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The VHA Male Osteoporosis Program: A National Model for Bone Health

As people age, the risk of osteoporotic fracture increases, but much more attention has been given to osteoporosis in women than in men. The VHA has identified osteoporosis as a major health concern and has begun new initiatives to identify and treat veterans with prior fractures or veterans at high risk for osteoporosis. While these initiatives will benefit female veterans as well, men comprise more than 90% of the 400,000 veterans identified as being at highest risk. This article will focus on the VA approach to male osteoporosis, including identifying men at risk, evaluation of those at risk, and clinical management, including benefits and harms of treatment. We will describe national surveillance of the implementation of this initiative in the Patient Aligned Care Team (PACT) in collaboration with the Pharmacy Benefits Management (PBM) Medication Safety Center, as well as new initiatives for clinical pharmacists.

EVIDENCE SYNTHESIS

Recently published VHA Information Letters rely on an evidence synthesis from the VHA and external evidence reviews. Several organizations have recommended that all men older than 70 years should be screened for osteoporosis by measuring bone density with dual energy x-ray absorptiometry (DXA).[1-4] In contrast, the United States Preventive Services Task Force (USPSTF) determined there was insufficient evidence to recommend DXA screening of older men.[5]

The VHA Office of Patient Care Services commissioned a VHA Health Services Research and Development Evidence Based Synthesis Review of male osteoporosis, which became the basis for the VHA approach, as published in an Information Letter on Osteoporosis in Men, as well as an American College of Physicians Clinical Guideline.[6,7] The VHA approach is to identify those men who are most likely to fracture, evaluate them, and then treat them. The Information Letter in September 2009, updated in March 2011, contains an algorithm for male osteoporosis evaluation and treatment (Figure 1).

Among the men at highest risk are those who have already had an osteoporotic fracture (Table 1). It is clear that many of these men have not had appropriate evaluation and treatment of their underlying osteoporosis.[8] This problem is also common in the community.[9] Patients taking oral glucocorticoid therapy for more than 3 months form a second group at high risk for osteoporosis and fracture.[10] It is possible to demonstrate a significant increase in fracture risk in patients on 5 mg to 7.5 mg of prednisone daily for as little as 3 months.[11] At any one time about 1% to 2% of all veterans are taking oral glucocorticoids. Finally, a third high-risk group includes men receiving androgen deprivation therapy (ADT) for prostate cancer.[12] Men with localized prostate cancer or with a rising PSA who are given ADT have a good overall outlook, but they can have a frac-

