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The Prevention of Osteoporosis and Sarcopenia in Older Adults

Healthy Aging: Prevention of Osteoporosis & Sarcopenia

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Tables 5

Key Points. Osteoporosis and sarcopenia are both common in older adults.

Osteoporosis and sarcopenia can both cause disability, functional impairment and dependency.

Osteoporosis and sarcopenia can be prevented from occurring, identified in their early stages and treated to reduce progression and in some instances, reverse existing disease.

Why does this paper matter?

This paper provides up to date information for geriatrics care providers to help them promote optimal musculoskeletal health for older adults.

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Abstract

Osteoporosis and sarcopenia are common in older adults. Osteoporosis is a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture. Bone fractures can result in changes in posture, pain, the need for surgical repair and functional impairment.

Sarcopenia is the progressive and generalized loss of skeletal muscle mass, strength and/or physical performance. Older adults with sarcopenia experience increased risk of frailty, disability, hospitalizations, mortality, and a reduced quality of life. In this narrative review we provide guidance regarding the prevention of both osteoporosis and sarcopenia, including interventions that prevent both conditions from occurring, recommended screening and treatment to prevent progression.

Introduction

Musculoskeletal health is an important component of healthy aging. Bone and muscle are the two most important components of the musculoskeletal system. Though age-related changes in both bone and muscle structure do occur, diseases that either directly or indirectly affect bone and muscle, and age associated lifestyle changes, have a greater impact on bone and muscle health. Poor bone and muscle integrity and strength predispose older adults to impaired function, disability, dependency, falls, pain, high medical care costs and death. Osteoporosis

and sarcopenia are common in older adults. This review addresses the prevention of osteoporosis and sarcopenia for older adults.

Osteoporosis

Osteoporosis is defined as a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture.¹ Osteoporosis is also defined by the World Health Organization (WHO) as bone mineral density (BMD) which is less than 2.5 standard deviation (SD) below the mean level for a young adult.² It may also be diagnosed based on the occurrence of a fragility fracture. Osteopenia is present when BMD is between 1.0 and 2.5 SDs below the mean level for a young adult. Bone mass is regulated by several mechanisms including; bone cells (osteoclasts, osteoblasts and osteocytes), hormones (vitamin D and parathyroid hormone) growth factors (FGF-23), skeletal loading and gene polymorphisms. These mechanisms maintain bone density in young adults, but with increasing age bone mass begins to decrease at a rate of approximately 0.5% per year.³

Epidemiology & Clinical Significance

Osteoporosis is common in older adults, especially older women.⁴ Risk factors for osteoporosis are listed in Table 1. Alterations in bone density and architecture results in fragile bone. Micro fractures in the vertebral spine result in loss of height and curvature of the spine. Low bone

density also results in long bone fractures that can occur with minimal trauma. These fractures are painful, may require surgical repair and can result in mortality or long-term disability. Common fracture sites are the hip, wrist, spine, pelvis and upper arm. Almost one third of fractures occur in older men.⁵

Primary Prevention.

Achieving good bone density when younger may be an important way of preventing low bone density and associated complications when older.⁶

Nutrition

The efficacy of calcium supplementation and the ideal serum level of vitamin D to prevent osteoporosis are controversial, with different recommendations from different sources. A meta-analysis from the National Osteoporosis Foundation (NOF) on the use of combined calcium and vitamin D supplementation showed a 15% reduced risk of total fractures and a 30% reduced risk of hip fractures.⁷ A meta-analysis of randomized studies in postmenopausal women 60 years of age and older, found a significant reduction in hip and nonvertebral fractures with vitamin D supplementation at doses of 700IU to 800IU per day.⁸ However the United States Preventive Services Task Force (USPSTF) concludes that the current evidence is insufficient to assess the balance of the benefits and harms of vitamin D and calcium supplementation, alone or combined, for the primary prevention of fractures in men and premenopausal women.⁹ Table 2 It is worth noting however that the USPSTF recommendations may not be applicable for patients at high risk for osteoporosis, including those who reside in

long-term care facilities. For some high risk patients' supplementation with vitamin D may still be appropriate.¹⁰ Calcium supplements can cause constipation in some patients and excessive vitamin D intake can result in hypercalcemia.

