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The latest physician jobs brought to you by the NEJM CareerCenter
How to Prepare for Your Physician Job Interview

By Nisha Mehta, MD, a physician leader whose work focuses on physician empowerment, community building, and career longevity in medicine

Finally! You've done countless interviews at this point, but for many of you, this is the first one where you are interviewing for a "real job." Some of the same rules apply, but others are very different.

To start, the dynamic in this interview is much different than others. You are likely interviewing with people who will be your colleagues, and your impression of them counts just as much as their impression of you. Depending on the job market in your field, there's a distinct possibility that they may even need you more than you need them.

Additionally, in an ideal scenario, you are picking a job that will last longer than a set time period of training. You are designing what potentially decades of life could look like for you and your family. Since this isn't just a stepping stone to the next thing, your approach will need to be more all-inclusive. Also, unlike residencies and fellowships, where a similar core set of responsibilities and expectations are already outlined, there is a lot of variability between jobs, even within the same city and specialty. It's important you are able to leave the interview with a 360-degree view of the position and the life you will build around it.
Keeping all of that in mind, here are some of my core tips for preparing for an interview:

1. **Do your research about a job ahead of time.** Not doing this is one of the biggest mistakes I see applicants making. Showing up to a job and asking basic questions whose answers can easily be found online will cause interviewers to question why you’re at the interview and how serious you are about the job. You want to come in knowing how the group is structured from a management perspective, what its patient population looks like, who the referral base may be, and what areas within your field the group specializes in, as well as some areas or topics where you may be able to add value. Look at the group's website and the members and see if there are any connections that you might have where you might be able to find common ground. Call the people you know who may be familiar with the group and ask them for insights. Find out if people have left the group recently, as it may raise some red flags. This will all lead to more sophisticated questions that you can ask and more valuable information to consider when you are making your decision. It will also tell group members you are serious about the opportunity, which will help your chances as they decide whether to extend a job offer. Time and resources are precious in this process, and many won’t want to waste their time if they feel they are one of 100 possibilities.

2. **Try and allot time to get to know the city you are interviewing in.** For those of you who are trying to return to a known place, this may be less of an issue, but nonetheless, training somewhere or growing up somewhere is different from living there as an adult and potentially raising a family in that location. Make sure the place offers outlets to foster your interests outside of work, as it will play into your happiness and burnout. Tour neighborhoods you may want to live in, and if you have educational preferences for your children, take some time to explore your options. If applicable, bring your significant other with you so that you’re on the same page about pros and cons of living there.

3. **When interviewing with potential future colleagues, don’t be afraid to be yourself.** It’s important that the fit feels natural and that there is a mutual desire to work together. As the saying goes, you can’t choose your family, but you can choose your friends. Similarly, you can choose colleagues that you are confident will contribute to your happiness at the job, whether it be via friendships, accommodating emergencies when they arise, splitting work in a way that feels equitable, or being respected.

You should see yourself fitting into the culture of the group’s members and in line with the standards, ethics, and practice patterns that they embrace.

4. **In a similar vein, take note of how colleagues are interacting with each other.** As the landscape of health care delivery gets more challenging and complicated, it’s important that you feel that the group is cohesive and supports each other. If there are obvious tensions within the group, it may be a sign that there is more beneath the surface that’s resulting in conflict, whether it’s RVU (relative value unit) structures, partnership issues, different beliefs about the direction the company is taking, etc.

5. **Talk about money and opportunities for growth.** After all, this is a job. Put some effort into figuring out how revenue is generated, when you get to share in those profits, and what the plans of the group are in terms of expansion. If the compensation structure is complicated, ask for details. You don’t have to take up your entire interview time talking about it, but get a basic sense and then ask the interviewer to send you a summary with details later. Understand the benefits. If the group’s members do something a lot different from other groups you've interviewed with or your colleagues are interviewing with, ask them why they chose to structure things in that way.

6. **If possible, spend some time shadowing someone whose job is similar to the one you’re interviewing for.** Make sure you can see yourself happy in his or her shoes, and if there are obvious pain points or dealbreakers, take note of them. You may not be able to do this on the day of the interview, but if you have doubts about whether you’d enjoy the particular setting ahead of time, see if an interviewer can incorporate this on a later date. Again, it’s in everybody’s best interest to ensure a job is a good fit for you.

I could go on, but your goal on your interview day is to confirm the job is one you can see yourself enjoying for years to come. You’re really picking more than a job — you’re picking a lifestyle and a vision for your future, and you want to make sure you are keeping a keen eye out for pros, cons, and red flags.

