Published in final edited form as:

Best Pract Res Clin Rheumatol. 2006 August ; 20(4): 695–706.

Osteoporotic fractures in older adults

Cathleen S. Colón-Emeric* and

Center for the Study of Aging and Human Development, Duke University Medical Center and the Durham VA Medical Center Geriatrics Research Education and Clinical Center, Duke University Medical Center, Durham, NC, USA

Kenneth G. Saag

Center for Education and Research on Therapeutics of Musculoskeletal Disorders, University of Alabama at Birmingham, Division of Clinical Immunology and Rheumatology, Birmingham, AL, USA

Abstract

Osteoporotic fractures are emerging as a major public health problem in the aging population. Fractures result in increased morbidity, mortality and health expenditures. This article reviews current evidence for the management of common issues following osteoporotic fractures in older adults including: (1) thromboembolism prevention; (2) delirium prevention; (3) pain management; (4) rehabilitation; (5) assessing the cause of fracture; and (6) prevention of subsequent fractures. Areas for practice improvement and further research are highlighted.

Keywords

osteoporosis; fractures; aged

As the population ages, osteoporosis is emerging as a major public health problem. At 50 years of age, 4 in 10 women will experience a hip, vertebral or forearm fracture in their remaining lifetime, and are more likely to die from complications of fracture than from breast cancer.¹ Although osteoporosis is frequently considered to be a disease of elderly women, men account for 30% of hip fractures worldwide^{2,3}, and mortality after such fractures is greater in men than in women.⁴

Osteoporotic fractures result in substantial healthcare resource utilization; more than 400 000 hospitalizations, 3.4 million outpatient visits and 179 000 nursing home stays were reported in the USA in 1995. The direct medical costs of treating osteoporotic fractures total \$13.8 billion.⁵ Furthermore, patients who survive an osteoporotic fracture use more than twice the healthcare resources compared with similar patients without fractures for at least 3 years after their event.⁶ More difficult to calculate is the human cost associated with osteoporotic fractures. Increased mortality, pain, disability, depression and loss of independence have been well documented after hip and vertebral fractures.^{7–11}

Due to the high risk of morbidity and mortality after an osteoporotic fracture, older adults require an interdisciplinary approach to their care. In particular, attention must be given to the prevention of common fracture complications, rehabilitation, assessment of the cause of fracture, and prevention of subsequent fractures. This paper will review current evidence and recommendations in each of these areas.

* Corresponding author. Address: Center for the Study of Aging and Human Development, Duke University Medical Center, Durham, NC 27710, USA. Tel.: +1 919 660 7517; Fax: +1 919 684 8569., E-mail address: colon001@mc.duke.edu (C. S. Colón-Emeric)..

PREVENTION OF COMMON FRACTURE COMPLICATIONS

When caring for an older adult presenting with an acute fracture, the most immediate complications that must be addressed are thromboembolism, delirium and pain management. Fortunately, effective preventive measures are available for each of these problems.

Thromboembolism

Deep vein thromboembolism (DVT) occurs in over 40% of hip fracture patients without prophylaxis.¹² A single study reported that patients with pelvic and lower extremity fractures have a similarly high risk of DVT¹³, although in a younger trauma population. The incidence of DVT in other types of fractures is unknown.

A meta-analysis of randomized controlled trials showed that unfractionated or low-molecular-weight heparin (LMWH) reduces the absolute incidence of DVT by 16%, suggesting that about six hip fracture patients need to be treated for 7–10 days to prevent one DVT.¹² There is insufficient evidence to suggest that LMWHs are superior to unfractionated heparins. However, a separate meta-analysis of head-to-head trials of the selective factor Xa inhibitor fondaparinux compared with the LMWH enoxaparin showed an additional reduction in the incidence of DVT by 6% with fondaparinux.¹⁴ It is unclear whether symptomatic DVT or pulmonary embolism are reduced significantly with this agent. A large trial of aspirin in addition to 'usual' venous thromboembolism prophylaxis showed an absolute reduction of 1% in pulmonary embolism or symptomatic DVT, but an excess of transfusion-requiring bleeding episodes.¹⁵ Mechanical pumping devices reduce the absolute incidence of DVT by 15%, although compliance remains problematic.¹² Nevertheless, mechanical pumping devices are a reasonable alternative for patients with contra-indications to anticoagulants.

The duration of DVT prophylaxis in randomized trials of patients undergoing hip surgery is generally 7–10 days. However, since the increased risk of DVT persists for several months, longer durations of therapy have been tested. A randomized trial of a 28-day course vs a 7-day course of fondaparinux showed a 2.4% absolute decrease in the incidence of symptomatic DVT, but a 1.4% increase in the risk of major bleeding.¹⁶ A longer duration of therapy could be considered for patients at highest risk. Further head-to-head trials and economic analyses will be helpful to guide the choice and duration of DVT prophylaxis after hip fracture.

