ΘΕΡΑΠΕΥΤΙΚΟΙ ΣΤΟΧΟΙ ΣΤΗΝ ΟΣΤΕΟΠΟΡΩΣΗ

ΓΙΩΡΓΟΣ ΤΡΟΒΑΣ

ΕΝΔΟΚΡΙΝΟΛΟΓΟΣ

ΕΡΓΑΣΤΗΡΙΟ ΕΡΕΥΝΑΣ ΠΑΘΗΣΕΩΝ ΜΥΟΣΚΕΛΕΤΙΚΟΥ ΣΥΣΤΗΜΑΤΟΣ <Θ.ΓΑΡΟΦΑΛΙΔΗΣ> ΠΑΝΕΠΙΣΤΗΜΙΟ ΑΘΗΝΩΝ

ΣΚΟΠΟΙ ΦΑΡΜΑΚΕΥΤΙΚΗΣ ΑΓΩΓΗΣ ΓΙΑ ΤΗΝ ΟΣΤΕΟΠΟΡΩΣΗ

- **Πρωταρχικοί σκοποί είναι:**
- Η μείωση του πρώτου κατάγματος και των επομένων όπως επίσης
- Η βελτίωση της Οστικής πυκνότητας.
- Η οστική πυκνότητα που επιτυγχάνεται στο ολικό ισχίο με την θεραπεία είναι από τους πιο αξιόπιστους προγνωστικούς δείκτες της μείωσης των σπονδυλικών και μη σπονδυλικών καταγμάτων.
- Οι θεραπευτικές αποφάσεις επίσης πρέπει να λαμβάνουν υπόψη τις βασικές περιοχικές τιμές της Οστικής πυκνότητας (ΟΜΣΣ,ΙΣΧΙΟ),
- Παράγοντες εξατομίκευσης (ηλικία, συννοσηρότητες, φάρμακα) και πιθανή πρόβλεψη διάρκεια της θεραπείας.

Cosman F, Lewiecki EM, Ebeling PR, et al. T-Score as an indicator of fracture risk during treatment with romosozumab or alendronate in the ARCH trial. *J Bone Miner Res*. 2020;35(7):1333-1342.

Bouxsein ML, Eastell R, Lui LY, et al. Change in bone density and reduction in fracture risk: a meta-regression of published trials. *J Bone Miner Res*. 2019;34(4):632-642.

ΠΟΙΑ ΚΑΤΑΓΜΑΤΑ;

- Κατάγματα ευθραυστότητας
- Μείζονα οστεοπορωτικα κατάγματα
- Χαμηλής ενέργειας
- Υψηλής ενέργειας
- Όλα τα κλινικά κατάγματα (εκτός κάποιων εξαιρέσεων)

NEWS

A Fracture Is a Fracture Is a Fracture

Using levels of trauma to define osteoporotic fractures may be a thing of the past

Neil A. Andrews

Managing Editor, IBMS BoneKEy

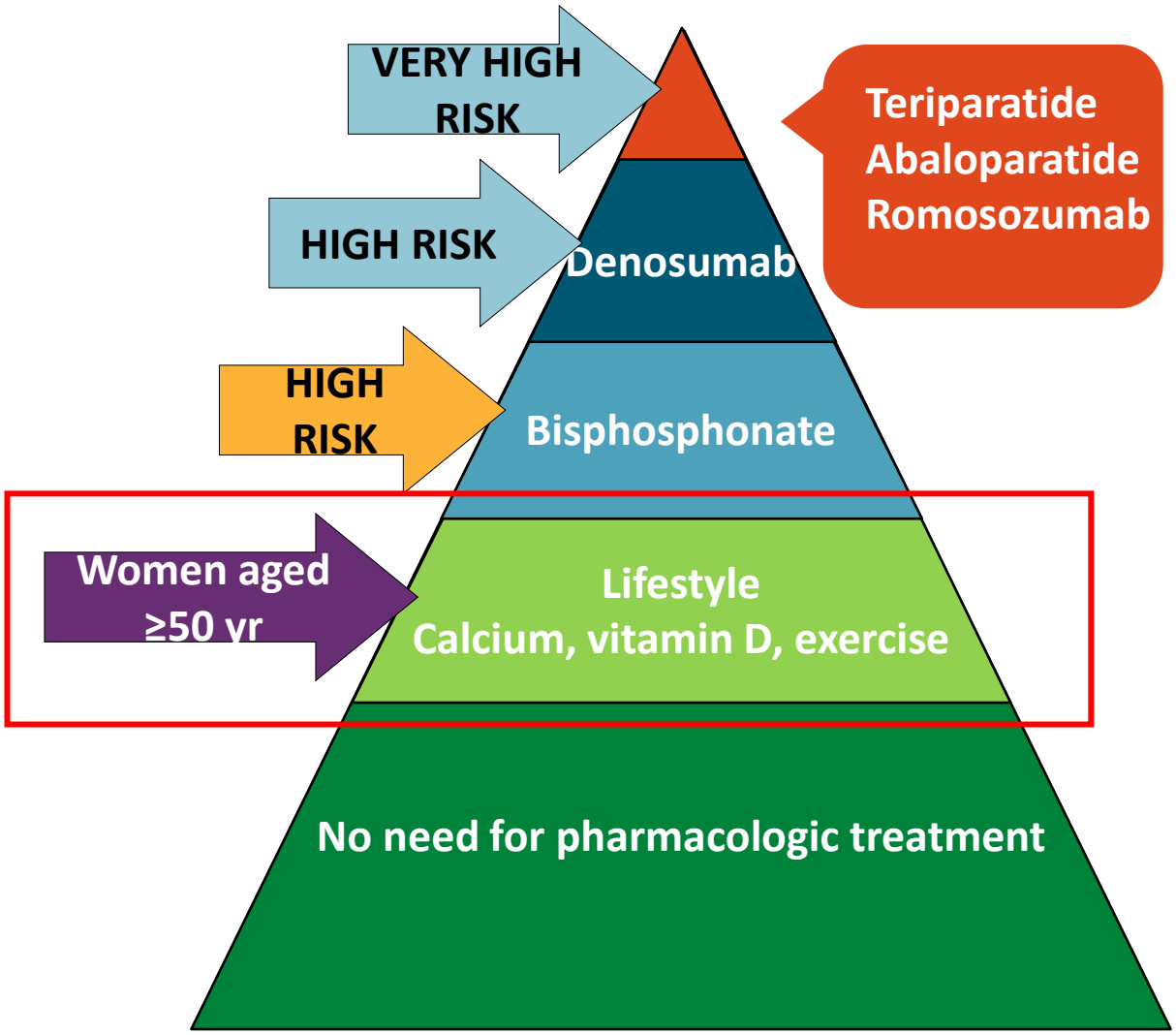
- Γυναίκα μετεμηνοπαυσιακή 50-60 ετών με οστεοπενία, χαμηλού κινδύνου για κάταγμα η οποία δεν θέλει η υπάρχει αντένδειξη ΟΘΥ.

Fracture Prevention in Women 50 to 60 Years of Age

- Fractures in postmenopausal women younger than 65 years are relatively common;
- approximately 1 in 10 of these women will have a fracture during a 10-year period
- And fractures in adults 50 to 65 years of age account for approximately one fourth of all fractures in adults over 50 years of age.

- Siris ES, Brenneman SK, Barrett-Connor E, et al. The effect of age and bone mineral density on the absolute, excess, and relative risk of fracture in postmenopausal women aged 50-99: results from the National Osteoporosis Risk Assessment (NORA). Osteoporos Int 2006; 17:565-74.
- Abrahamsen B. Treating osteoporosis in the oldest old. J Bone Miner Res 2024;39: 629-30.

