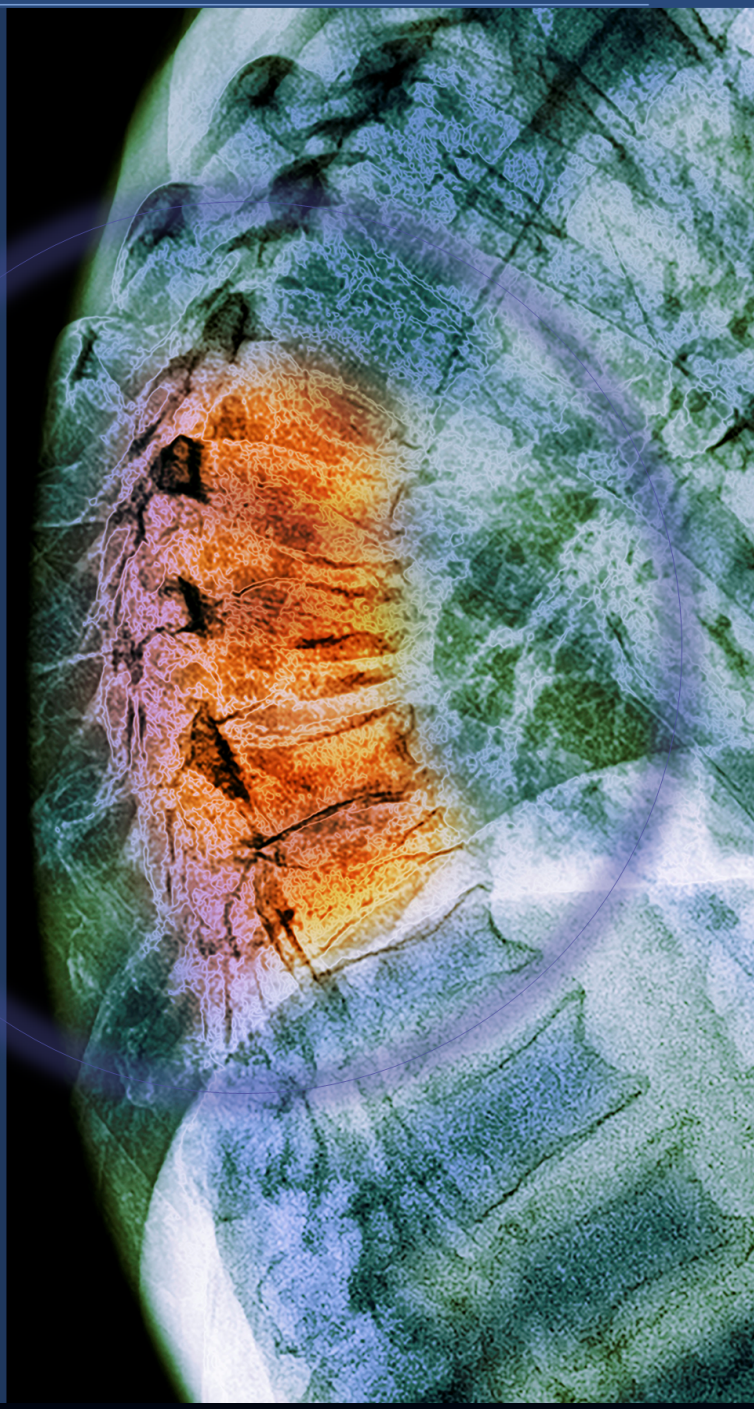
Managing Patients with OSTEOPOROSIS

Staying Current with Updated Guidelines



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Contents:

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ACTIVITY OVERVIEW

As the most common bone disease, osteoporosis continues to be a major healthcare burden in the U.S. It is characterized by increased bone turnover as well as decreased bone mass, resulting in skeletal fragility and increased risk of bone fractures in the hip, spine, wrist and other sites. In many patients, osteoporosis is a silent disease. In those who have not received proper screening, it can remain undetectable for years, often until a fracture event occurs. Though some fractures do occur with trauma, many occur with little to no impact. For both men and women, osteoporosis is associated with significant morbidity and mortality in the aging population. In the U.S. alone, more than 53 million adults either have osteoporosis or are at high risk because of low bone mass. Despite its significant prevalence and impact on older Americans, osteoporosis remains under-diagnosed and under-treated in this population. In order to deliver quality care for patients with osteoporosis and those at risk for osteoporosis, PAs must remain up to date on all aspects of disease management.

AAPA TAKES RESPONSIBILITY FOR THE CONTENT, QUALITY, AND SCIENTIFIC INTEGRITY OF THIS CME ACTIVITY.

EDUCATIONAL OBJECTIVES

- At the conclusion of this activity, the PA should be better able to:
- Use screening guidelines when evaluating a patient for osteoporosis.
- Stratify patients based on osteoporosis risk according to latest guidelines.
- Initiate pharmacologic therapies appropriately.
- Provide appropriate patient education in the post-fracture setting and facilitate hand-off for continuing care.

ACCREDITATION STATEMENT

This activity has been reviewed by the AAPA Review Panel and is compliant with AAPA CME Criteria. The activity is designated for 1.5 AAPA Category 1 CME credits. PAs should only claim credit commensurate with the extent of their participation. Approval is valid through December 31, 2022.

Estimated time to complete this activity: 90 minutes.

HOW TO RECEIVE CREDIT

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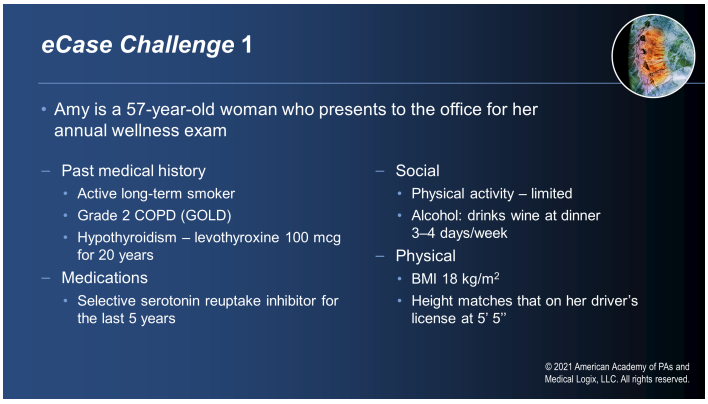
eCASE CHALLENGE #1

Catherine Sweeney, PA-C, CCD: Hello, and welcome to this video *eCase Challenge*, "Managing Patients with Osteoporosis: Staying Current with Updated Guidelines." I'm PA Catherine Sweeney, Coordinator of Emerge Ortho's Bone Health Clinic. Joining me today is PA Patrick Cacchio. Patrick is a PA at the Duke University Endocrinology Clinic.

Many thanks to you for your involvement in this important continuing medical education activity. This activity will consist of two video *eCase Challenges*. So, let's get started.

Our first *eCase Challenge* is focused on a patient we will call Amy. Amy is a 57-year-old woman who presents to the office for her annual wellness exam. She is an active long-term smoker and has grade 2 COPD according to GOLD guidelines. She has a history of hypothyroidism and has been on a stable dose of levothyroxine for 20 years at around 100 mcg every other day.

She has been treated with a selective serotonin reuptake inhibitor for the last 5 years. Her physical activity is limited, and she drinks wine at dinner 3 to 4 days a week. She has a thin frame, with a BMI of 18 kg/m^2, and her current height matches that on her driver's license at 5 foot, 5 inches. With this brief initial information, let's pose our first clinical question.



Question 1

For this patient, which of the following is not a risk factor for the development of osteoporosis?

A. Low BMI
B. Smoking
C. SSRI use
D. Hypothyroidism

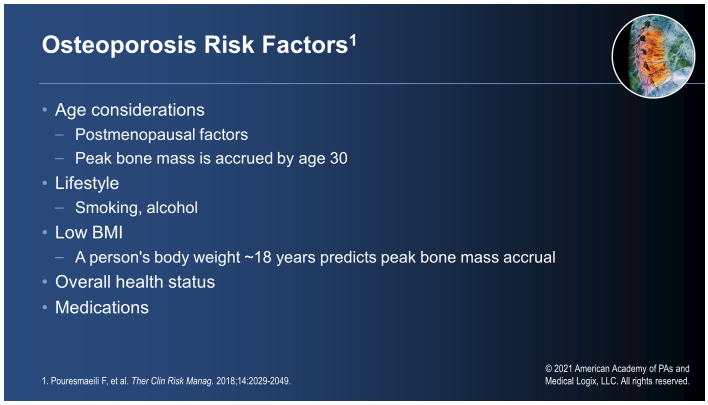
So, Patrick, this brings us into a good conversation about what are risk factors for osteoporosis? What are some things that you think with this patient are somewhat red flags or possible indicators for osteoporosis?

Patrick Cacchio, PA-C, MHS: Sure. There are so many things that can go into this and put someone at risk for bone loss. And I talk to patients, I talk to students a lot, that we focus on the postmenopausal factors, which play a big role. But our peak bone mass is accrued by age 30, so there are a lot of things that affect that even early in life, long before the first bone density test is often done.

So, things that stood out in this case: obviously smoking, but also the low BMI. So, we know that a person's body weight around age 18 is likely to predict their peak bone mass accrual. So anything that affects their health overall early in life certainly can affect the peak bone mass.

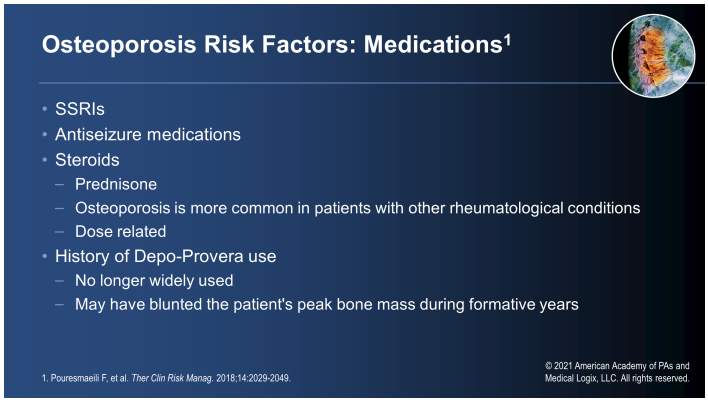
But then, of course, there's also the postmenopausal factors, too, that we're all very familiar with, right? So all the lifestyle things. And in this case, again, the cigarette smoking stands out, but also the alcohol consumption is something that can certainly influence bone mass accrual, as I'm sure we've all seen.

And then you think about other things in terms of medications and their effects, as well.



Catherine Sweeney: A lot of these medications are fairly common. The SSRIs are some that can certainly contribute to low bone mass. Of course, if people are on antiseizure medications -- the steroids are certainly the big ones to look out for, with your prednisone. So we see this a lot in patients with other rheumatological conditions.

And also, for women, too, we don't use it as much anymore, but in the past there was a birth control, Depo-Provera, that was used that could have blunted the patient's peak bone mass during their formative years.



Patrick Cacchio: But I think it's important that whenever I see a patient for the first time, I want to understand, I don't want to just prescribe a medicine and say, "Here, take this pill," but understand what's gone into their overall bone health.

And some of these things are correctable, right, in terms of smoking cessation, reducing her alcohol intake in this particular patient.

And then you pointed out steroids. That's a big part of my practice, too, right? So, so many good uses for steroids, but, in the bone world, we deal with the bad effects of it in terms of bone density. And very much dose-related, too, right?

Catherine Sweeney: Absolutely. And then we have the ones that, like you had mentioned earlier, are not modifiable. So knowing that family history with genetics, especially if mother or father had suffered a hip fracture, that absolutely could increase that patient's risk of fracture.

And if mother or father had osteoporosis, it is something that can be passed on genetically. And same with body type. And having that low BMI, like you said, certainly puts patients at higher risk.

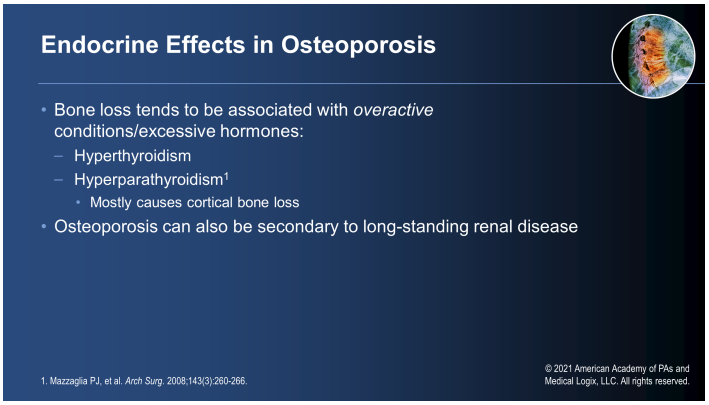
And we see this, too, in women a lot like you said with younger years, maybe someone who was an athlete, or their menstrual cycles were not regular. So, all those things are good questions to ask that could then affect that patient later in life and be a reason. Like you said, sometimes it's not just the loss of the estrogen.

And then I know with the question that was posed here, we did touch on some endocrine problems. And I know that's certainly your specialty, for sure. And it can get a little confusing. Hypothyroidism versus hyperthyroidism, hypothy -- parathyroidism, hyperparathyroidism. Which are the ones that tend to predispose patients to having osteoporosis?

