

Osteoporoza – diagnostic si tratament. Exista vreo exagerare?

Cristian Baicus

Medicina Interna Colentina

www.baicus.ro

Diagnostic

- HTA, diabet, colesterol crescut, **osteoporoza**
 - Aceste boli sunt definite printr-un **numar (prag)**, nu prin simptome
 - Medicii incearca sa o ia inaintea simptomelor – dg precoce, pentru a **preveni** efectele
 - **Supradiagnostic (*overdiagnosis*)**
 - Multi dintre pacienti nu vor dezvolta niciodata simptome si nu vor muri din cauza afectiunii
 - **Nu exista nici un RCT care sa demonstreze beneficiile screening-ului pentru osteoporoza**

Diagnostic

- înainte de 1992, osteoporoza se diagnostica in momentul unei fracturi vertebrale dureroase
- Masurarea densitatii osoase
 - Scorul T normal (0): BMD medie a unei femei de 20-29 ani
 - 1992: OMS+Intl Osteoporosis Found. (org nonprofit, Advisory Board 31 companii medicamente & echipamente medicale):
osteoporoza = $T < -2,5$; osteopenia: $-1, -2,5$.
 - 1997: Testul: rambursat de asigurari
 - 2003: National Osteoporosis Foundation: <2

- National Osteoporosis Foundation:

“Osteoporoza este deseori denumita “boala tacuta”, pentru ca pierderea osoasa are loc fara simptome. Oamenii nu stiu ca au osteoporoza pana cand oasele lor devin atat de slabe, incat o tensiune, lovitura sau cadere bruste determina o fractura, sau prabusirea unei vertebre”

National Osteoporosis Foundation. Viewed at <http://www.nof.org/osteoporosis/stats.htm>.

- 20% dintre femeile >50a (40%, osteopenie)
- 25% >65a
- 50% >75a

Abramson, John . Overdosed America: The Broken Promise of American Medicine.

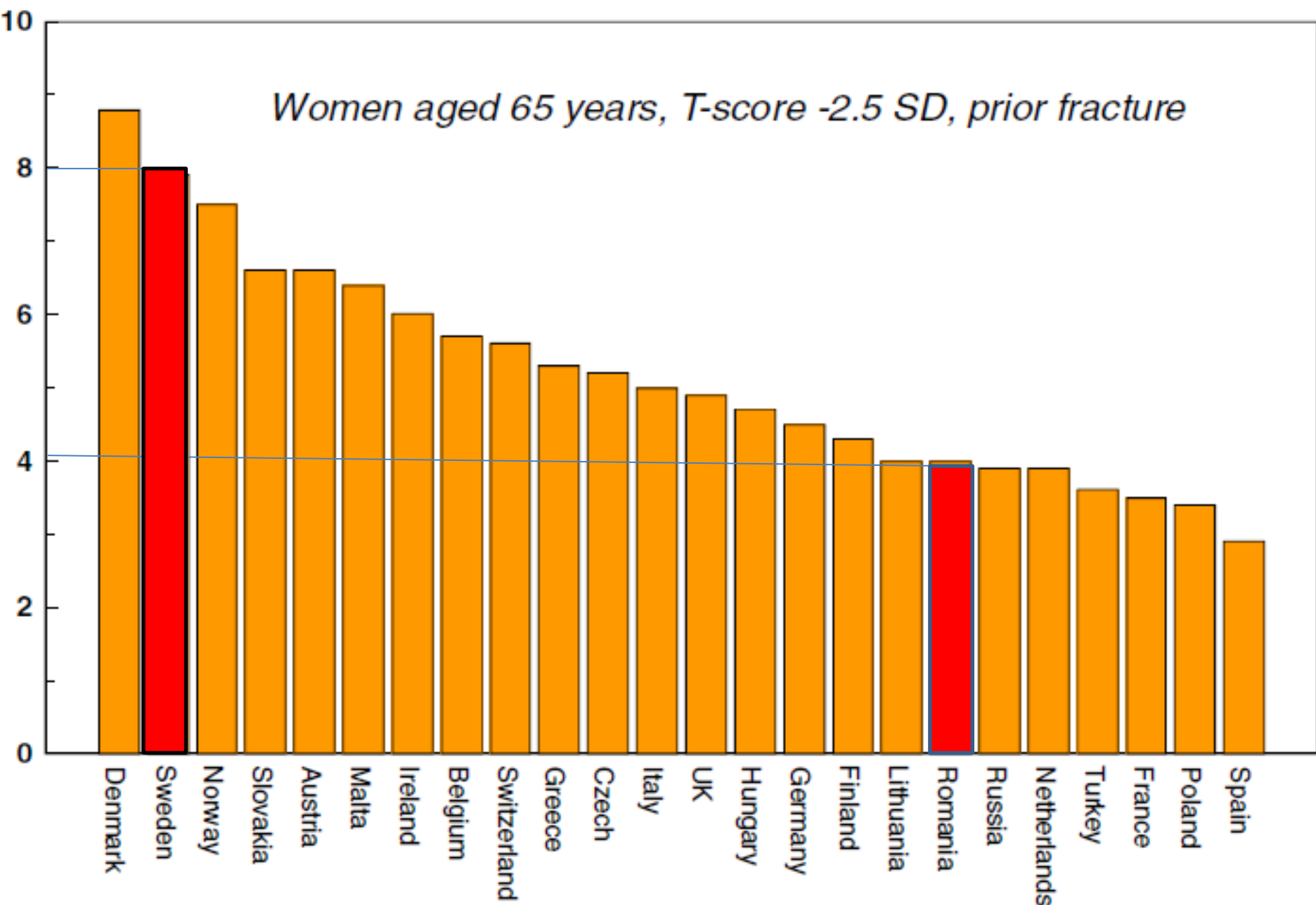
Condition	Disease Prevalence				
	Change in Threshold	Old Definition	New Definition	New Cases	Increase
Diabetes					
Fasting sugar 140 → 126	11,697,000	13,378,000	1,681,000	14%	
Hypertension					
Systolic BP 160 → 140	38,690,000	52,180,000	13,490,000	35%	
Diastolic BP 100 → 90					
Hyperlipidemia					
Total cholesterol 240 → 200	49,480,000	92,127,000	42,647,000	86%	
Osteoporosis in women					
T score -2.5 → -2.0	8,010,000	14,791,000	6,781,000	85%	

Efectul scaderii pragului diagnostic asupra numarului de americani “bolnavi”

Table 1 Remaining lifetime probability of a major fracture at the age of 50 and 80 years in men and women from Sweden [10] (with kind permission from Springer Science and Business Media)

Site	At 50 years		At 80 years	
	Men	Women	Men	Women
Forearm	4.6	20.8	1.6	8.9
Hip	10.7	22.9	9.1	19.3
Spine	8.3	15.1	4.7	8.7
Humerus	4.1	12.9	2.5	7.7
Any of these	22.4	46.4	15.3	31.7

Ten-year probability (%) fractură de șold



Fracture probability (%)