Spectrum of Fracture Risk



Fracture Prevention with Infrequent Zoledronate in Women 50 to 60 Years of Age

Mark J. Bolland, M.B., Ch.B., Ph.D., Zaynah Nisa, B.Nurs., Anna Mellar, B.Sc.,Chiara Gasteiger, Ph.D., Veronica Pinel, M.D., Borislav Mihov, B.Phty.,Sonja Bastin, M.B., Ch.B., Andrew Grey, M.D., Ian R. Reid, M.D.,Greg Gamble, M.Sc., and Anne Horne, M.B., Ch.B.

N Engl J Med 2025;392:239-48.

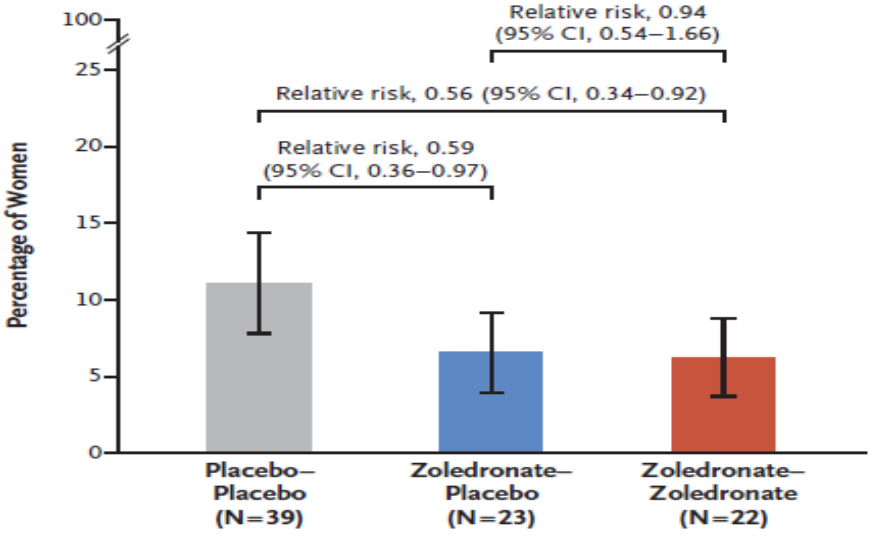
- **Participants**
- Postmenopausal women 50 to 60 years of age were randomly selected from the electoral roll in Auckland, New Zealand, and invited by letter to participate in the trial.
- Women were eligible if their bone mineral density T score at the lumbar spine, femoral neck, or total hip was lower than 0 (scores of −1 or higher typically indicate normal bone density).
- Exclusion criteria were a T score of−2.5 or less at any of these sites,
- any major systemic illness or metabolic bone disease,
- a previous clinical spine or hip fracture,
- use of any bisphosphonates or hormone-replacement therapy within 12 months before randomization, any previous use of zoledronate,
- or use of oral glucocorticoid drugs equivalent to an average dose of prednisone of 2.5 mg per day or more during the preceding 6 months.

- **Study Design**
- We conducted a 10-year, prospective, double blind, randomized, placebo-controlled trial designed to determine whether very infrequent zoledronate infusions prevent vertebral fractures in a total of 1054 early postmenopausal women,
- The participants were randomly assigned in a 1:1:1 ratio to receive infusions of zoledronate at a dose of
- 5 mg at baseline and again at 5 years (zoledronate–zoledronate group -352),
- an infusion of zoledronate at a dose of 5 mg at baseline and an infusion of normal saline (placebo) at 5 years (zoledronate–placebo group 351),
- or infusions of normal saline at baseline and at 5 years (placebo– placebo group 351).
- of these, 1003 (95.2%) completed 10 years of follow-up.

End Points

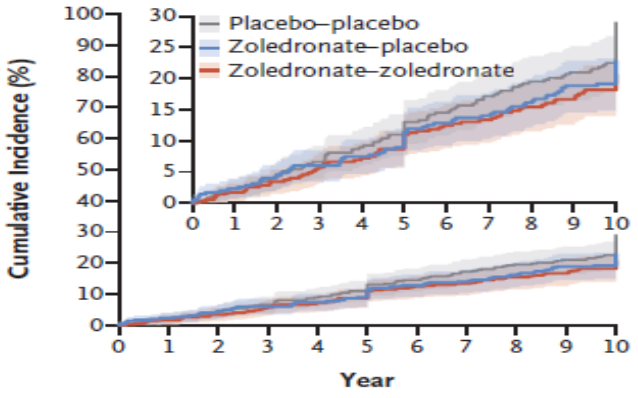
- **The primary end point was a new morphometric vertebral fracture, which was determined with the use of spinal radiograph**s.
- **Secondary end points** were fragility fracture, any fracture, and major osteoporotic fracture.
- **Fragility fractures** were defined as any fracture, including radiographic vertebral fractures, but excluding fractures involving toes, metatarsals, fingers, metacarpals, the skull, or the face.
- **Major osteoporotic fractures** were defined as fractures of the wrist, spine, shoulder, hip, or pelvis.
- **Fractures were not excluded on the basis of trauma severity** but pathologic fractures were excluded from all end points.
- Other secondary end points included changes in bone mineral density at the proximal femur and lumbar spine and changes in markers of bone turnover.

A Risk of Morphometric Vertebral Fracture



B Fragility Fracture

Zoledronate–zoledronate vs. placebo–placebo hazard ratio, 0.69 (95% CI, 0.51–0.94)
Zoledronate–placebo vs. placebo–placebo hazard ratio, 0.77 (95% CI, 0.57–1.04)
Zoledronate–zoledronate vs. zoledronate–placebo hazard ratio, 0.91 (95% CI, 0.66–1.25)

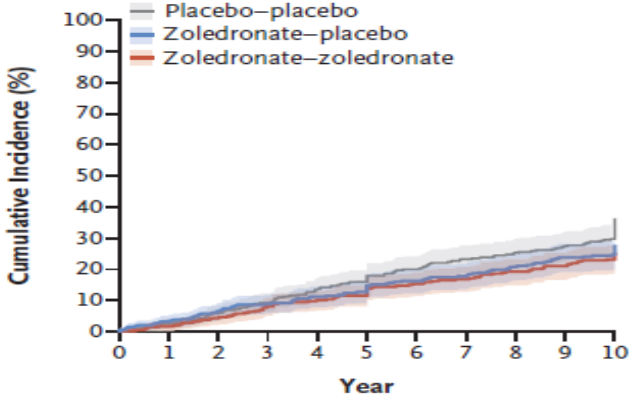


No. at Risk

Placebo–placebo	351	342	332	323	314	304	291	281	273	267	258
Zoledronate–placebo	351	342	332	324	316	306	292	287	278	266	260
Zoledronate–Zoledronate	352	344	336	327	319	313	297	291	281	274	267

C Any Fracture

Zoledronate–zoledronate vs. placebo–placebo hazard ratio, 0.66 (95% CI, 0.50–0.87)
Zoledronate–placebo vs. placebo–placebo hazard ratio, 0.74 (95% CI, 0.57–0.97)
Zoledronate–zoledronate vs. zoledronate–placebo hazard ratio, 0.91 (95% CI, 0.68–1.22)

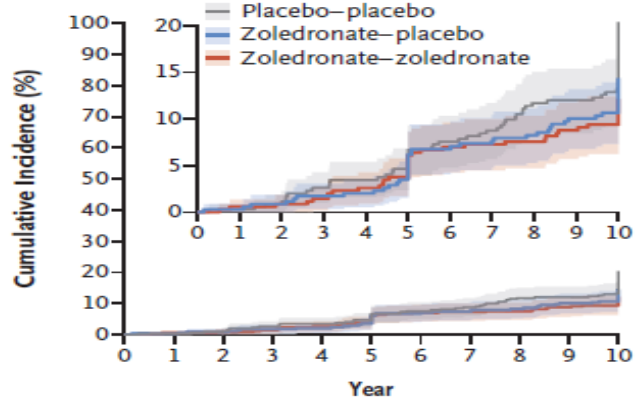


No. at Risk

Placebo–placebo	351	341	326	314	298	287	272	260	253	245	235
Zoledronate–placebo	351	339	325	314	303	293	280	274	263	250	242
Zoledronate–Zoledronate	352	344	333	319	309	303	287	279	268	259	250

