Osteoporosis and Lupus

Andrew Ruthberg, MD

University Rheumatologists

Forget the medical terminology (osteoporosis, osteopenia, low bone mass, DEXA, DXA, T score etc)

The bottom line is that you don't want to break (fracture) any bones after your childhood years

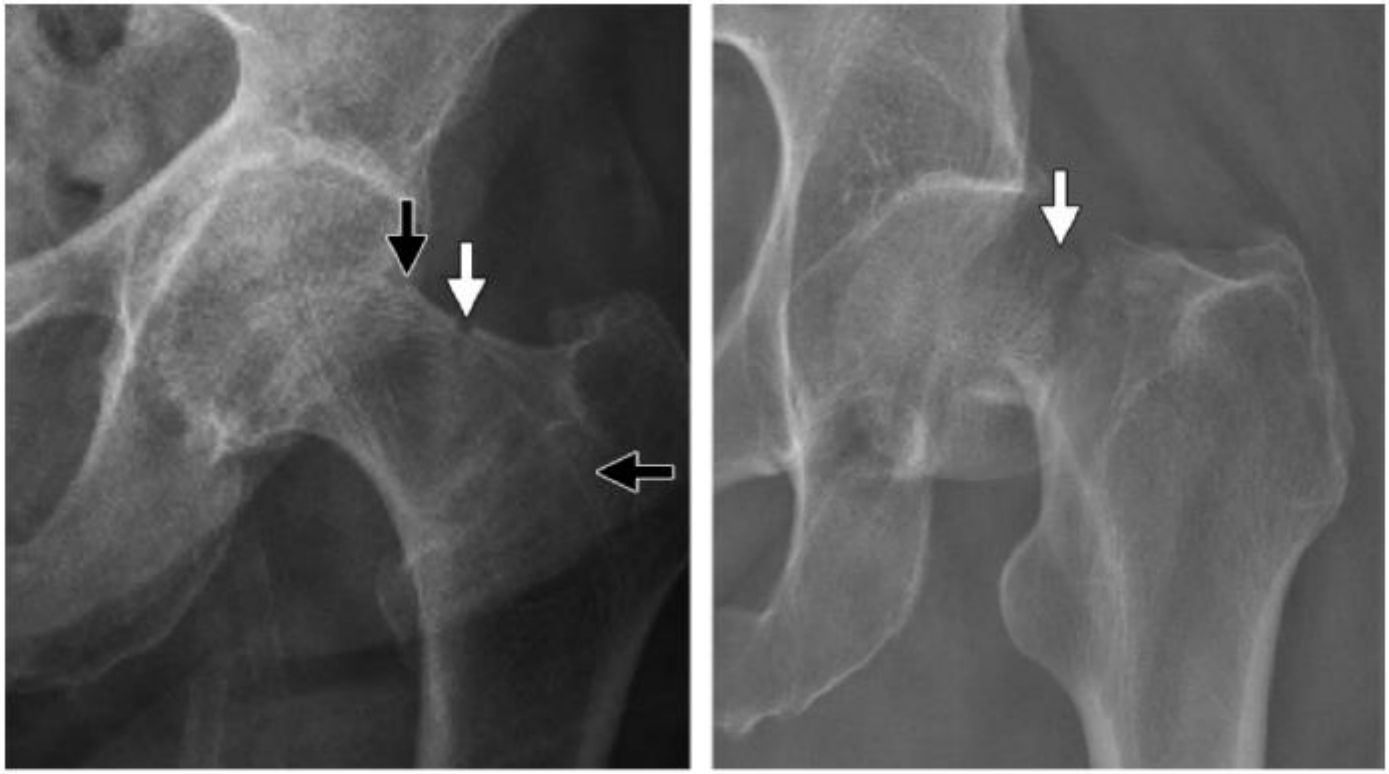
If Nik Wallenda had fallen from his tightrope and landed on Wacker Drive he would have broken many bones (and probably died) even though he is a younger (and hopefully healthy) man. Those would have been “traumatic fractures”

Insufficiency/Fragility fractures

- Our issue today
- They are fractures caused more by weaker bones than extraordinary trauma
- One definition might be a fracture with a fall from normal standing height

A distal radial fracture (wrist fracture) – a common insufficiency fracture

A femoral neck/hip fracture-much less common but much more serious



a. b.

Figure 16. Sequential images of the left hip in an 85-year-old woman with osteoporosis and complaints of groin pain. **(a)** Initial anteroposterior radiograph demonstrates focal disruption of the lateral femoral cortex (white arrow) with the fracture line oriented perpendicular to the primary tensile trabeculae (black arrows). The patient was diagnosed with an incomplete insufficiency-type stress fracture and was placed under strict activity restrictions. **(b)** Follow-up anteroposterior radiograph obtained after acute atraumatic exacerbation of groin pain demonstrates completion of the now-displaced femoral neck fracture (arrow).

A severe spinal compression fracture-they can be much milder and may occur without a patient being aware of the event

RadioGraphics
RG • Volume 31 Number 5

Figure 3. Lateral radiograph of the dorsal spine shows a wedge fracture (arrow) associated with severe osteopenia and causing a kyphotic deformity.

Bone is living tissue

- You were able to detect conversion from soft cartilage to hard bone at the “fontanelles” at the skull of your children or grandchildren when they were babies
- All of us had our arm and leg bones grow longer as kids and teenagers
- Most broken bones (fractures) that we had as kids and teenagers healed back to normal
- Even when we are 60, 70, 80 or older are bones are slowly breaking down and rebuilding themselves (remodeling)

A few technical terms that relate to targets for treatment

- Osteoclasts-the cells in charge of bone breakdown
- Osteoblasts-the cells in charge of bone formation starting with cartilage
- Calcification-an important process as our body tries to make stronger bone from the softer cartilage. Vitamin D is a factor