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Physician Employment Contracts: Strategies for Avoiding Pitfalls

By Bonnie Darves, a Seattle-based freelance health care writer

As physicians increasingly opt for practice opportunities in employed-model arrangements and hiring entities move toward standardizing employment contracts to simplify matters and ensure equitable treatment of existing and incoming physicians, it might appear that there’s scant room for negotiating contract terms.

That’s not a prudent attitude to take about such an important document, contract lawyers maintain. That employment agreement not only dictates the next year or two of a physician’s career but also could potentially negatively affect his or her personal and professional life for years into the future. Benjamin J. Mayer, JD, MBA, a Denver lawyer whose firm specializes in physician contracts, advises physicians to take the position that any terms that aren’t favorable can — and should — be made more reasonable. “The physician might not be able to get a higher starting salary or a larger signing bonus but definitely should negotiate anything that’s explicitly unfair or clearly intentionally ambiguous,” Mr. Mayer said.

Key examples he cites are contracts with onerous non-compete provisions that would prevent a departing physician from working within, say, a 60-mile radius of any of the employer’s locations, or contracts that contain little detail about weekly work hours and schedules, or call requirements.

Essentially, anything that is vague or an overreach should be modified and specified. “The physician needs to require reasonable boundaries on all of the contract’s terms,” Mr. Mayer said. For example, any non-compete radius should be drawn from a single primary location, not from all of a sprawling mega–health system’s hospitals and clinics. Similarly, regarding schedules, the contract should at least specify a cap on total weekly hours or days worked and should dictate an equitable call schedule.

“Duties, hours, and responsibilities should be spelled out, and if the call coverage isn’t specified, the contract should at least state that those duties will be ‘equally divided among all physicians’ in the group,” Mr. Mayer said. He acknowledged that some young physicians might be willing to shoulder commensurately more call duty than their peers if they’re trying to pay off medical school loans, for example, but such special arrangements are best addressed outside of the contract.

Michael Schaff, cochair of health law for Wilentz, Goldman & Spitzer, P.A. in Woodbridge, New Jersey, suggests that young physicians in surgical and other call-intensive specialties should determine whether practice culture or bylaws issues might translate into an inordinate call burden that they’re not willing to assume. For example, Mr. Schaff noted, some practices enable physicians who reach a certain age — 55 or 60 is common — to opt out of call altogether. If several senior doctors stop taking call, younger physicians’ “equally divided duties” might be unmanageable. To be safe, the contract should specify a “not to exceed” number of call days per week or month, Mr. Schaff and other sources advised.

Emerging “super groups” affect contracts

On a global scale, practice acquisition and management trends — specifically, the growing influence of private equity on physician practice and facility management and the creation of huge organizations that operate scores of groups — are affecting physician employment. Rebecca Gwilt, a Richmond, Virginia, lawyer and partner in Nixon Law Group, said she is witnessing a “trickle-down effect” on contracts as private equity-operated super groups emerge.

“We’re seeing a more sophisticated framework for physician contracts,” Ms. Gwilt said, as well as a tendency toward both shorter employment terms and slimmer benefits. “Legally, these companies aren’t permitted to influence the delivery of services, but in general, they’re non-physician companies, which means that the MBAs are making contract decisions, not physicians,” said Ms. Gwilt, who frequently speaks on physician contract
issues. "So, as this [model] becomes more common, market salaries and benefits could change."

Although the trend toward super-group formation isn't inherently negative — such groups have more bargaining power regarding physicians' reimbursement rates than smaller ones do, generally — it does call for due diligence and research on the part of physicians who consider interviewing with such entities. "You first should find out who runs the company, because you will have less room to negotiate a contract than with a physician-owned practice," Ms. Gwilt said. "You want to know what it's like to work there, so I advise clients to ask for the name of the last physician hired — someone who's been there for a year — and then talk to that physician."

The movement toward "corporatization" of medicine, in tandem with the fluctuating health care economic, reimbursement, and policy environment, is prompting employers to reduce their financial risk wherever possible. One example is instituting shorter contract employment terms, which enables employers to more easily let go of poor-performing physicians. Another recent development is the setting of limits on how much individual physicians can earn, regardless of their productivity, according to Kyle Clausen, CEO of Resolve Physician Agency, a Missouri-based firm that counsels physicians on contract issues.

"It's becoming more prevalent to see clauses with caps on compensation, such as the 75th or 90th percentile in a major national survey such as the Medical Group Management Association survey," Mr. Clausen said. Although such caps aren't likely to affect most physicians coming out of residency because starting salaries are rarely set at those percentiles, the caps could penalize high-income specialties such as neurosurgery and orthopedic surgery as those physicians move into their second and third years of practice. "I've seen some high-income specialists walk away from those potential jobs," he said. He added — and other sources concurred — that sign-on bonuses are less common now than they were a few years ago, possibly for some of the same economic reasons.

