The PROMIS® of Improved Bone Health in Older Adults

Supported by an educational grant from Pfizer Inc.

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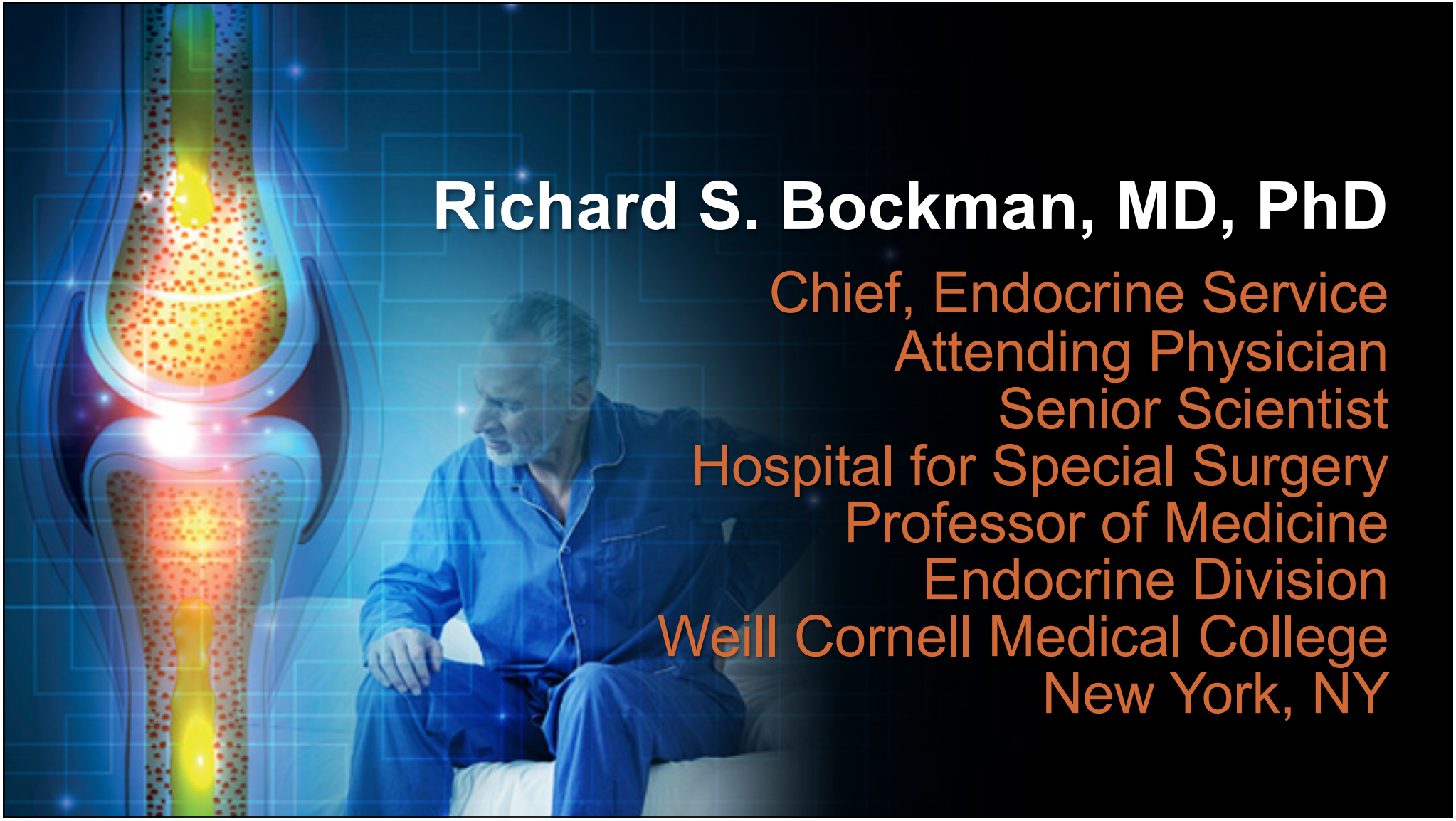

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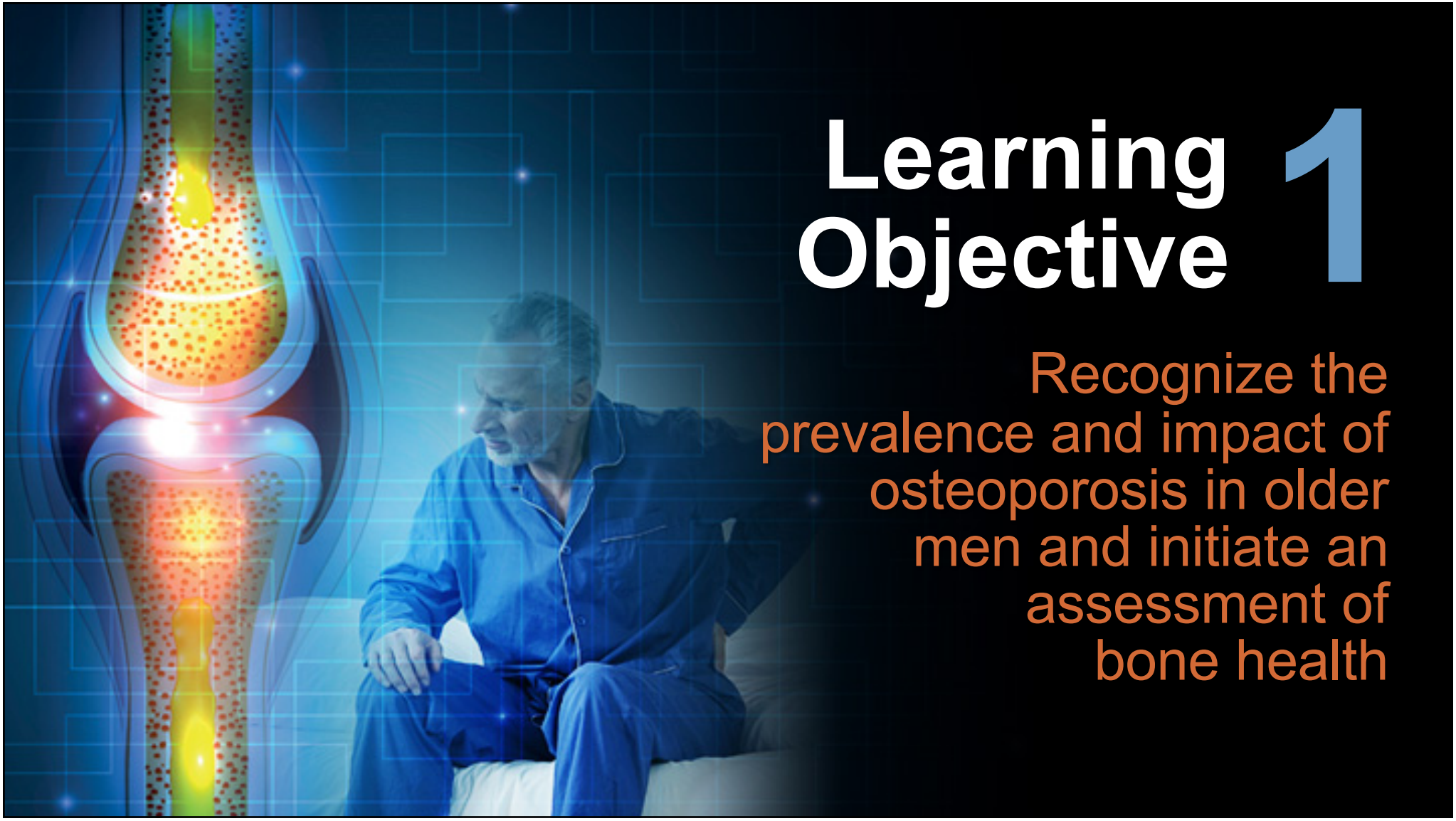
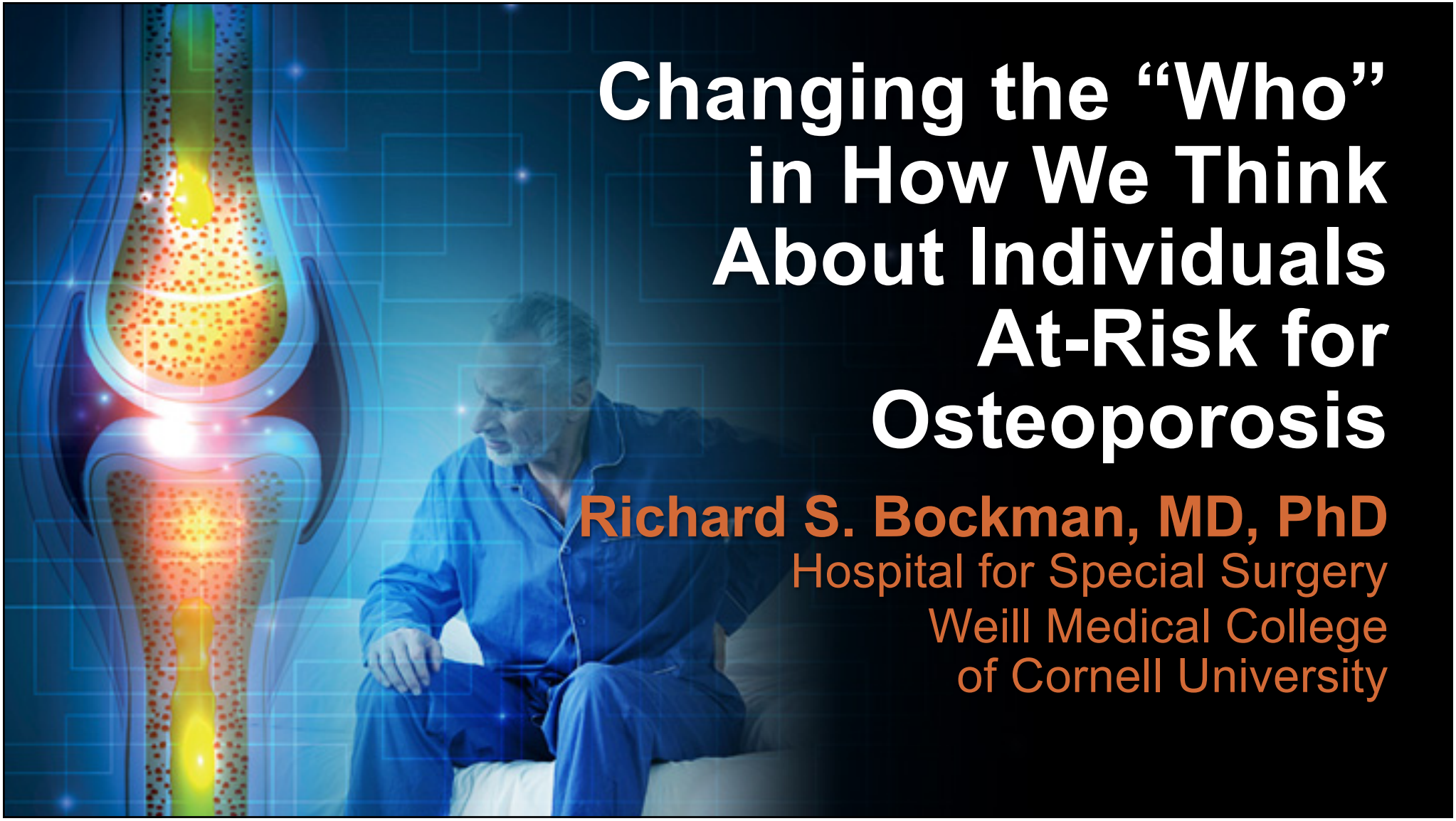

Learning Objective 1
Recognize the prevalence and impact of osteoporosis in older men and initiate an assessment of bone health

Learning Objective 2

Assess the safety and efficacy data for calcium and vitamin D supplementation in patients who do not meet dietary needs

Learning Objective 3

Implement PROs into clinical workflow to measure change in function and quality of life in patients with osteoporosis



Changing the "Who" in How We Think About Individuals At-Risk for Osteoporosis

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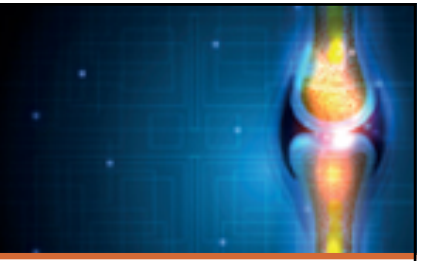
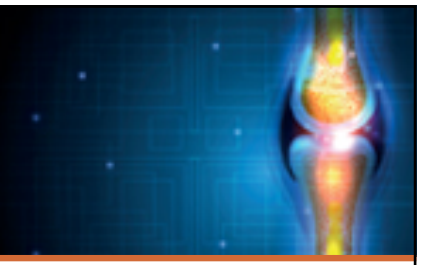
US Preventive Task Force



- By 2020, ~12.3 M Americans > 50 years old will have osteoporosis
- Osteoporotic fractures associated with limited ambulation, pain, disability, loss of independence, and decreased quality of life
- 21% - 30% of patients with hip fractures die within one year, Men>Women
- Screening Update (USPSTF) occurred in 2018 (last update 2011)
- B recommendation for screening in postmenopausal women > 65 years old
- B recommendation for women <65 based on formal risk tools (e.g., FRAX)
- Insufficient evidence for screening to prevent fractures in MEN
  - Bone density accurate for detecting osteoporosis and predicting fracture risk
  - Drug therapies are effective in reducing fracture risk in postmenopausal women
  - Drug therapies – evidence in MEN without prior fracture – Inadequate
  - **Time to get some answers for men**

Curry SJ, et al. *JAMA*. 2018;319(24):2521-2531.