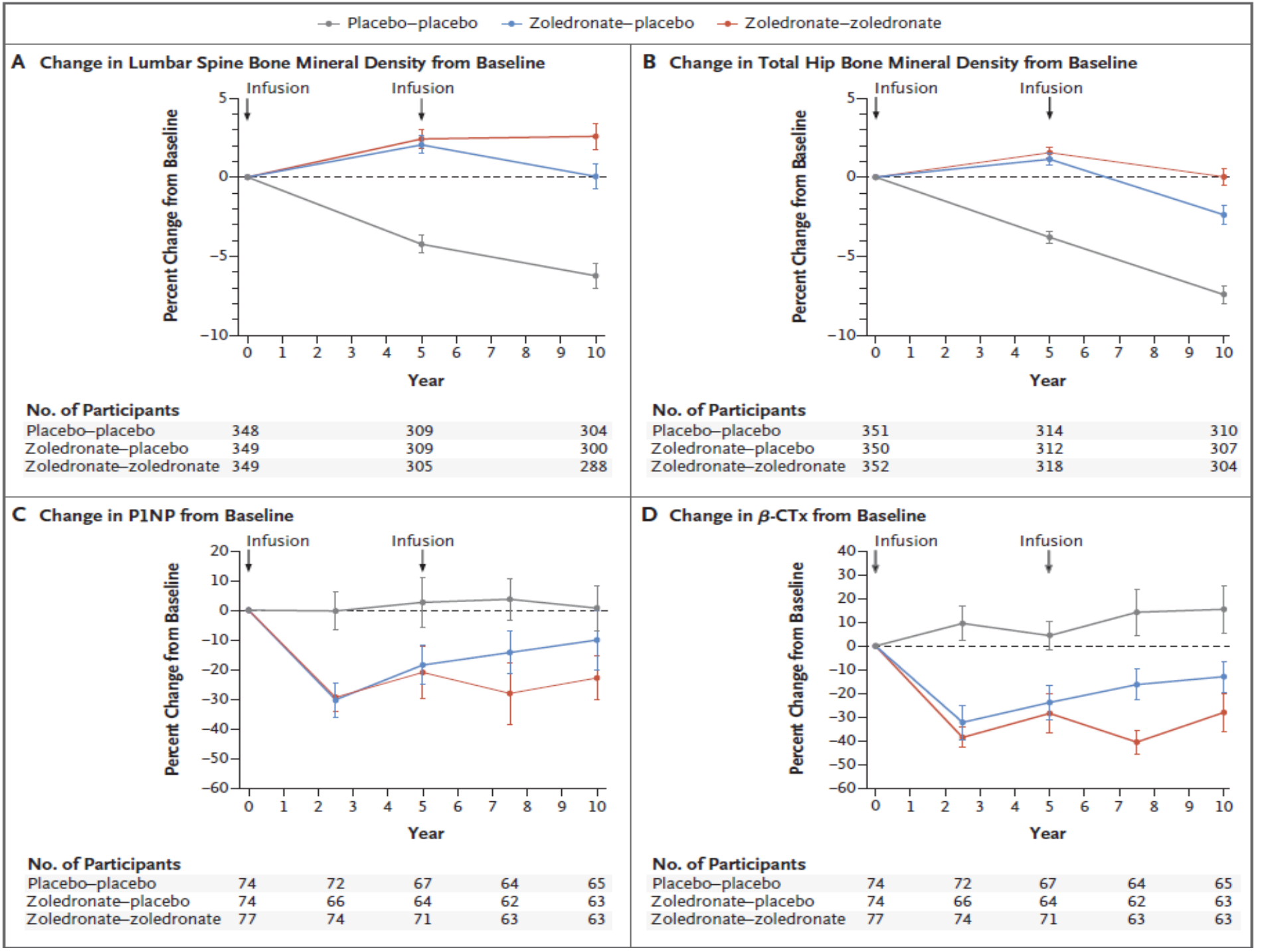
D Major Osteoporotic Fracture

Zoledronate–zoledronate vs. placebo–placebo hazard ratio, 0.58 (95% CI, 0.39–0.85)
Zoledronate–placebo vs. placebo–placebo hazard ratio, 0.69 (95% CI, 0.48–1.00)
Zoledronate–zoledronate vs. zoledronate–placebo hazard ratio, 0.84 (95% CI, 0.55–1.28)



No. at Risk

Placebo–placebo	351	349	343	337	333	325	314	309	299	297	289
Zoledronate–placebo	351	349	345	339	335	325	313	309	305	296	289
Zoledronate–Zoledronate	352	348	345	342	335	330	316	312	308	301	297


Placebo–placebo
Zoledronate–placebo
Zoledronate–zoledronate
A Change in Lumbar Spine Bone Mineral Density from Baseline
Infusion
Infusion
Percent Change from Baseline
Year
No. of Participants
Placebo–placebo 348 309 304
Zoledronate–placebo 349 309 300
Zoledronate–zoledronate 349 305 288
B Change in Total Hip Bone Mineral Density from Baseline
Infusion
Infusion
Percent Change from Baseline
Year
No. of Participants
Placebo–placebo 351 314 310
Zoledronate–placebo 350 312 307
Zoledronate–zoledronate 352 318 304
C Change in P1NP from Baseline
Infusion
Infusion
Percent Change from Baseline
Year
No. of Participants
Placebo–placebo 74 72 67 64 65
Zoledronate–placebo 74 66 64 62 63
Zoledronate–zoledronate 77 74 71 63 63
D Change in β-CTx from Baseline
Infusion
Infusion
Percent Change from Baseline
Year
No. of Participants
Placebo–placebo 74 72 67 64 65
Zoledronate–placebo 74 66 64 62 63
Zoledronate–zoledronate 77 74 71 63 63

The NEW ENGLAND JOURNAL of MEDICINE

Fracture Prevention with Infrequent Zoledronate

A PLAIN LANGUAGE SUMMARY

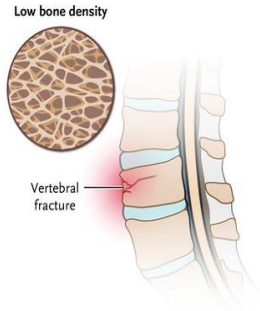
Based on the NEJM publication: Fracture Prevention with Infrequent Zoledronate in Women 50 to 60 Years of Age by M.J. Bolland et al. (published January 16, 2025)

In this trial, researchers assessed whether very infrequent zoledronate infusions would prevent vertebral fractures in early postmenopausal women without osteoporosis.

Decreases in **bone mineral density** start before menopause, with an average loss of bone density of 0.5 to 1% per year thereafter.

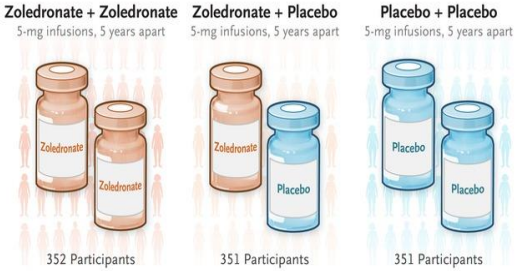
WHY WAS THE TRIAL DONE?

Zoledronate, given every 12 or 18 months for prevention of fractures in older women, has a prolonged duration of action; the effects of a single 5-mg dose on bone mineral density and bone turnover are stable and persist well beyond 5 years. Whether even-more-infrequent dosing could maintain bone mineral density and prevent fractures in early postmenopausal women is unknown.