I will use slides from the NOF

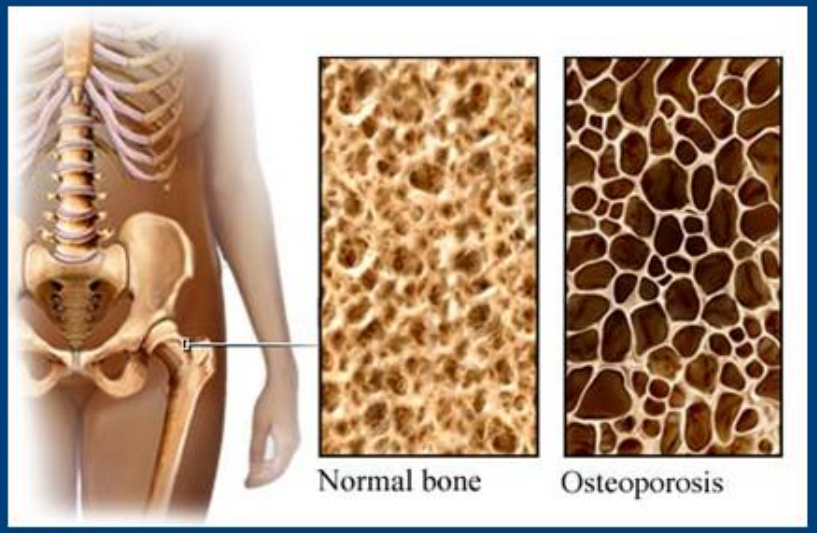
What is Osteoporosis?

Osteoporosis, or porous bone, is a disease characterized by low bone mass and structural deterioration of bone tissue, leading to bone fragility and an increased susceptibility to fractures, especially of the hip, spine and wrist, although any bone can be affected.

World Health Organization. Assessment of Fracture Risk and Its Application to Screening for Postmenopausal Osteoporosis. Report of a WHO Study Group. World Health Organ Technical Report Series 843. 1994:1-129.

Osteoporosis as defined by NIH

A skeletal disorder characterized by compromised *bone strength* predisposing to an increased risk of fracture



Bone strength = Bone quality including bone density, architecture and bone turnover

National Institutes of Health. *Osteoporosis Prevention, Diagnosis, and Therapy.* NIH Consensus Conference, 2000. March 27-29; 17:1-36.

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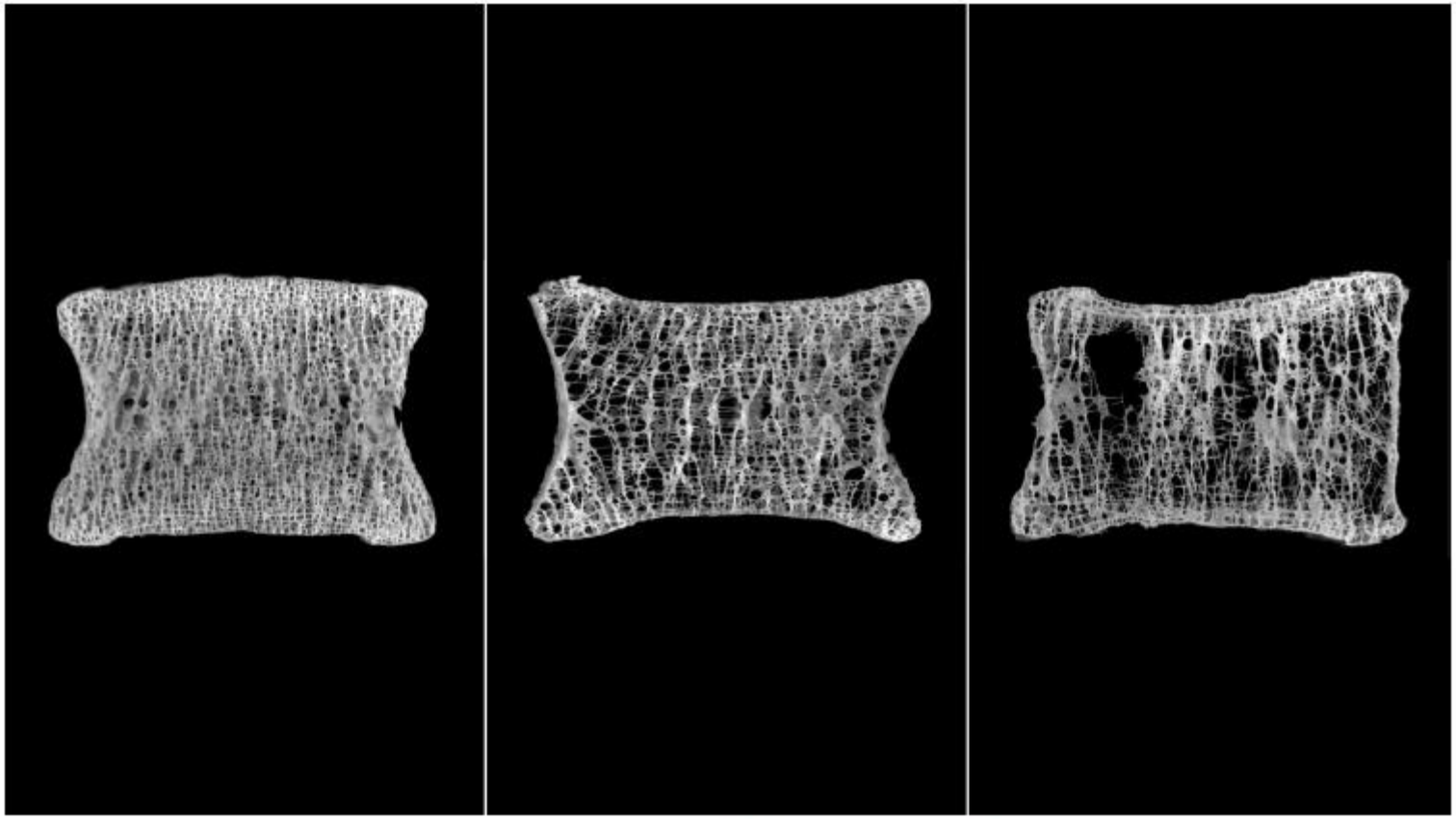


CT scans show the progression of one patient's vertebra over a six- to eight-year period, from normal bone density to moderate osteoporosis and severe osteoporosis.
A. Boyde and P.D. Miller