Incidence of Osteoporosis and Osteopenia in the United States

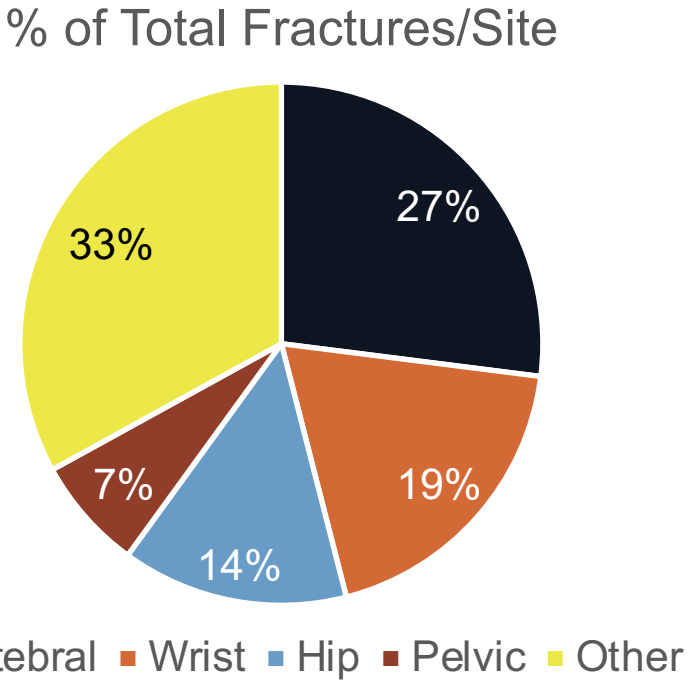


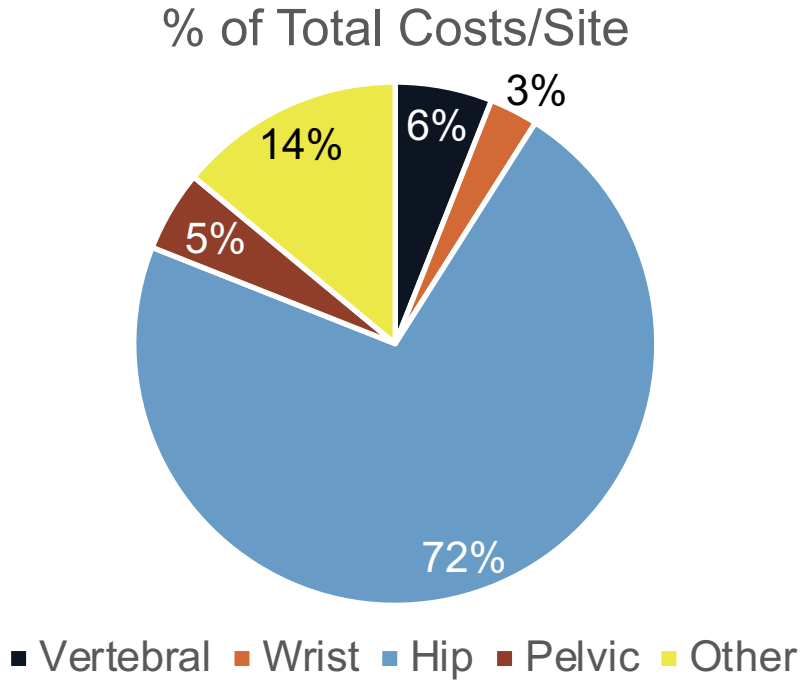
- ~33-54 million Americans have osteoporosis and low bone mass, placing them at increased risk for fracture
- 1 in 2 women and **1 in 4 men** age ≥50 will break a bone due to osteoporosis
- In 2005: >2 million incident fractures 2005;
  - Projected to grow to >3 million in 2025
  - Cost $17 B in 2005; projected to go to $25.3 B in 2025
- Men:
  - 29% of fractures
  - ≥25% of the cost
  - Men are definitely a major part of the public health problem

National Osteoporosis Foundation website. Available at https://www.nof.org/patients/what-is-osteoporosis/
Burge R, et al. *J Bone Miner Res*. 2007;22(3):465-475.

Fractures by Incidence and Cost

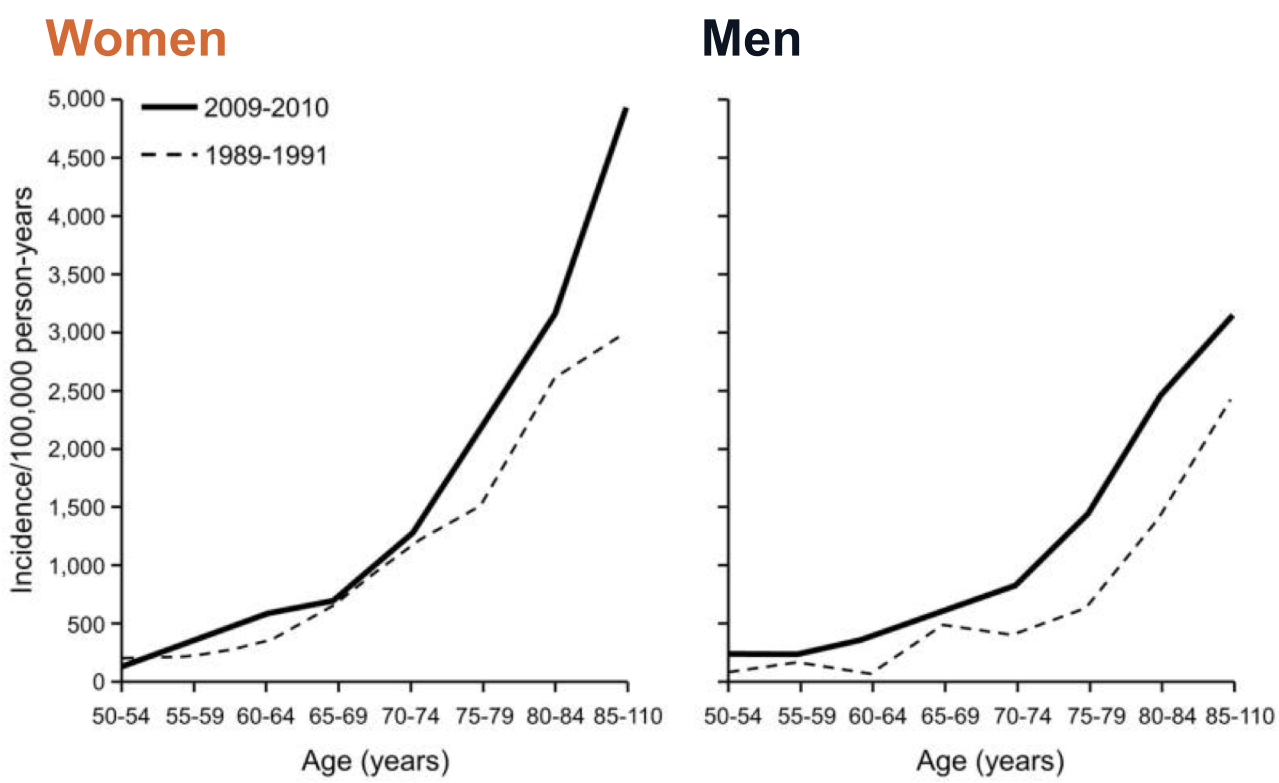
Total Incident Fractures Site and Cost





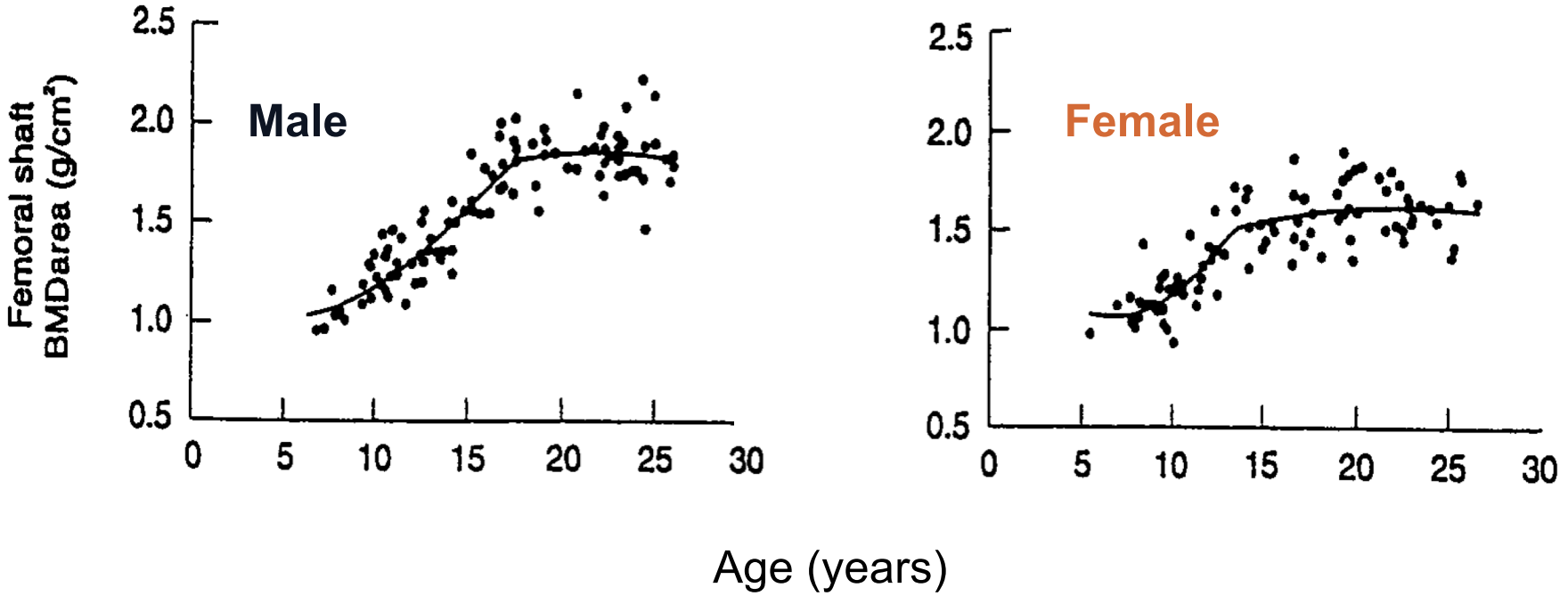
Burge R, et al. *J Bone Miner Res*. 2007;22(3):465-475.

Population-Based Increased Incidence of Vertebral Fractures in Women and Men ≥ 50 Years Old



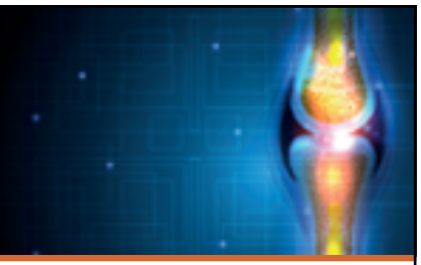
Amin S, et al. *J Bone Miner Res*. 2014;29(3):581–589.

Bone Size (Areal Density) Does Change During Puberty with Boys > Girls



Lu PW, et al. *J Clin Endocrinol Metab*. 1996;81(4):1586-1590.

Sex Steroids in Men



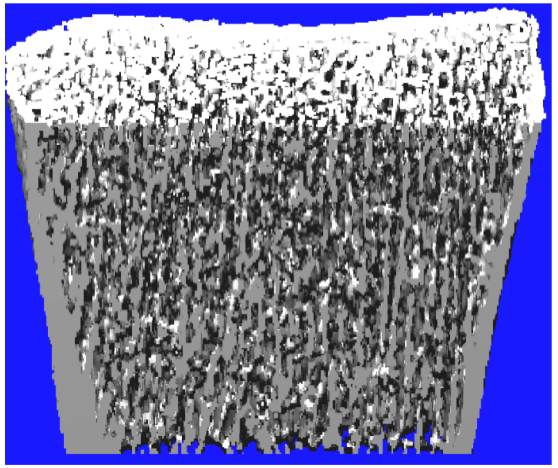
- Both estrogens and androgens are important for the achievement of peak AREAL bone mass in men

What about micro architecture?

Microarchitectural Features of Bone: Men vs. Women

- High Resolution pQCT Imaging: **Peak Bone Mass**

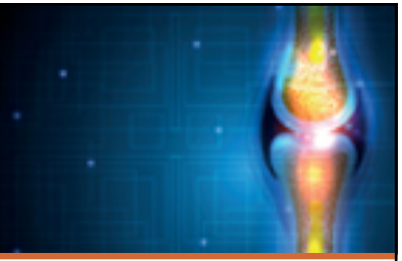
Index	Men vs. Women
Trabeculae	28% thicker
TBV/TV	26% greater
Trabecular #	No difference



TBV = trabecular bone volume; TV = tissue volume

Khosla S, et al. *J Bone Min Res.* 2006;21:124-131.

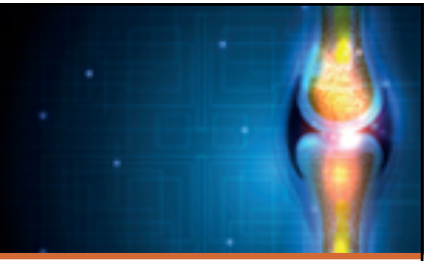
Microarchitectural Changes with Aging in Men and in Women

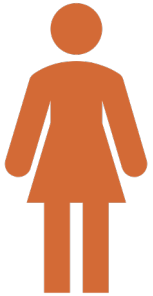


Index	Men	Women
TBV/TV	26% ↓	27% ↓
Trabecular #	**7% ↑**	**13% ↓**
Trabecular Separation	**2% ↓**	**24% ↑**
Trabecular Thickness	24% ↓	18% ↓

Khosla S, et al. *J Bone Min Res.* 2006;21:124-131.

