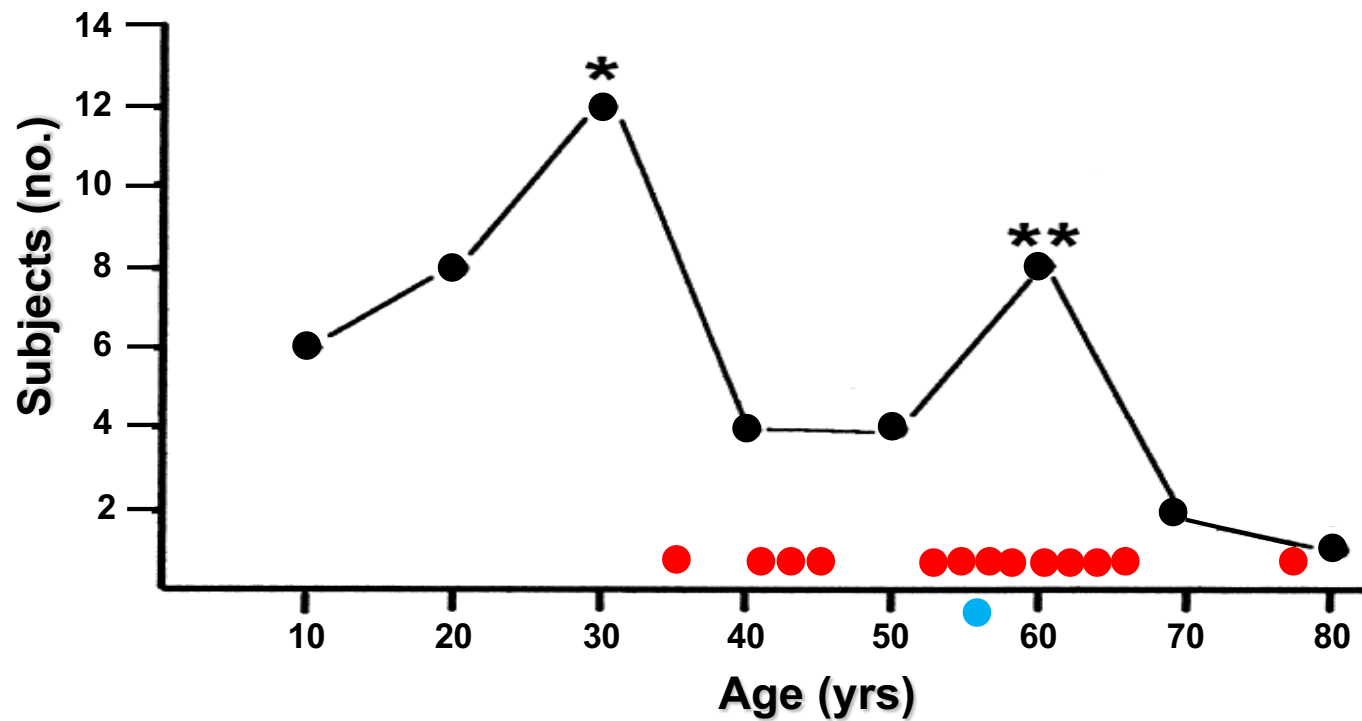


Vazquez H, et al. *AJG* 2000

INCIDENCE OF FRACTURES AND VERTEBRAL DEFORMITIES IN CD



THE CLINICAL IMPACT OF METABOLIC BONE DISEASE IN COELIAC DISEASE



Fickling WE, et al. *Postgrad Med J* 2001

AGE AND RISK OF FRACTURES IN COELIAC DISEASE

Osteoporos Int (2005) 16: 1150–1155
DOI 10.1007/s00198-004-1822-z

ORIGINAL ARTICLE

Excess non-spine fractures in women over 50 years with celiac disease: A cross-sectional, questionnaire-based study

Michael W. Davie · I. Gaywood · E. George
P.W. Jones · T. Masud · T. Price · G.D. Summers

	Original data		
	<i>n</i> #	<i>p</i>	OR (95% CI)
Any fracture	817	< 0.01	1.51 (1.13:2.02)
Any fracture after age 50 years	801	< 0.001	2.20 (1.49:3.25)