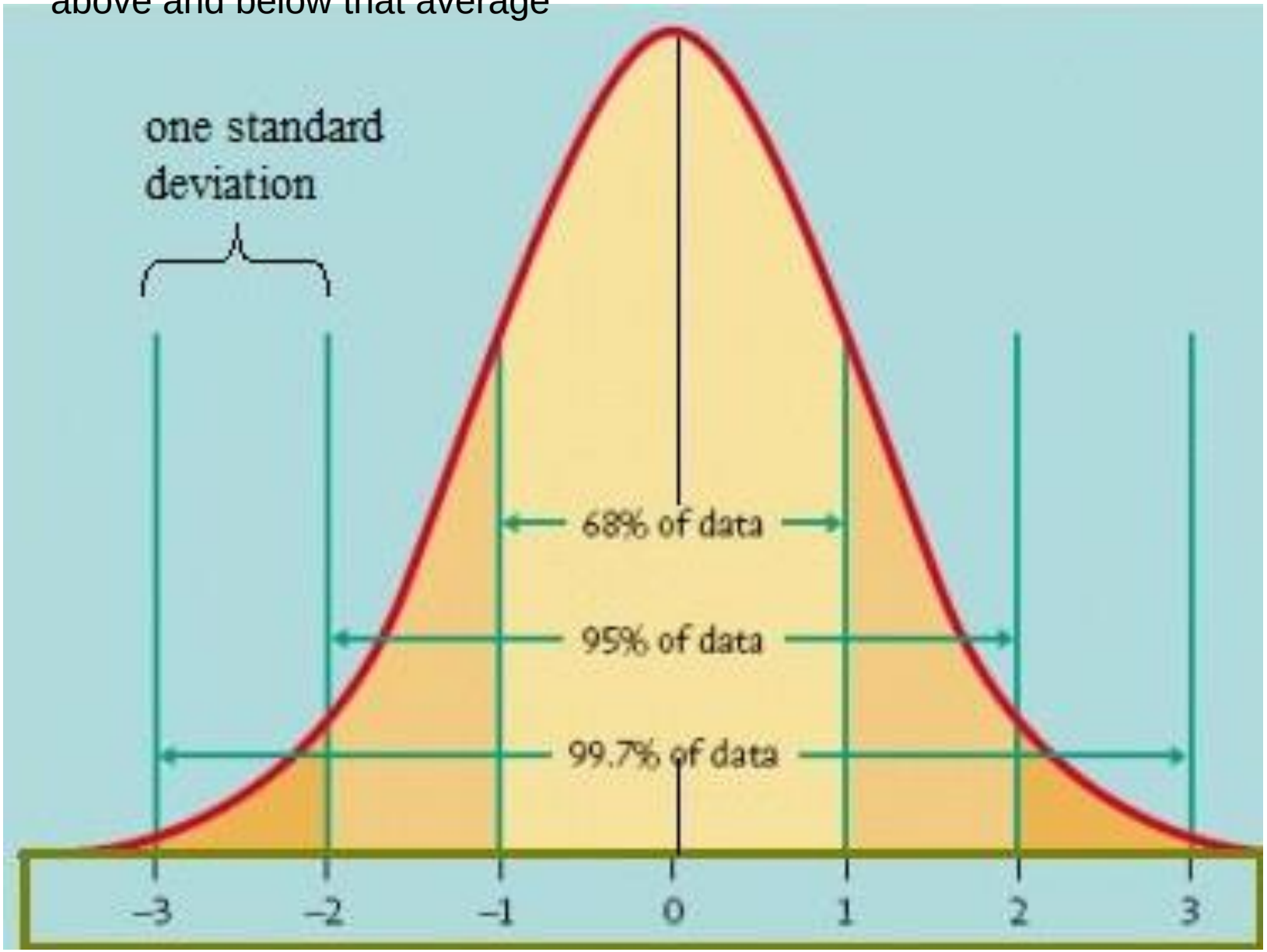
The New York Times

WHO Diagnostic Classification using T scores (this is the labeling system we use with DEXA scans)

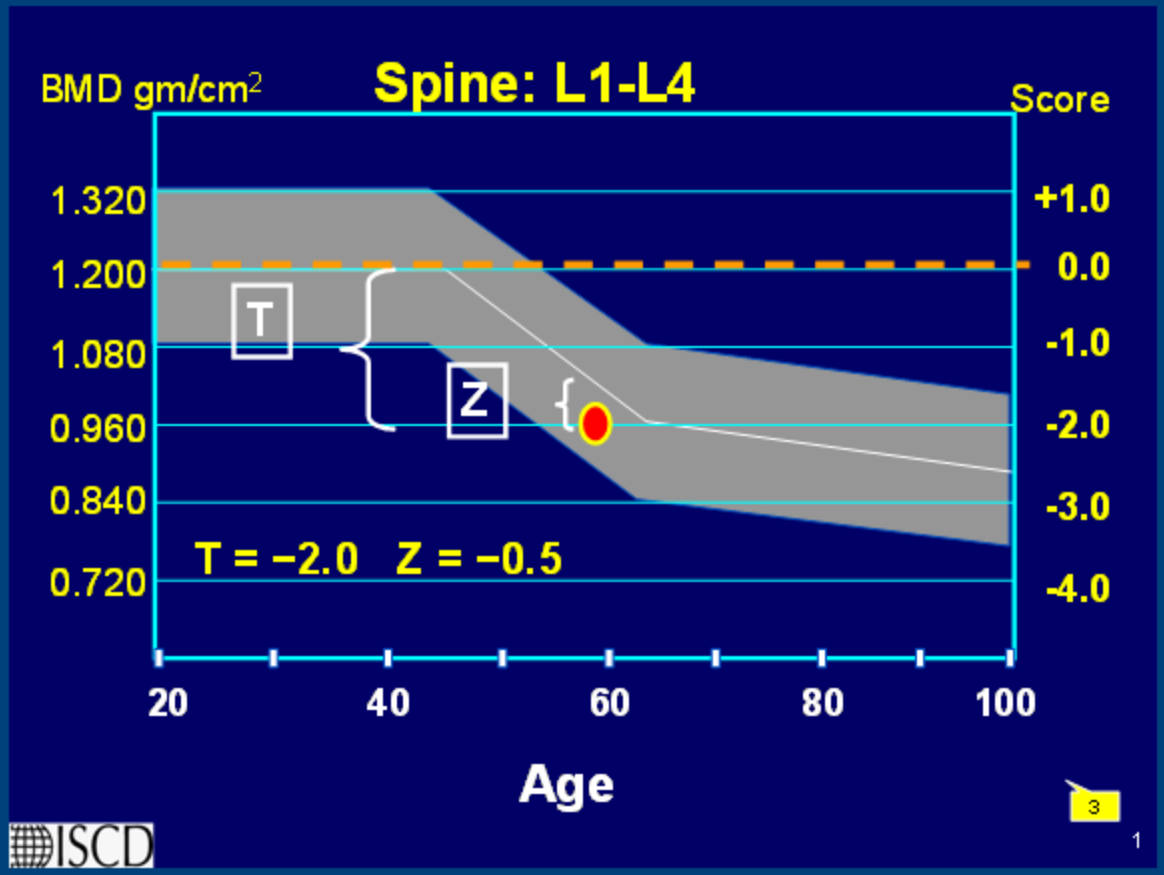
Classification	T-score
Normal	-1.0 or greater
Osteopenia	Between -1.0 and -2.5
Osteoporosis	-2.5 or less
Severe Osteoporosis	-2.5 or less and fragility fracture