Delirium

Delirium complicates the hospital stay of 10–40% of older adults with hip fracture.^{17,18} The risk of delirium after other fracture types is not known. Delirium can occur both before and after surgery, and is most frequently attributed to infection, cardiopulmonary dysfunction, drugs, and fluid and electrolyte imbalances. However, 60% of delirium cases are considered to be multifactorial with no single precipitating event.¹⁸ Patients with an attributable cause are more likely to recover by the time of hospital discharge. Delirium has been shown to prolong hospital stay, increase mortality and increase the risk of nursing home placement.^{19,20}

A randomized trial of an interdisciplinary consultation service compared with usual care after hip fracture showed an 18% absolute risk reduction in episodes of delirium, and a 17% reduction in cases of severe delirium.¹⁹ The team made recommendations to the orthopaedic surgeons based on a structured protocol with attention to 10 domains. These included oxygen delivery, fluid and electrolyte balance, treatment of pain, reduction of inappropriate medications, bowel and bladder function, early mobilization, prevention of postoperative complications, nutrition, environmental stimuli, and pharmacological treatment of agitated delirium. This study highlighted the importance of careful, comprehensive general medical care in frail older adults after fracture.

Pain control

Pain is a universal result of acute fracture, and a complete discussion of pain management is beyond the scope of this paper. However, it is important to recognize that older patients are frequently undertreated for fracture pain, with a resulting increase in adverse outcomes.

Clinicians are frequently hesitant to prescribe opiate medications to older adults because of concerns about precipitating or worsening delirium. One cohort study suggested that while 40% of cognitively intact hip fracture patients reported severe or very severe pain, 80% had no standing order for an analgesic agent. Patients with dementia fared even worse, receiving only one-third of the amount of opioids as cognitively intact patients.²¹

Surprisingly, however, older patients who received less than the equivalent of 10 mg/day morphine sulphate were five times more likely to develop delirium after hip fracture compared with patients who received more opiates. Furthermore, cognitively intact patients reporting severe pain had a nine-fold higher risk of developing delirium compared with those whose pain was adequately treated.²² These studies underscore the importance of aggressive pain control in older fracture patients, both to relieve suffering and to reduce the risk of delirium and its attendant complications.

REHABILITATION

Disability following fracture is common and increases with age. For example, patients with lumbar fracture report an average of 158 limited activity days after their event, although the range is highly variable. Substantial disability has also been reported for other fracture sites²³, and may especially impact frail adults with limited functional reserve. Physical therapy (PT) and occupational therapy (OT) are therefore important parts of the treatment plan of older adults with fractures.

Timing and duration

Unfortunately, much is still unknown about the optimal timing, intensity and type of rehabilitation in fracture patients.²⁴ While cohort studies have consistently shown that patients receiving earlier, more intensive PT after hip fracture recover more rapidly²⁵, these study designs are confounded by the fact that patients who are able to participate in therapy earlier are likely to be healthier than those whose therapy is delayed. Some evidence from randomized trials suggests that earlier PT may reduce acute pain and disability in patients with humeral and radial fractures.^{26,27} It seems clear that the earliest possible referral to PT is not harmful and may be beneficial for fracture patients.

The duration and delivery mode of therapy is also of debate. One randomized trial showed that 6 months of supervised PT after standard rehabilitation for hip fracture improved physical performance and functional status compared with home exercise.²⁸ However, a randomized trial of a prolonged home-based PT and OT intervention in a similar population had no effect.²⁹ Extended group and home-based PT appear to increase balance, trunk strength and psychological status in women with vertebral fractures.^{30,31} At the present time, the type and duration of therapy is often dictated by availability and reimbursement rather than by evidence. Nevertheless, early referral to a therapist experienced in treating patients with osteoporosis is advisable.

Vertebroplasty and kyphoplasty

In recent years, a growing number of patients with acute vertebral fractures have undergone vertebroplasty or kyphoplasty in an effort to reduce pain and restore vertebral body height. In vertebroplasty, a canula is inserted into the collapsed vertebral body and

polymethylmethacrylate (PMMA) cement is injected, while in kyphoplasty, balloon expansion of the vertebral body precedes PMMA injection. Case series and cohort studies have suggested a reduction in acute pain scores with vertebroplasty and kyphoplasty compared with patients treated conservatively, although outcomes at 6 weeks and 6–12 months are similar.³² Reported complications include leakage of PMMA into the spinal canal, PMMA pulmonary embolism, and collapse of adjacent vertebral bodies.³³ Of long-term concern is a heightened risk for fractures above and below the spinal level being treated.^{34,35} Randomized trials to assess the safety and efficacy of these procedures are needed before its place in the management of acute vertebral fracture can be understood.

