
# Νόσος Paget των οστών

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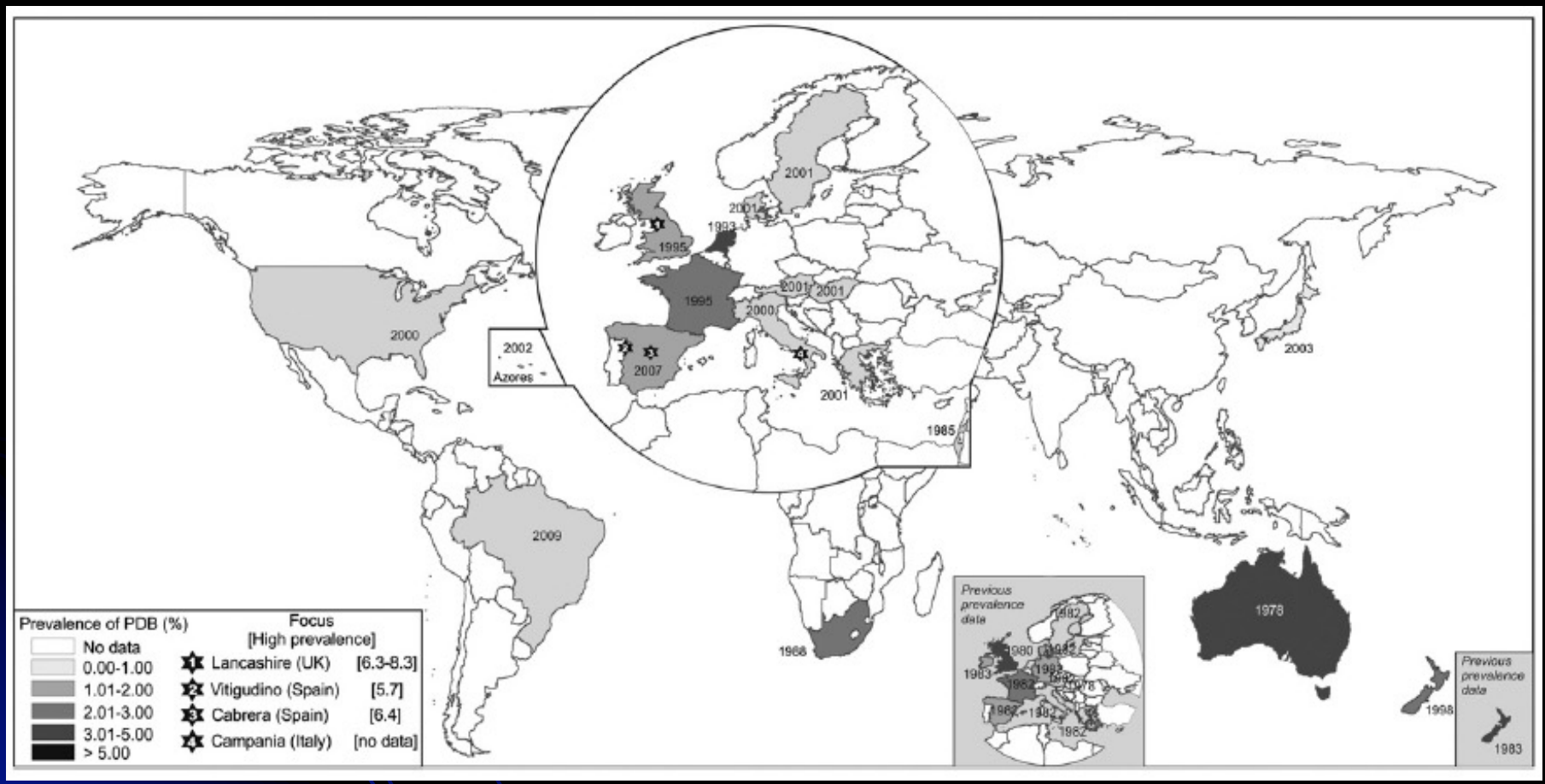
Τμήμα Ιατρικής Α.Π.Θ.

# Σύγκρουση Συμφερόντων

- Καμία

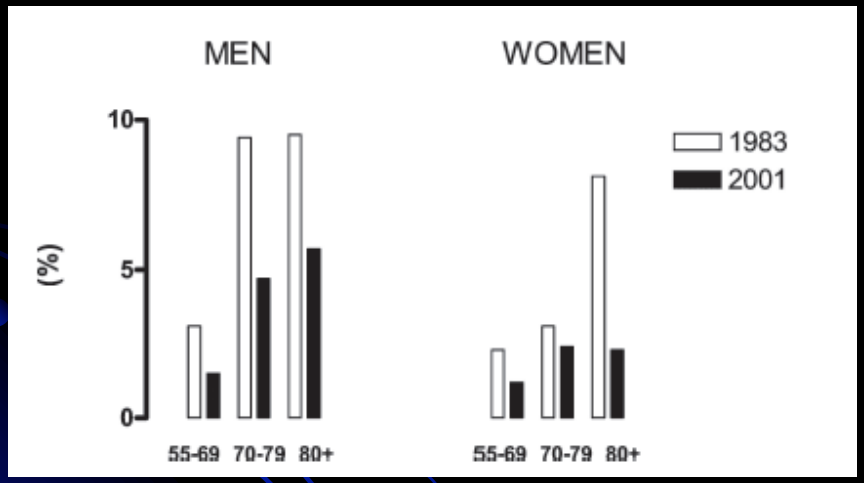
# Επιπολασμός




L Corral-Gudino et al. Bone 2013

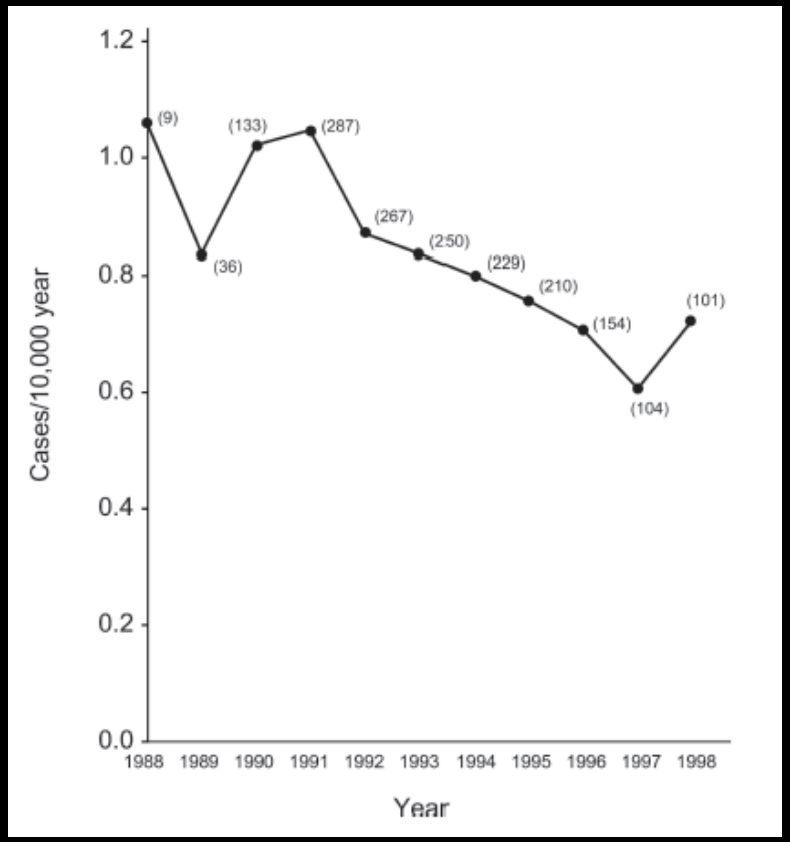
# Ελάττωση επιπολασμού και επίπτωσης

**Dunedin, Νέα Ζηλανδία**




T Cundy J Bone Miner Res 2006

**Hv. Βασίλειο**



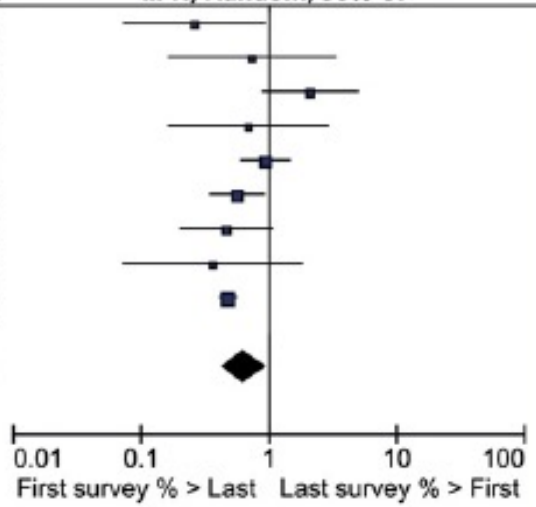

C Cooper et al. J Bone Miner Res 2006

# Ελάττωση επιπολασμού

| Study or Subgroup | Last X-ray survey Events | Total | First X-ray survey Events | Total | Weight | Odds Ratio M-H, Random, 95% CI |
|---|---|---|---|---|---|---|
| Denmark (1982-2001) | 3 | 950 | 12 | 1006 | 6.0% | 0.26 [0.07, 0.93] |
| Greek (1982-2001) | 3 | 912 | 4 | 901 | 4.6% | 0.74 [0.17, 3.32] |
| Italy (1986-2001) | 11 | 1219 | 10 | 2305 | 10.2% | 2.09 [0.89, 4.93] |
| Norway (1982-2001) | 3 | 890 | 5 | 1027 | 4.9% | 0.69 [0.16, 2.90] |
| NZ Auckland (1998-2006) | 87 | 3350 | 27 | 979 | 18.3% | 0.94 [0.61, 1.46] |
| NZ Dunedin (1982-1998) | 27 | 1019 | 46 | 1000 | 17.2% | 0.56 [0.35, 0.92] |
| Spain (1982-2001) | 8 | 1587 | 19 | 1766 | 10.6% | 0.47 [0.20, 1.07] |
| Switzerland (1982-2001) | 2 | 950 | 6 | 1041 | 4.1% | 0.36 [0.07, 1.81] |
| UK (1977/1980-1995) | 252 | 9828 | 496 | 9515 | 24.1% | 0.48 [0.41, 0.56] |
| **Total (95% CI)** | | **20705** | | **19540** | **100.0%** | **0.64 [0.45, 0.91]** |
| Total events | 396 | | 625 | | | |