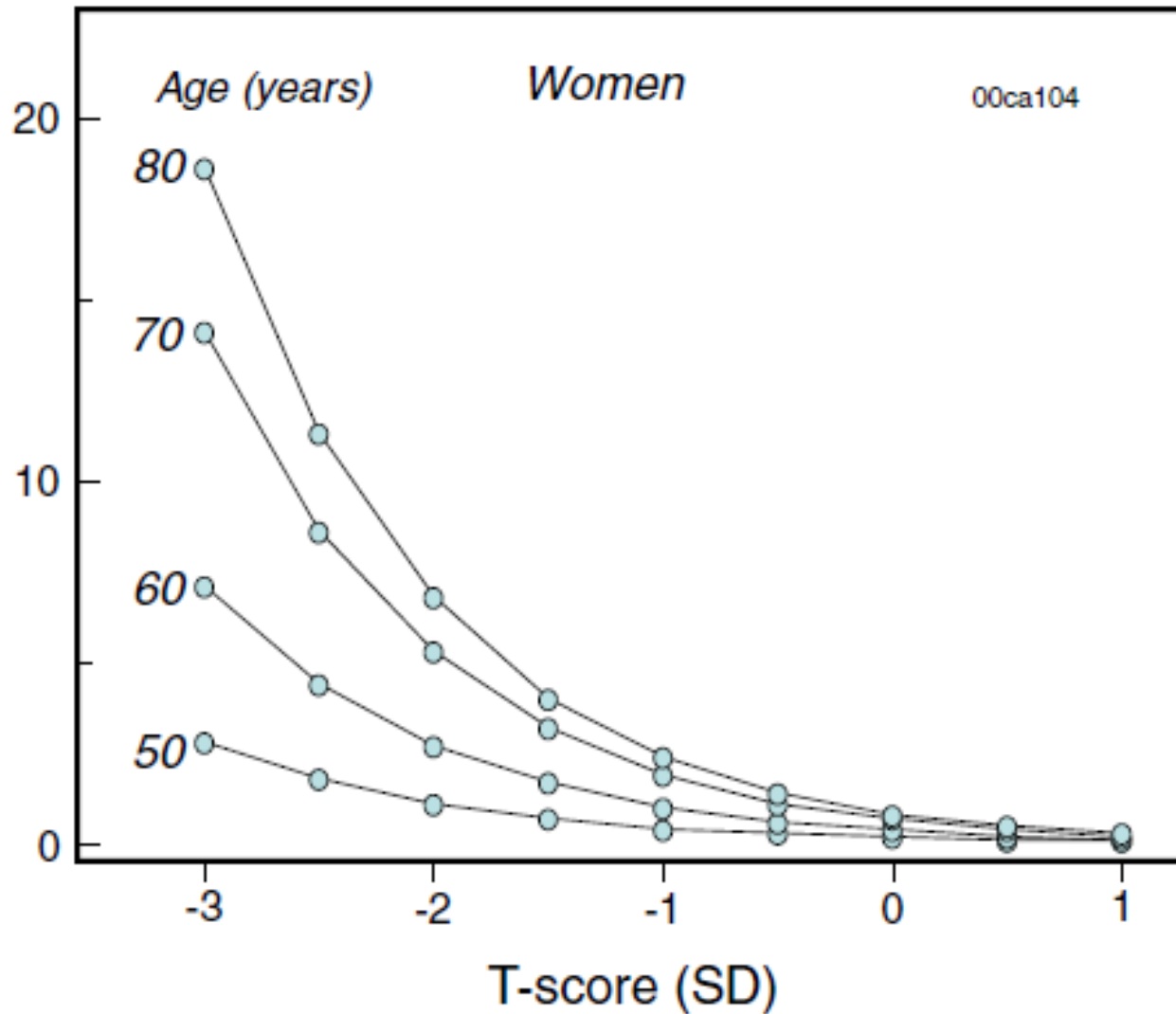
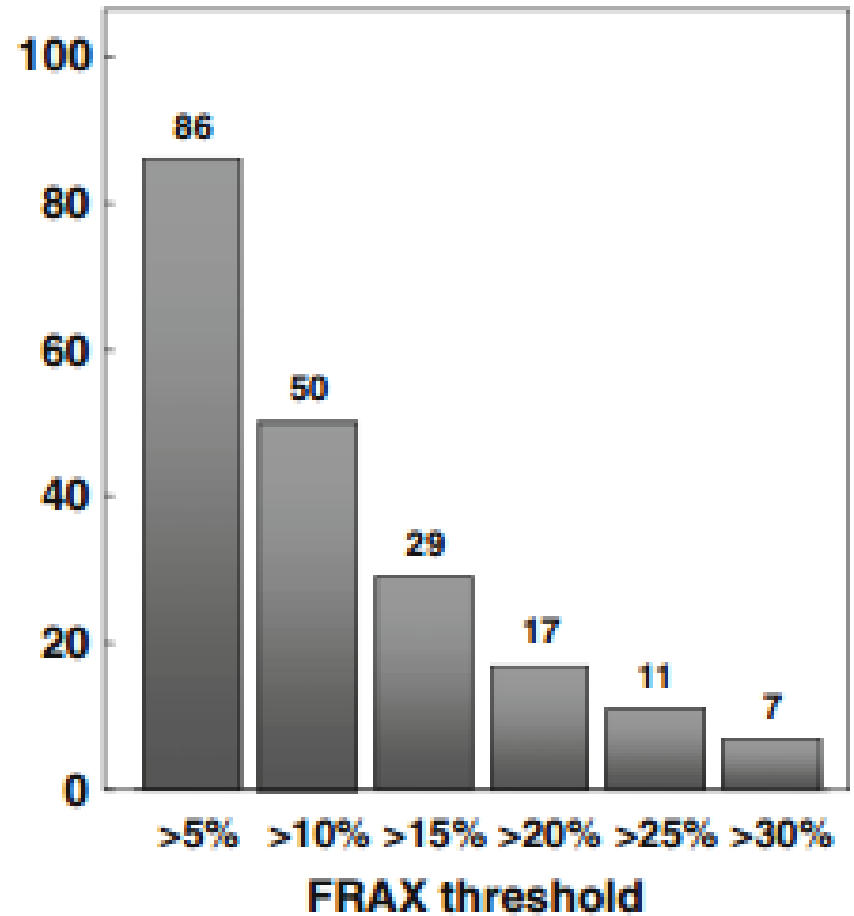
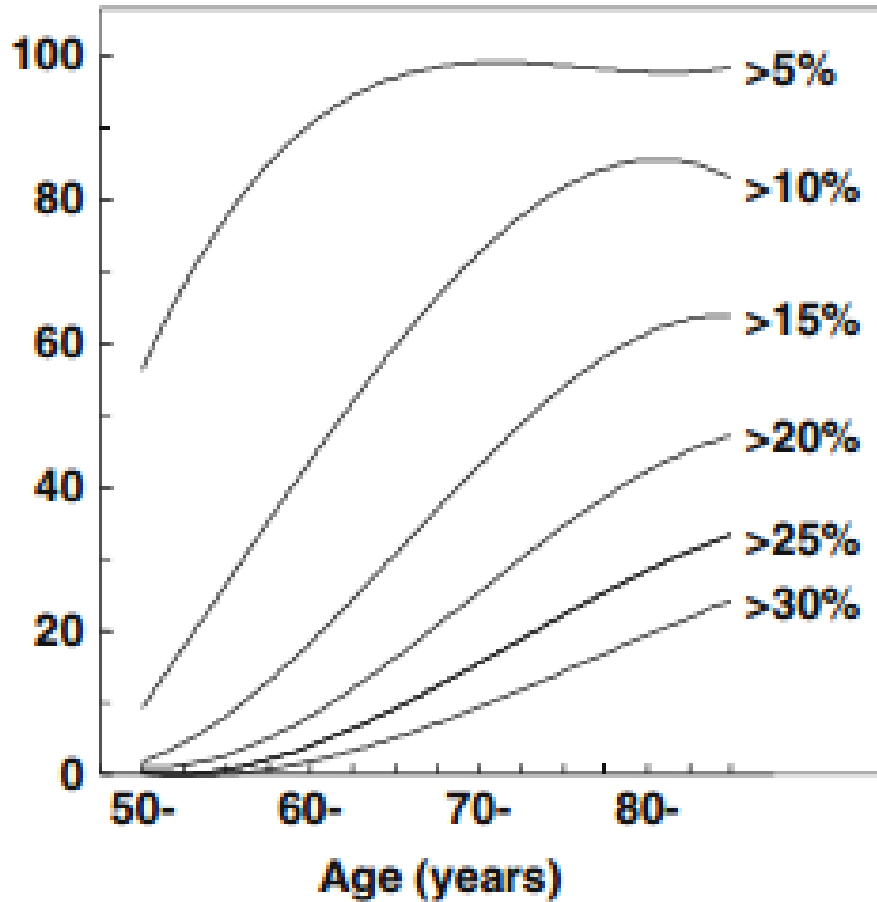