ASSESSMENT OF CAUSE OF FRACTURE

While a host of systemic diseases can secondarily cause or worsen osteoporosis, few data are available to guide the appropriate evaluation after fracture in older adults. A careful history and physical examination is essential to avoid unnecessary and expensive testing.

Laboratory testing

Although primary osteoporosis remains a ‘diagnosis of exclusion’, it is by far the most likely cause of a low trauma fracture in an older adult. As a result, the authors suggest that the laboratory evaluation for most fracture patients can be limited to those (1): needed prior to initiation of therapy; or (2) indicated on the basis of history and examination findings. Most clinical practice guidelines recommend, at a minimum, measurement of serum calcium, creatinine, alkaline phosphatase, liver enzymes and complete blood count.³⁶ These tests will inform selection of osteoporosis therapy and exclude severe underlying illnesses and some forms of metabolic bone diseases. To exclude other forms of metabolic bone diseases, further tests may include serum protein electrophoresis, thyroid function tests, 24-h urine calcium (or a spot urine calcium:creatinine ratio as a screening test), parathyroid hormone and 25-OH vitamin D levels. With the exception of vitamin D, discussed below, the diagnostic yields of these tests are likely to be low when applied routinely to older people. However, more thorough metabolic bone testing may be indicated for some patients. Men may be more likely to have an underlying cause for osteoporosis, particularly hypogonadism³⁷, and history and physical examination should include a genital examination and pertinent history. Free serum testosterone may be assessed, but providing routine testosterone supplements to older men without symptoms of severe hypogonadism is not recommended.

Vitamin D deficiency is now recognized as a common problem in older adults, with prevalence ranging from 6% in healthy community-dwelling older adults to 85% in medical inpatients.^{38,39} In addition to causing osteomalacia, vitamin D deficiency has been associated with increased fall rates which in turn increase the risk of further fractures.⁴⁰ Even healthy premenopausal women may have a high burden of vitamin D deficiency (typically defined as a 25-OH vitamin D of < 10 ng/mL) or insufficiency (level of between 10 and 25 ng/mL) by late winter in northern latitudes.^{41,42} Moreover, initiating bisphosphonate therapy in patients with uncorrected vitamin D deficiency can cause serious hypocalcaemia.⁴³ It is therefore important to consider vitamin D deficiency in all older adults presenting with fractures. A challenge in the diagnosis and management of vitamin D deficiency is the expense and lack of availability of high-quality vitamin D assays, many of which do not accurately measure levels of 25 hydroxycholecalciferol (25-OH vitamin D3) received from dietary sources. The authors generally recommend checking vitamin D levels in all older adults with low bone mass, and then treating everyone with a level below 25 ng/mL (80 nmol/dL) with 50 000 IU ergocalciferol twice a week for 8–12 weeks followed by at least 800 IU/day of vitamin D3 (equivalent to a multivitamin and two calcium pills with vitamin D added). An alternative to measuring vitamin D levels is to simply supplement all older fracture patients. If this approach is chosen, the

authors typically give 100 000 IU ergocalciferol followed by 800–1000 IU vitamin D3 daily; a dose associated with lower falls and fracture risk.

Measurement of bone mass

By definition, older adults with low trauma fracture are highly likely to have low bone mineral density (BMD), heightened bone turnover and/or poor bone quality. Moreover, bone loss appears to be accelerated in the perifracture period.⁴⁴ These facts, coupled with the high risk for additional fractures observed in this population, have led several expert panels to recommend osteoporosis treatment for fracture patients regardless of their BMD.³⁶ Many older patients with a recent fracture experience disability and pain that render BMD measurement impractical. Therefore, while some advocate using bone density to determine baseline BMD and to monitor the response to therapy, the authors believe that BMD measurement is not necessary for all fracture patients and should only be used when it will influence current or future management decisions.

PREVENTION OF SUBSEQUENT FRACTURES

Older adults with low trauma fracture have approximately twice the risk for subsequent fractures compared with similar patients without fracture.⁴⁵ After a hip fracture, for example, 10–14% of survivors will suffer another fracture each year.⁴⁶ Thus, clinicians caring for older fracture patients must consider options for secondary fracture prevention. Presently, few patients with osteoporotic fractures receive interventions to reduce this risk. Studies in both the UK and the USA consistently show that fewer than 25% of women with recent osteoporotic fracture receive any therapy to prevent further fractures, with practice even worse among men.^{47,48} Economic analyses suggest that osteoporosis therapies become more cost effective in older patients and in patients with fractures.³⁶ Thus, there is a significant imbalance between the current state of medical knowledge in secondary fracture prevention and current clinical practice.