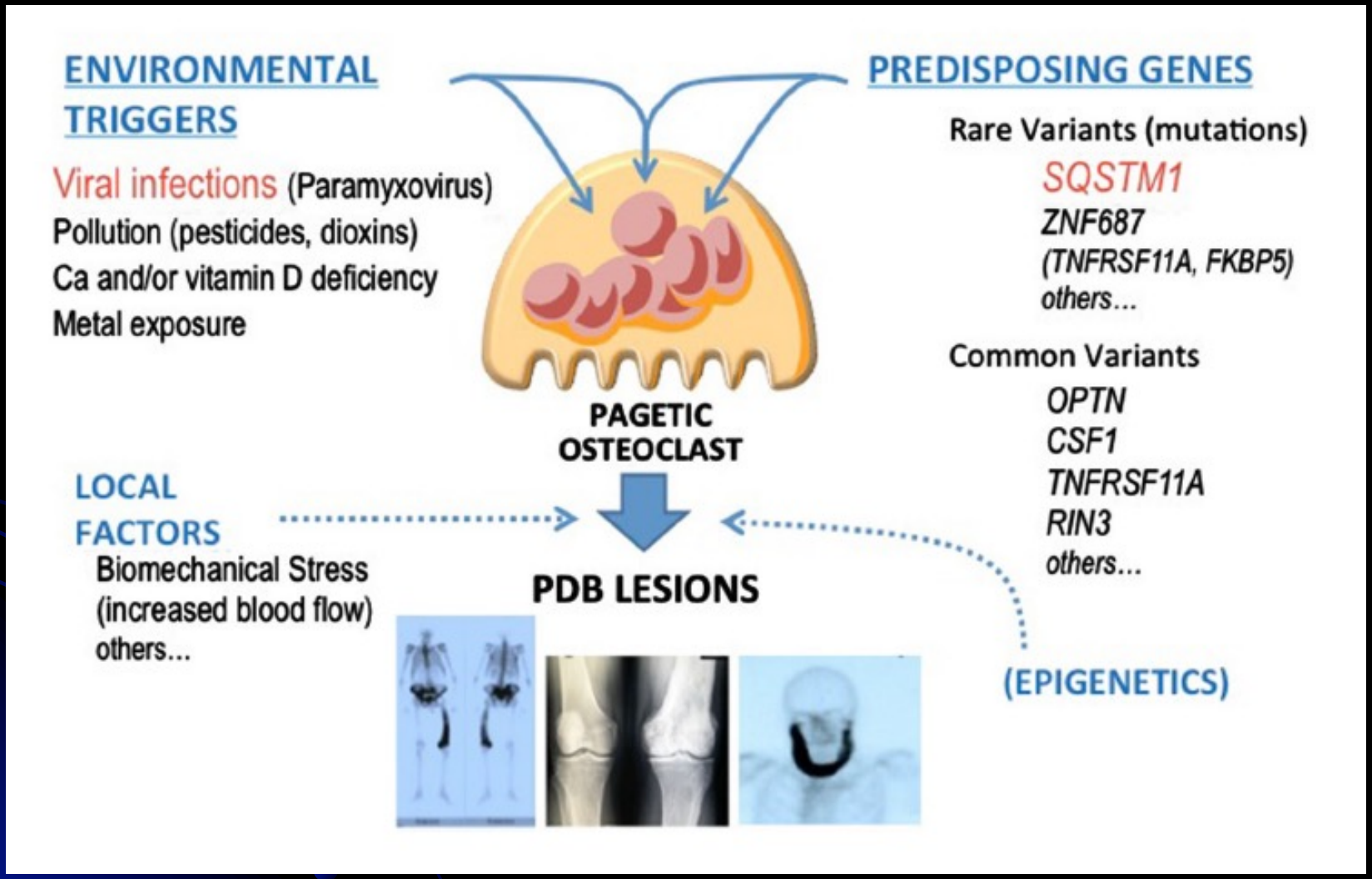
Heterogeneity: $Tau^2 = 0.13$; $Chi^2 = 19.93$, df = 8 (P = 0.01); $I^2 = 60\%$

Test for overall effect: Z = 2.47 (P = 0.01)