>10 yrs before diagnosis

Between 10 yrs before diagnosis
and 5 yrs after diagnosis

>5 yrs after diagnosis

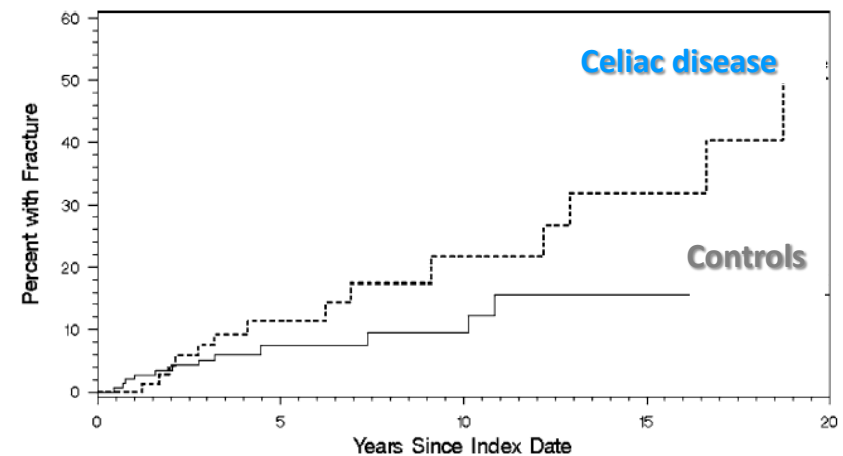


LONG-TERM FRACTURE RISK IN PATIENTS WITH COELIAC DISEASE: A POPULATION-BASED STUDY IN OLMSTED COUNTY, MINNESOTA

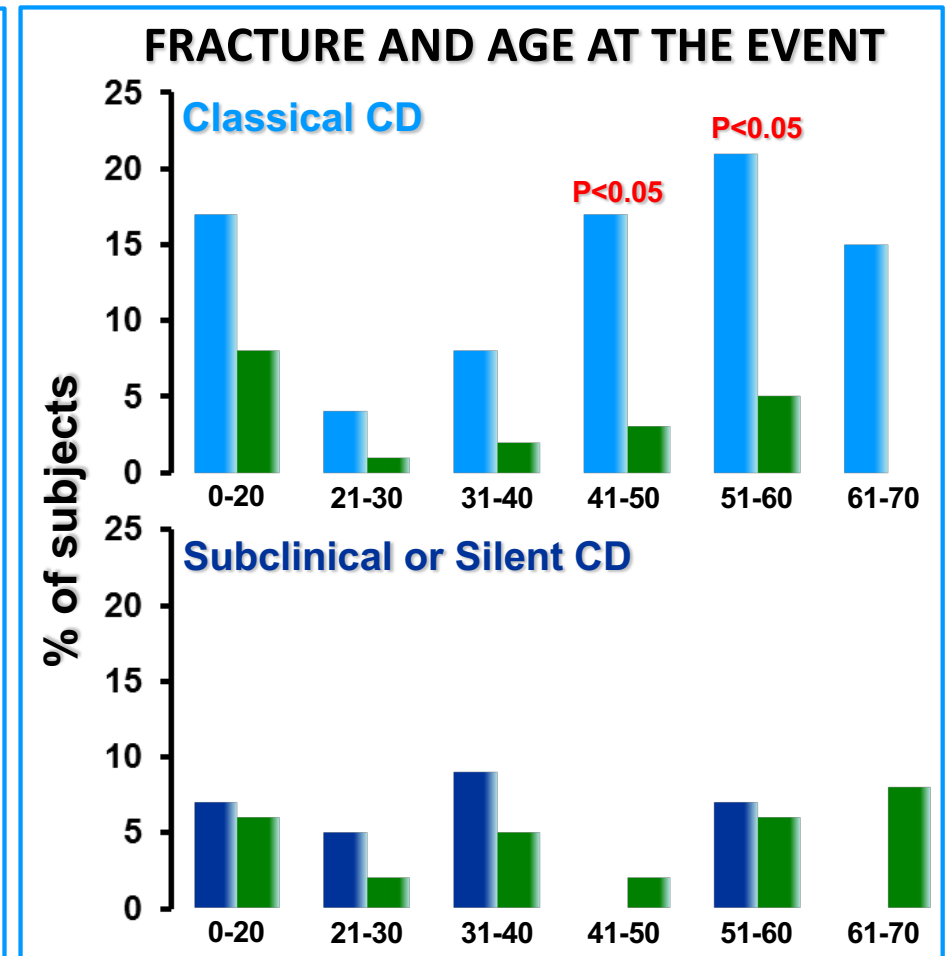
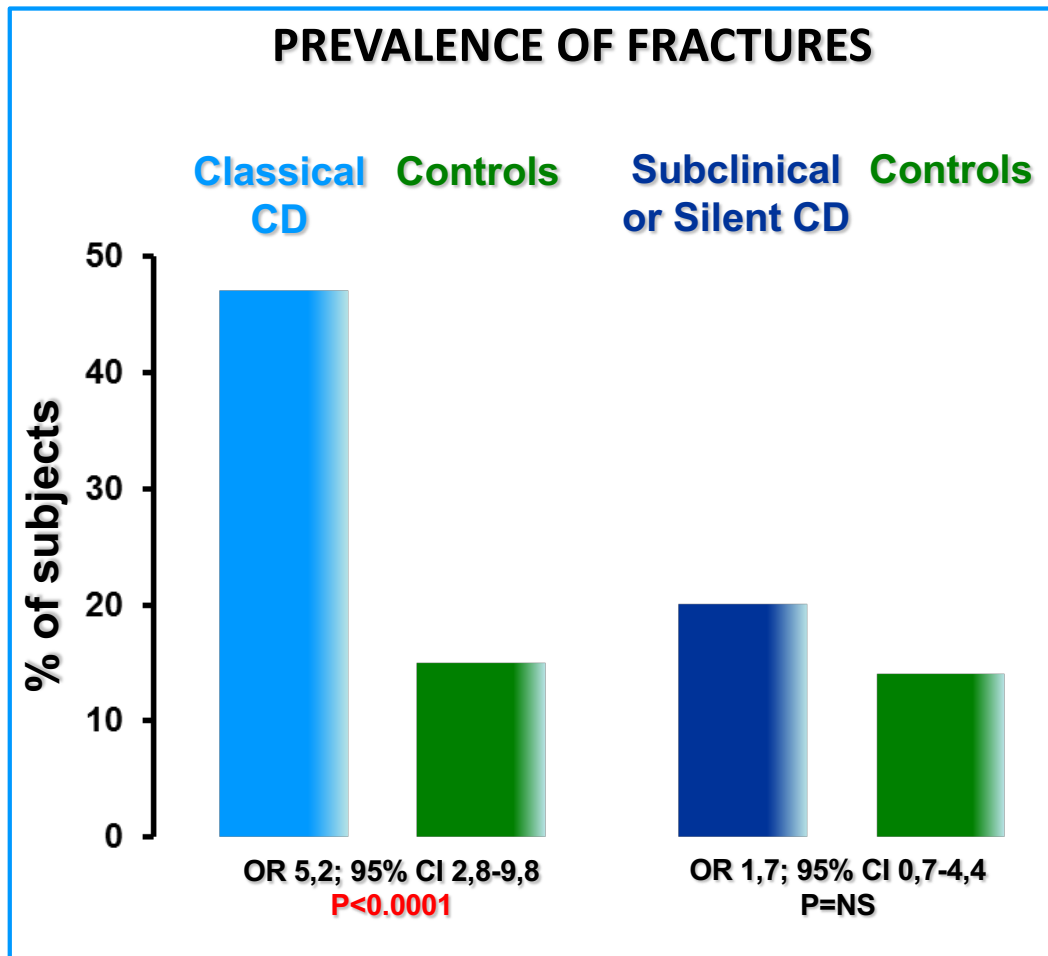
Fracture risk before diagnosis

Fracture type	Unadjusted odds ratio ^a (95% CI)	<i>P</i>
Any fracture	2.0 (1.0, 3.9)	0.045
Peripheral	2.0 (1.0, 3.8)	0.052
Axial	1.7 (0.7, 4.1)	0.273
Osteoporotic	8.0 (0.9, 72)	0.063