Calcium and vitamin D

Calcium and vitamin D supplementation in older adults is an effective means of preventing fractures, and possibly falls, regardless of BMD or fracture history.^{49,50} Calcium and vitamin D have also been included as part of therapy in nearly all secondary fracture prevention trials, and thus form an essential part of the treatment of older fracture patients. Practical issues include ensuring absorption of calcium, which requires an acidic environment, in older patients with achlorhydria or who are taking acid-suppressing drugs. Administration of calcium supplements with meals or in the form of calcium citrate may be helpful for such patients. Achieving the recommended daily dose of 800–1000 IU vitamin D often requires a multivitamin in addition to combination calcium and vitamin D products, which generally contain only 200 IU per tablet. For those with vitamin D deficiency or insufficiency, a more aggressive approach to vitamin D repletion, as discussed previously, is used prior to initiating daily supplements.

Bisphosphonates

The bisphosphonate medications reduce the relative risk of both vertebral and non-vertebral fractures in patients with established osteoporosis by 40–50%.^{51–53} Beyond the large-scale clinical trials showing risk reduction in secondary fractures, several randomized trials have demonstrated specific safety and efficacy even in the oldest and frailest populations, with patients randomized to bisphosphonates reporting gastrointestinal symptoms no more often than those taking placebo.^{54,55} Daily, weekly and monthly oral preparations are available, and yearly intravenous preparations are under study.⁵⁶ Clinicians need to consider whether their frail or cognitively impaired older patients can safely follow the dosing requirements;

patients must take the medication while fasting and remain upright for at least 1 h after the dose to maximize absorption and minimize risk for upper gastrointestinal complications. Hypocalcaemia, common in older patients, should be corrected prior to beginning therapy.

Although there is a theoretical concern that inhibiting osteoclast activity with bisphosphonates could impair the remodelling that occurs during fracture healing, most animal models and at least one human randomized trial suggest that early use of bisphosphonate may actually improve callus formation and mechanical bone strength.⁵⁷ Therefore, recent fracture need not be considered as a contra-indication to bisphosphonate use.⁵⁸

Calcitonin

Calcitonin is the most frequently prescribed osteoporosis medication in US nursing homes⁵⁹, probably because of its intranasal administration and low side-effect profile. Calcitonin reduces the relative risk of vertebral fractures in women with established osteoporosis by 40%.⁶⁰ However, calcitonin has not been proved to reduce fractures at non-vertebral sites and is thus considered by many to be a second- or third-line agent. Similar to emerging data with other anti-osteoporotic agents, calcitonin may have an analgesic effect in acute vertebral fractures.⁶¹ Calcitonin is therefore an alternative choice for patients with isolated spine osteoporosis or who have painful acute vertebral fracture and cannot tolerate other agents.

Teriparatide

The 1–34 parathyroid hormone teriparatide is a potent anabolic agent that reduces the relative risk of both vertebral and non-vertebral fractures in men and women with established osteoporosis by 35–65%.⁶² Although combinations of the anabolic effects of teriparatide with the anti-osteoclastic activity of bisphosphonates is theoretically attractive, the effectiveness of teriparatide to increase BMD is reduced by concomitant administration of alendronate.⁶³ In contrast, there is emerging data that starting an antiresorptive agent after a 24-month course of teriparatide is beneficial.⁶⁴ Presently, the high cost and subcutaneous administration of teriparatide make it less attractive for some older adults with osteoporosis, although it is an effective alternative for those who have severe osteoporosis, cannot tolerate oral bisphosphonates, or who have failed other therapies. Alternative administration methods for teriparatide are under investigation.

Raloxifene

The selective oestrogen receptor modulator raloxifene reduces the relative risk of vertebral fractures by 50% in women with osteoporosis.⁶⁵ Reduction of fractures at non-vertebral sites by raloxifene has not been clearly demonstrated, suggesting that raloxifene may be a weaker antiresorptive agent. Raloxifene significantly increases the risk of DVT; this adverse drug event is particularly problematic for patients with recent fracture whose DVT risk is already high. However, a reduction in the risk of breast cancer incidence may make raloxifene attractive for some patients.⁶⁶

External hip protectors

External hip protectors are undergarments with side pads that attenuate the force delivered to the trochanteric region during a fall. Certain individual randomized trials of hip protectors in residents of homes for the aged have shown impressive relative reductions in hip fracture rates of up to 60%.⁶⁷ However, meta-analysis of all experimental and quasi-experimental trials of hip protectors have failed to find a significant benefit.⁶⁸ One explanation may be the highly variable force attenuation capacities of different hip protector brands observed in biomechanical studies, with some brands consistently exceeding the fracture threshold during

simulated fall conditions.⁶⁹ Few trials have evaluated the use of hip protectors in community-dwelling older adults. Regrettably, compliance with hip protectors in real-world settings is generally poor, although educational interventions substantially increase their use. As hip protectors are safe, relatively inexpensive and take effect immediately, they may be a potentially attractive secondary prevention option.⁷⁰ Thus, it appears reasonable to recommend brands of hip protectors with proven efficacy to older fracture patients at high risk for falls or residing in nursing homes, although additional trials are needed to fully understand their utility.