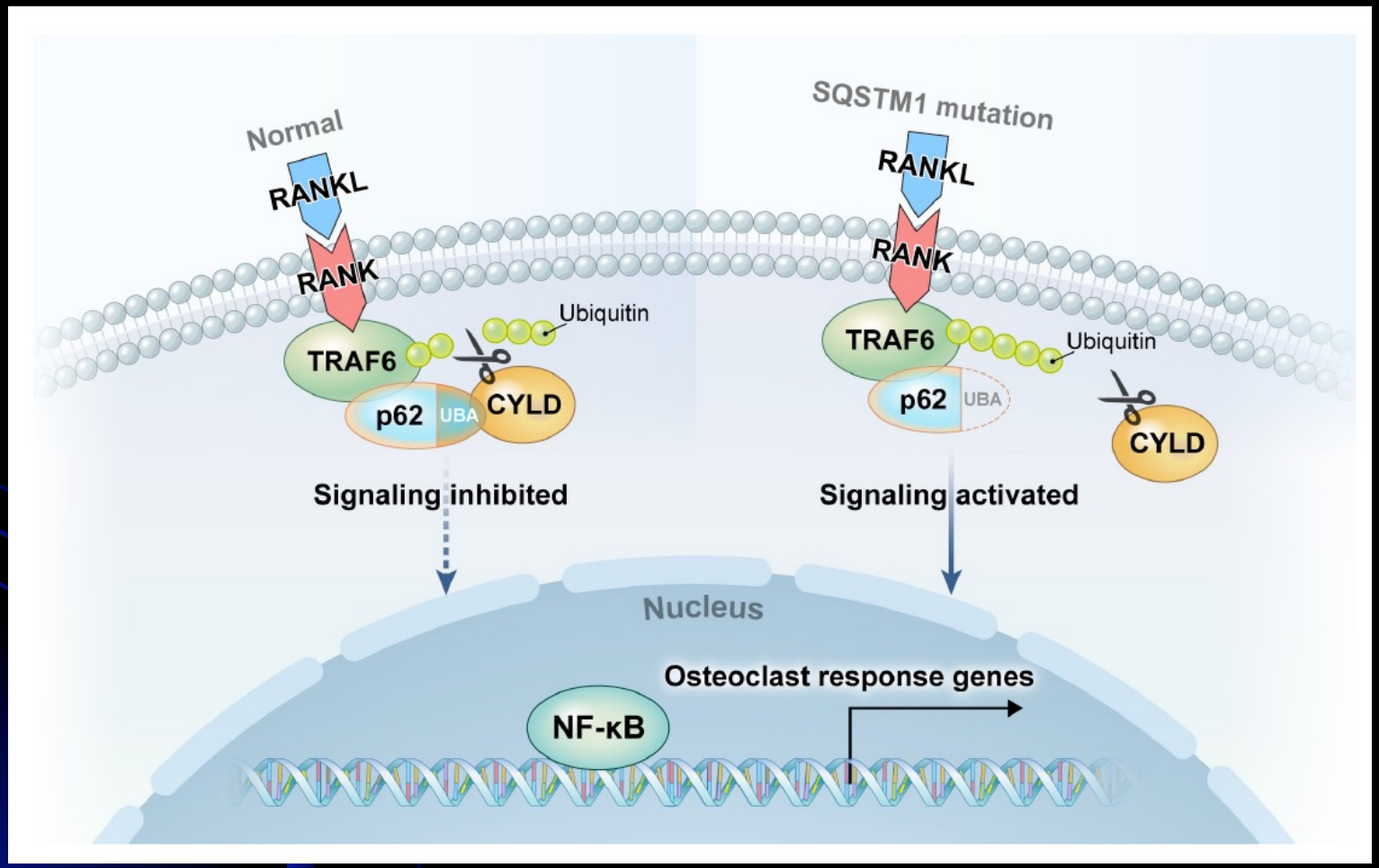

L Corral-Gudino et al. Bone 2013

# Παθογένεια



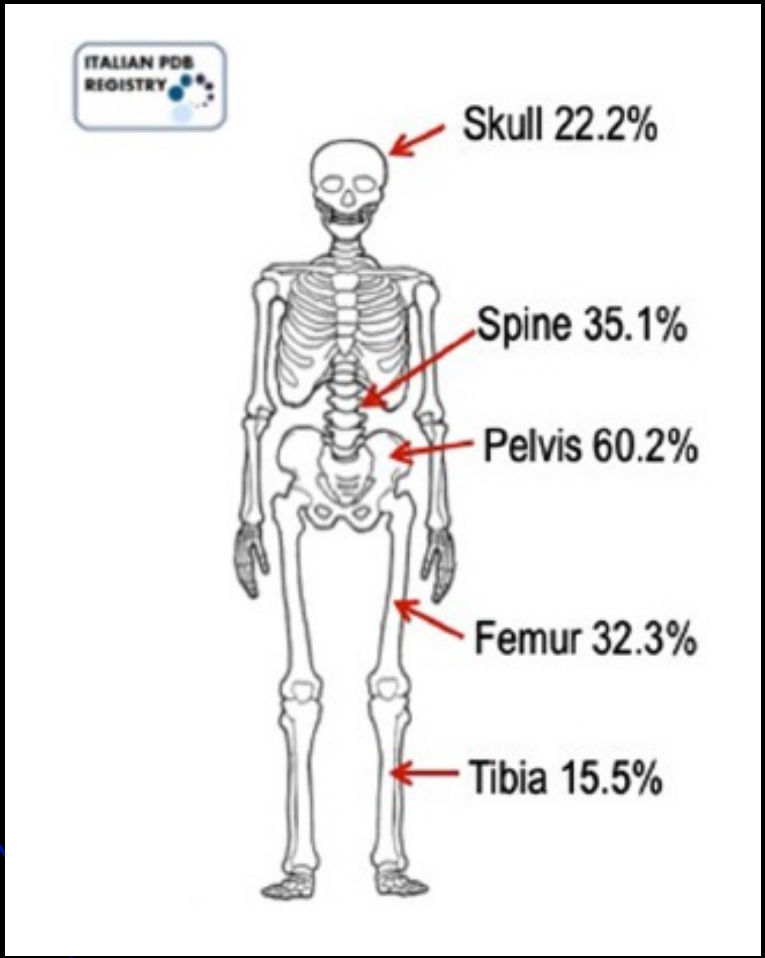

L Gennari et al. Calcif Tissue Int 2019

# Ενεργοποίηση οστεοκλαστών σε sequestosome 1 gene (SQSTM1) mutations




YJ Choi et al. Endocrinol Metab 2022

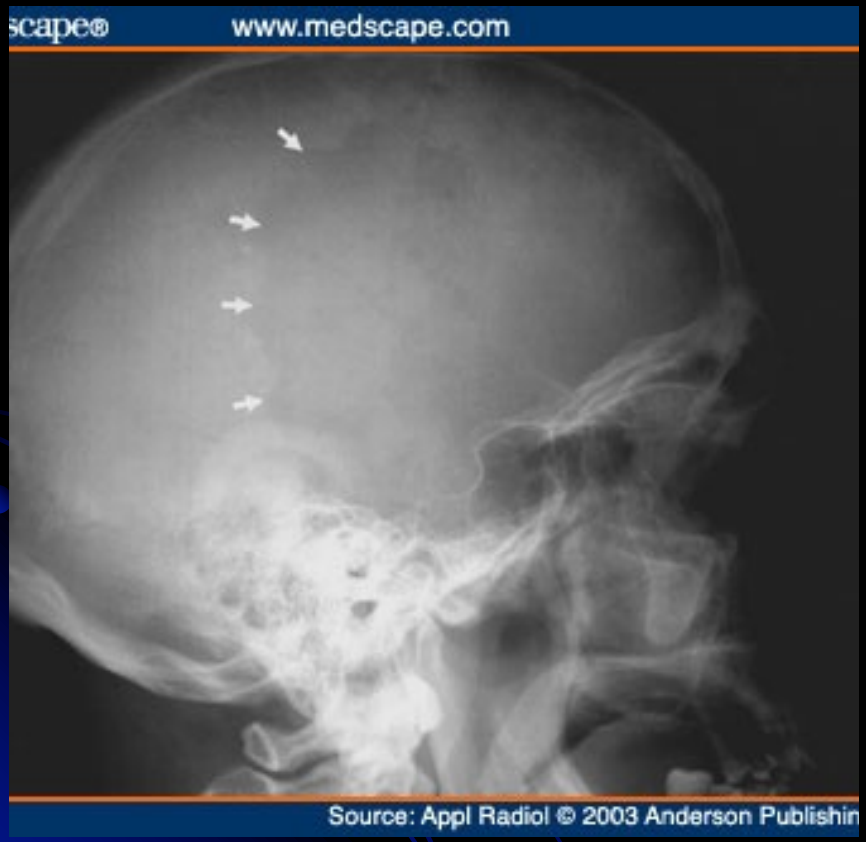
# Συχνότερες οστικές εντοπίσεις




L Gennari et al. Calcif Tissue Int 2019

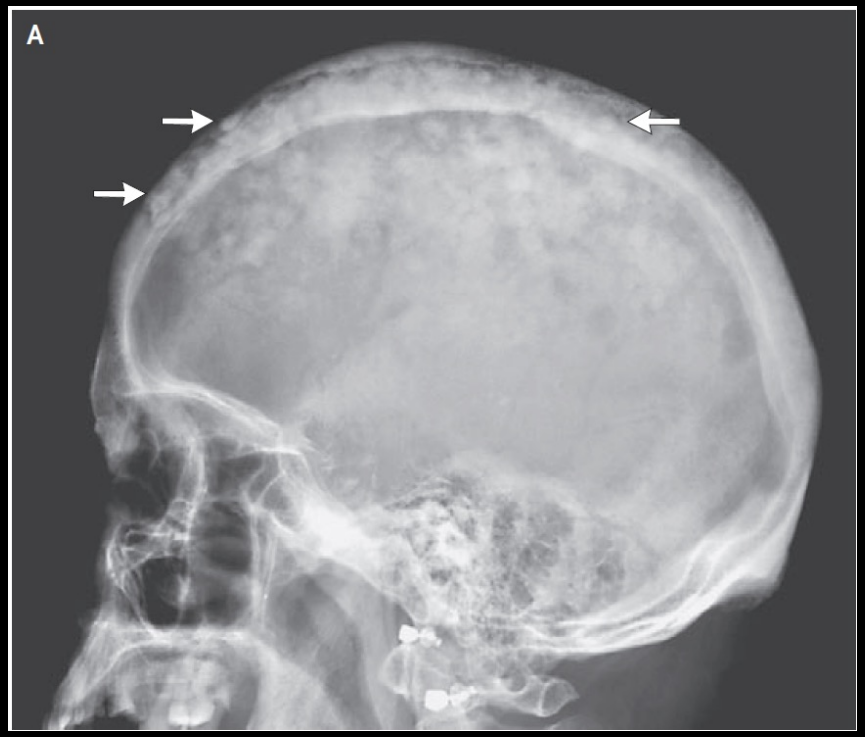
