Research Article

Role of Bone Supplement(Ca, Vit D) In Elderly Fragility Fracture

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ABSTRACT

Fragility fractures are a significant public health issue among the aged population because they have a significant influence on quality of life and healthcare expenses. As individuals grow older, their bone mineral density decreases and they become more prone to low-trauma fractures due to an increased risk of falls. Sufficient consumption of calcium and vitamin D has been widely acknowledged as crucial for preserving bone health and potentially decreasing the likelihood of fractures.

Objectives: This review analyses the existing evidence from randomized controlled trials and meta-analyses to determine the effectiveness of calcium and vitamin D supplementation, either alone or in combination, in avoiding fragility fractures in older persons.

Conclusion: Supplementing calcium and vitamin D has potential in decreasing the likelihood of fragility fractures in older individuals by enhancing bone health and strength. Nevertheless, the effectiveness of these supplements is contingent upon variables such as dosage, initial nutrient levels, and dietary circumstances. Although the evaluation suggests that customized approaches could be advantageous, additional research is required to build thorough protocols and comprehend the enduring effects.

Keywords: *fragility fractures, elderly, calcium, vitamin D, management, prevention.*

Introduction

Fragility fractures; also referred to as osteoporotic fractures for being the main consequence of osteoporosis ^[1], are fractures that are caused by a mechanical force or impact that would not break a healthy bone (low energy trauma) that is less or equals force resulted from a fall from a standard height^[1, 2,3].

Fragility fractures as a sequel of osteoporosis are crucial because of resulted disabilities, impaired quality of life for the patient and his family with social impact and high medical costs, complications and increased mortality rate ^[4].

Dr. Mohammed Mubarak Mohammed Ahmed , (2024). Role of Bone Supplement(Ca, Vit D) In Elderly Fragility Fracture. *MAR Orthopedics & Trauma (2024) 6:2*

Risk factors

There are many factors that have a remarkable impact on the incidence of fragility fractures. They include, first and foremost decreased bone mass (bone mineral density BMD) in osteoporotic patients ^[4]. Increased age as the elderly are at high risk for fractures due to bone aging and concomitant comorbidities ^[4]. Gender and hormonal changes; as females especially after menopause are notably more affected by the disease than males ^[1,4]. Family history of osteoporosis, and a previous fracture as a one fragility fracture significantly increases the risk of a secondary fracture particularly within two years after the first fracture ^[2]. The utilization of some medication such as systemic glucocorticoids ^[3,5]. Insufficient dietary intake of calcium and vitamin D , inadequate physical activity and frequent falls ^[5].

Epidemiology

Musculoskeletal disorders with osteoporosis and osteoporotic fractures on the top, are prevalent issues that are particularly prominent in the elderly population ^[6].

Fragility fractures have been a significant global health problem that increases with time due to population aging . In 2019 Global Burdens of Diseases, injuries, and risk factors study (GBD) 2019 estimating fractures at all sites and all ages, there were a 178 million fractures in 204 nations and regions ,with the highest incidence among the elderly , every year up to 37 million fragility fractures occur in people who are 55 years and above ^[7].

Women are commonly more affected than men, with a risk of a lifetime osteoporotic fracture in women of 44% compared to 25% in men at the same age ^[8].

Fragility fractures commonest sites are the vertebrae (clinical), hip, distal radius and proximal humerus (MOF major osteoporotic fractures)^[9]. hip fractures are considered the most severe form of fractures with the highest mortality rate particularly in men^[9] with a percentage of 33% for men compared to 12-24% for women with a hip fracture die within the first year ^[10]. Hospitalization is almost always mandatory, with a high risk of disability, partial if not complete loss of function, dependency and even death ^[9].

Vertebral fractures is the most frequent presentation of osteoporosis, and usually present with back pain. Most of them, about 75%, are subclinical and can only by identified on X rays when there's a visible alteration in the shape of the vertebral body ^[1,9]. they may end with unbearable back pain, immobility, deformity of spine and even impaired pulmonary function and eventually death ^[9].

The third commonest fragility fracture among elderly population is distal radius fractures, they usually occur first then followed by a hip or vertebral fracture ^[9].