Fall prevention strategies

Since most fractures in older adults occur after a fall, interventions to prevent falls are an important part of the care of older fracture patients. The aetiology of falls is frequently multifactorial; therefore, most effective interventions have involved multiple risk factor reduction by an interdisciplinary team.⁷¹ Risk factors that should be addressed include medication review, correction of orthostatic hypotension, environmental safety evaluations, balance and strengthening exercises, correction of sensory deficits, and provision of ambulatory aids.⁷² In high-risk populations such as nursing home residents, these interventions have been shown to reduce fracture rates significantly.⁷³ Specifically requesting fall prevention services in addition to standard rehabilitation after a fracture is warranted.

SUMMARY AND CONCLUSIONS

A fracture event in an older adult nearly always indicates osteoporosis and places them at very high risk for both short- and long-term adverse outcomes. Fortunately, a growing body of evidence suggests that many of these events, including DVT, delirium, functional decline and subsequent fractures, can be effectively prevented with existing drug therapies and physical modifications. The complexities of caring for older fracture patients in today's healthcare environment requires an individualized and multidisciplinary approach to care that is frequently challenging but also immensely rewarding.

Practice points

Thromboembolism prevention

- use a pharmacological agent (subcutaneous heparin, LMWH or factor Xa inhibitor) or mechanical pumping device for 7–10 days in most hip fracture patients, and consider in patients with other high-risk fractures
- consider longer duration therapy (28 days) or the addition of aspirin in high-risk patients

Delirium prevention

- a strategy of early detection and treatment of postoperative complications reduces the risk of delirium in hip fracture patients

Pain control

- undertreatment of pain is common, particularly in cognitively impaired patients, and is associated with a higher risk of delirium

Rehabilitation

- early mobilization and referral to PT is not harmful and is associated with improved outcomes

Assessment of cause of fracture

- basic laboratory evaluation should include serum calcium, creatinine, alkaline phosphatase, liver enzymes and complete blood count
- further diagnostic testing should be guided by a thorough history and physical examination
- vitamin D deficiency is common; levels should be measured or supplements provided to most patients
- BMD should be measured when results will change current or future management, but most patients should be treated for osteoporosis regardless of their BMD

Prevention of subsequent fractures

- most patients should be offered secondary prevention with a proven pharmacological agent, calcium and vitamin D
- some brands of external hip protectors may be useful for patients in residential facilities
- assess for and reduce risk factors for falls

Research agenda

- economic evaluation comparing thromboembolism prevention strategies
- randomized trials to determine optimal rehabilitation strategies and duration
- randomized trials of vertebroplasty and kyphoplasty including long-term follow-up for late complications to establish safety and efficacy
- randomized trials to establish the safety and efficacy of pharmacological agents in institutionalized patients
- interventions to improve the use of effective osteoporosis therapies in high-risk populations

Acknowledgements

Dr. Colón-Emeric is supported by a K23-Brookdale Fellowship, NIA AG024787-01. Dr. Saag is supported by 1 K24 AR052361-01 and by grant U18 HS10389 from the Agency for Healthcare Quality and Research.

References

1. US Department of Health and Human Services. Bone Health and Osteoporosis: a Report of the Surgeon General. Rockville, MD; US Department of Health and Human Services, Office of the Surgeon General: 2004.
2. Cooper C, Campion G, Melton L. Hip fractures in the elderly: a world-wide projection. *Osteoporosis International* 1992;2:285–289. [PubMed: 1421796]
3. Cooper C, Melton L. Epidemiology of osteoporosis. *Trends in Endocrinology and Metabolism* 1992;3:224–229.
4. Diamond T, Thornley S, Sekel R, Smerdely P. Hip fracture in elderly men: prognostic factors and outcomes. *The Medical Journal of Australia* 1997;167:412–415. [PubMed: 9364155]
5. Ray N, Chan J, Thamer M, Melton L. Medical expenditures for the treatment of osteoporotic fractures in the United States in 1995: report from the National Osteoporosis Foundation. *Journal of Bone and Mineral Research* 1997;12:24–35. [PubMed: 9240722]
6. Zimmerman S, Chandler J, Hawkes W, et al. Effect of fracture on the health care use of nursing home residents. *Archives of Internal Medicine* 2002;162:1502–1508. [PubMed: 12090887]

