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Improving the Pharmacologic Management of Patients after Osteoporotic Hip Fractures

Joseph Klaus, Milad Modarresi, Rodrigo Aguilar, Nasreen BenHamed, and Franklin D. Shuler

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References with DOI

1. Shuler FD, Conjeski J. Defining bone health and fracture risk in West Virginia: the World Health Organization FRAX assessment tool. *The West Virginia Medical Journal*. 2011;107(5):12-7.
2. Cosman F, de Beur SJ, LeBoff MS, Lewiecki EM, Tanner B, Randall S, et al. Clinician's Guide to Prevention and Treatment of Osteoporosis. *Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA*. 2014;25(10):2359-81. <https://doi.org/10.1007/s00198-014-2794-2>
3. Jacobsen SJ, Goldberg J, Miles TP, Brody JA, Stiers W, Rimm AA. Hip fracture incidence among the old and very old: a population-based study of 745,435 cases. *American Journal of Public Health*. 1990;80(7):871-3. [https://doi.org/10.1016/0022-4375\(91\)90022-n](https://doi.org/10.1016/0022-4375(91)90022-n)
4. Boonen S, Autier P, Barette M, Vanderschueren D, Lips P, Haentjens P. Functional outcome and quality of life following hip fracture in elderly women: a prospective controlled study. *Osteoporosis International : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA*. 2004;15(2):87-94. <https://doi.org/10.1007/s00198-003-1515-z>
5. Schroder HM, Petersen KK, Erlandsen M. Occurrence and incidence of the second hip fracture. *Clinical Orthopaedics and Related Research*. 1993(289):166-9. <https://doi.org/10.1097/00003086-199304000-00022>
6. Ensrud KE, Barrett-Connor EL, Schwartz A, Santora AC, Bauer DC, Suryawanshi S, et al. Randomized trial of effect of alendronate continuation versus discontinuation in women with low BMD: results from the Fracture Intervention Trial long-term extension. *Journal of Bone and Mineral Research : the official journal of the American Society for Bone and Mineral Research*. 2004;19(8):1259-69. <https://doi.org/10.1359/jbmr.040326>
7. Chesnut CH, 3rd, Skag A, Christiansen C, Recker R, Stakkestad JA, Hoiseth A, et al. Effects of oral ibandronate administered daily or intermittently on fracture risk in postmenopausal osteoporosis. *Journal of Bone and Mineral Research : the official journal of the American Society for Bone and Mineral Research*. 2004;19(8):1241-9. <https://doi.org/10.1359/jbmr.040325>
8. Chesnut CH, 3rd, Silverman S, Andriano K, Genant H, Gimona A, Harris S, et al. A randomized trial of nasal spray salmon calcitonin in postmenopausal women with established osteoporosis: the prevent recurrence of osteoporotic fractures study. PROOF Study Group. *The American Journal of Medicine*. 2000;109(4):267-76. [https://doi.org/10.1016/s0002-9343\(00\)00490-3](https://doi.org/10.1016/s0002-9343(00)00490-3)
9. Ettinger B, Black DM, Mitlak BH, Knickerbocker RK, Nickelsen T, Genant HK, et al. Reduction of vertebral fracture risk in postmenopausal women with osteoporosis treated with raloxifene: results from a 3-year randomized clinical trial. Multiple Outcomes of Raloxifene Evaluation (MORE) Investigators. *Jama*. 1999;282(7):637-45. <https://doi.org/10.1001/jama.282.7.637>
10. Cummings SR, San Martin J, McClung MR, Siris ES, Eastell R, Reid IR, et al. Denosumab for prevention of fractures in postmenopausal women with osteoporosis. *The New England Journal of Medicine*. 2009;361(8):756-65. <https://doi.org/10.1097/01.ogx.0000363236.41902.96>
11. Neer RM, Arnaud CD, Zanchetta JR, Prince R, Gaich GA, Reginster JY, 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(19):1434-41. <https://doi.org/10.3171/foc.2001.11.2.8>

