

Handout

Osteoporosis Update

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Disclosure

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Learning Objectives

- Define current methods for diagnosing osteoporosis and assessing fracture risk
- Identify pharmacologic options for reducing fracture risk
- Describe innovative strategies to reduce the osteoporosis treatment gap

Osteoporosis: Good News

- Improving awareness
- Excellent diagnostic methods
- Validated fracture risk assessment tools
- Effective, safe, inexpensive treatments
- Better understanding of pathogenesis
- Emerging treatments
- Federal initiatives to improve care

Osteoporosis: Bad News

- Underdiagnosis
- Undertreatment
- Poor adherence to therapy
- Poor understanding of risk/benefit ratio
- DXA quality suboptimal
- Restrictions on insurance coverage
- Medicare cuts in DXA reimbursement

A Real Story

- 76 year-old woman falls and breaks her hip
- ORIF in hospital goes well
- Discharged to rehab facility, then home
- 18 months later she falls, breaking her other hip
- Survives surgery, but eating poorly and ambulating with difficulty using walker
- Discharged to nursing home in poor condition
- Dies 2 months later

What went wrong?

- No diagnostic tests for factors contributing to skeletal fragility
- No DXA
- No calcium, vitamin D, or medications to reduce fracture risk
- No attention to reducing fall risk

FRACTURE IS A SENTINEL EVENT

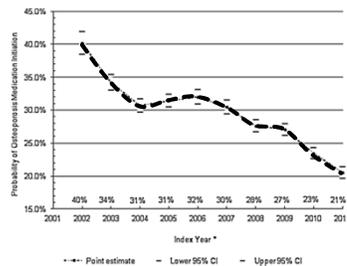
Prior Fracture Increases the Risk of Subsequent Fracture

Site of Prior Fracture	Site of Subsequent Fracture		
	Wrist	Vertebra	Hip
Wrist	3.3	1.7	1.9
Vertebra	1.4	4.4	2.3
Hip	NA	2.5	2.3

Klotzbuecher CM et al. J Bone Miner Res. 2000;15:721-739.

Osteoporosis Treatment After Hip Fx

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.

Indications for BMD Testing

- Women age 65 and older, men age 70 and older
- Younger postmenopausal women, perimenopausal women, and younger men with risk factors
- Adults with a fragility fracture
- Adults with a disease, condition, or medication associated with bone loss
- Anyone being considered for pharmacologic therapy
- Anyone treated for osteoporosis to monitor treatment effect
- Anyone not being treated when evidence of bone loss would lead to treatment

ISCD. Official Positions. 2015.

DXA Quality Matters

Best Practices for Dual-Energy X-ray Absorptiometry Measurement and Reporting: International Society for Clinical Densitometry Guidance

E. Michael Lewiecki,^{1,2} Neil Binkley,² Sarah L. Morgan,³ Christopher R. Shuhart,⁴ Bruno Muzzi Canargos,⁵ John J. Carey,⁶ Catherine M. Gordon,⁷ Lawrence G. Jankowski,⁸ Joon-Kiong Lee,⁹ and William D. Leslie¹⁰ on behalf of the International Society for Clinical Densitometry

Open access (free download) at www.iscd.org

DXA Best Practices. Lewiecki EM et al. J Clin Densitom. 2016;19(2):127-140.

Assessing DXA Quality

- Ask about the following
 - ISCD certification for DXA tech and interpreter
 - ISCD facility accreditation
 - Precision assessment has been done and least significant change is known
- Look at report
 - Make and model of DXA instrument are identified
 - One diagnosis per patient, not different diagnosis for each skeletal site
 - One fracture risk assessment per patient, not different one for each skeletal site

DXA Best Practices. Lewiecki EM et al. J Clin Densitom. 2016;19(2):127-140.

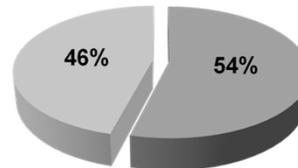
WHO Classification of BMD

	T-score
Normal	-1.0 or higher
Osteopenia	Between -1.0 and -2.5
Osteoporosis	-2.5 or lower
Severe Osteoporosis	-2.5 or lower + fragility fracture

Reference standard for calculating T-scores is Caucasian female NHANES III database

WHO Study Group. 1994. ISCD. Official Positions. 2015.

Most Women with Hip Fractures Do Not have a T-score ≤ -2.5



Wainwright SA et al. J Clin Endocrinol Metab. 2005;90:2787-2793.