WHO Study Group. 1994.

Based on DEXA results for a group of younger women noting the average for the group and how many people are different amounts above and below that average



World Health Organization
Osteoporosis Guidelines



From ISCD Bone Densitometry Clinician Course, Lecture 5 (2008).

A more flexible definition from the Bone Health Alliance

- A T score of -2.5 or lower at the spine, total hip or femoral neck noted with a DEXA scan
- Someone who has had a spinal compression fracture or hip fracture without major trauma
- Someone with calculated risk for major osteoporotic fracture of 20% or more or risk of hip fracture of 3% or more during the next 10 years using a tool called FRAX

There are other causes for "weak bones" that we have to keep in mind

- Osteogenesis imperfecta causing fractures from very early childhood is an example
- Severe vitamin D deficiency (Osteomalacia or Rickets)
- Overactive parathyroid gland (Hyperparathyroidism)
- Bone diseases associated with kidney disease (renal failure)

Risk Factors for Osteoporosis

- Low bone density
- Advancing age
- History of prior fracture
- Parental history of hip fracture
- Use of certain medications e.g. glucocorticoids
- Race
- Small frame
- Low estrogen in women
- Low testosterone in men

Fractures

Caucasian more than Hispanic more than African American

Medications Associated with Reduced Bone Mass in Adults

- Anticoagulants
- Anticonvulsants Seizure medications
- Aromatase inhibitors
- Barbiturates
- Cancer chemotherapeutic drugs
- Cyclosporin A
- Glucocorticoids - oral and high-dose inhaled Key for people with Lupus

Special issues for many Lupus patients

- Need to avoid the sun increases risk for Vitamin D deficiency
- Increased rate of early menopause
- Renal (kidney) failure creates risk for other forms of bone disease (renal osteodystrophy)

Curr Osteoporos Rep (2017) 15:187–193
DOI 10.1007/s11914-017-0367-y

Renal Osteodystrophy—Time for Common Nomenclature

Susan M. Ott[1]

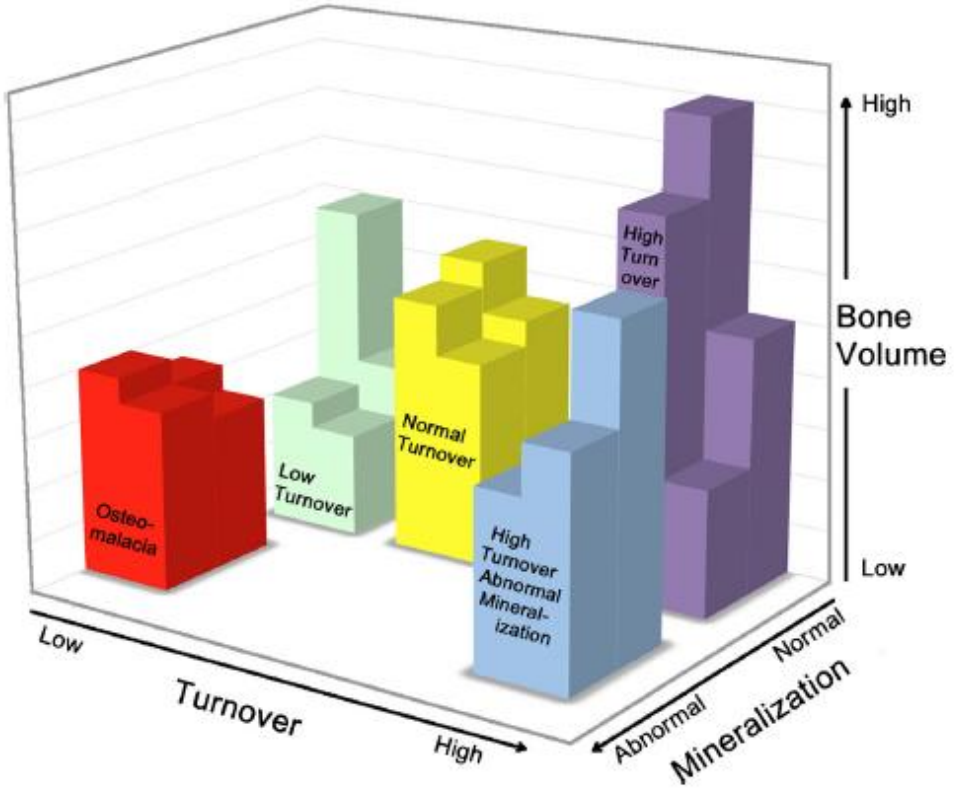


Fig. 2 Theoretical construction of the Turnover-Mineralization-Volume framework. Patients with renal osteodystrophy group into categories depending on the degree of osteoid and of turnover as shown in this figure. The bone volume, however, remains a theoretical construct and it is likely that both low and high bone volume will be seen in each of the other groups

Current concepts on osteonecrosis of the femoral head

Joaquin Moya-Angeler, Arianna L Gianakos, Jordan C Villa, Amelia Ni, Joseph M Lane

Figure 3 Bilateral osteonecrosis of the femoral head with flattening of the surface and early sings of osteoarthritis.