There is limited evidence regarding the impact of a specific diet on bone density, including eating foods rich in phytoestrogens.¹¹

Exercise

There is evidence for both older women and older men that weight bearing exercise and progressive resistance training can help maintain and in some cases increase bone density.¹²

Recommended exercises can be adjusted based on the estimated risk of developing osteoporosis and the ability of the person to perform the activity. Impact loading (jumping and hopping), progressive resistance training (PRT) and balance training have been demonstrated to help maintain bone density and prevent fragility fractures.¹²⁻¹⁴

Tobacco and Alcohol

Both smoking cigarettes and drinking excessive amounts of alcohol have been demonstrated to reduce bone density.¹⁵

High Risk Medications

Where and when possible medications which reduce bone density should be avoided or minimized. Table 3

Screening

The appropriate time to initiate screening for osteoporosis is determined by age, gender and clinical risk assessment.

Risk Assessment

The most commonly used clinical fracture risk assessment is the Fracture Risk Assessment Tool (FRAX[®]) developed by the University of Sheffield.²¹ FRAX[®] is a 10-year prediction model for hip or major osteoporotic fractures. FRAX[®] integrates eight clinical risk factors, which in addition to age and sex, contribute to a 10-year fracture risk estimate independently of BMD. Table 2 BMD from the femoral neck is an optional input variable when FRAX is used to calculate 10-year fracture probability. FRAX has been demonstrated to predict fracture risk for both women and men, and has the most utility in clinical decision making around treatment in those with T-scores that meet criteria for osteopenia.

Bone Imaging

The USPSTF recommends bone density screening in women 65 years and older.²² Dual-Energy X-Ray Absorptiometry (DXA) is the preferred method of screening for low bone density. It is not clear how often older women should have their bone density measured. There are data which indicate that a 15 year interval is appropriate for women who have an initial normal bone density or mild osteopenia, 5 years for women with moderate osteopenia, and 1 year for women with advanced osteopenia.²³ There is no universal agreement about the use of screening for low bone density with DXA in men. The USPSTF concluded that the evidence was insufficient to assess the balance of benefits and harms of screening in men.²² The NOF recommends that high risk men should be screened including those with hypogonadism and

those over 70 years of age.²⁴ In the United States, Medicare will pay for a screening bone density by DXA every two years for women 65 years of age and older and for men 70 years of age and older.

The Prevention of Further Bone Loss in Patients with Osteoporosis.

All of the interventions that prevent osteoporosis, including vitamin D, physical exercise, avoiding excessive alcohol intake, not smoking and avoiding or minimizing the use of medications that reduce bone density, also help prevent further loss of bone density for those who have osteoporosis.

Medications

There are a number of pharmacologic options for patients diagnosed with osteoporosis. These may be broadly divided into four groups; bisphosphonates, monoclonal antibody targeted against the *receptor activator of nuclear factor- κ B ligand (RANKL)*, monoclonal antibody targeted against sclerostin and anabolic therapy. Table 4 The NOF recommends pharmacologic treatment for patients with osteoporosis based on either bone density measurement or the occurrence of a fragility fracture.²⁴

Bisphosphonates.

Bisphosphonates are pyrophosphate analogs with a high affinity for bone mineral matrix, and incorporate into sites of active bone remodeling as is seen in osteoporosis. In the bone mineral they are taken up by osteoclast cells, and through several mechanisms decrease osteoclast-

mediated bone resorption. They may persist in the bone matrix for months to years, and thus, the recommendation for a drug holiday after long-term use. There is compelling evidence that bisphosphonates can preserve and increase bone density in patients with osteoporosis while also significantly reducing the incidence of future fractures.²⁵ Several bisphosphonates are available. They differ by frequency of administration and mode of administration. Depending on future fracture risk, bisphosphonate treatment should be considered for discontinuation between 5 and 10 yrs. after initiation. There are significant side effects associated with the use of bisphosphonates including esophagitis, spontaneous long bone fractures and osteonecrosis of the jaw, most commonly of the mandible.