As an osteoporotic patient with a previous fragility fracture has a huge risk for a second fracture in addition to the mortality risk ; prevention and risk factors modification is the key to increase disease control and reduce subsequent complications and disabilities. Falls prevention, regular follow up with TUG (timed up and go), physical activity and exercises, and last but not least; pharmacological treatments with Bisphosphonates , calcium , vitamin D &C, RANKL inhibitors and PTH agonists supplements ^[4,10] and hormone replacement therapy for postmenopausal women ^[10].

In this study we focus on the role of bone supplements, particularly calcium, vitamin D and vitamin C in elderly fragility fractures.

Methodology

In order to investigate the role of calcium and vitamin D supplementation on the prevention of fragility fractures in the elderly, an exhaustive review of the scientific literature was undertaken, encompassing multiple electronic databases such as PubMed and Google Scholar. The preliminary investigation covered a wide timeframe, commencing in January 2000 and continuing to the present day. The search terms and keywords utilized in this procedure comprised a combination of: bone supplement, calcium, vitamin D, elderly, fragility fracture, osteoporosis, bone health.

To refine the search, Boolean operators ("AND," "OR," "NOT") were implemented. The search results were filtered by publication date, article type (e.g., clinical trials, observational studies, reviews), and relevance to the review's topic. The final assemblage of research articles adhered to the subsequent inclusion criteria: studies that specifically targeted elderly populations; studies that investigated the effects of calcium and/or vitamin D supplementation on fragility fractures or bone health; and published meta-analyses and randomized controlled trials (RCTs).

Studies were excluded if they did not specifically address bone supplements' effects on elderly fragility fractures, were not in English, were case reports, opinion pieces, or editorials without supporting empirical data, did not include interventions, not blinded or couldn't be retrieved. Following the preliminary search, the eligibility of the articles was assessed through a review of their titles and abstracts. In order to mitigate bias and maintain uniformity, the selection process was carried out by four independent reviewers.

Dr. Mohammed Mubarak Mohammed Ahmed , (2024). Role of Bone Supplement(Ca, Vit D) In Elderly Fragility Fracture. *MAR Orthopedics & Trauma (2024) 6:2*

Disagreements were resolved via deliberation and, when required, by consultation with a fifth reviewer. Data were extracted from the selected studies, focusing on the following information: Study design study population characteristics, type and dosage of bone supplements, primary and secondary outcomes related to fragility fractures, and study results and conclusions.

The extracted data were synthesized into a comprehensive narrative review, the findings were summarized and critically discussed, providing insights and recommendations for future research and clinical practice in bone health management for elderly populations.

Discussion

In recent years, the perception of osteoporosis has shifted significantly. It was once considered an inevitable part of aging, but now it is recognized as a clearly defined chronic non-communicable disease. There are established diagnostic criteria, effective risk assessment methods, and a broad array of treatment options available^[11]. The treatment of fragility fractures should be approached through a multidisciplinary clinical system^[12]. Recent guidelines emphasized on principles to manage and prevent fragile fracture coming to recommend, Exercise, balanced die, pharmacological therapies, fracture risk assessment ,monitoring and long-term follow-up^[13,14].

Patients with osteoporosis and/or fragility fractures should undergo investigation for underlying causes, including the necessity for routine blood tests ^[14,15], fragility fractures should be treated within a multidisciplinary clinical system, ensuring proper preoperative assessment and preparation of patients. This includes providing sufficient pain relief, managing fluid intake appropriately, and scheduling surgery within 48 hours of the injury. Patients should receive proper pain management as soon as possible and before beginning diagnostic tests. Using nerve blocks can help alleviate acute pain in patients with hip fractures. A comprehensive and systematic multidisciplinary assessment upon admission should evaluate the patient's medical conditions, focusing on modifiable factors such as malnutrition, electrolyte or volume imbalances, anemia, cardiac or pulmonary issues, dementia, delirium, and glycemic control. Preoperative investigations should encompass a chest X-ray, ECG, full blood count, clotting studies, blood group typing, and renal function tests, as well as cognitive baseline function assessment. This thorough approach aids in identifying and treating acute medical issues or exacerbations of chronic conditions when necessary. Prompt and safe transfer from the emergency room to an orthogeriatric ward, followed by definitive treatment including

Dr. Mohammed Mubarak Mohammed Ahmed , (2024). Role of Bone Supplement(Ca, Vit D) In Elderly Fragility Fracture. *MAR Orthopedics & Trauma (2024) 6:2*

Dr. Mohammed Mubarak Mohammed Ahmed, MAR Orthopedics & Trauma (2024) 6:2 Page 6 of 14

early surgery within 24-48 hours of admission, can greatly reduce short-term and mid-term mortality rates. It also minimizes medical complications stemming from immobility, such as pressure ulcers, pneumonia, and prolonged hospital stays. Delaying surgery to manage acute medical problems must be carefully balanced against the drawbacks of extending pain and immobility ^[12,16].

