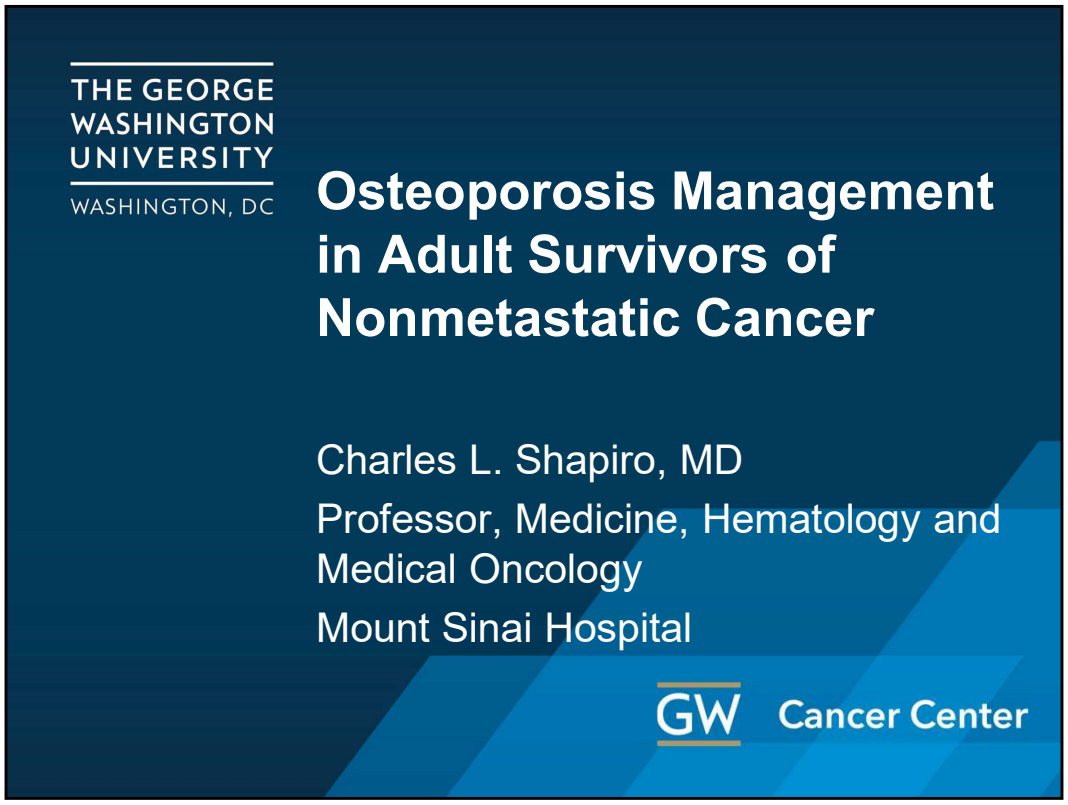

Hello and welcome to this module on osteoporosis management in adult survivors of nonmetastatic cancer. My name is Charles Shapiro and I am a Professor of Medicine, Hematology and Medical Oncology at Mount Sinai Hospital.

Disclosure

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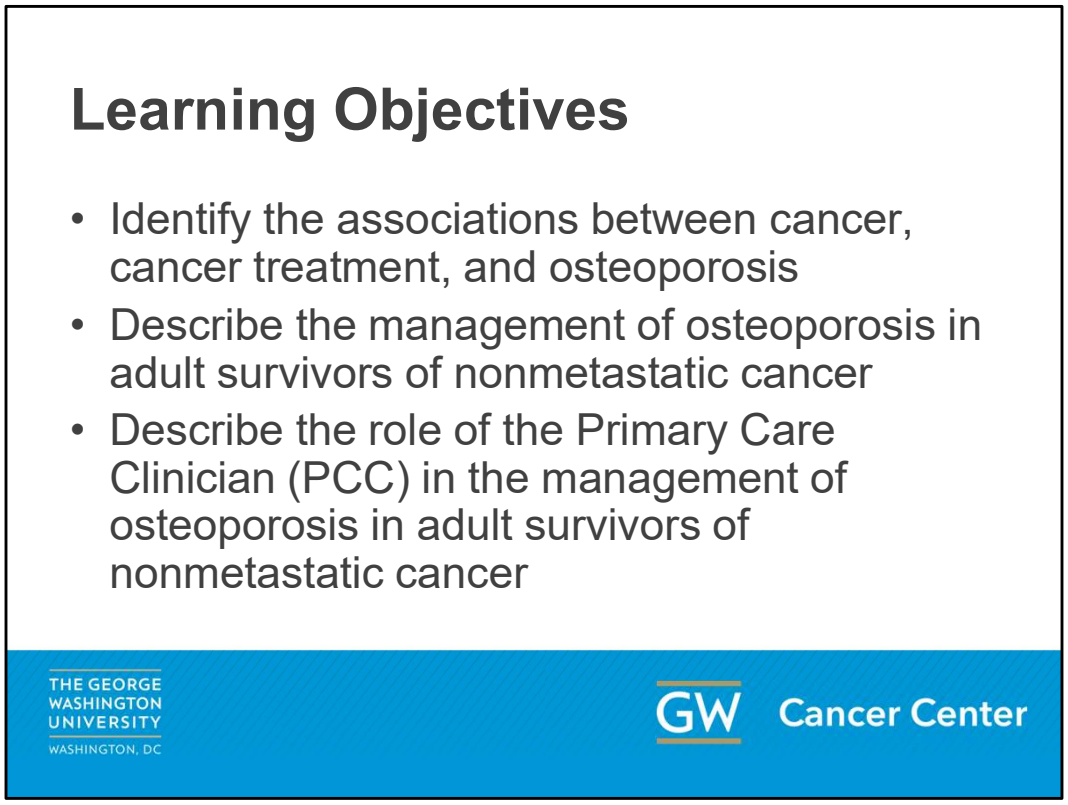
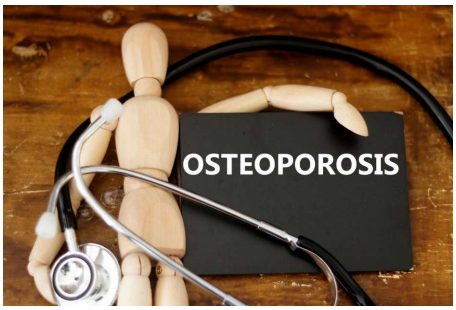