Monoclonal antibody targeted against *RANKL*

RANK-L is a cytokine required for the formation, function, and survival of osteoclasts, which breakdown bone. When denosumab binds to RANK-L, it prevents RANKL from binding with its receptor RANK on osteoclast precursors, and reversibly inhibits osteoclast-mediated bone resorption. It is administered every 6-months by subcutaneous injection in a clinical setting. There is evidence that denosumab reduces future fracture risk in both older women and older men with osteoporosis.²⁶ To prevent a rapid decrease in bone density and to mitigate an increased risk of vertebral fractures, particularly in those with a history of prior vertebral fractures, patients should be transitioned to another antiresorptive medication when denosumab is discontinued. Side effects include possible infections of the upper respiratory and GI tracts.

Monoclonal antibody targeted against sclerostin

Romozosumab works by binding and inhibiting activity of sclerostin, a product of the SOST gene, produced by osteocytes and part of the Wnt signaling pathway. It promotes bone formation, decreases bone resorption and reduce fracture risk.²⁷ In April 2019 the Food and Drug Administration (FDA) approved romozosumab to treat postmenopausal women with osteoporosis at high risk for fracture. This includes women with a history of a fracture, multiple risk factors for fracture, those who cannot take other osteoporosis therapies or those for whom other treatments have not been successful. It is administered by SC injection every month (in 2 injections) for 12 months. Similar to denosumab, discontinuation must be followed by an anti-resorptive therapy in order for gains in BMD and fracture efficacy to be maintained. Further, romozosumab may increase risk of cardiovascular events and side effects include joint pain and headaches.²⁸

Anabolic Therapy

Anabolic therapy, including teriparatide (recombinant parathyroid hormone) and abaloparatide (a synthetic analogue of PTH-related protein) are unique therapies that produce large increases in bone mass through stimulation of bone formation ahead of bone resorption. Both of these agents significantly increase bone density at all sites (with exception of the radius) and significantly reduce the risk of new vertebral fractures and non-vertebral fractures in postmenopausal women.^{29, 30} Patients who have prevalent vertebral fractures or very low T-scores (below -3.0) should be considered for these agents. They are given as daily injections and are approved for use for up to 24-months in total. When they are discontinued they need to be followed by anti-resorptive therapy in order to maintain BMD gains that occurred during treatment. The FDA requires a black box warning on their label because of concerns regarding

an increased risk of osteosarcoma. These medications are contraindicated in patients who have had radiation therapy, Pagets disease of bone and an elevated alkaline phosphatase of unknown origin.

Sarcopenia

Introduction

Sarcopenia is the progressive and generalized loss of skeletal muscle mass, strength and/or physical performance.³¹ Since sarcopenia was coined by Rosenberg in the late 80's,³² a number of sarcopenia definitions have emerged; with the currently accepted definitions listed in Table 5. The rationale for the multitude of diagnostic criteria are due to the differing body mass phenotypes between populations and ethnicities. It is important to note the accepted definitions also used different cut points for sarcopenia components such as muscle mass, strength and/or physical performance, with some studies using mean/median population values and other cut points predictive of future outcomes.^{31,33-35} Thus a clinical assessment of sarcopenia should first involve identifying a single set of diagnostic criteria relevant to the population, and thereafter that criteria should be consistently applied as prevalence rates of sarcopenia can vary greatly within, and between, definitions.³⁶ The Sarcopenia Definitions and Outcomes Consortium (SDOC)³⁵ was created in 2020 and it is recommended that their diagnostic criteria are followed for US populations, especially when a measurement of muscle mass is not available in clinical practice. The SDOC criteria have been validated in low and high risk populations.³⁷ As the sarcopenia field evolves, these definitions will continue to be revised.

Epidemiology & Clinical Significance

Noticeable losses of muscle mass and strength begin in middle age (40-50 years) and by age 80, an older adult may have lost a large portion of muscle mass (~30%) and strength (~50%) which predisposes to sarcopenia.³⁴ As the world population continues to grow with an increase in the oldest old, the prevalence of sarcopenia will inevitably increase. It is projected that by 2045, 32 million older adults in Europe will be classified as sarcopenic, a remarkable increase of 64% compared to 2016. In both older Japanese and Italian adults, sarcopenia prevalence was found to increase significantly with advancing age.^{38,39} Between the ages of 70-74 years women report a higher prevalence of sarcopenia than men (2.6 vs and 1.2 %), and among those in their 80s this rises to 31.6% in women and 17.4% men.⁴⁰ An explanation for this disparity between sexes may be due to men possessing greater levels of peak muscle mass and strength than their female counterparts during young adulthood, which may offer protective effects against this muscle disease in later life.⁴¹