Exercise: Incorporating both regular weight-bearing and muscle-strengthening exercises is important. As engaging in balance and functional training at least twice a week to minimize the risk of falls. It is also beneficial to perform progressive resistance training twice weekly, focusing on strengthening abdominal and back extensor muscles. guidance from exercise professionals knowledgeable about osteoporosis for exercise selection, intensity, progression, and activity modification, particularly after a recent fracture or when there is a high risk of fracture ^[14,17].

Nutrition: Ensure an adequate intake of calcium through foods and water that are high in calcium. If calcium intake from meals is insufficient, consider using supplements, but only in the minimum dose needed to meet requirements. Daily vitamin D supplementation is a more natural approach, but for better adherence, weekly or monthly doses are also acceptable from a pharmacological standpoint ^[13,14,18,19].

Pharmacological treatments are categorized into antiresorptive therapy, which suppresses osteoclastic activity, and anabolic therapy, which promotes the formation of new bone. Antiresorptive treatments include bisphosphonates such as alendronate, risedronate, and zoledronic acid, as well as denosumab, raloxifene, and menopausal hormone therapy. Anabolic treatments comprise teriparatide and romosozumab.Moderate-to-high certainty was observed in the effectiveness of pharmacotherapy. Typically, bisphosphonate therapy is administered for a duration of 3 to 5 years ^[14,15,20,21,22].

Regarding vertebral fractures two currently suggested methods to stabilize or stabilize-reduce vertebral fractures are vertebroplasty and kyphoplasty. In vertebroplasty, cement is injected at high pressure, which carries a higher risk of leakage and potential pulmonary embolism. In kyphoplasty, cement is injected at a lower pressure, which lowers the risk of leakage. This procedure involves inflating a balloon within the vertebral body, often resulting in a partial reduction of the deformity ^[18].

Fracture risk assessment involves evaluating osteoporosis and fracture risks by identifying risk factors and checking for signs of undiagnosed vertebral fractures. A FRAX assessment should be conducted for any postmenopausal woman or man aged 50 years and older who has a clinical risk factor for fragility fracture. This helps guide bone mineral density (BMD) measurement, ensuring timely referral and/or appropriate

Dr. Mohammed Mubarak Mohammed Ahmed , (2024). Role of Bone Supplement(Ca, Vit D) In Elderly Fragility Fracture. *MAR Orthopedics & Trauma (2024) 6:2*

Role of Vitamin D and Calcium supplements in managing fragility fractures in the elderly:

The efficacy of vitamin D and calcium supplements in reducing the risk of osteoporotic fractures remains a controversial topic with conflicting evidence, while deficiencies of calcium and vitamin D are invariably associated with lower bone-health and an increased risk of fractures ^[25,26], the benefits of their routine use as supplements in reducing the risk of fragility fractures remains under considerable debate.

A randomized controlled trial (RCT) conducted by Trivedi, Doll and Khaw in 2003 which utilized fourmonthly 100,000 IU oral vitamin D supplements found that among people aged 65 – 85 the use of vitamin D supplements was associated with a 22% lower rate of a first fracture in general and a 33% lower rate of fractures occurring in common osteoporotic sites (vertebrae, hips, wrists and forearms) ^[27]. In contrast, Lyons et al. also conducted an RCT similarly employing four-monthly 100,000 IU oral vitamin D supplements and found no significant difference in the risk of osteoporotic fractures between the intervention and control groups ^[28], the authors postulate that the difference between their results and those of Trivedi et al. could be related to a difference in the dose or type of vitamin D used or the study population ^[28]. The same verdict of no benefit in reducing the risk of fractures by vitamin D supplementation was reached by Glendenning et al. when measuring the effects of three-monthly 150,000 IU vitamin D supplements on the risk of fractures in older postmenopausal women ^[29].