After this module, you will be able to:

- Identify the associations between cancer, cancer treatment, and osteoporosis
- Describe the management of osteoporosis in adult survivors of nonmetastatic cancer
- Describe the role of the Primary Care Clinician (PCC) in the management of osteoporosis in adult survivors of nonmetastatic cancer

What is Osteoporosis?

- The peak bone mass achieved by age 30 minus ongoing losses due to age and menopause
- T-score of -2.5 or less in femoral neck, total hip, or lumbar spine



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Mayo Clinic, n.d.; Shapiro et al, 2019

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Osteoporosis can be thought of as an equation, where you take the peak bone mass achieved by age 30 and subtract the ongoing losses due to age and menopause.

Osteoporosis is assessed by x-rays measuring how many grams of calcium and other essential minerals are present in the bones. A good indication if someone has osteoporosis is T-score, which usually is -2.5 or less in femoral neck, total hip, or lumbar spine areas.

Who Is Susceptible to Osteoporosis?

- At least 40% of postmenopausal women and 15-30% of men will experience a fragility fracture
- Lifestyle factors, including cigarette smoking and excessive alcohol consumption affect bone loss

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Cauley, 2011; Salari et al, 2021; Shapiro et al, 2019

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In the general population, at least 40% of postmenopausal women and 15-30% of men will experience a fragility fracture in their lifetime. Worldwide it has been estimated that more than 200 million people are suffering from osteoporosis.

Risk factors for osteoporosis can be either modifiable or nonmodifiable. For example, modifiable risk factors are low body weight, tobacco and alcohol consumption, calcium deficiency, and long-term use of glucocorticoid (medication that is commonly used to reduce inflammation). Being older, non-Hispanic white or Asian female, having genetic predisposition are non-modifiable risk factors.

Cancer Survivors in the United States

- In 2019, there were approximately 17 million cancer survivors in the US
- It is projected that the number will increase to 22 million by 2023

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NCI, 2019

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The number of cancer survivors has been exponentially growing not only in the US, but worldwide as well. In 2019, there were approximately 17 million cancer survivors in the US, which represents 5.0% of the population. It has been projected that there will be approximately 22 million survivors by 2030.

The largest groups of cancer survivors are:

- Women with early-stage breast cancer
- Men with nonmetastatic prostate cancer

Osteoporosis and Cancer

- Patients with nonmetastatic cancer may experience challenges in skeletal integrity due to the disease and disease treatment