Patrick Cacchio: Sure. So I see an awful lot of questions about this, both from patients and even colleagues and clinicians, too, in terms of what the effects can be.

It's really the overactive conditions, the excessive hormones. So when you have hyperthyroidism and this sort of hypermetabolic state, we can see bone loss associated with that.

And then also, hyperparathyroidism, right? So that's a big one that will cause predominantly cortical bone loss. So we'll see that from things like the hip and the wrist on a bone density when we have someone who has hyperparathyroidism, either primary or even secondary can certainly cause bone loss, as well, when it's secondary to renal disease and things like that in long standing.



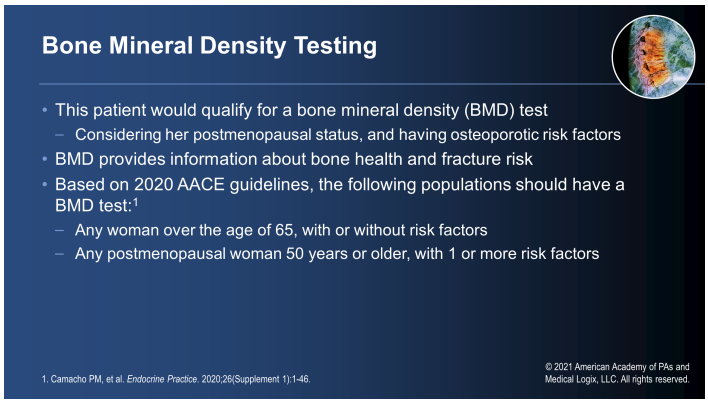
Catherine Sweeney: Absolutely. So, kind of putting all that together, then, with this particular patient that we're talking about, what do we think? I think this patient would classify as someone who should get a bone mineral density test.

Patrick Cacchio: Absolutely. I mean, it's almost never the wrong answer, right, to offer someone who's postmenopausal, especially with some of these risk factors -- and the guidelines support that, too, right? So, any postmenopausal female who has any one of these risk factors -- and we've already identified potentially several for this particular case that would meet the criteria for bone mineral density testing.

So it's a great screening test. It's not a perfect test, but it gives us a lot of good information about someone's bone health, and then, as a result their fracture risk, which is really what we ultimately care about here.

Catherine Sweeney: And according to the guidelines, like you said, often we use the AACE guidelines, which is the endocrinology guidelines, and they published a new set of guidelines back just recently in 2020, which kind of clarified, okay, who should get these bone mineral density tests? And I get that question a lot, I'm sure you do in clinic, too "Will my insurance pay for this? You know, do I qualify?"

But according to the guidelines, any woman, no matter what your risk factor, over the age of 65 can get a bone mineral density test. And then if we have those risk factors, any postmenopausal woman 50 or older certainly qualifies, and insurance is usually very amenable to that. I'm not sure if you've had any issues with getting them approved in your clinic or anything.



Patrick Cacchio: No, no, no. Really, not. It's just such a cost-effective test, particularly in the postmenopausal population. It's been well demonstrated, and I think, its utility is very clear particularly as a screening test.

Catherine Sweeney: Absolutely. Well, let's review the question that was posed. Which of the following is not a risk factor for the development of osteoporosis? The correct answer is (D) hypothyroidism.

Several factors increase one's risk for osteoporosis, including several endocrine factors, such as hyperthyroidism, hyperparathyroidism and estrogen deficiency. However, hypothyroidism, which is quite common, is not one of these factors.

After screening for other risk factors and performing a clinical examination, based on her risk factors, you offer her a bone mineral density testing. The results come back. This brings us to our next clinical question.

Question 2

Amy's DEXA scan results show that she has a T score of -1.5 standard deviations at the hip and -2.5 at the spine. Which of the following is the most accurate interpretation of these results?

A. She has osteoporosis in both areas.
B. She has osteoporosis at the spine and osteopenia at the hip.
C. This is a normal examination.
D. She has osteoporosis of the hip and osteopenia at the spine.

So this then brings us into what are these definitions of osteopenia versus osteoporosis? And so we have guidelines according to the World Health Organization that give us criteria for your T scores. And so, Patrick, would you mind explaining what the different T scores mean?

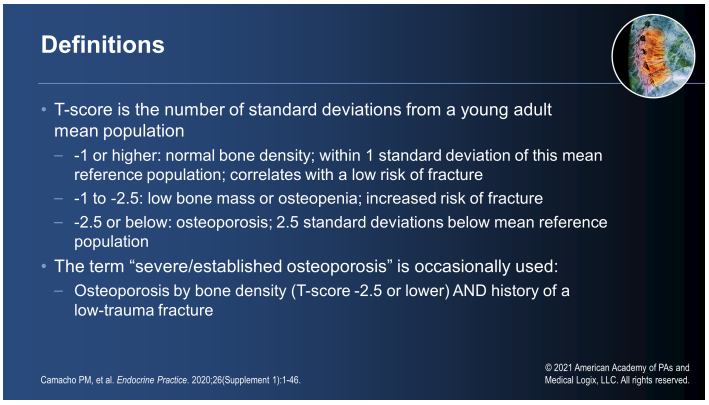
Patrick Cacchio: Sure. I do this every day, right? So what does a T score mean? What does a Z score mean? What are all these things? So for a postmenopausal female, we use a T score for diagnostic purposes based on a bone density.

And the criteria, a T score is the number of standard deviations from a young adult mean population. So that's the sort of scientific criteria here. But in layman's terms, a score of -1 or higher is considered normal bone density. So it's within 1 standard deviation of that mean population. We think that's pretty normal, pretty good bone density, and correlates with a pretty low risk of fracture.

We call low bone mass, or another term that's used, osteopenia, for anyone who has a T score between -1 and -2.5. And so that's folks that are at an increased risk of fracture versus someone who would have normal bone density.

And then we use the term osteoporosis for anyone who has -2.5 or below on a bone density. So 2 and a half standard deviations below that mean population.

And they also mention the idea of severe, or established osteoporosis is a term that sometimes is used. And that's for someone who has osteoporosis by bone density so -2.5 or below on a T score and also has a fracture, a low-trauma fracture that they've sustained as part of their history.



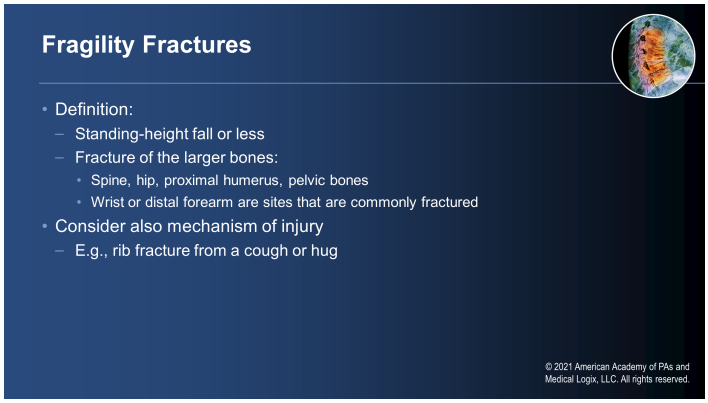
So for folks that haven't had a fracture, these T scores are really our best way to sort of help stratify someone's risk of a fracture. And so that's very useful information for patients and clinicians to understand their fracture risk.

Catherine Sweeney: Absolutely. And when we talk about fragility fractures, can we clarify which ones? Because I know we get a lot of referrals, you know, foot fractures, or, "I had a stress fracture in my ankle." This person has osteoporosis. Which ones are really deemed fragility fractures according to the guidelines?

Patrick Cacchio: Sure. And this can be a pretty big gray area sometimes, right, Catherine?

But the definition is really a standing-height fall or less in terms of the degree of trauma involved, and then we think particularly of the, as I tell patients, the bigger bones, right? So the spine, the hip, the proximal humerus, the pelvic bones, and then also the wrist or the distal forearm are sites that are most commonly fractured from a standing-height fall in patients with osteoporosis.

So those are the ones we think about. They're the ones that are often studied in clinical trials. So I think that's another important thing to think about as we're starting to think towards treatment is, what fractures do we know our treatments are good at preventing?



Catherine Sweeney: And it's something that how that fracture happens, too, matters, just like you said. You know, maybe I coughed, and I broke a rib. Or my spouse gave me a hug, and I broke a rib. Or kind of these strange scenarios.

And then what about that, I call it the gray area, osteopenia. So because there's, like we said, it's not just about the bone density test, there's all these other risk factors that we have to take into consideration to really understand someone's fracture risk. And so I'm sure many people have seen on the bone density reports, you get what's called a FRAX score. So can you explain what that takes into consideration?

Patrick Cacchio: So the FRAX score -- I mean, it's one of my favorite tools I use every day with almost every patient. As one colleague once said, there's no FRAX police, so you can use this fairly liberally in practice. It was designed initially with Dr. Kanis and the World Health Organization to answer the question that you just posed, what do you do with these folks with osteopenia? Which ones are at a high risk of fracture, and which ones aren't?

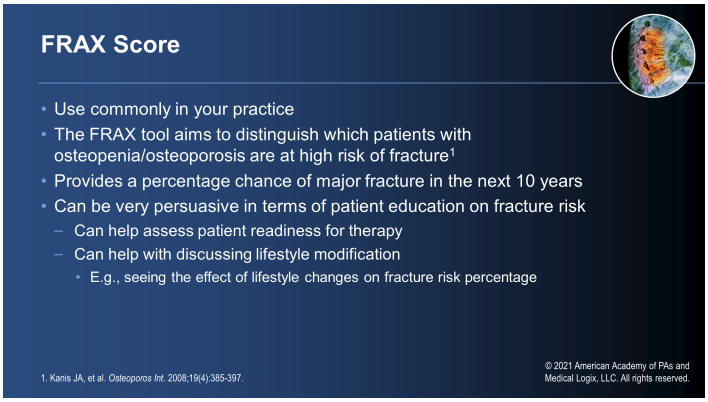
So, it's a very robust tool. I think it's very meaningful for patients, too. I always sort of like to put it in front of a patient and gauge their reaction sometimes, and that helps me in terms of the discussion that follows, right, how do they react to this number? Does this upset them? Is this something that they're concerned about? Or do they kind of say, "Oh, that's not so bad?" So, I don't know what your experience has been using it with patients. I'm sometimes surprised by different thresholds that different folks have for these things.

Catherine Sweeney: Right. And it is. This can be kind of eye-opening, and I think it helps to educate the patient in that the bone density, your T score, is not the only factor. So, we may go over their T scores, and, they might not be so bad. Maybe it's a -1.8, but then when you add all these other risk factors in there, then they see

the fracture risk goes up. You know, maybe even a 1 in 3 chance they're going to break something. Then that light bulb goes off. "Okay, yes, this is important. You know, we need to address this."

And you're right. That helps as a clinician to be able to judge, "Okay, is this person ready to take that step for medication, or can we wait and work on lifestyle modifications, as well?

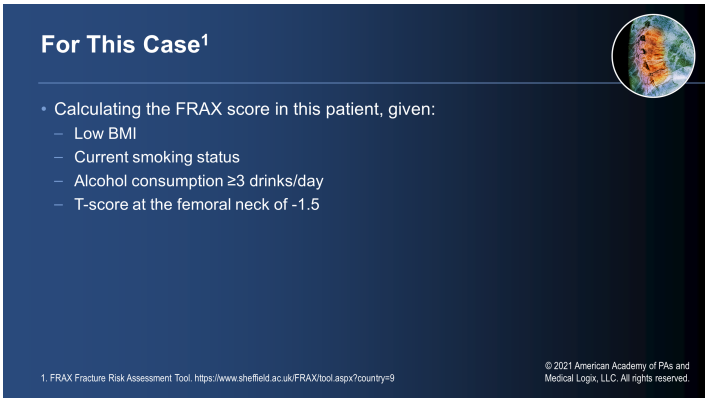
Patrick Cacchio: And that's another sort of little tip or pearl, I guess. But, sometimes -- so some of those modifiable risk factors that we talked about -- alcohol use and smoking -- are in the FRAX tool. And so sometimes you can kind of put that in front of a patient, side by side, and say, you know, "Here's your risk while you're smoking. Here's your risk if you were to be able to successfully quit."



Because sometimes when you put a number on these things, it can be a little more meaningful to folks.

Catherine Sweeney: Absolutely, absolutely. And so with the patient in our case here, FRAX could be a useful tool for this patient. And so if we calculated her FRAX score, she has a low BMI. She is a current smoker. She does drink alcohol, three or more drinks daily, which can be a risk factor.

And then when we factor in the T score, this particular patient has an 11% risk of major osteoporotic fracture in the next 10 years, and a 2.7% risk of hip fracture in the next 10 years. So, this, according to the guidelines, doesn't necessarily qualify her for treatment. But she's close enough where I think that conversation could be had, especially with these other risk factors that she has.