Another contract area where shifts are occurring involves bonuses and productivity-based compensation, several sources mentioned. As employers, as well as government and commercial insurers, move toward providing monetary incentives to physicians for performance on measures ranging from patient satisfaction to hospital readmissions, it's important to know how such payments are handled on the employer side. This is particularly the case with any bonuses or incentive payments that may be due a physician, Mr. Schaff pointed out.

For example, if the contract states that incentives and bonuses are paid only through the employment period or only at the end of a calendar year, the physician might lose out on a substantial sum if he or she leaves the job on, say, Dec. 22, rather than Jan. 1 of the following year. Ideally, the contract should call for payment of "all bonuses earned through the time of termination."

Ditto for accounts receivable monies that physicians might be due. It's very common for such monies to continue flowing to the practice for several months after a physician departs, so ideally, Mr. Schaff suggested, the contract should call for reporting on such funds for a specific period after termination and ultimately paying out what's due at, say, 60, 90, or even 180 days post-termination of employment. "This is all over the map in contracts I've seen," Mr. Schaff said. "I've even seen contracts that state that the physician only receives payments through the last day of employment. This is something that should be negotiated."

At the other end of the spectrum, physicians whose contracts set minimum or expected productivity or quality performance targets in order to continue the base salary beyond year one should understand not only what those requirements are but also — and more importantly — whether they're achievable and reasonable. That means talking to other physicians at the prospective practice to see how they've fared in year two in productivity. It's also helpful to find out how much personal effort is required to track the performance metrics that underlie performance payments, several sources advised. Mr. Mayer said that when a base salary arrangement converts to a totally productivity-based one at the end of the first year, he often negotiates for something less dramatic, such as continuation of the base salary for an extended period or perhaps a part-base/part-productivity structure.

"The point is that your contract governs how your money works, and compensation structures are becoming increasingly complicated," Ms. Gwilt said. "That's why it's really important that physicians understand those structures and obtain legal review: It's not uncommon for compensation methodologies to incorporate a half-dozen components beyond base salary, such as incentive bonuses or "clawbacks" (monies returned to the employer for underperformance or other reasons) based on quality measures, cost metrics, patient-specific clinical measure reporting, compliance, and shared savings, to name a handful."
Unreasonable benefit start dates. One pitfall with benefits is not ensuring that they commence at a reasonable time, Mr. Schaff observed. For example, if a contract stipulates that health insurance benefits start on the first day of the month following hiring or 90 days hence, he said, “The physician could be on the hook for paying the premiums for COBRA [continued coverage from the previous employer]. At the least, if the benefits start date can’t be modified, the incoming physician might try to negotiate that the employer pay the COBRA premiums until the coverage starts.”

Onerous — or unspecific — indemnification or liquid damages clauses, especially regarding malpractice claims. The first order of business here is to understand any limitations that employer-paid malpractice coverage might have, and then ensure that the employed or contracted physician isn’t on the hook fully for additional damages that the policy doesn’t cover, Mr. Mayer advised. For example, if the malpractice coverage tops out at $1 million and the judgment comes in at $1.25 million, some contracts might shift the entire shortfall to the physician, explicitly or not so explicitly. “Such a provision might say that ‘the practice and the doctor agree to indemnify and hold each other harmless for any liability caused by the other,’” Mr. Mayer said. “It sounds and seems fair, but in practice, the malpractice claim will usually follow the physician, not the practice. This is something that requires careful review and possibly negotiation.”

On a final note, all sources stressed the importance of physicians reading every word of the contract and obtaining expert review. The point is to make sure that physicians understand what the contract entails and what its provisions would look like in their daily lives, by requesting specific examples of not only what’s expected of them but also what might happen should they leave the position prematurely. “One thing that physicians need to think about but are reluctant to ask is this: What happens if they want to get out or if the employer wants to terminate the contract?” Ms. Gwilt said. “If there’s a penalty clause, that should be highly negotiated.”

Contract pitfalls to watch for

Contract language that’s vague and highly employer-favorable. Such language might show up in any area of the contract, but it’s especially problematic when it comes to physician schedules and duties, according to Ms. Gwilt. “You want to beware of anything that states, ‘X will be determined by the practice at its discretion,’” she said. That leaves the physician open to whatever the employer decides at any time during the contract period. At the least, physicians should negotiate to add that the terms be “fair and reasonable, and in accordance with [requirements] for all like colleagues.”