7. Salkeld G, Cameron I, Cumming R, et al. Quality of life related to fear of falling and hip fracture in older women. A time trade off study *BMJ* 2000;320:341–346.
8. Lyles K, Gold D, Shipp K, et al. Association of osteoporotic vertebral compression fractures with impaired functional status. *The American Journal of Medicine* 1993;94:595–601. [PubMed: 8506884]
9. Fox K, Hawkes W, Hebel J, et al. Mobility after hip fracture predicts health outcomes. *Journal of the American Geriatrics Society* 1998;46:169–173. [PubMed: 9475444]
10. Crans G, Silverman S, Genant H, et al. Association of severe vertebral fractures with reduced quality of life: reduction in the incidence of severe vertebral fractures by teriparatide. *Arthritis and Rheumatism* 2004;50:4028–4034. [PubMed: 15593198]
11. Picavet H, Hoeymans N. Health related quality of life in multiple musculoskeletal diseases: SF-36 and EQ-5D in the DMC3 study. *Annals of the Rheumatic Diseases* 2004;63:723–729. [PubMed: 15140781]
12. Handoll H, Farrar M, McBirmie J, et al. Heparin, low molecular weight heparin and physical methods for preventing deep vein thrombosis and pulmonary embolism following surgery for hip fractures. *Cochrane Database of Systematic Reviews* 2002;4:CD000305.
13. Britt S, Barker D, Maxwell R, et al. The impact of pelvic and lower extremity fractures on the incidence of lower extremity deep vein thrombosis in high-risk trauma patients. *The American Surgeon* 2003;69:459–463. [PubMed: 12852501]
14. Turpie A, Bauer K, Eriksson B, Lassen M. Fondaparinux vs enoxaparin for the prevention of venous thromboembolism in major orthopedic surgery: a meta-analysis of 4 randomized double-blind studies. *Archives of Internal Medicine* 2002;162:1833–1840. [PubMed: 12196081]
15. PEP Trial Collaborative Group. Prevention of pulmonary embolism and deep vein thrombosis with low dose aspirin: Pulmonary Embolism Prevention Trial. *Lancet* 2000;355:1295–1302. [PubMed: 10776741]
16. Eriksson B, Lassen M, Colwell CJ. Efficacy of fondaparinux for thromboprophylaxis in hip fracture patients. *The Journal of Arthroplasty* 2004;19(supplement 2):78–81. [PubMed: 15457423]
17. Francis J. Delirium in older patients. *Journal of the American Geriatrics Society* 1992;40:829–838. [PubMed: 1634729]
18. Brauer C, Morrison R, Silberzweig S, Siu A. The cause of delirium in patients with hip fracture. *Archives of Internal Medicine* 2000;160:1856–1860. [PubMed: 10871981]
19. Marcantonio E, Flacker J, Wright R, Resnick N. Reducing delirium after hip fracture: a randomized trial. *Journal of the American Geriatrics Society* 2001;49:516–522. [PubMed: 11380742]
20. Edelstein D, Aharonoff G, Karp A, et al. Effect of postoperative delirium on outcome after hip fracture. *Clinical Orthopaedics and Related Research* 2004;422:195–200. [PubMed: 15187857]
21. Morrison R, Siu A. A comparison of pain and its treatment in advanced dementia and cognitively intact patients with hip fracture. *Journal of Pain and Symptom Management* 2000;19:240–248. [PubMed: 10799790]
22. Morrison R, Magaziner J, Gilbert M, et al. Relationship between pain and opioid analgesics on the development of delirium following hip fracture. *The Journals of Gerontology Series A* 2003;58:76–81.
23. Fink J, Ensrud K, Nelson D, et al. Disability after clinical fracture in postmenopausal women with low bone density: the Fracture Intervention Trial (FIT). *Osteoporosis International* 2003;14:69–76. [PubMed: 12577187]
24. Handoll H, Sherrington C, Parker M. Mobilisation strategies after hip fracture surgery in adults. *Cochrane Database of Systematic Reviews* 2004;4:CD001704.
25. Penrod J, Boockvar KL, Litke A, et al. Physical therapy and mobility 2 and 6 months after hip fracture. *Journal of the American Geriatrics Society* 2004;52:1114–1120. [PubMed: 15209649]
26. Hodgson S, Mawson S, Stanley D. Rehabilitation after two-part fractures of the neck of the humerus. *The Journal of Bone and Joint Surgery* 2003;85:419–422.
27. Liow R, Cregan A, Nanda R, Montgomery R. Early mobilisation for minimally displaced radial head fractures is desirable. A prospective randomized study of two protocols. *Injury* 2002;33:801–806. [PubMed: 12379391]
28. Binder E, Brown M, Sincamore D, et al. Effects of extended outpatient rehabilitation after hip fracture: a randomized controlled trial. *JAMA* 2004;292:837–846. [PubMed: 15315998]