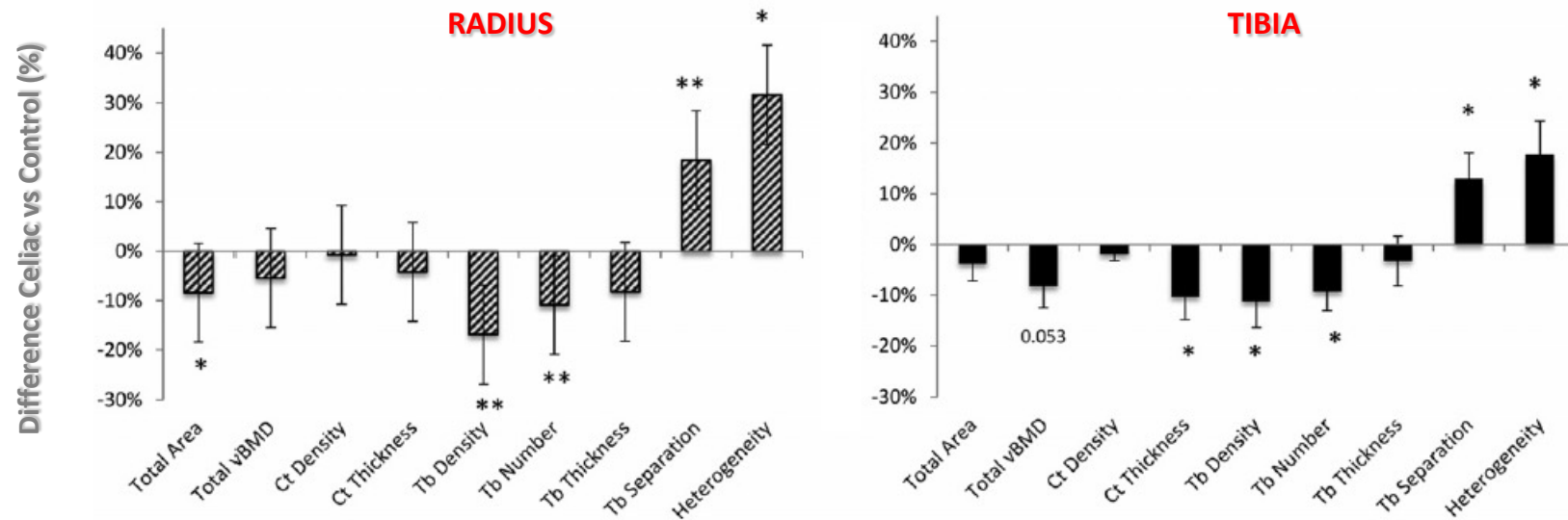
Fracture risk after diagnosis



STRATIFICATION OF BONE FRACTURE RISK IN PATIENTS WITH CD

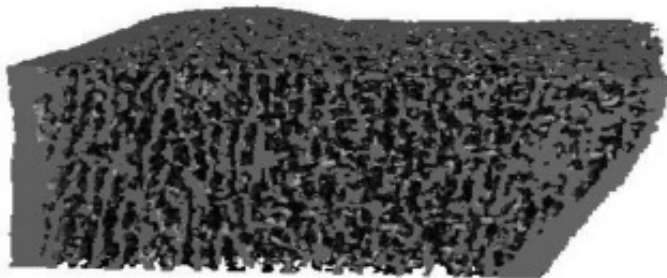


ABNORMAL SKELETAL STRENGTH AND MICROARCHITECTURE IN UNTREATED PRE-MENOPAUSAL WOMEN WITH COELIAC DISEASE

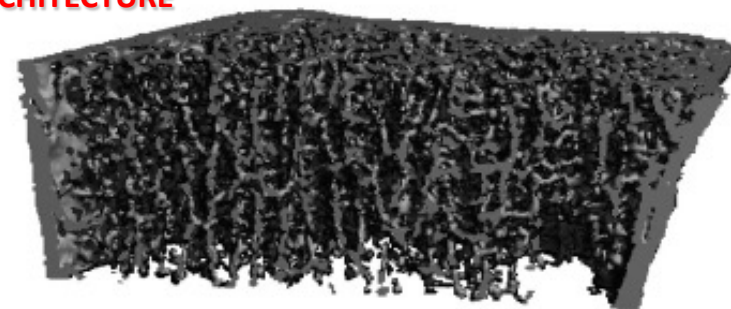