Similarly Hin et al. Conducted an RCT in 2016 that compared participants taking either 4000 IU or 2000 IU of vitamin D supplements per day to a placebo group, results showed no significant difference in the risk of fractures between the three groups ^[30]. And more similar results were reported in a recent study by LeBoff et al., it showed that a daily 2000 IU dose of vitamin D lead to no significant effect on the risk of fractures compared to the control group ^[31]. Lastly Aloia et al. conducted an RCT to determine whether maintaining a serum 25(OH)D level above 30 ng/ml had a protective effect against falls and fractures in elderly African American women, results showed that there was no benefit on the risk of falls and fractures when compared to the control group with serum 25(OH)D levels below 30 ng/ml ^[32].

A stark contrast arises when considering an RCT by Sanders et al. conducted among women aged 70 and older, results revealed that an annual single 500,000 IU oral dose of vitamin D was associated with a statistically significant 15% increase in the risk of falls and a significant 26% increase in the risk of fractures

Dr. Mohammed Mubarak Mohammed Ahmed , (2024). Role of Bone Supplement(Ca, Vit D) In Elderly Fragility Fracture. *MAR Orthopedics & Trauma (2024) 6:2*

Dr. Mohammed Mubarak Mohammed Ahmed, MAR Orthopedics & Trauma (2024) 6:2 Page 8 of 14

^[33]. However the authors speculate that this adverse outcome is likely related to the dose-regiment ^[33]. Smith et al. conducted a similar study on the effects of an annual 300,000 IU intramuscular injection of vitamin D on the risk of fractures among elderly patients, results showed the intervention to be ineffective in reducing the risk of fractures in general but there was notably a small but statistically significant increase in the risk of hip fractures in the intervention group, with the increase being more pronounced in women ^[34].

When considering the efficacy of combining Vitamin D with calcium we see a similar pattern of conflicting evidence, In a study by Robbins et al. on the value of calcium plus vitamin D supplements in reducing the risk of fractures among women taking postmenopausal hormonal therapy, results revealed that the supplements significantly reduced the risk of hip fractures among the intervention group using 1000 mg calcium carbonate plus 400 IU vitamin D along with hormonal therapy compared to the control group using only hormonal therapy ^[35]. In contrast an RCT was conducted by Jackson et al. on the efficacy of vitamin D and calcium supplements on reducing the risk of fractures in postmenopausal women aged 50 -79, results showed that while the intervention group had a 1.06% higher hip bone density, the difference on the risk of hip, spine and total fractures was not statistically significant ^[36]. Notably the study also showed that the use of calcium and Vitamin D supplements was associated with a small but statistically significant increase in the risk of renal stones ^[36]. Quite similarly a study by Grant et al. on elderly patients who already suffered a low-trauma fracture compared supplementation with vitamin D or Calcium or a combination to a placebo and found no significant difference in the risk of fractures between the groups ^[37]. The authors conclude that routine use of vitamin D and calcium supplementation as means of secondary prevention is not effective ^[37].

An RCT conducted by Porthouse et al. among elderly women where the intervention group received daily oral 1000 mg calcium combined with 800 IU vitamin D again found no benefit of supplementation in the reduction of falls or fractures ^[38]. The same result was reached by Salovaara et al. when assessing the efficacy of twice daily tablets containing 400 IU vitamin D and 500 mg calcium^[39].

On the effect of calcium monotherapy a study by Reid et al. testing the effects of 1000 mg calcium citrate on bones showed that while the intervention had beneficial effects on bone mineral density, it failed to show similar benefits on the risk of fractures and even significantly increased the risk of hip fractures ^[40]. Finally an RCT by Prince et al. conducted over 5 years among elderly women on the effects of calcium supplementation on the risk of fractures and the structure of bones showed that twice-daily 600 mg calcium carbonate tablets didn't provide a statistically significant reduction in the risk of fractures ^[41], Discussing

Dr. Mohammed Mubarak Mohammed Ahmed , (2024). Role of Bone Supplement(Ca, Vit D) In Elderly Fragility Fracture. *MAR Orthopedics & Trauma (2024) 6:2*

their results the authors note that the lack of efficacy is likely related to the lack of compliance among the intervention group ^[41], another explanation provided is that perhaps the vitamin D status in the intervention group was not sufficient for optimal utilization of calcium ^[41].

Safety of vitamin D and Calcium supplements:

Calcium supplements have been associated with an increased risk of kidney stones, constipation and various other gastrointestinal symptoms ^[41,42], and some studies even showed potential for an increase in the risk of hip fractures ^[40]. Use of calcium supplements for extended periods of time has also been associated with a significant increase in the risk of myocardial infarction ^[43].