29. Tinetti M, Baker D, Gottschalk M, et al. Home-based multicomponent rehabilitation program for older persons after hip fracture: a randomized trial. *Archives of Physical Medicine and Rehabilitation* 1999;80:916–922. [PubMed: 10453768]
30. Gold D, Shipp K, Pieper C, et al. Group treatment improves trunk strength and psychological status in older women with vertebral fractures: results of a randomized clinical trial. *Journal of the American Geriatrics Society* 2004;52:1471–1478. [PubMed: 15341548]
31. Papaioannou A, Adachi J, Winegard K, et al. Efficacy of home-based exercise for improving quality of life among elderly women with symptomatic osteoporosis-related vertebral fractures. *Osteoporosis International* 2003;14:677–682. [PubMed: 12879220]
32. Diamond T, Champion B, Clark W. Management of acute osteoporotic vertebral fractures: a non-randomized trial comparing percutaneous vertebroplasty with conservative therapy. *The American Journal of Medicine* 2003;114:257–265. [PubMed: 12681451]
33. Laredo J, Hamze B. Complications of percutaneous vertebroplasty and their prevention. *Skeletal Radiology* 2004;33:493–505. [PubMed: 15205925]
34. Fribourg D, Tang C, Sra P, et al. Incidence of subsequent vertebral fracture after kyphoplasty. *Spine* 2004;29:2270–2276. [PubMed: 15480139]
35. Uppin A, Hirsch J, Centenera L, et al. Occurrence of new vertebral body fracture after percutaneous vertebroplasty in patients with osteoporosis. *Radiologia* 2003;226:119–124.
36. Nelson, H.; Morris, C.; Kraemer, D., et al. *Osteoporosis in Postmenopausal Women: Diagnosis and Monitoring*. Rockville, MD: Agency for Healthcare Policy and Research; 2002.
37. Kelepouris N, Harper K, Gannon F, et al. Severe osteoporosis in men. *Annals of Internal Medicine* 1995;123:452–460. [PubMed: 7639446]
38. Thomas M, Lloyd-Jones D, Thadhanai R, et al. Hypovitaminosis D in medical inpatients. *The New England Journal of Medicine* 1998;338:777–783. [PubMed: 9504937]
39. Semba R, Garrett E, Johnson B, et al. Vitamin D deficiency among older women with and without disability. *The American Journal of Clinical Nutrition* 2000;72:1529–1534. [PubMed: 11101482]
40. Bischoff-Ferrari H, Dawson-Hughes B, Willet W, et al. Effect of vitamin D on falls: a meta-analysis. *JAMA* 2004;291:1999–2006. [PubMed: 15113819]
41. Steingrimsdottir LG, Indridason O, Franzson L, Sigurdsson G. Relationship between serum parathyroid hormone levels, vitamin D sufficiency, and calcium intake. *JAMA* 2005;294:2336–2341. [PubMed: 16278362]
42. Tangpricha V, Pearce E, Chen T, Holick M. Vitamin D insufficiency among free-living healthy young adults. *The American Journal of Medicine* 2002;112:659–662. [PubMed: 12034416]
43. Rosen C, Brown S. Severe hypocalcemia after intravenous bisphosphonate therapy in occult vitamin D deficiency. *The New England Journal of Medicine* 2003;348:1503–1504. [PubMed: 12686715]
44. Fox K, Magaziner J, Hawkes W, et al. Loss of bone density and lean body mass after hip fracture. *Osteoporosis International* 2000;11:31–35. [PubMed: 10663356]
45. Klotzbuecher C, Ross P, Landsman P, et al. Patients with prior fractures have an increased risk of future fractures: a summary of the literature and statistical analysis. *Journal of Bone and Mineral Research* 2000;15:721–739. [PubMed: 10780864]
46. Colón-Emeric C, Kuchibhatla M, Pieper C, et al. The contribution of hip fracture to risk of subsequent fractures: data from two longitudinal studies. *Osteoporosis International* 2003;14:879–883. [PubMed: 14530910]
47. Torgerson D, Dolan P. Prescribing by general practitioners after an osteoporotic fracture. *Annals of the Rheumatic Diseases* 1998;57:378–379. [PubMed: 9771215]
48. Colón-Emeric C, Yballe L, Sloane R, et al. Expert physician recommendations and current practice patterns for evaluating and treating men with osteoporotic fracture. *Journal of the American Geriatrics Society* 2000;48:1261–1263. [PubMed: 11037013]
49. Chapuy M, Arlot M, Duboeuf F, et al. Vitamin D3 and calcium to prevent hip fractures in elderly women. *The New England Journal of Medicine* 1992;327:1637–1642. [PubMed: 1331788]
50. Dawson-Hughes B, Harris S, Krall E, Dallal G. Effect of calcium and vitamin D supplementation on bone density in men and women 65 years of age or older. *The New England Journal of Medicine* 1997;337:670–676. [PubMed: 9278463]