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Shapiro et al, 2019

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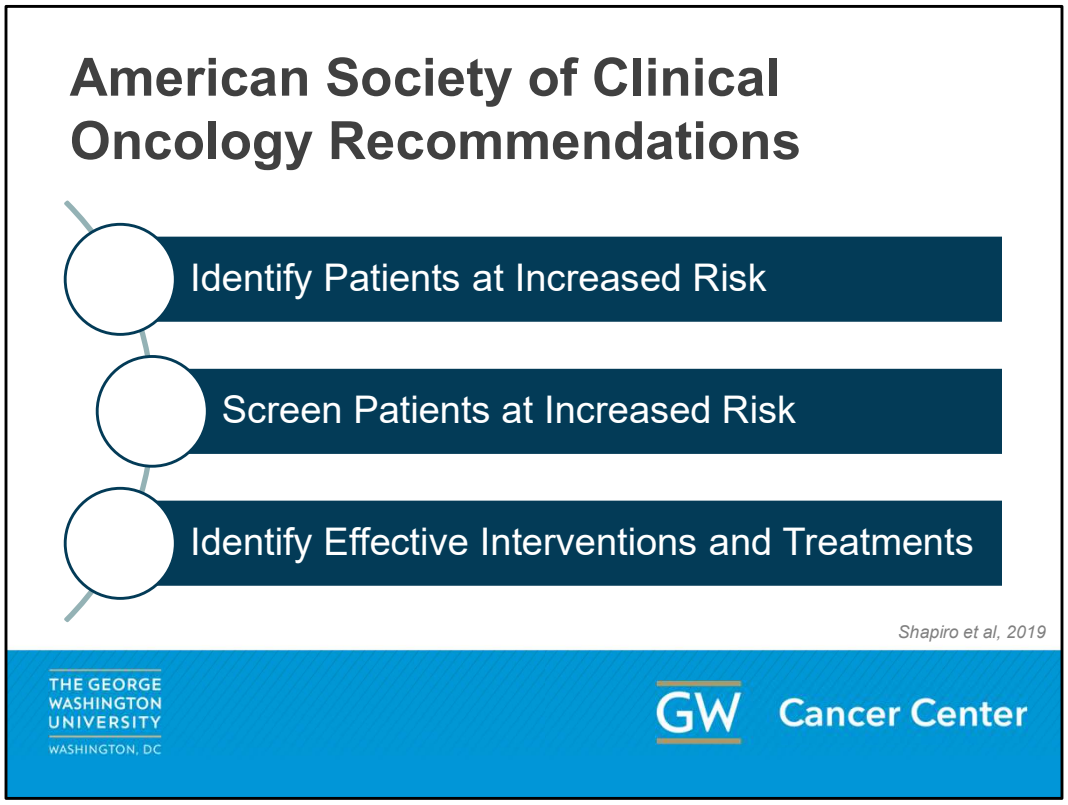
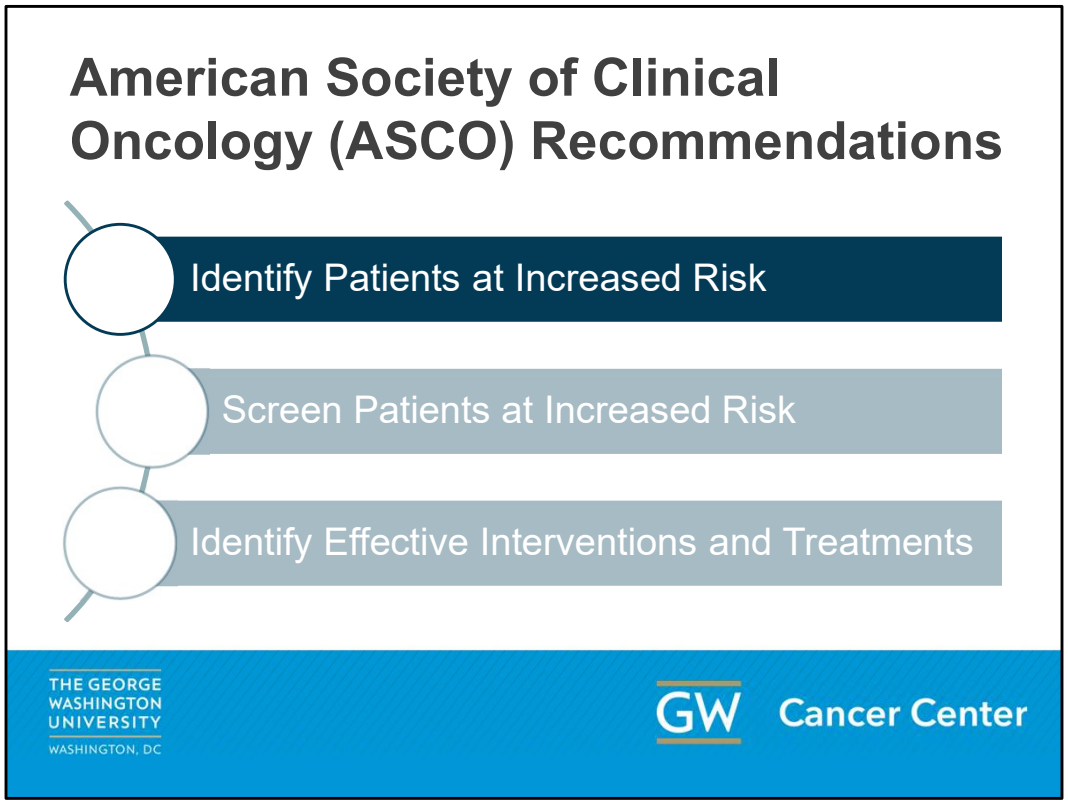
Patients with nonmetastatic cancer may experience challenges in skeletal integrity as a result of the disease or the disease treatment.