Mr. Mayer provides an example of where “at the practice’s discretion” could have a serious lifestyle effect: unspecified practice locations. As organizations merge and/or add satellite facilities, a vague location clause might mean that physicians could be required to commute to or travel among four different clinics or hospitals. Mr. Mayer suggests that physicians ask prospective employers to specify locations and limit their number contractually, or at least give the physician the opportunity to decide if she or he is willing to expand the number.

Highly restrictive non-compete clauses. Syracuse, New York, attorney Andrew Knoll, JD, MD, cautions physicians to beware of and negotiate onerous non-compete terms when employers aim to keep physicians from working for a slew of specific competitors. “I’ve seen clauses that state, ‘Within two years of leaving the practice, the physician cannot work for health system Y or hospitals A, B, or C.’ That’s overly broad. Others might restrict the employee from going to a particular large health system, but not to smaller hospitals or systems in the same urban area,” Mr. Knoll said. “These clauses should always be reviewed.”

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Postmenopausal Osteoporosis

Marcella Donovan Walker, M.D., and Elizabeth Shane, M.D.

This Journal feature begins with a case vignette highlighting a common clinical problem. Evidence supporting various strategies is then presented, followed by a review of formal guidelines, when they exist. The article ends with the authors’ clinical recommendations.

A 69-year-old woman presents to review the results of her first dual-energy x-ray absorptiometry (DXA) scan. Her T scores are –2.6 at the lumbar spine and –2.3 at the total hip. She fell while walking 18 months ago and fractured her left humerus. Imaging of the spine, performed to investigate 5 cm (2 in.) of height loss and moderate thoracic kyphosis, reveals two vertebral fractures. How should this patient be evaluated and treated?

THE CLINICAL PROBLEM

Postmenopausal osteoporosis is caused by estrogen deficiency, which leads to increased osteoclast differentiation and activation, accelerated bone resorption that outpaces formation, and rapid bone loss, particularly in the years immediately before and after menopause. This results in low bone mineral density, deteriorated bone microarchitecture, decreased bone strength, and increased risk of fragility fractures. Postmenopausal osteoporosis is diagnosed on the basis of the occurrence of a fragility fracture (with no associated trauma or with trauma equivalent to falling from a standing height or less) or bone mineral density at the spine, total hip, or femoral neck that is at least 2.5 standard deviations below the mean of that in a young adult reference population (T score of –2.5 or less), as measured with the use of DXA. In the United States, approximately 20% of women age 65 years or older meet DXA criteria for osteoporosis. Postmenopausal osteoporosis is more common among White, Asian, and Hispanic women than among non-Hispanic black women. An additional 40% of postmenopausal women have low bone risks (osteopenia; defined as a T score between –1.0 and –2.4). Approximately 50% of postmenopausal women will have fragility fractures, which cause pain, disability, and decreased quality of life. After a hip fracture, many women never regain independence, 20% are institutionalized, and the risk of death within 1 year doubles. Approximately 10% of women who have hip fractures are more likely to die within 6 months, are less likely to regain independence, and have less timely surgery and rehabilitation than White women who have hip fractures. The annual health care cost associated with fractures related to postmenopausal osteoporosis in the United States, currently $57 billion, is projected to exceed $95 billion by 2040.

STRATEGIES AND EVIDENCE

DIAGNOSIS AND EVALUATION

Osteoporosis is asymptomatic until the first clinical fracture. Bone mineral density as measured with the use of DXA is the gold standard for identifying patients at risk. Each standard deviation reduction below a T score of 0 is associated with a doubling or tripling in the risk of fracture. Most guidelines recommend DXA of the spine and hip for postmenopausal women 65 years of age or older and for postmenopausal women younger than 65 years who have risk factors (Table 1). Forearm bone mineral density predicts fracture and can be measured if recommended sites are not evaluable or if hyperparathyroidism is present. Fragility fractures of the spine, hip, forearm, humerus, and pelvis are diagnostic of osteoporosis, even with T scores higher than –2.5. The occurrence of a fragility fracture is associated with a marked increase in the imminent risk of additional fractures.

