Menopause: Bone and Muscle Health

A focus on prevention
10/11/25

Rachel Cady, MD, FACOG, NCMP.

Objectives

1. Risk factors for osteoporosis
2. Preventive measures
3. What is the scope of the problem?
4. What does the data show?


Disclosure: speaker for Astellas

Why is this topic important?

Panel 1

People age 65 and older represented 17% of the population in the year 2020 but are expected to grow to be 22% of the population by 2040.

The 85 and older population is projected to more than double from 6.7 million in 2020 to 14.4 million in 2040 (a 117% increase).

**Number of Persons Age 65 and Older, 1900-2060 (numbers in millions)**

Year	Value
1900	3.1
1920	4.9
1940	9
1960	16.2
1980	25.5
2000	35
2020	55.7
2040	80.8
2060	94.7
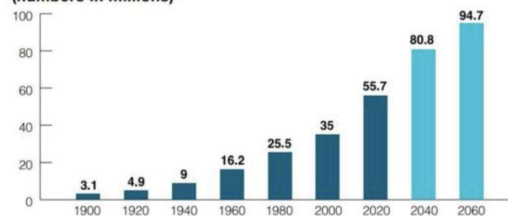
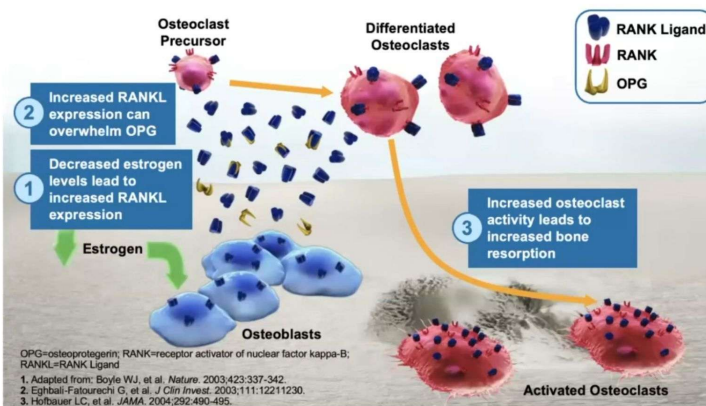Note: Lighter bars (2040 and 2060) indicate projections.
Source: U.S. Census Bureau, Population Estimates and Projections

Panel 2

Bone mineral density, age and menopause

From the beginning of the menopausal transition, reduced estrogen levels lead to a decrease in critical bone mass[3]

Panel 3
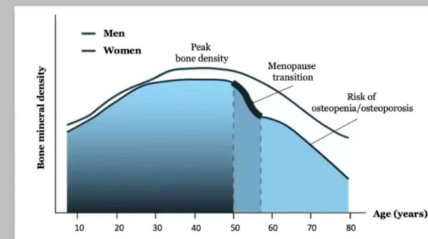
Decreased estrogen levels lead to Increased RANK Ligand expression and accelerated Bone Resorption [1-3]

- RANK Ligand
- RANK
- OPG

Osteoclast Precursor

Differentiated Osteoclasts

2 Increased RANKL expression can overwhelm OPG

1 Decreased estrogen levels lead to increased RANKL expression

Estrogen

3 Increased osteoclast activity leads to increased bone resorption

Osteoblasts

Activated Osteoclasts

OPG=osteoprotegerin; RANK=receptor activator of nuclear factor kappa-B; RANKL=RANK Ligand
1. Adapted from: Boyle WJ, et al. Nature. 2003;423:337-342.
2. Eghbali-Fatourechi G, et al. J Clin Invest. 2003;111:12211230.
3. Hofbauer LC, et al. JAMA. 2004;292:490-495.

Panel 4

What have we learned from SWAN?

Study of Women's health Across the Nation. Longitudinal study of 3302 women followed from perimenopause >20 years. 2407 BMD subset.

- Accelerated bone loss occurs from 1-2 years before the final menstrual period till 3-4 years after the final menstrual period at both the lumbar spine and femur neck.

- Bone loss is maximal in the period one year before FMP and for 2 years after FMP.

- Cumulative BMD loss averages during this time were 10.6% at lumbar spine and 9.1% at the femur neck amounting to a lowering of about 1 standard deviation(1 T-score unit).

Greendale et al. J Bone Miner Res. 2012:27:1118

Slide 1

What have we learned from SWAN?
Study of Women's health Across the Nation. Longitudinal study of 3302 women followed from perimenopause >20 years. 2407 BMD subset.