Fig. 1 Ten-year probability of hip fracture in women from Sweden according to age and T-score for femoral neck BMD [52] with kind permission from Springer Science and Business Media

Identified for treatment (%)



Pharmacologic Treatment of Low Bone Density or Osteoporosis to Prevent Fractures: A Clinical Practice Guideline from the American College of Physicians

Amir Qaseem, MD, PhD, MHA; Vincenza Snow, MD; Paul Shekelle, MD, PhD; Robert Hopkins Jr., MD; Mary Ann Forciea, MD; and Douglas K. Owens, MD, MS, for the Clinical Efficacy Assessment Subcommittee of the American College of Physicians*

Description: The American College of Physicians (ACP) developed this guideline to present the available evidence on various pharmacologic treatments to prevent fractures in men and women with low bone density or osteoporosis.

Methods: Published literature on this topic was identified by using MEDLINE (1966 to December 2006), the *ACP Journal Club* database, the Cochrane Central Register of Controlled Trials (no date limits), the Cochrane Database of Systematic Reviews (no date limits), Web sites of the United Kingdom National Institute of Health and Clinical Excellence (no date limits), and the United Kingdom Health Technology Assessment Program (January 1998 to December 2006). Searches were limited to English-language publications and human studies. Keywords for search included terms for osteoporosis, osteopenia, low bone density, and the drugs listed in the key questions. This guideline grades the evidence and recommendations according to the ACP's clinical practice guidelines grading system.

Recommendation 1: *ACP recommends that clinicians offer pharmacologic treatment to men and women who have known osteoporosis and to those who have experienced fragility fractures (Grade: strong recommendation; high-quality evidence).*

Recommendation 2: *ACP recommends that clinicians consider pharmacologic treatment for men and women who are at risk for developing osteoporosis (Grade: weak recommendation; moderate-quality evidence).*

Recommendation 3: *ACP recommends that clinicians choose among pharmacologic treatment options for osteoporosis in men and women on the basis of an assessment of risk and benefits in individual patients (Grade: strong recommendation; moderate-quality evidence).*

Recommendation 4: *ACP recommends further research to evaluate treatment of osteoporosis in men and women.*

Ann Intern Med. 2008;149:404-415.

For author affiliations, see end of text.

See related article in 5 February 2008 issue (volume 148, pages 197-213).

www.annals.org

Is too much intervention recommended in the ACP osteoporosis treatment guidelines?

P Alonso-Coello, L Pencille, V Montori

- Recomandat tratamentul in osteoporoza sau fracturi
- “osteoporoza afecteaza 44 milioane = 55% din indivizii >50a”
 - Chiar vor sa spuna ca trebuie sa ia medicamente $\frac{1}{2}$ din populatia SUA?
 - pacienta de 50 de ani cu osteoporoza: risc <9%/<3%
 - De ce nu se foloseste evaluarea riscului (FRAX)/ decizia impartasita?

RASPUNS

- FRAX poate fi un instrument util
- Totusi, nu exista RCT care sa arate eficacitatea tratamentului la pacientii selectati pe baza FRAX
- Aproape toate studiile care au demonstrat beneficiu au inrolat pacienti pe baza BMD (scor T) +/- fracturi de fragilitate in antecedente

- Testele de densitate minerala identifica o mica parte din riscul de fractura de șold
- Femei 60-80a:
 - 1/6 din risc e identificat de BMD
 - La fel de importanți: fragilitate (*frailty*), slăbiciune musculară, efectele adverse ale altor medicații, scăderea vederii, fumatul

DeLaiet 1997, *BMJ*.

- 2/3 fracturi de șold la >80a
- 90% din fracturile de șold: din căderi.

Table 31: Clinical summary of findings: AUC ranges [95% CI] (see appendix D for forest plots)

	Untreated	High adherence current treatment	Low adherence current treatment	Past treatment
FRAX without BMD, Major osteoporotic fracture	0.63 [0.61-0.65]	0.67 [0.65-0.69]	0.69 [0.67-0.71]	0.67 [0.62-0.72]
FRAX with BMD, Major osteoporotic fracture	0.66 [0.64-0.68]	0.64 [0.62-0.66]	0.71 [0.70-0.73]	0.69 [0.64-0.74]
BMD alone, Major osteoporotic fracture	0.65 [0.62-0.67]	0.65 [0.63-0.67]	0.69 [0.67-0.71]	0.66 [0.61-0.71]
FRAX without BMD, Hip fracture	0.78 [0.74-0.82]	0.76 [0.72-0.79]	0.83 [0.80-0.86]	0.83 [0.80-0.86]
FRAX with BMD, Hip fracture	0.82 [0.79-0.85]	0.80 [0.77-0.83]	0.85 [0.83-0.87]	0.85 [0.83-0.88]
BMD alone, Hip fracture	0.78 [0.74-0.83]	0.77 [0.73-0.80]	0.82 [0.79-0.85]	0.79 [0.70-0.88]

POOR

FAIR

BMD nu aduce nimic semnificativ pe lângă FRAX

Table 32: Clinical summary of findings for hip fractures: sensitivity and specificity ranges [95% CI]

Outcome	Sensitivity	Specificity
FRAX with BMD (3% threshold) ^{4,21,46}	46–77 [39–81]%	72–80 [69–81]%
FRAX without BMD (3% threshold) ^{4,21,28,46}	59–79 [51–82]%	39–86 [36–86]%
QFracture (3% threshold) ²⁸	55 [54–56]%	88 [88–88]%
FRAX with BMD (5% threshold) ^{4,20,21,45}	29–76 [23–80]%	63–89 [61–90]%
FRAX without BMD (5% threshold) ^{4,20,21,28,45}	39–78 [31–82]%	50–92 [49–92]%
QFracture (5% threshold) ²⁸	39 [38–40]%	93 [93–93]%

Table 33: Clinical summary of findings for major osteoporotic fractures: sensitivity and specificity ranges [95% CI]

Outcome	Sensitivity	Specificity
FRAX with BMD (10% threshold) ^{4,20,21,45}	42–97 [35–98]%	15–76 [14–78]%
FRAX without BMD (10% threshold) ^{4,20,21,45}	50–100 [46–100]%	0–72 [0–73]%
QFracture (10% threshold) ²⁸	22 [22–23]%	94 [94–95]%
FRAX with BMD (20% threshold) ^{4,20,21,45}	9–28 [6–30]%	81–96 [80–97]%
FRAX without BMD (20% threshold) ^{4,20,21,45}	16–29 [13–31]%	81–93 [80–94]%
QFracture (20% threshold) ²⁸	2 [2–2]%	100 [100–100]%
FRAX with BMD (30% threshold) ^{4,20,21,45}	0–18 [0–21]%	94–99 [93–99]%
FRAX without BMD (30% threshold) ^{4,20,21,45}	4–10 [3–11]%	96–99 [95–99]%
QFracture (30% threshold) ²⁸	0 [0–0]%	100 [100–100]%

What is my risk of breaking a bone?