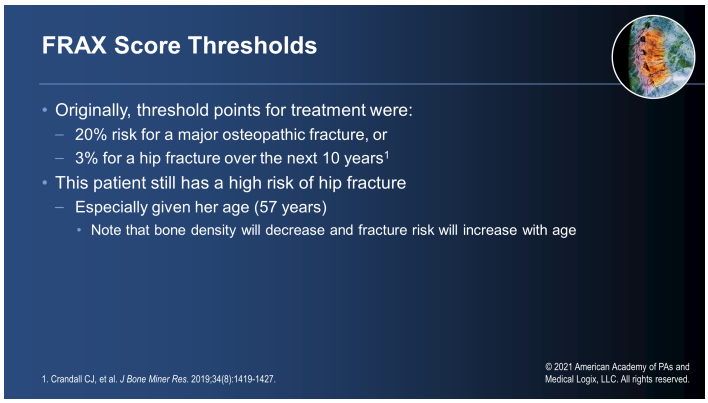


And so what are the thresholds for your FRAX score, as far as what would be a good patient for treatment?

Patrick Cacchio: So, again, getting back to sort of the original utility and thought behind FRAX. So, in that patient who has osteopenia, the sort of decision points were cut at 20% risk for a major osteopathic fracture, or 3% for a hip fracture over the next 10 years. And that's based on data in terms of treatment.

So, as you've pointed out, she doesn't quite meet those thresholds. That hip fracture risk is fairly high, especially for someone her age, right? So that's the other thing I always keep in mind: these risks are going to increase as someone gets older.

And so that's another thing you can sometimes put in front of a patient and say, "This is where it is now. This is where it will be in 5 years if nothing changes. And the odds are that without therapy, bone density might get worse, and so that will also increase the fracture risk."



Returning to our question, after BMD testing, our patient Amy has a T score of -1.5 standard deviations at the hip and -2.5 at the spine. Which of the following is the most accurate interpretation of these results?

The correct answer is (B) she has osteoporosis at the spine and osteopenia at the hip. The T score is the number of standard deviations a patient's bone mineral density from the mean of young adult white women. A score between -1.0 and -2.5 defines osteopenia, whereas a score of -2.5 standard deviations defines osteoporosis.

Continuing with Amy's case, given her osteoporosis, you and Amy begin discussing therapeutic options. She has heard that there are several options, some of which are oral, and others injectable. She is concerned about convenience. She would like more perspective on the best option for her and would like to learn more about her choices. This leads into the next question.

Question 3

She has heard there are several options, some of which are classified as antiresorptive, and others as anabolic. Which of the following is an anabolic agent for the treatment of osteoporosis?

A. Alendronate
B. Denosumab
C. Raloxifene
D. Romosozumab

So these are common drugs that we use in practice. What are your thoughts in terms of anabolic agents, antiresorptive agents, Catherine, in your practice?

Catherine Sweeney: In my clinical practice, at least, we're seeing a lot of patients post-fracture.

And the data now supports that perhaps if you can, start with an anabolic agent in those patients. That will help them to improve

their bone mineral density more than perhaps starting with an antiresorptive.

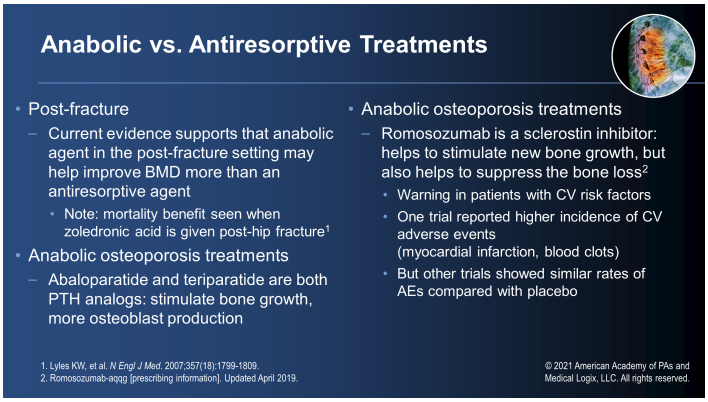
And the anabolics, we now have three. So, like you mentioned in the question there, they mentioned a few. Abaloparatide, teriparatide, and then the newer one now, which is romosozumab. The abaloparatide and teriparatide are both PTH analogs. So they help the body basically stimulate more bone growth, more osteoblast production.

The romosozumab is what is called a sclerostin inhibitor. So this is a new mechanism of action. We've never had a medication like this before. So it's almost like a dual-acting medication, where it not only helps to stimulate new bone growth, but also helps to suppress the bone loss.

So in my particular practice, we do use these anabolic agents quite a bit to help in, of course, good fracture prevention for the future, building an excellent-quality bone, which I think is unique to some of these medications, and providing a good foundation of bone to then build upon later in life, because we do have to think about this.

This is a lifelong disease. So none of these medicines, unfortunately, are cures at this point. So positioning these medications is becoming quite strategic now, and I think a really hot topic of research. So the anabolics, I think, are a lovely option.

With, romosozumab there is a warning about cardiovascular risk factors. So in one of the big clinical trials that got this to the market, they did see a higher incidence of adverse cardiovascular effects. So things like stroke or myocardial infarction, blood clots. In the other two big studies that got it to market, they did not see these adverse effects any more than placebo.



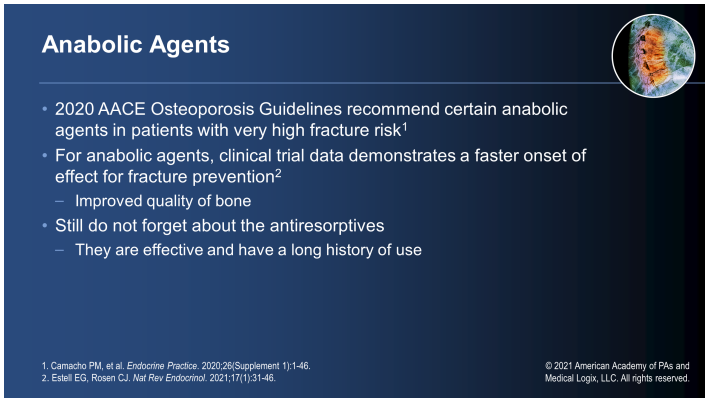
So just a word of caution if someone especially had a myocardial infarction, perhaps within the last 12 months, or known congestive heart failure, maybe not the best choice for this patient. But otherwise, the side effect profile seems to be quite favorable. Have you used any of these in practice, as well?

Patrick Cacchio: Sure. And, to your point, I think one of the things I alluded to earlier was the new AACE guidelines in terms of this idea of a very high fracture risk, and really positioning some of these agents ahead of others, and in part, yes, these are folks that maybe need a stronger medication.

But I think if we look at the clinical trial data, one of the other benefits these drugs have is generally a much faster onset of efficacy in terms of fracture prevention.

And so once you have a fracture, we know the bone is prone to probably fracturing again without intervention. And so, these drugs really do, as you said, improve the quality of the bone and really substantially and quickly -- relatively quickly speaking, in terms of from a bone standpoint, reduce fracture risk. So that's really important.

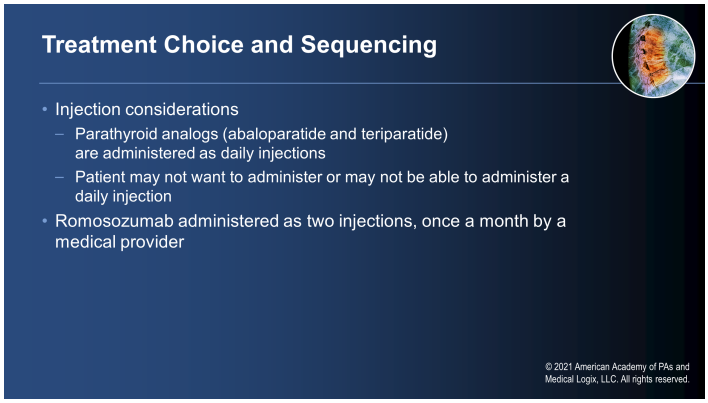
You know, that being said, the antiresorptives are also a good class of drugs that have been around a long time and we have a good track record with.



And to your point, one of the big areas of emphasis right now in terms of osteoporosis research, is how do we sequence these treatments, and what's the best way to use these drugs? Which patients are most appropriate for an anabolic versus an antiresorptive, and when do you follow them up with each other and that sort of thing?

Catherine Sweeney: The anabolics, especially the parathyroid analogs, although very, very effective, sometimes, sure, someone doesn't want to give themself daily injections, which is understandable. So, what are some other alternatives you might use in those patients who really don't want to do that daily injection therapy but still are at a really high risk?

Patrick Cacchio: So, obviously, romosozumab is a really nice option there, being a once-a-month injection that's given by a nurse, not a self-injection. So that's an advantage for that in some of these patients that -- the burden of the daily injection.



I have lots of patients with such horrible rheumatoid disease that they couldn't even give themself a daily injection functionally. So that's something you have to factor in, is just, the patient's ability to do that. And so that's where romosozumab is a nice agent as an alternative anabolic that doesn't require that burden of daily injections.

Catherine Sweeney: So let's return to the clinical question, which asked, which of the following is an anabolic agent for the treatment of osteoporosis? The correct answer is (D) romosozumab. Other anabolic osteoporotic treatments include abaloparatide and teriparatide. These anabolic agents, as well as denosumab and zoledronate, are recommended for the treatment of very high-risk patients and/or those with prior fractures.

So, going back to Amy's case, you and Amy together decide to initiate bisphosphonates. She is compliant with the medication. Much later in your care of Amy, she is lost to regular follow-up due to her life circumstances.

At this point in time, Amy has been treated with a bisphosphonate for 5 years, and she comes back to see you. She states that she is more concerned about her bone health after seeing her close friend suffer from a hip fracture that drastically affected her life.

She is relatively compliant with her medication, but does complain of heartburn she occasionally gets. She asks about how long she should remain on this agent and whether she should switch agents. Offhandedly, she wonders if she has been getting shorter. This leads to the next clinical question.

Question 4

Which of the following statements is true regarding the 2020 AACE guideline recommendations for the treatment of osteoporosis?

A. Switching from bisphosphonates to denosumab produces additional gains in BMD.
B. Drug holidays with denosumab are recommended.
C. Antiresorptive agents are not recommended following the discontinuation of an anabolic agent.
D. Switching from a bisphosphonate to an anabolic agent should not be considered.

So what do the guidelines say now with regards to therapies? This is a really hot topic of research, and like we talked about earlier, sequencing of these medications is becoming more and more important, and we're learning more about what are the better ways to sequence these therapies. Because, like you said, you don't just take one medication, and you're done for the rest of your life usually. So what types of sequencing do you practice at your work?

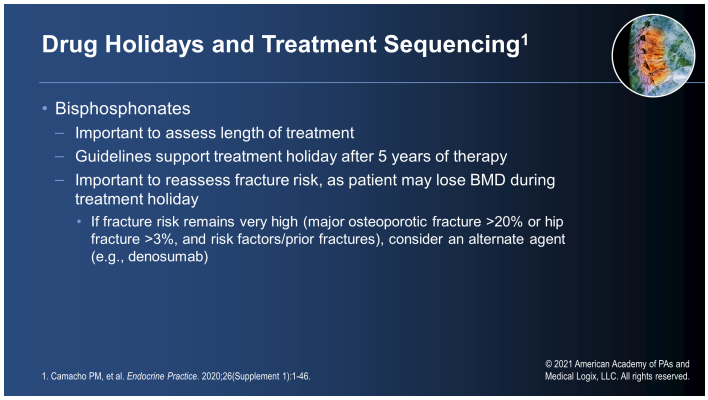
Patrick Cacchio: So, this is a great topic here. This is a common question I get asked by colleagues. You have a patient who's completed 5 years of a bisphosphonate, and it's important always, I think, and I tell residents and folks that are working with me, if you have a patient who's on a bisphosphonate, make sure you know how long they've been taking it, right?

So we know that there is a concern about adverse effects with long-term use, generally after 5 years. And so the guidelines would support considering a treatment holiday sometimes in these patients. But, it's also important to assess their fracture risk, because we do see and I see it all too frequently patients that do fracture or even lose bone density while on a treatment holiday from a bisphosphonate.

So it's important to think about how we're sequencing this. And, if this is a patient who's at high risk of fracture, if they still have significant osteoporosis by bone density or if we, recalculate that fracture risk, and we think it's still really high, there was a really nice study looking at the idea of a holiday, and utilizing FRAX at that 5-year time point as in this patient case.

And if the fracture risk for a major fracture over the next 10 years is greater than 23%, that may be somebody that's too high of a risk to probably offer a treatment holiday, and that you want to think about sequencing with additional treatment.

And so, in that case, I think you don't want to give more bisphosphonate. Again, we know there's an increased potential risk of adverse effects. So, an alternative agent like denosumab may make a lot of sense in this case.



But, you know, the other thing you have to think about is the opposite, too, right? You have a patient who's on denosumab. What do you do in that case after they've been on it for a period of time? And, fortunately, we haven't seen the side effects, at least I certainly haven't in practice. And I know that the FREEDOM extension trial's been reassuring in that regard. So I don't know what you do with denosumab in terms of transitioning off of that, or in many cases just continue in your practice. What are your thoughts?