BMD at time of menopause is a highly significant predictor of the risk of future osteoporosis as significant bone loss (and loss of bone structure) will lead to earlier attainment of fracture thresholds.

Other risk factors
- Low BMI
- Rate of bone loss
- History of fracture
- Family history of osteoporosis/fractures
- Medical conditions associated with bone loss

Zaitlin et al. Arch Osteoporos. 2023;18:78.

Slide 2

**Bone Mineral Density, Menopause and Age**

Key Points:

- Bone loss is a continuous process beginning in midlife, including an interval of relatively rapid loss that occurs across the menopausal transition

Slide 3
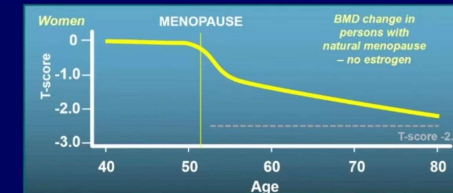
Key Points:

- Bone loss in perimenopausal women occurs before increases in bone resorption or declines in serum estradiol (1,2)
- In SWAN, higher serum FSH was weakly correlated with increased NTX levels and rates of bone loss (3)
- FSH inhibitors prevent bone loss in ovariectomized rats (4)
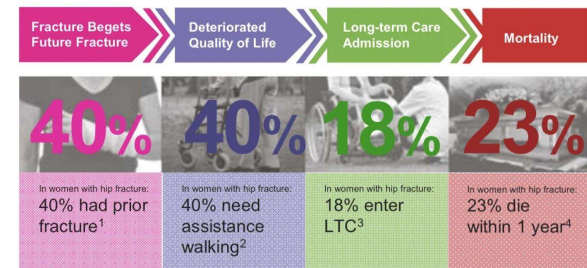 - clinical trials are evaluating this therapy in humans
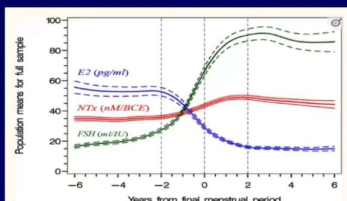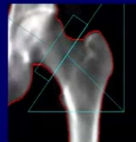
1. Ausmanas MK et al. *Climacteric* 2007;10: 427–37
2. Zaidi M et al. *Curr Rheumatol Rep* 2009;11: 191–5
3. Sowers MR et al. *J Clin Endocrinol Metab* 2013;98: 2854–63
4. Liu S et al. *J Endod* 36: 658–63

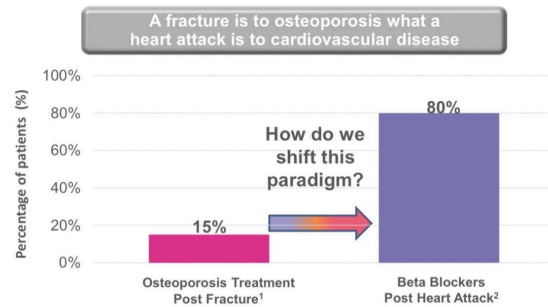## Slide 4

Timeline: Consequences post fracture

Lifetime risk of hip fracture in women >50 is **12.1%**[5]

Fracture Begets Future Fracture	Deteriorated Quality of Life	Long-term Care Admission	Mortality
40%	**40%**	**18%**	**23%**
In women with hip fracture: 40% had prior fracture[1]	In women with hip fracture: 40% need assistance walking[2]	In women with hip fracture: 18% enter LTC[3]	In women with hip fracture: 23% die within 1 year[4]

1. Hajcsar EE, et al. CMAJ 2000;163:819-822; 2. Cooper C. Am J Med. 1997:103:12S-19S; 3. Jean S, et al. J Bone Miner Res. 2013; 28:360-71; 4. Ioannidis G, et al. CMAJ 2009;181: 265-271; 5. Hopkins RB, et al. Osteoporos Int. 2012; 23:921-927.

Slide 1

Which Raises the Question: Why do 80% of Patients Post-MI vs. 15% Post Fracture Leave the Hospital on Treatment?

> A fracture is to osteoporosis what a heart attack is to cardiovascular disease

How do we shift this paradigm?