3-D TRABECULAR ARCHITECTURE

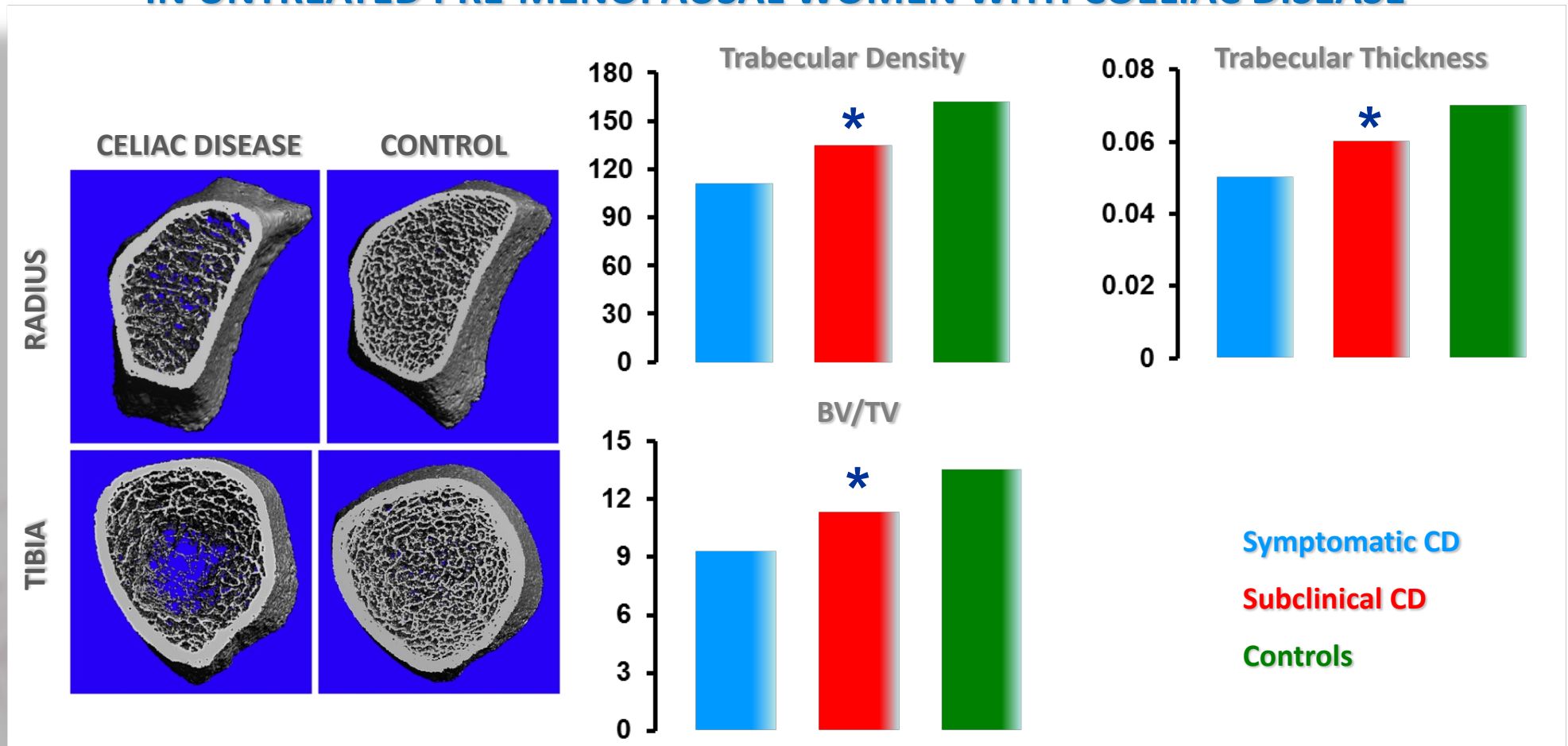
HEALTHY
CONTROL



COELIAC
DISEASE

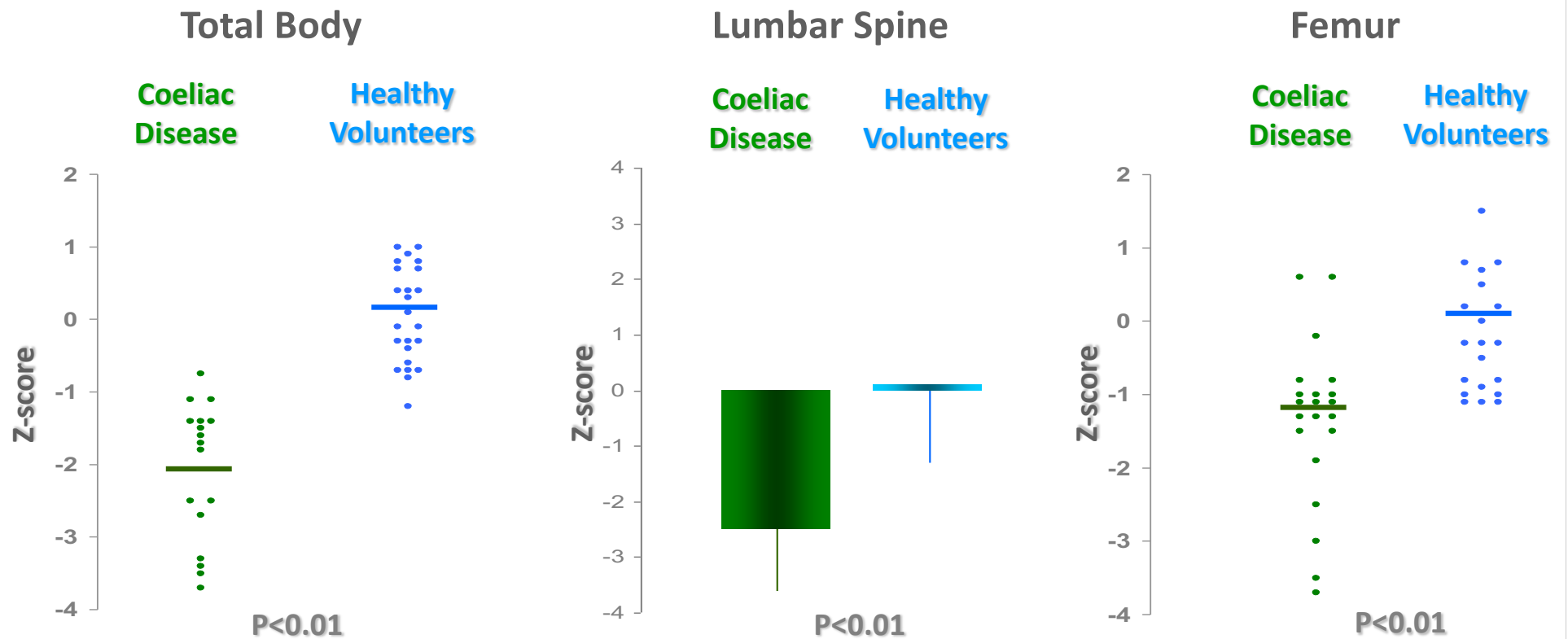


BONE MICROARCHITECTURE IMPAIRMENT IN UNTREATED PRE-MENOPAUSAL WOMEN WITH COELIAC DISEASE



Zanchetta MB, et al. *Bone* 2015

BONE MINERAL DENSITY IN UNTREATED ADULT COELIAC DISEASE