Similarly large doses of vitamin D are associated with hypercalcemia and thus an increased risk of calciumrelated effects ^[44], Symptoms of vitamin D toxicity can range from confusion and drowsiness to psychosis and coma ^[45]. While some evidence exists on the benefit of vitamin D supplements on reducing the risk of fractures ^[27], studies using very high doses (300,000 – 500,000 IU) of vitamin D conversely reported an increased risk of fractures ^[33,34].

Conclusion:

Fragility fractures pose a significant health challenge, particularly in the aging population. The prevention and management of fragility fractures require a comprehensive approach that includes identifying and modifying risk factors such as decreased bone mass, aging, gender differences, family history, and medication use. Strategies such as falls prevention, appropriate exercise, and balanced nutrition can play a key role in mitigating the risk of fractures.

While bone supplements such as vitamin D and calcium have potential benefits, their routine use requires careful consideration due to inconsistent evidence and possible side effects as some studies suggest benefits from supplementation, others find no significant impact and even potential adverse effects. It is clear that more research is needed to establish clear guidelines and optimal dosing strategies. In the mean time, healthcare providers must approach each patient's case individually, considering their specific needs and risks. Continuous monitoring and long-term follow-up are essential to assess the effectiveness of interventions and adjust treatment plans as needed., combining preventive measures, targeted lifestyle

Dr. Mohammed Mubarak Mohammed Ahmed , (2024). Role of Bone Supplement(Ca, Vit D) In Elderly Fragility Fracture. *MAR Orthopedics & Trauma (2024) 6:2*

Dr. Mohammed Mubarak Mohammed Ahmed, *MAR Orthopedics & Trauma (2024) 6:2* Page 10 of 14 modifications, pharmacological treatment, and patient education, is crucial for effectively managing fragility fractures and improving patient outcomes.

Reference

1.Borgström F, Karlsson L, Ortsäter G, Norton N, Halbout P, Cooper C, Lorentzon M, McCloskey EV, Harvey NC, Javaid MK, Kanis JA. Fragility fractures in Europe: burden, management and opportunities. Archives of osteoporosis. 2020 Dec;15:1-21.

2. Center JR. Outcomes following osteoporotic fractures. InOsteoporosis 2013 Jan 1 (pp. 841-852). Academic Press.

3. National Institute for Health and Clinical Excellence. Osteoporosis: assessing National Institute for Health and Clinical Excellence; 2012.the risk of fragility fracture

4. Migliorini F, Giorgino R, Hildebrand F, Spiezia F, Peretti GM, Alessandri-Bonetti M, Eschweiler J, Maffulli N. Fragility fractures: risk factors and management in the elderly. Medicina. 2021 Oct 17;57(10):1119.

5. Voulgaridou G, Papadopoulou SK, Detopoulou P, Tsoumana D, Giaginis C, Kondyli FS, Lymperaki E, Pritsa A. Vitamin D and calcium in osteoporosis, and the role of bone turnover markers: A narrative review of recent data from RCTs. Diseases. 2023 Feb 8;11(1):29.

6. Veronese N, Kolk H, Maggi S. Epidemiology of fragility fractures and social impact. Orthogeriatrics: the management of older patients with fragility fractures. 2021:19-34.

7. Wu AM, Bisignano C, James SL, Abady GG, Abedi A, Abu-Gharbieh E, Alhassan RK, Alipour V, Arabloo J, Asaad M, Asmare WN. Global, regional, and national burden of bone fractures in 204 countries and territories, 1990–2019: a systematic analysis from the Global Burden of Disease Study 2019. The Lancet Healthy Longevity. 2021 Sep 1;2(9):e580-92.

8. Cawthon PM. Gender differences in osteoporosis and fractures. Clinical Orthopaedics and Related Research®. 2011 Jul 1;469(7):1900-5.

9. van Oostwaard M. Osteoporosis and the nature of fragility fracture: an overview. Fragility fracture nursing: holistic care and management of the orthogeriatric patient. 2018:1-3.