Bar chart:
- Osteoporosis Treatment Post Fracture[1]: 15%
- Beta Blockers Post Heart Attack[2]: 80%

Y-axis: Percentage of patients (%), 0%–100%

1. Bessette L, et al. Osteoporos Int. 2008;19:79-86.
2. Austin PC, et al. CMAJ. 2008;179:895-900.

Slide 2

Definition of Osteoporosis

A systemic skeletal disease characterized by **low bone mass** and **microarchitectural deterioration** of bone tissue leading to enhanced **bone fragility** and a consequent **increase in fracture risk** when falling from own body height
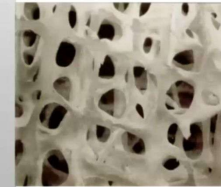
Normal bone | Osteoporosis

Consensus development conference. Am J Med 1993;94:646-650

Slide 3

- Osteoporosis is the most common bone disorder affecting humans
- The risk of hip fracture doubles for every 5- to 6-y increase in age from ages 65-85 y
- Of the 10 million Americans estimated to have osteoporosis, 8 million are women (80%)
- 1 in 2 women aged older than 50 y will sustain osteoporosis-related fracture in their lifetimes
- A prior low-trauma fracture (fragility fracture) is also a diagnosis of osteoporosis regardless whether dual energy x-ray absorptiometry (DXA) is available or reported
  — Excludes fingers, toes, face, skull, or pathologic or traumatic fractures

Kim SH, et al. *Arthritis Care Res (Honoken)*. 2012;64(5):751-75.7

Slide 4

Latest recommendations for screening
The U.S. Preventive Task Force (USPSTF)
JAN 14 2025 JAMA

Recommendation Summary

Population	Recommendation	Grade
Women age 65 years or older	The USPSTF recommends screening for osteoporosis to prevent osteoporotic fractures in women age 65 years or older.	B
Postmenopausal women younger than age 65 years with one or more risk factors for osteoporosis	The USPSTF recommends screening for osteoporosis to prevent osteoporotic fractures in postmenopausal women younger than age 65 years who are at increased risk for an osteoporotic fracture as estimated by clinical risk assessment.	B

Screening is defined as central DXA examination with or without risk factors

Risk factors for fracture

For the clinical risk factors a yes or no response is asked for. If the field is left blank, then a "no" response is assumed. See also notes on risk factors.
The risk factors used are the following:

Age	The model accepts ages between 40 and 90 years. If ages below or above are entered, the programme will compute probabilities at 40 and 90 year, respectively.
Sex	Male or female. Enter as appropriate.
Weight	This should be entered in kg.
Height	This should be entered in cm.
Previous fracture	A previous fracture denotes more accurately a previous fracture in adult life occurring spontaneously, or a fracture arising from trauma which, in a healthy individual, would not have resulted in a fracture. Enter yes or no (see also notes on risk factors).
Parent fractured hip	This enquires for a history of hip fracture in the patient's mother or father. Enter yes or no.
Current smoking	Enter yes or no depending on whether the patient currently smokes tobacco (see also notes on risk factors).
Glucocorticoids	Enter yes if the patient is exposed to oral glucocorticoids or has been exposed to oral glucocorticoids for more than 3 months at a dose of prednisolone of 5mg daily or more (or equivalent doses of other glucocorticoids) (see also notes on risk factors).
Rheumatoid arthritis	Enter yes where the patient has a confirmed diagnosis of rheumatoid arthritis. Otherwise enter no (see also notes on risk factors).
Secondary osteoporosis	Enter yes if the patient has a disorder strongly associated with osteoporosis. These include type I (insulin dependent) diabetes, osteogenesis imperfecta in adults, untreated long-standing hyperthyroidism, hypogonadism or premature menopause (<45 years), chronic malnutrition, or malabsorption and chronic liver disease.
Alcohol 3 or more units/day	Enter yes if the patient takes 3 or more units of alcohol daily. A unit of alcohol varies slightly in different countries from 8-10g of alcohol. This is equivalent to a standard glass of beer (285ml), a single measure of spirits (30ml), a medium-sized glass of wine (120ml), or 1 measure of an aperitif (60ml) (see also notes on risk factors).
Bone mineral density (BMD)	BMD of the femoral neck is entered either as a T-score or as a Z-score. In patients without a BMD test, the field should be left blank (see also notes on risk factors).

Why is FRAX without DXA not appropriate at peri/post menopause

- FRAX is based on risk factor for fracture.