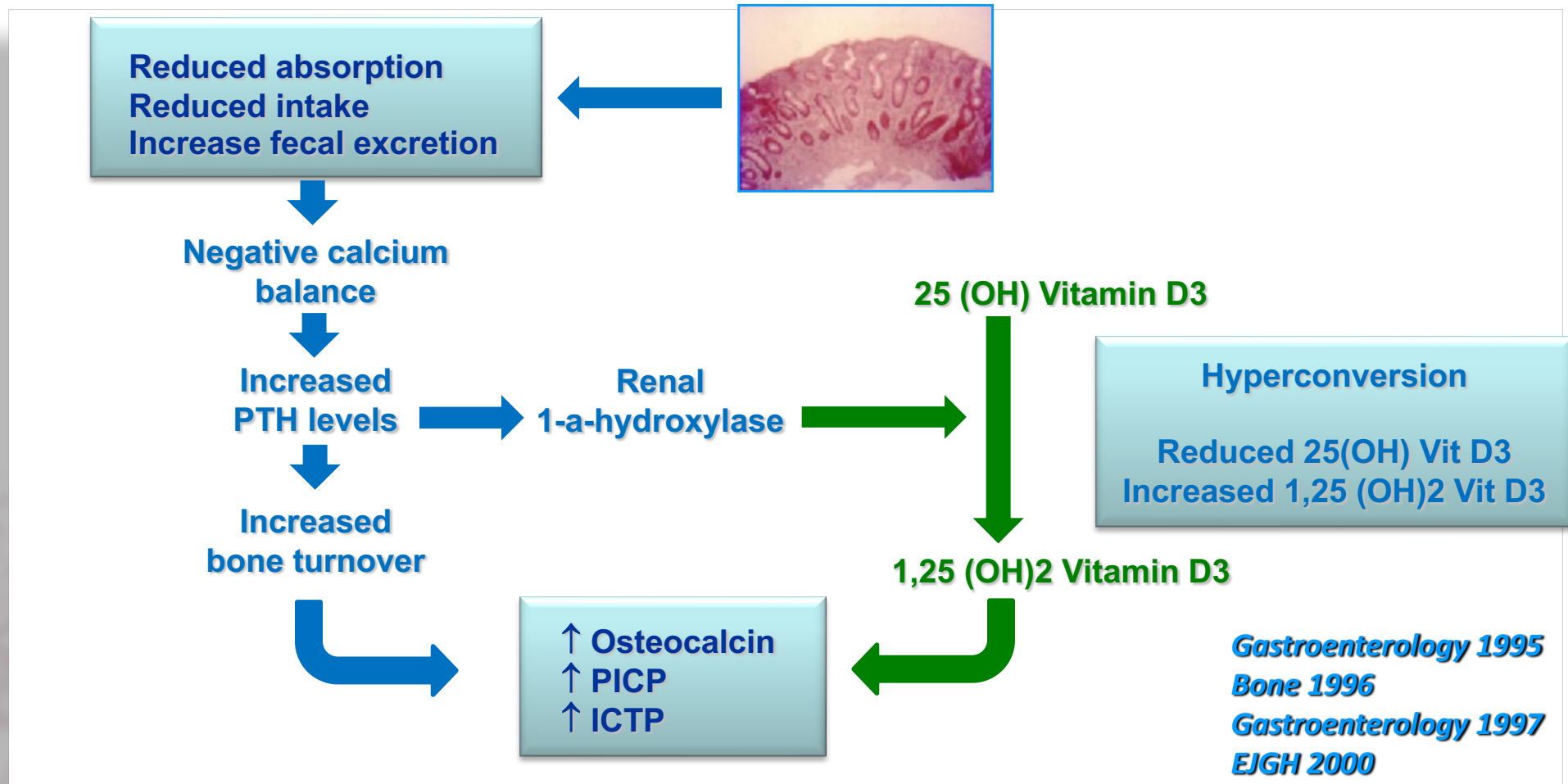


Corazza et al, *Gastroenterology* 1995

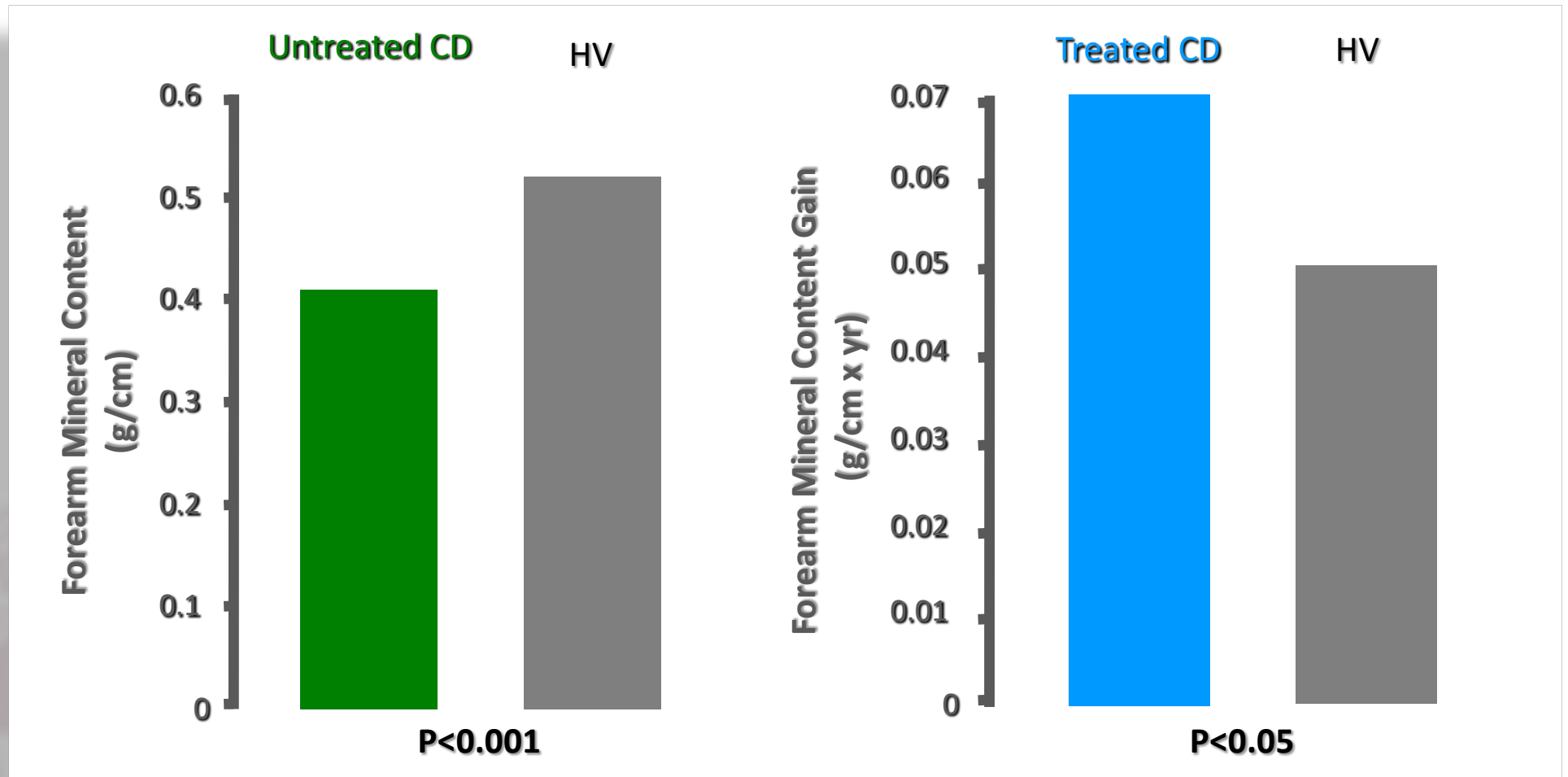
Gonzalez et al, *AJG* 1995

McFarlane et al, *Gut* 1996

PATHOPHYSIOLOGY OF BONE LOSS IN UNTREATED ADULT COELIAC DISEASE

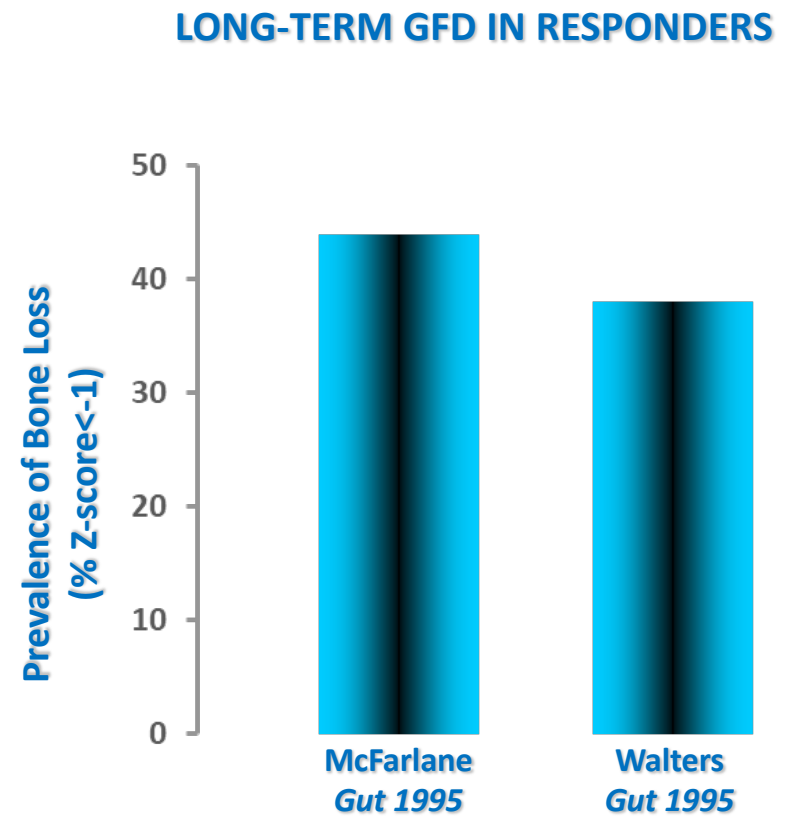
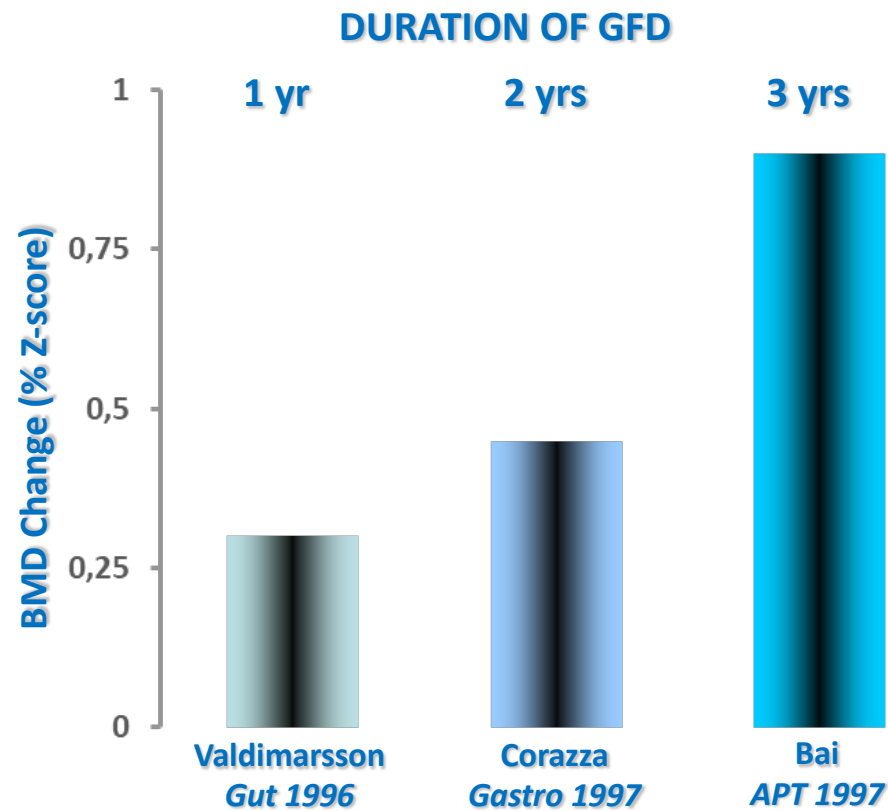