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12. Lyles KW, Colon-Emeric CS, Magaziner JS, Adachi JD, Pieper CF, Mautalen C, et al. Zoledronic acid and clinical fractures and mortality after hip fracture. *The New England Journal of Medicine*. 2007;357(18):1799-809. <https://doi.org/10.1056/nejmoa074941>
 13. Ogrinc G, Davies L, Goodman D, Batalden P, Davidoff F, Stevens D. SQUIRE 2.0 (Standards for Quality Improvement Reporting Excellence): revised publication guidelines from a detailed consensus process. *BMJ quality & safety*. 2016;25(12):986-92. <https://doi.org/10.7812/tpp/15-141>
 14. Kanis JA. Osteoporosis and osteopenia. *Journal of bone and mineral research : the official journal of the American Society for Bone and Mineral Research*. 1990;5(3):209-11. *8 Marshall Journal of Medicine*, Vol. 3 [2017], Iss. 3, Art. 12 <http://mds.marshall.edu/mjm/vol3/iss3/12> DOI: <http://dx.doi.org/10.18590/mjm.2017.vol3.iss3.12>; <https://doi.org/10.1002/jbmr.5650050302>
 15. Kamel HK, Hussain MS, Tariq S, Perry HM, Morley JE. Failure to diagnose and treat osteoporosis in elderly patients hospitalized with hip fracture. *The American Journal of Medicine*. 2000;109(4):326-8. [https://doi.org/10.1016/s0002-9343\(00\)00457-5](https://doi.org/10.1016/s0002-9343(00)00457-5)
 16. Kiebzak GM, Beinart GA, Perser K, Ambrose CG, Siff SJ, Heggeness MH. Undertreatment of osteoporosis in men with hip fracture. *Archives of internal medicine*. 2002;162(19):2217-22. <https://doi.org/10.1001/archinte.163.10.1236-b>
 17. LeBoff MS, Kohlmeier L, Hurwitz S, Franklin J, Wright J, Glowacki J. Occult vitamin D deficiency in postmenopausal US women with acute hip fracture. *Jama*. 1999;281(16):1505-11. <https://doi.org/10.1001/jama.281.16.1505>
 18. Diamond T, Smerdely P, Kormas N, Sekel R, Vu T, Day P. Hip fracture in elderly men: the importance of subclinical vitamin D deficiency and hypogonadism. *The Medical journal of Australia*. 1998;169(3):138-41.
 19. Recker RR, Hinders S, Davies KM, Heaney RP, Stegman MR, Lappe JM, et al. Correcting calcium nutritional deficiency prevents spine fractures in elderly women. *Journal of Bone and Mineral Research : the official journal of the American Society for Bone and Mineral Research*. 1996;11(12):1961-6. <https://doi.org/10.1002/jbmr.5650111218>
 20. Chapuy MC, Arlot ME, Duboeuf F, Brun J, Crouzet B, Arnaud S, et al. Vitamin D3 and calcium to prevent hip fractures in the elderly women. *The New England Journal of Medicine*. 1992;327(23):1637-42. <https://doi.org/10.1097/00006254-199305000-00026>
 21. Dawson-Hughes B, Harris SS, Krall EA, Dallal GE. 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(10):670-676. <https://doi.org/10.1056/nejm199709043371003>
 22. Marshall D, Johnell O, Wedel H. Meta-analysis of how well measures of bone mineral density predict occurrence of osteoporotic fractures. *Bmj*. 1996;312(7041):1254-9. <https://doi.org/10.1136/bmj.312.7041.1254>
 23. Cummings SR, Bates D, Black DM. Clinical use of bone densitometry: scientific review. *Jama*. 2002;288(15):1889-97. <https://doi.org/10.1001/jama.288.15.1889>
 24. Unnanuntana A, Gladnick BP, Donnelly E, Lane JM. The assessment of fracture risk. *The Journal of Bone and Joint Surgery American volume*. 2010;92(3):743-53. <https://doi.org/10.2106/jbjs.i.00919>
 25. Dawson-Hughes B, Tosteson AN, Melton LJ, 3rd, Baim S, Favus MJ, Khosla S, et al. Implications of absolute fracture risk assessment for osteoporosis practice guidelines in the USA. *Osteoporosis*

international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA. 2008;19(4):449-58. <https://doi.org/10.1007/s00198-008-0559-5>