# Διάγνωση

**Osteoporosis circumscripta**



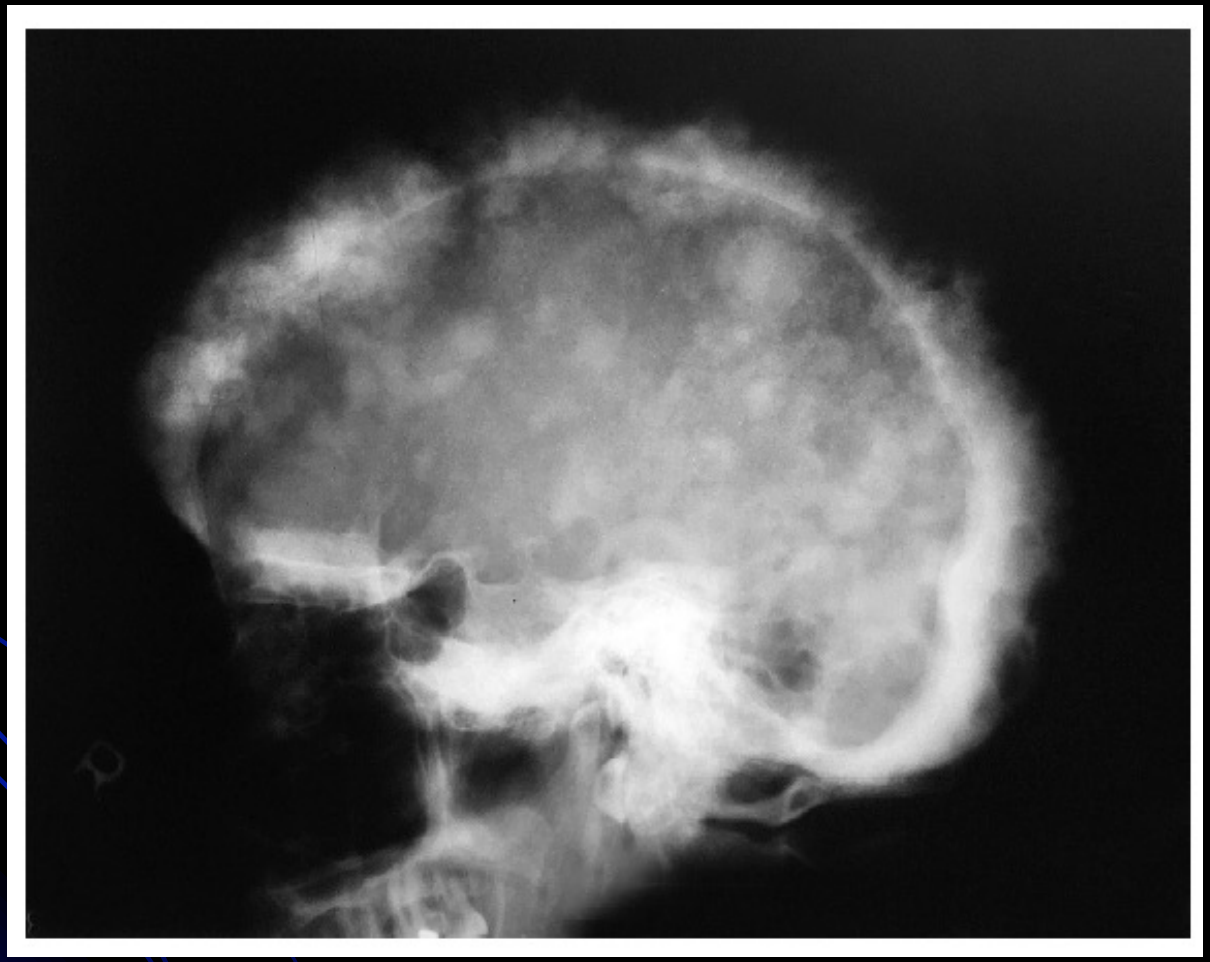

**Χρόνια «ιγμορίτιδα» & μετωπιαία κεφαλαλγία, TALP=434 IU/L**

**"Cotton Wool"**




P Bhargava et al. NEJM 2010

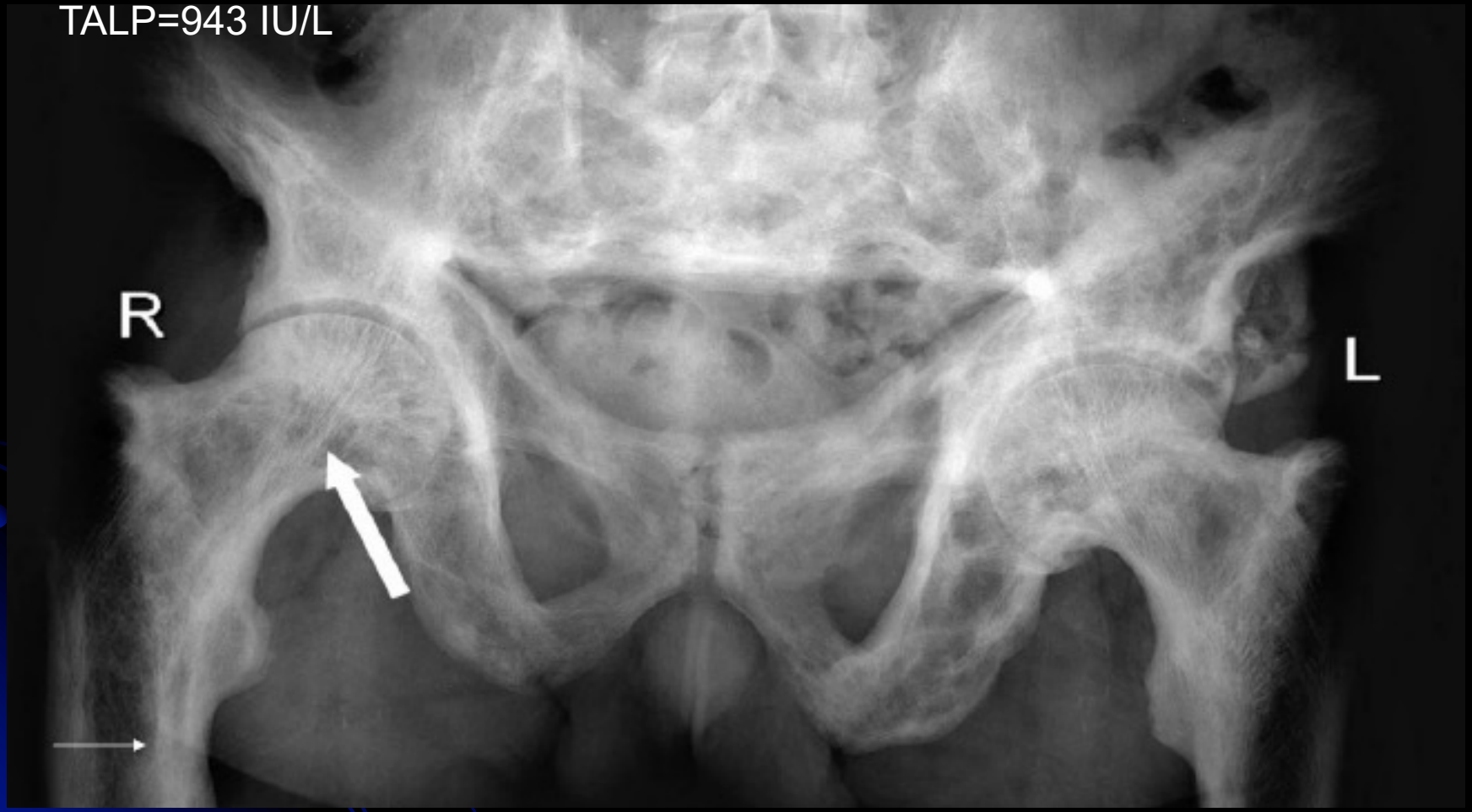
# Διάγνωση



FR Singer. Best Pract Res Clin Rheumatol 2020

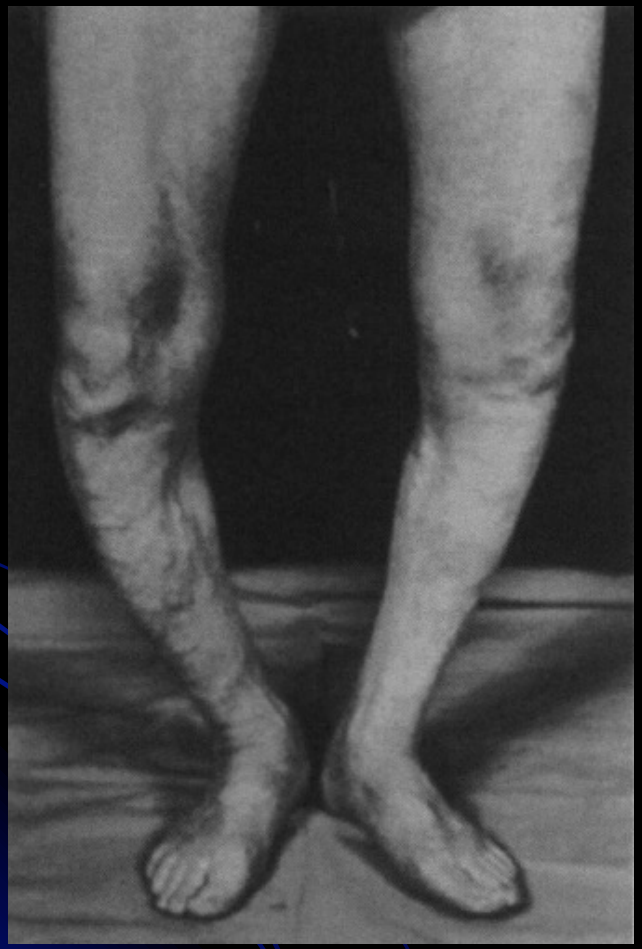
# Διάγνωση

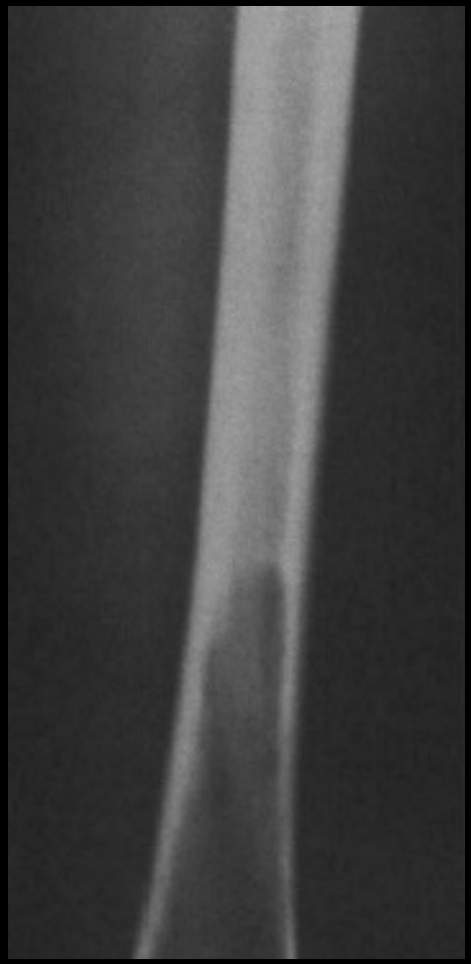
Προοδευτικό άλγος λεκάνης, ισχίου ΔΕ, γόνατος ΑΡ, ώμων άμφω και οσφύος
TALP=943 IU/L