Several modifiable (i.e., lifestyle) and non-modifiable (i.e., genetics) risk factors for sarcopenia have been identified. Table 1

A number of chronic diseases including cardiovascular disease and diabetes are associated with sarcopenia.⁴² There is a bidirectional relationship between osteoporosis and sarcopenia and when either condition is present, screening for the other should be conducted.^{43,44}

For irreversible risk factors, advancing age⁴⁵⁻⁴⁷ along with female sex⁴⁸ are among the leading risk factors. Modifiable risk factors include sedentarism and low protein intake.⁴⁵⁻⁴⁷ Low physical

activity, poor mobility, low body mass index (BMI), smaller calf circumference and lower albumin levels all show a strong association with sarcopenia incidence.⁴⁶ Associated biomarkers include, increased pro-inflammatory cytokines (interleukin-6, tumor necrosis factor alpha and C-reactive protein), low testosterone and insulin-like growth factor 1.^{39,40}

Sarcopenia associates with a number of adverse health outcomes with a recent quantitative analyses of over 30 studies and 40,000 participants demonstrating those with sarcopenia were at a 1.89 and 1.71 increased odds of suffering from a fall or fracture respectively.⁴⁹ Sarcopenic older adults also experience increased levels of frailty, disability, hospitalizations and mortality,^{50,51} and a reduced quality of life.⁵²

Primary Prevention

Both physical activity and nutritional interventions have been demonstrated to prevent sarcopenia. Table 2

Exercise

Resistance exercise (RE) improves muscle mass, strength and physical performance, with attention to protein, amino acids and vitamin D intake providing additive effects in some, but not all, trials⁵³. High intensity RE has been noted to have a larger impact on muscle strength than low intensity RE, with the degree of intensity referring to the amount of resistance used.⁵⁴ However, adjusting training components (sets, repetitions and rest intervals) may partially

compensate for not using high resistance.⁵⁵ Older adults doing RE for the first time should start with less resistance and gradually progress by adjusting training components.

Nutrition

The recommended dietary allowance (RDA) for protein is set at 0.8 grams per kilogram of body-weight per day (g/kg/day) for adults of all ages. However, a higher protein intake in older adults helps maintain muscle mass. A recent umbrella review⁵³ showed low-moderate evidence in favor of supplementing above the RDA with protein, leucine or hydroxymethylbutyrate (HMB) for increases in muscle mass, but inconclusive evidence for muscle strength or physical performance. Vitamin D deficiency is linked to declines in both strength and physical performance.⁵⁶ Vitamin D supplementation in adults ≥ 60 years has demonstrated increased muscle strength and improved balance in those with deficiencies.⁵⁷ As noted above, nutritional interventions to improve aspects of sarcopenia work best when combined with RE.

Screening

The Strength, Assistance with walking, Rise from a chair, Climb stairs and Falls (SARC-F) is a rapid, 5 item screening questionnaire which can detect those at risk for sarcopenia.⁵⁸ It has been demonstrated to have high specificity for predicting functional deterioration, hospitalization, quality of life and mortality.⁵⁹⁻⁶² SARC-F screening should be conducted annually beginning at age 65.⁶³ For a confirmed diagnosis of sarcopenia, a definition can then be employed. Table 5

Prevention of Further Loss of Muscle Mass & Strength in Patients with Sarcopenia

Exercise

A recent systematic review and meta-analysis found strong improvements in appendicular lean mass, strength and physical performance in sarcopenic older adults, following prolonged RE.⁶⁴

Of note, the FrOST study, a randomized controlled trial of older men with

osteopenia/osteoporosis and sarcopenia (termed osteosarcopenia), showed significant

improvements in muscle mass and hip/leg extensor strength and maintenance of lumbar spine