HOW WAS THE TRIAL CONDUCTED?

Participants without osteoporosis were randomly assigned to receive zoledronate infusions at baseline and again at 5 years, a zoledronate infusion at baseline and a placebo infusion at 5 years, or placebo infusions at baseline and at 5 years. Spinal radiographs were obtained at baseline and at 5 and 10 years. The primary end point was a new vertebral fracture.



PARTICIPANTS

WHO

1054 women

50 to 60 years of age; mean, 56 years

CLINICAL STATUS

Bone mineral density T scores between 0 and −2.5 at the lumbar spine, femoral neck, or total hip (scores of −1 or higher typically indicate normal bone density)

No previous clinical spine or hip fracture

No use of bisphosphonates or hormone-replacement therapy within the previous 12 months and no use of zoledronate

TRIAL DESIGN

- RANDOMIZED
- DOUBLE-BLIND
- PLACEBO-CONTROLLED
- DURATION: 10 YEARS
- LOCATION: NEW ZEALAND

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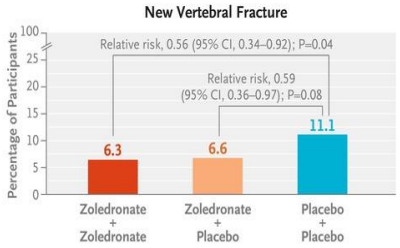
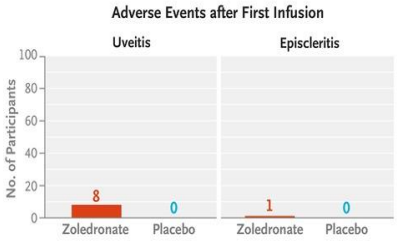
RESULTS

The percentage of women with a new vertebral fracture was lower in the two zoledronate groups than in the placebo–placebo group, but the difference between the zoledronate–placebo group and the placebo–placebo group was not statistically significant.

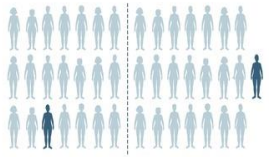
Findings with respect to fragility fracture, any fracture, and major osteoporotic fracture (secondary end points) suggested a potential benefit with zoledronate but were not conclusive.



Few adverse events occurred. Some cases of uveitis and episcleritis were reported after the first infusion of zoledronate but not after the infusion of placebo.



NUMBER NEEDED TO TREAT



The researchers estimated that 21 women would need to receive two doses of zoledronate and 22 would need to receive one dose of zoledronate during a 10-year period to prevent one woman from having a new vertebral fracture.

No cases of osteonecrosis of the jaw and no atypical femoral fractures occurred during the trial.

LIMITATIONS AND REMAINING QUESTIONS

- Participants were women in early menopause without osteoporosis, so the results may not apply to older women, men, or persons with osteoporosis.
- Results for secondary end points should be interpreted with caution, because there was no adjustment for multiple testing.

CONCLUSIONS

Among women in early postmenopause without osteoporosis, zoledronate infusions given every 5 years led to a lower risk of new vertebral fracture at 10 years than placebo.

LINKS: FULL ARTICLE | NEJM QUICK TAKE | EDITORIAL

FURTHER INFORMATION

Trial registration: Australian New Zealand Clinical Trials Registry number, ACTRN12612000270819

Trial funding: Health Research Council of New Zealand

Full citation: Bolland MJ, Nisa Z, Mellar A, et al. Fracture prevention with infrequent zoledronate in women 50 to 60 years of age. N Engl J Med 2025;392:239-48. DOI: 10.1056/NEJMoa2407031.

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The American Society for Bone and Mineral Research and the United States Bone Health and Osteoporosis Foundation Task Force on Goal-Directed Osteoporosis Treatment

- The task force suggests that treatment decisions should be individualized in part based on starting T-scores at different skeletal sites and
- on the probability of achieving BMD treatment targets within 3 years of treatment.
- **Initial treatment**
- **Sequence of treatment**

The American Society for Bone and Mineral Research and the United States Bone Health and Osteoporosis Foundation Task Force on Goal-Directed Osteoporosis Treatment

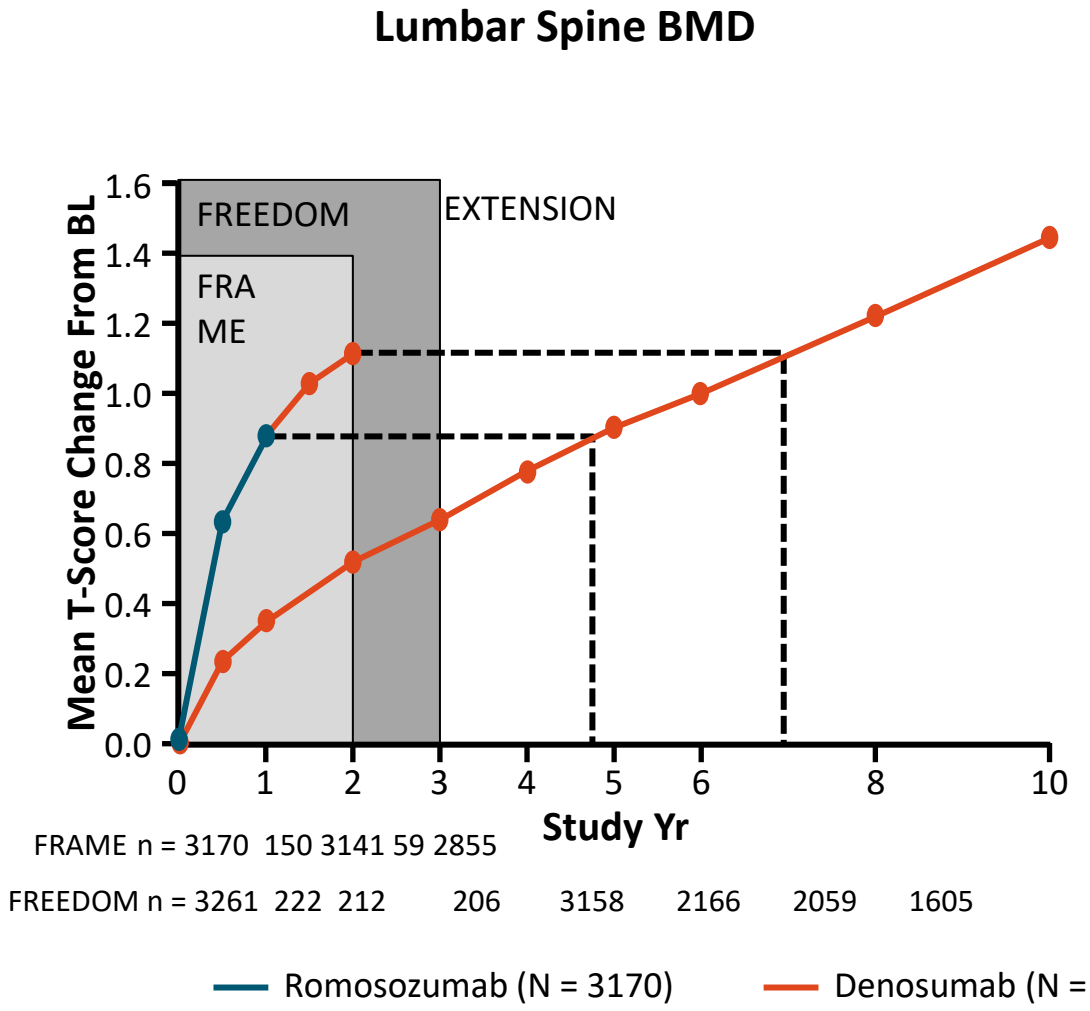
Initial treatment:

- Selection of initial treatment should consider the probability that a treatment target can be attained over a reasonable period of time,
- with greater urgency for patients at imminent fracture risk (recent fracture or some multiple prior fractures).
- Data to guide these decisions include the likelihood that a treatment can provide at least a 50%probability of attaining the T score target over 3yr, depending on the initial BMD.
- For some patients, it might be appropriate to select treatment to achieve
- a higher T score target,
- reach the treatment target faster or
- provide a higher probability of achieving the treatment target.

