# Updated Guidelines from NOF, NBHA, ISCD, IOF



#### October 11-12, 2018

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# Disclosure

- Institutional grant/research support from Amgen, Radius, PFEnex, Mereo
- Scientific advisory boards for Amgen, Radius, Alexion, Ultragenyx, Sandoz
- Speakers' bureaus for Alexion, Radius
- Board positions with the ISCD, NOF, OFNM

# **Guideline Development Disclosure**

- NOF Clinician's Guide
- ISCD Official Positions
- ISCD DXA Best Practices
- AACE Clinical Practice Guidelines
- IOF Committee of Scientific Advisors

# "All guidelines are wrong, but good ones are useful."

### "Perfect is the enemy of good."

#### Voltaire (1694-1778)



# Types of "Guidelines"

- Evidence-based reviews
  - Examples: ACP, USPSTF
- Clinical practice guidelines (guides)
  - Examples: NOF, AACE
- Health plan policies
  - Examples: BCBS, United Healthcare
- Concepts (guidance, recommendations, considerations, suggestions)
  - Examples: ASBMR reports on drug holidays, TTT
- Standards
  - Examples: ISCD Official Positions, DXA Best Practices, FRAX

Developed by Committees/Task Forces: Assumptions, Compromises, Costs

# Guideline Conundrum

#### Scientifically Rigorous vs.

- Evidence-based
- RCTs
- Cost-utility analysis
- Often very detailed
- Limited applicability
- Overly complex
- Difficult to remember

#### **Clinically Useful**

- Simple
- Intuitive
- Flexible
- Memorable
- Broadly applicable
- Allow for clinical judgment
- Not tied to reimbursement

### **Problems with Guidelines**

- Too many guidelines
- Conflicting guidelines
- Often not followed
- Do not always protect from lawsuits
- Do not replace shared decision making
- Do not account for individualizing care

### Poor Adherence to Guidelines

Review of US insurance claims data (commercial + Medicare) in 96,887 patients hospitalized with hip fracture, 2002-2011



Solomon DH et al. J Bone Miner Res. 2014;29:1929–1937.

# Following Guidelines Does Not Prevent Lawsuits

Following the Standard of Care Can Still Get You Sued



Standards of care are only guidelines, and following them does not always shield medical professionals from lawsuits. Acts of omission and commission can both be used in a lawsuit, so good chart documentation is key to reducing exposure.

- An "expert witness" might testify that inappropriate application of a guideline harmed the patient
- Treatment might be indicated according to a guideline, yet the specific drug chosen might result in harmful effects

Medscape. April 6, 2015.

#### Different Indications for Bone Density Testing

	ISCD 2015 Women and Men	NOF 2016 Women and Men	AACE 2016 Women Only	NAMS 2010 Women Only	ACOG 2012 Women Only	USPSTF 2011 Screening Only
Women age ≥ 65						
Younger postmenopausal women with risk factors						*
Perimenopausal women with risk factors						
Men age ≥ 70						
Younger men with risk factors						
Adults with fragility fracture						
Adults with med, disease, or condition, causing low BMD						
Monitor treatment						

\* FRAX MOF risk  $\geq$  9.3%

# NOF Treatment Guidelines

# For postmenopausal women and men age 50 and older, after appropriate evaluation for secondary causes

Osteoporosis by T-score

• T-score -2.5 or less at FN, TH, or LS, or . . .

Clinical Osteoporosis

• Hip or vertebral (clinical or morphometric) fracture, or . . .

Low BMD + High Fracture Risk

- T-score between -1.0 and -2.5 at FN, TH, or LS, and . . .
- FRAX 10-year probability of hip fracture ≥ 3% or major osteoporotic fracture ≥ 20%

National Osteoporosis Foundation. Clinician's Guide to Prevention and Treatment of Osteoporosis. 2014.

# NOF Guide Cost-effectiveness Analysis

- Treatment with BP for 5 years with 100% persistence
- Linear offset of effect for next 5 years
- 35% fracture risk reduction (all types of fractures)
- Drug cost = \$600 per year
- Societal willingness to pay = \$60,000 per QALY gained
- Treatment cost-effective with 3% 10-year HF risk
- FRAX MOF risk not part of the analysis

Tosteson ANA et al. Osteoporos Int. 2008;19:437-447.