Vertebral compression fractures, the most common osteoporotic fractures, are frequently asymptomatic. Vertebral fractures are associated with increased mortality, and the presence of vertebral fractures influences diagnosis, risk stratification, and therapeutic decisions. Vertebral fracture analysis, a low-radiation spine image obtained on a densitometer when bone mineral density is measured, has high sensitivity and specificity to detect moderate or severe (≥25%) vertebral compressions. Vertebral fracture analysis, spine radiography should be performed when suspicion is high (e.g., height loss of >1.5 inches or >3.8 cm) or if the management strategy may be affected (Fig. 1). Vertebral fracture risk can be estimated with the use of the fracture risk assessment tool (FRAX®) or other validated calculators. FRAX estimates the 10-year probability of major osteoporotic fracture and hip fracture on the basis of the clinical risk factors (Table 1), with or without a measurement of bone mineral density. Many authorities recommend designating patients who have an elevated fracture risk but do not have T scores of –2.5 or less as a fragility fracture as having osteoporosis.

Bone microarchitecture contributes to bone strength and can be assessed by means of several methods. The trabecular bone score — a Food and Drug Administration (FDA)–cleared, Medicare-covered, indirect measure of spine trabecular microarchitecture that is obtained from a DXA image with the use of additional commercially available software — predicts fracture risk independent of bone mineral density. FRAX-estimated fracture risk or T scores can be adjusted by means of the trabecular bone score to enhance risk stratification. The trabecular bone score is most useful when it influences treatment decisions (e.g., for osteopenia or when fractures are osteopenic). Results of the trabecular bone score are least as well as DXA. Measurement of bone microstructure and strength by means of high-resolution peripheral quantitative CT (HRpQCT) predicts fracture risk independent of bone mineral density but is not FDA-approved for diagnosis.
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Clinical Practice

OTHER EVALUATIONS
Medical history, medications, and risk factors should be assessed. Other metabolic bone diseases that are associated with low bone mineral density, such as osteomalacia, are important diagnostic considerations (Fig. 1). Conditions (e.g., celiac disease) and medications (e.g., glucocorticoids) that cause removably bone loss should be addressed (Table 1). Because there is no consensus regarding the most cost-effective laboratory evaluation, testing depends on the clinical situation but must, at minimum, identify contra-indications to specific therapies (Fig. 1 and Table 2).

TREATMENT
The fundamental goal of treatment is to prevent fractures in women at high risk before their first fracture (primary prevention) or before a subsequent fracture (secondary prevention). Lifestyle modifications are applicable to all of these patients. Pharmacologic interventions (Table 2) are targeted to women at high risk for fracture. Intervenion thresholds vary according to different guidelines (Table 3), but many guidelines recommend treating women who have fragility fractures of the hip or spine, regardless of bone mineral density; those with T scores of −2.5 or less at the lumbar spine, total hip, or femoral neck; and those with high 10-year fracture risk as assessed with the use of FRAX (hip fracture risk of ≥3% or major osteoporotic fracture risk of ≥20%).12 Findings from randomized, controlled trials support the fracture-risk-reduction efficacy of FDA-approved treatments based on T scores or fracture criteria (or both). Evidence that supports treatment based on FRAX-estimated fracture risk is less robust.13,14

LIFESTYLE CHANGES
Patients should be encouraged to stop smoking, avoid excessive alcohol, increase weight-bearing exercise, and prevent falls.15 Most guidelines recommend 1000 to 1200 mg of calcium daily in women with postmenopausal osteoporosis, prefer embly obtained from diet,16 and 400 to 1000 UI of vitamin D daily.17 Some experts and guidelines recommend adjusting vitamin D intake to achieve serum 25-hydroxyvitamin D levels higher than 20 to 30 ng per milliliter, but this approach is controversial and not supported by rigorous data.18,19 Whether calcium and vitamin D supplementation reduces fractures remains debated. Limited evidence suggests supplemental calcium combined with vitamin D significantly reduces hip fractures, but not nonvertebral or vertebral fractures, in patients with postmenopausal osteoporosis.20 Because the efficacy of most osteoporosis medications has been studied in conjunction with calcium and vitamin D supplementation, and some osteoporosis medications can cause hypercalceemia, adequate calcium and vitamin D intake is prudent. Risks associated with calcium supplementation include nephrolithiasis and, according to some meta-analyses, increased incidence of cardiovascular events, although studies included in the meta-analyses were not designed to assess cardiovascular outcomes.21

PHARMACOLOGIC APPROACHES
Therapies for postmenopausal osteoporosis act by reducing bone resorption (antiresorptive therapies), stimulating bone formation (anabolic therapies), or both. All pharmacologic approaches reduce vertebral fracture risk, and some reduce the risk of nonvertebral and hip fractures.17 Table 2 summarizes available therapies and fracture risk reductions that have been assessed in randomized, controlled trials. Selection of a therapy must include the consideration of osteo-

Table 1. Risk Factors for Postmenopausal Osteoporosis and Fracture.