Sequence of treatment

- Treatment sequence is important for attaining T score targets particularly in patients with baseline T scores far below the treatment target.
- Selection of initial therapy should acknowledge the differential impact on BMD for osteoanabolic-first versus antiresorptive-first treatment sequences.
- Greater and faster BMD increases at the hip and spine are seen with osteoanabolic first followed by antiresorptive treatment strategies, compared with the reverse order.

BMD Increase With Dmab After Romo



- FRAME vs FREEDOM + FREEDOM Extension
- 1 yr of Romo followed by 1 yr of Dmab gives same BMD increase as 7 yr of continuous Dmab

Cosman. J Bone Miner Res. 2018;33:1219.

Ασθενής με πρόσφατο κάταγμα (< 2 έτη) και επαπειλούμενο κίνδυνο νέου κατάγματος

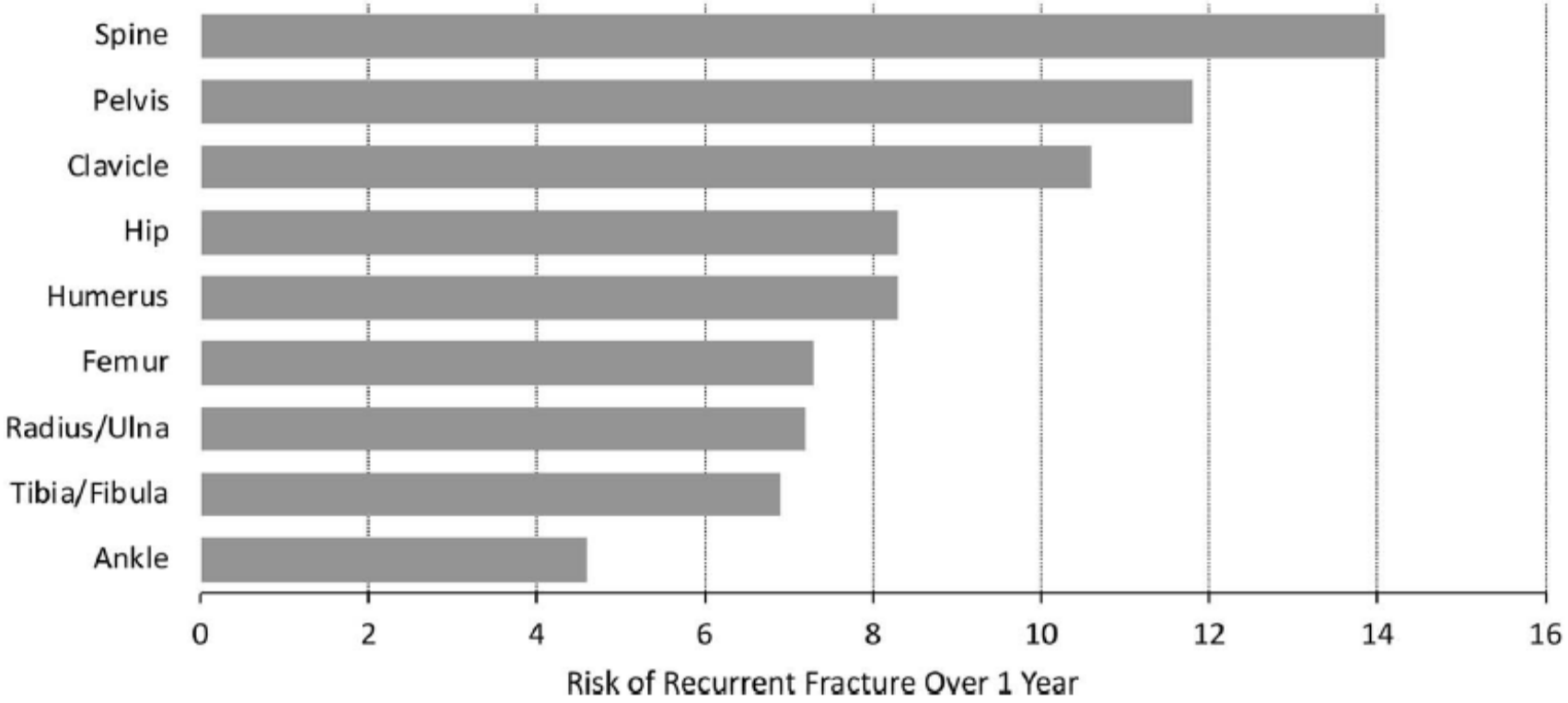
- **Σπονδυλικό, ισχίου, λεκάνης**

- Αναβολική αγωγή πρώτη εκλογή
- Διφωσφονικα-Dmab δεύτερη εκλογή

- **Άλλα κατάγματα**

- Αναβολική αγωγή, ΔΦ-dmab
- Χρειάζεται consesus ποιά

<< άλλα κατάγματα>> χρήζουν αντιμετώπισης με αναβολική αγωγή και ποια με αντικαταβολική.



Μέσος Όρος νέου κατάγματος είναι 10% το πρώτο χρόνο και 18% το δεύτερο

BalasubramanianA,ZhangJ,ChenL,etal.Risk of subsequent fracture after prior fracture among older women.*OsteoporosInt*.2019;30(1):79–92.

Γυναίκα με αρχική Οστική πυκνότητα THip Tscore <-2,5εως-2,8 LS Tscore <-2,5εως -3

- **Ασθενής χωρίς ιστορικό κατάγματος**
- **Στόχος να φτάσει σε ένα T score τουλάχιστον >-2,5.**

  -διφωσφονικα η denosumab
- **Ασθενής υπό Αλενδρονάτη και Tscore-2,7 έχει >50 πιθανότητες να φτάσει ένα**

  Tscore >-2,5 σε 3 έτη.

Denosumab

- Στο ολικό ισχίο ένα αρχικό **T score -2,8** επιτρέπει σε >50 των γυναικών να φτάσουν ένα Tscore>-2,5 σε 3 έτη Αντίστοιχα στη ΟΜΣΣ το αρχικό Tscore είναι

  -3,1.
- Τέλος **ένα T score -2,7** επιτρέπει >70 των γυναικών να φτάσουν Tscore >-2,5 ΤΗ.

Γυναίκα με αρχική Οστική πυκνότητα ΤΗ Tscore <-2,5εως-2,8 LS Tscore <-2,5εως -3

- **Ασθενής με ιστορικό κατάγματος (ισχίου, σπονδυλικού, λεκάνης>2 έτη αλλά <10ετη)**

  -Αναβολική αγωγή

- **Άλλα κατάγματα:**

- ΔΦ-DENOSUMAB

Γυναίκα με αρχική Οστική πυκνότητα
ΤΗ Tscore <-2,8
LS Tscore < -3

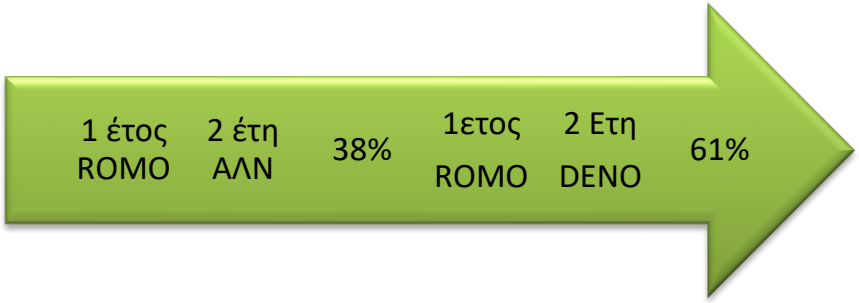
- **Αναβολική αγωγή ως αρχική θεραπεία εάν είναι δυνατόν.**
- **Εναλλακτικά ΔΦ-DEN**
- **Με Αλενδρονάτη 9% εάν το αρχικό ΤΗ Tscore είναι -3 μετα από 3 χρόνια**
- **Με Denosumab Η πιθανότητα ενός Tscore ΤΗ >2,5 είναι 12% όταν η αρχική ΟΠ είναι ΤΗ Tscore<-3 μετά από 3 χρόνια αγωγής**

Table 2. Lowest baseline T-score that permits > 50% of women to achieve a T-score > −2.5 in approximately 3 yr.