With Aging

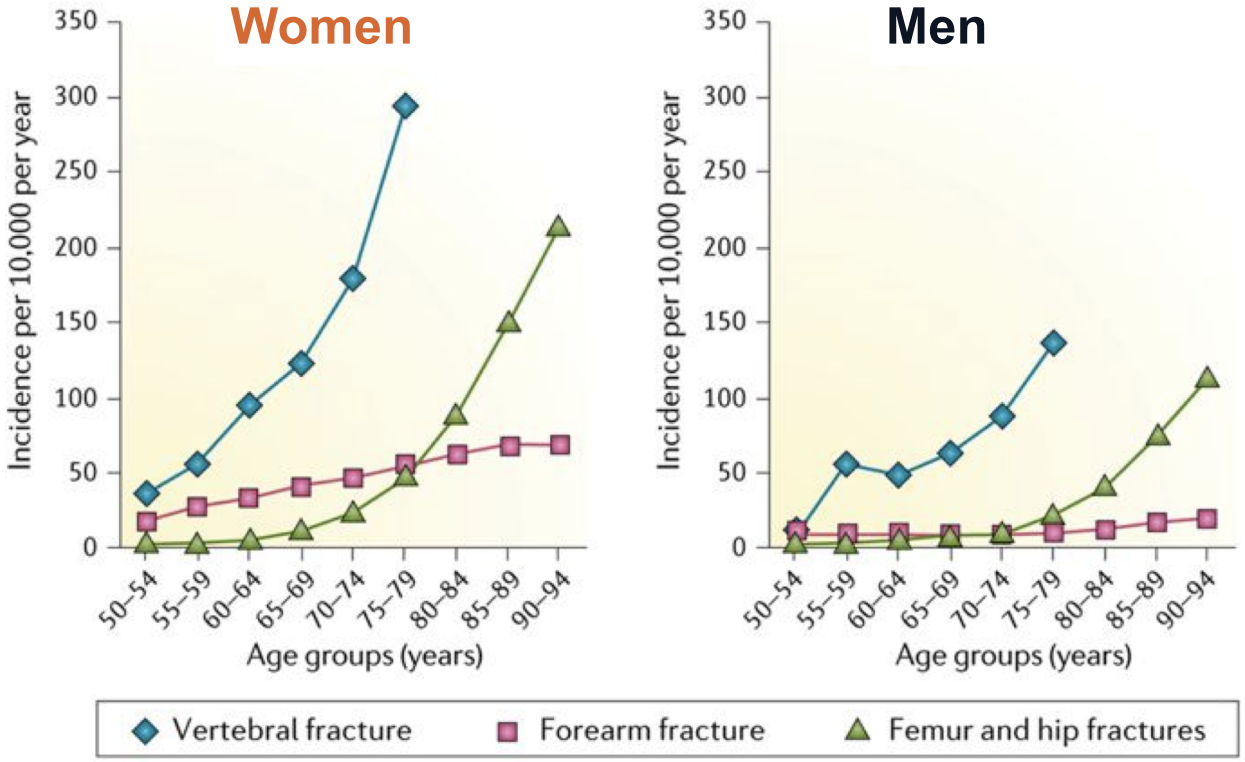




Women:
Trabeculae are lost and become thinned

Men:
Trabeculae become thinned but are not lost

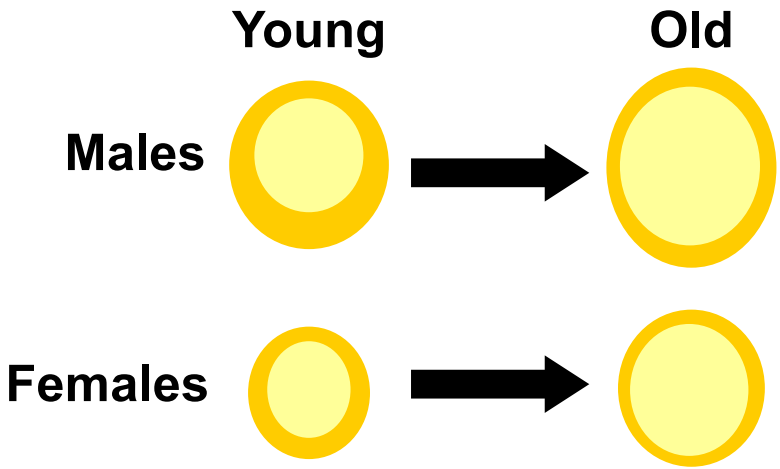
Fractures Increase with Age in Men and Women



Eastell R, et al. *Nat Rev Dis Primers.* 2016;2:16069.

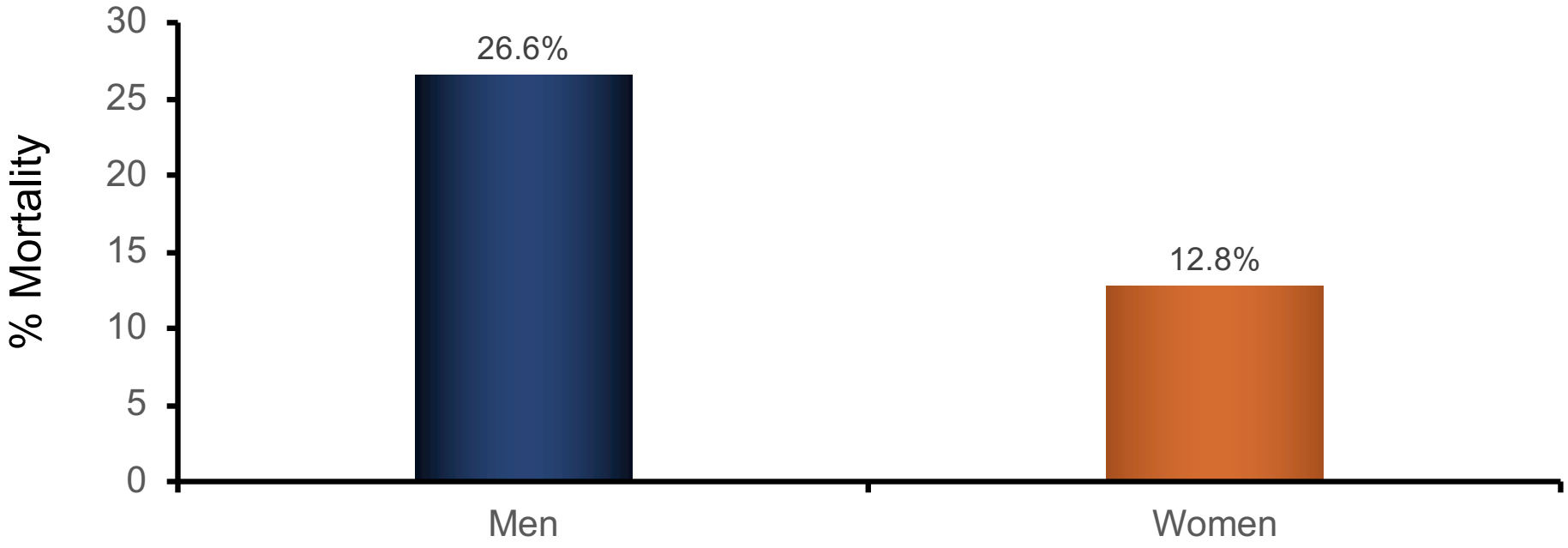
Changes in Bone Geometry with Aging: Men vs. Women

- Both sexes show cortical thinning, but males show a greater compensatory increase in cross-sectional diameter with age.



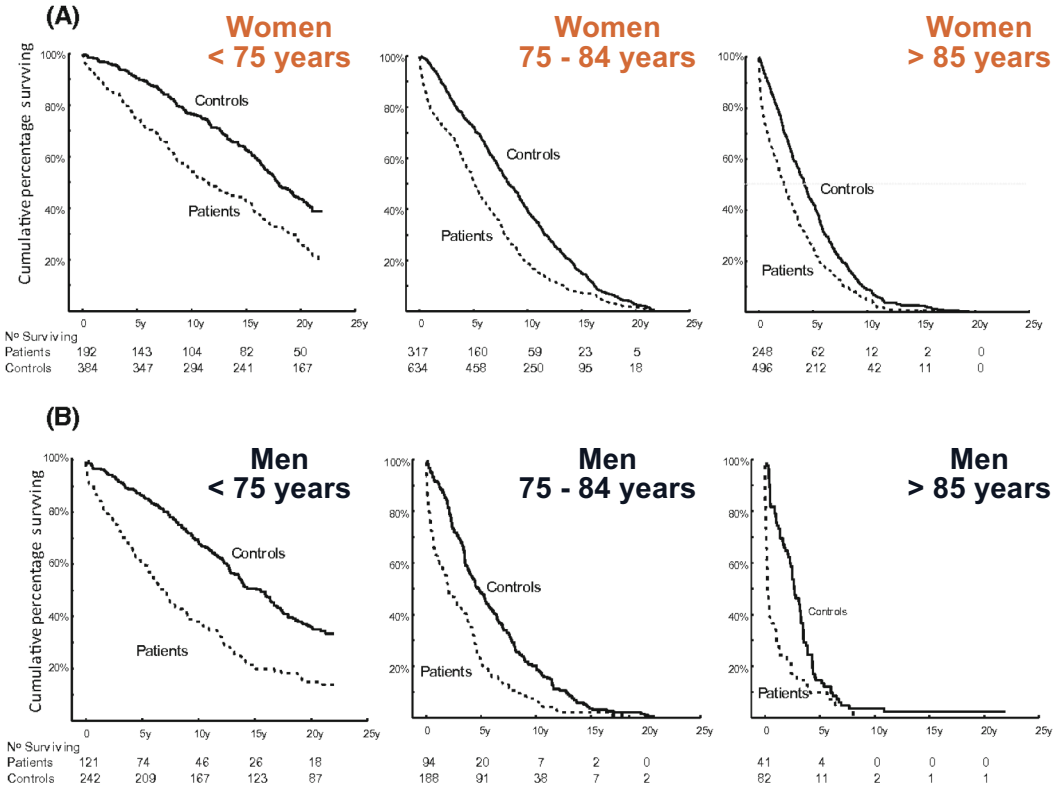
Milovanovic P, et al.. *J Gerontol A Biol Sci Med Sci.* 2015;70(10):1269-1275; Beck TJ, et al. *Calcif Tiss Int.* 1992;50:24-29.

Mortality One Year After Hip Fracture



Katelaris AG, et al. *Am J Public Health.* 1996;86:557-60; Orwoll ES, et al. *Endocrinol Metab Clin.* 1998;72:349-67; Forsen L, et al. *Osteoporos Int.* 1999;10:73-8; Hannan EL, et al. *JAMA.* 2001;285:2736-42.

Probability of Survival Following Hip Fracture is Higher in Women (A) Than Men (B)

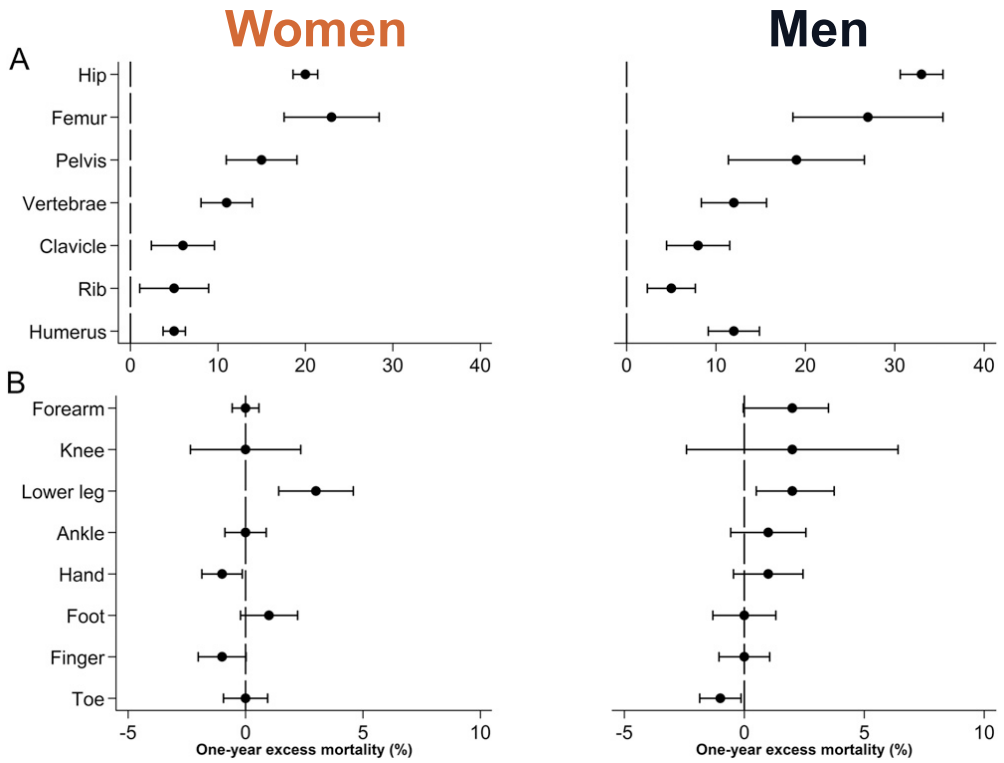


Friesendorff MV, et al. *Osteoporosis International.* 2016;27:2945-2953.

Excess Mortality 1 Year After Individual Types of Fragility Fracture

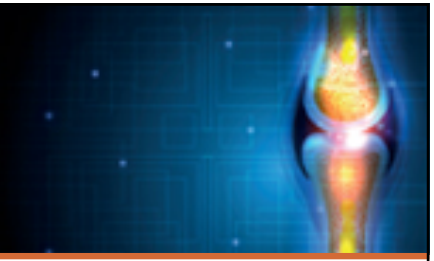
A: Proximal Fractures

B: Distal Fractures



Tran T, et al. *J Clin Endocrinol Metab,* 2018;103(9):3205–3214.

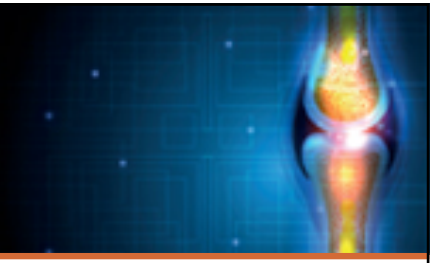
When to Measure Bone Density in Men



- 70 years and older
- Prior fracture, after the age of 50
- Osteopenia or vertebral deformity on X-ray
- Diseases and medications causing bone loss such as
  - Hypogonadism
  - Alcoholism
  - Hyperparathyroidism
  - Hyperthyroidism
  - GnRH analogues
  - COPD
  - Steroids
  - Gastrectomy/malabsorption
  - Antiepileptics
  - Delayed puberty

Watts NB, et al. *J Clin Endocrinol Metab*. 2012;97(6):1802-1822.

Screening Tests for Osteoporosis and Risk of Osteoporosis

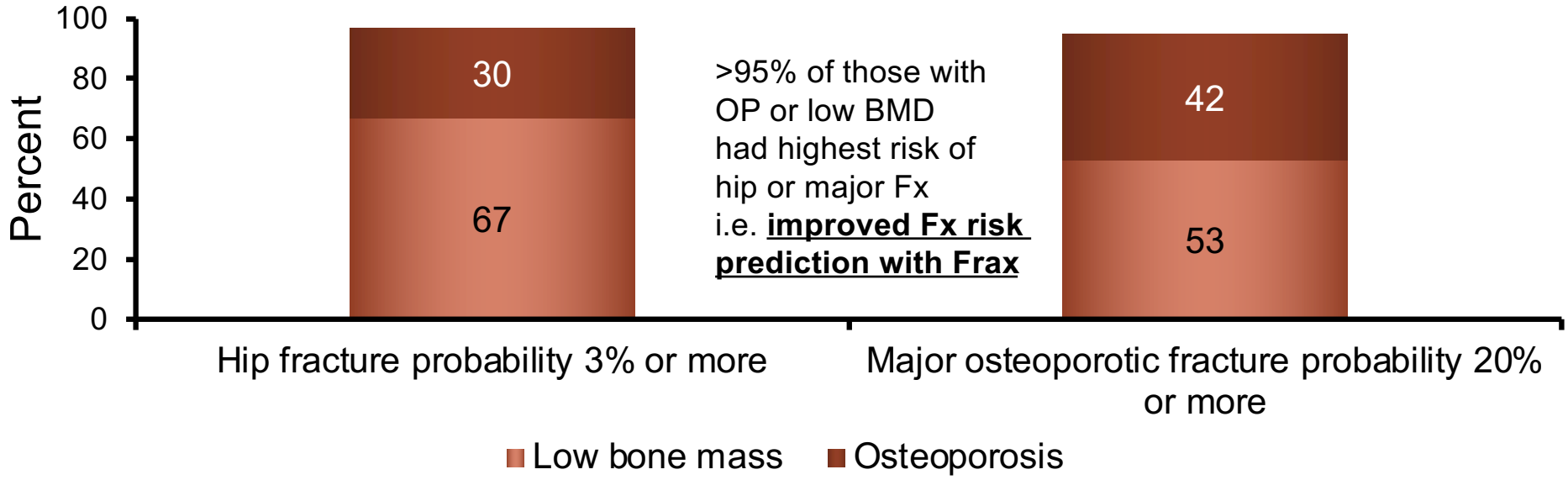


- Quantitative Ultrasound (QUS)
  - Uses ultrasound to evaluate peripheral bone sites; similar accuracy to central DXA
- Risk Assessment Tools
  - FRAX (Fracture Risk Assessment Tool)
    - Assesses 10-year risk of fracture
  - Simple Calculated Osteoporosis Risk Estimation (SCORE)
  - Osteoporosis Risk Assessment Instrument (ORAI)
  - Osteoporosis Index of Risk (OSIRIS)
  - Osteoporosis Self-Assessment Tool (OST)

USPSTF. *JAMA*. 2018;319(24):2521-2531.