Look for Vertebral Fractures

- VFs are common
- Most VFs are not diagnosed
- VFs have serious consequences
- VFs predict future fractures
- Detection of VFs may change diagnostic classification, assessment of fracture risk, and clinical management*

*NOF Guide: VF is indication for treatment regardless of BMD

Indications for Vertebral Imaging

- All women \geq age 70 and all men \geq age 80 with T-score ≤ -1.0
- Women age 65-69 and men age 70-79 with T-score ≤ -1.5
- Postmenopausal women and men \geq age 50 with risk factors for fracture
 - Prior low trauma fracture
 - HHL ≥ 1.5 inches or PHL ≥ 0.8 inches
 - Recent or ongoing glucocorticoid treatment

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

VFA = Vertebral Fracture Assessment

A non-invasive method of diagnosing vertebral fractures by DXA with greater patient convenience, less cost, and lower radiation exposure than conventional X-ray



FRAX Tips

- Input for previous fracture includes radiographic VFs but output is for clinical VFs
- Best to enter FN BMD not T-score
- Secondary osteoporosis is a "dummy" risk factor that does nothing if BMD is provided
- Major osteoporotic fracture = clinical VF, hip, proximal humerus, forearm
- Risk of any osteoporotic fracture is about twice major osteoporotic fracture
- May over- or under-estimate fracture risk in individual patients
 - Risk factor input is dichotomous, important risk factors are not included, fractures are stochastic events

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
- T-score between -1.0 and -2.5 with low trauma vertebral, proximal humerus, pelvis or some distal forearm fractures
- FRAX MOF risk \geq 20% or HF risk \geq 3%

Siris ES et al. Osteoporos Int. 2014;25:1439-1443.

NOF Treatment Guidelines

For postmenopausal women and men age 50 and older, consider treatment to reduce fracture risk, after appropriate evaluation for secondary causes, when . . .

- T-score \leq -2.5 or less at FN, TH, or LS, or . . .
- Hip or vertebral (clinical or morphometric) fracture, or . . .
- T-score between -1.0 and -2.5 at FN, TH, or LS, and FRAX 10-year probability of hip fracture \geq 3% or major osteoporotic fracture \geq 20%

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

Laboratory Evaluation

- CBC
- Blood chemistries
 - Creatinine
 - Calcium
 - Phosphorus
 - Albumin
 - Alkaline phosphatase
 - Liver enzymes
- 25-OH-vitamin D
- 24-hour urine for calcium, sodium
- TSH
- Celiac antibodies
- Bone turnover markers
- Urinalysis
- sIFE, kappa/lambda light chain ratio
- Intact PTH
- Dexamethasone suppression or urinary free cortisol

Adapted from Lewiecki EM. Evaluation of Osteoporosis. Chapter 63 in Osteoporosis. Marcus R et al, eds. 2013.

Rare Bone Diseases You Should Never Miss

- Tumor Induced Osteomalacia
 - Suspect: low P; confirm with renal P wasting, high FGF23
 - Manage: P, calcitriol
 - Cure: resection of tumor
- Hypophosphatasia
 - Suspect: low alk phos; confirm with high B6
 - Manage: avoid bisphosphonates
 - Cure: asfotase alfa for severe forms
- Hypoparathyroidism
 - Suspect: low albumin-corrected Ca; confirm with low PTH
 - Manage: Ca, calcitriol
 - Cure: PTH(1-84) when poorly controlled

Universal Recommendations

- Calcium 1000-1200 mg/day, ideally from diet
- Vitamin D 800-1000 IU/day, target \geq 30 ng/mL
- Regular weight-bearing and muscle-strengthening exercise
- Fall prevention
- Avoid tobacco use and excess alcohol
- Identification and treatment of risk factors for fracture
- Measure height annually (stadiometer)

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

Medications for Osteoporosis

Inhibit Bone Resorption	Stimulate Bone Formation
Alendronate (Fosamax, generic)	Teriparatide (Forteo)
Risedronate (Actonel, Atelvia, generic)	
Ibandronate (Boniva, generic)	
Zoledronate (Reclast, generic)	
Denosumab (Prolia)	
Raloxifene (Evista, generic)	
Calcitonin (Miacalcin, Fortical)	
Estrogen (various)	
CE/BZA (Duavee)	

Compounds in late stage clinical development:
abaloparatide, romosozumab, odanacatib

Initial Choice of Therapy

- Oral bisphosphonate (ALN, RIS) first line for most patients
- Injectable antiresorptive agent (ZOL, Dmab) also good first line therapy or when oral therapy contraindicated, adverse effects, poor adherence, malabsorption, not responding
- IBN is second-line agent
- Teriparatide for patients at very high risk of fracture
- Raloxifene for postmenopausal women up to about age 70, especially those at high risk for breast cancer
- [Estrogen is still a good drug for osteoporosis in "young" postmenopausal women when benefits > risks]

Adapted from AACE Guidelines. Endocr Pract. 2010;16(Suppl 3).