AVN or avascular necrosis.

This another bone disorder associated with prednisone use but is different from Osteoporosis

How can we identify a person at risk before they have a fracture?

Recognize clinical risk factors

Consider a DEXA scan (likely appropriate for anyone on prednisone)

Who Should Have a BMD Test?

- Women age 65 and older and men age 70 and older
- Younger postmenopausal women and men age 50-69 with concern based on risk factors
- Women in menopausal transition if there is a specific risk factor
- Adults who have had a fracture after age 50
- Adults with a condition or taking a medication associated with bone loss prednisone

A DEXA or DXA scan is the most standard BMD test

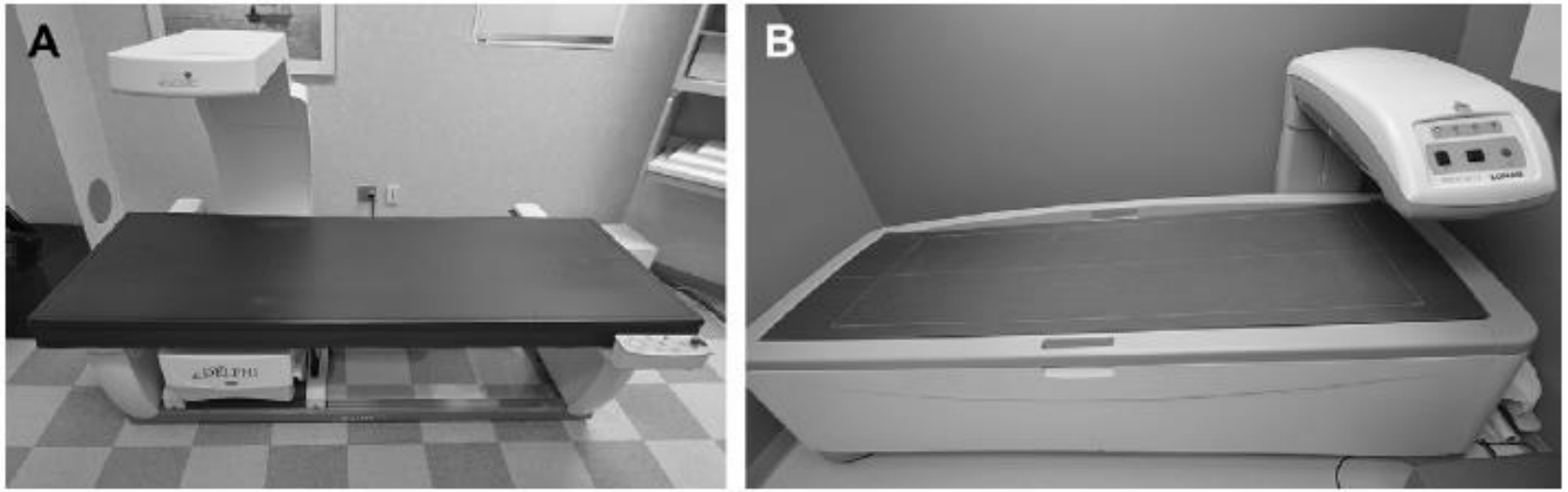


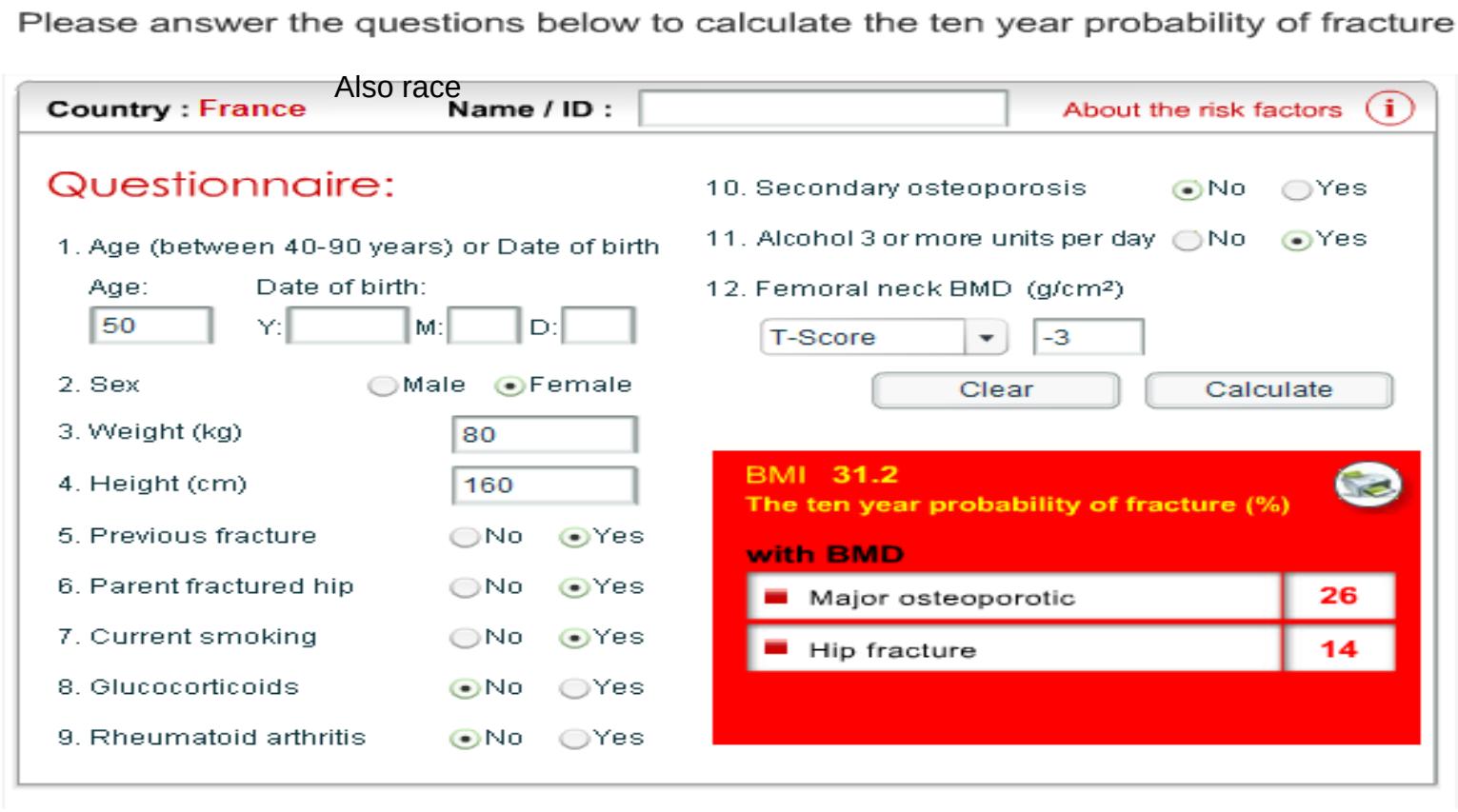
Fig. 1. Central dual x-ray absorptiometry (DXA) scanners. (*A*) Hologic's Delphi fan-beam scanner. (*B*) General Electric's Prodigy fan-beam scanner.