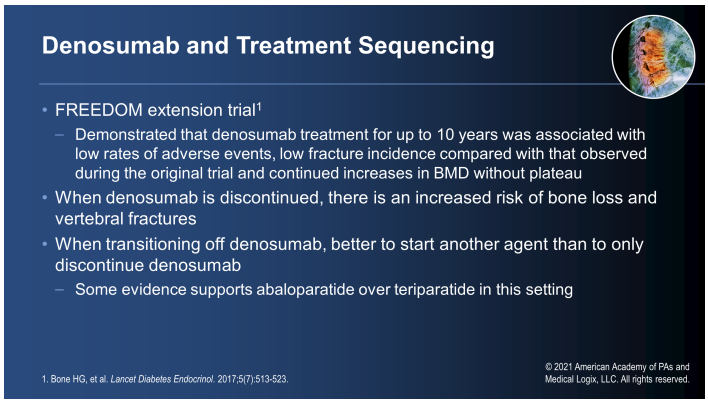
Catherine Sweeney: It's a hot topic and patients ask, "How long can I take denosumab?" or, "My primary care said I need to stop after 5 years," and so, I turn to the studies that have been done.

And there have been quite a number of studies now where we're trying to figure this out, you know, where they've transitioned from denosumab to perhaps alendronate, or denosumab to zoledronic acid, and see, are there declines in bone density?

And I think when transitioning off of denosumab for whatever reason, a big takeaway point is it's better to transition to something than to just stop completely, because then that person certainly could be at risk for a more rapid decline in the bone density and potentially vertebral fractures.

And from what I've seen in the data, it's a bit mixed. You know, still not quite clear which agent is best to follow denosumab with. But some promise with both alendronate and the zoledronic acid, and even some promise with switching to anabolic agents, as well.

I think the best data supports more so abaloparatide versus teriparatide in that transition. But again, still a little unclear. But we do know if someone does have to stop denosumab for whatever reason, it is best to try to transition to something to help blunt that potential rapid loss of bone density.



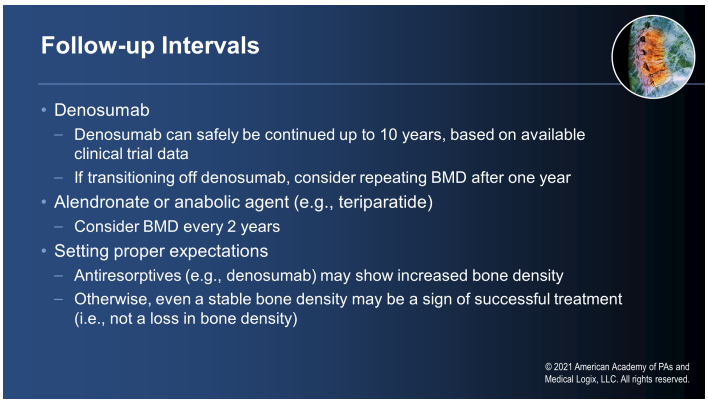
Patrick Cacchio: How often do you follow these folks when they're on therapy in terms of bone density, and sort of that discussion to monitor these things?

Catherine Sweeney: When transitioning from denosumab, again, thankfully we don't have to do that too often, since the data supports, it seems to be very safe to continue, as long as it is providing a clinical benefit. But if I am transitioning off of denosumab, I often will repeat a bone density test at a year, just to watch those patients a little bit more closely.

In other patients, where maybe we're on alendronate or we're doing an anabolic agent, such as teriparatide, every 2 years is usually when we'll order the bone density test to monitor their progress, and then make decisions based on that, what the next step in therapy will be.

Patrick Cacchio: I have a similar approach. And I think the other point that I like to think about is making sure the patient and myself have reasonable expectations for the bone density, right?

And so, I see a lot of patients that will come to me, and they say, "Oh, you know, I took alendronate before, and I stopped because it wasn't doing anything." Well, that probably meant it was working, right, if the bone density wasn't changing, and it was maintaining. That's typically how an antiresorptive agent should work.



Denosumab's a little bit unique in that most patients will improve their bone density because it's such a potent antiresorptive agent. But, you know, even then you have to have a reasonable expectation for yourself in terms of, how is this drug supposed to work? What should I see as an appropriate response, and how soon should I see that, too, right? So that's part of that sort of every-couple-of-years updating of bone density to assess the response. If you follow some of these agents too quickly, you may not be able to capture change on bone densities.

So, you can tell a patient, "Yes, your bone density's stable, but that means your risk of fracture is now significantly reduced from where it was 2 years ago."

Well, let's review the answer to our clinical question. Which of the following statements is true regarding the 2020 AACE guideline recommendations for the treatment of osteoporosis? The correct answer is (A) Switching from bisphosphonates to denosumab produces additional gains in BMD.

However, as noted, the discontinuation of denosumab can cause a rapid decrease in BMD, with risk of multiple vertebral fractures and spontaneous fractures within a short period. Therefore, drug holidays with denosumab are not recommended.

Though current guidelines do not recommend switching from denosumab to an anabolic agent because of the associated loss of hip bone mineral density, switching from a bisphosphonate to an anabolic agent may be considered.

Getting back to our case, with Amy's new concern regarding osteoporosis and hip fracture risk, she asks what more she can do aside from taking her medication diligently. She knows calcium helps with bone health, but one of her friends said there is some downsides to taking it, as well. This leads to the final question.

Question 5

For this patient, what is the recommended daily intake of calcium and vitamin D?

A. Calcium intake of 800 mg/day and vitamin D intake of 600 IU/day.
B. Calcium intake of 1,200 mg/day and vitamin D intake of 600 IU/day.
C. Calcium intake of 1,200 mg/day and vitamin D intake of 800 IU/day.
D. Calcium intake of 1,600 mg/day and vitamin D intake of 800 IU/day.

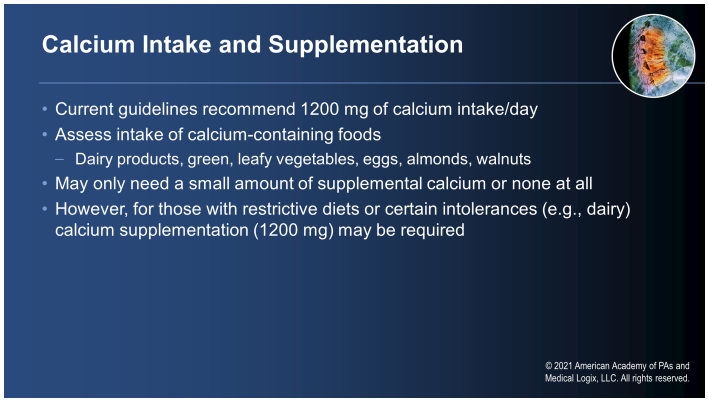
Catherine, what do you recommend to your patients about calcium and vitamin D?

Catherine Sweeney: I can relate to that scenario, as well, which is great. People are very conscious of what they're putting into their bodies, and that's a huge component of this. It isn't just about medication.

So I do follow the guidelines, which recommends 1,200 mg of calcium per day. However, I do always ask about their diet, because your food counts just as much, if not more, in my opinion than the supplements do.

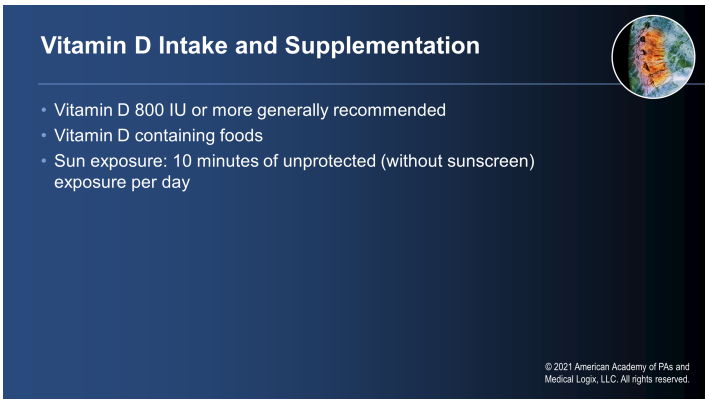
So we go over, are you eating dairy products, green, leafy vegetables, eggs, almonds, walnuts, those types of foods? If they eat all of that, you know, then maybe we don't even need a calcium supplement depending on their bloodwork, of course, and everything, too. But for most, I would say most people can at least get half of what they need from their food, and maybe supplement with 500 to 600 mg of calcium.

And then, of course, there are patients who perhaps are just lactose intolerant or just only eat apples and bananas, and we don't get any calcium-rich foods. So for those patients, absolutely, take the 1,200 mg, so that way we're ensuring our bodies are getting what they need.



And with vitamin D, I do tend to recommend 800 IU, or even more, especially depending on their bloodwork.

And that, again, I counsel my patients about the foods that do contain vitamin D, which certainly, there's a shorter list there. But getting some sunshine, 10 minutes a day of unprotected sunshine without the sunscreen, and then supplementing as needed, I think, is very helpful.

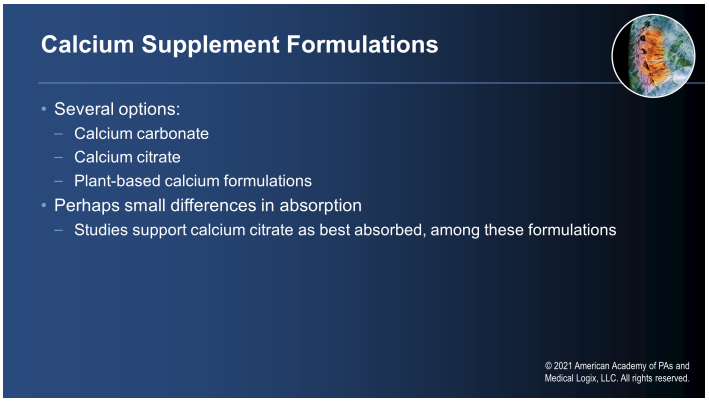


Is there particular calciums that you tend to recommend at all, because that's another hot question we get, too.

Patrick Cacchio: I think I tell patients, if you're doing well with what you're taking, and it's not bothering you, then that's fine. And that brings up the point of what are the concerns with calcium supplements?

in terms of the different formulations, you know, there's calcium carbonate. There's calcium citrate. And now there's a lot of these plant-based calciums that are out there, as well.

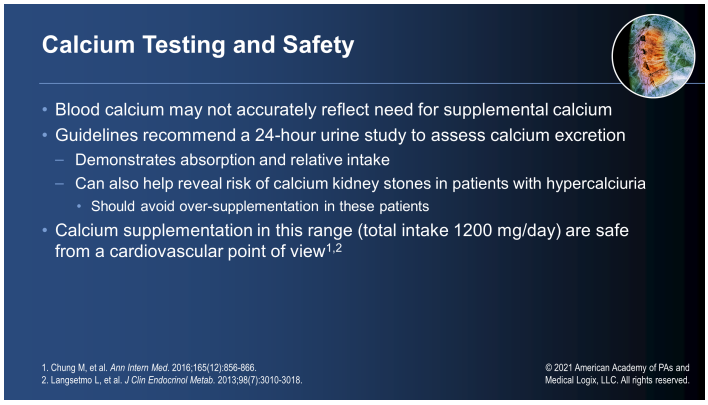
And there's probably some differences in absorption. How clinically meaningful is that for the average patient? Probably not so much, but, you know, I see a lot of folks that are post-bariatric surgery and have some issues in terms of absorption, obviously. And so I think the studies would support calcium citrate as probably the best absorbed from that standpoint. And so I do tend to recommend that, especially if I have some concerns.



And then if I have the patient who really wants to know, am I getting enough just from my diet? Do I need to take a calcium supplement? Well, a lot of times the blood calciums not the best indicator of that. And so the guidelines would suggest a 24-hour urine study to look at calcium excretion. And if that's normal, then that can give you some reassurance that they're probably absorbing their calcium pretty well and getting a normal amount.

In addition, it's a helpful secondary screening tool, as well. I see a number of folks that have hypercalciuria, and those are folks I really want to be careful about taking extra calcium supplements, because I don't want them to end up with kidney stones, and many of them may have already had them.

I get a lot of questions, you know, "My cardiologist told me not to take calcium," and all these sort of things. And I always defer to the cardiologist when it comes to heart health. But the data and the Preventive Cardiology Association did look at this data, and at the doses we're recommending, the effects from a cardiovascular risk standpoint are minimal, if any.



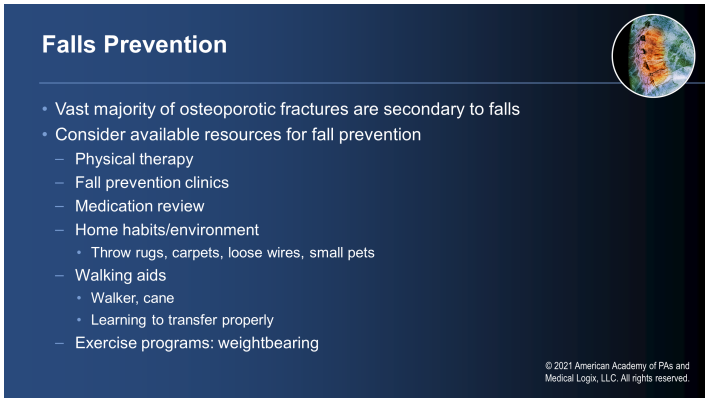
And so I think calcium supplements are safe. But, you also don't want to overdo it.

But, what else can patients do to help beyond just, you know, their diet and supplements? And so I always tell folks when they come in, both from a patient and a family standpoint, but falls, right? That's the big thing. How many fractures occur from a fall? Almost all of the ones that we see. Not all, but almost all.