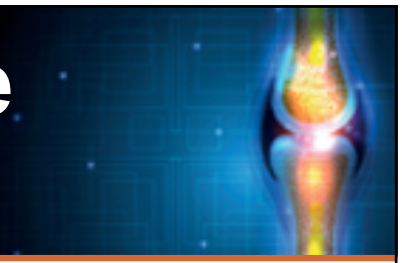
Prevalence of Osteoporosis or Low Bone Mass Density Among Adults >50 Years Old in the US with High Probability (by FRAX) to Fracture

Osteoporosis at the femoral neck in adults with elevated FRAX-based 10-year probability of hip or major osteoporotic fracture.



Looker AC, et al. *Natl Health Stat Report*. 2017 Mar;(103):1-16.

Osteoporosis in Men: An Endocrine Society Clinical Practice Guideline

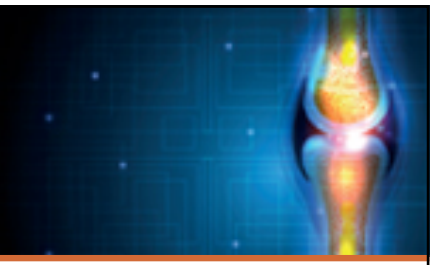


- Recommend testing higher risk men [aged ≥70 and men aged 50-69 who have risk factors (e.g. low body weight, prior fracture as an adult, smoking, etc.)]
  - Central dual-energy x-ray absorptiometry (DXA) of the spine and hip
    - Forearm DXA
      - when spine and hip cannot be interpreted
      - men with hyperparathyroidism and those receiving androgen-deprivation therapy

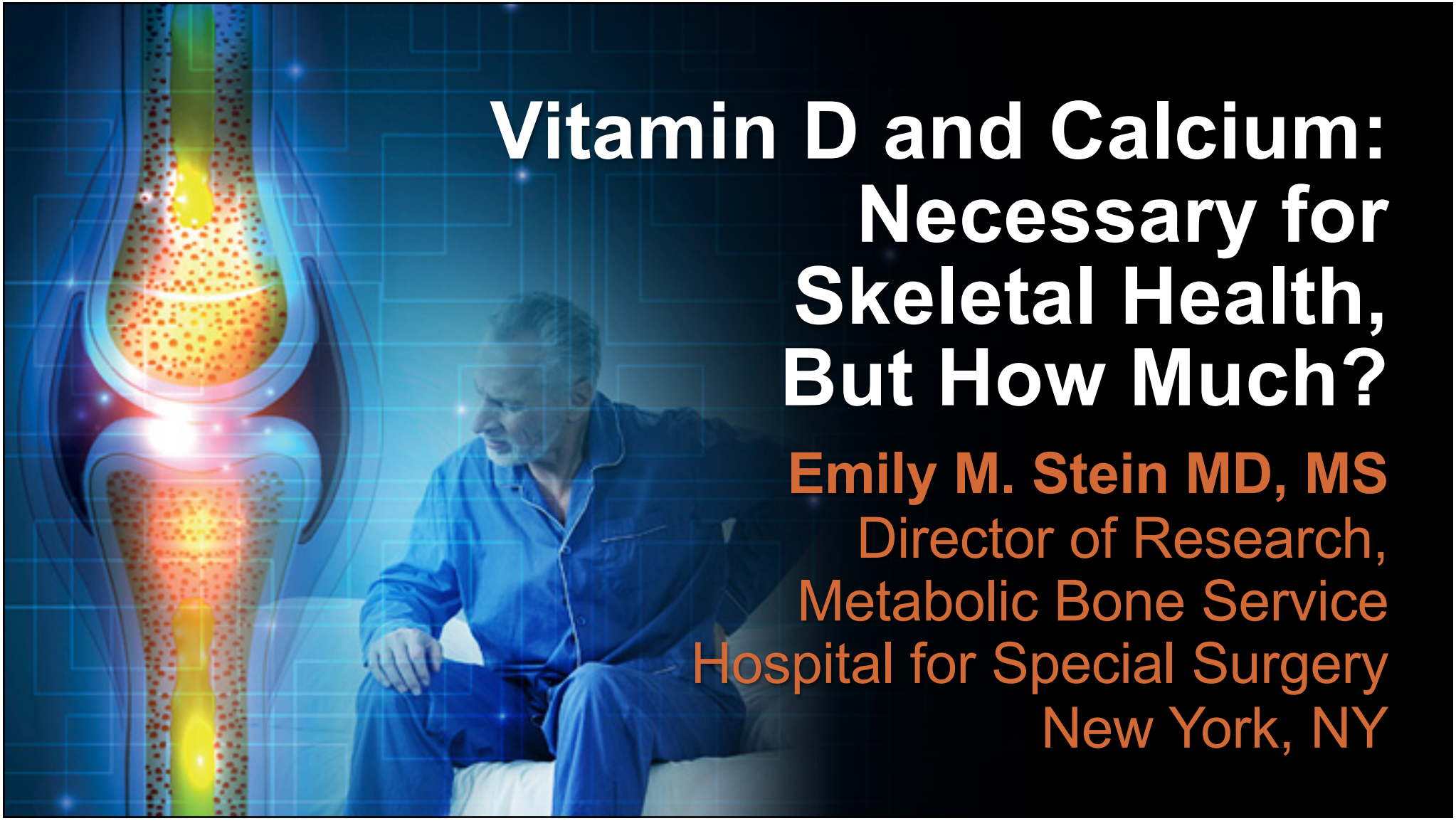
      (And include a predictive tool, e.g., FRAX)
  - History and physical
    - Medications used; chronic diseases; alcohol or tobacco abuse; hx of falls/fractures as an adult; family hx of osteoporosis
    - Pt height, kyphosis, balance, mobility, frailty, and causes of secondary osteoporosis

Watts NB, et al. *J Clin Endocrinol Metab*. 2012;97(6):1802-1822.

Take Away Points



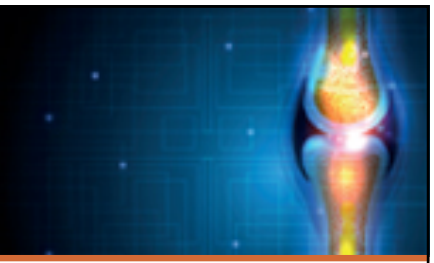
- Screening methods and tools are available to identify men and women at risk for fracture
- The outcomes for men who fracture can be devastating - **more men die within a year of a hip fracture than from nearly any other disease associated morbidity**
- We have an obligation to identify and treat those at risk to improve healthcare and patient related outcomes



Vitamin D and Calcium: Necessary for Skeletal Health, But How Much?

Emily M. Stein MD, MS
Director of Research,
Metabolic Bone Service
Hospital for Special Surgery
New York, NY

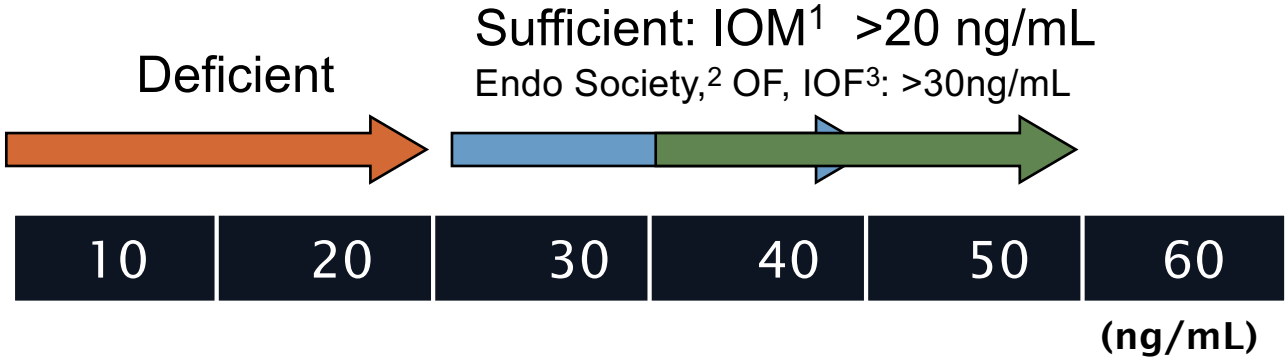
Clinical Case



- Mr. Jones is a 75-year-old man who presents after a recent fall in which he sustained a hip fracture. As part of his osteoporosis management, you would like to evaluate him for vitamin D deficiency.

Diagnosis of Vitamin D Deficiency

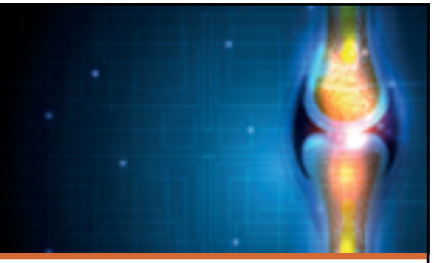
- 25-hydroxyvitamin D (25-OH-VitD) used to assess D stores/diagnose deficiency
- Optimal concentration for skeletal health is controversial
- Levels < 20 ng/mL (50nmol/L) are sub-optimal for skeletal health



Sufficiency defined as: Level below which PTH is stimulated; Level necessary for calcium absorption; Relationship to BMD; Relationship to fracture

1. Institute of Medicine, *Food and Nutrition Board. Dietary Reference Intakes for Calcium and Vitamin D*. 2011;
2. Holick MF, et al. *J Clin Endocrinol Metab*. 2011;96:1911-1930; 3. Mithal DA, et al. *Osteoporos Int*. 2009;20(11):1807-1820.

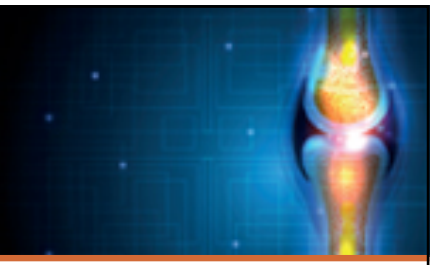
Optimal Intake to Prevent Deficiency



- IOM [National Academy of Medicine]:[1]
  - 600 IU vitamin D (up to 70 years), 800 IU vitamin D (over 71 years)
- National Osteoporosis Foundation (NOF):[2]
  - In women, 800-1000 IU of vitamin D daily (50 years and older)
  - In men, 400 – 800 ID of vitamin D daily (< 50 years old); 800 – 1000 IU daily (ages > 50)
- American Geriatric Society:[3]
  - > 1000 IU vitamin D daily

1. Institute of Medicine, Food and Nutrition Board. Dietary Reference Intakes for Calcium and Vitamin D. 2011;
2. NOF. Available at https://cdn.nof.org/wp-content/uploads/2016/04/Calcium-and-Vitamin-D-are-Essential-for-Bone-Health.pdf;
3. AGS. *Ann Longterm Care*. 2014;22(1):12-13.

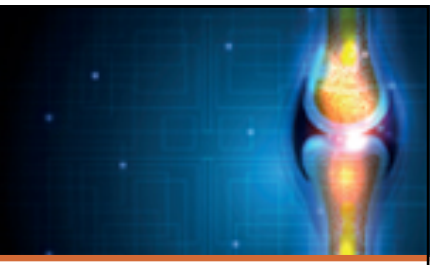
Dosing Vitamin D



- In patients with normal absorptive capacity, for every 100 units (2.5 mcg) of added vitamin D3 serum 25OHD increases ~1.0 ng/ml
- Larger increments seen in patients with lower baseline
- Typical regimen for D deficient patient:
  50,000 IU of D2 or D3 per week for 8 weeks
- Continue treatment until patient is sufficient
- Follow with maintenance dose of at least 800 IU/d

Schwartz JB, et al. *J Am Geriatr Soc*. 2016;64(1):65-72; Vieth R. *J Nutr*. 2006;136(4):1117-1122; Heaney RP, et al. *Am J Clin Nutr*. 2003;77(1):204-210; Gallagher JC, et al. *Ann Intern Med*. 2012;156(6):425-437.

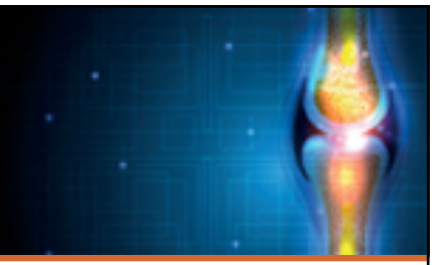
Vitamin D Toxicity



- IOM: Tolerable upper limit 4000 IU per day
- More common now as patients often use high doses of supplements
- Earliest manifestation will be hypercalciuria
- Hypercalcemia may occur later
- Caution repleting patients with a history of nephrolithiasis or concurrent idiopathic hypercalciuria
- Prolonged sun exposure does not produce toxic levels
  - Photoconversion of previtamin D3 and D3 to inactive metabolites
  - Melanin production inhibits D

Gailor K, et al. *Nutrients*. 2018;10(8):953; Holick MF. *J Cell Biochem.* 2003;88(2):296-307.