As you get older, your risk of breaking a bone, often through a fall, increases. This increased risk may be due to weakened bones or *osteoporosis*.

Your risk is estimated primarily by:

Your age: _____

Your Bone Mineral Density (T score): _____

It is also affected by:

- If you have had a fracture
- If a parent had a fracture
- If you currently smoke
- If you drink more than 2 drinks of alcohol a day
- If you have taken prescription steroid medications

Based on these risk factors, we estimate your risk is

<10% 10-30% >30%

Your fracture risk can be lowered with medications called *bisphosphonates*, which work to reduce bone loss. This decision aid will walk you through the benefits and downsides of bisphosphonates, so that we can make an informed choice about whether or not they are right for you.

Benefits

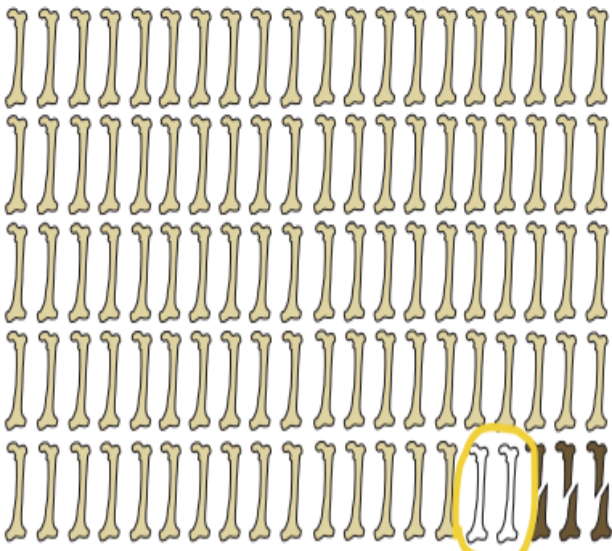
Without Medication

Roughly 5 in 100 have a fracture within the next 10 years. 95 will not.



With Medication

Roughly 3 in 100 have a fracture within the next 10 years. 97 will not. 2 have avoided a fracture because of the medication.



Downsides

Directions

This medication must be taken

- Once a week
- On an empty stomach in the morning
- With 8 oz of water
- While upright (sitting or standing for 30 min)
- 30 minutes before eating

Possible Harms

Abdominal Problems

About 1 in 4 people will have heartburn, nausea, or belly pain. However, it may not be from the medication. If the medication is the cause, the problem will go away if you stop taking it.

Osteonecrosis of the Jaw

Fewer than 1 in 10,000 (over the next 10 years) will have bone sores of the jaw that may need surgery.

Out of Pocket Cost

with insurance \$30 | without insurance \$70-90

What would you like to do?

Benefits

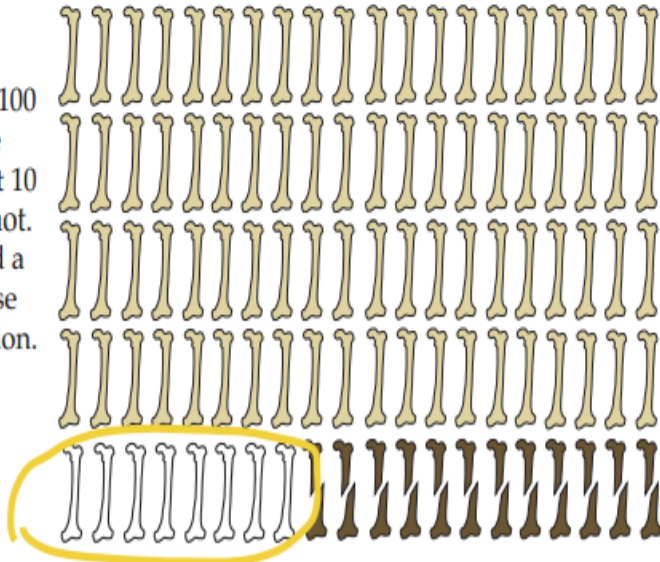
10-30%

Downsides

Without Medication
Roughly 20 in 100 have a fracture within the next 10 years. 80 will not.



With Medication
Roughly 12 in 100 have a fracture within the next 10 years. 88 will not. 8 have avoided a fracture because of the medication.



Directions

This medication must be taken

- Once a week
- On an empty stomach in the morning
- With 8 oz of water
- While upright (sitting or standing for 30 min)
- 30 minutes before eating

Possible Harms

Abdominal Problems

About 1 in 4 people will have heartburn, nausea, or belly pain. However, it may not be from the medication. If the medication is the cause, the problem will go away if you stop taking it.

Osteonecrosis of the Jaw

Fewer than 1 in 10,000 (over the next 10 years) will have bone sores of the jaw that may need surgery.

Out of Pocket Cost

with insurance \$30 | without insurance \$70-90

What would you like to do?

Benefits

>30%

Downsides

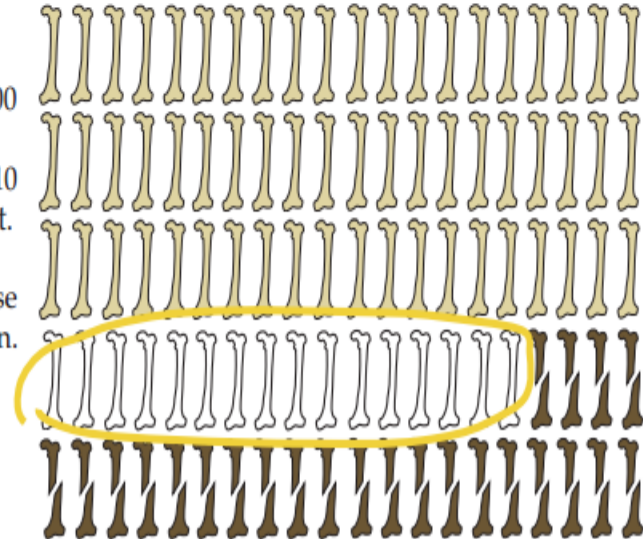
Without Medication

Roughly 40 in 100 have a fracture within the next 10 years. 60 will not.



With Medication

Roughly 24 in 100 have a fracture within the next 10 years. 76 will not. 16 have avoided a fracture because of the medication.



Directions

This medication must be taken

- Once a week
- On an empty stomach in the morning
- With 8 oz of water
- While upright (sitting or standing for 30 min)
- 30 minutes before eating

Possible Harms

Abdominal Problems

About 1 in 4 people will have heartburn, nausea, or belly pain. However, it may not be from the medication. If the medication is the cause, the problem will go away if you stop taking it.

Osteonecrosis of the Jaw

Fewer than 1 in 10,000 (over the next 10 years) will have bone sores of the jaw that may need surgery.