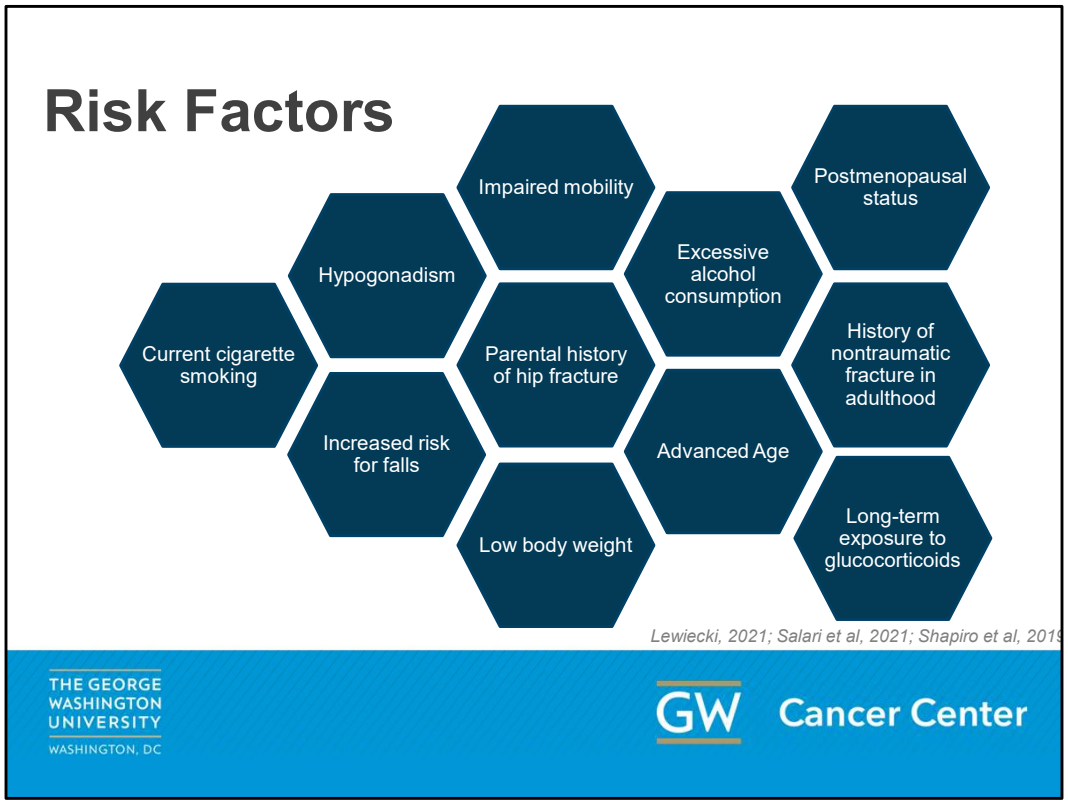
Nonmetastatic cancer increases susceptibility to osteoporosis due to the local and systemic inflammation associated with the disease which can promote bone loss. Treatments are also associated with more rapid and severe bone loss. The rate of bone loss may be more than seven-fold higher than the rate associated with normal aging.



The American Society of Clinical Oncology (ASCO) has published three recommendations for osteoporosis management in adult patients with nonmetastatic cancer.



We will start with identifying patients at increased risk for osteoporosis.



As I have mentioned earlier, there are modifiable and nonmodifiable risk factors. This figure presents the most common risk factors.

Few studies have looked at cancer patients specifically, so these factors were identified based on risk in the general population.

- Advancing age, defined as age 65 years or older in women and 70 years or older in men, has been reported to be the most critical determinant of fracture than bone mass
- Increasing alcohol intake to greater than 10 servings per week was also a statistically significant risk factor, as were current smoking and history of chronic glucocorticoid use
- Body weight less than 58 kg (127 lbs), low body mass index (20kg/m2) and loss off 5% of weight can also increase clinical risk, as well as history of a prior fracture in adulthood

Risks from Treatment

- Aromatase inhibitors (AIs) - increase the risk of fractures
- Antiandrogen therapy (ADT) - accelerate and disrupt the bone turnover process
- Radiation therapy can affect the bone in the treatment field

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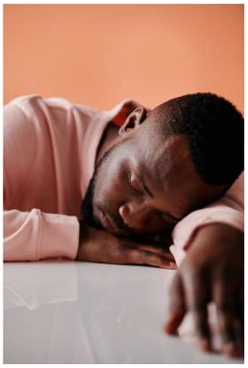
Anticancer therapies may increase the risk of osteoporotic fracture in either the short- or long-term. This slide presents some notable therapies that providers should be aware of when assessing a patient's baseline fracture risk.

Aromatase inhibitors may increase the risk of fracture in postmenopausal women with estrogen receptor positive early breast cancer. Antiandrogen therapy in men with prostate cancer can accelerate and disrupt the bone turnover process and men on this therapy have increased bone loss and fracture risk. Radiation therapy can affect the bone within the treatment field, and also indirectly effect bone through vascular changes.