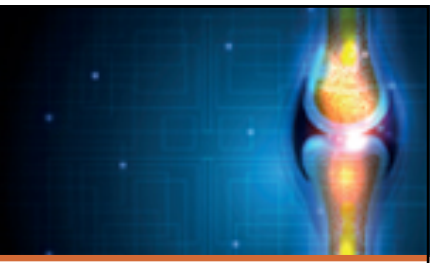
Vitamin D Supplementation and Fracture Risk



- Some studies have found a reduction in fractures with supplementation
- Others have not seen an effect
- Conflicting results may relate to differences in baseline vitamin D status of participants, range of doses used, and compliance
- Reduction in hip fractures and non-vertebral fractures seen with doses ~800 IU/day or greater

Zhao JG, et al. *JAMA*. 2017;318(24):2466-2482; Pundole X, et al. *JAMA*. 2018;319(19):2041-2042; Bischoff-Ferrari HA, et al. *N Engl J Med*. 2012;367(1):40-49.

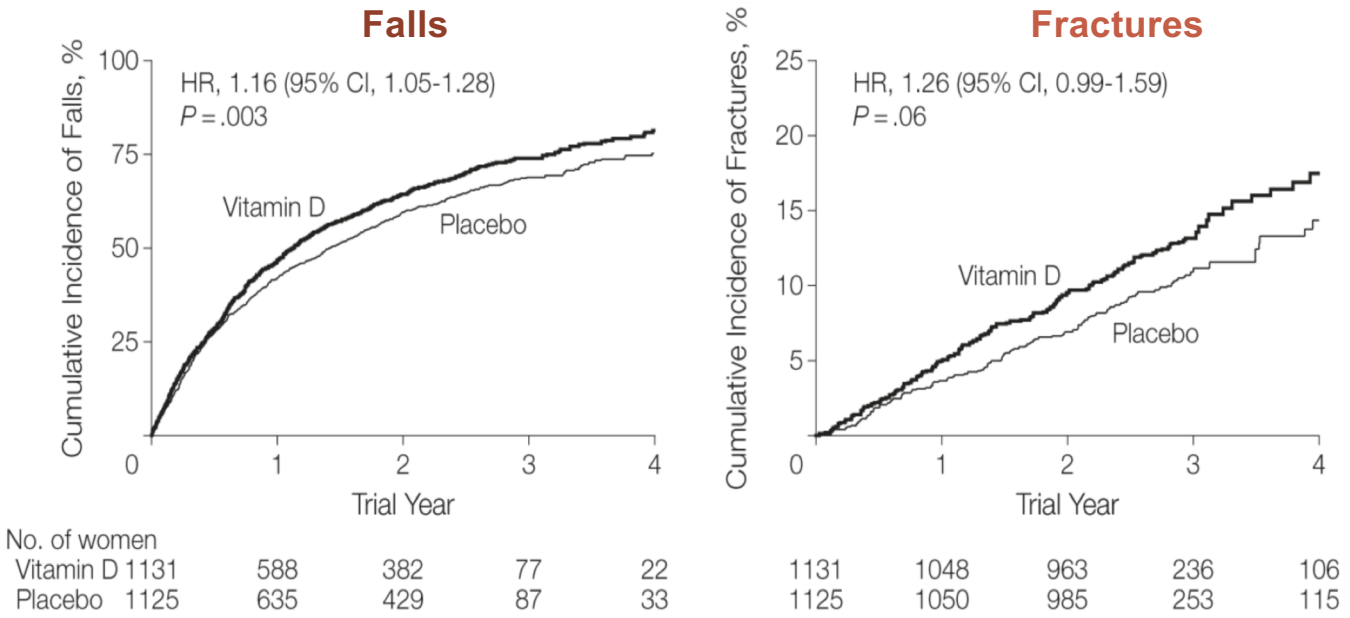
25OHD Status and Falls



- Men and women over 65 with low serum 25OHD (<10 ng/ml) are at greater risk for falls and hip fracture because of
  - Loss of muscle mass
  - Lower strength
- Vitamin D supplementation may reduce fall risk
  - Effect may relate to dose and baseline level
  - Majority of studies finding a beneficial effect have used doses ≥ 800 IU/day

Visser M, et al. *J Clin Endocrinol Metab*. 2003;88(12):5766-5572.; Cauley J, et al. *Ann Intern Med*. 2008;149(4):242-250; Michael Y et al. *Ann Intern Med*. 2010;153(12):815-825; Gillespie LD, et al. *Cochrane Database Syst Rev*. 2012;Sep 12(9):CD007146.

Annual High-Dose Oral Vitamin D and Falls and Fractures in Older Women:
The More the Better?



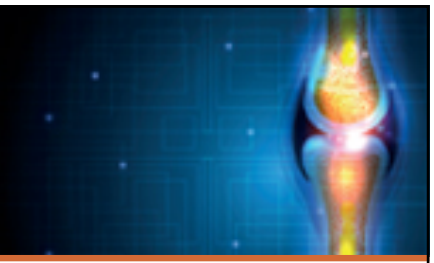
INCREASED risk of falls and fractures

Temporal pattern in fall risk highest first 3 months after dose

Sanders KM, et al. *JAMA*. 2010;303(18):1815-1822.


What About
Calcium?

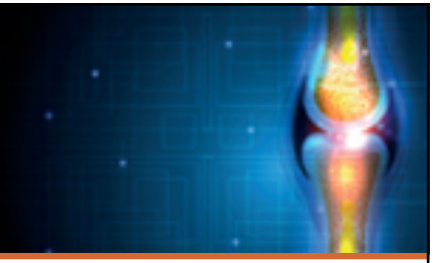
IOM: Recommendations for Calcium Intake



- As with vitamin D, optimal calcium intake is uncertain
  - 1000 mg daily for premenopausal women and men < 70
  - 1200 mg daily for postmenopausal women and men > 70
- Recommended intakes based on combined intake from diet and supplements
- Intake should be spaced with ≤ 500 mg - 600 mg at one time

Institute of Medicine, Food and Nutrition Board. Dietary Reference Intakes for Calcium and Vitamin D. 2011.

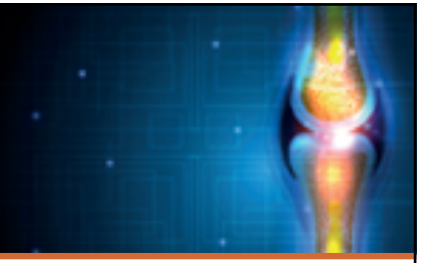
Adverse Effects of Calcium Intake



- Nephrolithiasis
  - Associated with calcium supplements not dietary calcium (which may offer some protection)
- Cardiovascular disease, linked with use of supplements
  - Effects are controversial
  - Some studies and meta-analyses have found increased risk of MI, CVD from calcium supplements alone and calcium + vitamin D, other studies no increased risk
  - Possible protective effect of dietary calcium on CVD, MI, CVA
  - Hypothesized that sudden elevation from supplements may increase vascular resistance, calcification and arrhythmias

Anderson JJ, et al. *J Am Heart Assoc*. 2016;5(10).pii:e003815; Paik JM, et al. *Osteoporos Int.* 2014;25(8):2047-2056; Rejnmark L, et al. *J Clin Endocrinol Metab.* 2012;97(8):2670-2681; Bolland MJ, et al. *BMJ.* 2011;342:d2040.

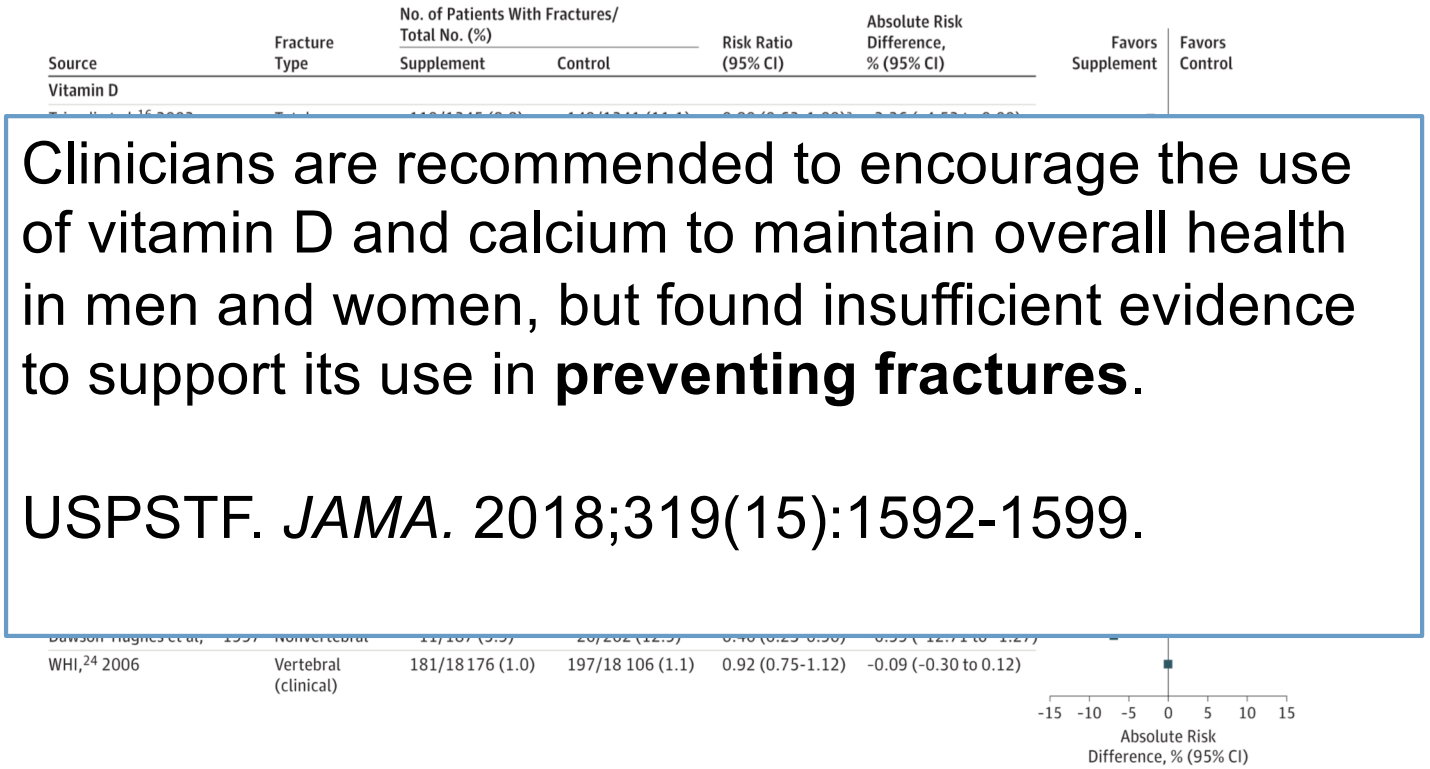
Efficacy of Calcium on BMD



- Critical during period of bone mass accrual
- In older individuals, small, consistent effects of calcium alone or calcium + vitamin D on improving BMD
- Effects on fracture reduction less clear
  - Epidemiological evidence showing fracture reduction
  - No benefits in large RCTs or meta-analyses when analyzed as ITT
  - However, sub-group analysis showed calcium + vitamin D fracture risk reduction in Women's Health Initiative
    - 15% reduced risk of total fractures; 30% reduction of hip fractures

Weaver CM, et al. *Osteoporos Int*. 2016;27:367–376; Jackson RD, et al. *N Engl J Med*. 2006;354(7):669-683; Kim KM, et al. *Clin Endocrinol Metab*. 2014;99(7):2409-2417; Key TJ, et al. *Public Health Nutr*. 2007;10(11):1314-1320; Bolland MJ, et al. *BMJ*. 2015;351:h4580.

RCTs Comparing Vitamin D, Calcium, or Both vs Placebo on Fracture Prevention



Source	Fracture Type	No. of Patients With Fractures/ Total No. (%) Supplement	Control	Risk Ratio (95% CI)	Absolute Risk Difference, % (95% CI)
Vitamin D					
WHI,[24] 2006	Vertebral (clinical)	181/18 176 (1.0)	197/18 106 (1.1)	0.92 (0.75-1.12)	-0.09 (-0.30 to 0.12)

Clinicians are recommended to encourage the use of vitamin D and calcium to maintain overall health in men and women, but found insufficient evidence to support its use in **preventing fractures**.

USPSTF. *JAMA.* 2018;319(15):1592-1599.

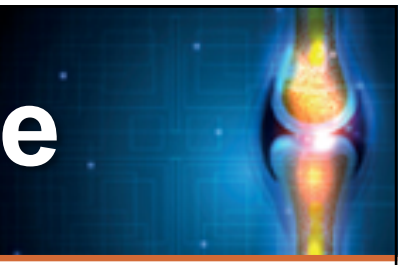
Kahwati LC, et al. *JAMA.* 2018;319(15):1600-1612.

Promote Dietary Intake of Calcium

- While calcium and vitamin D are not sufficient to prevent fractures in high-risk patients, they are necessary for proper mineralization of bone
- Patients who are deficient in calcium or vitamin D prior to initiation of bisphosphonate or denosumab treatment are at risk for hypocalcemia as well as a suboptimal treatment response

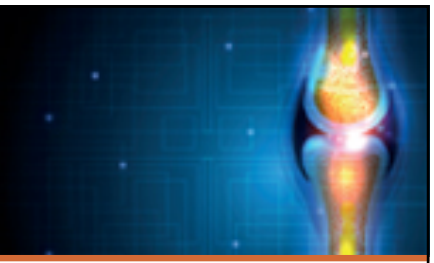
Use supplements if dietary intake is inadequate

Let's Revisit Our Clinical Case



- Mr. Jones, our 75-year-old patient, presents after a recent fall in which he sustained a hip fracture. As part of his osteoporosis management, you would like to evaluate him for vitamin D deficiency

Conclusions

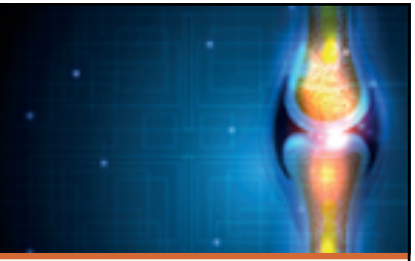


- Vitamin D insufficiency is widespread and has clear skeletal sequelae
  - Supplementation lowers risk of fractures and falls – in deficient patients, using optimal doses of ~800 IU daily
  - Potential risks with very high doses and 25OHD levels
- Adequate intake of calcium is important for building and maintaining the skeleton
  - Potential risks with high doses of supplements
  - Goal intake for older patients 1000-1200mg, dietary sources are preferable
- Vitamin D and calcium are necessary for skeletal health
- Moderate intakes of both will maximize efficacy and minimize potential risks

Integrating Patient-Reported Outcomes into Clinical Workflow

Kirsten Grueter, RN
Hospital for Special Surgery
New York, NY

Categories of Patient Outcomes

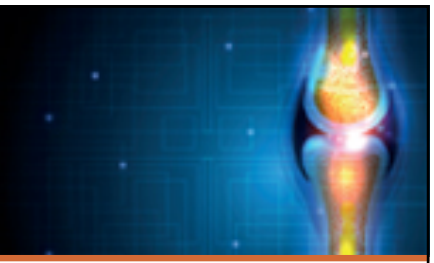


Patient Outcomes Assessment Sources and Examples

Clinician-Reported	Physiological	Caregiver-Reported	Patient-Reported
• Global impressions • Observations & tests of function	• T-scores • Lab values • Bone markers	• Dependency • Functional status	• Global impressions • Functional status • Well-being • Symptoms • HRQoL • Satisfaction with TX • Treatment adherence • Utility/preference-based measures

Adapted from Acquadro C, et al. *Value in Health*. 2003;6(5)5:522-531.