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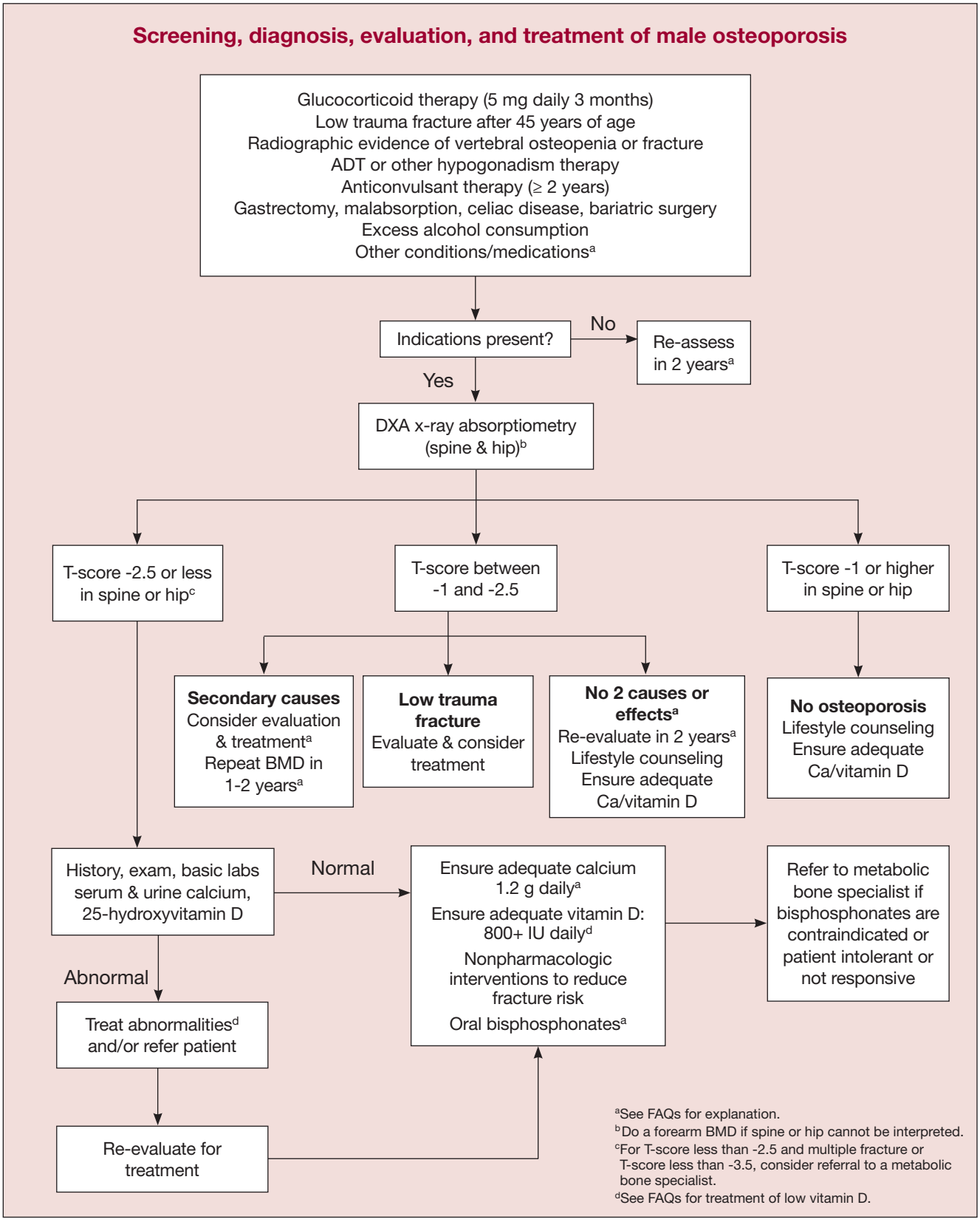
The VHA's Specialty Care Services includes medical services with a wide range of subspecialties; emergent and urgent care and patient support services, such as nutrition; spiritual care and other specific-purpose programs, such as cancer registry and Centers of Excellence for multiple sclerosis, epilepsy, and Parkinson disease. The Office of Specialty Care Services brings you "Updates in Specialty Care," sharing the latest evidence-based approaches, each column featuring a different topic and providing updates on existing programs, and introducing new programs. Special thanks to Margaret (Maggi) Cary, MD, MBA, MPH, director of the VA's Physician Leadership Development Program, who coordinates and edits the column. Please send suggestions for future columns to margaret.cary@va.gov.

Figure 1. Male osteoporosis algorithm[7]



Adapted from the Under Secretary for Health's Information Letter: Osteoporosis in Men.[7]

Table 1. Estimates of veterans with prior fracture or at risk for osteoporosis

Cohorts	Fracture diagnosis	Patients with ≥ 1 prescription for an oral glucocorticoid (≥ 90 days)	Patients with ≥ 1 prescription for ADT	Osteoporosis/ osteopenia diagnosis
Patients (N)	178,882	72,669	29,644	115,821
Mean age (SD)	59.53 (16.45)	67.19 (12.68)	74.17 (10.68)	69.46 (13.08)
Gender (%)				
Male	164,426 (91.92)	68,934 (94.87)	28,923 (97.57)	88,830 (76.70)
Female	14,456 (8.08)	3,724 (5.13)	720 (2.43)	26,991 (23.30)
Age (%)				
≤ 49	42,474 (23.74)	6,028 (8.30)	728 (2.46)	7,462 (6.44)
50-64	74,296 (41.53)	24,924 (34.30)	4,861 (16.40)	35,201 (30.39)
65-74	23,727 (13.26)	17,727 (24.39)	7,311 (24.66)	24,507 (21.16)
≥ 75	38,385 (21.46)	23,990 (33.01)	16,744 (56.48)	48,651 (42.01)

Source: Department of Veterans Affairs PBM Service.

ture risk as high as 20% in 5 years.[13] To summarize, 3 categories of male veterans are at the highest risk for osteoporosis: postfracture patients, patients on chronic oral glucocorticoid treatment, and patients on ADT.