10. Zaheer S, LeBoff MS. Osteoporosis: prevention and treatment. Endotext [Internet]. 2022 Dec 27.

Dr. Mohammed Mubarak Mohammed Ahmed , (2024). Role of Bone Supplement(Ca, Vit D) In Elderly Fragility Fracture. *MAR Orthopedics & Trauma (2024) 6:2*

Dr. Mohammed Mubarak Mohammed Ahmed, MAR Orthopedics & Trauma (2024) 6:2 Page 11 of 14

11. Curtis EM, Woolford S, Holmes C, Cooper C, Harvey NC. General and Specific Considerations as to why Osteoporosis-Related Care Is Often Suboptimal. Current Osteoporosis Reports. 2020 Feb;18(1):38–46.2.Lems WF, Dreinhöfer KE, Bischoff-Ferrari H, Blauth M, Czerwinski E, da Silva J, et al. EULAR/EFORT recommendations for management of patients older than 50 years with a fragility fracture and prevention of subsequent fractures. Annals of the Rheumatic Diseases [Internet]. 2016 Dec 22 [cited 2019 Dec 16];76(5):802–10. Available from: https://ard.bmj.com/content/76/5/802

12. Lems WF, Dreinhöfer KE, Bischoff-Ferrari H, Blauth M, Czerwinski E, da Silva J, et al. EULAR/EFORT recommendations for management of patients older than 50 years with a fragility fracture and prevention of subsequent fractures. Annals of the Rheumatic Diseases [Internet]. 2016 Dec 22 [cited 2019 Dec 16];76(5):802–10. Available from: https://ard.bmj.com/content/76/5/802

13. LeBoff MS, Greenspan SL, Insogna KL, Lewiecki EM, Saag KG, Singer AJ, et al. The clinician's guide to prevention and treatment of osteoporosis. Osteoporosis International. 2022 Apr 28;33(10).

14. Gregson CL, Armstrong DJ, Bowden J, Cooper C, Edwards J, Gittoes NJL, et al. UK clinical guideline for the prevention and treatment of osteoporosis. Archives of Osteoporosis. 2022 Apr 5;17(1).

 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 [Internet]. 2014 Aug 15;25(10):2359– 81. Available from: https://cdn.nof.org/wp-content/uploads/2016/01/995.pdf

16. O'Connor MI, Switzer J. AAOS Clinical Practice Guideline Summary: Management of Hip Fractures in Older Adults. Journal of the American Academy of Orthopaedic Surgeons. 2022 Jun 17;Publish Ahead of Print.

17. Hartley GW, Roach KE, Nithman RW, Betz SR, Lindsey C, Fuchs RK, et al. Physical Therapist Management of Patients With Suspected or Confirmed Osteoporosis: A Clinical Practice Guideline From the Academy of Geriatric Physical Therapy. Journal of Geriatric Physical Therapy. 2022 Mar 11;44(2):E106–19.

18. Nuti R, Brandi ML, Checchia G, Di Munno O, Dominguez L, Falaschi P, et al. Guidelines for the management of osteoporosis and fragility fractures. Internal and Emergency Medicine. 2018 Jun 13;14(1):85–102.

19. Tomaž K, Janez P, Marija P, Mojca JS, Jensterle ČM, Andrej Z. Guidelines for the detection and treatment of osteoporosis. Slov Med J. 2013;84.

Dr. Mohammed Mubarak Mohammed Ahmed , (2024). Role of Bone Supplement(Ca, Vit D) In Elderly Fragility Fracture. *MAR Orthopedics & Trauma (2024) 6:2*

Dr. Mohammed Mubarak Mohammed Ahmed, MAR Orthopedics & Trauma (2024) 6:2 Page 12 of 14

20. Piotr Głuszko, Sewerynek E, Waldemar Misiorowski, Jerzy Konstantynowicz, Marcinowska-Suchowierska E, Tomasz Blicharski, et al. Guidelines for the diagnosis and management of osteoporosis in Poland. Update 2022. Endokrynologia Polska. 2023 Feb 27;74(1):5–15.

21. Gregson CL, Compston JE. New national osteoporosis guidance—implications for geriatricians. Age and Ageing [Internet]. 2022 Apr 1 [cited 2022 Jun 18];51(4):afac044. Available from: https://academic.oup.com/ageing/article/51/4/afac044/6565793?login=true

22. Khan AA, Alrob HA, Ali DS, Dandurand K, Wolfman W, Fortier M. Guideline No. 422g: Menopause and Osteoporosis. Journal of Obstetrics and Gynaecology Canada. 2022 May;44(5):527-536.e5.