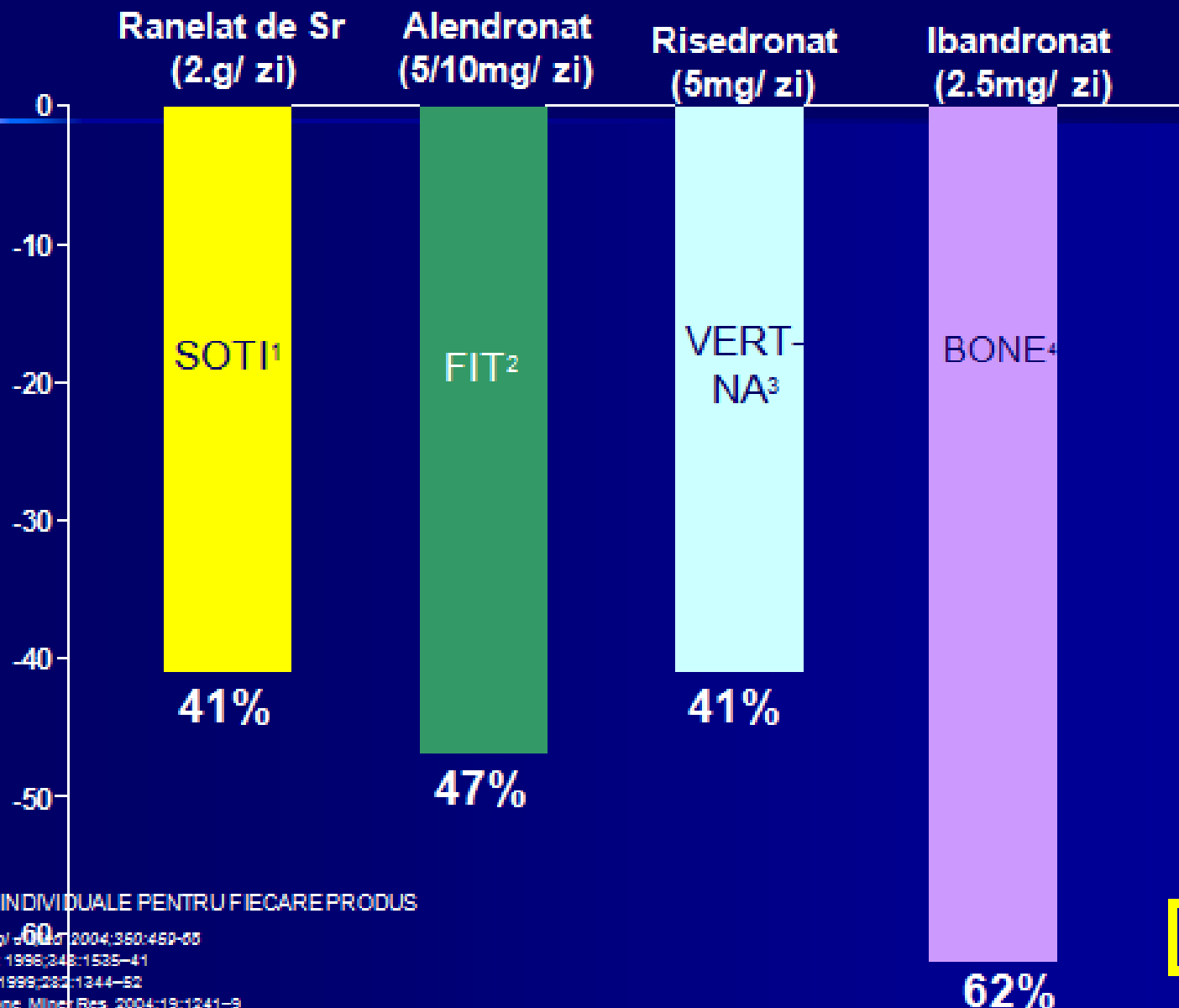
Out of Pocket Cost

with insurance \$30 | without insurance \$70-90

What would you like to do?

TRATAMENT

Reducerea RR pentru fracturi vertebrale noi dupa 3 ani



Dar..

DATE DIN STUDII INDIVIDUALE PENTRU FIECARE PRODUS

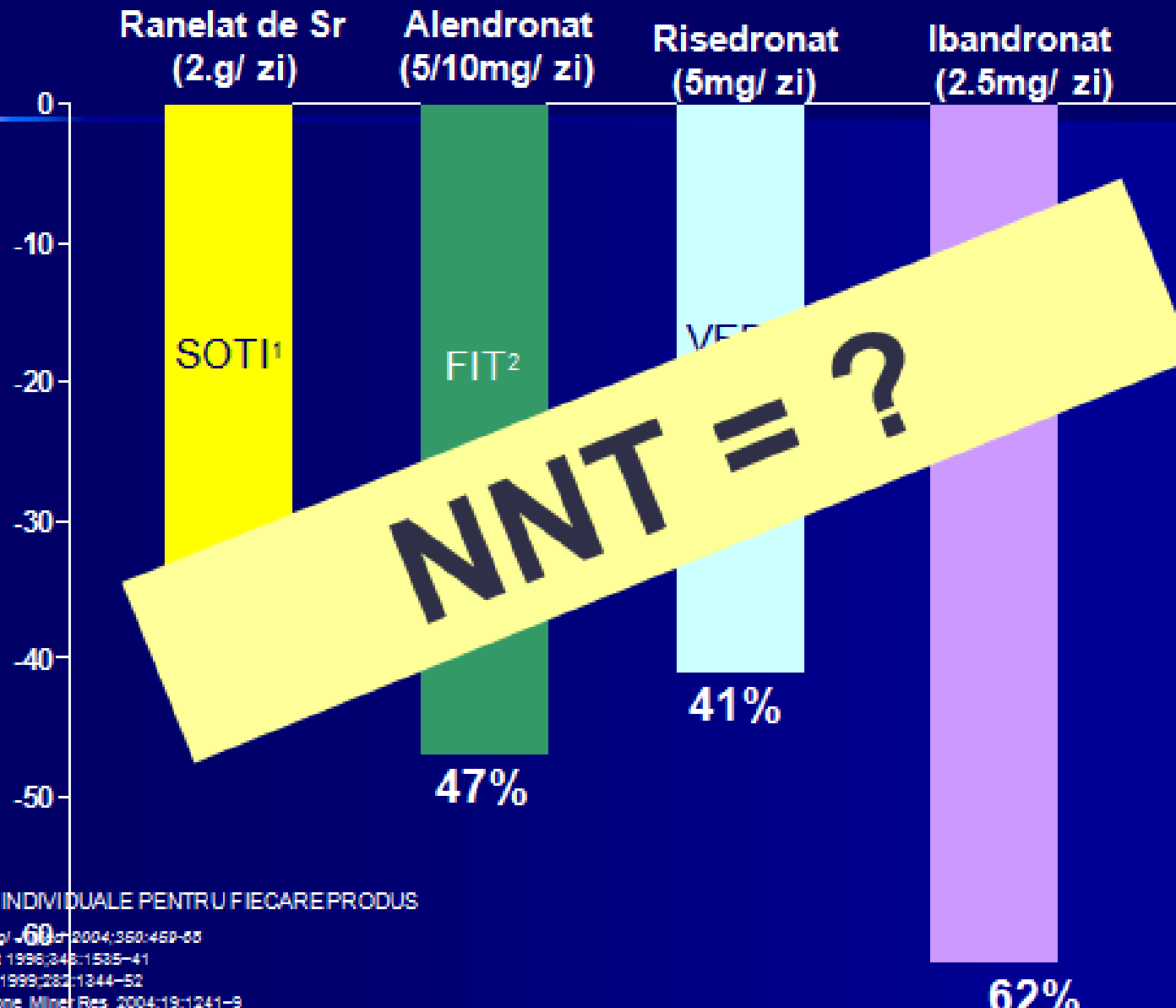
¹Meunier PJ, et al. *N Engl J Med* 2004;350:469-80