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Improving the pharmacologic management of patients after osteoporotic hip fractures

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Abstract

Background

Osteoporotic hip fractures have become an increasingly common healthcare burden with significant morbidity and mortality in the geriatric population. Pharmacological management of the underlying osteoporosis is critical. Our objective is to determine the percentage of patients older than 65 who receive pharmacologic treatment of osteoporosis at Cabell Huntington Hospital within six months after a fragility fracture.

Methods

Data was extracted from medical records for patients age 65 or older who sustained a hip fracture during June 2013 - March 2015. Patients who received any form of pharmacologic treatment within six months after their fractures were identified. All analyses were performed using SAS version 9.3 (SAS Institute, Cary, North Carolina).

Results

Among the 193 patients who met the inclusion criteria, 26% (n=50) received pharmacologic treatment within six months after fracturing versus 74% (n=143) who did not receive any type of pharmacologic therapy after the fracture. Female was the predominant gender in pharmacologic treatment group (74% vs 71%). Mean age was 81 years old in both groups (81±9 vs 82±8), mean BMI was 25 in both groups (25±5 vs 25±6). There was no significant difference in pharmacologic management when the patients were stratified according to age group.

Conclusion

Patients were pharmacologically undertreated after an osteoporotic hip fracture, regardless of the age of fracture presentation. Due to potential benefits of pharmacologic treatment after osteoporotic hip fracture, treatment should be initiated prior to discharge, if possible. If this is not feasible for the patient, specific and detailed instructions should be given to the patient's primary care physician, or endocrinologist if medically complicated, for initiating therapy and proper management of the patient.

Key Words

Osteoporosis, Hip fracture, Geriatrics, FRAX, PTAF, Pharmacologic management of fractures

Introduction

Due to the growing elderly population, fragility hip fractures have become a common healthcare burden. Fragility fracture is defined by the World Health Organization (WHO) as "a fracture caused by an injury that would be insufficient to fracture a normal bone." According to National Osteoporosis Foundation recommendations, any patient age 50 or older who suffers a fragility fracture or vertebral fracture can be clinically diagnosed with osteoporosis.² The lifetime risk of

osteoporotic fractures in men and women age 50 or older is 25% and 50%, respectively.¹ Most patients are not aware that they have osteoporosis until they suffer a fragility fracture (i.e. fracture when falling from standing height).² Osteoporotic hip fractures are a well-established source of morbidity and mortality in the geriatric population. They are associated with a significant increase in health care service utilization, as well as all forms of post-acute care. This includes post-acute hospitalizations, home health care, and physical and occupational therapy. Further, patients who were originally community-dwelling have an increased likelihood of living in a nursing home after hip fracture.^{3,4} There is also substantial evidence that prior osteoporotic hip fracture results in an increased risk of subsequent fracture.⁵ The greatest risk appears to be soon after fracture, particularly in the first year. Hip fractures are also associated with increased mortality rates. The reported one year mortality rate due to hip fracture for women over 50 years is 24% and for men up to 49%.¹

The acute management of hip fractures is very well established. It includes optimization of vitamin D and calcium levels, optimizing the patient for surgery, and surgical repair of the fracture. Patients may be discharged as soon as one or two recovery days after surgery. Those patients who demonstrate low vitamin D levels are also discharged with vitamin D replacement therapy.