Department of Radiology, Wake Forest University Baptist Medical Center, Medical Center Boulevard, Winston-Salem, NC 27157, USA
* Corresponding author.
E-mail address: llenchik@wfubmc.edu

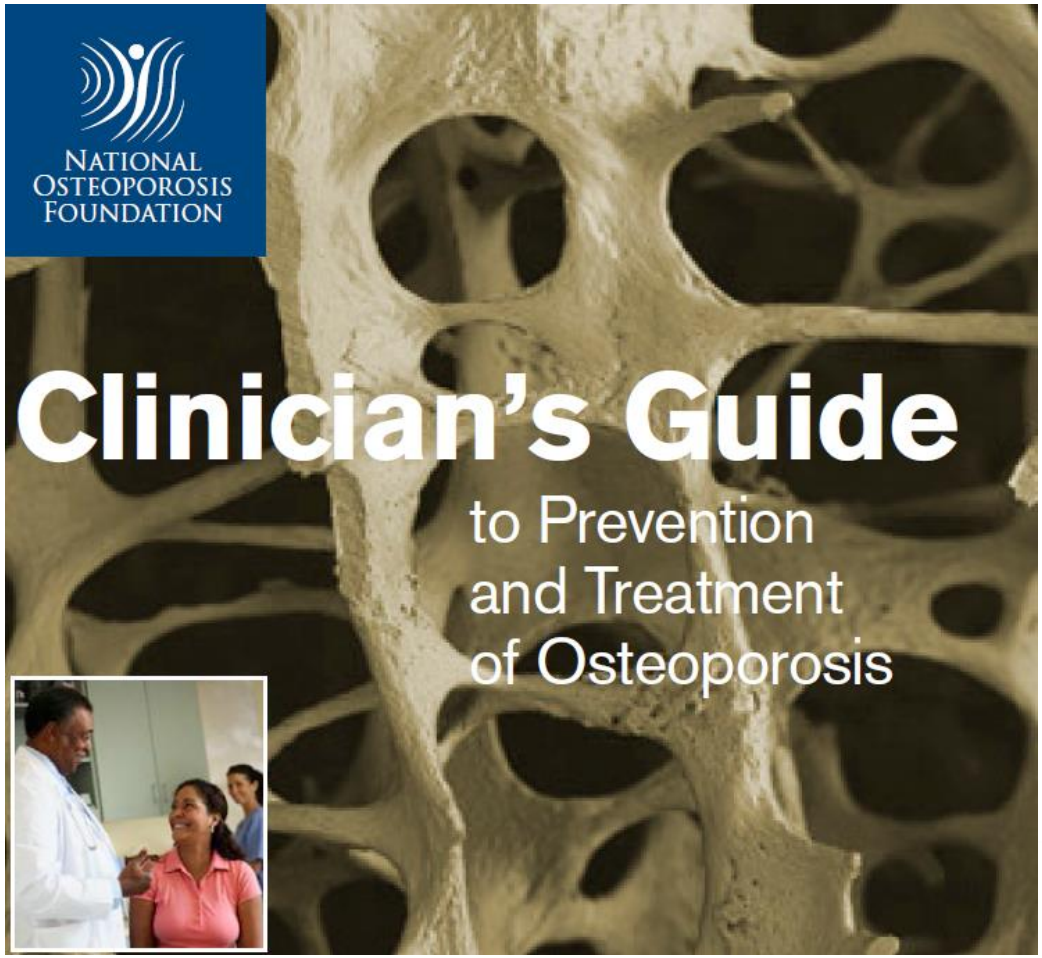
Radiol Clin N Am 48 (2010) 541–560
doi:10.1016/j.rcl.2010.02.019
0033-8389/10/$ – see front matter

Fig. 2. Correct patient positioning for DXA scan of posterior-anterior (PA) spine. (*A*) Lateral photograph shows the positioning block under the subject's feet. (*B*) Frontal photograph shows the subject is centered on the scanner table and aligned with the scanner's long axis.

The FRAX calculation combines the DEXA results with “clinical” risk factors and allows us to get a more concrete estimation of fracture risk over the next 10 years



Who to treat and how?