Clinical Challenges after Starting Treatment

- Motivating the patient to fill the prescription and take it correctly, regularly, and for a sufficient length of time to benefit
- Monitoring to assure that benefit is achieved
- Managing nonresponders / suboptimal responders
- Deciding when (if ever) to stop or change therapy
- Knowing when (if ever) to restart, if treatment is stopped
- Managing side effects, perceived side effects, and fear of side effects

Controversies

- Drugs
 - Best initial therapy
 - Safety - ONJ, AFF
 - How long to treat, when to change
- Calcium
 - What kind is best and how much
 - Safety - cardiovascular
- Vitamin D
 - Supplementation - D2 vs. D3, OTC vs. pharmacological
 - Monitoring
- Exercise
 - What is best and safest
- Fall prevention
 - What works and doesn't work
- Combination therapy
 - Good or bad?

Bisphosphonate Safety Issues

Side Effects

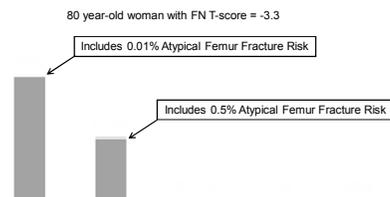
- Short-term
 - GI distress
 - Acute phase reaction
 - Hypocalcemia
 - Renal toxicity
- Long-term
 - Osteonecrosis of the jaw
 - Atypical femur fractures
- Questionable
 - Chronic musculo-skeletal pain
 - Atrial fibrillation
 - Esophageal cancer
 - Impaired fracture healing

"Side Benefits"

- Improved implant survival
- ↓ risk of breast cancer
- ↓ risk of endometrial cancer
- ↓ risk of colorectal cancer
- ↓ risk of stroke
- ↓ risk of gastric cancer
- ↓ risk of MI in RA patients
- ↓ risk of type 2 DM
- ↓ mortality

Prieto-Ahambra D et al. Arthritis Rheum. 2014;66:3233-3240.
 Chlebowski RT et al. J Clin Oncol. 2010;28:3582-3590.
 Newcomb PA et al. J Clin Oncol. 2015;33:1186-1190.
 Dryfus JH, CA Cancer J Clin. 2010;60:343-344.
 Newcomb PA et al. Br J Cancer. 2010;102:799-802.
 Rennert G et al. J Clin Oncol. 2010;28:3577-3581.
 Vestergaard P et al. Calcif Tissue Int. 2011;88:255-262.
 Rennert G et al. J Clin Oncol. 2011;9:1146-1150.
 Kang JH et al. Osteoporos Int. 2012;23:2551-2557.
 Abrahamson B et al. J Bone Miner Res. 2012;27:678-686.
 Center JR et al. J Clin Endocrinol Metab. 2011;96:1008-1014.
 Wolfe F et al. J Bone Miner Res. 2013;28:984-991.
 Konstantinos A et al. J Clin Endocrinol Metab. 2015;100:1933-1940.
 Sambrook PN et al. Osteoporos Int. 2011;22:2551-2556.
 Lee P et al. J Clin Endocrinol Metab. 2016;101:1945-1953.

10-Year Probabilities



Untreated probability of major osteoporotic fracture calculated by FRAX. ONJ estimate is ~1/100,000 patient-treatment-years from ASBMR Task Force by Khosla S et al. J Bone Miner Res 2007;22:1479-149. AFF estimate untreated is ~0.01/10,000 and treated is ~5/10,000 patient-years from Schlicher J et al. N Engl J Med. 2011;364:1728-1737. Risk estimates assume long-term bisphosphonate therapy resulting in 50% reduction in fracture risk. MVA and murder data from the CDC at http://www.cdc.gov/nchs/data/nvsr/nvsr56/nvsr56_10.pdf. Image copyright © 2011 Lewiecki EM. Slide version.

How Long to Treat

- Only one drug has a time limit— 24 months with teriparatide
- All drugs except bisphosphonates stop working when stopped
- Bisphosphonates have a persistent antiresorptive effect when withheld after at least 3-5 years of treatment
- Rationale for a bisphosphonate "holiday" is persistence of anti-fracture benefit while possibly reducing long-term risks
 - NOT "drug retirement"
 - NOT "stopping treatment"
 - NOT for non-bisphosphonates
- Consider for patients no longer at high fracture risk
- End drug holiday when fracture risk is again high

Adapted from Whitaker M et al [FDA]. N Engl J Med. 2012;366:2048-2051. Black DM et al. N Engl J Med. 2012;366:2051-2053. Bonnick SL. J Clin Densitom. 2011;14:377-383. Watts NB et al. J Clin Endocrinol Metab. 2010;95:1555-1565.