Given concerns that veterans at known risk are undertreated, the VHA has developed and is now implementing a headquarters-administered program that leverages the VHA national leadership in data management to identify individual veterans at highest risk so that care can be coordinated for their evaluation and treatment within the PACT. For the primary care provider (PCP), the Information Letter includes a simple algorithm (Figure 1) to be used at the point of care to identify all male veterans who may be candidates for evaluation by DXA. These include those men who have low bone mass (often called osteopenia) detected on x-ray or have an incidental finding of a fracture (usually in the spine or ribs) on a chest or other x-ray. Other high-risk groups include men taking antiseizure medications for at least 2 years, particularly anticonvulsants (such as phenytoin and carbamazepine) that induce enzymes involved in the catabolism of vitamin D.

Years ago, peptic ulcer treatment included gastric surgery. These patients, as well as those who had more recent procedures or bariatric surgery for obesity, have an elevated osteoporosis risk. Patients with inflammatory bowel disease, malabsorption, and celiac disease may also have osteoporosis. Excess alcohol is defined as greater than 3 units (drinks) per day, and men who ingest this amount are at higher fracture risk, as are current smokers, particularly those with chronic obstructive pulmonary disease (COPD). Validated risk factors have been used to create fracture risk calculators, such as the FRAX, which can be accessed online.[14,15]

Other high-risk groups to be considered for evaluation are those men who have had an organ transplant, men with rheumatoid arthritis, and men with mobility disorders, such as stroke and Parkinson disease.[16] VHA will focus its osteoporosis resources on the men most likely to fracture and most likely to benefit from evaluation and treatment. As men live longer, and long enough to fracture, the incidence of fracture and its consequent morbidity and increased mortality rate will likely climb rapidly unless we seek out and manage osteoporosis in the high-risk male veteran.

VHA IMPLEMENTATION PLAN

The initial national approach to implementation will focus on veterans with fractures. The VISN Primary Care Leaders will receive lists of veterans who have incurred a new onset vertebral fracture or veterans who have undergone hip fracture surgery in the VHA within the prior 6 months. This approach will enable us to assess the success of communication strategies, the accuracy of administrative data compared with chart review, and identify possible best practices at the facility level, including potential clinical reminders. Other high-risk groups to be targeted include men on oral glucocorticoids for ≥ 3 months and men on ADT. These men will have their care coordinated by the PACT. Clinical pharmacists (PharmDs) are a major resource for PACT teams, especially at major facilities.

PharmDs whose scope of practice includes osteoporosis can be authorized to order DXA tests and to man-

Table 2. Evaluation of men at risk for osteoporsis[18-24]

History	Laboratory tests
Risk factors: Disorders and medications listed in algorithm (Figure 1)	Serum chemistries (including calcium and creatinine)
Secondary causes of osteoporosis	25-hydroxyvitamin D
Physical examination	Complete blood count
Kyphosis, vertebral tenderness	In specific cases
Evidence for secondary causes of osteoporosis	Serum/urine protein electrophoresis Parathyroid hormone Thyroid function tests, TSH Testosterone, LH, FSH Celiac antibodies
Fall risk, frailty	Imaging (in addition to DXA)
	Spine x-rays or vertebral fracture assessment

age pharmaceutical therapy once the PCP has ordered initial treatment. As part of a new program to expand the role of clinical pharmacists in PACT, in 2011, 277 VA pharmacists received training about osteoporosis in collaboration with the VA Central Office National Endocrinology and Diabetes Program, which is responsible for treatment recommendations for male osteoporosis. These pharmacists will, in turn, teach their colleagues about osteoporosis.