²Bleck DM, et al. *Lancet* 1998;348:1535-41

³Harris ST, et al. *JAMA* 1999;282:1344-52

⁴Cheesnut CH, et al. *J Bone Miner Res* 2004;19:1241-9

Reducerea RR pentru fracturi vertebrale noi dupa 3 ani



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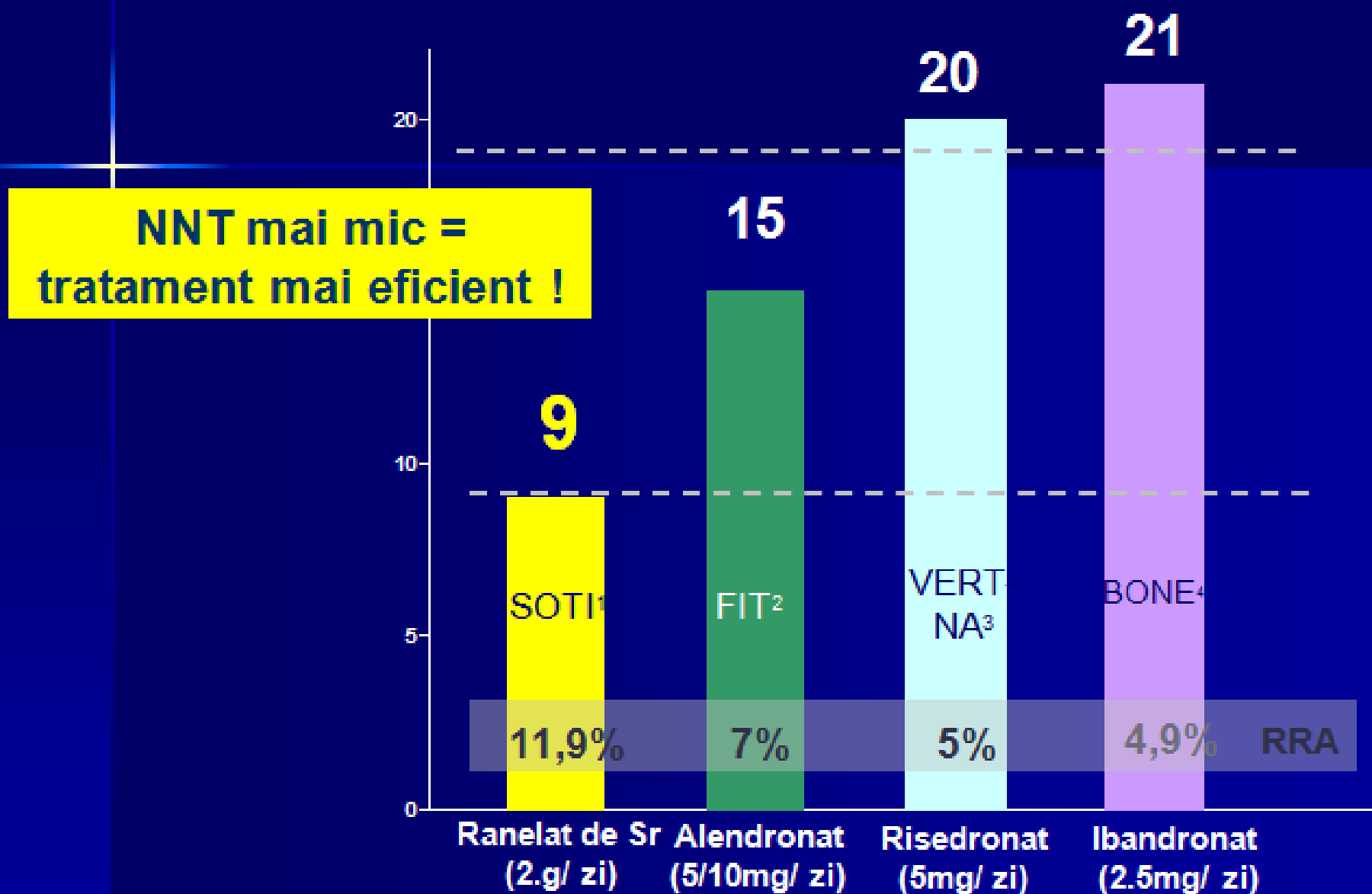
¹Meunier PJ, et al. *N Engl J Med* 2004;350:459-66

²Black DM, et al. *Lancet* 1996;348:1535-41

³Harris ST, et al. *JAMA* 1999;282:1344-52

⁴Chesnut CH, et al. *J Bone Miner Res* 2004;19:1241-9

NNT pentru reducerea riscului de F.V. noi la 3 ani

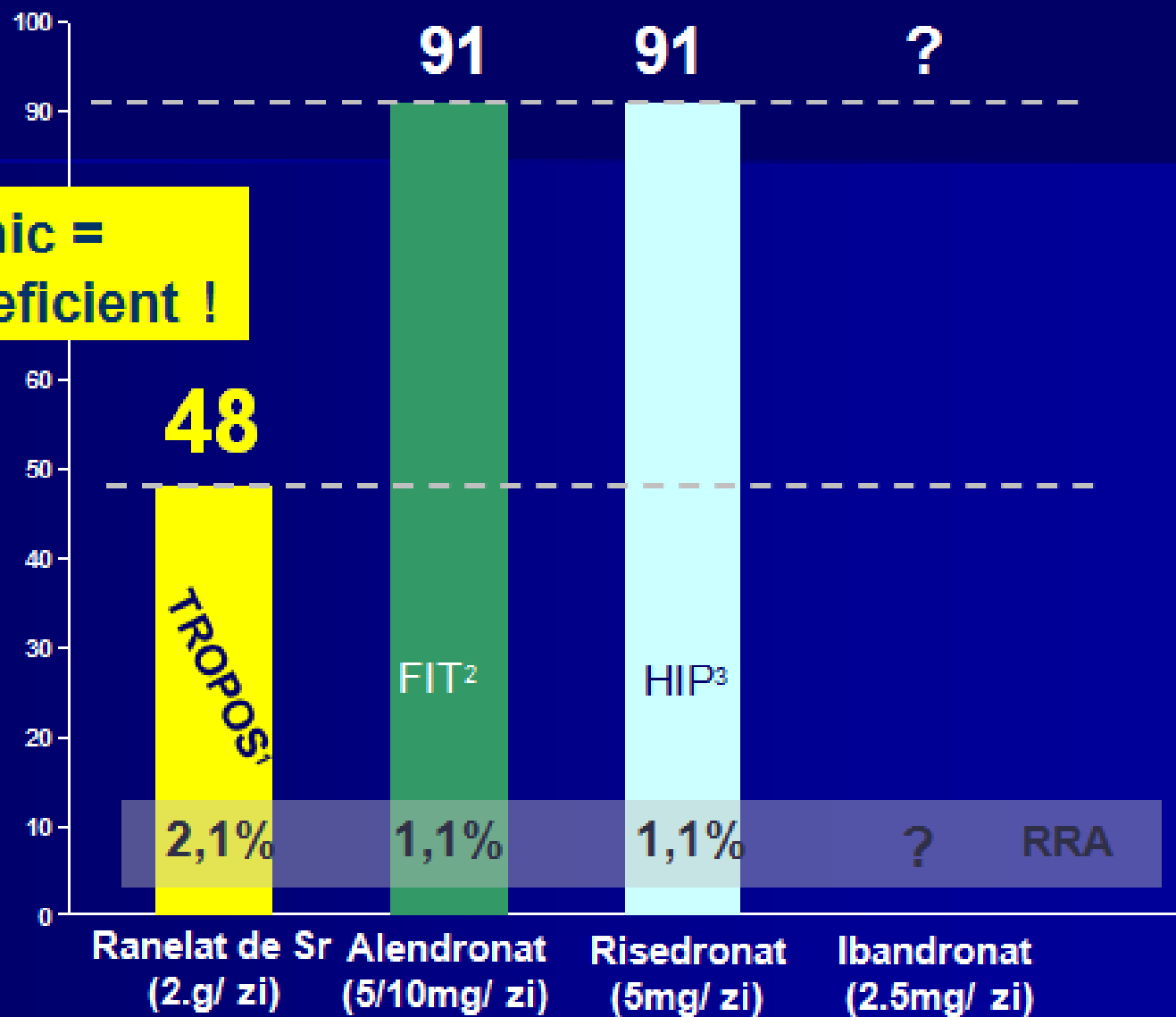


DATE DIN STUDII INDIVIDUALE PENTRU FIECARE PRODUS

¹Meunier PJ et al. *N Engl J Med* 2004;350:450-55 ²Black DM, et al. *Lancet* 1996;348:1535-41 ³Harris ST, et al. *JAMA* 1999;282:1344-52 ⁴Chesnut CH, et al. *J Bone Miner Res* 2004;19:1241-9