ACR Glucocorticoid Treatment Guidelines

ARTHRITIS & RHEUMATOLOGY
Vol. 00, No. 00, Month 2017, pp 00–00
DOI 10.1002/art.40137

SPECIAL ARTICLE

2017 American College of Rheumatology Guideline for the Prevention and Treatment of Glucocorticoid-Induced Osteoporosis

Lenore Buckley,[1] Gordon Guyatt,[2] Howard A. Fink,[3] Michael Cannon,[4] Jennifer Grossman,[5]

Treatment or prevention starts with simple things

Diet/nutrition, exercise, fall prevention

Prevention and Treatment Strategies

- Counsel on risk reduction
- Instruct on adequate daily intake of calcium and vitamin D
- Provide guidelines for regular weight-bearing and muscle strengthening exercise
- Provide strategies for fall prevention and balance training
- Counsel on avoiding tobacco smoking and excessive alcohol intake

Rx For Strong Bones: Calcium

Recommended Calcium Intake

Children and Adolescents	mg/day
1 through 3 years	500
4 through 8 years	800
9 through 18 years	1,300
Adult Women and Men	
19 through 49 years	1,000
≥ 50 years	1,200

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Vitamin D recommended daily allowance (RDA)

- 600-800 units in theory for most of you
- We can measure 25 hydroxyvitamin D levels and use that result to guide supplementation
- Target blood level is debated (20 or 30 ng/ml or another number, unclear if African Americans should have a different target level)
- Many people will seem to need more than the standard RDA

The Role of Exercise

Benefits of exercise related to osteoporosis:

- Decreased risk of falling
- Improved bone mass and strength
- Enhanced muscle strength
- Improved balance, flexibility and posture
- Improved cardiovascular fitness
- Improved mood
- Recommend weight-bearing and muscle-strengthening exercises

Major bone loss has been documented among astronauts after months with loss of normal weight bearing "exercise" impact

NOF Recommendations for Initiation of Therapy (con't)

If the T-score is:

Referring to prescription drugs

- ≤ -2.5 in spine or total hip or femoral neck after evaluation to exclude secondary causes, or
- between -1.0 and -2.5 and 10-yr probability of hip fracture ≥ 3 percent or a 10-yr probability of any major osteoporosis-related fracture ≥ 20 percent based on US-adapted FRAX®

Or if someone has had a hip or spinal fracture already

Prescription drugs

Drugs that slow bone breakdown targeting osteoclast function (most of them)

Drugs that stimulate bone formation targeting osteoblast function (teriparatide/Forteo and recently abaloparatide/Tymlos)

US FDA-Approved Options

Antiresorptives (bone retaining):

- Bisphosphonates
- Calcitonin
- Estrogen agonists/antagonists, also called SERMs
- Estrogen/Hormone Therapy

They are referring to drugs approved for post menopausal osteoporosis here

Anabolics (bone forming):

- Teriparatide (PTH (1-34)

Newer drug abaloparatide/Tymlos is similar

Human monoclonal antibody to RANK-ligand

Denosumab /Prolia

Drugs not specifically approved for steroid induced osteoporosis as of today

- Denosumab/Prolia
- Abaloparatide/Tymlos

Generic and brand names

Generic	Brand name(s)
• Alendronate	• Fosamax
• Risedronate	• Actonel and Atelvia
• Ibandronate	• Boniva
• Zoledronate	• Reclast
• Denosumab	• Prolia
• Teriparatide	• Forteo
• Abaloparatide	• Tymlos
• Raloxifene	• Evista

How do we judge effectiveness?

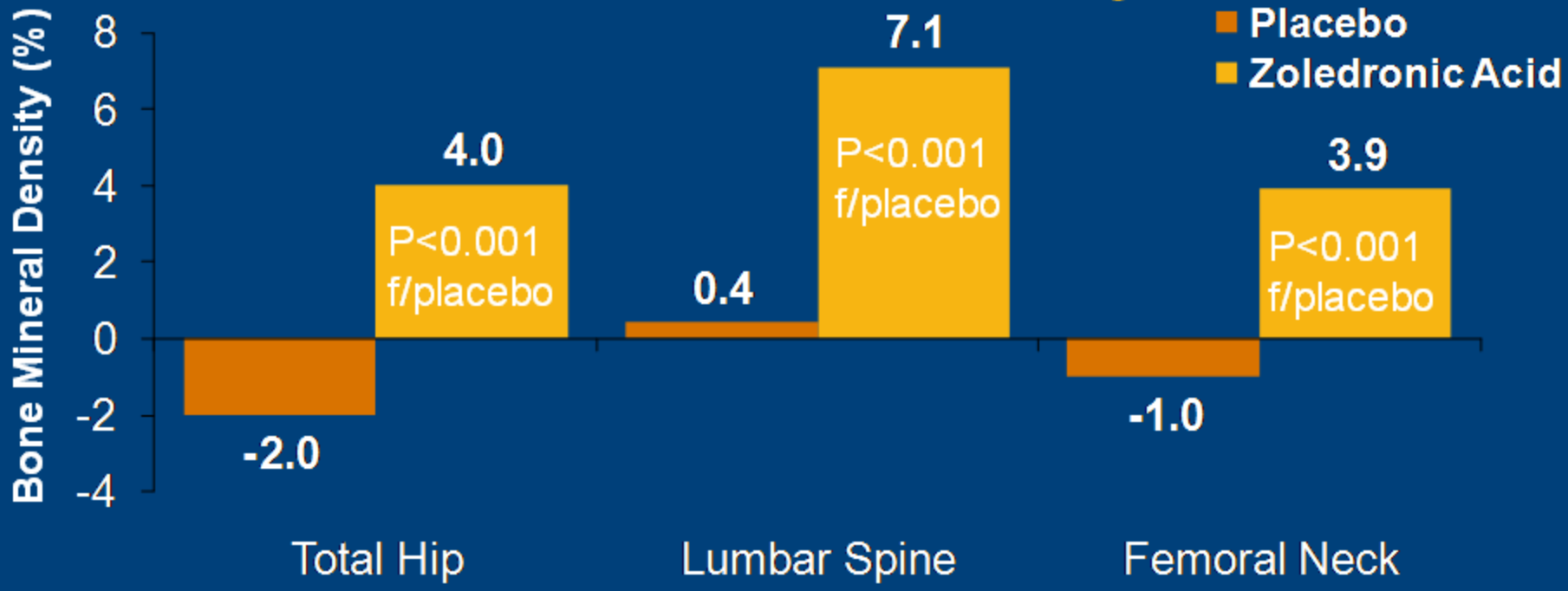
- Looking for an increase in bone mineral density (BMD) with a follow up DEXA
- Looking for reduction of a lab bone breakdown marker or increase of a lab bone formation marker (done less often in routine practice)
- Documenting a reduction in the number of new fractures over time (vertebral fractures seen with x rays, clinical vertebral fractures, non-spinal fractures, hip fractures)

It is easier to achieve some goals than others

- It is usually easy to show an increase in BMD with a DEXA
- It is usually easy to show a change of a bone turnover marker
- Radiographic vertebral fracture reduction is usually easier to prove than other types of fracture reduction because they are more common
- Hip fracture reduction may be the hardest to show because they don’t occur that often

Zoledronic Acid HORIZON Pivotal Fracture Trial

Bone Mineral Density



Black DM, et al. Once-yearly zoledronic acid for treatment of postmenopausal osteoporosis. *N Eng J Med* .2007;356:1809-1822.