BMD, following 12 months of high-intensity RE, compared to non-exercising controls.⁶⁵ In frail

populations too (>75 years old), evidence for RE is well established, with improvements in gait

speed⁶⁶, lower limb strength⁶⁷, increases in lean mass⁶⁸, and decreases in intramuscular fat⁶⁸, as

well as reversal of frailty.⁶⁶

Nutrition

Supplementation above the RDA with protein, leucine or HMB has shown to augment the

benefits of RE on muscle mass,⁵³ however these effects are maximized with sufficient vitamin D

levels (≥ 50 nmol/L).⁶⁹ For sarcopenic individuals who are not willing to partake in RE or who are

non-ambulatory (i.e., bed ridden, post-hip fracture), protein, leucine or HMB supplementation

has shown to attenuate the loss of muscle mass but the evidence for muscle strength or

physical function is inconclusive.⁵³ Creatine is another nutrient which has received less

attention, although there is consistent evidence in older adults showing enhancements of lean

mass and strength when added to RE.⁵³ Creatine has little effect without RE.⁵³

Medications

Pharmacological treatments for sarcopenia are of increasing interest in clinical trials, although there are currently no approved drugs. These interventions have focused on improving muscle mass via administration of testosterone, selective androgen receptor modulators (SARMS), growth hormones and myostatin inhibitors.⁷⁰ SARMS and myostatin inhibitors, in particular, demonstrate anabolic effects on muscle mass, although equivocal results on strength and mobility.⁷¹ In short, side effects and effectiveness in comparison to inexpensive lifestyle interventions (resistance exercise and nutrition) have impeded their development.⁶⁷

Conclusion

Maintaining good bone and muscle strength promotes healthy aging. Though some changes in bone and muscle may be inevitable with increasing age, there are many interventions that can preserve and in some instances increase both bone and muscle strength in older adults. Good bone and muscle strength promotes good posture, maintains functional independence, reduces pain, reduces falls and reduces fractures and disability associated with falls.

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Table 1. Risk Factors for Osteoporosis & Sarcopenia in Older Adults.

Osteoporosis	Sarcopenia
Older Age	Older Age
Female Gender	Low Educational Level
White Race	Low Income (men)
Low Body Mass Index (BMI)	Low Body Mass Index (BMI)
Genetics	Low Physical Activity
Low Estrogen (women)	Low Protein Intake
Low Testosterone (men)	Diabetes Mellitus
Smoking Cigarettes	Cardiovascular Disease
Heavy Alcohol Intake	Mobility Limitations
Hyperthyroidism	Osteoporosis
Vitamin D Deficiency	
Inadequate Calcium Intake	

Table 2 Internet Resources regarding the Prevention of Osteoporosis and Sarcopenia

Osteoporosis
Prevention
USPSTF. Vitamin D & Calcium Supplementation https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/vitamin-d-calcium-or-combined-supplementation-for-the-primary-prevention-of-fractures-in-adults-preventive-medication
Risk Assessment
FRAX https://www.sheffield.ac.uk/FRAX/tool.aspx?country=9
Screening Guidelines
USPSTF. Screening for osteoporosis https://www.uspreventiveservicestaskforce.org/uspstf/document/RecommendationStatementFinal/osteoporosis-screening
ISCD. Indications for bone mineral density testing https://iscd.org/learn/official-positions/adult-positions/
USPSTF. Screening for Vitamin D deficiency https://www.uspreventiveservicestaskforce.org/uspstf/recommendation/vitamin-d-deficiency-screening
AACE/ACE Guidelines for the diagnosis and treatment of post-menopausal osteoporosis https://journals.aace.com/doi/pdf/10.4158/GL-2020-0524SUPPL
Patient Education Resources
NOF. What is osteoporosis & what causes it https://www.nof.org/patients/what-is-osteoporosis/
NOF. Bone density exam/ testing https://www.nof.org/patients/diagnosis-information/bone-density-examtesting/
NOF. Calcium & Vitamin D https://www.nof.org/patients/treatment/calciumvitamin-d/
NOF. Exercise https://www.nof.org/preventing-fractures/exercise-to-stay-healthy/weight-bearing/
Health In Aging Foundation. Osteoporosis https://www.healthinaging.org/a-z-topic/osteoporosis
Sarcopenia
Risk Assessment
SARC-F Questionnaire https://41e5fc1d-e404-4830-8c07-64690e79acce.filesusr.com/ugd/2a1cfa_b868e55b12a241028d69b9e7a2fce7a8.pdf
Patient Education
Preserve Your Muscle Mass https://www.health.harvard.edu/staying-healthy/preserve-your-muscle-mass