NNT pentru reducerea riscului de F.S. la 3 ani

**NNT mai mic =
tratament mai eficient !**



DATE DIN STUDII INDIVIDUALE PENTRU FIECARE PRODUS

¹Reginster JY, et al. *J Clin Endocrinol Metab.* 2005;90(5):2816-2822 ²Mac Clung MR, Gensens P, Miller PD et al. *New Engl J Med* 2001, 344:333-340

Cea mai mică dobândă, dar cel mai mare câștig!?

	RRR (dobânda)	RAR (câștigul)	NNT (câștigul)	Riscul bazal %
RANELAT DE STRONTIU (SOTI)	41 %	11,9 %	9	30%
ALENDRONAT (FIT)	47 %	7 %	15	15%
RISEDRONAT (VERT-NA)	41 %	5 %	20	12%
IBANDRONAT (BONE)	62 %	4,9 %	21	8%
DENOSUMAB (FREEDOM)	68 %	4,9 %	21	7%



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

10 January 2014
EMA/10206/2014

PRAC recommends suspending use of Protelos/Osseor (strontium ranelate)

The PRAC has now conducted an in-depth review taking into account available data on the benefits and risks of the medicine. The Committee noted that for every 1,000 patient-years¹ there were 4 more cases of serious heart problems (including heart attacks) and 4 more cases of blood clots or blockages of blood vessels with Protelos/Osseor than with placebo (a dummy treatment). In addition,

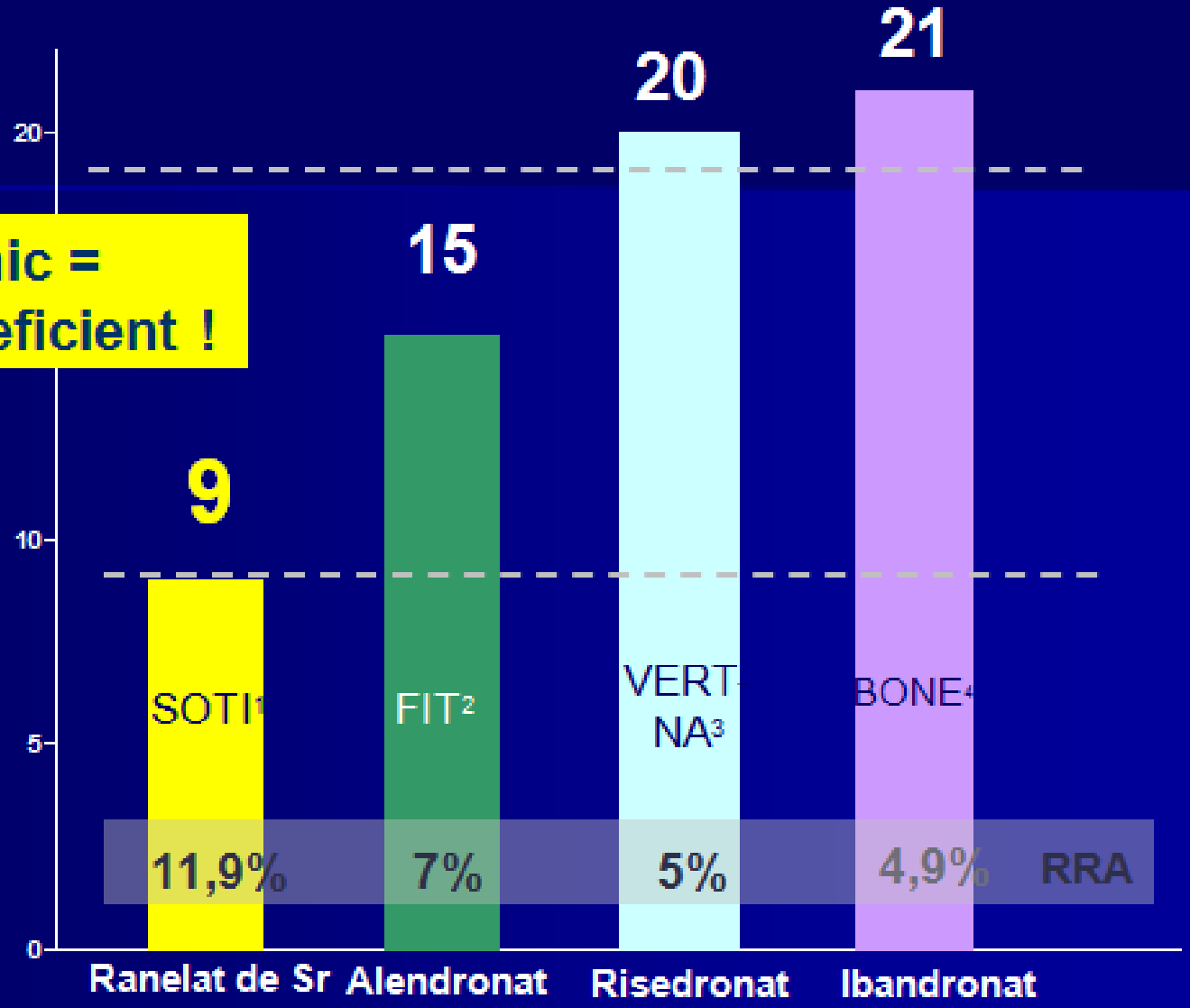
$$\text{NNH} = 250 + 250 = 125$$

With regard to its benefits, Protelos/Osseor has been shown to have a modest effect in osteoporosis, preventing about 5 non-spinal fractures, 15 new spinal fractures and 0.4 hip fractures for every 1,000 patient-years.

NNT: 200 (fr nonvert); 67 (fr vert); 2500 (fr sold) !!!???