The evaluation of the high-risk veteran is straightforward. DXA of the spine and hip should be performed on these men, with forearm (usually distal 1/3 radius) performed in men in whom the spine or hip DXA cannot be interpreted. Those with osteoporosis by DXA (a bone mineral density [BMD] 2.5 standard deviations below the normal young mean, a T-score of < –2.5) or those with osteopenia (T-score between –1 and –2.4) but with high-risk of fracture because of glucocorticoid therapy, ADT, or other important risk factors, should have further evaluation.[10-16]

The evaluation should consist of a careful history and physical examination, looking for secondary causes of osteoporosis.[17] In a VA study, laboratory evaluation identified many secondary causes of and risk factors for osteoporosis (Table 2).[18] Among the important tests is the best measure of vitamin D status, the 25-hydroxyvitamin D concentration. Although the Institute of Medicine (IOM) determined that for the population at large a serum level of 20 ng/mL was adequate for bone health, some experts recommend a higher level of 30 ng/mL.[19,20] This range can be achieved with cholecalciferol therapy, usually 1,000 or 2,000 units daily. For the older population, the IOM suggests dosing levels from 600 units to 800 units daily and states that up to 4,000 units daily is probably safe for almost all people.

Vitamin D increases gut absorption of calcium, and the IOM suggests that men older than 70 years should ingest 1,200 mg of elemental calcium daily, with up to 2,000 mg daily considered safe for most patients. Dairy products and fortified foods can supply most calcium needs, but supplements of calcium carbonate and calcium citrate are available. There have been some recent reports that calcium supplements may increase cardiovascular risk in women, but other studies in women have not confirmed this finding.[21,22] All studies of modern osteoporosis therapy have included adequate calcium and vitamin D as part of the therapeutic regimen.

Attention to fall prevention is an important component of reducing fracture risk.[23] Patients' vision should be corrected, and medications that affect cognition or balance should be minimized. Patients can be instructed in home safety measures (eg, nightlights, elimination of throw rugs, and loose extension cords, etc). Veterans should also be evaluated for assistive devices to improve balance while walking and, in some cases, a home evaluation for adaptive equipment should be considered. Some evidence suggests that for women, exercise to improve lower body strength and balance may decrease fracture risk.[24] Thus, lifestyle counseling should include encouragement of weight-bearing exercise.

The 2 main types of osteoporosis treatment are antiresorptive drugs, which decrease osteoclast activity, and anabolic drugs, which increase osteoblast activity. Most patients will be treated with antiresorptives, slowing bone resorption and allowing bone formation to "catch up." Oral alendronate and risedronate and intravenous (IV) zoledronic acid are approved by the FDA for osteoporosis in men.

In the VHA, the most commonly used antiresorptive, generic alendronate, is taken as a 70-mg tablet once weekly, on an empty stomach with a glass of water, while postponing ingestion of other medications and food/beverages for at least 30 minutes. After taking an oral bisphosphonate, patients should not lie down, thereby allowing the pill to be washed into the stomach. Remaining erect helps avoid esophageal irritation, a potential adverse effect (AE). Patients with gastroesophageal reflux disease should have the condition under control before an oral bisphosphonate is started. Patients with esophageal motility disor-

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Table 3. Annual cost of osteoporosis therapy in the VA

Drug	Cost
SC teriparatide, 20 µg daily	$6,136.00
SC denosumab, 60 mg twice yearly	$1,200.00
IV zoledronic acid, 5 mg yearly	$761.00
Oral risedronate, 150 mg monthly	$672.00
Oral alendronate, 70 mg weekly	$20.00
Vitamin D3 1,000, international units (UI) daily	$5.00
Calcium carbonate, 500 mg elemental Ca daily	$3.00
Vitamin D2 50,000, UI monthly	$2.00

Source: PBM Service, Hunter Holmes McGuire VA Medical Center, December 2011.

ders or Barrett's esophagus should not receive oral bisphosphonates. There is a monthly alternative, risedronate 150 mg, but it is not FDA-approved for male osteoporosis (although the 35-mg dose of risedronate weekly is) and is more expensive (Table 3). For patients intolerant of oral bisphosphonates, IV zoledronic acid infusion (5 mg intravenously over at least 15 minutes, once yearly) may be used.