### Case

- 54 year-old postmenopausal Caucasian woman with family history of osteoporosis has a screening DXA according to standard indications
- Fallen twice in past year due to vestibular disorder
- L1-L4 T-score = -2.5, FN T-score = -2.1
- FRAX shows MOF 7.1%, HF 1.0%
- Do you treat or not treat?

Conundrum: NOF indication for treatment but fracture risk is low

# What to do?

#### **Arguments for treating**

- NOF guide
- Protects from irreversible degradation of bone
- FRAX may underestimate fracture risk
- Garvan 10-year risk is 19% for any fragility fracture and 5% for hip fracture

#### **Arguments against treating**

- FRAX risk is low (7.1%/1.0%)
- Difficult to reduce risk when baseline risk is very low
- Osteoporosis drugs will not prevent falls
- More cost-effective to wait until fracture risk is high

### FRAX

#### Benefits

- Robust supporting data
- Included in DXA printouts
- Smartphone app
- Works without BMD
- Part of NOF guide
- Diagnosis (USA, NBHA)

#### Limitations

- "Spineless"
- Falls not considered
- Age competing risk factor
- Unclear range of uncertainty
- MOF = only 4 fracture types
- 4 ethnicities in USA

FRAX Development, Brussels, Belgium, 2004

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WHO Scientific Group Meeting

## Garvan Institute Fracture Risk Calculator



Sex	Female
Age	54
Fractures since age of 50	Nil
Falls over last 12 months	2
T-Score	-2.5

https://www.garvan.org.au/promotions/bone-fracture-risk/calculator/

## What do you do now?

- Shared decision making
  - Well-informed patient who understands benefits/risks
  - Provider who listens, recommends, negotiates, follows
- Patient viewpoint (2 types?)
  - Pro-active, prevention-oriented: Wants to do something now before fracture risk is high and irreversible microarchitectural degradation of trabecular bone
  - Afraid of side effects, likes "natural": Wants to postpone decision to treat as long as possible

### Case

- 73 year-old Asian woman with history of wrist fracture at age 52 from fall in garden
  - L1-L2 T-score = -1.7 (osteoarthritis)
  - FN T-score = -2.1
  - TH T-score = -1.9
  - -33% Radius T-score = -2.8
- FRAX shows MOF 10.0%, HF 2.5%
- Do you treat or not treat?

Conundrum: ISCD dx of osteoporosis but NOF treatment not indicated



# **Diagnosis of Osteoporosis**

- T-score  $\leq$  -2.5 at LS, TH, or FN
- In certain circumstances, the 33% (1/3) radius may be used
- Forearm BMD should be measured when
  - Hip and spine cannot be measured or interpretted
  - Hyperparathyroidism
  - Very obese patient exceeds weight limit of DXA table
- Application may vary according to local requirements



**Official Position** 

# Indications for VFA/Imaging

- T-score < -1.0 and one or more of the following:
- Woman age  $\geq$  70, man age  $\geq$  80
- HHL > 1.5 inches
- Self-reported but undocumented VF
- Glucocorticoid therapy ≥ prednisone 5 mg/day for at least 3 months

### **VFA Results**

- Previously unrecognized VF is identified
- Fracture risk is higher than previously estimated
- Treatment now indicated according to NOF guide
- Another "tiebreaker" marker of bone turnover (not part of NOF treatment algorithm)



### Case

- 81 year-old Native American man trips on shoes at night after getting up to urinate for 3<sup>rd</sup> time, falls to floor and breaks 3 ribs, complicated by pneumothorax
- Hospitalized for 3 days with a chest tube, then discharged
- PCP sees him 6 weeks later to manage his diabetes and hypertension
- 3 months after fracture, FLS coordinator realizes he has had no osteoporosis evaluation and no DXA
- She orders DXA
  - LS not valid due to severe OA
  - FN T-score = -1.8
  - 33% Radius T-score = -1.1
  - FRAX MOF 10.0%, HF 4.2%
- An anabolic agent is prescribed

#### Conundrum: Insurance coverage is denied because T-score > -2.5

# NBHA Position Statement: Clinical Diagnosis of Osteoporosis

In postmenopausal women and men age 50 years and older, osteoporosis may be diagnosed by....