BJ Sheane et al. J Clin Rheumatol 2008

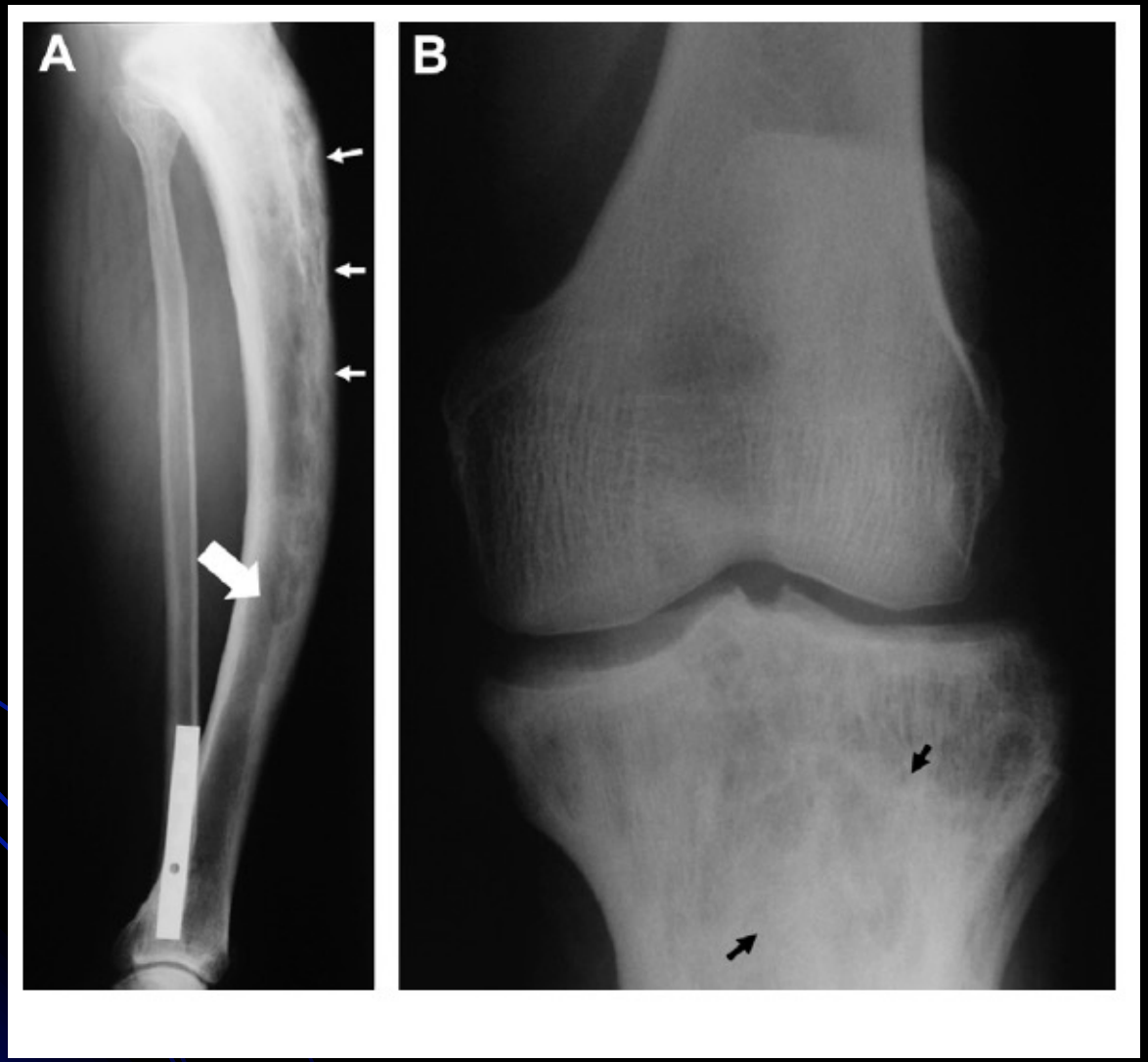
# Διάγνωση





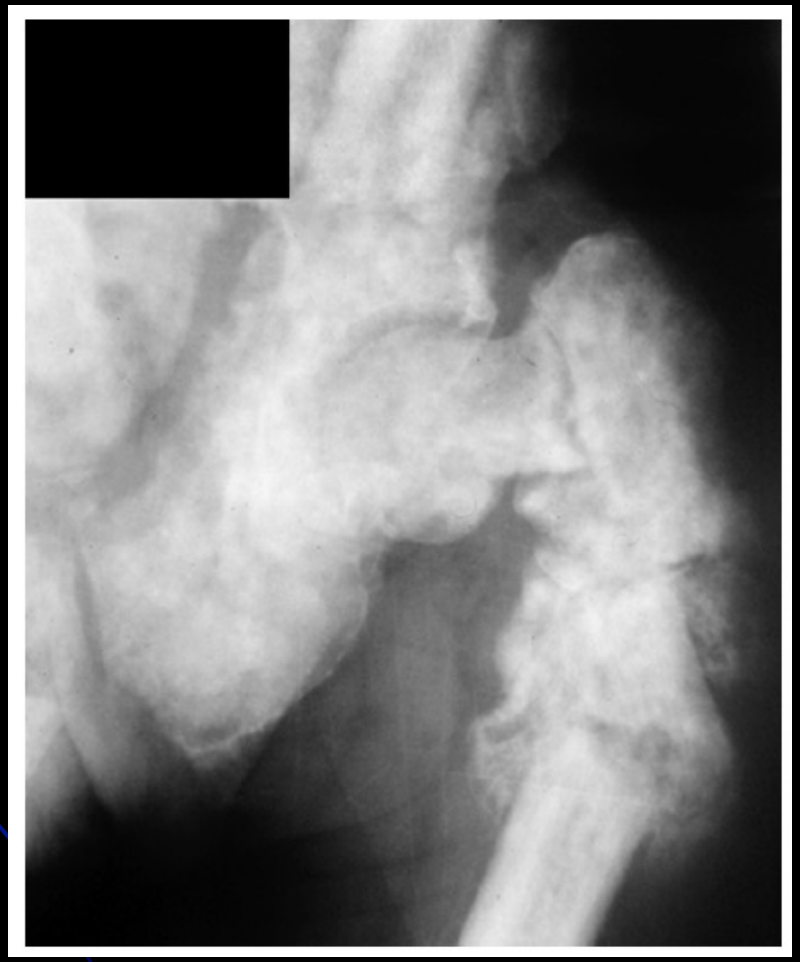
A Abelson. Curr Med Res Opin 2008

# Διάγνωση



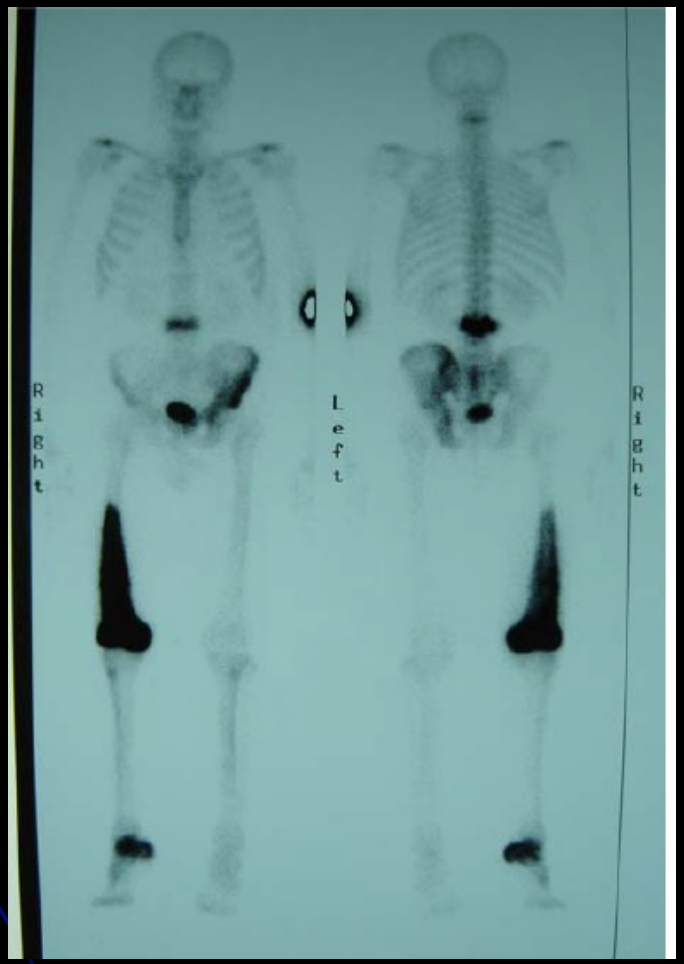

AF Lombardi Radiol Clin N Am 2022

# Οστεοσάρκωμα επί νόσου Paget

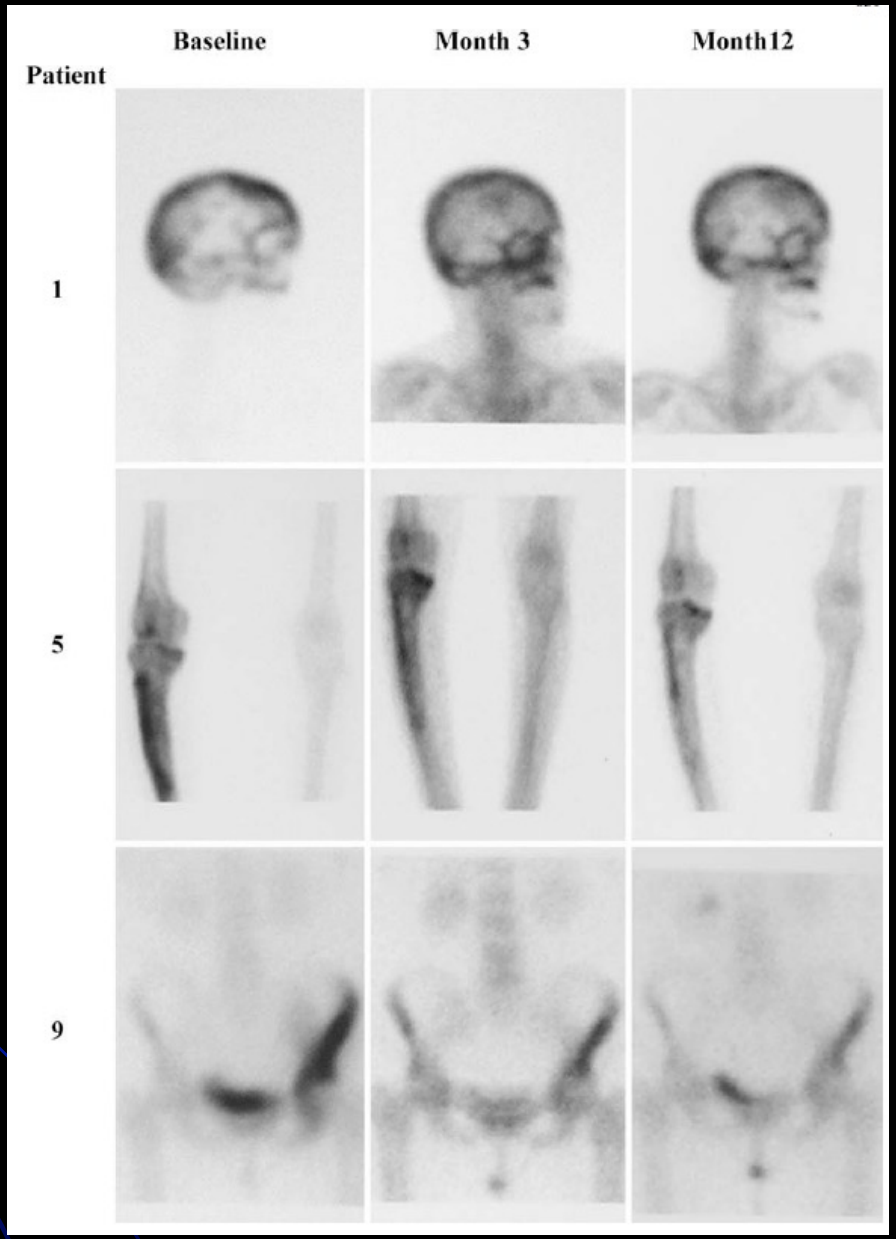


AF Lombardi Radiol Clin N Am 2022

# Έκταση νόσου




M Colina et al. Rheumatol Int 2008




SA Polyzos et al. J Bone Miner Metab 2008

# Follow-up

- TSAP (+γGT)
- P1NP
- BSAP (20% cross-reactivity με ηπατική ALP)
- CTx (αCTx vs. βCTx)
- Σπινθηρογράφημα
  - Όταν φυσιολογικοί BT markers

SA Polyzos et al. Expert Rev Endocrinol Metab 2009

Endocrine Society Guidelines JCEM 2014

# Επιπλοκές

| System | Complications | |
|---|---|---|
| | Common | Rare (< 1%) |
| Osteoarticular | Bone pain<br>Bone deformity<br>Osteoarthritis at adjacent joints<br>Fractures | Spinal stenosis |
| Neurological | Hearing loss<br>Tinnitus | Cranial nerve deficits<br>Basilar impression<br>Hydrocephalus<br>Paraplegia, paraparesis<br>Vascular steal syndrome |
| Metabolic | Hyperparathyroidism[a] | Hyperuricemia<br>Hypercalcemia<br>Nephrolithiasis |
| Cardiovascular | | High output heart failure<br>Generalized atherosclerosis<br>Endocardial calcifications<br>Aortic stenosis |
| Neoplastic | | Sarcomas<br>Giant cell tumor |

L Gennari et al. Calcif Tissue Int 2019

# Νοσηρότητα

TABLE 3. PREVALENCE OF MORBIDITIES IN PAGET'S DISEASE PATIENTS AND CONTROLS[6]

| | *Paget's disease group (n = 2465)* | | *Control group (n = 7395)* | | *Crude relative risk* | |
|---|---|---|---|---|---|---|
| | *No. of cases* | *Rate (%)* | *No. of cases* | *Rate (4%)* | *Ratio* | *95% CL* |
| Back pain | 601 | 10.2 | 887 | 4.9 | 2.1 | 1.9–2.3 |
| OA–osteoarthritis | 352 | 5.6 | 619 | 3.4 | 1.7 | 1.5–1.9 |
| Dizziness/giddiness | 322 | 5.0 | 678 | 3.7 | 1.3 | 1.2–1.5 |
| Fracture | 194 | 2.8 | 437 | 2.3 | 1.2 | 1.0–1.5 |
| Femur/hip fracture | 71 | 1.0 | 137 | 0.7 | 1.4 | 1.1–1.9 |
| Hearing loss | 170 | 2.4 | 296 | 1.5 | 1.6 | 1.3–1.9 |
| Hip arthroplasty | 104 | 1.5 | 93 | 0.5 | 3.1 | 2.4–4.1 |
| Knee arthroplasty | 25 | 0.3 | 43 | 0.2 | 1.6 | 1.0–2.6 |
| Tinnitus | 47 | 0.6 | 85 | 0.4 | 1.5 | 1.1–2.2 |
| Cranial nerve disorder | 17 | 0.2 | 39 | 0.2 | 1.2 | 0.7–2.1 |
| Malignant neoplasm of bone | 1 | 0.1 | 0 | 0 | ∞ | 5.0–∞ |

HG Bone J Bone Miner Res 2006

# Ελάττωση σοβαρής νόσου

| Sociodemographic data and comorbidities at first visit for PDB | | Historical cohort ($N = 173$) | Contemporary cohort ($N = 195$) | Unadjusted p-value[a] | Adjusted p-value[b] |
|---|---|---|---|---|---|
| Sex, n (%) | Women | 67/173 (38.7 %) | 91/195 (46.7 %) | 0.1400 | 1.0000 |
| | Men | 106/173 (61.3 %) | 104/195 (53.3 %) | | |
| Age at PDB diagnosis, mean ± standard deviation | | 58.5 ± 10.1 | 68.7 ± 10.7 | <0.0001 | <0.0001 |
| Positive family history of PDB, n (%) | | 47/140 (33.6 %) | 23/167 (13.8 %) | <0.0001 | 0.0024 |
| Ever smoker, n (%) | | 8/18 (44.4 %) | 47/99 (47.5 %) | 1.0000 | 1.0000 |
| Marital status, n (%) | Single | 0/3 (0.0 %) | 4/26 (15.4 %) | 0.5161 | 1.0000 |
| | Divorced | 0/3 (0.0 %) | 2/26 (7.7 %) | | |
| | Married | 3/3 (100 %) | 14/26 (53.8 %) | | |
| | Widowed | 0/3 (0.0 %) | 6/26 (23.1 %) | | |
| Ethnicity, n (%) | Arabic | 0/7 (0.0 %) | 1/85 (1.2 %) | 1.000 | 1.0000 |
| | African | 0/7 (0.0 %) | 1/85 (1.2 %) | | |
| | Caucasian | 7/7 (100 %) | 83/85 (97.6 %) | | |
| Primary osteoarthritis, n (%) | | 13/34 (38.2 %) | 40/118 (33.9 %) | 0.6852 | 1.0000 |
| Hypertension, n (%) | | 11/34 (32.4 %) | 67/118 (56.8 %) | 0.0187 | 1.0000 |
| Atherosclerotic coronary disease, n (%) | | 7/34 (20.6 %) | 21/118 (17.8 %) | 0.8021 | 1.0000 |
| Rheumatoid arthritis, n (%) | | 1/34 (2.9 %) | 5/118 (4.2 %) | 1.0000 | 1.0000 |
| Chronic obstructive pulmonary disease, n (%) | | 1/34 (2.9 %) | 3/118 (2.5 %) | 1.0000 | . |
| Osteoporosis, n (%) | | 4/34 (11.8 %) | 19/118 (16.1 %) | 0.6018 | 1.0000 |

[a] Based on Chi-square exact test or Wilcoxon Mann Whitney test.
[b] Based on Bonferroni correction method.

E Gendron et al. Bone 2023

# Ελάττωση σοβαρής νόσου

| Clinical characteristics at first visit for PDB | Historical cohort (N = 173) | Contemporary cohort (N = 195) | Unadjusted p-value[a] | Adjusted p-value[b] |
|---|---|---|---|---|
| Incidental diagnosis, n (%) | 16/24 (66.7 %) | 97/113 (85.8 %) | 0.0369 | 1.0000 |
| Bone pain related to PDB, n (%) | 20/38 (52.6 %) | 64/123 (52.0 %) | 1.0000 | |
| Number of bones affected, median (interquartile range) | 2 (1; 5) | 1 (1; 3) | <0.0001 | <0.0001 |
| Rénier's index[c], mean ± SD (%) | 12.5 ± 9.5 | 8.2 ± 7.6 | <0.0001 | <0.0001 |
| Monostotic, n (%) | 53/173 (30.6 %) | 118/195 (60.5 %) | <0.0001 | <0.0001 |
| Skull, n (%) | 33/106 (31.1 %) | 43/150 (28.7 %) | 0.6793 | 1.0000 |
| Lower limb, n (%) | 59/106 (55.7 %) | 60/150 (40.0 %) | 0.0157 | 0.9281 |
| Upper limb, n (%) | 35/105 (33.3 %) | 24/150 (16.0 %) | 0.0015 | 0.0897 |
| Pelvis, n (%) | 68/105 (64.8 %) | 83/150 (55.3 %) | 0.1547 | 1.0000 |
| Spine, n (%) | 39/105 (37.1 %) | 34/149 (22.8 %) | 0.0165 | 0.9762 |
| Other, n (%) | 9/105 (8.6 %) | 11/150 (7.3 %) | 0.8140 | 1.0000 |
| | | | | |
| Complications of PDB | | | | |
| Bone deformity, n (%) | 26/48 (54.0 %) | 15/115 (13.0 %) | < 0.0001 | <0.0001 |
| Fracture of pagetic bone, n (%) | 11/30 (36.7 %) | 7/105 (6.7 %) | 0.0001 | 0.0078 |
| Orthopedic surgery related to PDB complications, n (%) | 6/21 (28.6 %) | 8/91 (8.8 %) | 0.0237 | 1.0000 |
| Secondary osteoarthritis, n (%) | 16/31 (51.6 %) | 46/107 (43.0 %) | 0.4188 | 1.0000 |
| Gait instability, n (%) | 3/8 (37.5 %) | 10/24 (41.7 %) | 1.0000 | 1.0000 |
| Hearing disorder, n (%) | 11/18 (61.1 %) | 27/52 (51.9 %) | 0.5885 | 1.0000 |
| Spinal stenosis, n (%) | 5/9 (55.6 %) | 12/24 (50.0 %) | 1.0000 | 1.0000 |
| Urinary lithiasis, n (%) | 1/1 (100.0 %) | 4/10 (40.0 %) | 0.4545 | 1.0000 |
| Osteosarcoma, n (%) | 0/7 (0.0 %) | 0/78 (0.0 %) | – | – |

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# Θεραπεία-Πότε;

**Table 1** Indications for therapy in asymptomatic Paget's disease of bone

| |
|---|
| Age at diagnosis: lower than 50 |
| Location of the bone lesion [2–4, 7, 8, 10, 26] |
| Limbs (close to joints) (risk of osteoarthritis) |
| Lytic lesions (risk of fracture) |
| Hip |
| Cervical and thoracic spine (risk of neurologic complications: spinal stenosis or pagetic steal syndrome) |
| Skull (particularly the base: risk of hearing loss and/or other neurologic complications) |
| Jaws (facial deformity, buccal malocclusion) |
| Elevated values of TAP [25, 28] (more than twice the upper limit of normal) |
| Planned orthopaedic intervention |