Adherence to therapy is important, because patients must take 75% to 80% of prescribed doses to ensure decreased fracture risk.[25] Even in the VHA persistence with osteoporosis therapy, which does not make the patient feel differently, is low.[26] Most patients need treatment for at least 5 years, so reinforcement of adherence to therapy is important.[27] The ideal duration of therapy has not been established in women, and there is even less information on treatment duration in men. A recent review provides some guidance on when to continue and when to stop bisphosphonate therapy.[27] Although atrial fibrillation (AF) has been suggested as a potential AE of bisphosphonates, AF is probably not an AE of therapy.[28] More important, osteonecrosis of the jaw, defined as exposed bone that does not heal, has been found in the mandible or maxilla in a small number of patients treated with bisphosphonates for osteoporosis.[29] Men who have dental conditions that may require invasive surgery should consider postponing bisphosphonate therapy until after they have recovered. Overall, good dental hygiene is encouraged for all patients on bisphosphonates.[30]

More recently, another potential AE is an atypical femoral fracture below the greater trochanter in the femur in patients who have usually taken bisphosphonates for > 7 years.[31] The background incidence of these unusual fractures is not known, nor is it proven that bisphosphonates cause them. While more information is needed to understand atypical fractures, for now, experts estimate that for every atypical fracture potentially caused by bisphosphonates, 30 to 100 typical fractures are prevented.[32]

As previously stated, most experts continue to recommend that patients on bisphosphonate therapy be treated for 5 years. A repeat DXA, which should be done on the same densitometer as the first evaluation, can be done at 2-year intervals to determine whether the patient is responding and help encourage the patient to continue therapy.[26] Repeating a DXA earlier than 2 years is not recommended, because most densitometers are unable to reliably detect the small changes in BMD in response to therapy. Good DXA practice requires a substantial quality control program and special training for the DXA technologist. At 5 years, another DXA can be performed to help determine whether the patient can have a so-called drug holiday for 1 to up to 2 years.[27]

Despite the potential AEs, bisphosphonates decrease fracture risk. Interestingly, both IV and oral bisphosphonates have been shown to decrease overall mortality as well.[33,34] Several alternatives to oral bisphosphonates are available for patients who cannot tolerate oral bisphosphonates, for complicated patients, and for patients with AEs. Alternatives include IV zoledronic acid, subcutaneous (SC) denosumab, or teriparatide. PBM is developing a strategy to identify the place of these drugs in therapy and to ensure they are available to veterans for whom an oral bisphosphonate is not an option. Complicated patients should be referred to an internist or specialist with expertise in osteoporosis, most often an endocrinologist, rheumatologist, geriatrician, or a general internist with a special interest in osteoporosis. The VA Patient Care Services Office of Specialty Care has implemented an electronic consultation mechanism to enable specialists to provide advice based on chart review, which can improve patient access and minimize travel costs.

PLANS FOR NATIONAL SURVEILLANCE

The PBM Center for Medication Safety (VAMedSAFE) was established to improve the safety of drug prescribing practices and medication administration for veterans receiving treatment in the VA health care system. As one of its many pharmacovigilance efforts, VAMedSAFE has developed a pilot Osteoporosis Registry, which uses administrative data to identify veterans with prior fractures or veterans who are receiving medications that warrant evaluation for possible osteoporosis. In FY 2010, approximately

179,000 veterans were identified with a history of fracture, 115,000 had a diagnostic code for osteoporosis or osteopenia, 73,000 received oral glucocorticoids for over 90 days, and 30,000 received ADT therapy (Table 1). Most likely, many men with other risk factors discussed previously have undiagnosed osteoporosis. In the future, the VAMedSAFE program may be able to expand its surveillance to identify these men without a DXA scan or antiresorptive agent. Because administrative data have limitations in identifying non-VA care (including hospice or nursing home care), its appropriate use would be to monitor trends in population health only, rather than used as a benchmark.

CONCLUSION

The VHA's approach to male osteoporosis is based on case findings in high-risk populations, using a national administrative database registry. By emphasizing those men for whom the risk is highest and treatment efficacious based on level A evidence, the program approach prioritizes clinical efficacy, safety, and thus, pharmacologic resources. The expectation is that the rates of treatment will rapidly increase in these veteran cohorts over the next 1 to 2 years. Additionally, the interactions between PCPs and clinical pharmacists, if proven successful, can be replicated in the private sector. ●

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