| Older age | Low weight (<127 lb [<58 kg]) | Previous fracture during adulthood (particularly hip, spine, or wrist); recent fracture indicates a higher risk than remote or unclear history |
| Parental history of hip fracture | Current or past glucocorticoid treatment (<5 mg prednisolone daily or equivalent for 3 mo or more) | Other medications that cause bone loss* |
| Current smoking | Excess alcohol intake | Causes of secondary osteoporosis† |
| Rheumatoid arthritis | Premature menopause (<40 yr of age) or hypogonadism | Frequent falls |

* These medications include (but are not limited to) aromatase inhibitors, suppressive doses of thyroid hormone, chemotherapy, cyclosporine, unfractured and low-molecular-weight heparins, antidepressants, thiazolidinediones, selected antiviral drugs, and proton-pump inhibitors. Some drug categories have been associated with higher fractures in epidemiologic studies but have not been causally linked.

† Causes include (but are not limited to) organ transplantation, primary hyperparathyroidism, chronic kidney disease, type 1 and type 2 diabetes, anorexia nervosa, hypopituitarism, malabsorption, bariatric surgery, immobility, untreated hyperparathyroidism, chronic pulmonary disease, human immunodeficiency virus infection, Cushing’s disease, osteogenesis imperfecta, Gaucher’s disease, and Marfan syndrome.

Table 2 summarizes available therapies and fracture risk reductions that have been assessed in randomized, controlled trials. Selection of a therapy must include the consideration of osteoporosis medications that cause bone loss.* Consider alternate diagnoses and medications (e.g., glucocorticoids) that cause removably bone loss should be addressed (Table 1).
Biphosphonates

For women with postmenopausal osteoporosis who are at high risk for fracture, most guidelines recommend biphosphonates as initial treatment, given their efficacy, safety, convenience, low cost, and enduring effects after discontinuation (Table 2). Four oral and intravenous biphosphonates are FDA-approved for postmenopausal osteoporosis. All reduce the risk of vertebral fracture.19 All but ibandronate reduce the risk of hip and nonvertebral fractures.23,24 When administered within 90 days after hip fracture repair and annually for 3 years, zoledronic also reduced the risk of death, although the mechanism is unclear.

Oral biphosphonates are poorly absorbed and may cause upper gastrointestinal mucosal irritation (Table 2). Intravenous zoledronic is preferred in patients who have this side effect and those with esophageal dysfunction. Acute-phase reactions may occur with zoledronic but can be mitigated with preinfusion and postinfusion oral hydration and acetaminophen. Long-term use of biphosphonates has been associated with osteonecrosis of the jaw and atypical femur fractures. Osteonecrosis of the jaw is an area of exposed jaw bone that does not heal within 8 weeks after identification by a health care provider.25 Atypical femur fractures are low-trauma subtrochanteric or femoral-shaft fractures with specific radiographic criteria.26 In patients receiving biphosphonates at doses used for postmenopausal osteoporosis, the estimated risks of osteonecrosis of the jaw and atypical femur fracture are very low.

Denosumab

In randomized, controlled trials conducted over a period of 3 years, denosumab lowered the risk of spine, hip, and nonvertebral fractures as compared with placebo.27 In long-term, open-label extension studies, the lower risk of fractures was maintained.28 Although gains in bone mineral density are greater with denosumab than with biphosphonates, evidence for greater reduction of fracture risk is limited.29 Denosumab is also rarely associated with osteonecrosis of the jaw and atypical femur fracture30 and with hypocalcemia in patients with advanced chronic (stage 4 or 5) kidney disease or vitamin D deficiency (Table 2).
Anabolic agents, PTH receptor agonists

PTH analogue — teriparatide (PTH 1-34)
Increases bone formation
20 μg daily subcutaneously
74 ND 39 Hypercalcemia, muscle cramps, nausea, headache, diziness, hypotension
Bone metastases, skeletal cancers, increased risk of osteosarcoma, Paget's disease, hypercalcemic crisis, unexplained elevated alkaline phosphatase, hypercalcemia

PPTH-IP analogue — abaloparatide (PTH-P 1-34)
Increases bone formation
80 μg daily subcutaneously
87 ND 46 Same as for teriparatide (PTH 1-34)
Same as for teriparatide (PTH 1-34)

Sclerostin inhibitor — romosozumab
Human monoclonal antibody against sclerostin; increases bone formation, decreases bone resorption
210 mg per mg subcutaneously
73 38† 19†† Arthralgia, headache, MSK pain, hypocalcemia, CV events, rarely ONJ, AFF
Recent stroke or MI; other CV risks, hypocalcemia, or hypercalcemia; important to ensure vitamin D sufficiency