- DXA BMD is based on risk for osteoporosis

Fracture Risk Assessment Tool: FRAX

- FRAX helps identify women with osteopenia at high risk of fracture who should be treated

- Uses epidemiologic risk factors

  - independently associated with poor bone quality, falls, fracture

  - ....Doesn't get at bone quality directly

High Risk of Fracture: ≥ 20% Major osteoporotic ≥ 3% Hip fracture

https://frax.shef.ac.uk/FRAX/tool.aspx?country=9

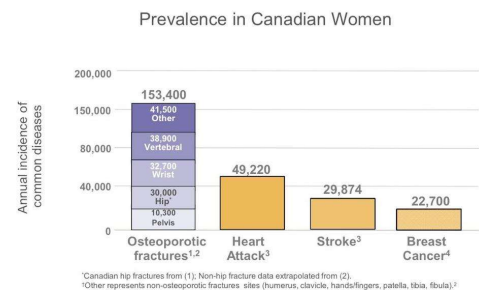## BONE HEALTH: *It is all about PREVENTION and having a lifelong plan.*

Identification of those at risk of low bone density

- Tools such as FRAX can be useful, even without information on actual bone density
- Risk factors such as age, gender, BMI and absolute weight, previous fracture, smoking, family hx, chronic disease, alcohol use, medications are taken into consideration
- ★ Lifestyle modification (diet, exercise, Vitamin D) will not prevent the early menopause bone loss, will not significantly increase BMD in postmenopausal women and will not be considered adequate treatment for women with osteoporosis

Pharmacotherapy—prevention or treatment?

- ★ Guidelines generally don't recognize the effect of menopause transition-related bone loss and are focused on treating osteoporosis to prevent fracture, not prevention of bone loss
- MHT has been shown to prevent bone loss, and even increase density from 2-5%. This is dose dependent and product specific, and after discontinuation, bone loss of 3-6% in the first year is seen
- MHT may be considered for this (indication) in appropriately selected individuals[1,2]

Fractures from Osteoporosis are more Prevalent than Heart Attack, Stroke and Breast Cancer Combined[1]

Prevalence in Canadian Women

Annual incidence of common diseases

- Osteoporotic fractures[1,2]: 153,400 (41,500 Other; 38,900 Vertebral; 32,700 Wrist; 30,000 Hip*; 10,300 Pelvis)
- Heart Attack[3]: 49,220
- Stroke[3]: 29,874
- Breast Cancer[4]: 22,700

*Canadian hip fractures from (1); Non-hip fracture data extrapolated from (2).
*Other represents non-osteoporotic fractures sites (humerus, clavicle, hands/fingers, patella, tibia, fibula).[2]

1. Leslie WD, et al. Osteoporos Int. 2010; 21:1317-1322; 2. Burge J, et al. J Bone Miner Res. 2007;22:465-475;
3. Canadian Institute for Health Information (2009) Health Indicators; 4. Canadian Cancer Society. 2009.

Risk for Osteoporosis - new data

Dr. Michael McClung

Key Points:

- Strongest risk factors for developing osteoporosis are
  - advanced age
  - body weight
  - medical problems causing bone loss
  - history of fracture
  - family history of osteoporosis

- BMD at menopause is a strong risk factor for fracture later in life
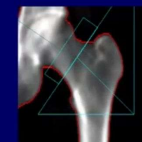
Baseline characteristic	Not diagnosed N=1572	Diagnosed N=113	P value
Body weight Kg	72.6+/-19.1	65.0+/-18.4	<0.0001
BMI	27.4+/-6.7	25.2+/-6.9	0.0006
Maternal history of osteoporosis	14.1%	23.9%	0.0146
Lumbar spine BMD	1.08+/-0.13	0.95+/-0.13	<0.0001
Total hip BMD	0.96 ± 0.14	0.85+/-0.14	<0.0001

- In a subset of women in SWAN, baseline pre- or perimenopausal characteristics were evaluated for predicting the clinical diagnosis of osteoporosis over follow-up of 10 years
- Small size and BMD at the time of menopause were highly significant predictors of the likelihood of being diagnosed with osteoporosis

Zeitlin J et al. Arch Osteoporos 2023 Jun 5;18:78

Approach to Bone Health in the Perimenopause and Postmenopause

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So we have identified risk factors and the gravity of bone loss, now let's shift to talk about prevention.