What are Patient-Reported Outcomes (PROs)?

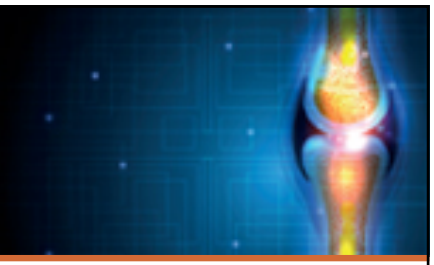


Patient Outcomes:

- PROs = any report of the status of a patient's health condition, health behavior, or healthcare experience that comes directly from the patient, without interpretation by a clinician or anyone else*

*FDA. 2009. Available at https://www.fda.gov/downloads/drugs/guidances/ucm193282.pdf

What is a PROM?



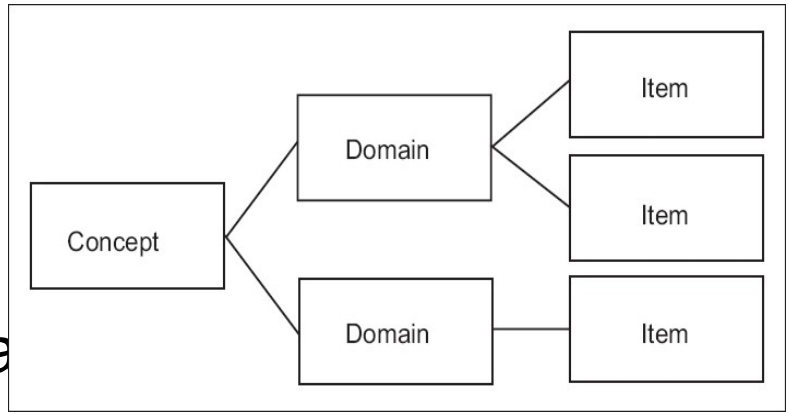
- PROM = Patient Reported Outcome Measure
- Tools – questionnaires - used to gain insight from the perspective of the patient
- Best source of information
  - Symptoms: pain, fatigue, physical function
  - Impact of symptoms on meaningful activities
  - Knowledge, attitude, behaviors
- Variability in correlation between clinician and patient reports
- HRQoL predicts survival in many conditions[1]
- Same biological value in 2 patients ≠ same impact

[1]Hahn EA, et al. *Mayo Clin Proc*. 2007;82:1244-1254.

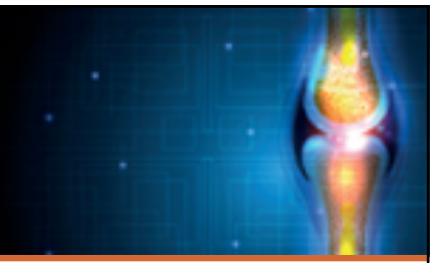
How PROs are Measured

Instruments (questionnaires) capture PRO data

- Concept: thing/event being measured
  - physical health, mental health, social health
- Domain: unidimensional content area
  - anxiety, pain, fatigue, physical function, depression
- Item: individual question, statement, or task



When to Measure PROs?



Clinical trials

- HRQoL assessment required for drug and medicinal product approval

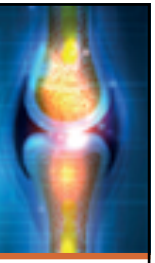
Clinical care

- Monitor disease and treatment/interventions
- Detect physical or psychosocial issues
- Improve patient-physician communication
- Improve patient engagement

Quality of Care

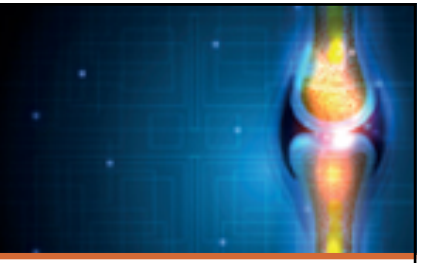
- Audit and quality assurance by payors or insurance companies

Selecting the Appropriate PROM



- ***Crucial*, *arguably the most important part***
- Need to make sure you are measuring what you want to measure and what you think you are measuring
- Avoid responder burden
- Choosing sub-type of question
  - **Generic**: Measure domains which can be compared between conditions
  - **Disease-specific**: Developed specifically to capture elements of health and QoL that are relevant to a *specific patient group or condition*

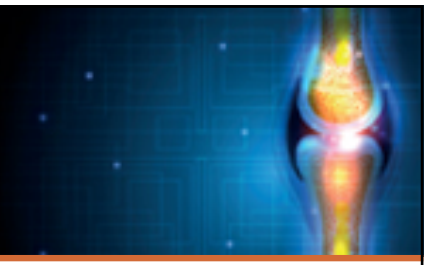
Patient Reported Outcome Measurement Information System (PROMIS®)



- Originally NIH-funded initiative to develop and validate PROs for clinical research and practice
- ”A psychometrically validated, dynamic system to measure [patient reported outcomes] efficiently in study participants with a wide range of chronic diseases and demographic characteristics."
- Over 300 measures of physical, mental, and social health
  - Can be used in general population
  - May be particularly helpful for those living with chronic conditions

NIH website. Available at https://commonfund.nih.gov/promis/index.

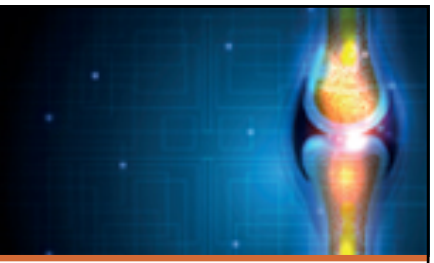
HealthMeasures PROMIS® Assessment Center



- Web-based management tool
- Enables creation of specific surveys
- Participant interface → data collection
- PROMIS® has created electronic item banks of validated questions for a variety of domains
- Administration of questions via short forms and computer adaptive testing (CATs)
  - Short form: fixed set 4-10 items for one domain

HealthMeasures website. Available at http://www.healthmeasures.net/explore-measurement-systems/promis.

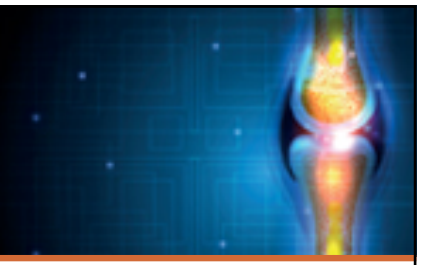
PROMIS® Item Banks



Domains	Items in Bank	Items in Short Form
Emotional Distress – Anger	29	8
Emotional Distress – Anxiety	29	7
Emotional Distress – Depression	28	8
Fatigue	95	7
Pain – Behavior	39	7
Pain – interference	41	6
Physical Function	125	10
Satisfaction with Discretionary Social Activities	12	7
Satisfaction with Social Roles	14	7
Sleep Disturbance	27	8
Wake Disturbance (sleep related impairment)	16	8
Global Health		10

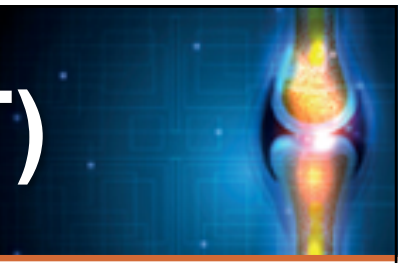
Witter J. *Rheum Dis Clin North Am*. 2016;42(2):377-394.

Item Response Theory (IRT)



- A psychometric measurement method
- Family of mathematical models that assumes responses on a set of items/questions are related to an unmeasured “trait”
- Most effective administered electronically
- Strength of PROMIS®

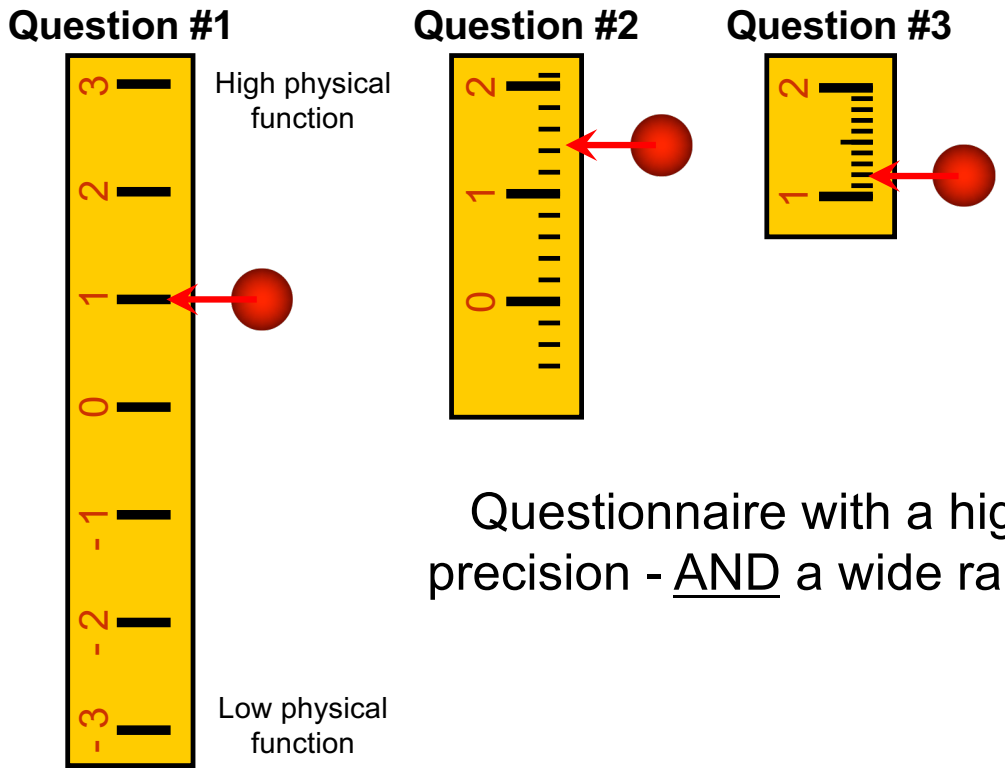
Computer Adaptive Testing (CAT)



- Utilizes IRT
- Answer to one question affects the next question administered
- Measurement is “adapted” to individual
- Skips uninformative items to minimize response burden

Allows determination of person’s standing on a domain without a loss in measurement precision

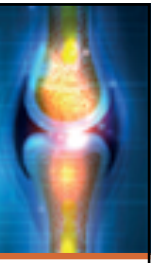
Computerized Adaptive Tests



Questionnaire with a high precision - AND a wide range

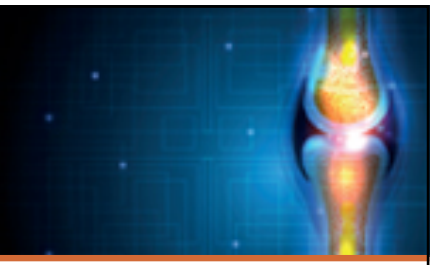
Courtesy of Dr. James Witter (CSO PROMIS®)

CAT – Advances in Clinical Research



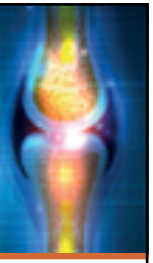
- Precision – improved measurement precision across the full range of patient-reported outcomes
- Efficiency – less respondent burden
- Standardization – more interpretable research with standard terminology and metrics
- International clinical trial applications
- Avoids ceiling and floor effects common to “Legacy” instruments

PROMs: Challenges



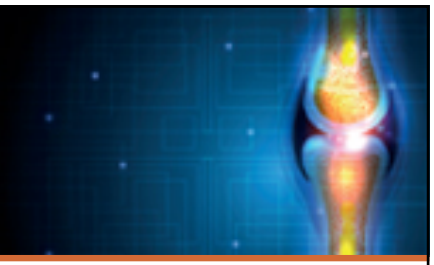
- Engage users – whether in clinical practice or research
- Both study subjects/patient and physicians/other providers must be engaged and have bought into the concept
- The person administering must be well-trained
- Need some infrastructure to effectively utilize PROMs at point-of-care
- Many institutions are building PROMs into their EMR

PROMs at Hospital for Special Surgery (HSS)



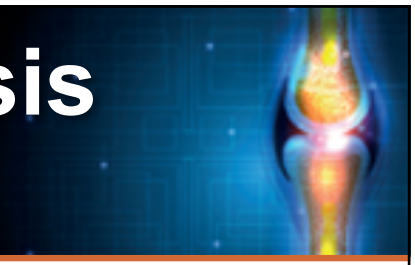
- Has been used extensively in patient registries
- EPIC: Short-form PROMIS® -10 and a disease-specific measure for all patients treated at HSS

Piloting PROs in Osteoporosis at HSS/Weill Cornell Medicine



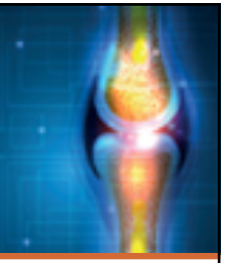
- Trial of PROMIS® in hip fracture patients with IRT and CAT in-house → failure
  - Cognitive impairment
  - Unfamiliar with iPad technology
  - Post-operative medication
  - Distortion of results by family or caregivers
- Resolution
  - "6-Item Screener:" validated tool to identify cognitively intact and can consent to participate in clinical research
  - PROMIS®-29 Short Form, alternative to CAT

Piloting PROMIS®-29 in Osteoporosis at HSS/Weill Cornell Medicine



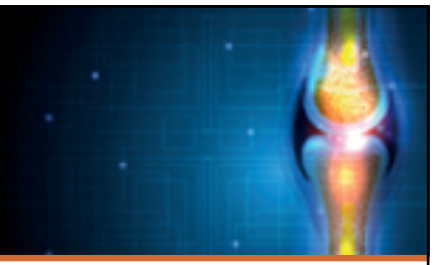
- PROMIS®-29 Short Form: generic, health-related quality of life survey
- Assess each of 7 domains
  - Anxiety
  - Depression
  - Physical function
  - pain interference
  - Fatigue
  - Sleep disturbance
  - Ability to participate in social roles and activities

Piloting PROMIS®-29 in Osteoporosis at HSS/Weill Cornell Medicine (cont.)