Table 3. Intervention and Treatment Guidelines.*

<table>
<thead>
<tr>
<th>Guideline</th>
<th>Intervention Threshold</th>
<th>Initial Treatment</th>
<th>Duration</th>
</tr>
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<tbody>
<tr>
<td>AACE-AACE 2020† †</td>
<td>T score of −2.5 or less at the spine, femoral neck, total hip, or 53% radius; osteopenia (T score between −1.0 to −2.49) and history of a history of a fracture of the hip or spine; osteopenia and high probability of fracture as estimated with the use of FRAX</td>
<td>Alendronate, denosumab; abaloparatide, denosumab; zolendronic acid; antiresorptive therapy is alendronate and risedronate</td>
<td>Oral bisphosphonate† — treat for 5 yr, then consider holiday if fracture risk is no longer high; if fracture risk remains high, continue treatment for up to an additional 5 yr; in patients at very high risk, consider holiday after 6–10 yr of stable BMD; zoleodronic acid‡ — consider holiday after 3 yr of high risk or until fracture risk is no longer high; continue for 6 yr in patients at very high risk; holiday not recommended for non-bisphosphonate antiresorptive therapies; abaloparatide or teriparatide — treat for 2 yr, then follow with antiresorptive therapy; romosozumab — treat for 1 yr, then follow with antiresorptive therapy † †</td>
</tr>
<tr>
<td>American College of Physicians 2013*</td>
<td>T score of −2.5 or less; individualize in those &lt;45 yr of age with osteopenia</td>
<td>Bisphosphonates; denosumab if contraindications to or adverse effect from bisphosphonates</td>
<td>Bisphosphonate use for &gt;3–5 yr reduces vertebral fracture but not other fractures, with increased risk of long-term harms; consider stopping after 5 yr unless strong indication to continue</td>
</tr>
<tr>
<td>Bone Health and Osteoporosis Foundation‡</td>
<td>T score of −2.5 or less at the femoral neck, total hip, lumbar spine, 33% radius, fracture of the hip or vertebra regardless of BMD by DXA; osteopenia at the femoral neck or total hip by DXA with 10 yr hip fracture risk ≥1% or MFR ≥20% by FRAX; osteopenia with fracture of proximal humerus, pelvis, or distal forearm; individualized approach for those with proximal humerus, pelvis, or distal forearm fractures without osteopenia</td>
<td>Generally follows Endocrine Society algorithm</td>
<td>Generally follows Endocrine Society algorithm</td>
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</tbody>
</table>
Although denosumab is an alternative treatment option for women at high risk for fracture who have contraindications to bisphosphonates or cannot take them owing to unacceptable adverse effects, there is concern about accelerated bone resorption and rapid bone loss after discontinuation of denosumab therapy. Whether denosumab should be used as initial therapy in women who are at high risk — but not at very high risk — for fracture who have other treatment options is debated among some experts. In a post hoc analysis of a trial that compared denosumab with placebo, the incidence of vertebral fractures increased from 1.2 to 7.1 per 100 participant-years after treatment with denosumab was discontinued, a finding similar to that observed after discontinuation of placebo, but the incidence of multiple vertebral fractures was higher after discontinuing denosumab than after discontinuing placebo (3.4% vs. 2.2%).

Therefore, patients must continue denosumab therapy indefinitely or transition to treatment with bisphosphonates to maintain bone mineral density and prevent incident vertebral fractures. Weekly administration of alendronate, initiated 6 months after receipt of the last dose of denosumab, may prevent bone loss. The efficacy of zoledronate may depend on the timing among patients whose risk of fracture remains at or returns to high or very high levels or who do not have a response to other therapies.

Romosozumab
Romosozumab, given monthly as subcutaneous injections, is the newest FDA-approved therapeutic for postmenopausal osteoporosis. In a phase 2 study, romosozumab increased bone mineral density more than teriparatide. In the Fracture Study in Postmenopausal Women with Osteoporosis (FRAME), romosozumab reduced the risk of vertebral and clinical (composite symptomatic vertebral and nonvertebral) fractures at 12 months as compared with placebo. The risk of vertebral fracture remained lower in the romosozumab group after 1 year of treatment with denosumab.
Similar to treatment with PTH receptor agonists, romosozumab therapy must be followed by treatment with bisphosphonates or denosumab.41 In another trial that investigated treatment with romosozumab in combination with ibandronate, 1 year, both followed by alendronate for 1 year,31 romosozumab reduced vertebral, nonvertebral, and hip fractures more than alendronate. Although not observed in FRAME, a higher incidence of serious cardiovascular events with romosozumab (2.5% vs. 1.9%) led to a black-box warning against the use of romosozumab within 1 year after myocardial infarction or stroke.41 Many guidelines recommend romosozumab as initial therapy only for persons at very high risk for fracture, with use limited to 1 year (Table 3).