And so, thinking about fall prevention and if you have resources in your community that you can refer someone to, whether it's physical therapy or fortunately, at Duke, we have a falls prevention clinic that helps folks go through their medications and their habits and their home and things like that to make them safer, and reduce their risk of a fall.

Catherine Sweeney: And I think physical therapy and the fall prevention clinic that you all have is fantastic, because they can walk those patients through, "Okay, do I need a walker? Do I need a cane? How do I use it? How do I transfer properly?" Those things about throw rugs. You know, wires, little pets, which we see a lot. The little dogs and cats are so cute, but they're that perfect height to trip people up. So just kind of having the time with the patient to go over those things can be really effective in helping to prevent those falls.

And of course, doing the exercises that help with bone density. Our weightbearing exercises, of course, is the catchall term. But walking, again, that yoga or tai chi to work on balance. If you can do weights, wonderful, or those exercise bands. All of that can really help to complete the picture of your treatment for the patient.



Patrick Cacchio: I think it's a good thing that we have these resources now, and they're publicly available and really, we need to make sure we're utilizing them, because they help. They do help.

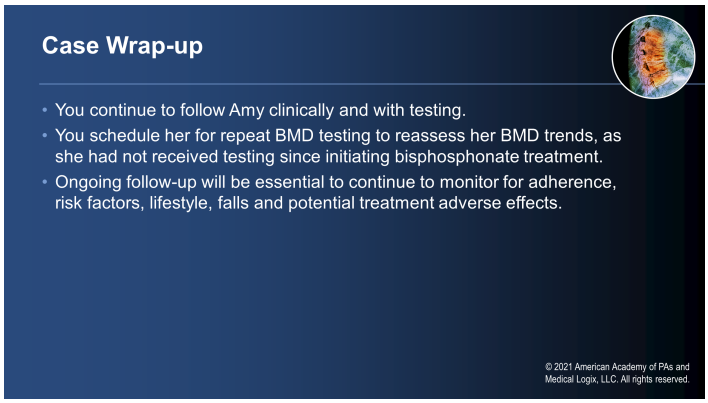
Catherine Sweeney: And so returning to our question, the recommended total daily intake of calcium is 1,200 mg, and for vitamin D, it is 800 IU/day. The correct answer is therefore (C).

There is some debate about the relative risks of calcium supplementation. However, staying within recommended supplementation limits is not associated with adverse cardiovascular outcomes. As well, sufficient calcium and vitamin D intake is associated with maintained bone mineral density or slowed bone loss.

Several other lifestyle considerations have been shown to improve bone mineral density and related outcomes, including regular exercise, weightbearing exercise, smoking cessation and alcohol reduction. Fall prevention interventions can help prevent major falls.

Amy is pleased with your counseling and continues with her treatment and follow-up with renewed vigor.

Patrick Cacchio: As we close this case, you continue to follow Amy clinically and with testing. You schedule her for repeat BMD testing to reassess her BMD trends, and she had not received testing since initiating bisphosphonate treatment. Ongoing follow-up will be essential to continue to monitor to adherence, risk factors, lifestyle, falls, and potential treatment adverse effects.



Catherine Sweeney: I would like to thank our expert faculty, PA Cacchio, for your great insights and discussion. And I would like to thank you, our audience, for participating in this video *eCase Challenge*.

CLINICAL PEARL

The AACE recommendations acknowledge that BMD testing is powerful, but other clinical risk factors influence fracture risk. The FRAX tool incorporates key risk factors into fracture risk assessment.

For patients at high risk of fracture, an oral bisphosphonate remains a reasonable frontline agent per AACE guidelines.

Anabolic agents for the treatment of osteoporosis include romosozumab, abaloparatide and teriparatide. Notably, romosozumab was approved for use in osteoporosis in 2019. These anabolic agents, as well as denosumab and zoledronate, are recommended for the treatment of very high-risk patients and/or those with prior fractures.

The AACE guidelines support that switching from bisphosphonates to denosumab produces additional gains in BMD. However, since the discontinuation of denosumab can cause a rapid decrease in board with risk of multiple vertebral fractures and spontaneous fractures within a short period, drug holidays with denosumab are not recommended because of the increased fracture risk, and patients should transition to an alternative antiresorptive therapy.

As per the guidelines, a holiday is not recommended for non-bisphosphonate antiresorptive drugs, and treatment with such agents should be continued for as long as clinically appropriate.

To prevent loss of BMD and maintain fracture efficacy, antiresorptive agents, denosumab, bisphosphonates or raloxifene are recommended following the discontinuation of an anabolic agent, abaloparatide, romosozumab, teriparatide.

The recommended total daily intake of calcium is 1,200 mg, and for vitamin D it is 800 IU/day.

There is some debate about the relative risks of calcium supplementation. However, staying within recommended supplementation limits is not associated with adverse cardiovascular outcomes. As well, sufficient calcium and vitamin D intake is associated with maintained BMD or slowed losses.

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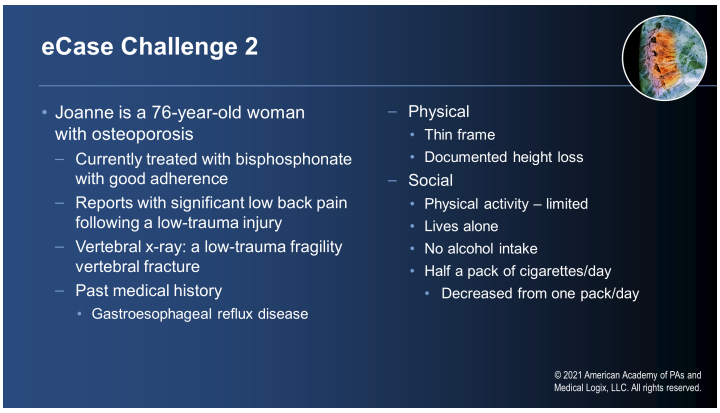
eCASE CHALLENGE #2

Catherine Sweeney, PA-C, CCD: Hello, and welcome to this ideo *eCase Challenge*, "Managing Patients with Osteoporosis: Staying Current with Updated Guidelines." I'm PA Catherine Sweeney, Coordinator of Emerge Ortho's Bone Health Clinic. Joining me today is PA Patrick Cacchio. Patrick is a PA at the Duke University Endocrinology Clinic. My thanks to you for your involvement in this important continuing medical education activity.

We will be discussing the second *eCase Challenge* during this activity. So, let's get started.

Our second *eCase Challenge* is focused on a patient we will call Joanne. Joanne is a 76-year-old woman with a history of osteoporosis and gastroesophageal reflux disease. She has been taking an oral bisphosphonate with good adherence. She reports with significant low back pain following a low-trauma injury.

On vertebral x-ray, a low-trauma fragility vertebral fracture is confirmed. She has a thin frame, and she has documented height loss. Her physical activity is limited, and she lives alone. She does not drink, but she continues to smoke half a pack of cigarettes per day, decreased from one pack per day.



With this brief initial information, let's pose our first clinical question.

Question 1

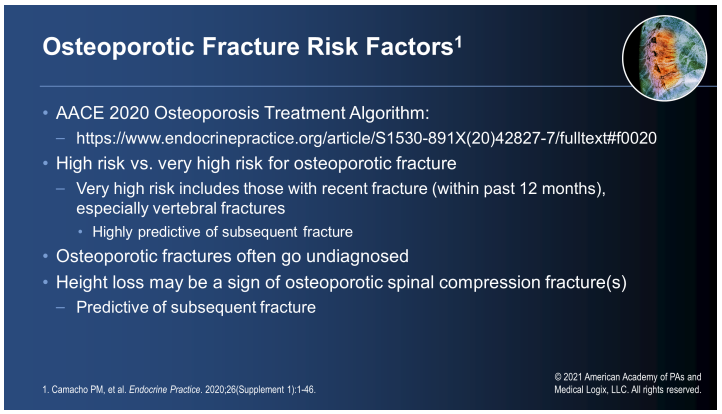
What key features put this patient at very high risk for fracture?

A. Distant history of fracture after motor vehicle accident
B. Recent fracture within the past 12 months
C. Treatment with proton pump inhibitor
D. T score less than -2

Patrick Cacchio, PA-C, MHS: So, Catherine, allow me to review some important points. What are some of the risk factors? How do we stratify someone's fracture risk based on the new AACE guidelines? Well, I really like the algorithm that they came up with, and there's a nice graphic in the guideline document that talks about high risk versus very high fracture risk.

And so, patients can be at a high risk, which is concerning. But very high fracture risk are those who have had a recent fracture, and that's defined within the past 12 months, particularly vertebral fractures. You know, those are very predictive of subsequent fracture.

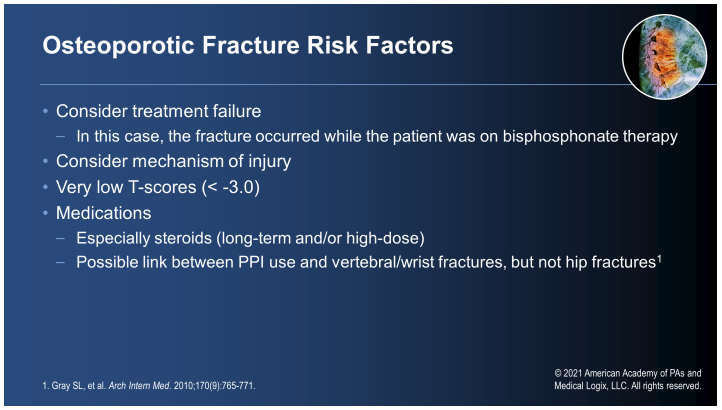
And a lot of them go undiagnosed. And so, when you hear a patient talk about height loss or, in our clinic, we measure height every time we see a patient to see if there's any objective height loss between their visits, that can be very predictive of someone's risk of a subsequent fracture, and really something that should be actionable from a clinical standpoint.



The other things to think about as it relates to this case: fractures while on therapy. This is a patient that's on a bisphosphonate. So, the whole reason we're treating osteoporosis is to try to prevent fracture. So is this indicative of a potential treatment failure if someone's fractured while on therapy?

So understanding, as we've talked about, low-trauma fracture, understanding the mechanism of the injury. And then, folks that have very low T scores certainly are those that are at very high risk of fracture, as well. And the guidelines would suggest anything less than -3.0 as a very low T score.

Medications, high-risk fracture medications, so things like steroids and very much long-term use of steroids, high-dose steroids are all really important things.



And then the FRAX calculator, right? So that's so important here, and that gives us a number. And the guidelines really for the first time define very high fracture risk using FRAX as a major fracture risk greater than 30%, or a hip fracture risk greater than 4 and a half percent.

So how do you counsel patients to sort of talk about very high fracture risk versus high fracture risk, and what that means to that individual person in terms of their risks?

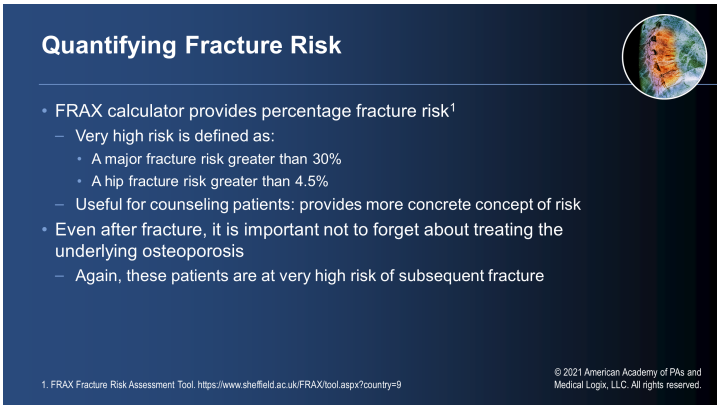
Catherine Sweeney: Exactly. And I think these guidelines do kind of help us counsel patients in that way, because now we have certain thresholds where we can say, "Okay, we know this certain threshold puts you at much higher risk." So, like you said, if I see

patients with vertebral fractures, especially if we discover them on maybe a DEXA scan, and they didn't even know they had them, that can put you at that very-high-risk category.

So, someone who maybe falls below those thresholds still, of course, may have osteoporosis, and the fracture risk is still high. But now we know what are the factors that really put someone almost over the edge, where they really need to kind of perk up and maybe do something more aggressive as far as treatment goes to help prevent that next fracture.

And I agree, it was kind of interesting that they incorporated FRAX with this, too, because, again, a lot of times we don't even calculate that when someone's T score is at a -2.5 or lower, more negative. So it's nice to kind of again see that stratification.

Patrick Cacchio: And I think that's a key point, too, in terms of what type of therapy, because I see a lot of times in practice -- and I'm sure you see this, too, in the osteoporotic fracture world, especially in an orthopedic clinic -- that, you know, you focus on treating the fracture, and we'll deal with the bone density and the bone health later.



But, there's some urgency here, and that's when we talk about a recent fracture within 12 months, these are folks that are at very high risk of another fracture now, not a year from now, but right now. And that's where, again, having a clinician that's aware of these new guidelines is really important to be able to act upon them.

Catherine Sweeney: Absolutely. So let's review the question posed, which asked, what key features put this patient at very high risk for fracture? The correct answer is (B) Recent fracture within the past 12 months.