4 Keys to Strength Building and Muscle Mass

<https://www.eatright.org/fitness/training-and-recovery/building-muscle/strength-building-and-muscle-mass>

NCHPAD. Sarcopenia Aging & Resistance Training

<https://www.nchpad.org/1583/6596/Sarcopenia~~Aging~~and~Resistance~Training>

CDC. Growing Stronger. Strength Training for Older Adults

https://www.cdc.gov/physicalactivity/downloads/growing_stronger.pdf?fbclid=IwAR0qhbb3fHVLZ5nhGRkMdsErEGGTiZ5BiSBusezGeFa_79ErJBWVQLlxpHU

USPSTF: United States Prevention Services Task Force. FRAX: Fracture Risk Assessment Tool.

ISCD: International Society for Clinical Densitometry. AACE: American Association of Clinical Endocrinologists. ACE: American College of Endocrinology. NOF: National Osteoporosis

Foundation. SARC-F: Strength, Assistance with walking, Rise from a chair, Climb stairs and Falls.

NCHPAD: National Center on Health, Physical Activity and Disability. CDC: Centers for Disease Control.

Table 3 Medications that decrease bone density.

Long Term Oral Steroid Administration ¹⁶
Aromatase Inhibitors ¹⁷
GnRH Agonists ¹⁷
Thiazolidinediones (TZDs) ¹⁸
Protein Pump Inhibitors (PPIs) ¹⁹
Selective serotonin receptor inhibitors (SSRIs) ²⁰

Table 5. Recommended diagnostic criteria for commonly used sarcopenia definitions

Definition	Year	Lean (Muscle) Mass	Muscle Strength	Physical Performance
Asian Working Group for Sarcopenia (AWGS) ³¹	2020	ALM/h ²	Handgrip strength	Gait Speed <1.0 m/s
		Men <7.0 kg/m ² Women <5.4 kg/m ²	Men <28 kg Women <18 kg	
Revised European Working Group on Sarcopenia in Older Persons (EWGSOP2) ³²	2019	ALM/h ²	Handgrip Strength	Gait Speed ≤0.8 m/s
		Men <7.0 kg/m ² Women <5.5 kg/m ²	Men <27 kg Women <16 kg	
Sarcopenia Definitions and Outcomes Consortium (SDOC) ³³	2020	n/a	Handgrip Strength Men <35.5 kg Women <20 kg	<0.8 m/s

Appendicular lean mass (ALM), corrected for height squared (h²).

TABLE 4: OSTEOPOROSIS MEDICATIONS APPROVED FOR USE IN OLDER MEN AND WOMEN

Medication	DOSING	MEN	WOMEN	FRACTURE EFFICACY		COMMENTS/CAUTIONS
				VERT	NON-VERTEBRAL	
ALENDRONATE	70 mg po Q week	✓	✓	✓	✓	Potential adverse GI side effects Use if Cr Cl > 30 cc/min
RISEDRONATE	35 mg/wk or 150 mg/month	✓	✓	✓	✓	Potential adverse GI side effects Use if Cr Cl > 30 cc/min
ZOLEDRONIC ACID	5 mg/yr or Q other yr	✓	✓	✓	✓	Use if Cr CL > 35 cc/min Caution re; A Fib
DENOSUMAB	60 mg SC q 6-months	✓	✓	✓	✓	Monitor for Hypocalcemia – can use if Cr CL 15-30 cc/min. Also approved for GIOP, women on AIs, men on ADT
TERIPARATIDE	Daily SC 20 ug	✓	✓	✓	✓	Use up to 24-months, Black box osteosarcoma warning, avoid in pts with h/o RT. Can cause orthostatic hypotension, hypercalcemia, hypercalciuria and urolithiasis.
ABALOPARATIDE	Daily SC 80 ug		✓	✓	✓	Use up to 24-months, Black box osteosarcoma warning, avoid in pts with h/o RT. Can cause orthostatic hypotension, hypercalcemia, hypercalciuria and urolithiasis.

ROMOSUZAMAB	Monthly 210 mg SC		√ Dec by 76% c/w PL	√		Monitor for Hypocalcemia if Cr Cl 15-30 cc/min.
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AI = Aromatase Inhibitors (breast cancer Rx)

ADT = Androgen Deprivation Therapy (prostate cancer Rx)