North American Menopause Society (now The Menopause Society)

- "Estrogen or bisphosphonates can be considered to prevent bone loss in young postmenopausal women with low BMD (T-score <1) and other risk factors for fracture (eg, family history) who do not meet criteria for osteoporosis treatment."

McClung M et al. Menopause

Preventing Bone Loss in Young Postmenopausal Women: *General Measures*

Key Points:

- It would be ideal – and most women want to believe – that good nutrition, regular physical activity and avoiding bad habits are sufficient to prevent bone loss in early menopause

While general measures are important for overall health,
no non-pharmacological intervention prevents
perimenopausal bone loss

Key Points

- In the WHI studies, estrogen with or without progestin significantly reduced the risk of vertebral, hip and other fractures in a population with low fracture risk

E only:
- Mean age 63.6 years
- 14% had previous fracture
- Mean LS T-score -1.16
- Mean TH T-score -0.81

E+P study
- Mean age 63.6 years
- 39% had previous fracture
- Mean LS T-score -1.28
- Mean TH T-score -0.92

	Risk reduction	
Fracture type	E only	E + P
Vertebral	39%	34%
Hip	38%	34%
Total	30%	24%

E = estrogen; E+P = Conjugated equine estrogen + medroxyprogesterone acetate
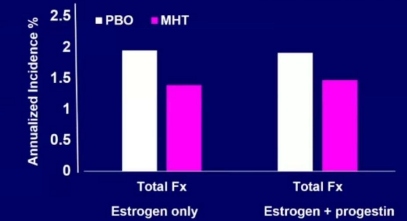
Rossouw JE et al. *JAMA* 2002;288:321
Anderson G L et al. *JAMA* 2004;291:1701

***BONE HEALTH:* It is all about PREVENTION**

and having a lifelong plan.

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Preventing vs Treating Osteoporosis

Osteoporosis treatment

Identify patients at risk of fracture
Treat to prevent fractures

vs

Osteoporosis prevention

Identify women at risk for osteoporosis
Treat to maintain BMD

Therapies approved for osteoporosis prevention
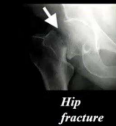*All are anti-remodeling agents that inhibit bone turnover*

- estrogen, oral or transdermal
- conjugated estrogen 0.45 mg daily with bazedoxifene 20 mg daily
- raloxifene 60 mg po dailypo daily
- tibolone 0.625 mg

- Bisphosphonates, oral and IV
  - alendronate po 35 mg/week
  - risedronate po 35 mg/week
  - ibandronate po 150 mg/month
  - zoledronate 5 mg IV Q 2 years

Why is Bone Quality Important ?

- 1 in 3 women age 50+ have a fragility fracture
  - Trauma = fall from standing height or less
- Pain, disability, cost, increase risk of death after hip fracture
- Assess bone quality to
  - Identify those at risk before a fracture (or subsequent fracture) occurs

Vertebral fracture

Hip fracture

http://www.iofbonehealth.org/what-osteoporosis-0; http://www.4bonehealth.org/world-osteoporosis-day-stop-at-one/

Muscle

Impact of Sarcopenia

Postmenopausal women with sarcopenia have 13 times the risk of having osteoporosis as those without sarcopenia.

Musculoskeletal Syndrome of Menopause

What is MSM?

- Declining levels of estradiol leads to five primary MSK changes:
  - 1. inflammation (tendinopathy, arthralgia)
  - 2. sarcopenia (loss of 0.6% of muscle mass per year)
  - 3. decreased satellite cell proliferation (inability to gain muscle)
  - 4. decreased bone mineral density
  - 5. arthritis (cartilage and subchondral bone)

Slide 1: Mortality

Mortality

Survival time according to sarcopenic obesity status in participants with BMI ≥27 (n=2918)

- Lower muscle function alone had 29% increase in all-cause mortality
- Sarcopenic obesity had 94% higher risk of all-cause mortality
- Highest mortality risk in high %BF with both low SMM *and* poor muscle function
- Limitation: homogenous population

Legend:
- No sarcopenic obesity
- Normal HGS and altered BC (1 component)
- Normal HGS and altered BC (2 components)
- Low HGS and normal BC
- Low HGS and altered BC (1 component)
- Low HGS and altered BC (2 components)

Benz E, Pinel A, Guillet C, et al. Sarcopenia and Sarcopenic Obesity and Mortality Among Older People. JAMA Netw Open. 2024;7(3):e243604