Combination – Sequential Therapy

Antiresorptive	PTH	Delay or attenuation of anabolic effect with potent antiresorptive (Dmab); no delay or attenuation with less potent antiresorptive
PTH	Antiresorptive	Antiresorptive therapy is essential after PTH to maintain or enhance skeletal benefits of PTH
Antiresorptive	PTH	No benefit with ALN; small additive effect on BMD with ET, RLX, RIS; faster but transient BMD increase with ZOL; additive effect on BMD with PTH+Dmab (most promising)
Antiresorptive	Antiresorptive	Small additive effect on BMD with some combinations; adds to cost and possible adverse effects; no evidence of improved anti-fracture efficacy; not advised

Calcium Tips

- Get enough calcium, but not too much
- Most people can get sufficient amount in diet
- Limited benefit and possible harm with calcium intake > 1200-1500 mg/day
- Does calcium supplementation cause cardiovascular disease?
 - Inconsistent findings on observational studies and secondary analyses of clinical trials
 - No conclusive evidence that calcium supplements increase cardiovascular risk
- Follow the guidelines

McDaniel MH et al. J Clin Densitom. 2013;16:389-393.
Wang L et al. Am J Cardiovasc Drugs. 2012;12:105-116.

Vitamin D Tips

- Measure serum 25-OH-D, NOT 1,25-(OH)₂-D
- Target of 30-50 ng/ml is reasonable
- Supplemental vitamin D3 1000 IU/day increases serum 25-OH-D by about 6-10 ng/mL
- Pharmacological doses of vitamin D (≥ 50,000 IU per day) rarely necessary except for symptomatic deficiency (eg, osteomalacia, myopathy)
- Non-skeletal benefits of vitamin D include improved balance and reduced falls
- Takes at least 3 months for new steady-state

National Osteoporosis Foundation. Clinician's Guide to Prevention and Treatment of Osteoporosis. 2014.
Institute of Medicine. Report on Dietary Reference Intakes. 2011.
Binkley N et al. J Clin Densitom. 2013;16:402-408.
Watts NB et al. AACE Guidelines. 2010.

New Strategies to Reduce the Osteoporosis Treatment Gap

Fracture Liaison Service (FLS)

- Secondary fracture prevention by systematic identification and management of fracture patients
- Objectives
 - Assess risk of future fractures
 - Evaluate for factors contributing to skeletal fragility
 - Educate about skeletal health
 - Start on treatment to reduce fracture risk if needed
 - Follow to assure that objectives are achieved
- Key person: dedicated coordinator - often a hospital based nurse educator or discharge planner
- Technology: dedicated fracture management software - patient registry, task tracker, quality measures, etc.

Fracture Prevention Central. National Bone Health Alliance. Curr Osteoporosis Rep. 2013;11:348-353.
Capture the Fracture. International Osteoporosis Foundation. Osteoporosis Int. 2013;24:2135-2152.
Own the Bone. American Orthopedic Association. J Bone Joint Surg Am. 2008;90:163-173.

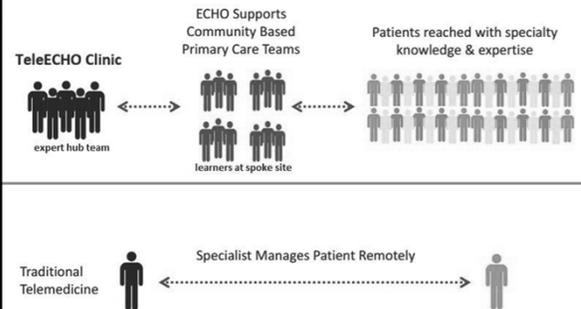


Extension for Community Healthcare Outcomes

Project ECHO

- A collaborative strategy of medical education and care management using videoconferencing technology with case-based learning
- ECHO aims to democratize medical knowledge and develop specialty care capacity in underserved communities
- Established at University of New Mexico in 2003 with chronic hepatitis C as the model disease
- Now about 90 ECHO hubs in 12 countries for 45 diseases
- Goal: To touch 1 billion lives by 2025

ECHO vs. Telemedicine



Bone Health ECHO



- Launched October 6, 2015
- Model for replication/innovation
- Goal: to reduce the burden of osteoporotic fractures worldwide

Who Can Benefit from Bone Health ECHO

- Physicians, CNPs, and PAs who seek a higher level of expertise in the care of patients with skeletal diseases
 - Case-based learning
 - Free CME
 - Relief of professional isolation in rural areas
 - Collegial relationships with peers
 - Collaboration in patient care
 - Development of community center of excellence
- Residents and fellows at training programs lacking local expertise in bone diseases
- FLS coordinators
- Most importantly: patients benefit from better care, closer to home, with greater convenience and lower cost

Bone Health ECHO Learners



More on Bone Health ECHO

- To participate in Bone Health ECHO register at www.ofnm.org
- To find out more about Project ECHO, go to <http://echo.unm.edu/bone-health/>
- For additional information contact me at mlewiecki@gmail.com
- Or just Google Bone Health ECHO