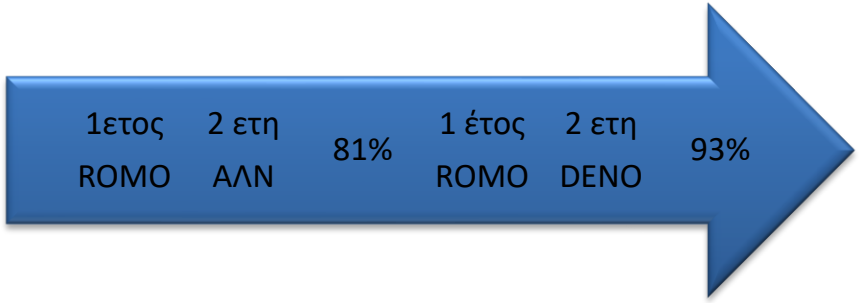
	Total Hip	Lumbar Spine
Alendronate	−2.7	−3.0
Denosumab	−2.8	−3.1
Romosozumab/Alendronate	−2.9	−3.5
Abaloparatide/Alendronate	−2.9	−3.5
Romosozumab/Denosumab	−3.1	−3.7

ROMOSOZUMAB

ΤΗ>-2,5 σε 3 έτη



ΟΜΣΣ >-2,5 σε 3 ετη



Ασθενής με καταγμα(τα) πέραν των 2 ετών

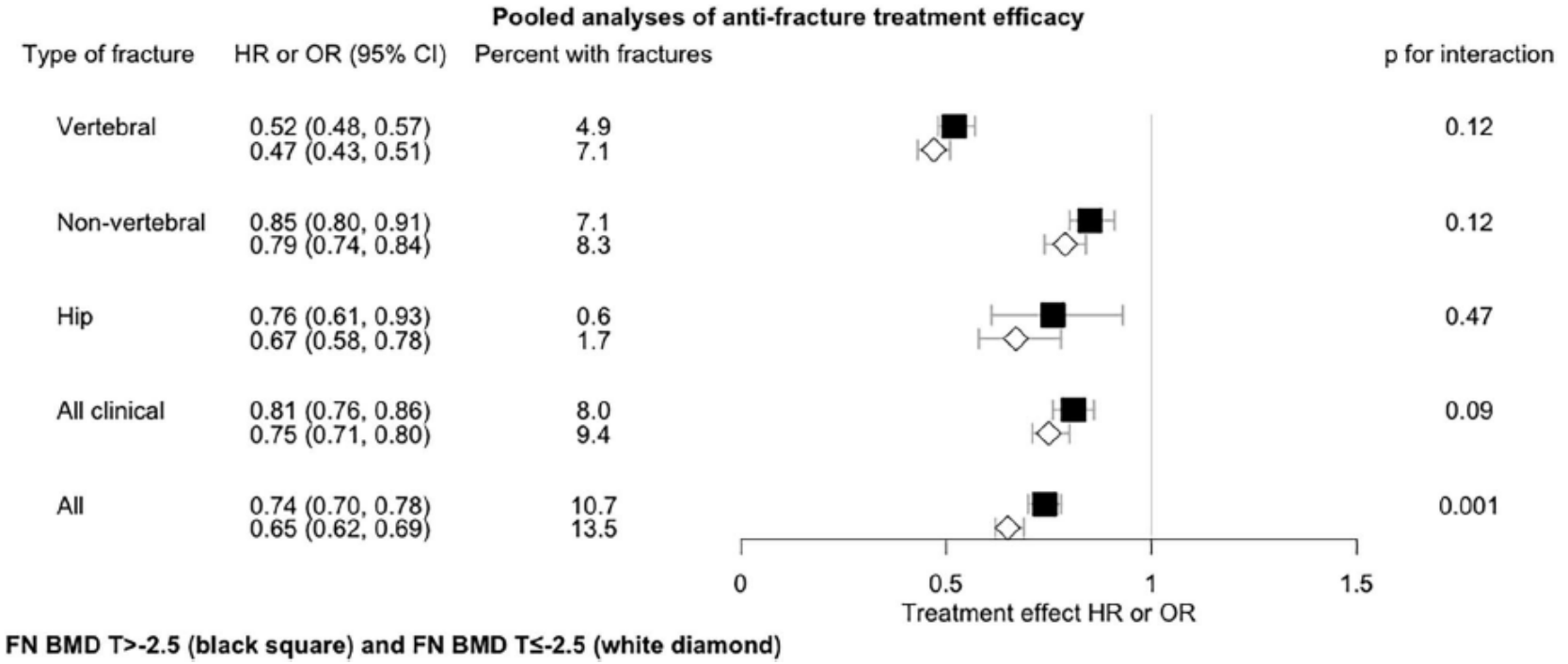
Tscore >-2,5

- **Σπονδυλικό, κάταγμα ισχίου, λεκάνης:**
- **ΠΡΩΤΗ ΕΠΙΛΟΓΗ: Αναβολική αγωγή**
- **Εναλλακτικά ΔΦ-DENO**
- **ΑΛΛΑ ΚΑΤΑΓΜΑΤΑ: ΔΦ-DENO**
- **Ασθενείς χωρίς κατάγματα αλλά αυξημένο κίνδυνο κατάγματος(FRAX) :**
- **Όσον αφορά την ΟΠ ο στόχος είναι να αυξηθεί 3% (0,2 T score)στο ισχίο και 6% (0,5Tscore)στην ΣΣ σε 3 ετη.**

Schini M, VilacaT,LuiL-Y, et al.

Pre-treatment bone mineral density(BMD) and the benefit of pharmacologic treatment on fracture risk and BMD change: analysis from the FNIH-ASBMR-SABREproject.

JBoneMinerRes.2024;39(7):867–876.