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Slide 2: Sarcopenia
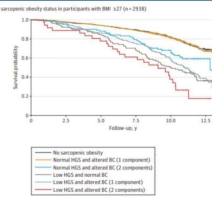
Sarcopenia

- Peak muscle mass is achieved at age 30, and decreases by 3-8% per decade until age 75, when loss may be 1% per year[1]
- Sarcopenia is age related loss of lean muscle mass and is characterized by atrophy of muscle fibres with increase in intramuscular adipose tissue[2]
- Sarcopenia is **probable** when low muscle strength is detected, **diagnosed** when the quality and quantity of muscle is low, and considered **severe** when low muscle strength and performance are present[3]

Definition of sarcopenia from 2022

1. International Journal of Women's Health 2022;14:805-809 2. Climacteric epub 30 July 2024 3. Age Ageing 2019;48(1):16-31

The Menopause Society

Slide 3: Musculoskeletal Syndrome of Menopause

Musculoskeletal Syndrome of Menopause

The Menopause Society

Taylor & Francis

CLIMACTERIC
https://doi.org/10.1080/13697137.2024.2390341

REVIEW ARTICLE

OPEN ACCESS

The musculoskeletal syndrome of menopause

Vonda J. Wright[a], Jonathan D. Schwartzman[a], Rafael Itinoche[a] and Jocelyn Wittstein[b]

[a]University of Central Florida College of Medicine, Orlando, FL, USA; [b]Duke University School of Medicine, Durham, NC, USA

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  - 5. arthritis (cartilage and subchondral bone)

The Menopause Society

Slide 4: Women need more protein to maintain SMM

Women need more protein to maintain SMM.

Changes in dietary intake:
- Decreased appetite
- Changes in taste and smell
- Poor dentition/trouble swallowing
- Food insecurities

Macronutrient changes
- 10-25% of adults consume <0.8g/kg/day protein
- 5-9% older adults consume < EAR of protein

Micronutrient changes
- Polypharmacy- PPI/H2 blockers, metformin
- NHANES- older women deficient in calcium, magnesium and potassium and lower consumption of vitamins D, E and K

Khanal et al examined 281 PMP women >60 yo, threshold of 1.17 g/kg/d protein required to maintain high SMM and consuming more than this threshold was associated with lower BMI, lower fat mass, higher MM and improved QOL scores

Khanal, Praval et al. "Dietary Protein Requirement Threshold and Micronutrients Profile in Healthy Older Women Based on Relative Skeletal Muscle Mass." Nutrients vol. 13.9 3076. 1 Sep. 2021
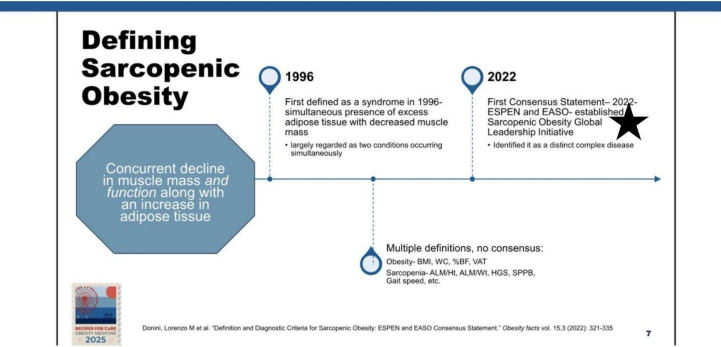
Defining Sarcopenic Obesity

1996
First defined as a syndrome in 1996- simultaneous presence of excess adipose tissue with decreased muscle mass
- largely regarded as two conditions occurring simultaneously

2022
First Consensus Statement– 2022- ESPEN and EASO- established Sarcopenic Obesity Global Leadership Initiative
- Identified it as a distinct complex disease

Concurrent decline in muscle mass *and function* along with an increase in adipose tissue

Multiple definitions, no consensus:
Obesity- BMI, WC, %BF, VAT
Sarcopenia- ALM/Ht, ALM/Wt, HGS, SPPB, Gait speed, etc.