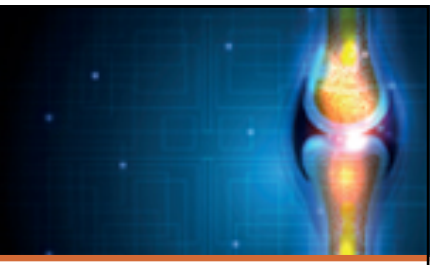
- Administered post-operatively at:
  - Day 2, 3 months, 1 year
- Able to follow trajectory of responses and individually tailor patient care
- Hypothesis is we will be able to identify specific patient trajectories
- Goal is early identification of potential patients in jeopardy

PROMs in Outpatient Osteoporosis Patients



- Metabolic Bone Disease Service at HSS has standardized information on patients with diagnosis of osteoporosis
- PROMIS®-29 for variety of domains
- Strengths: easy, information on several domains, takes only 5 minutes to complete

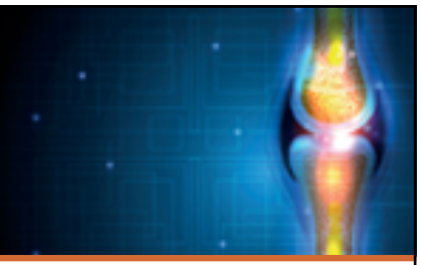
Take-Away



- PROMIS® is a powerful tool that can be used to phenotype osteoporotic patients beyond lab and DEXA values
- Patients enjoy being asked about their emotional and physical well-being → increased patient engagement and satisfaction
- Can allow for more feasible choice of drug therapy by identifying domains which may be barriers to compliance

SMART Goals

Specific, **M**easurable, **A**ttainable, **R**elevant, **T**imely



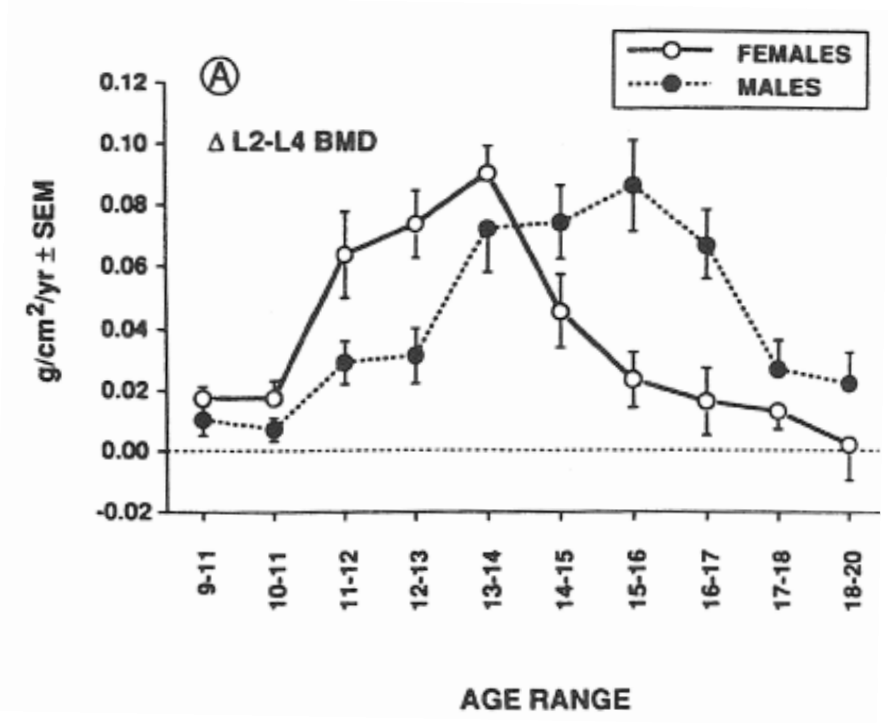
- Implement the use of evidence-based tools and strategies to assess bone health and risk of fracture in older men
- Identify patient-specific, optimal repletion regimens for patients who are calcium and/or vitamin D deficient to reduce the risk of fracture
- Incorporate the use of PROMs to provide a more global assessment of osteoporotic patients' disease progression, effectiveness of treatment, and quality of life

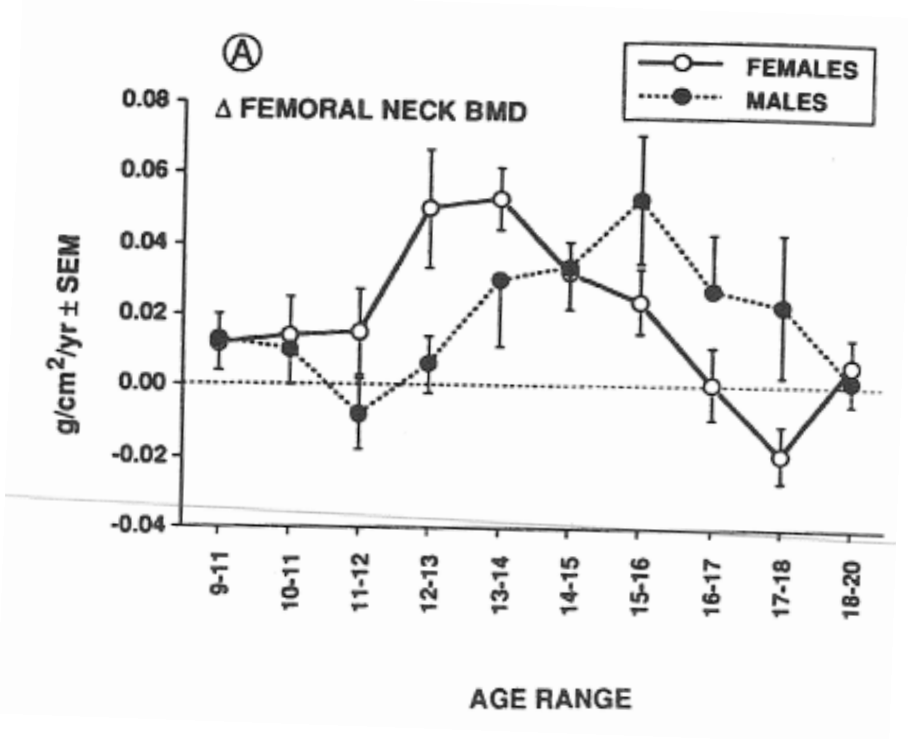

Questions
& Answers


Thank You
To receive credit, please complete the demographics survey upon login and the evaluation during Q&A on your mobile device. You will receive an email with your certificate after the event.


Resource Slides

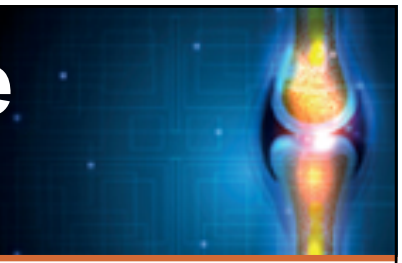
Bone Mass Density Changes During Puberty: Males > Females





Kemper HCG. *Pediatric Exercise Science*. 2000;12:198-216.

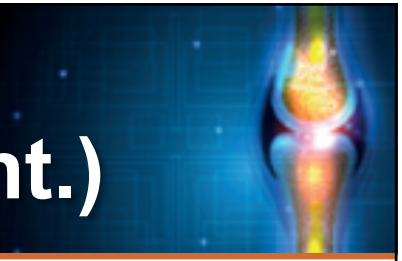
Osteoporosis in Men: An Endocrine Society Clinical Practice Guideline



- Recommend testing higher risk men [aged ≥70 and men aged 50-69 who have risk factors (e.g. low body weight, prior fracture as an adult, smoking, etc.)]
  - Central dual-energy x-ray absorptiometry (DXA) of the spine and hip
    - Forearm DXA
      - when spine and hip cannot be interpreted
      - men with hyperparathyroidism and those receiving androgen-deprivation therapy
  - History and physical
    - Medications used; chronic diseases; alcohol or tobacco abuse; hx of falls/fractures as an adult; family hx of osteoporosis
    - Pt height, kyphosis, balance, mobility, frailty, and causes of secondary osteoporosis

Watts NB, et al. *J Clin Endocrinol Metab*. 2012;97(6):1802-1822.

Osteoporosis in Men: An Endocrine Society Clinical Practice Guideline (cont.)

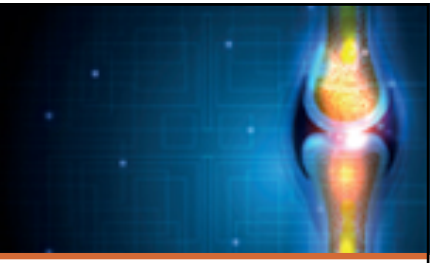


- Lab tests
  - Serum calcium
  - Phosphate
  - Creatinine (with GFR)
  - Alkaline phosphatase
  - Liver function
  - 25-hydroxyvitamin D [25(OH)D],
  - Total testosterone,
  - CBC
  - 24-hr urinary calcium (creatinine and sodium) excretion

- Vertebral Fracture Assessment (VFA) using DXA equipment
  - In men with osteopenia or osteoporosis who might have previously undiagnosed vertebral fractures

Watts NB, et al. *J Clin Endocrinol Metab*. 2012;97(6):1802-1822.

Individuals at High Risk for Vitamin D Deficiency



- Low dietary intake
- Elderly
- Dark-skinned
- Limited sun exposure (institutionalized, sun screen)
- Medications that accelerate vitamin D metabolism (i.e. phenytoin)
- Malabsorption (inflammatory bowel and celiac disease)
- Rheumatologic Disease: SLE, RA, polymyositis/dermatomyositis
- Obese
- Critically ill

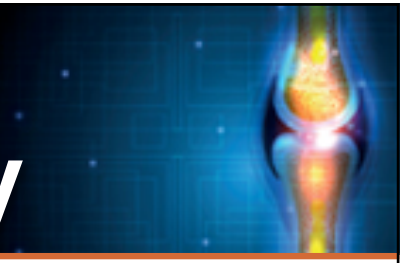
Liu X, et al. *Br J Nutr*. 2018;119(8):928-936; Gröber U, et al. *Dermatoendocrinol*. 2012;4(2):158-166.

Vitamin D for Extra-skeletal Health

- In addition to its role in calcium and bone homeostasis, vitamin D may regulate many other cellular functions
- Epidemiologic data suggest higher risk of cancer, infections, autoimmune and CV disease with low 25OHD
- A causal relationship between vitamin D deficiency and these diseases has not been clearly established in RCTs

Bouillon R. *Best Pract Res Clin Endocrinol Metab*. 2011;25(4):693-702. Ahn J et al. *J Natl Cancer Inst*. 2008;100(11):796; Michaëlsson K, et al. *Am J Clin Nutr*. 2010;92(4):841-848.

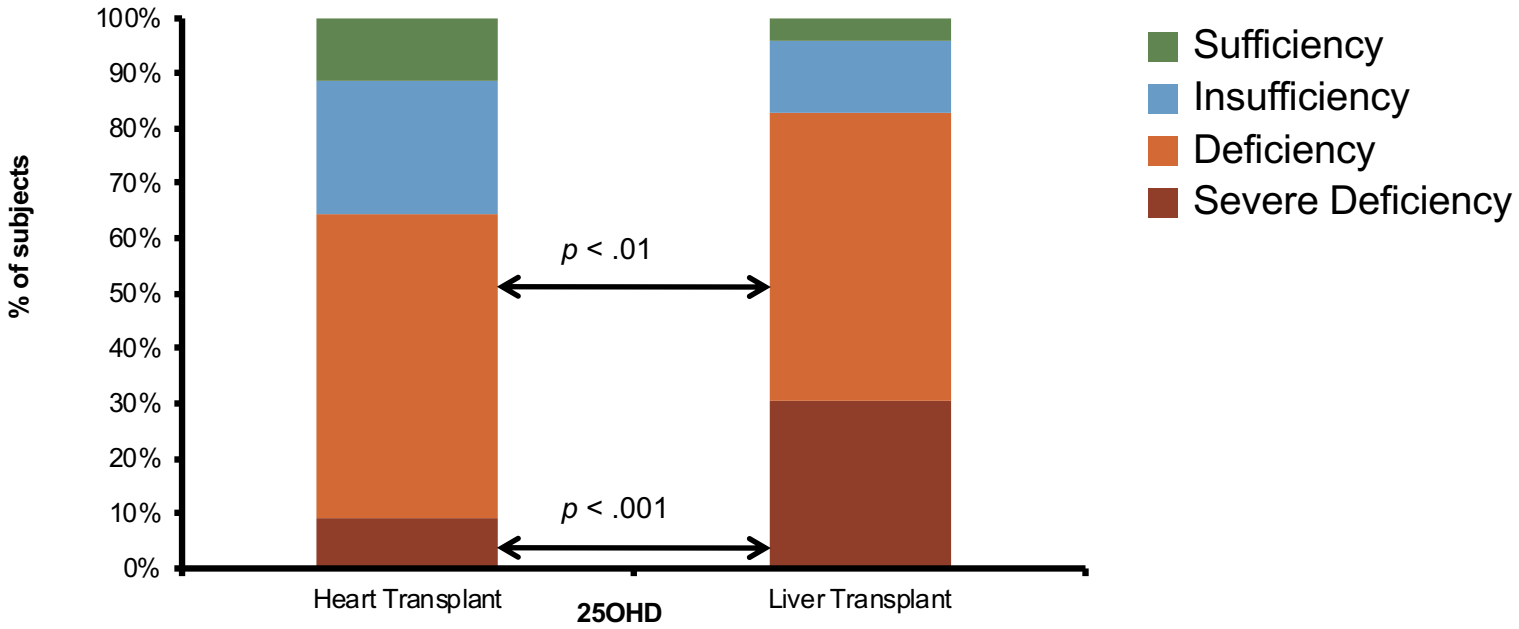
Vitamin D for Extra-skeletal Health: Malignancy and Mortality



- Low levels associated with increased risk of certain malignancies (e.g., colon cancer)
- High levels may be associated with increased risk of pancreatic cancer and prostate cancer
  - No RCT of vitamin D supplementation with mortality as primary endpoint
- Many studies have found low 25OHD <10-20 ng/mL associated with increased mortality
- U-shaped relationship between 25OHD and mortality in observational studies
  - Higher risk of mortality at 25OHD >40-50 ng/mL (stronger effect in women)

Bouillon R. *Best Pract Res Clin Endocrinol Metab*. 2011;25(4):693-702. Ahn J et al. *J Natl Cancer Inst*. 2008;100(11):796; Michaëlsson K, et al. *Am J Clin Nutr*. 2010;92(4):841-848; Melamed ML, et al. *Arch Int Med.* 2008;168(15):1629-1637; Bjelakovic G, et al. *Cochrane Database Syst Rev*. 2014;Jan 10;(1):CD007470.