TAP = total alkaline phosphatase activity

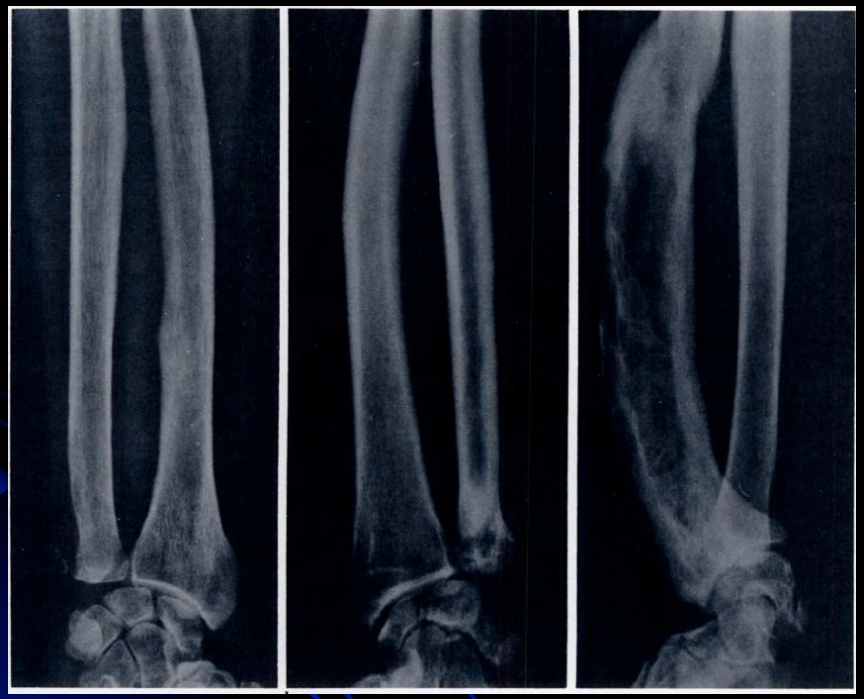
*"We recommend treatment with a bisphosphonate for most patients with active Paget's disease who are at risk of future complications."*

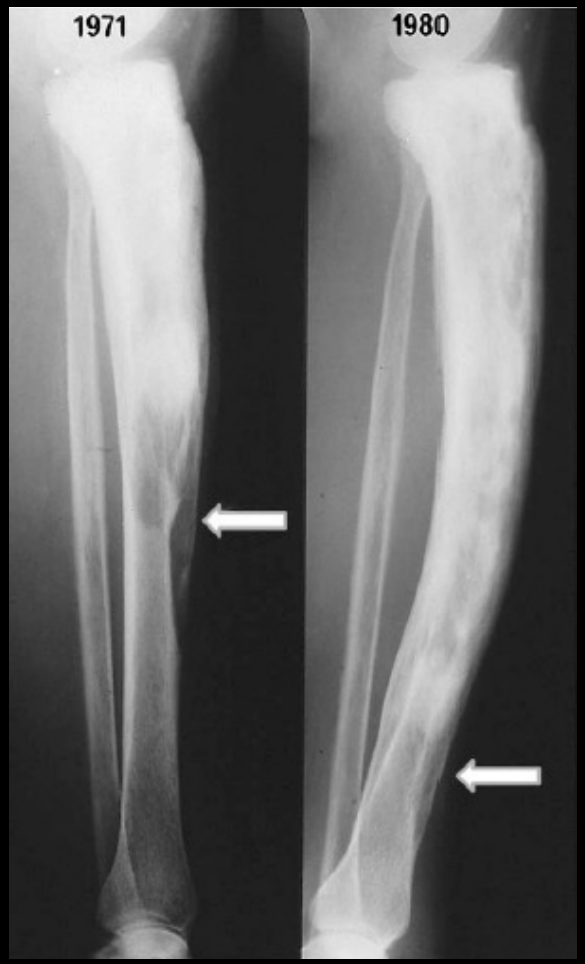
Burned-out?

Belgian Bone Club Guidelines Osteoporos Int 2007

Endocrine Society Guidelines JCEM 2014

# Χωρίς Θεραπεία






CJ Vellenga Radiology 1984

IR Reid Bone 2010

# Θεραπεία

**Table 2.** Recommended Bisphosphonate Dosing Regimens

| Drug | Dosage |
|---|---|
| Zoledronate[a] | 5 mg given as a single infusion over 15 min. Retreatment is seldom required within 5 y |
| Alendronate | 40 mg/d for 6 mo. Retreatment may be required between 2 and 6 y |
| Risedronate | 30 mg/d for 2 mo. Retreatment may be required between 1 and 5 y |

[a] The authors recognize that the official generic name for this drug is "zoledronic acid." However, that is a misnomer. In fact, it is the sodium salt, not the acid, that is used in medical practice. Therefore, we have elected to use "zoledronate," which is consistent with the usual nomenclature for bisphosphonates.

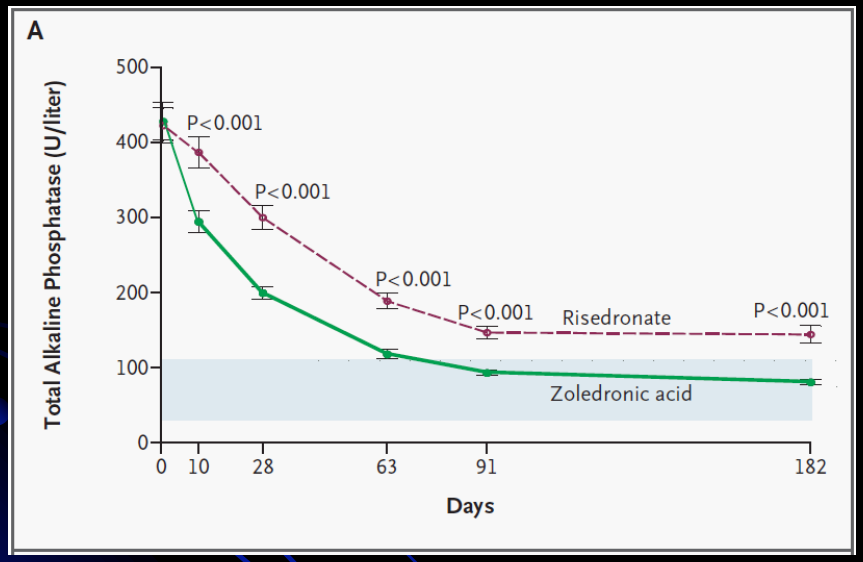
?

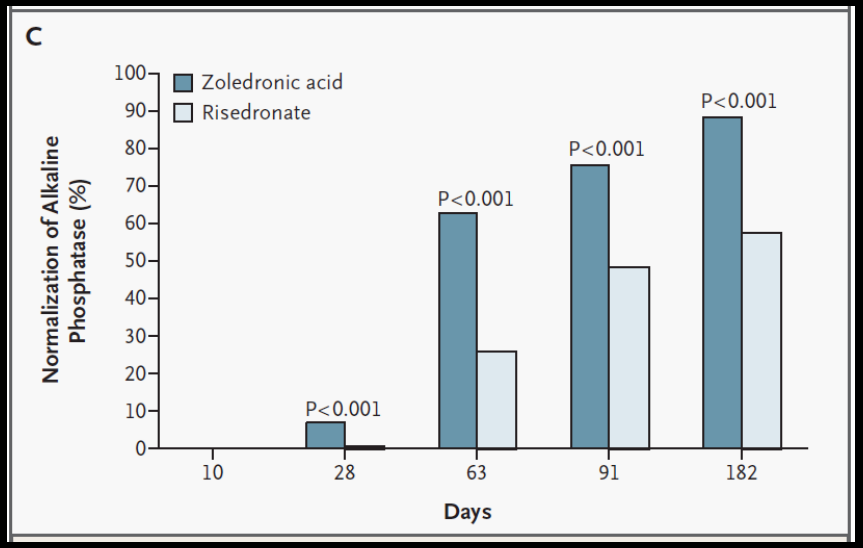
- Καλσιτονίνη ✖
- Ετιδρονάτη ✖
- Κλοδρονάτη ✖
- Τιλουδρονάτη ✖
- Ιμπανδρονάτη ?

- Παμιδρονάτη

Endocrine Society Guidelines JCEM 2014

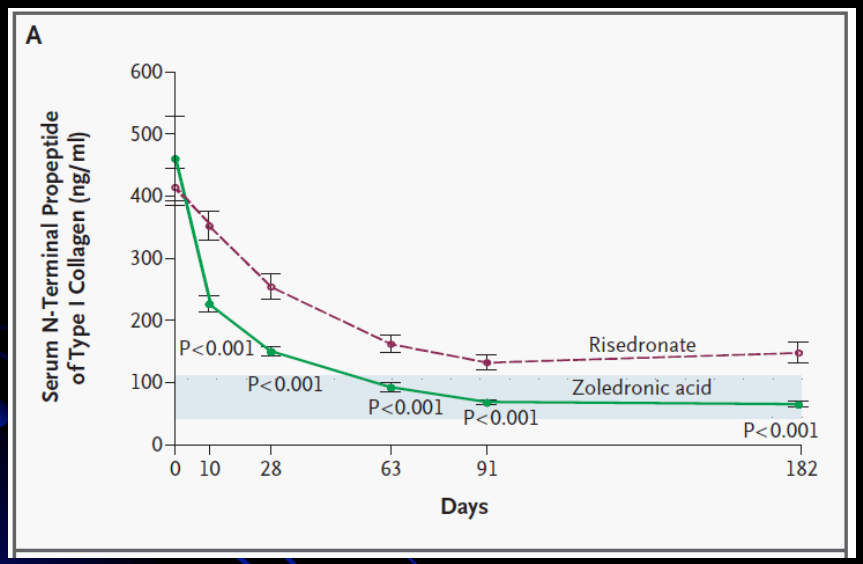
# Ρισεδρονάτη vs. Ζολεδρονικό (RCT)