EFFECT OF GFD ON BONE MINERAL DENSITY IN CHILDHOOD CD



Mora et al, *AJCN* 1993

EFFECT OF GFD ON BONE MINERAL DENSITY IN ADULT CD



EFFECT OF MINERALO-ACTIVE DRUGS ON BMD IN ADULT CD

Osteoporosis in a North American Adult Population With Celiac Disease

Douglas Meyer, M.D., Stavros Stavropoulos, M.D., Beverly Diamond, D.S.W., Elizabeth Shane, M.D., and Peter H. R. Green, M.D.

Department of Medicine, College of Physicians and Surgeons, Columbia University, New York, New York

AJG 2001

Celiac Disease Presenting as Severe Osteopenia

Christopher J. Mulder DO; Anthony P. Cardile DO; and Judith Dickert MD

Hawaii Med J 2011

Effect of zoledronic acid on bone mineral density in patients of celiac disease: A prospective, randomized, pilot study

Mukul Kumar, Ashu Rastogi, Sanjay Kumar Bhadada, Anil Bhansali, Kim Vaiphei* & Rakesh Kochhar**

Indian J Med Res 2013

No effect of Calcium and VitaminD supplementation

Positive effect of Teriparatide, calcium and VitaminD supplementation (1 patient)

zoledronic acid = calcium and vitaminD supplementation

RANK/RANKL/OPG SYSTEM AND BONE LOSS IN ADULT CD

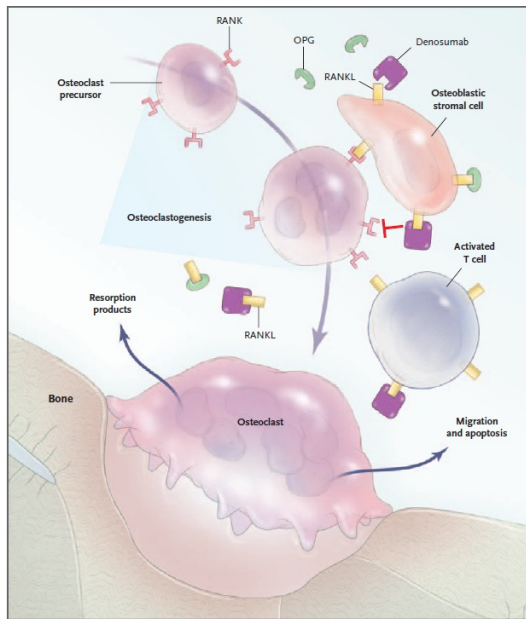
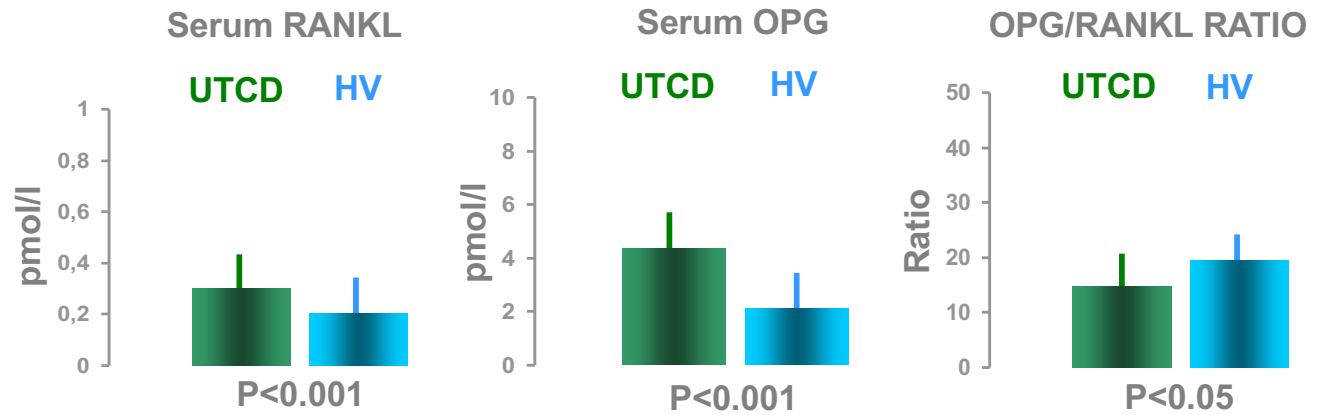
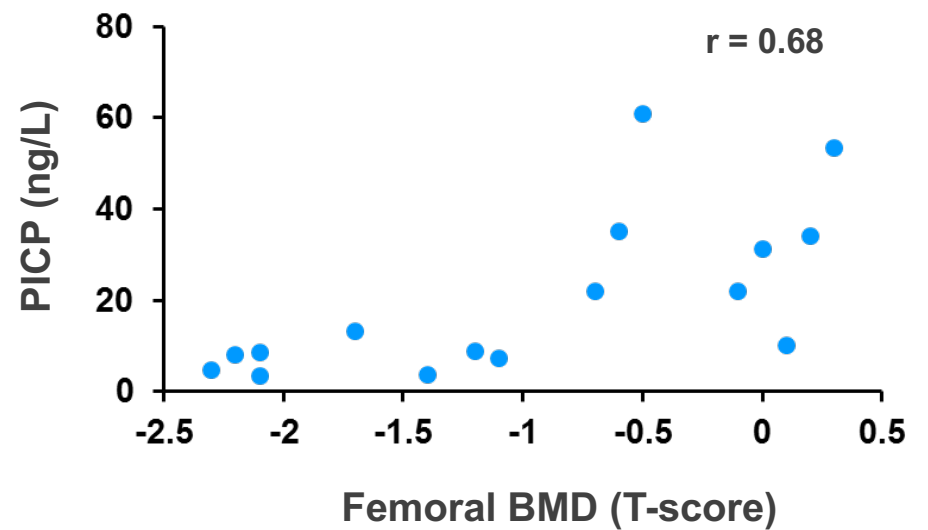
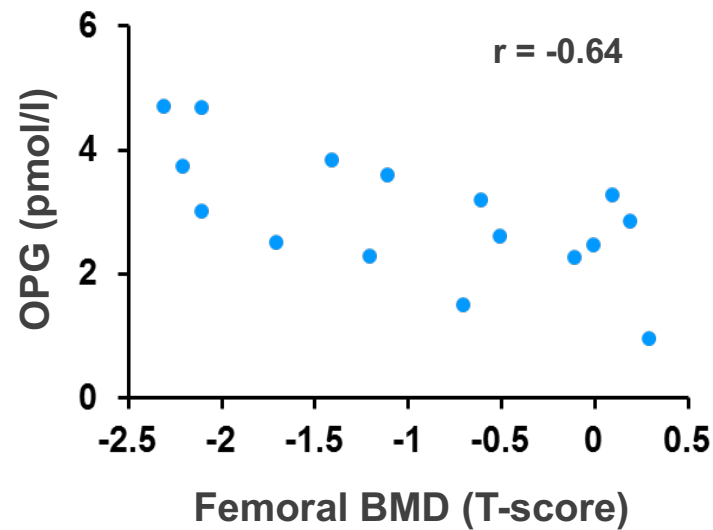