The prevention of recurrence via investigation for osteoporosis and initiation of pharmacologic treatment after fracture (PTAF) is poorly executed. According to National Osteoporosis Foundation recommendations, any patient age 50 or older who suffers an osteoporotic fracture should receive PTAF.² It is crucial to treat these patients pharmacologically in order to medically optimize them for functional recovery. Further, FDA-approved medications for osteoporosis have been shown to reduce the risk of subsequent osteoporotic fractures.⁶⁻¹² It is also important to initiate PTAF early due to increased risk of subsequent fracture within one year.¹² Despite the current recommendations, PTAF is often overlooked.

Our objective is to determine the percentage of patients older than 65 who receive PTAF within six months after a fragility fracture. It is our hypothesis that this vulnerable population is being undertreated. We further hope to determine possible causes of this disparity and propose solutions to improve management and patient outcomes.

Methods

Study Design

A retrospective cohort study. SQUIRE 2.0 guideline was used to prepare this quality improvement paper.¹³

Cohort generation

Medical records for patients age 65 or older who sustained hip fracture during June 2013 - March 2015 were collected from electronic medical records with IRB approval (874559-3). Patients with a prior diagnosis of osteoporosis, pathologic hip fracture due to tumor, and those who were already on pharmacologic treatment of osteoporosis were excluded. Medications included in calculations were bisphosphonates (alendronate, ibandronate, risedronate, zoledronic acid),

parathyroid hormone (teriparatide), and RANK ligand inhibitors (denosumab). Vitamin D and calcium supplementation were not included in our calculations of pharmacologic treatment. Descriptive analysis was performed to extract demographics of our cohort. Age, gender, BMI, and whether patients received a DXA scan (dual x-ray absorptiometry) before and after treatment were extracted to assess for the difference in treatment with respect to these variables.

Assessment of Risk of Future Fracture

Next, the International Osteoporosis Foundation's Fracture Risk Assessment Tool (FRAX) was used to calculate each patient's ten-year risk of hip and major osteoporotic fracture using pre-fracture data. The FRAX tool integrates each patient's independent risk factors to determine their ten-year risk. These risk factors include country of origin, age, gender, BMI, previous fracture, parental history of hip fracture, current smoking, use of glucocorticoids, rheumatoid arthritis, secondary osteoporosis, alcohol consumption, and, when available, bone mineral density (BMD). Patients were excluded from FRAX analysis for the following reasons: age greater than or equal to 90 and missing relevant historical information. In clinical practice, patients with greater than or equal to a 20% ten-year risk of major osteoporotic fracture or greater than or equal to a 3% ten-year risk of hip fracture are treated if they have osteopenia demonstrated by DXA scan. Most patients in this study did not have a DXA scan. Therefore FRAX scores will not be used as an indication for therapy, but rather, as an assessment of fracture risk.

Statistical Analysis

All categorical variables were compared using Pearson's χ^2 test, while continuous variables were compared using t-test. All analyses were performed using SAS version 9.3 (SAS Institute, Cary, North Carolina). All p-values were based on 2-sided tests and were considered statistically significant when $p < 0.05$.

Results

Among the 193 patients who met the inclusion criteria, 26% (n=50) received PTAF within six months versus 74% (n=143) who did not receive PTAF (**Figure 1**). Female was the predominant gender in both groups (74% vs 71%). Mean age was 81 years old in both groups (81±9 vs 82±8), mean BMI was 25 in both groups (25±5 vs 25±6). Demographics and DXA scan histories of the 193 patients who met the inclusion criteria are presented in **Table 1**.

Figure 1: Out of 193 patients who met inclusion criteria, 50 (26%) received PTAF within six months of fracture.