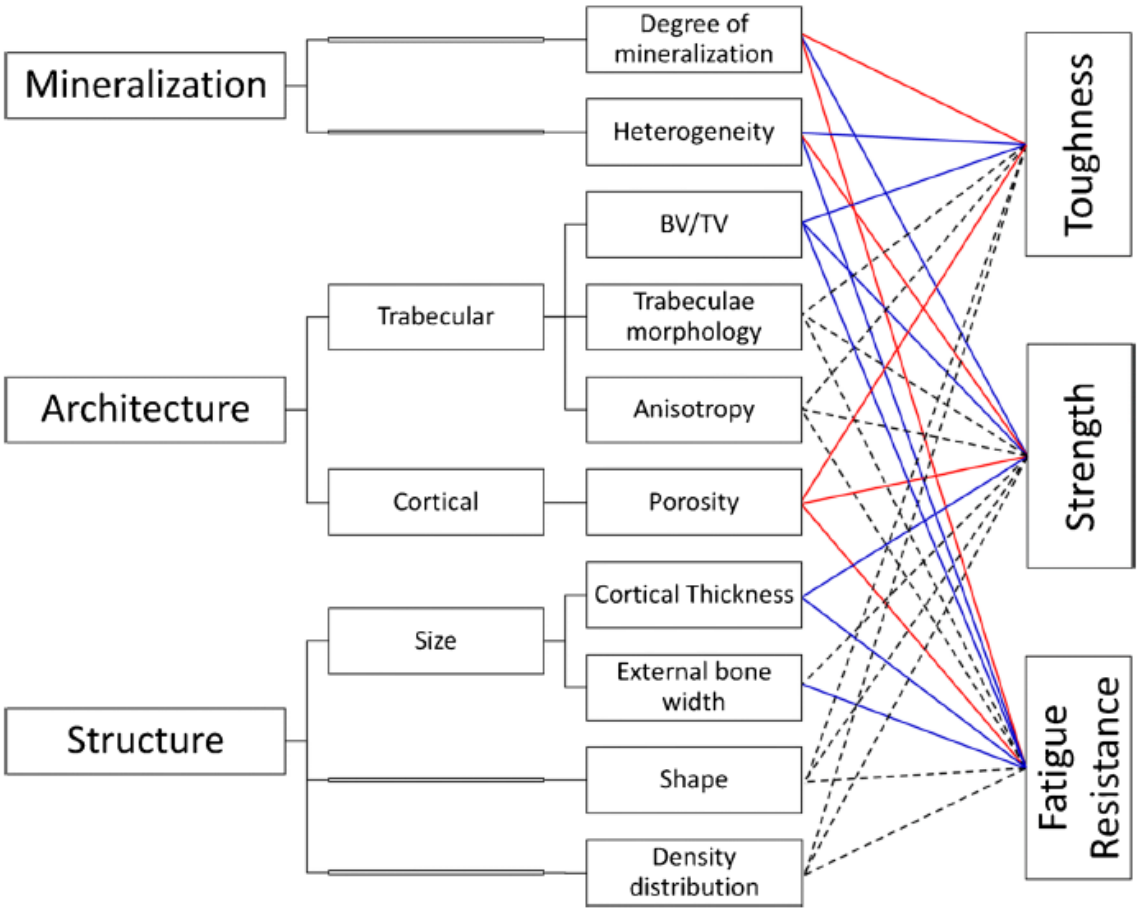
Πως ελέγχουμε εάν οι στόχοι έχουν επιτευχτεί

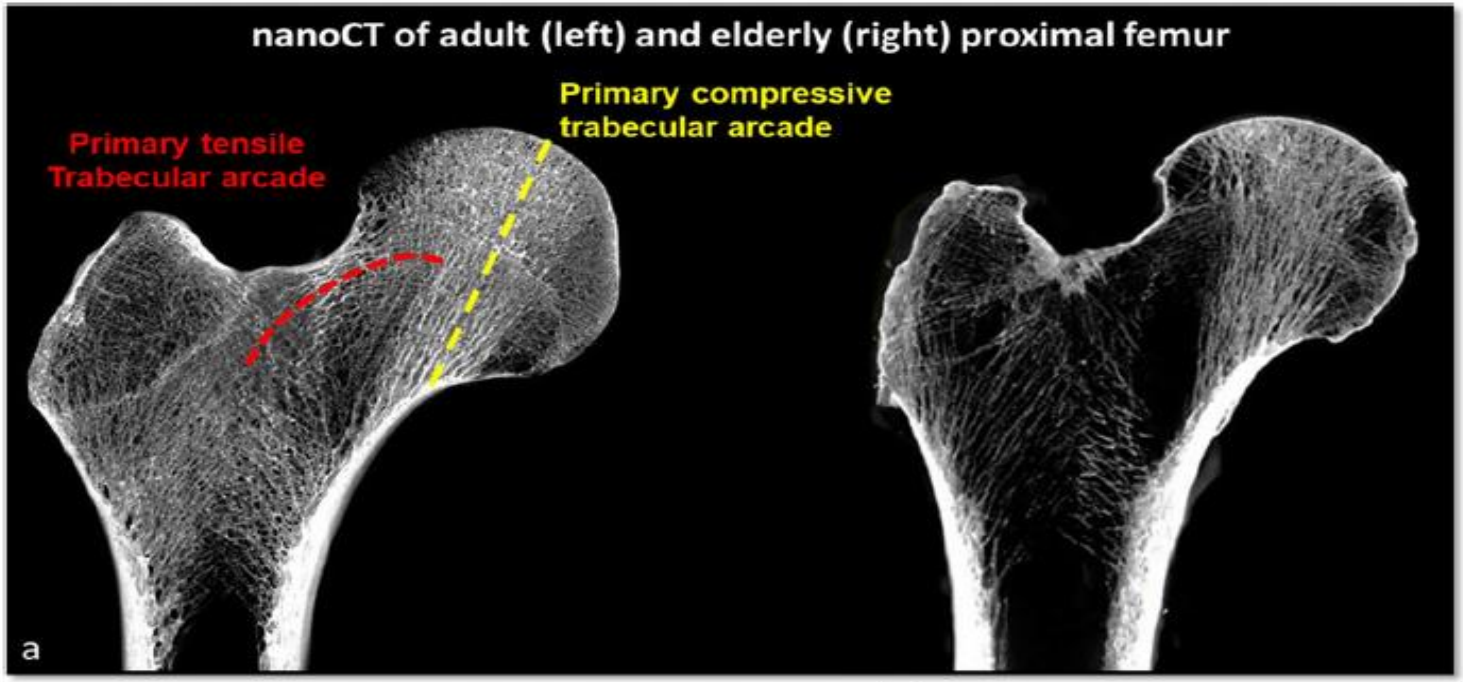
- **Επανάληψη ΟΠ**
- **Ανίχνευση νέων καταγμάτων**
- Έχοντας μια βασική απεικόνιση της ΣΣ μπορούμε να ανακαλύψουμε νέα σπονδυλικά κατάγματα
- Εάν ο ασθενής παρουσιάζει νέα κατάγματα ο στόχος δεν επιτυγχάνεται ανεξάρτητα από τη ΟΠ
- Οι ασθενείς μπορεί να ανταποκρίνονται στη θεραπεία αλλά είναι μακριά από το στόχο