Figure 1. The Skeletal Action of Denosumab.
RANKL, a member of the tumor necrosis factor superfamily of ligands and receptors, promotes the differentiation, activation, and survival of bone-resorbing osteoclasts. Osteoprotegerin (OPG) that is produced by osteoblasts, the key modulator of RANKL, acts as a natural soluble decoy receptor for RANKL and blocks its effects. Denosumab functions like OPG and has the effect of decreasing osteoclastogenesis, as revealed by diminished biochemical markers of bone resorption.



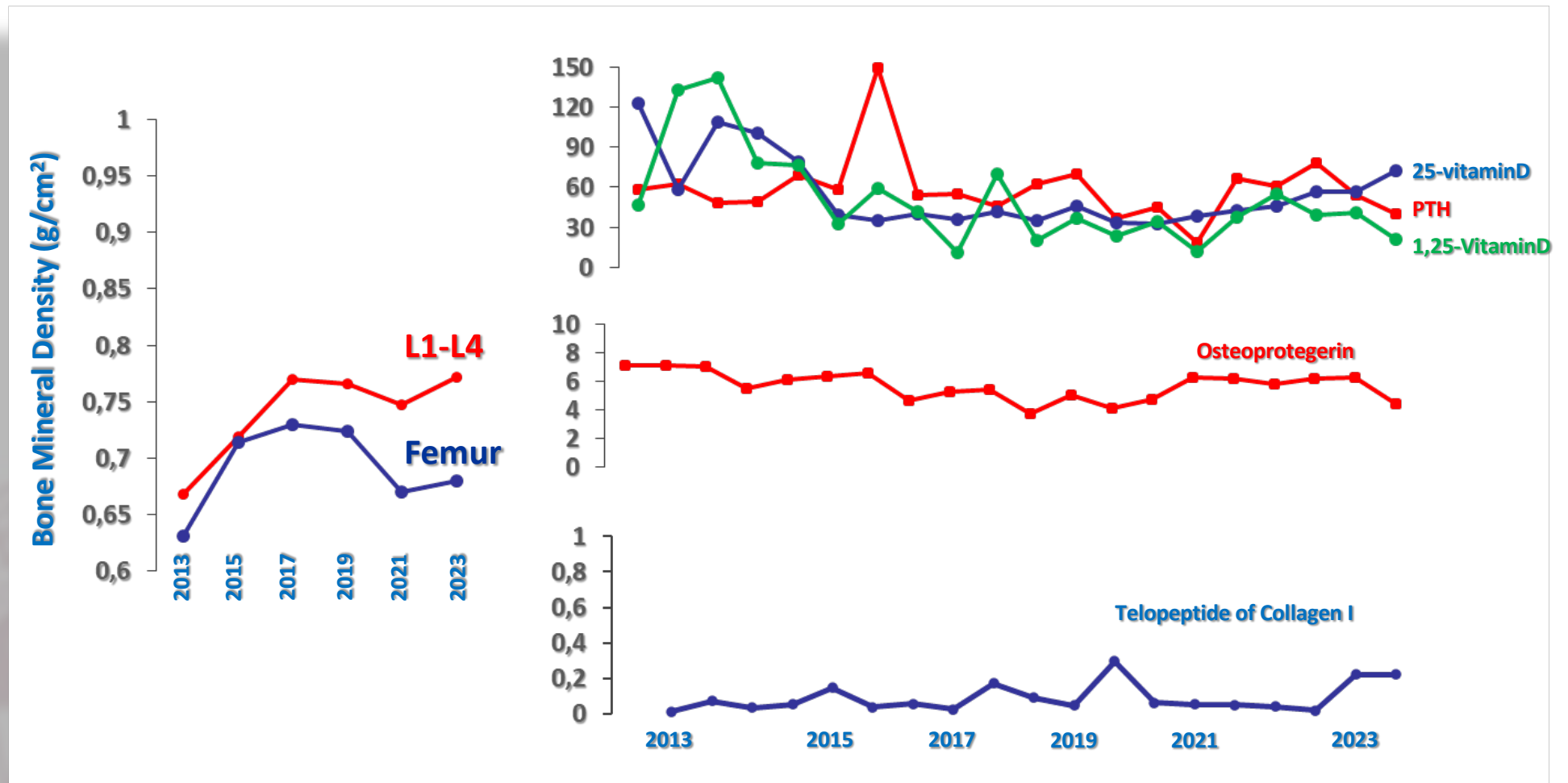
Fiore et al, *Horm Metab Res* 2006

RANK/RANKL/OPG SYSTEM AND PICP IN ADULT CD ON LONG-TERM GLUTEN-FREE DIET WITH PERSISTENTLY LOW BMD



Di Stefano M et al, *JCG* 2013

EFFECT OF DENOSUMAB IN SEVERE OSTEOPOROTIC FEMALE CD PATIENT



TIMING FOR DEXA EVALUATION ACCORDING TO GUIDELINES

ACG guidelines

DEXA at diagnosis and every 2-3 years

European Society for the Study of CD guidelines

DEXA at diagnosis, follow up for abnormal index values

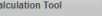
British Society of Gastroenterology guidelines

DEXA in pts with risk factors or >55 yr old, follow up for abnormal index values

NICE guidelines

Preliminary risk assessment through clinical scores, DEXA in high risk patients, follow up in pts receiving treatment

FRAX SCORE AND PREDICTION OF 10-yr MAJOR OSTEOPOROTIC FRACTURE PROBABILITY IN CD


FRAX® Fracture Risk Assessment Tool

[Home](#)
[Calculation Tool](#)
[Paper Charts](#)
[FAQ](#)
[References](#)
[CE Mark](#)
[English](#)

Calculation Tool

Please answer the questions below to calculate the ten year probability of fracture with BMD.