As discussed, based on the most recent 2020 AACE osteoporosis guidelines, several factors place one at very high risk of fracture, including recent fracture, fracture while on approved therapy, very low BMD T score, less than -3.0, and very high FRAX score.

Regarding the incorrect options, while PPI use does seem to decrease calcium absorption, the link between PPI use and increased fracture risk is not as clear. There may be a link between PPI use and vertebral and wrist fractures, though not hip fracture, based on one large analysis.

High-velocity fractures in the past are not associated with later risk of osteoporotic fractures.

Getting back to our case, given the recent documented low-trauma vertebral fracture and fracture while on osteoporosis therapy, Joanne is at very high risk for subsequent fracture. Aside from managing the pain of this fracture, you will need to make decisions regarding the next steps in treating her osteopetrosis. This brings us to our next clinical question.

Question 2

Based on the 2020 AACE osteoporosis guidelines, which agent would be considered second-line therapy for very-high-risk patients?

A. Denosumab
B. Ibandronate
C. Romosozumab
D. **Teriparatide**

So this brings an important point to light with patients who have fractured versus patients who have not fractured. So what are some of the things you think about when you see this post-fracture patient? Which agents do you tend to reach for first?

Patrick Cacchio: Again, to my earlier point, this is a setting where we know this is someone who's at high risk of fracture. So it's important to think about certainly the mechanism of action of these drugs, as well as the onset of fracture efficacy.

So, we know in general, oral bisphosphonates are good medicines, but they take a while to demonstrate meaningful fracture risk reduction in clinical trials. So, some of newer agents, particularly anabolic drugs, have shown a much faster onset in terms of risk reduction.

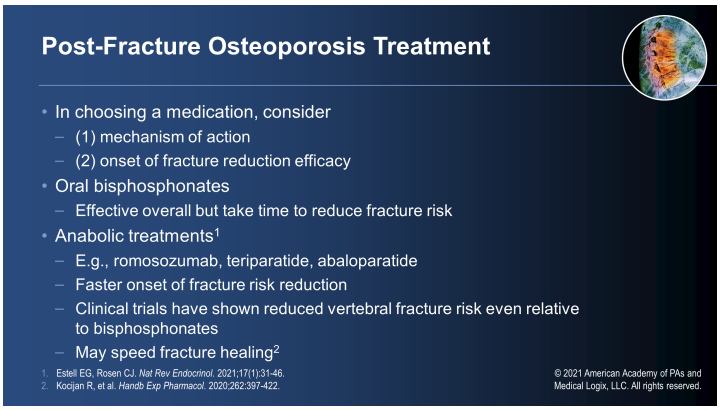
And in addition, we also know that there may be superiority demonstrated in some of these trials. So, particularly when we're talking about vertebral fracture risk reduction, a lot of our anabolic drugs have shown superiority to bisphosphonates in terms of preventing a fracture, a future vertebral fracture.

So this is a setting where we have someone who's already fractured. They have a vertebral fracture. You know, we really want to use a drug that's going to be most effective at preventing that, again, without causing other harm to the patient and not otherwise contraindicated. But, I really think about -- when I see someone who's had a recent fracture, starting with hopefully the most effective therapy as long as it's not contraindicated.

So the anabolics, like romosozumab, like teriparatide or abaloparatide, are really good agents in these settings, I think. And as we get more and more experience in clinic and in clinical trials, I think that keeps showing up again and again, that these are really effective treatments.

Catherine Sweeney: Absolutely. And it's something -- I think we have a little bit of data now, too, that some of these anabolic agents can actually help with fracture healing a little bit. So, again, like you said, the quickness that these medications can work, especially things like abaloparatide, where it showed significant improvements in bone density within the first 3 months, that's pretty fast, considering the bone turnover process and remodeling process.

So these types of anabolic agents I think can not only help, again, prevent that future fracture, but can also help speed along the healing a little bit of these recent fractures, as well.



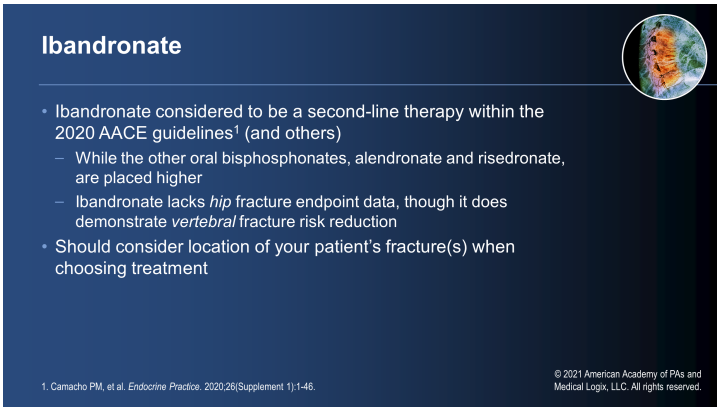
And so what's different about ibandronate? We're going to kind of answer the question there a little bit. But why is that maybe considered a second-line therapy?

Patrick Cacchio: So this is always sort of, I think, a nuance in the guidelines, and it's not unique to the AACE guidelines. If you go through any of the iterations of osteoporotic treatments, guidelines, ibandronate's almost always positioned beneath alendronate or risedronate among the oral bisphosphonates.

And it's primarily because it does not have hip fracture endpoint data. So in their clinical trial program, it's an effective treatment at vertebral fracture risk reduction, but did not show the same efficacy as alendronate and risedronate. So many clinicians would view it as a lesser agent.

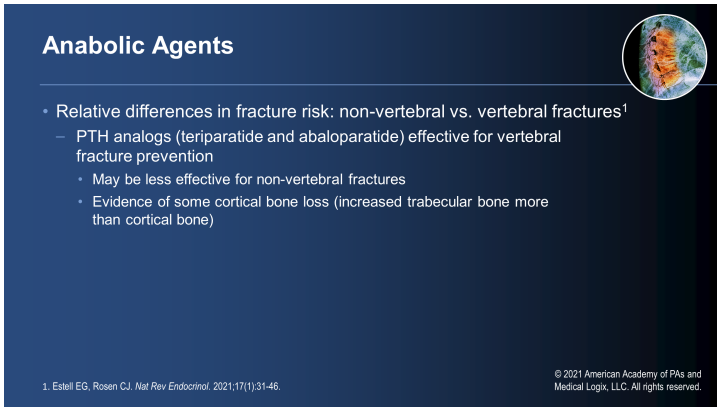
You know, there's probably some debate about clinical trial design and power and those sorts of things, as well. But if we're going to be purists about the data, I do think it's probably a little bit lesser agent compared to alendronate or risedronate as it relates to non-vertebral fracture risk reduction.

And that's where, again, the site of a fracture matters -- and also the pattern of bone loss on a bone density matters. So if you have someone who has a significant risk of hip fracture or recently sustained a non-vertebral fracture risk, you want an agent that's going to have a meaningful effect on non-vertebral fractures. So, you're not going to pick a drug like ibandronate probably as your first choice, if possible, and think about something that has demonstrated efficacy in those settings.



You know even among the anabolic agents, I think there are some differences there, too, in terms of fracture risk reduction at non-vertebral versus vertebral fracture sites. And certainly, the PTH analogs -- teriparatide, abaloparatide are very effective at the spine, but probably less so at other sites.

And, certainly in the trials even at cortical bone, there can be some bone loss associated with those treatments, because of the PTH effect. So you have to think through these things in terms of what are you hoping to achieve with these treatments?



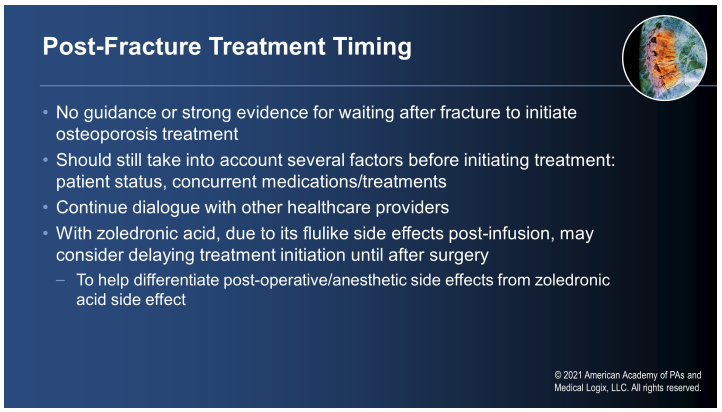
Catherine Sweeney: Absolutely. And is there any guidelines or data that we have that help us to decide timing of this treatment? So I know I have a lot of orthopedic surgeons who will say, "I have to do a kyphoplasty. Can you please wait a month before starting therapy?" Is there really any data to support waiting on therapy if someone does have to have surgery or an ORIF or anything like that?

Patrick Cacchio: No, certainly not in the guidelines, and not high-level evidence at this point, I don't think. But, you know, you have to take into account the patient status and how much you want to throw at this person at one time.

If they are going to have a procedure, a surgical fixation or a stabilization of a fracture, we want to be proactive, but we want the patient to be feeling well and giving the treatment a good chance of success, as well.

So I think it's very much individualized, and it's important to be able to have that conversation with the treating orthopedic provider and understand their concerns and understand your concerns, that this is someone who's at high risk of additional fractures. And so we want to get them on therapy as soon as we can safely do so.

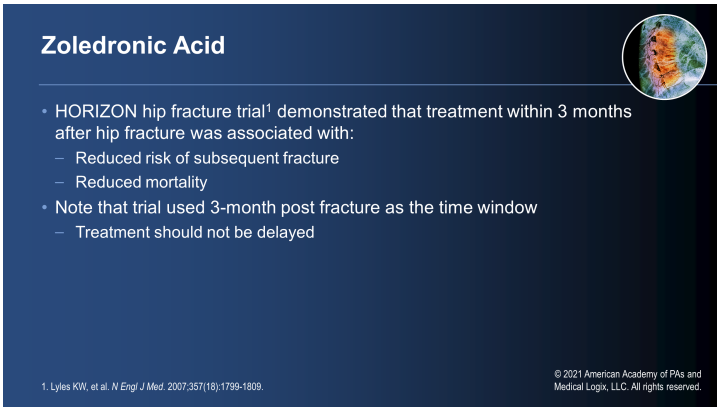
Catherine Sweeney: Absolutely. And I think one thing -- one timing I do in my clinical practice is perhaps with zoledronic acid, because sometimes it can cause those flulike side effects immediately after the infusion, sometimes I find it to be helpful to delay that until someone is postoperative, where we know it's, the difference between if it's an anesthesia side effect or a side effect from the zoledronic acid.



But otherwise, I would agree, just working in conjunction with the orthopedic surgeon or whoever else is advisable, because the data doesn't really quite support any reason to delay otherwise.

Patrick Cacchio: And you raise a good point there. In terms of zoledronic acid, the HORIZON hip fracture trial, so, using zoledronic acid after hip fracture has been shown to not just prevent subsequent fracture, but actually reduce mortality, which we know is such a big factor with these hip fractures in our older patients.

So delaying treatment is really in some ways hindering potentially that mortality benefit. The trial was designed to give it within the first 3 months of the fracture, post-fracture. So we want to delay it, to your point, to the patient's feeling well and reasonably recovered, and their renal function is stable and that sort of thing. But if that's the treatment of choice in that setting, delaying it too long post-fracture may minimize some of the benefit that you get clinically.



So, returning to our question, the correct answer is (B) ibandronate. The remaining medications are all recommended for the treatment of patients at very high risk for osteoporotic fracture, which includes those with previous fracture. The main agents included are abaloparatide, denosumab, romosozumab, teriparatide and zoledronate.

As you begin to consider next medication options, you consider factors contributing to poor response to osteoporosis treatment. This leads us to the next question.

Question 3

Which factor does not contribute to poor osteoporosis therapeutic response?

A. Poor intestinal absorption
B. Hypocalcemia
C. Hypoparathyroidism
D. Poor adherence

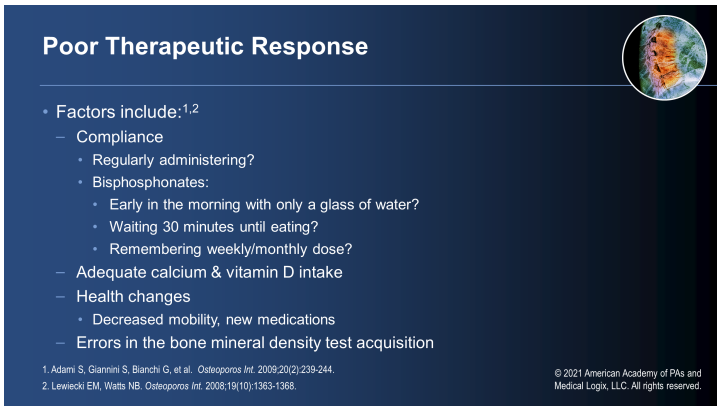
So this is a common concern, is someone who's not responding to therapy. What are some of the things that you think about and ask patients when you're trying to asses their response to therapy or promote a good response to therapy, Catherine?

Catherine Sweeney: Absolutely. So, things that we talk about is definitely compliance. So, number one, are you taking it? And that is a big factor, I would say, with the oral bisphosphonates. And even some of the anabolics, you know, with the daily injections, as well. Are you consistent? Do you take it every day?