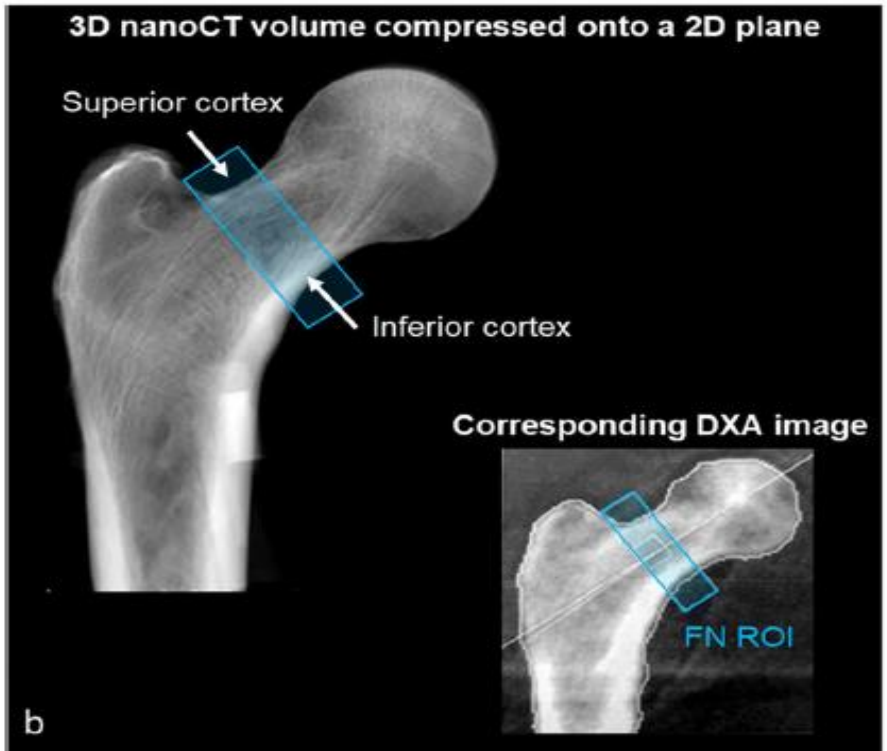
Όταν οι στόχοι δεν επιτυγχάνονται

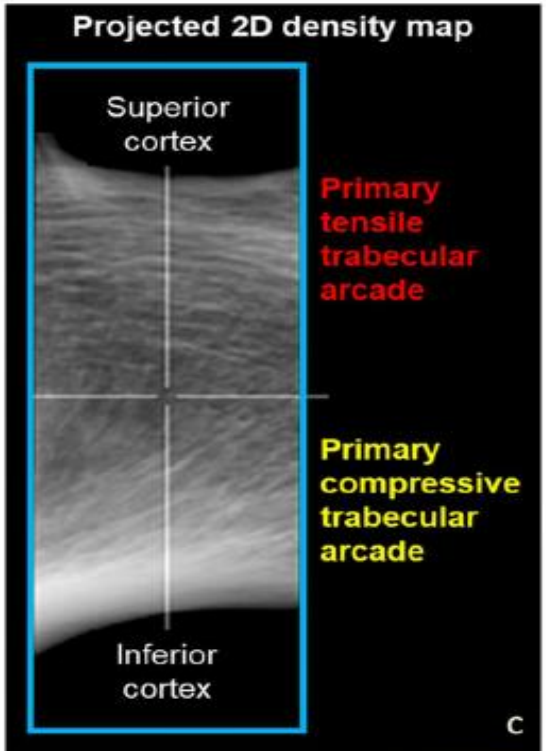
- Ενώ ένα κάταγμα υπό θεραπεία δεν αποτελεί αποτυχία αγωγής μπορεί να σημαίνει όμως ότι ο κίνδυνος κατάγματος είναι μεγαλύτερος από ότι είχε αρχικά υπολογιστεί.
- Έλεγχος για δευτεροπαθή αίτια, προσήλωση στην θεραπεία
- Αλλαγή η προσθήκη αναβολικού φαρμάκου στην αντικαταβολικη αγωγή
- Εάν ο ασθενής έχει λάβει αναβολική αγωγή και παραμένει υψηλού κινδύνου μια επανάληψη της σε όποιες χώρες επιτρέπεται μπορεί να δοκιμαστεί.

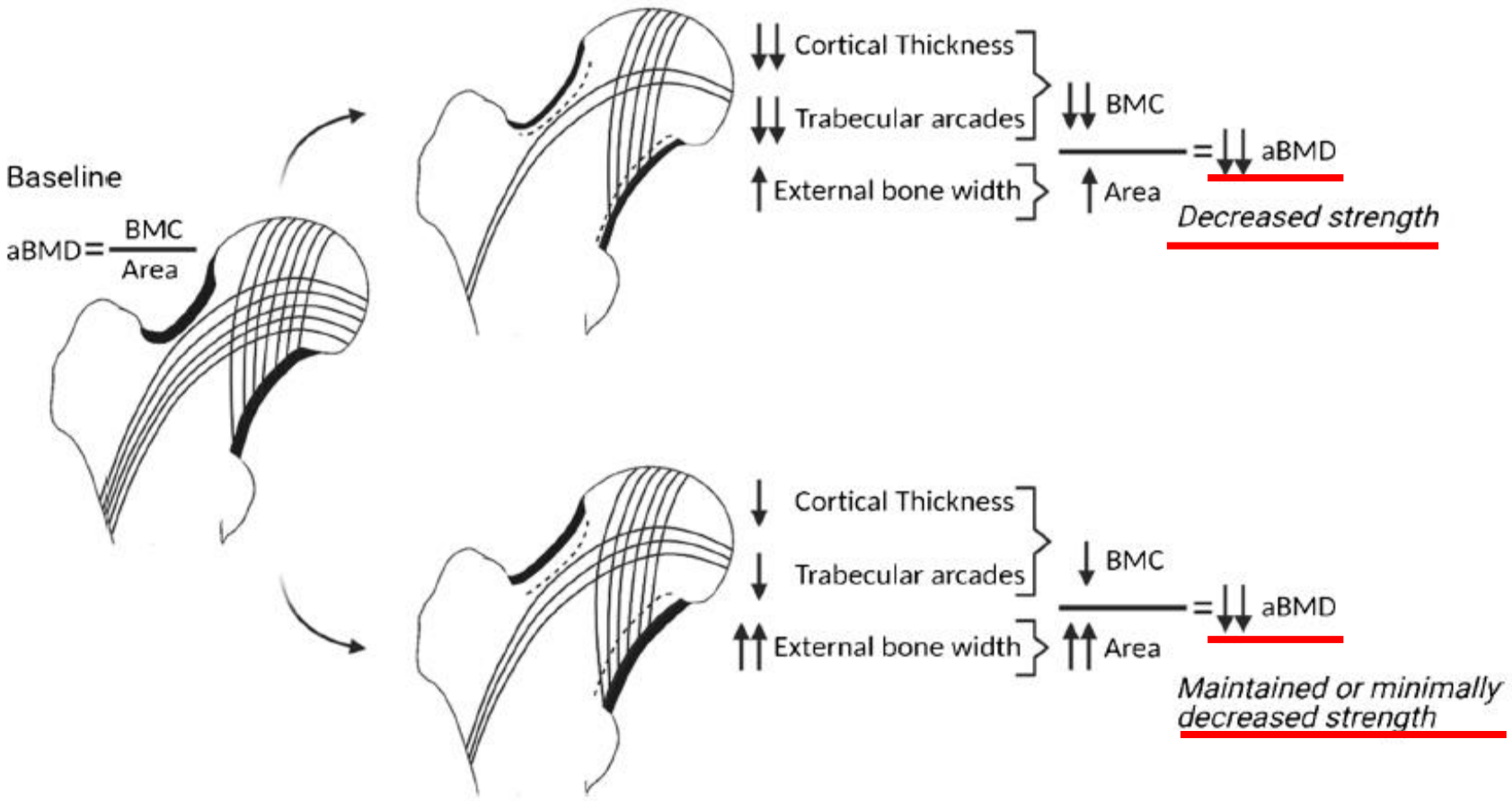
ΠΑΡΑΜΕΤΡΟΙ ΟΣΤΙΚΗΣ ΑΠΟΤΥΧΙΑΣ




nanoCT of adult (left) and elderly (right) proximal femur
Primary tensile
Trabecular arcade
Primary compressive
trabecular arcade
a


3D nanoCT volume compressed onto a 2D plane
Superior cortex
Inferior cortex
Corresponding DXA image
FN ROI
b


Projected 2D density map
Superior
cortex
Primary
tensile
trabecular
arcade
Primary
compressive
trabecular
arcade
Inferior
cortex
c


Baseline
aBMD = BMC / Area
Cortical Thickness
Trabecular arcades
External bone width
BMC
Area
aBMD
Decreased strength
Cortical Thickness
Trabecular arcades
External bone width
BMC
Area
aBMD
Maintained or minimally decreased strength

ΟΣΤΕΟΠΟΡΩΣΗ

5) MG Abies Pectinata D1 150mg

S: 50 σταγόνες πρωί.

Διάρκεια 1 εβδ. και επανάλ

c) Lamberts chewable Calcium 400mg

bt 1 (ένα)

S: 1 κάθε δεύτερο πρωί

ΕΥΧΑΡΙΣΤΩ