Risk from Disease Manifestation

- Physical, metabolic, and psychosocial changes in patients with cancer, can lead to bone atrophy
  - Cancer cachexia (“wasting”)
  - Cancer-related fatigue



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Dhanapal et al, 2011; Shapiro et al, 2019

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Physical, metabolic, and psychosocial changes in patients with cancer, such as malnourishment due to nausea, weight loss, and cancer-related fatigue, can similarly lead to bone atrophy. Nutritional deterioration can occur at any point in the timeline of cancer diagnosis, treatment, or management. Two cancer-related conditions to be aware of are:

- Cancer cachexia (”wasting”) which leads to diminished muscle strength and bone mass. Cachexia can be characterized by weight loss, anorexia, asthenia, and anemia
- Cancer-related fatigue which may reduce physical activity, can contribute to mechanical unloading, sarcopenia (a skeletal muscle disorder), and bone loss

Quantifying Risk Estimates

- Fracture Risk Assessment Tool (FRAX) assists in quantifying risk estimates in patients
- Assessment tools not yet validated in cancer patients

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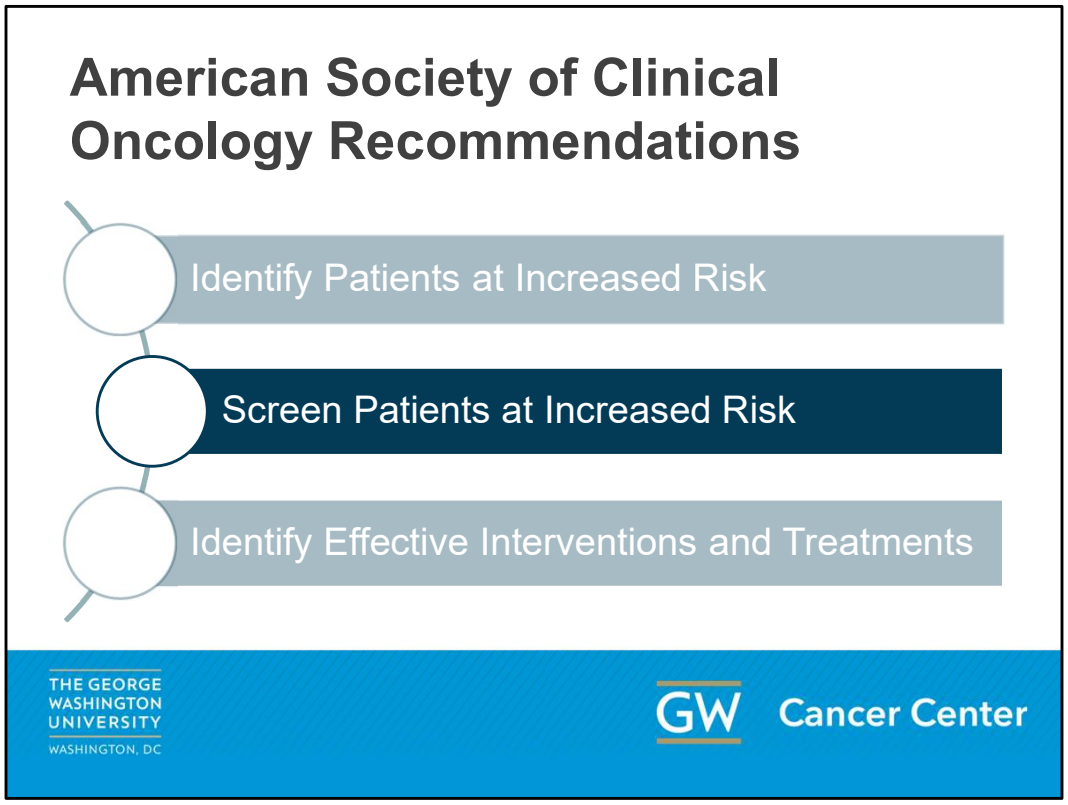
Clinicians may use risk assessment tools, such as the Fracture Risk Assessment Tool, known as “FRAX”, to quantify fracture risk estimates in patients. These calculators take into account risk factors, including age, sex, race, medical history, smoking and alcohol use, and family history. FRAX does not capture all risk factors though, and clinicians should consider additional evaluation if there is suspicion of rarer conditions, like high-risk medication use, causes of secondary osteoporosis, or collagen metabolism disorders that are not captured by FRAX.

It is important to note, that these assessment tools are used for the general population and have not been validated in cancer patients.



Next, we will discuss screening patients at increased risk for osteoporosis.

Bone Mineral Density Testing

- Bone mineral density (BMD) testing with central/axial dual x-ray absorptiometry (DXA)

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Patients with nonmetastatic cancer with one or more risk factors for osteoporosis fractures, such as the ones we previously discussed, should be offered bone mineral density testing using central/axial DXA. Central/axial DXA is considered the gold standard measure, but if DXA is not feasible or accessible, alternative BMD testing methods, such as quantitative ultrasound or calcaneal DXA, should be offered.

Bone Mineral Density Testing (Cont.)