With the oral bisphosphonates, are you taking it first thing in the morning, just with a glass of water? Are you waiting your 30 minutes? Do you forget? Which I find often, you know, it's common. The week goes by, and you forget to take your pill, or if you're taking something like ibandronate, the whole month goes by. It's very easy to forget that pill.

We also look at, again, their calcium and their vitamin D intake. Are you taking a supplement if necessary? Are you getting those foods in your diet?

Other things we think about is, did something happen in their health? Did they have to go to the hospital for a heart attack, and they haven't been able to be very mobile? Are they wheelchair-bound now for whatever reason? Did you have a knee replacement, and you couldn't put weight on that leg for a couple of months? You know, things like that that could have affected the rate of bone formation for the patient and ultimately the efficacy of the medication.



Also, I do take a look at the bone density test, because a lot of times there's errors there. You have to be a skilled technician to perform a bone density test, and there are certain places to put the markers.

There are certain differences in different brand machines. You have to know if you're comparing the same brand of machine on each exam, because if it's not, you can't compare the T scores apples to apples.

And so all those things can then affect your ultimate bone mineral density, and then your treatment decision. So I try to always get pictures of the scan itself so I can see where the markers were placed. Was it the same as the previous exam?

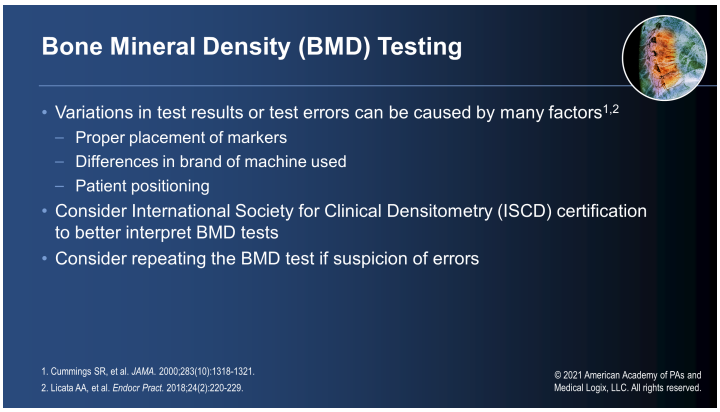
So all those different things can play a role where maybe it wasn't really a true decrease in bone density. Maybe there was some type of error there, and you have to kind of know when to recognize those things so then you can make your proper treatment decision.

Patrick Cacchio: And I know you've been involved with the ISCD and are certified from that standpoint. And it's really a great organization. Again, if bone density is part of someone's clinical practice, I encourage my students and learners to always get involved with that and take the courses and things to really understand what we're measuring and how to accurately interpret bone density.

But, a change in bone density, a negative change on therapy is certainly a concern that there is a treatment failure. So it's important to be thinking about why is the treatment not working? Is it the medicine itself, or are there other factors that we could modify that might make the treatment more effective?

Catherine Sweeney: Do you ever repeat a bone mineral density test or redo it, so to speak, if you find there are some errors?

Patrick Cacchio: So that's a challenge just in terms of sometimes insurance coverage and things like that. But if it's really important clinically, I think it's worth doing. And if you have the ability in your clinic to be able to repeat it and sort of almost write it off, so to speak, if necessary, but be able to do it, if it's going to affect your clinical decision-making, it's an important data point to get.



And so if you don't trust the data you're getting, you have to be able to have a quality scan. And so I do think it's important to repeat if necessary and confirm if it's a real finding.

And again, the ISCD has guidelines in terms of what's a least significant change, doing precision studies on a bone density machine. So all that information should be captured in a bone density report so that you have some assurance that it is a quality report and a quality study, and you can make your decision based on that.

Catherine Sweeney: Let's return to the clinical question, which asked, which factor does not contribute to poor osteoporosis therapeutic response? The correct answer is (C) hypoparathyroidism.

Causes leading to therapeutic failure may include poor adherence and poor medication supplement absorption. Other secondary factors may include endocrine causes, such as hyperthyroidism and hyperparathyroidism, though not hypoparathyroidism.

Going back to the case, as you mull over medication choice considerations, you also consider if adherence has become an issue for this patient. Perhaps some additional assistance is needed, and you consider an outside referral. This leads to the next question.

Question 4

Which of the following statements is correct regarding fracture liaison services?

A. Only offer treatment recommendations.
B. Are not associated with mortality risk improvement.
C. Associated with decreased refracture risk.
D. Are widely implemented in highly developed countries.

So this brings a new term to the discussion, a fracture liaison service. These certainly take many forms, depending on what practice you're in. And again, I know with your practice, Patrick, it's more of an endocrine-based clinic, where sometimes these fracture liaison services, we see them more either in primary care or orthopedic, where seeing a patient post-fracture is the more common patient type.

Do you all have one there at Duke, or how do you kind of capture these patients for your clinic?

Patrick Cacchio: So to your point, these can take many different forms. And, you know, certainly there are really good publications about specific programs at specific hospitals. And I think there are always going to be nuances to an individual health system or your practice that are going to make it take its own flavor.

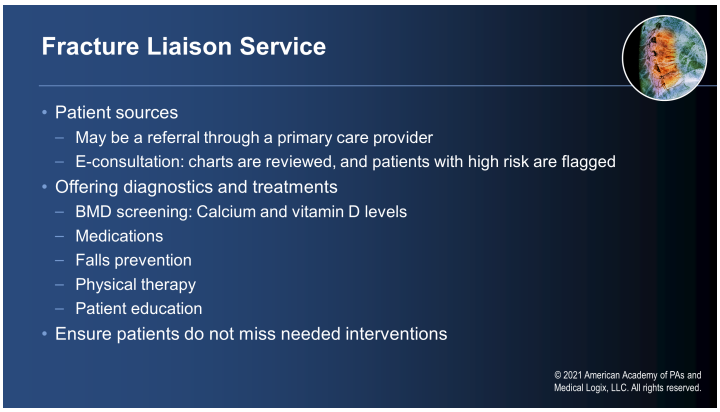
But, you know, the idea behind this is trying to identify folks at the time of their fracture and help get them to appropriate therapies, not just medications, but fall risk reduction and all those things that we've talked about from a lifestyle standpoint to help these folks prevent a subsequent fracture, because we know that these are really high-risk patients.

And so in our practice, yes, we're sort of the endgame for these folks, and so, we want to capture these patients, and so we want them from the inpatient services, from the orthopedic services, from the primary care community to be referring them to us.

And so there's a number of different initiatives that you can take on in your practice. We've piloted a lot of them in our practice, you know, using e-consultation, reviewing charts electronically and identifying, flagging patients through your electronic health record to say, "Hey, this patient's had a recent low-trauma fracture. They're at high risk of subsequent fracture. You know, you need to evaluate them and treat them if appropriately with the following modalities in terms of bone density screening and calcium and vitamin D and medications, as we've talked about, falls prevention, physical therapy, all these kind of things."

But also, partnering with those folks that are already taking care of these patients. A nurse case manager a lot of times is somebody who's really well positioned to help take the lead in terms of educating patients about their fracture.

And so, we've tried a number of different things to work with primary care and orthopedics and the case managers on the inpatient side to try to capture these patients and get them seen and evaluated. So I know your practice is doing this fairly proactively in an orthopedic clinic, which is really a unique setting for you to be working as a bone health specialist.

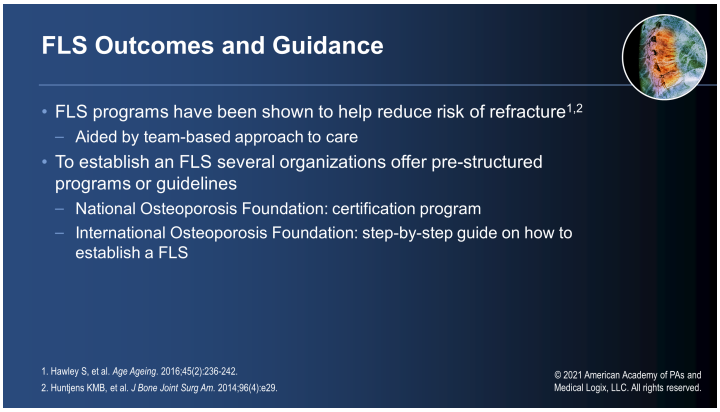


Catherine Sweeney: And it is. These fracture liaison services, I think the key takeaway is, it's a team approach, you know? So whether it looks like a nurse practitioner or a PA who leads the front or an MD, it's just a way to make sure these patients don't fall through the cracks, because so many of them do. They're seen for that fracture. They're treated. They walk out the door. You tell them to go follow-up with primary care. And nothing gets done.

So these services really have been shown to help reduce that risk of refracture, because you now created a team around this patient to help make sure that their bone health is optimized. And then it helps to really serve them in the future, and also take some things off the primary care doctors sometimes, as well, who have so much on their plates.

So these fracture liaison services, it doesn't necessarily have to be very complicated. And there's great resources that you have mentioned, kind of pre-structured programs or guidelines that people can follow.

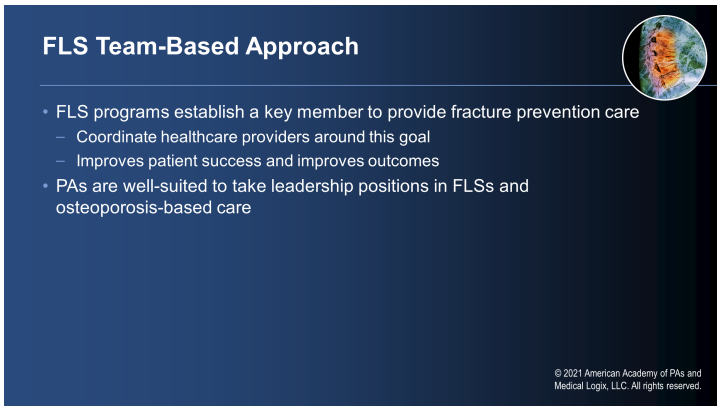
The National Osteoporosis Foundation has a wonderful program. You can get certified. The International Osteoporosis Foundation has a lovely step-by-step guide of how to establish these programs.



But basically, you're establishing a point person to be that person for the patient where, then you have the time to evaluate and say, "Okay, we broke a bone. How are we going to prevent this from happening again?"

And, like you said, working with the physical therapist, working with specialists like yourself, the endocrinologist, primary care and making sure that the medication, if you all choose medication, is adhered to, having those follow-up visits and having those touchpoints with that patient really makes them much more successful, and then therefore, much better outcomes for their overall health.

So these services are really just a way to kind of utilize us almost as PAs, too. This is a great role for a PA to take a leadership position and really be that point person for these patients to help reduce their chance of another fracture and keep them on track, be their coach, their motivator, and that will help them for the future years to come.



Patrick Cacchio: Absolutely. And I echo that. I think a lot of these case studies, when you go to these resources at the National Osteoporosis Foundation and elsewhere, it really all started with a single person. And a lot of times it is a midlevel provider, a PA, a nurse practitioner, sometimes even a nurse that takes a leadership role in seeing that there's a real need here.

So let's review the answer to our clinical question. Which of the following statements is correct regarding fracture liaison services? The correct answer is (C) They are associated with decreased refracture risk.

Similarly, they are also associated with 30-day and 1-year mortality risk benefits. These fracture liaison services are designed to identify patients who suffer a first fracture, assess their bone metabolic status and institute medical therapy as indicated to prevent a second fracture.

Returning to the clinical scenario, you are able to refer Joanne to a fracture liaison service, and they provide recommendations for follow-up, monitoring and treatment. Joanne has been taking her supplements diligently and her medication. Recently, she has been reading Internet forums about vibration platform therapies. She asks you about additional lifestyle modification to reduce her risk of osteoporotic fracture. This brings us to our final clinical question.

Question 5

Which of the following is true regarding lifestyle modification and osteoporosis?

A. Smoking one pack per day throughout adult life was associated with a 5 to 10% reduction in bone density.
B. Whole-body vibration platforms have shown improved BMD in randomized controlled testing.
C. Calcium supplementation should not be combined with other supplements/vitamins.
D. Increased protein intake is definitively associated with increased BMD.

So, Catherine, we've talked about lifestyle. We get lots of these questions in clinic, right, in terms of the latest technologies and things on the Internet, whether it's a supplement or things. How do you counsel your patients when they bring some of these things to you? I get messages, I think, almost every day from a patient

through our electronic record asking about some new supplement or technology to help their bones.

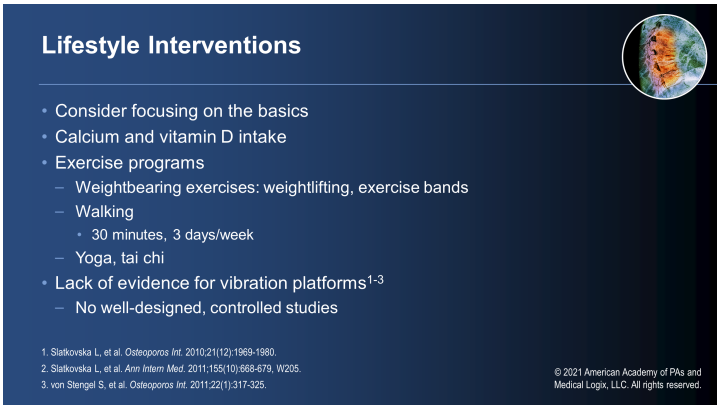
Catherine Sweeney: Absolutely. And there is. It's an ever-changing, ever-evolving body of data that we have. I tend to stick to the basics, of what the data supports. So, certainly, first and foremost, calcium and vitamin D to make sure that they're getting adequate nutritional intake of those vitamins, whether it be from food or their supplements.