51. Chestnut C, Skag A, Christiansen C, et al. Effects of oral ibandronate administered daily or intermittently on fracture risk in postmenopausal women. *Journal of Bone and Mineral Research* 2004;19:1241–1249. [PubMed: 15231010]
52. Cranney A, Waldegger L, Zytaruk N, et al. Risedronate for the prevention and treatment of postmenopausal osteoporosis. *Cochrane Database of Systematic Reviews* 2003;4:CD004523.
53. Bone H, Hosking DD, Devogelaer JP, et al. Ten years' experience with alendronate for osteoporosis in postmenopausal women. *The New England Journal of Medicine* 2004;350:1189–1199. [PubMed: 15028823]
54. Greenspan S, Schneider D, McClung M, et al. Alendronate improves bone mineral density in elderly women with osteoporosis residing in long-term care facilities. A randomized, double-blind, placebo-controlled trial. *Archives of Internal Medicine* 2002;136:742–746.
55. Boonen S, McClung M, Eastell R, et al. Safety and efficacy of risedronate in reducing fracture risk in osteoporotic women aged 80 and older: implications for the use of antiresorptive agents in the old and oldest old. *Journal of the American Geriatrics Society* 2004;52:1832–1839. [PubMed: 15507059]
56. Colon-Emeric C, Caminis J, Suh T, et al. The HORIZON recurrent fracture trial: design of a clinical trial in the prevention of subsequent fractures after low-trauma hip fracture repair. *Current Medical Research and Opinion* 2004;20:903–910. [PubMed: 15200749]
57. Adolphson P, Abbaszadegan H, Boden H, et al. Clodronate increases mineralization of callus after Colles' fracture: a randomized, double-blind, placebo-controlled, prospective trial in 32 patients. *Acta Orthopaedica Scandinavica* 2000;71:195–200. [PubMed: 10852328]
58. Fleisch H. Can bisphosphonates be given to patients with fractures? *Journal of Bone and Mineral Research* 2001;16:437–440. [PubMed: 11277260]
59. Jachna C, Shireman T, Whittle J, et al. Differing patterns of antiresorptive pharmacotherapy among nursing facility residents and community dwellers. *Journal of the American Geriatrics Society* 2005;53
60. Chestnut C, Silverman S, Andriano K, et al. A randomized trial of nasal spray salmon calcitonin in postmenopausal women with established osteoporosis: the Prevent Recurrence of Osteoporotic Fractures Study. *The American Journal of Medicine* 2000;109:267–276. [PubMed: 10996576]
61. Mehta N, Malootian A, Gilligan J. Calcitonin for osteoporosis and bone pain. *Current Pharmaceutical Design* 2003;9:2659–2676. [PubMed: 14529539]
62. Neer R, Arnaud C, Zanchetta J, et al. Effect of parathyroid hormone (1–34) on fractures and bone mineral density in postmenopausal women with osteoporosis. *The New England Journal of Medicine* 2001;344:1434–1441. [PubMed: 11346808]
63. Finkelstein J, Hayes A, Hunzelman J, et al. The effects of parathyroid hormone, alendronate, or both in men with osteoporosis. *The New England Journal of Medicine* 2003;349:1216–1226. [PubMed: 14500805]
64. Black D, Bilezikian J, Ensrud K, et al. One year of alendronate after one year of parathyroid hormone. *The New England Journal of Medicine* 2005;353:555–565. [PubMed: 16093464]
65. Ettinger B, Black D, Mitlak B, et al. Reduction of vertebral fracture risk in postmenopausal women with osteoporosis treated with raloxifene: results from a 3-year randomized clinical trial. *JAMA* 1999;282:637–645. [PubMed: 10517716]
66. Barret-Connor E, Cauley J, Kulkarni P, et al. Risk-benefit profile for raloxifene: 4-year data from the Multiple Outcomes of Raloxifene Evaluation (MORE) randomized trial. *Journal of Bone and Mineral Research* 2004;19:1270–1275. [PubMed: 15231013]
67. Kannus P, Parkkari J, Niemi S, et al. Prevention of hip fracture in elderly people with use of a hip protector. *The New England Journal of Medicine* 2000;343:1506–1513. [PubMed: 11087879]
68. Parker M, Gillespie W, Gillespie L. Hip protectors for preventing hip fractures in older people. *Cochrane Database of Systematic Reviews* 2005;3
69. Kannus P, Parkkari J, Poutala J. Comparison of force attenuation properties of four different hip protectors under simulated falling conditions in the elderly: an in vitro biomechanical study. *Bone* 1999;25:229–235. [PubMed: 10456390]
70. Colon-Emeric C, Datta S, Matchar D. An economic analysis of external hip protector use in ambulatory nursing facility residents. *Age and Ageing* 2003;32:47–52. [PubMed: 12540348]

71. Tinetti M. Preventing falls in elderly persons. *The New England Journal of Medicine* 2003;348:42–49. [PubMed: 12510042]
72. Gillespie L, Gillespie W, Robertson M, et al. Interventions for preventing falls in elderly people. *Cochrane Database of Systematic Reviews*. 2004
73. Ray W, Taylor J, Meador K, et al. A randomized trial of a consultation service to reduce falls in nursing homes. *JAMA* 1997;278:557–562. [PubMed: 9268276]