- T-score  $\leq$  -2.5 at the LS, TH, or FN
- Low trauma hip fracture regardless of BMD
- Osteopenia with low trauma vertebral, proximal humerus, pelvis or some distal forearm fractures
- FRAX MOF risk  $\geq$  20% or HF risk  $\geq$  3%

### Treatment

- Insurance denial is appealed
- Peer-to-peer meeting is arranged
- Coverage now allowed with new diagnosis of osteoporosis

# NBHA Position Statement on Dx by FRAX: Good Idea or Bad Idea?

#### **Benefits**

- Addresses USA-specific issue: diagnosis of osteoporosis often required for insurance coverage of treatment
- No ICD-10 code for high fracture risk
- Without this, treatment that is indicated may be denied because Tscore > -2.5

#### LImitations

- NOF treatment thresholds with FRAX are based on cost-effectiveness analysis
- Not appropriate for diagnosis to change when drug prices change
- Using FRAX for diagnosis leads to different diagnosis for same patient depending on country

### Case

- 67 year-old Hispanic woman has been treated with alendronate for 6 years
- She recently changed to a new Medicare Advantage plan and sees you for the first time
- DXA at your ISCD accredited facility shows
  - L1-L4 T-score = -3.2
  - TH T-score = -2.9
- She wants to know how that compares with her previous study at another facility that uses the same DXA manufacturer and model
- What do you tell the patient?

Conundrum: It is not helpful to tell her a comparison cannot be made but you don't want to send her back to a poor quality facility



**Official Position** 

# **BMD** Comparison

• It is not possible to quantitatively compare BMD or to calculate a LSC between facilities without cross-calibration

# **BMD** Comparison Between Facilities

- Cross-calibration is almost never done
- Quantitative comparison is not possible
- However, a large change in T-score may be clinically relevant
- Possible report: "While quantitative comparison with the previous study cannot be made due to technical differences, the T-score values are similar, consistent with a favorable response to therapy."

### Case

- 79 year-old Caucasian woman with baseline FN T-score = -3.6 has been treated with denosumab Q6M for 5 years, with most recent FN T-score = -2.5
- Mild aching in left thigh for 3 months
- She feels a snap in her left thigh walking up stairs and falls
- X-ray in ER shows subtroch fracture of left femur with features of AFF
- X-ray of right femur shows possible beaking of lateral cortex (no pain)
- IM nail is placed
- She then sees you with her daughter, who is very unhappy
- Is this treatment failure?
- What do you tell her?

#### Conundrum: AFF despite increase in BMD, fracture risk still high

# Image: Image:

Home - What We Do - Research -

#### **WORKING GROUPS**

Members of the Committee of Scientific Advisors are invited to join working groups based on their areas of expertise.



#### **Current CSA Working Groups**

The objectives of the working groups are to:

- Formulate global policy guidance, scientific guidelines and general statements to update IOF positions as appropriate
- Advise the Board in scientific matters related to the International Osteoporosis Foundation
- Develop educational and research projects of international relevance

#### Printer friendly



#### Research

- Working Groups
  - Adherence Working Group
  - APOA-IOF Orthopaedic Working group
  - Bone and Cancer Working Group
  - · Bone and Diabetes Working Group
  - Education Steering Comittee
  - Epidemiology/Quality of Life Working Group
  - Fracture Working Group
  - High Resolution Peripheral Computer Tomography (HR-pQCT) Working Group
  - Hip Bone Strength as a Therapeutic Target Working Group

Osteoporos Int (2012) 23:2769-2774 DOI 10.1007/s00198-012-2093-8

POSITION PAPER

#### Treatment failure in osteoporosis

A. Diez-Perez • J. D. Adachi • D. Agnusdei • J. P. Bilezikian • J. E. Compston • S. R. Cummings • R. Eastell • E. F. Eriksen • J. Gonzalez-Macias • U. A. Liberman • D. A. Wahl • E. Seeman • J. A. Kanis • C. Cooper for the IOF CSA Inadequate Responders Working Group

- Two or more incident fragility fractures, or
- One incident fracture and failure to suppress BTM with treatment and/or significant decrease in BMD, or
- Failure to suppress BTM and significant decrease in BMD

Diez-Perez A et al. Osteoporos Int. 2012;23:2769-2774.