Certainly, the vitamin D I think has excellent data behind it, as well.

And some of these exercise programs, yes, we get those questions, too. Which one is the best? Certainly, there are certain fads that come and go with exercise. But I think the basic principles is what I try to stick to.

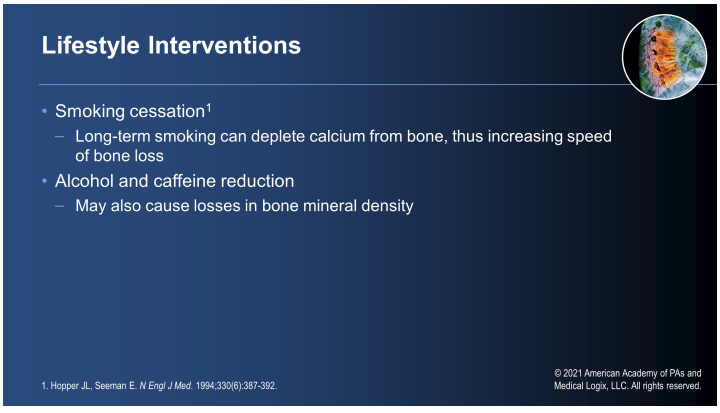
So, exercises that stress the bone and give a little bit of impact, within reason. So things like weightlifting, if they can, exercise bands, walking is great for the hips. You know, there are things like yoga and tai chi to help with balance.

The vibration platforms, not really great clinical data to support any real utility of those. So not something that I recommend on a regular basis.



With regards to the exercise, I try to encourage walking every day if they can. I think that's an easy enough exercise for most, and weather permitting, of course, that it does really help the hips, especially. But if they can do 30 minutes of exercise 3 days a week, that's fantastic.

And of course, those other lifestyle modifications that we talked about. So, absolutely working on quitting smoking if they can, offering as many resources as we can to help them along that journey, because certainly, smoking, especially long term, can deplete that calcium from the bone and really speed along the reduction in bone mineral density.

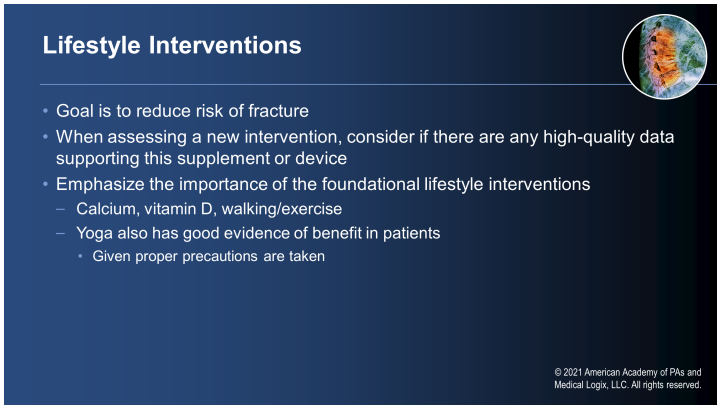


Same thing with alcohol and caffeine. We have those conversations, as well, and excess can also cause losses in bone mineral density. So taking a look at those lifestyle factors and trying to limit those things as much as possible.

Patrick Cacchio: And our goal here is to help this patient reduce their risk of fracture. And so, that's the question I always ask myself, is, "Is there any data that supports this modality or this supplement in terms of reducing this patient's risk of a fracture?" And for a lot of these newer things now, there are some claims and things. But there's no really high-quality data that support their use routinely for most patients.

It's sort of the commonsense things, as I tell patients. It's we want you to make sure you're getting enough calcium and D and exercise. Walking, if you're going to pick one thing, is important. But, you know, anything that helps with your strength and your balance is going to hopefully reduce your risk of a fall.

So, I feel strongly that things like yoga with appropriate precautions is perfectly reasonable for patients with osteoporosis. And I think it's probably helpful based on some pretty good data that has come out in the last few years.



Catherine Sweeney: Do you find that certain timelines are more useful to follow up with these patients? 3 months, 6 months?

Patrick Cacchio: It's going to vary on the patient. But, you know, I do find in our practice, we used to just spend a really long time in our first evaluation with patients, and then say, "Here's our recommendations," and sort of transition them back to their primary care provider.

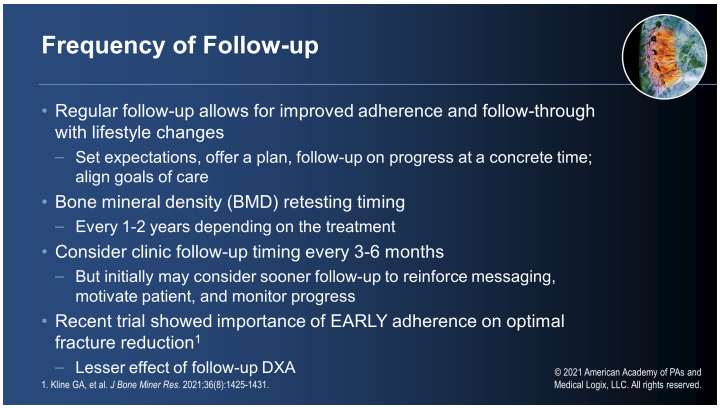
And what we learned is that without regular follow-up on these issues, particularly the medications and these questions, a lot of folks were falling off in terms of adherence and follow-through.

So we do like to try to follow our patients and see, and I try to give them expectations in terms of "This is what we're going to do today. This is what we're going to start. And then, I want to talk to you at this point."

So I think it's important for them to have that expectation, too, that we're invested. And I always say, "We're a team. We're trying to help you, and we don't want you to have another fracture. And so this is what we're going to do."

And then, from a bone density standpoint, as we've talked about, bone changes slowly. So, we don't want to foul up the bone density too soon, or we're not going to be able to capture any change meaningfully. So, certainly no sooner than a year on therapy for that is sometimes reasonable. But often, every 2 years, depending on the particular treatment for the patient.

Catherine Sweeney: Absolutely. And I would agree with that in our practice, as well, having those little more frequent touchpoints with the patient really does help with adherence, because a lot of times patients will have an adverse effect or get off track, and they don't think to call you and tell you. So you don't find out until 2 years later, when you do another test, that, "Oh, I have not been taking my medicine at all."



So having that 3-month checkpoint, 6-month checkpoint, whatever works best for your practice, but something a little sooner I think really helps with adherence and gives them some motivation, too, to keep it going.

Returning to our clinical question, which of the following is true regarding lifestyle modification and osteoporosis? In one twin study, smoking one pack per day throughout adult life was associated with a 5 to 10% reduction in bone density. This makes the correct answer (A).

Lifestyle modifications shown to BMD and fracture outcomes include calcium and vitamin D supplementation, weightbearing exercise and smoking cessation. Other interventions, such as whole-body vibration platforms, have not shown consistent improvements in BMD or fracture risk in randomized trials.

Getting back to the case, you review the relative dearth of evidence for vibration platforms. You again counsel Joanne on the importance of smoking cessation, not only for osteoporosis, but many other health outcomes.

Patrick Cacchio: As we close this case, you continue to counsel Joanne on the importance of modifiable risk factors and continue to support her smoking cessation efforts. Ongoing follow-up will be essential to continue to monitor risk factors, laboratory abnormalities, BMD testing and evaluate adherence to therapies.

Catherine Sweeney: I would like to thank our expert faculty, PA Cacchio, for your great insights and discussion, and I would like to thank you, our audience, for participating in this video *eCase Challenge*.

This concludes our second video *eCase Challenge*. On behalf of PA Cacchio and myself, we hope you enjoyed it. Thank you for joining us.

CLINICAL PEARL

Osteoporosis is a very common condition in the United States. While primarily affecting postmenopausal women, it also affects younger women, and even men. Before deciding treatment, the 2020 AACE guidelines recommend stratifying patients by fracture risk.

Several factors place one at very high risk of fracture, including recent fracture; fracture while on approved therapy; very low BMD, with a T score less than -3.0; and very high FRAX score, for example, a major osteoporosis fracture greater than 30% or a hip fracture risk greater than 4.5%.

Other factors include fractures while on drugs causing skeletal harm, such as long-term glucocorticoids, and high risk of falls or history of injurious falls.

In the case of therapeutic failure, causes may include poor adherence and poor medication supplement absorption. Other secondary factors may include endocrine causes, such as hyperthyroidism and hyperparathyroidism, though not hypoparathyroidism.

Fracture liaison services, or FLS, are designed to identify patients who suffer a first fracture, assess their bone metabolic status and institute medical therapy as indicated to prevent a second fracture. Interestingly, FLSs are associated with decreased refracture risk and improved 30-day and 1-year mortality risk.

Several lifestyle modifications have been shown to improve BMD and fracture outcomes, including calcium and vitamin D supplementation, weightbearing exercise and smoking cessation.

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CME POST-TEST: Participants must: 1) read the educational objectives and faculty disclosures; 2) study the educational materials; 3) complete the post assessments in Learning Central. See page 2 for further information.

Question #1

Which of the following is a risk factor for the development of osteoporosis?

A. Antiseizure medication use
B. High BMI
C. Hypothyroidism
D. Oral contraceptive pill use

Question #2

Based on 2020 AACE guidelines, which of the following patients should have a BMD test?

A. A 42-year-old woman with 2 osteoporotic risk factors
B. A healthy 47-year-old woman
C. A healthy 60-year-old woman
D. A healthy 67-year-old woman

Question #3

What information does the Fracture Risk Assessment (FRAX) tool provide?

A. Recommended osteoporotic treatment
B. Risk of major osteoporotic fracture in next 10 years
C. Risk of fracture at any site in next 5 years
D. T-scores at the hip and spine

Question #4

Which of the following agents is a sclerostin inhibitor?

A. Abaloparatide
B. Denosumab
C. Romosozumab
D. Teriparatide

Question #5

What did the FREEDOM extension trial find?

A. Denosumab treatment for up to 10 years was associated with low rates of adverse events and continued increases in BMD without plateau
B. Denosumab treatment past 10 years was associated with increased adverse events and decreased BMD at the spine
C. Ibandronate treatment was associated with improved vertebral fracture reduction risk, but not hip fracture risk reduction
D. Zoledronic acid treatment within 3 months after hip fracture was associated with reduced subsequent fracture risk

Question #6

For patients with osteoporosis, what is the recommended daily intake of calcium (dietary and supplemental sources)?

A. 800 mg/day

B. 1,200 mg/day

C. 1,600 mg/day

D. 2,000 mg/day

Question #7

A 70-year-old woman returns to your clinic after a DEXA scan to determine her bone mineral density. She has no previous osteoporotic fractures. She is currently taking denosumab. The results of her scan show that she has a T score of -2.7 at the hip and -2.0 at the spine. Which of the following is the most accurate interpretation of these results?

A. She has osteoporosis in both areas.
B. She has osteoporosis at the spine and osteopenia at the hip.
C. She has osteoporosis at the hip and osteopenia at the spine.
D. She has osteopenia in both areas.

Question #8

Which of the following is NOT considered to be an anabolic agent in the treatment of osteoporosis?

A. Romosozumab
B. Teriparatide
C. Ibandronate
D. Abaloparatide

Question #9

Which of the following agents is a parathyroid hormone (PTH) analog?

A. Abaloparatide
B. Denosumab
C. Pamidronate
D. Romosozumab

Question #10

Which of the following agents may give flulike side effects after administration?

A. Abaloparatide
B. Denosumab
C. Romosozumab
D. Zoledronic acid

Question #11

Ruth is an 88-year-old woman who presents to your clinic after repeat BMD testing. She has been taking a bisphosphonate for the past 3 years. Her results show BMD decreases more than you expect. You feel the test has been properly performed. You would like to question her on her adherence and administration of her oral bisphosphonate.

Which of the following is NOT associated with the administration of oral bisphosphonates?

A. Should be taken early in the morning with only a glass of water
B. Should wait at least 30 minutes until eating
C. Should not lie down for 30 minutes after taking
D. Should avoid if recent cardiovascular event

Question #12

Which of the following is NOT a factor associated with bone mineral density (BMD) test accuracy?

A. Differences in brand of machine used
B. Patient positioning
C. Proper placement of markers
D. Recent radiotherapy

Question #13

Which of the following statements is correct regarding fracture liaison services?

A. Only offer treatment recommendations
B. Are not associated with mortality risk improvement
C. Associated with decreased refracture risk
D. Are widely implemented in highly developed countries

Question #14

Tara is a 59-year-old woman who returns to the office after BMD testing. She has a bone mineral density of -2.8 at the hip and -2.0 at the spine. She has history of seizures necessitating the use of phenytoin. While she has risk factors for osteoporotic fracture, at this point she wishes to pursue lifestyle measures to improve her BMD.

Which lifestyle intervention has the largest evidence base supporting its use in treating osteoporosis?

A. Adequate calcium and vitamin D intake
B. Black cohosh
C. Swimming
D. Vibration platform therapy

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