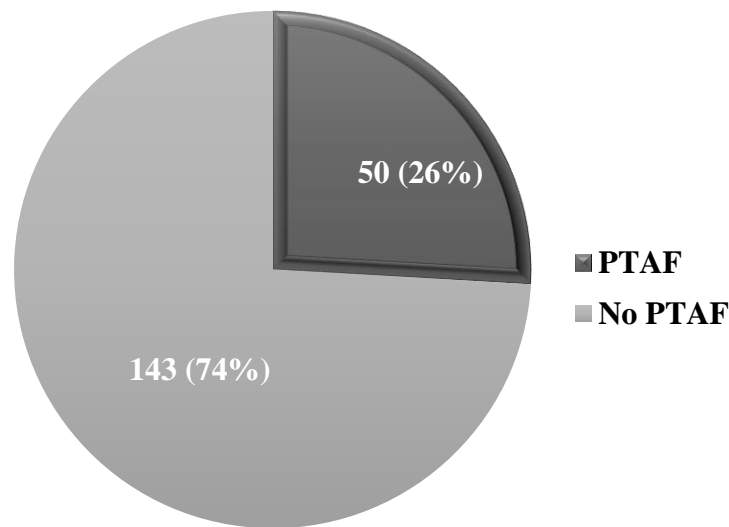


Table 1: Patient demographics and DXA scan histories. BMI: body mass index. \pm Standard deviation.

	Received PTAF (n=50)	Did not receive PTAF (n=143)
Mean age	81 \pm 9	82 \pm 8
Mean BMI	25 \pm 5	25 \pm 6
Female gender	37 (74%)	102 (71%)
DXA scan before fracture	5 (10%)	31 (22%)
DXA scan after fracture	1 (9%)	6 (22%)

Our analysis further showed there was no significant difference in pharmacologic management when the patients were stratified according to age group; most of our patients (n=71) were between 80 and 89 years old (**Table 2**).

Table 2: PTAF and non-PTAF patients stratified into ten-year age groups.

Age range (years)	Received PTAF (n=50)	Did not receive PTAF (n=143)
60-69	3 (20%)	12 (80%)
70-79	19 (29%)	47 (71%)
80-89	17 (24%)	54 (76%)
90-99	11 (27%)	30 (73%)

FRAX analysis was done on the group of patients that did not receive PTAF in order to quantify their risk of future fractures. Our results indicate that the majority of subjects who did not receive

PTAF were at high risk for future fracture (major osteoporotic fracture $\geq 20\%$, hip fracture $\geq 3\%$) (Tables 3 & 4).

Table 3: FRAX-derived ten-year risk of major osteoporotic fracture in patients who did not receive PTAF.

Ten-year risk of major osteoporotic fracture	Did not receive PTAF (n=121)
Low risk (<20%)	44
High risk (>20%)	77

Table 4: FRAX-derived ten-year risk of hip fracture in patients who did not receive PTAF.

Ten-year risk of hip fracture	Did not receive PTAF (n=121)
Low risk (<3%)	6
High risk (>3%)	115

Discussion

Non-traumatic fractures in the elderly are typically due to underlying osteoporosis.¹⁴ Uniform guidelines for prevention, assessment and management have been developed for this condition by various organizations. Results from this study and many others indicate a major need for attention to the pharmacological management of this condition.^{15,16}

One main area that can lead to definite improvement in management is the prevention and early detection of patients at risk. Deficiency in vitamin D and calcium have long been associated with increased risk of fractures.^{17,18} The addition of these supplements is proven to be beneficial in bone health.¹⁹⁻²¹ This is one of the limitations of our study since there are no records of previous vitamin D and calcium supplementation. Further, the serum levels of vitamin D and calcium, at the time of presentation, were not reviewed for each patient.

Early diagnosis is another important factor in initiating treatment. DXA-scan measures bone mineral density (BMD) and is a major tool used to identify patients with osteopenia or osteoporosis.^{22,23} Unfortunately, the state of West Virginia and many rural areas have limited access to DXA scans with only 24 of our 55 counties having this gold standard for osteoporosis/osteopenia detection.¹ This leaves a large number of rural patients without BMD scores, and thus, they are not given pharmacologic treatment. The FRAX analysis is a survey that does not require expensive equipment to administer. It has been used as an adjunct to determine patient need for pharmacologic treatment. FRAX provides a 10-year fracture risk and can be used with or without femoral neck bone mineral density.²⁴ However, current guidelines require that the patient has osteopenia demonstrated by DXA scan combined with FRAX results before pharmacologic treatment is indicated. Future studies should investigate the initiation of osteoporosis treatment using FRAX analysis with and without DXA scan results.