### Other Antiresorptive Agents

Owing to adverse effects, estrogen therapy and selective estrogen-receptor modulators are recommended only in selected populations or circumstances (Table 3). Calcitonin, a weak antiresorptive agent, is rarely used for postmenopausal osteoporosis.

### Combination Treatment

Concurrent treatment with teriparatide and bisphosphonates has no added benefit with respect to the bone mineral density of the spine and hip as compared with teriparatide alone.8 The combination of denosumab and teriparatide increases bone mineral density of the hip and spine more than either alone, but is not endorsed by guidelines or routinely covered by insurance.11

### Monitoring

Most guidelines suggest repeating DXA 1 to 2 years after initiating or changing therapy, but from these recommendations diverge.17,23-25 Non-response, defined as a decrease in bone mineral density greater than the least amount of change that can be considered clinically significant, may occur in 10% or more of patients.26 No treatment reduces fracture risk to zero. However, the presence of decreasing bone mineral density or the occurrence of multiple fractures should prompt evaluation and consideration of alternative therapy. Some clinicians measure bone-turnover markers 3 to 6 months after initiation of antiresorptive therapy to assess adherence and response. Although declines in bone-turnover markers are associated with a reduction in fracture risk in large trials, this approach is not routinely recommended.

### Areas of Uncertainty

The appropriate duration of bisphosphonate therapy is unclear. In extended trials of alendro- nate, among 23,180 women, participants who were assigned to discontinue therapy after 5 and 3 years, respectively, had lower bone mineral density at the study conclusion than pretreatment values and returns to pretreatment values, and returns to inter- vention thresholds.11 Likewise, the appropriate duration of denosumab may be unclued. The evidence does not suggest reasserting fracture risk after 5 to 10 years of denosumab therapy and continuing or switching therapy in patients who remain at high risk. Because the risk of multiple vertebral fractures after discontinuation of therapy may rise as the duration of denosumab therapy increases, recommendations may evolve.17

Limited data are available to guide the use of sequential pharmacologic treatment. Although antiresorptives are considered to be first-line therapy (Table 3), they blunt or delay bone mineral density gains in response to anabolic agents.40 The presentation of the patient described in the vignette is typical of postmenopausal osteoporosis in that the initial lumenus fracture was not recognized as indicating osteoporosis, which was later diagnosed by the T score of −2.6 and the FRAUM–F (fracture risk assessment using multiple fractures) tool.6,41

In patients receiving treatment with bisphosphonates, switching to romosozumab led to greater increases in bone mineral density than teriparatide.40 However, data regarding fractures are lack- ing.40,41-43 In contrast, switching patients from denosumab to teriparatide should be avoided owing to bone loss.26 Some experts recommend treat- ment approaches, in which bone loss is selectively modified and delayed, for patients whose fractures indicate a very high risk of additional fractures. Therefore, we favor therapy with anabolic agents first with either a PTH receptor agonist or romosozumab followed by treatment with a bisphosphonate or denosumab. If anabolic therapy was declined, we would favor denosumab over bisphosphonates, given her severe osteoporosis and the greater effects of denosumab on bone mineral density. Despite the debated utility of repeat DXA, we would reevaluate clinically and reassess bone mineral density with DXA 1 or 2 years after initiating therapy.

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### CONCLUSIONS AND RECOMMENDATIONS

The presentation of the patient described in the vignette is typical of postmenopausal osteoporosis in that the initial lumenus fracture was not recognized as indicating osteoporosis, which was later diagnosed by the T score of −2.6 and the FRAUM–F tool.6,41

In patients receiving treatment with bisphosphonates, switching to romosozumab led to greater increases in bone mineral density than teriparatide.40 However, data regarding fractures are lacking.40,41-43 In contrast, switching patients from denosumab to teriparatide should be avoided owing to bone loss.26 Some experts recommend treatment approaches, in which bone loss is selectively modified and delayed, for patients whose fractures indicate a very high risk of additional fractures. Therefore, we favor therapy with anabolic agents first with either a PTH receptor agonist or romosozumab followed by treatment with a bisphosphonate or denosumab. If anabolic therapy was declined, we would favor denosumab over bisphosphonates, given her severe osteoporosis and the greater effects of denosumab on bone mineral density. Despite the debated utility of repeat DXA, we would reevaluate clinically and reassess bone mineral density with DXA 1 or 2 years after initiating therapy.

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