# Issues Managing AFF on Denosumab

- No guideline to inform care
- Stopping denosumab may be followed by rapid increase in bone turnover, decrease in BMD, and possible increase in risk of multiple VFs
- Switching to anabolic agent may be followed by BMD decrease at the hip
- Switching to bisphosphonate may not reduce risk of AFF
- Considerations
  - Continue denosumab and add anabolic
  - Stop denosumab and switch to low dose bisphosphonate (ALN 35 mg weekly or every 2 weeks, RIS?)

Personal opinion.

# ACP Guideline 2017 Update

#	Recommendation	Strength
1	Offer ALN, RIS, ZOL, or Dmab to reduce risk of hip and VFs in women with osteoporosis	Strong
2	Treat osteoporotic women for 5 years	Weak
3	Offer BPs to reduce VF risk in men with osteoporosis	Weak
4	No BMD monitoring during 5 years of treatment in women	Weak
5	No E, E+P, or RLX for treatment of PMO	Strong
6	Decision to treat women age ≥ 65 with osteopenia and high fracture risk should be based on discussion of patient preferences, fracture risk profile, benefits, harms, and cost of medication	Weak

#### **Endorsed by AAFP**

Commentaries from ASBMR, AACE, ISCD, NOF, NBHA, and many letters to the editor

Qaseem A et al. Ann Intern Med. 2017;166:818-839.

# AACE Treatment Algorithm

Treat when LS, TH, or FN T-score  $\leq$  -2.5, fragility fracture, or high FRAX (MOF  $\geq$  20% or HP  $\geq$  3%) after evaluation for secondary causes

# No prior fracture or moderate fracture risk

- Alendronate, denosumab, risedronate, zoledronic acid
- Alternate: ibandronate, raloxifene

# Prior fragility fracture or indicators of higher fracture risk\*

- Denosumab, teriparatide, zoledronic acid
- Alternate: alendronate, risedronate

\*Higher fracture risk indicators include advanced age, frailty, glucocorticoids, very low T-score, increased fall risk

AACE Guidelines. Endocrine Practice. 2016;22(Suppl 4).

#### ANNALS OF THE NEW YORK ACADEMY OF SCIENCES MARROW

Perspective

#### Stop the war on DXA!

#### E. Michael Lewiecki,<sup>1</sup> Neil Binkley,<sup>2</sup> and John P. Bilezikian<sup>3</sup>

<sup>1</sup>New Mexico Clinical Research & Osteoporosis Center, Albuquerque, New Mexico. <sup>2</sup>University of Wisconsin, Madison, Wisconsin. <sup>3</sup>Columbia University College of Physicians and Surgeons, New York, New York

- Regression to the mean
- Choosing Wisely® campaign
- SOF analyses on when to repeat screening
- Reimbursement cuts
- Poor quality
- Fear of side effects
- Media reports

Lewiecki EM et al. Ann N Y Acad Sci. 2018; Epub.

Curr Osteoporos Rep DOI 10.1007/s11914-014-0203-6

INVITED COMMENTARY

#### Bone Density Testing: Science, the Media, and Patient Care

Micol S. Rothman • Paul D. Miller • E. Michael Lewiecki • John P. Bilezikian



Rothman MS et al. Curr Osteoporos Rep. 2014;12:227-229. Rothman MS et al. Am J Med. 2017;130:1133-1134.

#### US Hip Fracture Trends 2002-2015



Adapted from Lewiecki EM et al. Osteoporos Int. 2018;29:717-722.



Register at www.ofnm.org

### UNM Bone Health TeleECHO



# Summary

- Guidelines provide a structure for making clinical decisions but are not laws
- Guidelines are often based on clinical trials, cost-utility modeling, and expert opinion that may not apply to your patient
- Patient management decisions should be individualized considering all available clinical information

### Thank You, Paul