- BMD testing should be offered every 2 years to patients with nonmetastatic cancer who:
  - Are prescribed a drug that causes bone loss or
  - Have a baseline BMD near threshold of treatment

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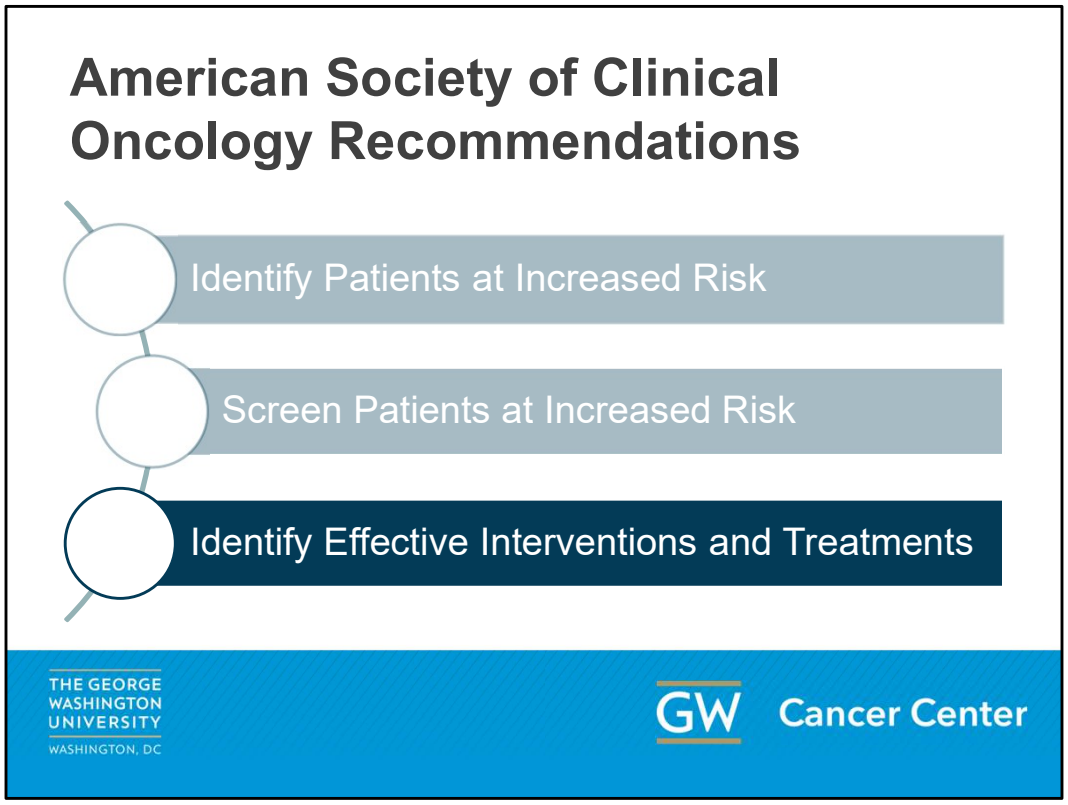
Bone mineral testing should be offered every 2 years to patients with nonmetastatic cancer who are prescribed a drug that causes bone loss or who have a baseline bone mineral density near the threshold of treatment.

Testing may be offered more frequently if medically necessary, but generally should not be conducted more than annually.



We will now discuss the final group of recommendations: identifying effective interventions and treatments

These are some nonpharmacologic interventions identified to limit bone loss, based on the interventions used in noncancer populations. We'll talk about a few of these.

- If daily intakes of calcium and vitamin D are below the suggested levels, patients should be encouraged to consume diet high in vitamin D and calcium in addition to taking supplements to attain these levels
- Combination of exercise types reduces the risk of fractures caused by falls. Exercises should be tailored to the needs of the abilities of the patient. Examples of such physical activities are balance, flexibility/stretching, endurance, resistance, and progressive strengthening exercises
- Patients with impairments that affect their gait and balance should be offered medical rehabilitation
- Smoking and alcohol consumption are risk factors for osteoporosis, so patients should aim to reduce or eliminate these behaviors

Nonpharmacologic Interventions – Cancer Populations

- Dosing suggestions in noncancer populations may not be adequate in oncology settings
- Checking levels of vitamin D is strongly recommended

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Checking levels of 25-OH(hydroxy) vitamin D is strongly recommended before initiation of Aromatase Inhibitors (AI), Androgen Deprivation Therapy (ADT), or any cancer therapy associated with bone loss, or when DXA(Dual energy x-ray absorptiometry) results indicate osteopenia or osteoporosis. The dosing suggestions in noncancer populations may not be adequate in cancer settings, due to the accelerated bone loss associated with cancer and cancer treatment.

Pharmacologic Interventions

- Bone-modifying agents (BMAs) may be offered to reduce fracture risk
- Hormonal therapies are generally avoided in patients with hormonal-responsive cancers

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In certain patients, bone-modifying agents (BMAs) may be appropriate to reduce fracture risk.