Post fracture management is another area that needs improvement. According to National Osteoporosis Foundation, pharmacologic treatment should be started in anyone with history of vertebral or hip fracture, patients with T score of ≤ -2.5 , patients with osteopenia according to

DXA scan or patients with ten year fracture risk assessment $\geq 3\%$ of vertebrae and hip or $\geq 20\%$ risk of fracture in other areas including the hip, clinical spine, forearm/wrist or proximal humerus.^{2,25} We found that only 18.6% of patients in our study had a DXA scan prior to their fracture, and only 3.6% after their fracture. Once we performed FRAX analysis on our patient group (without femoral neck bone mineral density), 54% (n= 77) had greater than 20% risk of major osteoporotic fracture and 77% (n= 110) of our patients had over 3% risk of major osteoporotic fracture. Findings from this study along with many others indicate under treatment in this vulnerable population and the need for attention and review of guidelines in place.

In conclusion, our study demonstrates the under-treatment of clinical osteoporosis and presents an opportunity to improve patient care. Using our results as a baseline, we can strive to increase the number of patients who initiate PTAF within six months of their events. We have proposed to implement a clinical pathway that discharges patients from the hospital with a prescription anti-resorptive medication and instructions to follow up with an endocrinologist or primary care physician. It is important to encourage patients to follow up with an endocrinologist if they have a complicated medical history that disqualifies them for first-line bisphosphonate therapy. In addition, a multidisciplinary hip fracture program at Cabell Huntington Hospital is using this data to narrow the post fracture pharmacological osteoporosis treatment gap.

References

1. Shuler FD, Conjeski J. Defining bone health and fracture risk in West Virginia: the World Health Organization FRAX assessment tool. *The West Virginia Medical Journal*. 2011;107(5):12-7.
2. Cosman F, de Beur SJ, LeBoff MS, Lewiecki EM, Tanner B, Randall S, et al. Clinician's Guide to Prevention and Treatment of Osteoporosis. *Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA*. 2014;25(10):2359-81.
3. Jacobsen SJ, Goldberg J, Miles TP, Brody JA, Stiers W, Rimm AA. Hip fracture incidence among the old and very old: a population-based study of 745,435 cases. *American Journal of Public Health*. 1990;80(7):871-3.
4. Boonen S, Autier P, Barette M, Vanderschueren D, Lips P, Haentjens P. Functional outcome and quality of life following hip fracture in elderly women: a prospective controlled study. *Osteoporosis International : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA*. 2004;15(2):87-94.
5. Schroder HM, Petersen KK, Erlandsen M. Occurrence and incidence of the second hip fracture. *Clinical Orthopaedics and Related Research*. 1993(289):166-9.
6. Ensrud KE, Barrett-Connor EL, Schwartz A, Santora AC, Bauer DC, Suryawanshi S, et al. Randomized trial of effect of alendronate continuation versus discontinuation in women with low BMD: results from the Fracture Intervention Trial long-term extension. *Journal of Bone and Mineral Research : the official journal of the American Society for Bone and Mineral Research*. 2004;19(8):1259-69.
7. Chesnut CH, 3rd, Skag A, Christiansen C, Recker R, Stakkestad JA, Hoiseth A, et al. Effects of oral ibandronate administered daily or intermittently on fracture risk in postmenopausal osteoporosis. *Journal of Bone and Mineral Research : the official journal of the American Society for Bone and Mineral Research*. 2004;19(8):1241-9.
8. Chesnut CH, 3rd, Silverman S, Andriano K, Genant H, Gimona A, Harris S, et al. A randomized trial of nasal spray salmon calcitonin in postmenopausal women with established osteoporosis: the prevent recurrence of osteoporotic fractures study. PROOF Study Group. *The American Journal of Medicine*. 2000;109(4):267-76.
9. Ettinger B, Black DM, Mitlak BH, Knickerbocker RK, Nickelsen T, Genant HK, et al. Reduction of vertebral fracture risk in postmenopausal women with osteoporosis treated with raloxifene: results from a 3-year randomized clinical trial. Multiple Outcomes of Raloxifene Evaluation (MORE) Investigators. *Jama*. 1999;282(7):637-45.
10. Cummings SR, San Martin J, McClung MR, Siris ES, Eastell R, Reid IR, et al. Denosumab for prevention of fractures in postmenopausal women with osteoporosis. *The New England Journal of Medicine*. 2009;361(8):756-65.
11. Neer RM, Arnaud CD, Zanchetta JR, Prince R, Gaich GA, Reginster JY, 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(19):1434-41.
12. Lyles KW, Colon-Emeric CS, Magaziner JS, Adachi JD, Pieper CF, Mautalen C, et al. Zoledronic acid and clinical fractures and mortality after hip fracture. *The New England Journal of Medicine*. 2007;357(18):1799-809.
13. Ogrinc G, Davies L, Goodman D, Batalden P, Davidoff F, Stevens D. SQUIRE 2.0 (Standards for Quality Improvement Reporting Excellence): revised publication guidelines from a detailed consensus process. *BMJ quality & safety*. 2016;25(12):986-92.
14. Kanis JA. Osteoporosis and osteopenia. *Journal of bone and mineral research : the official journal of the American Society for Bone and Mineral Research*. 1990;5(3):209-11.