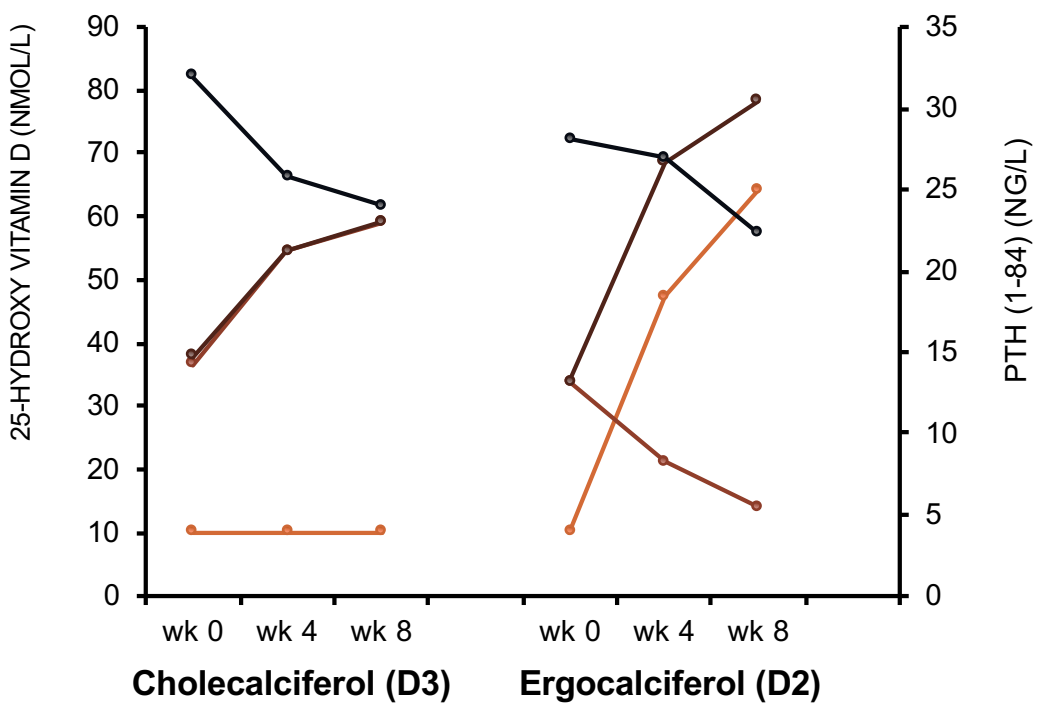
High Prevalence of Severe Vitamin D Deficiency Among Heart and Liver Transplant Recipients



Severe Deficiency (<10 ng/ml) in 10% heart transplant , 30% liver transplant, (22% undetectable); Sufficiency (≥30 ng/ml) in 10% heart transplant, 4% liver transplant

Stein EM, et al. *Clin Transplant*. 2009;23(6):861-865.

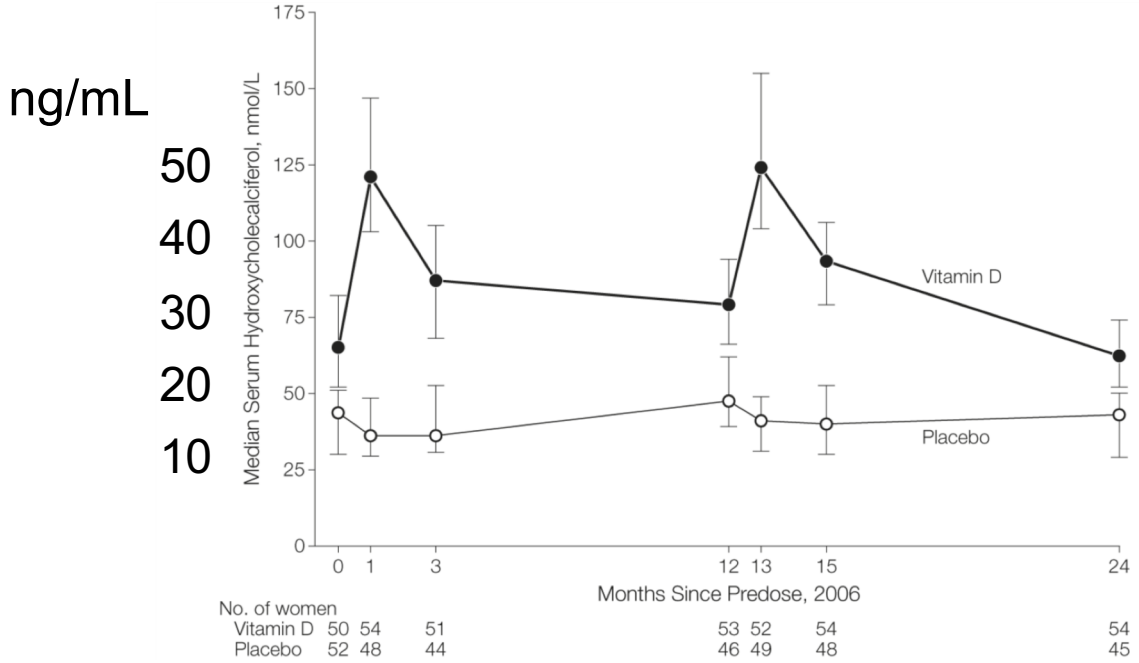
Effects of Vitamin D2 and Vitamin D3 Repletion in Severely Obese Subjects



- Both regimen significantly improved 25OHD, Decline in 25OHD3 with Ergo
- Despite lower weekly dose, suppression of PTH greater with D3

Stein EM, et al. *Clin Endocrinol (Oxf).* 2009;71(2):176-183.

Annual High-Dose Oral Vitamin D and Falls and Fractures in Older Women: The More the Better?



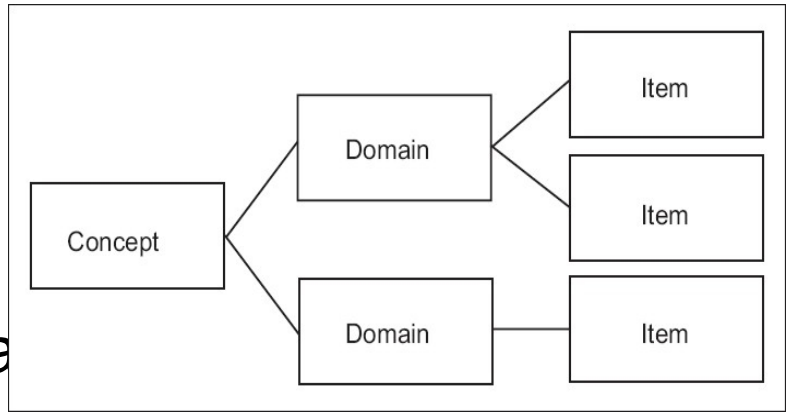
Single oral dose of 500,000 IU vitamin D3 or placebo annually for 3 years

Sanders KM, et al. *JAMA*. 2010;303(18):1815-1822.

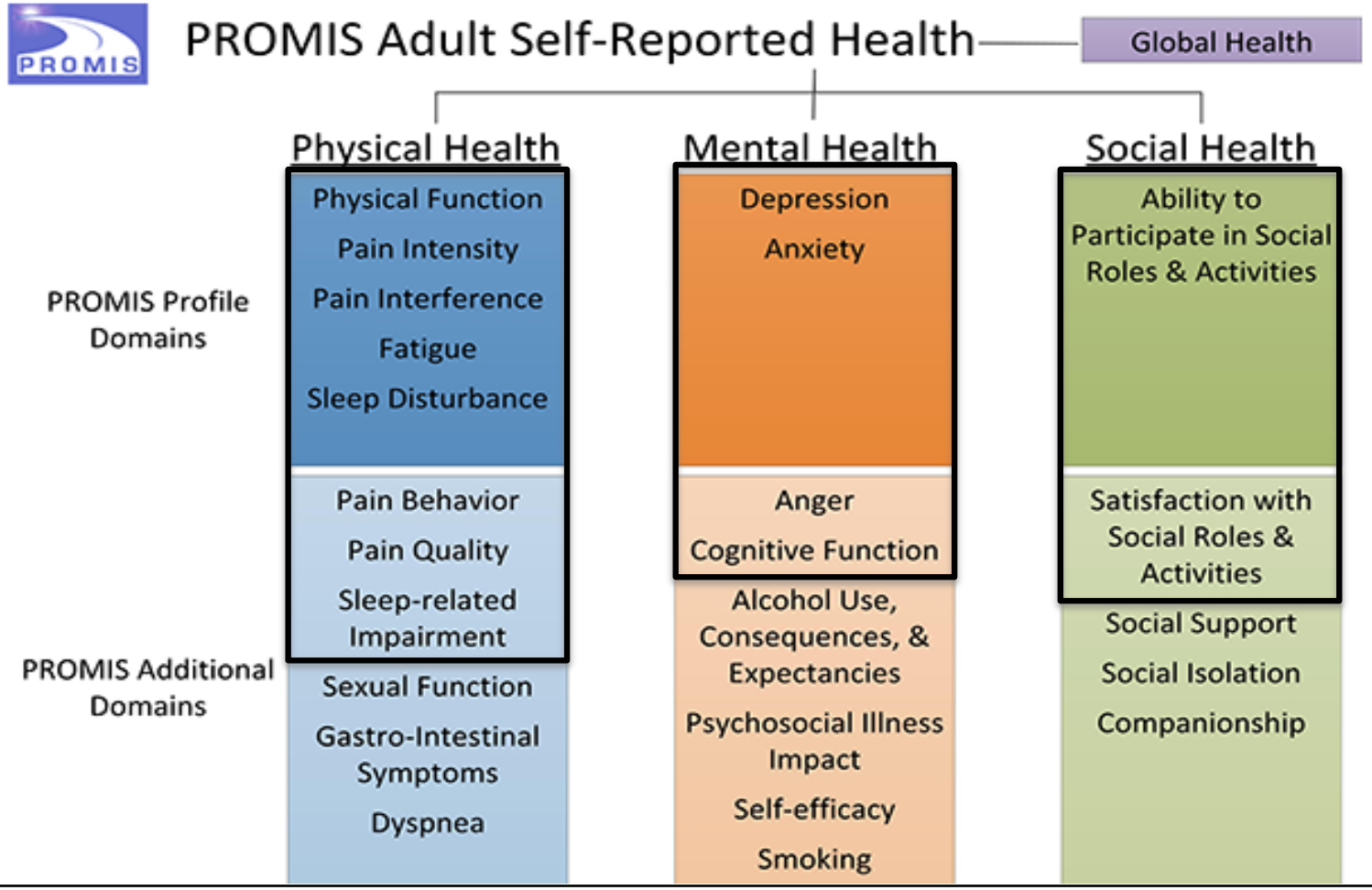
How PROs are Measured

Instruments (questionnaires) capture PRO data

- Concept: thing/event being measured
  - physical health, mental health, social health
- Domain: unidimensional content area
  - anxiety, pain, fatigue, physical function, depression
- Item: individual question, statement, or task



Domain Frameworks PROMIS® Adult Self-Reported Health



PROMIS® Pain Interference Short Form 8a

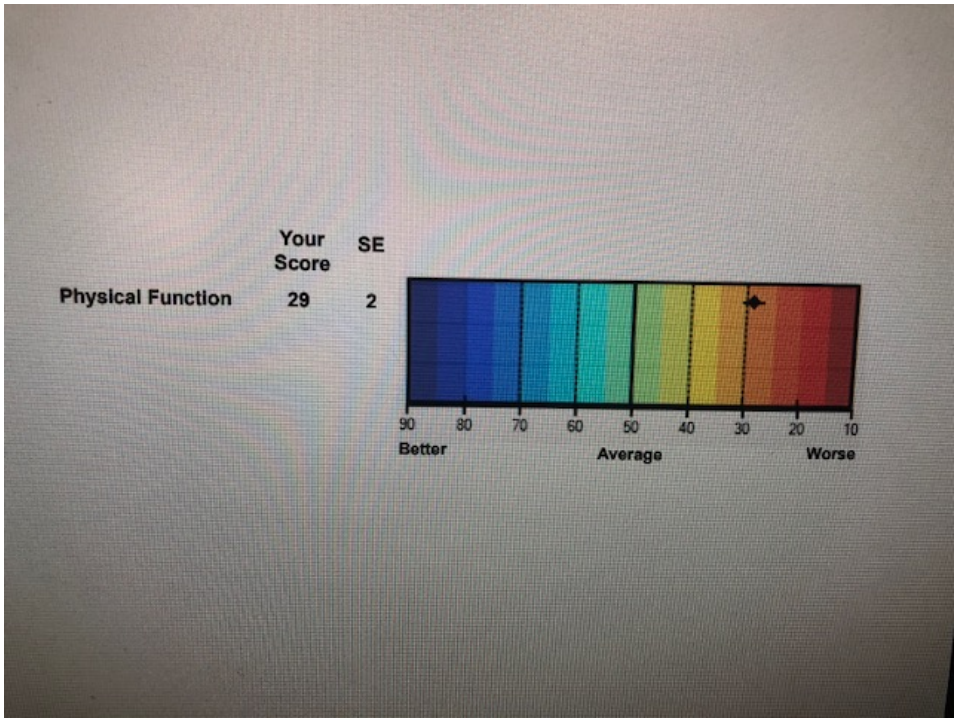
In the past 7 days…

		Not at all	A little bit	Somewhat	Quite a bit	Very much
PAININ9	How much did pain interfere with your day to day activities?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PAININ22	How much did pain interfere with work around the home?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PAININ31	How much did pain interfere with your ability to participate in social activities?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PAININ34	How much did pain interfere with your household chores?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PAININ12	How much did pain interfere with the things you usually do for fun?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PAININ36	How much did pain interfere with your enjoyment of social activities?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PAININ3	How much did pain interfere with your enjoyment of life?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
PAININ13	How much did pain interfere with your family life?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

Available at http://www.healthmeasures.net/index.php?option=com_instruments&task=Search.pagination&Itemid=992. Accessed September 14, 2018.

PROMIS® Scoring

- T Score
  Mean = 50
  SD = 10
- Referenced to the US general population



Witter J. Rheum Dis Clin North Am. 2016;42(2):377-394.