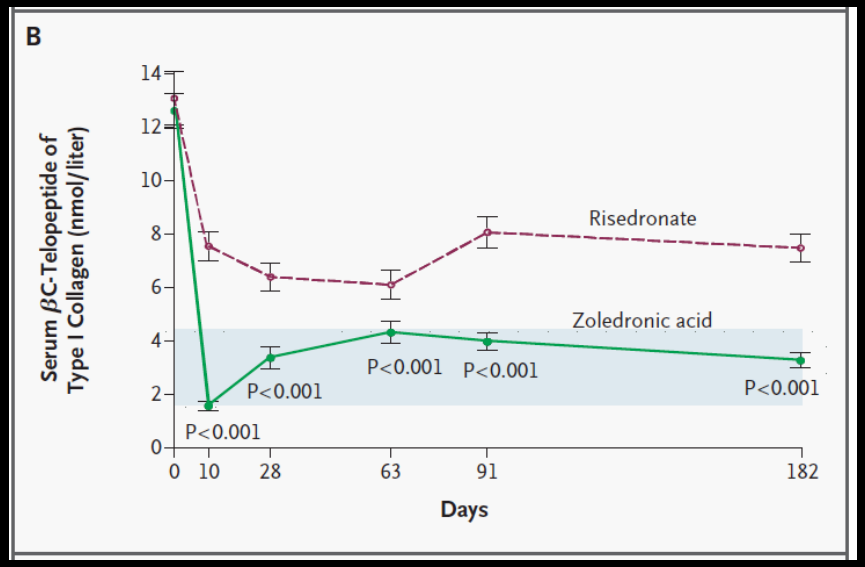


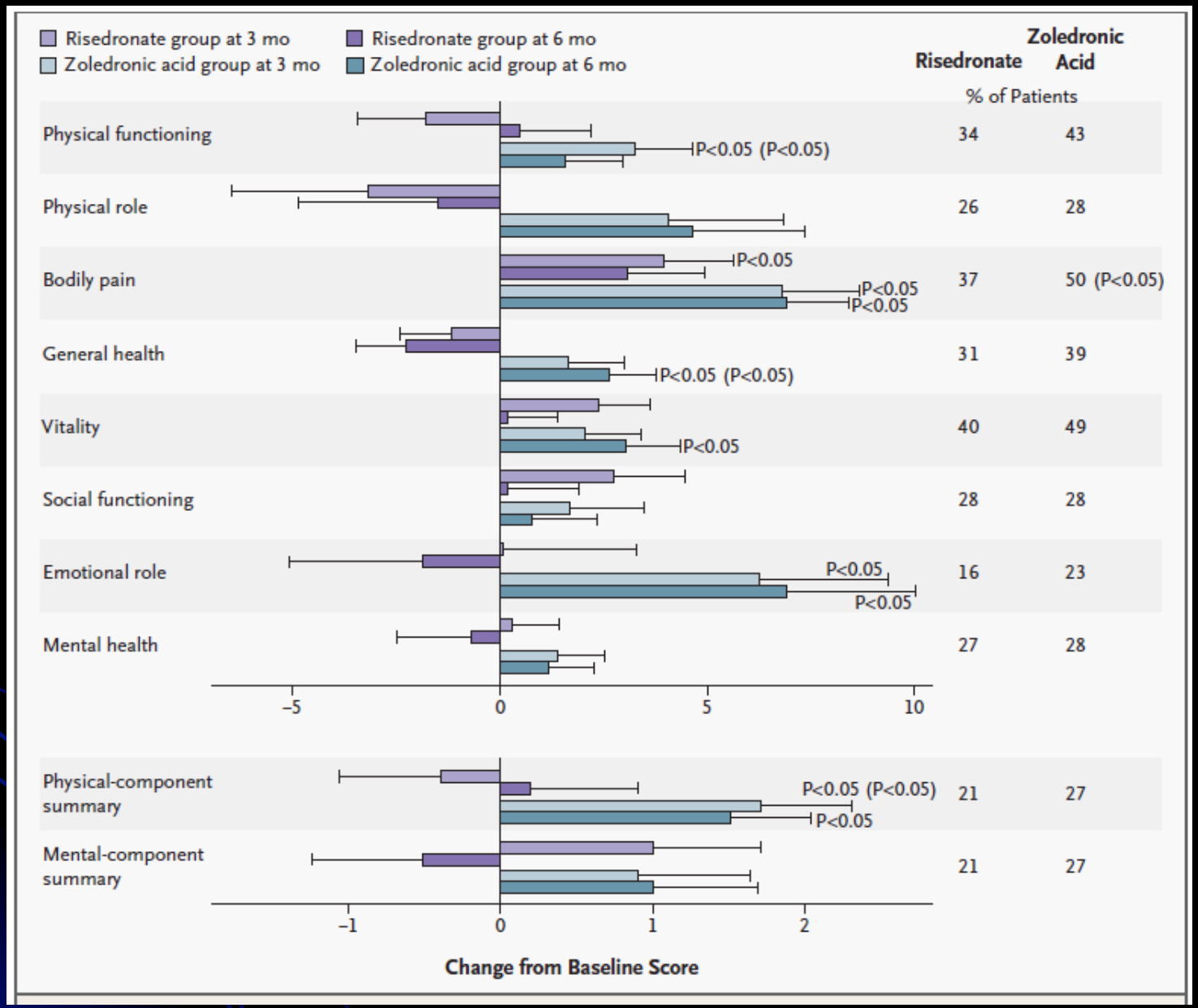

IR Reid et al. NEJM 2005

# Ρισεδρονάτη vs. Ζολεδρονικό (RCT)



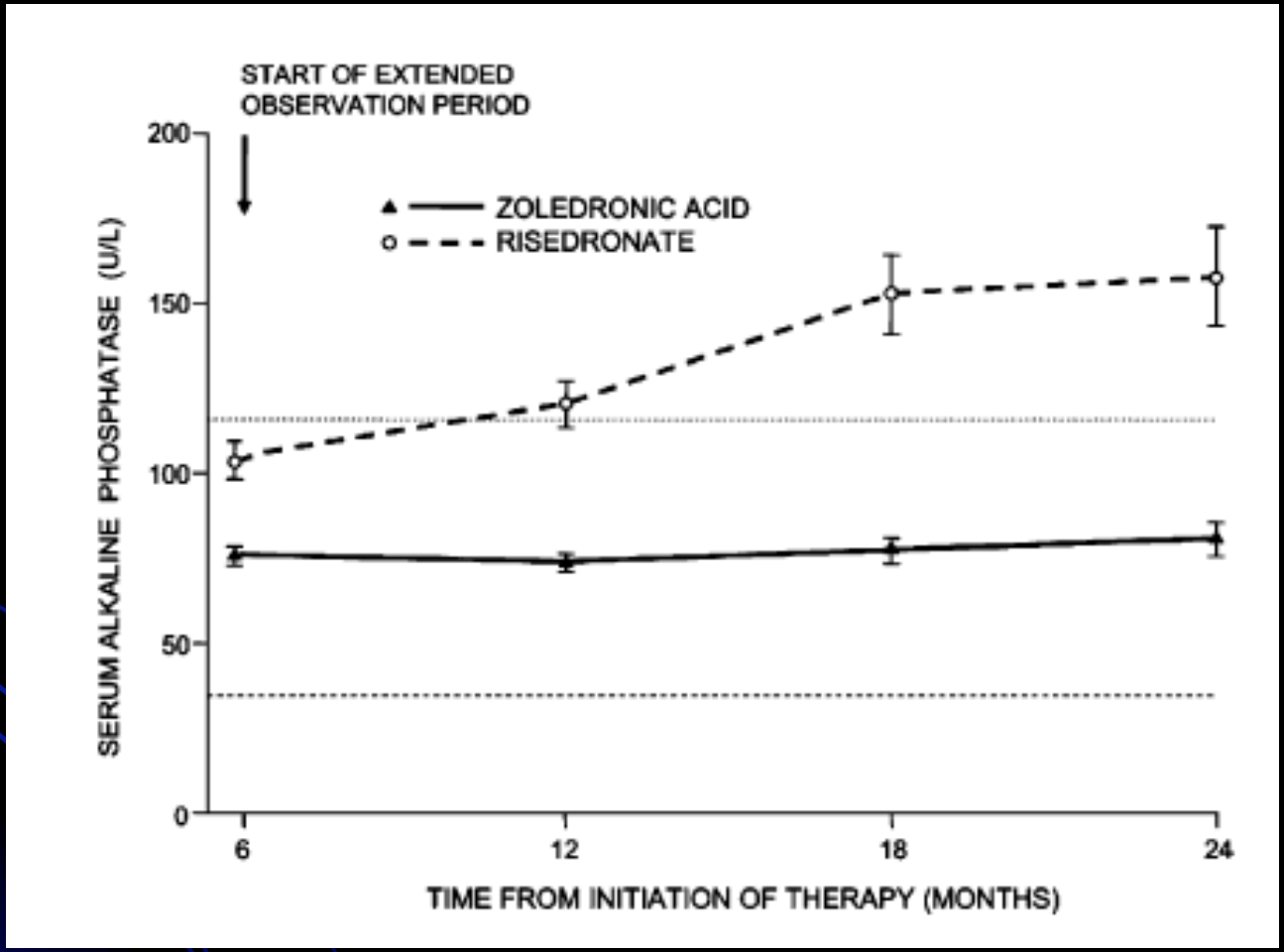




IR Reid et al. NEJM 2005




IR Reid et al. NEJM 2005

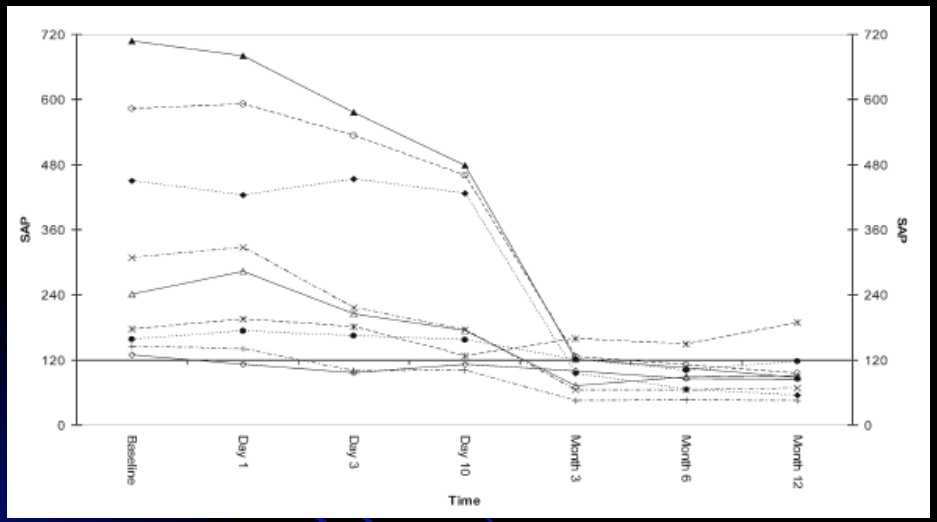
# Ρισεδρονάτη vs. Ζολεδρονικό - Επέκταση