15. Kamel HK, Hussain MS, Tariq S, Perry HM, Morley JE. Failure to diagnose and treat osteoporosis in elderly patients hospitalized with hip fracture. *The American Journal of Medicine*. 2000;109(4):326-8.
16. Kiebzak GM, Beinart GA, Perser K, Ambrose CG, Siff SJ, Heggeness MH. Undertreatment of osteoporosis in men with hip fracture. *Archives of internal medicine*. 2002;162(19):2217-22.
17. LeBoff MS, Kohlmeier L, Hurwitz S, Franklin J, Wright J, Glowacki J. Occult vitamin D deficiency in postmenopausal US women with acute hip fracture. *Jama*. 1999;281(16):1505-11.
18. Diamond T, Smerdely P, Kormas N, Sekel R, Vu T, Day P. Hip fracture in elderly men: the importance of subclinical vitamin D deficiency and hypogonadism. *The Medical journal of Australia*. 1998;169(3):138-41.
19. Recker RR, Hinders S, Davies KM, Heaney RP, Stegman MR, Lappe JM, et al. Correcting calcium nutritional deficiency prevents spine fractures in elderly women. *Journal of Bone and Mineral Research : the official journal of the American Society for Bone and Mineral Research*. 1996;11(12):1961-6.
20. Chapuy MC, Arlot ME, Duboeuf F, Brun J, Crouzet B, Arnaud S, et al. Vitamin D3 and calcium to prevent hip fractures in the elderly women. *The New England Journal of Medicine*. 1992;327(23):1637-42.
21. Dawson-Hughes B, Harris SS, Krall EA, Dallal GE. 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(10):670-
22. Marshall D, Johnell O, Wedel H. Meta-analysis of how well measures of bone mineral density predict occurrence of osteoporotic fractures. *Bmj*. 1996;312(7041):1254-9.
23. Cummings SR, Bates D, Black DM. Clinical use of bone densitometry: scientific review. *Jama*. 2002;288(15):1889-97.
24. Unnanuntana A, Gladnick BP, Donnelly E, Lane JM. The assessment of fracture risk. *The Journal of Bone and Joint Surgery American volume*. 2010;92(3):743-53.
25. Dawson-Hughes B, Tosteson AN, Melton LJ, 3rd, Baim S, Favus MJ, Khosla S, et al. Implications of absolute fracture risk assessment for osteoporosis practice guidelines in the USA. *Osteoporosis international : a journal established as result of cooperation between the European Foundation for Osteoporosis and the National Osteoporosis Foundation of the USA*. 2008;19(4):449-58.