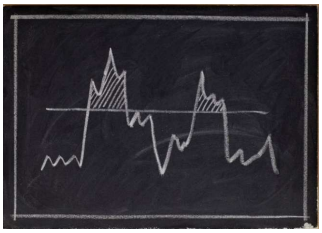
BMAs include:

- Oral bisphosphonates
- Intravenous bisphosphonates
- Subcutaneous denosumab

For patients without hormonally responsive cancers, hormonal therapy may be offered with other BMAs, when appropriate. However, the hormonal therapies are generally avoided in patients with hormonal-responsive cancers.

Candidates for BMAs

- If a T-score and/or risk assessment exceed the threshold for fracture, candidates may include:
  - Premenopausal women on GnRH therapy, AIs, CIOF or prior oophorectomy
  - Men who previously or currently receive ADT
  - Patients with history of current bone marrow transplantation or more than 3-6 months of glucocorticoid use



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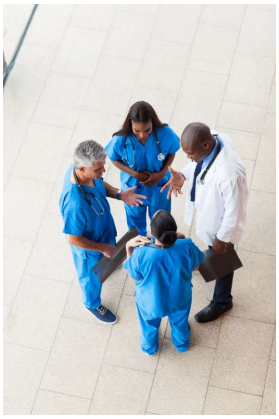
If T-score and/or risk assessment exceed the threshold for fracture, candidates for BMAs may include:

- Premenopausal women with GnRH (Gonadotropin-releasing hormone) therapy causing ovarian suppression
- Premenopausal women with CIOF (Chemotherapy induced ovarian failure) or prior to oophorectomy
- Postmenopausal women on Aromatase Inhibitors (AIs)
- Men who previously or currently receive ADT
- Patients with history or current bone marrow transplantation
- Patients with more than 3-6 months of glucocorticoid use

Treatment at higher bone density or T-score may be appropriate due to rapid short-term bone loss associated with these conditions.t

Conclusion

- Bone loss may occur without symptoms
- Effects of cancer treatment can increase fracture risk during and after treatment
- Providers should:
  - Integrate monitoring and management of bone health into the overall survival plan for adult patients with nonmetastatic cancer
  - Emphasize communication and shared decision-making across members of the care team
  - Adapt screening and treatment based on patient-specific risk factors



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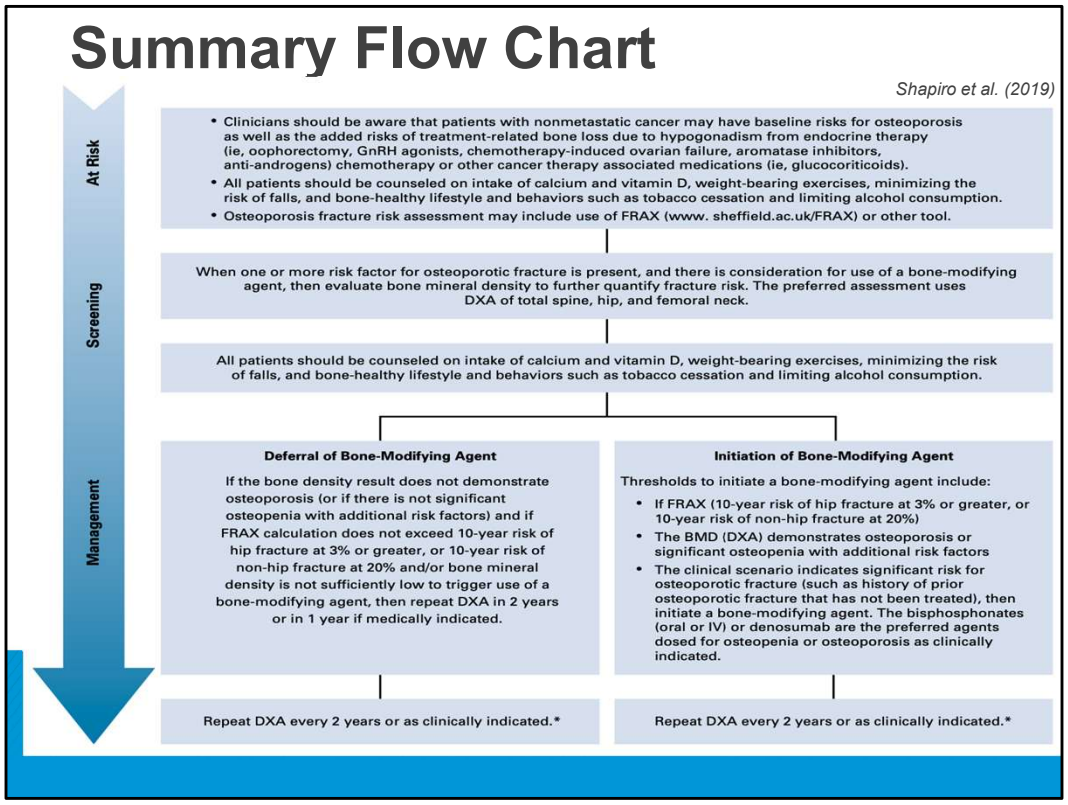
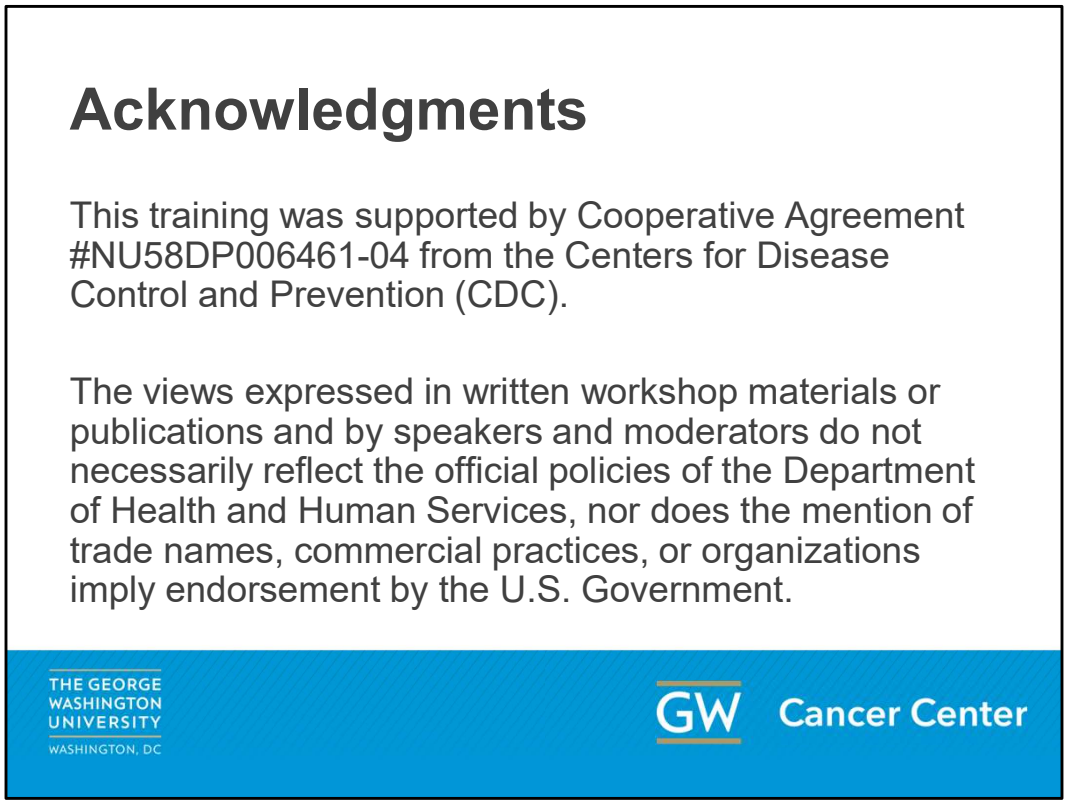
Some key takeaways for providers:

- Bone loss may occur without symptoms and the effects of cancer treatment may increase the risk of fracture during and after cancer treatment
- Providers should monitor and manage bone health as part of the overall survival plan for adult patients with nonmetastatic cancer, emphasize shared decision-making and communication with the patient and other members of the care team, and adapt screening and treatment based on patient-specific risk factors, including the ones discussed in this presentation.



Finally, this flow chart was created by the ASCO guidelines team and provides an overview of everything we've discussed today.



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References

Cauley J. A. (2011). Defining ethnic and racial differences in osteoporosis and fragility fractures. Clinical orthopaedics and related research, 469(7), 1891–1899. https://doi.org/10.1007/s11999-011-1863-5

Dhanapal, R., Saraswathi, T., & Govind, R. N. (2011). Cancer cachexia. *Journal of oral and maxillofacial pathology, 15*(3), 257–260. https://doi.org/10.4103/0973-029X.86670

Lewiecki EM. Osteoporosis: Clinical Evaluation. (2021). In: Feingold KR, Anawalt B, Boyce A, et al., editors. Endotext. South Dartmouth (MA): MDText.com, Inc.

Mayo Clinic. (n.d.). Bone Density Test. Retrieved from: https://www.mayoclinic.org/tests-procedures/bone-density-test/about/pac-20385273#:~:text=A%20bone%20density%20test%20determines,into%20a%20segment%20of%20bone.

National Cancer Institute. Office of Cancer Survivorship. (2019). Statistics and Graphs. Retrieved from: https://cancercontrol.cancer.gov/ocs/statistics.

Salari, N., Ghasemi, H., Mohammadi, L. et al. (2021). The global prevalence of osteoporosis in the world: a comprehensive systematic review and meta-analysis. *Journal of Orthopaedic Surgery and Research, 16*(609). https://doi.org/10.1186/s13018-021-02772-0

Shapiro, C.L., Poznak, C.V., Lacchetti, C., Kirshner, J., Eastell, R., Gagel, R.,…Neuner, J. (2019). Management of Osteoporosis in Survivors of Adult Cancers With Nonmetastatic Disease: ASCO Clinical Practice Guideline. *Journal of Clinical Oncology, 37*(31), 2916-2946. doi:10.1200/jco.19.01696

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Here are the references used to develop this presentation

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