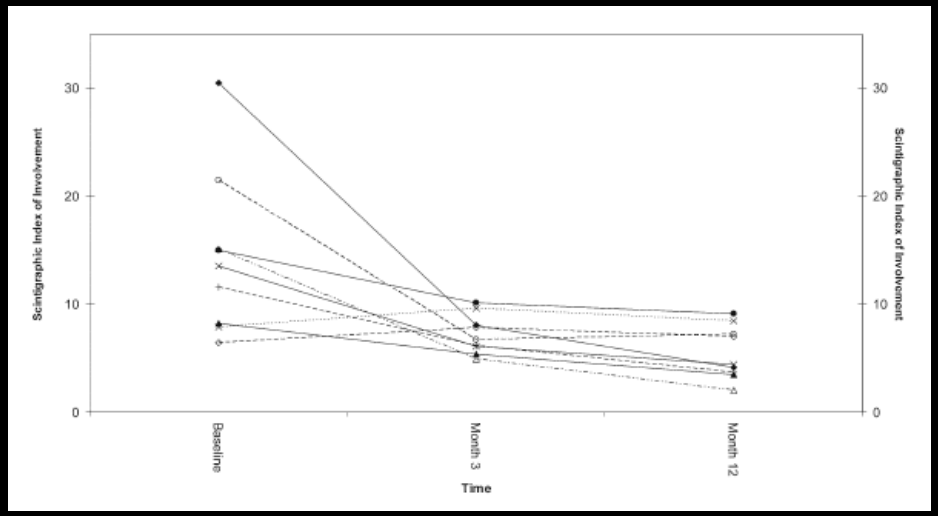

D Hosking et al. J Bone Miner Res 2007

# Ζολενδονικό σε νόσο Paget

**TSAP**

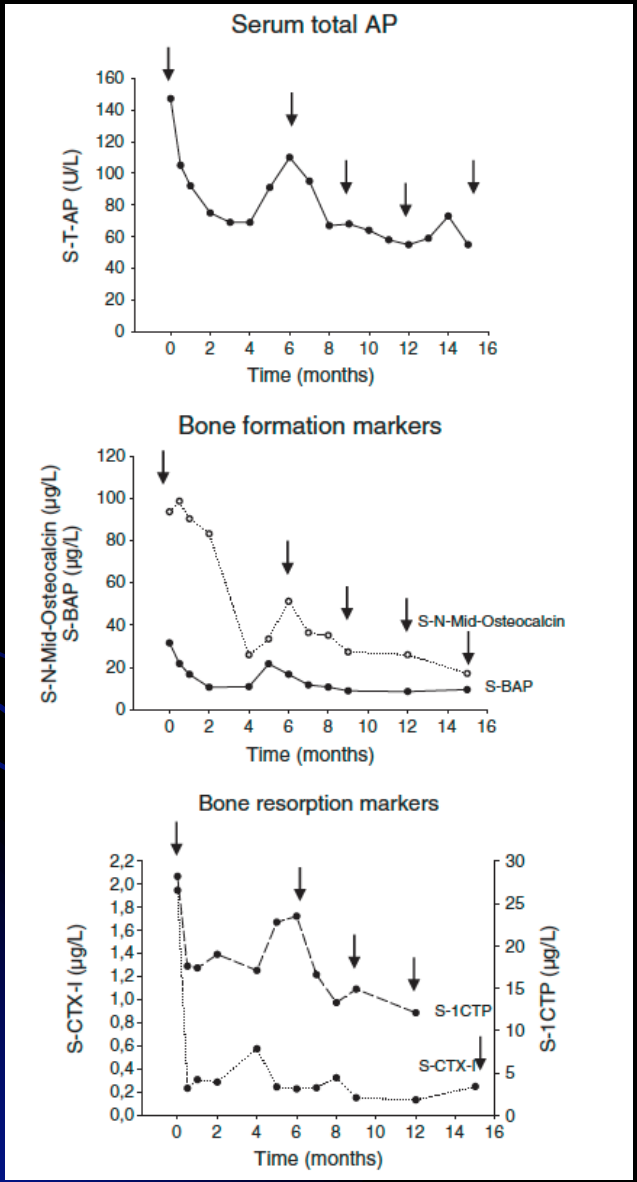


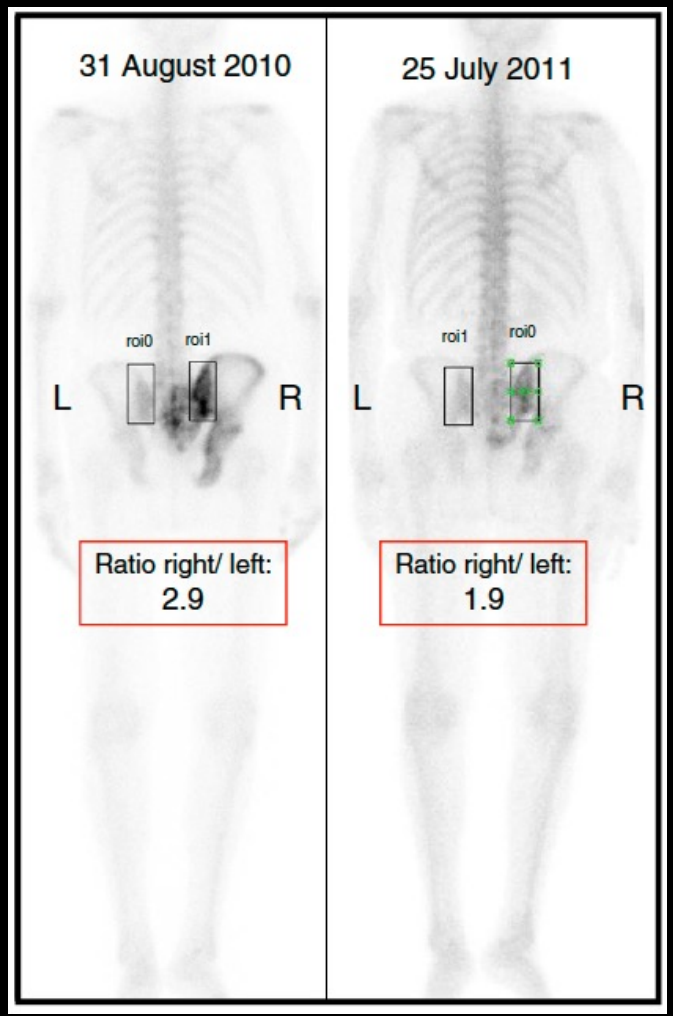

**Scintigraphic Index**




SA Polyzos et al. J Bone Miner Metab 2008

# Denosumab (60 mg) σε v. Paget



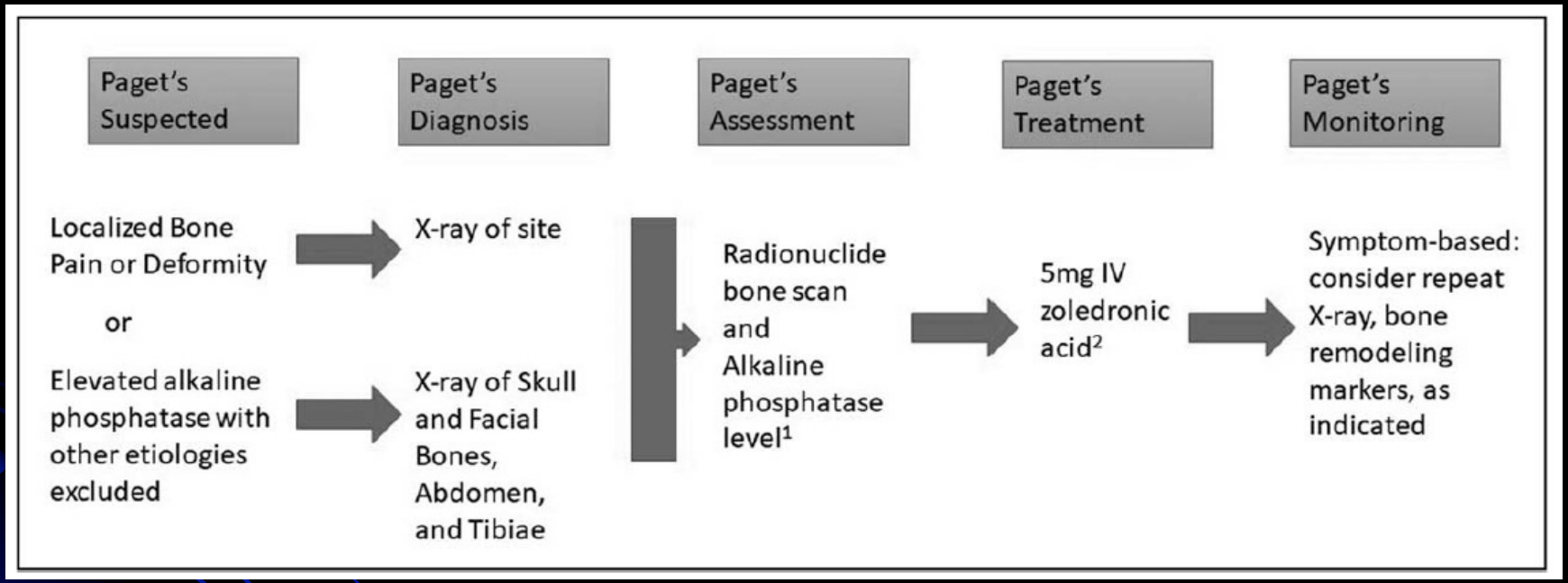

P Schwarz et al. Bone 2012

# Ασβέστιο, μαγνήσιο και βιταμίνη D

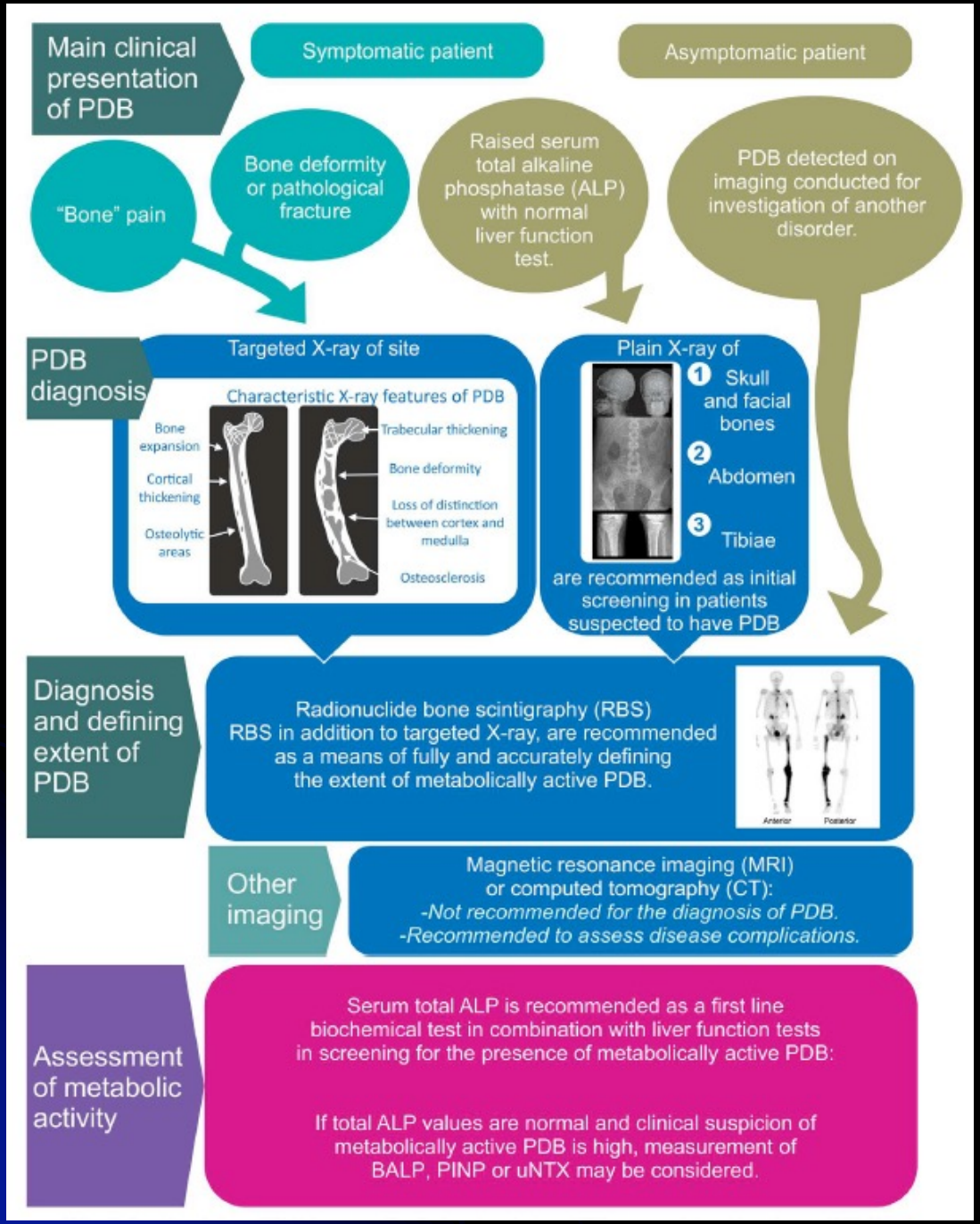
- Πολύ προσοχή προ της χορήγησης αντιοστεοκλαστικής αγωγής
  - Ειδικά σε υψηλό ρυθμό οστικής ανακατασκευής

SA Polyzos et al. Exp Clin Endocrinol Metab 2011

# Σύνοψη




E Hsu. Curr Opin Endocrinol Diabetes Obes 2019




SH Ralston et al. JBMR 2019 (guidelines)


Jason Borders