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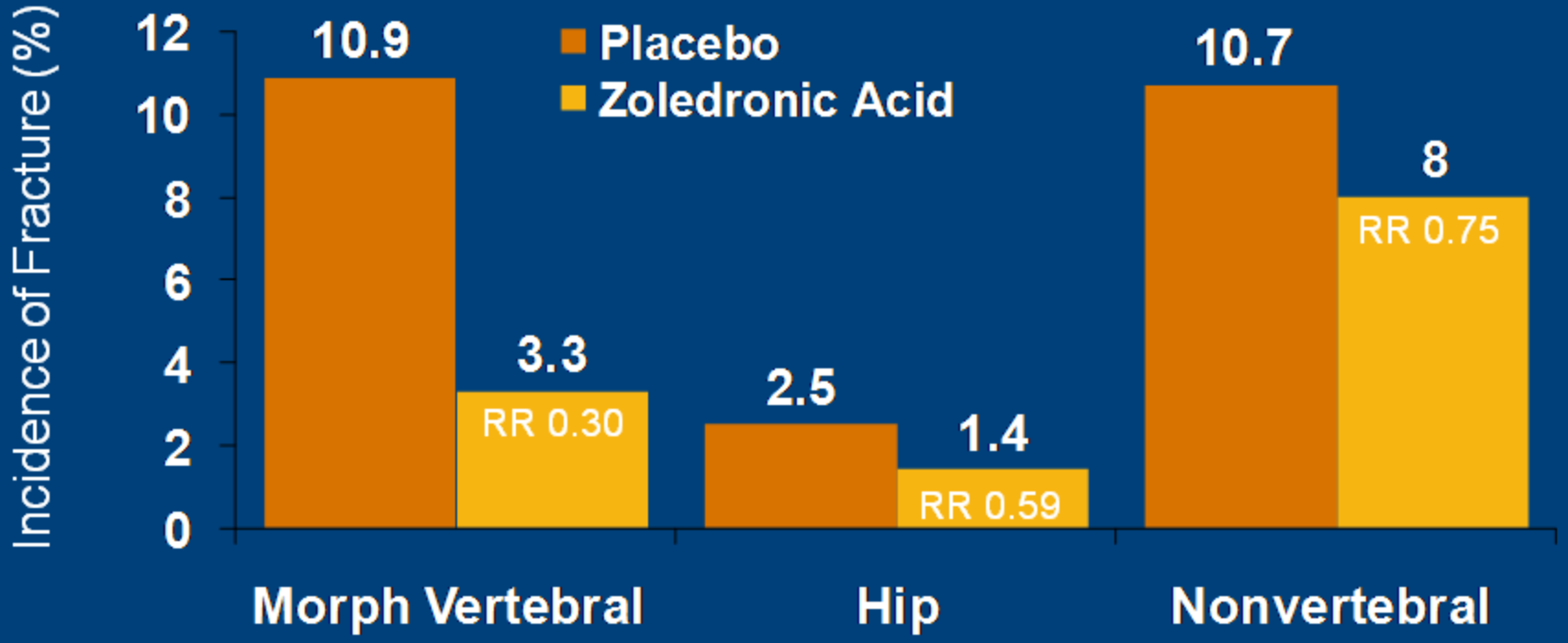
Zoledronic Acid HORIZON Pivotal Fracture Trial

Fracture Incidence



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The concept of “comparative efficacy”

- Do we know if one FDA approved drug is better than another?
- How can we get answers to this question
- Large studies to answer this type of question are rarely done
- Retrospective reviews of earlier studies called meta analyses attempt to give some guidance but they are far from perfect

Possible current opinion?

- Based on practice habits I think many doctors view Forteo, Prolia or Reclast as being more potent than the other available drugs
- There is no good study I know of that tells us which of those 3 is the best?
- The answer may be different for different patients.

The issue of drug cost

- Generic alendronate is probably the cheapest
- Reclast and Prolia are more expensive but covered by Medicare part B
- Forteo is more expensive and covered by Medicare part D. Tymlos will covered in a similar way
- Cost and insurance approval do influence treatment choices in many cases

An article in the NY Times indicating that many people are more afraid of the treatment than the disease

HEALTH

Fearing Drugs' Rare Side Effects, Millions Take Their Chances With Osteoporosis

By GINA KOLATAJUNE 1, 2016

The New York Times

Osteonecrosis of the Jaw

A condition in which bone in the jaw becomes exposed, typically after a dental extraction or some other trauma and the wound that occurs fails to heal in the usual time frame.

In patients receiving bisphosphonates for appropriate indications, the benefits far outweigh the risks.

Atypical Subtrochanteric and Femoral Shaft Fractures

- Rare type of fracture
- Distinctive fracture pattern
- More common in patients taking bisphosphonates for more than five years
- More common in patients on steroids or other medications that affect bone metabolism
- Pain in thigh precedes fracture; pain needs to be investigated
- More research is needed to understand relationship (currently under FDA review)

The possibility of a “drug holiday”

- There is evidence that some patients may be able to suspend alendronate (Fosamax) or zoledronate (Reclast) after 3-5 years and only have a modest extra risk fractures
- This concept does not apply to denosumab which has a “rapid offset of action” or to Forteo or Tymlos
- The concept is not so well documented for other drugs

Summary

- Work with your doctor to control your lupus with “steroid sparing” medicines when appropriate
- Take all your medicines as directed (for Lupus and for your bones)
- Do the simple things (exercise, fall risk reduction, proper diet and/or use of supplements)
- Don’t view the treatment as being “worse than the disease” regarding prescription drugs for Osteoporosis or Lupus