NNT pentru reducerea riscului de F.V. noi la 3 ani

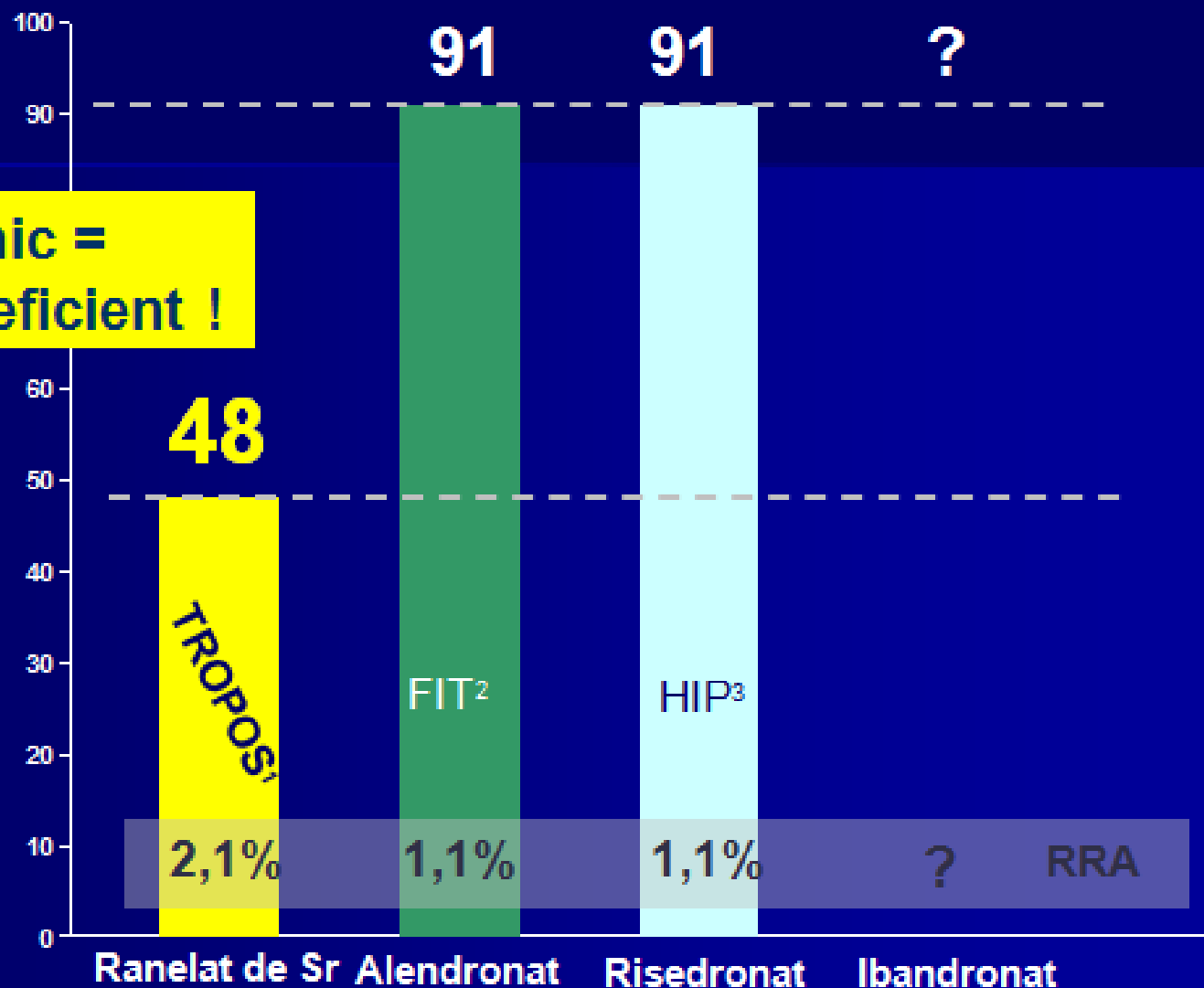
**NNT mai mic =
tratament mai eficient !**



NNT: 200 (fr nonvert); 67 (fr vert); 2500 (fr sold) !!!???

NNT pentru reducerea riscului de F.S. la 3 ani

**NNT mai mic =
tratament mai eficient !**



NNT: 200 (fr nonvert); 67 (fr vert); 2500 (fr sold) !!!???



All Trials Registered | All Results Reported

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It's time all clinical trial results are reported.

Patients, researchers, pharmacists, doctors and regulators everywhere will benefit from publication of clinical trial results. Wherever you are in the world please sign the petition:

Thousands of clinical trials have not reported their results; some have not even been registered.

Information on what was done and what was found in these trials could be lost forever to doctors and researchers, leading to bad treatment decisions, missed opportunities for good medicine, and trials being repeated.

All trials past and present should be registered, and the full methods and the results reported.

We call on governments, regulators and research bodies to implement measures to achieve this.

The petition has also been translated into [many different languages](#). If you would like to sign the petition on behalf of an organisation then please [contact us](#). Data will be held by Sense About Science. Read our [privacy policy](#) here.

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- [Effects of long-term strontium ranelate treatment on vertebral fracture risk in postmenopausal women with osteoporosis.](#)

Meunier PJ, Roux C, Ortolani S, Diaz-Curiel M, Compton J, Marquis P, Cormier C, Isaia G, Badurski J, Werk JD, Collette J, Reginster JY.
Osteoporos Int. 2009 Oct;20(10):1652-73. doi: 10.1007/s00198-009-0825-6. Epub 2009 Jan 20.
PMID: 19152673 [PubMed - indexed for MEDLINE] [Free PMC Article](#)
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- [Effects of long-term strontium ranelate treatment on the risk of nonvertebral and vertebral fractures in postmenopausal osteoporosis: Results of a five-year randomized, placebo-controlled trial.](#)

Reginster JY, Feisenberg D, Boonen S, Diaz-Perez A, Rizzoli R, Brandi ML, Spector TD, Briken K, Goemaere S, Cormier C, Balogh A, Delmas PD, Meunier PJ.
Arthritis Rheum. 2008 Jun;50(6):1657-65. doi: 10.1002/art.23461.
PMID: 18512759 [PubMed - indexed for MEDLINE] [Free Article](#)
[Related citations](#)
- [Vertebral fracture risk reduction with strontium ranelate in women with postmenopausal osteoporosis is independent of baseline risk factors.](#)

Roux C, Reginster JY, Fechtenbaum J, Kolta S, Sawicki A, Tulessey Z, Luisetto G, Padrino JM, Doyle D, Prince R, Fardellone P, Sorensen OH, Meunier PJ.
J Bone Miner Res. 2008 Apr;23(4):526-32. Epub 2008 Apr 5.
PMID: 18593773 [PubMed - indexed for MEDLINE]
[Related citations](#)
- [Strontium ranelate reduces the risk of nonvertebral fractures in postmenopausal women with osteoporosis: Treatment of Peripheral Osteoporosis \(TROPIS\) study.](#)

Reginster JY, Beaman E, De Vernejoul MC, Adami S, Compton J, Phenekos C, Devogelaer JP, Curiel MD, Sawicki A, Goemaere S, Sorensen OH, Feisenberg D, Meunier PJ.
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PMID: 15725210 [PubMed - indexed for MEDLINE]
[Related citations](#)
- [The effects of strontium ranelate on the risk of vertebral fracture in women with postmenopausal osteoporosis.](#)

Meunier PJ, Roux C, Seeman E, Ortolani S, Badurski JE, Spector TD, Cannata J, Balogh A, Lemmel EM, Fors-Nielsen S, Rizzoli R, Genant HK, Reginster JY.
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[Related citations](#)
- [Strontium ranelate phase 2 dose-ranging studies: PREVOS and STRATOS studies.](#)

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PMID: 12730797 [PubMed - indexed for MEDLINE]
[Related citations](#)
- [Design and methodology of the phase 3 trials for the clinical development of strontium ranelate in the treatment of women with postmenopausal osteoporosis.](#)

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PMID: 12730769 [PubMed - indexed for MEDLINE]
[Related citations](#)
- [Strontium ranelate: dose-dependent effects in established postmenopausal vertebral osteoporosis—a 2-year randomized placebo controlled trial.](#)

Meunier PJ, Slosman DO, Delmas PD, Sebret JL, Brandi ML, Albanese C, Lorenz R, Fors-Nielsen S, De Vernejoul MC, Rocas A, Reginster JY.
J Clin Endocrinol Metab. 2002 May;85(5):2060-6.
PMID: 11994341 [PubMed - indexed for MEDLINE]
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