Country: **UK**
Name/ID:
[About the risk factors](#)

Questionnaire:

- Age (between 40 and 90 years) or Date of Birth
Age: Date of Birth: Y: M: D:
- Sex
☐ Male ☐ Female
- Weight (kg)
- Height (cm)
- Previous Fracture
☒ No ☐ Yes
- Parent Fractured Hip
☒ No ☐ Yes
- Current Smoking
☒ No ☐ Yes
- Glucocorticoids
☒ No ☐ Yes
- Rheumatoid arthritis
☒ No ☐ Yes

- Secondary osteoporosis
☒ No ☐ Yes
- Alcohol 3 or more units/day
☒ No ☐ Yes
- Femoral neck BMD (g/cm²)
Select BMD

Weight Conversion
Pounds kg

Height Conversion
Inches cm

11000825
Individuals with fracture risk assessed since 1st June 2011



Table 2 Predictors of major osteoporotic fracture

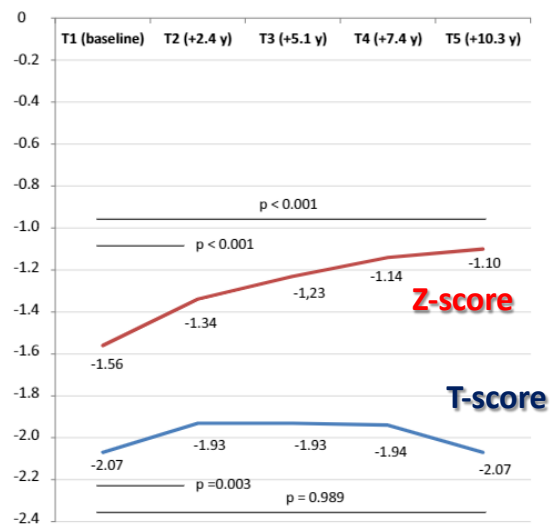
		Hazard ratio (95% CI)	p value
Model 1	Celiac disease (versus absent)	1.43 (1.11–1.86)	0.006
	FRAX (clinical without secondary osteoporosis) per SD increase	1.95 (1.89–2.00)	< 0.001
Model 2	Celiac disease (versus absent)	1.08 (0.84–1.40)	0.542
	FRAX (clinical with secondary osteoporosis) per SD increase	1.94 (1.89–2.00)	< 0.001
Model 3	Celiac disease (versus absent)	1.21 (0.93–1.57)	0.150
	FRAX (with BMD) per SD increase	2.09 (2.03–2.14)	< 0.001

CI confidence interval

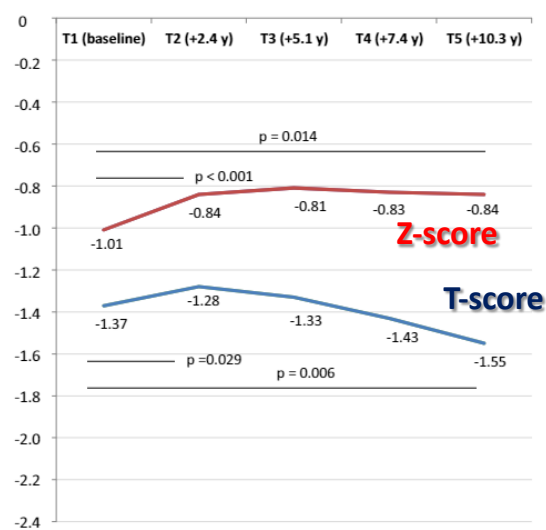
Duerksen DR et al, *Osteoporosis Int* 2021

BMD AND FRAX SCORE IN COELIAC DISEASE: A 10-yr PERSPECTIVE

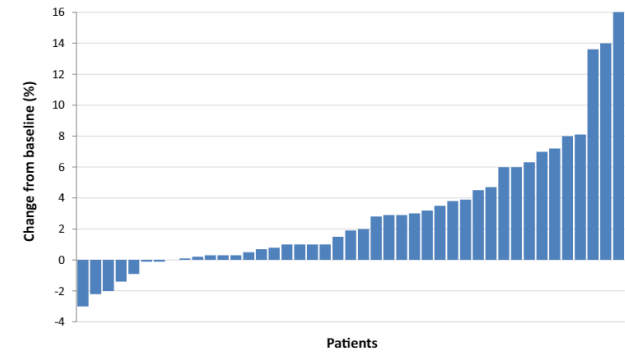
A – Lumbar spine



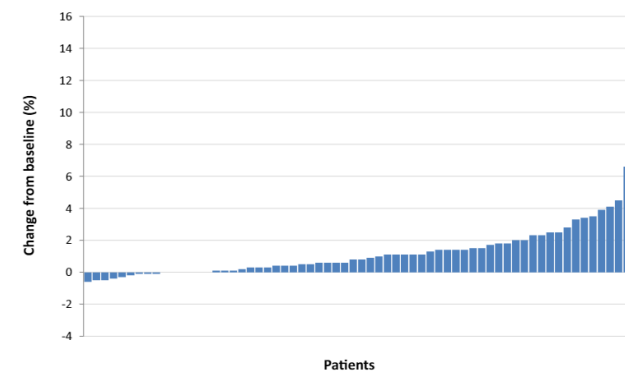
B – Femoral neck



Osteoporosis, at least one risk factor



Osteopenia and no risk factors



TIMING FOR DEXA EVALUATION ACCORDING TO PREDICTIVE DATA

ACG guidelines

DEXA at diagnosis and every 2-3 years

European Society for the Study of CD guidelines

DEXA at diagnosis, follow up for abnormal index values

British Society of Gastroenterology guidelines

DEXA in pts with risk factors or >55 yr old, follow up for abnormal index values

NICE guidelines

Preliminary risk assessment through clinical scores, DEXA in high risk patients, follow up in pts receiving treatment

METABOLIC BONE DISEASE AND COELIAC DISEASE - RESEARCH AGENDA -

- * Better selection of “at-risk” groups for **osteoporosis**
- * Better selection of “at-risk” groups for **fractures**
- * **Quality** of bone
- * Effect of **drugs** (bisphosphonates, teriparatide, denosumab....)
- * Redefinition of **guidelines**



**Grazie
per la Vostra Attenzione**