RECIPES FOR CARE OBESITY MEDICINE 2025

Donini, Lorenzo M et al. "Definition and Diagnostic Criteria for Sarcopenic Obesity: ESPEN and EASO Consensus Statement." Obesity facts vol. 15,3 (2022): 321-335

7

Assess muscle weakness:

Establish altered skeletal muscle functional parameters BEFORE assessing altered body composition

	Caucasian Male	Caucasian Female	Asian Male	Asian Female
Hand Grip Strength	<27 kg	<16 kg	<28 kg	<18 kg
Knee Extension Strength	<0.40 kg/kg Strength/W	<0.31 kg/kg Strength/W	<18 kg	<16 kg
Chair stand test	≥ 17 seconds			

RECIPES FOR CARE

Donini et al. , Obes Facts 2022; 15: 321-335, ESPEN and EASO Consensus Statement

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Table 5 Increases in BMD and associated estimated fracture risk reduction (FNIH Study)

% Increase in BMD	% Reduction in Vertebral Fracture	% Reduction in Hip Fracture
Total hip	Total hip	Total hip
2%	28%	16%
4%	51%	29%
6%	66%	40%
Femoral neck	Femoral neck	Femoral neck
2%	28%	15%
4%	55%	32%
6%	72%	46%
Lumbar spine	Lumbar spine	Lumbar spine
2%	28%	22%
4%	62%	38%
6%	79%	51%

Note: Larger improvements in DXA-based BMD are associated with greater reductions in fracture risk, particularly for vertebral and hip fractures

Caption

forearm BMD, or as dictated by clinical judgment [59, 62...

It is important to note that DXA of the lumbar spine difficult to accurately interpret. This is in large part degenerative changes in the lumbar spine, very comm older adults, that are typically characterized by localiz proliferation. In this setting, DXA findings can overes spinal BMD and underestimate fracture risk. Patient degenerative spinal changes may benefit from trabecul umetric BMD (vBMD) measured with quantitative con tomography (QCT), which is less affected by these ch although this technology is not widely available [63, 6...

These diagnostic classifications should not be appl everyone. Premenopausal women, men less than 50 y age, and children cannot be diagnosed on the basis of tometric criteria alone. In populations between 20 a years of age, the ISCD recommends that ethnicity- or adjusted Z-scores be used instead. Z-scores of − 2.0 or are classified as low BMD for chronological ag those above − 2.0 classified as within the expected

The fracture liaison service model of care

The FLS system of care in the USA was developed through the National Bone Health Alliance (NBHA), a public-private partnership of 50-plus member organizations along with representatives from the Centers for Disease Control and Prevention, Centers for Medicare & Medicaid Services, National Institutes of Health, and the US Food and Drug Administration [13].

In an FLS system, a multidisciplinary team of healthcare providers works in coordination to implement evidence-based diagnostic and treatment protocols to follow for post-fracture care. The process is overseen by an FLS coordinator (a nurse or other allied health professional) who is charged with overall organization, tracking, and documentation of post-fracture patient care. It is a simple concept, yet its implementation is complicated, requiring planning, division of responsibilities, coordination of staff, systematic and consistent patient monitoring, and knowledge of billing and coding technicalities. Beca management of osteoporosis is a multidimensional and lo term undertaking, treatment plan coordination is critical to its

Caption

The goal of the FLS model, like any practice management program is to ensure patients with a fracture are evaluated and treated for their underlying osteoporosis, while making the best use of clinician time and expertise. Creative approaches optimize use of electronic medical records and practice management software, delegate tasks, automate as much as possible, take advantage of the patient's waiting room time, and team up colleagues, specialists, allied health professionals, and support staff. There are many tools available for every type of practice, from sole practitioner to hospital-based multispecialty clinic.

Recommendations for secondary fracture prevention

In 2019, a coalition convened by the ASBMR published Clinical Recommendations for Secondary Fracture vention to treat the osteoporosis in women and men d 65 years or older who suffer a spine or hip frac ture. Here is a concise summary of the coalition's rec-

2090

indicate that 5 years of HT may decrease vertebral fractures by 35 to 50% and non-vertebral fractures by about 25%. Ten or more years of use might be expected to decrease the rate of all fractures by about 50%.

Vitamin D with Levels

Calcium (split up)

3 days of week weight training

Maybe creatine

Hormones, know your history.

Secondary fall prevention

IF YOU ARE NOT WEIGHTLIFTING , YOU ARE CHOOSING CHRONIC DISEASE

CLINICAL RESOURCES

1. MENOPAUSE.ORG
2. BHOF
3. INTERNATIONAL MENOPAUSE SOCIETY
4. PODCASTS: DR. LAUREN STREICHER
   DR. GABRIELLE LYONS
   DR. MARY CLAIRE HAVERS
   DR.PETER ATTIA