23. Arceo-Mendoza RM, Camacho P. Prediction of Fracture Risk in Patients with Osteoporosis: A Brief Review. Women's Health. 2015 Jul;11(4):477–84.

24. Yeap SS, Hew FL, Lee JK, Goh EML, Chee W, Mumtaz M, et al. The Malaysian Clinical Guidance on the Management of Postmenopausal Osteoporosis, 2012: A Summary. International Journal of Rheumatic Diseases. 2013 Jan 24;16(1):30–40.

25. Shlisky J, Mandlik R, Askari S, Abrams S, Belizan JM, Bourassa MW, et al. Calcium deficiency worldwide: prevalence of inadequate intakes and associated health outcomes. Annals of the New York Academy of Sciences. 2022 Mar 5;1512(1).

26. Lips P, van Schoor NM. The effect of vitamin D on bone and osteoporosis. Best Practice & Research Clinical Endocrinology & Metabolism [Internet]. 2011 Aug;25(4):585–91. Available from: https://www.sciencedirect.com/science/article/abs/pii/S1521690X11000418?via%3Dihub

27. Trivedi DP, Doll R, Khaw KT. Effect of four monthly oral vitamin D3 (cholecalciferol) supplementation on fractures and mortality in men and women living in the community: randomised double blind controlled trial. BMJ (Clinical research ed) [Internet]. 2003 [cited 2019 Oct 8];326(7387):469. Available from: https://www.ncbi.nlm.nih.gov/pubmed/12609940

28. Lyons RA, Johansen A, Brophy S, Newcombe RG, Phillips CJ, B. Lervy, et al. Preventing fractures among older people living in institutional care: a pragmatic randomised double blind placebo controlled trial of vitamin D supplementation. Osteoporosis international [Internet]. 2007 Feb 15 [cited 2024 Apr 27];18(6):811–8. Available from: https://link.springer.com/article/10.1007/s00198-006-0309-5

29. Glendenning P, Zhu K, Inderjeeth C, Howat P, Lewis JR, Prince RL. Effects of three-monthly oral

Dr. Mohammed Mubarak Mohammed Ahmed , (2024). Role of Bone Supplement(Ca, Vit D) In Elderly Fragility Fracture. *MAR Orthopedics & Trauma (2024) 6:2*

Dr. Mohammed Mubarak Mohammed Ahmed, MAR Orthopedics & Trauma (2024) 6:2 Page 13 of 14

150,000 IU cholecalciferol supplementation on falls, mobility, and muscle strength in older postmenopausal women: A randomized controlled trial. Journal of Bone and Mineral Research. 2011 Dec 22;27(1):170–6.

30. Hin H, Tomson J, Newman CE, Kurien R, Lay M, Cox JD, et al. Optimum dose of vitamin D for disease prevention in older people: BEST-D trial of vitamin D in primary care. 2016 Dec 16;28(3):841–51.

31. LeBoff MS, Chou SH, Ratliff KA, Cook NR, Khurana B, Kim E, et al. Supplemental Vitamin D and Incident Fractures in Midlife and Older Adults. New England journal of medicine/The New England journal of medicine [Internet]. 2022 Jul 28 [cited 2024 Apr 27];387(4):299–309. Available from: https://pubmed.ncbi.nlm.nih.gov/35939577/

32. Aloia JF, Rubinova R, Fazzari M, Islam S, Mikhail M, Ragolia L. Vitamin D and Falls in Older African American Women: The PODA Randomized Clinical Trial. Journal of the American Geriatrics Society. 2019 Jan 30;67(5):1043–9.

33. Sanders KM, Stuart AL, Williamson EJ, Simpson JA, Kotowicz MA, Young D, et al. Annual High-Dose Oral Vitamin D and Falls and Fractures in Older Women. JAMA [Internet]. 2010 May 12 [cited 2024 Apr 27];303(18):1815–5. Available from: https://pubmed.ncbi.nlm.nih.gov/20460620/

34. Smith H, Anderson F, Raphael H, Maslin P, Crozier S, Cooper C. Effect of annual intramuscular vitamin D on fracture risk in elderly men and women a population-based, randomized, double-blind, placebocontrolled trial. Rheumatology [Internet]. 2007 Aug 5 [cited 2024 Apr 27];46(12):1852–7. Available from: https://pubmed.ncbi.nlm.nih.gov/17998225/

35. Robbins JA, Aragaki A, Crandall CJ, Manson JE, Carbone L, Jackson R, et al. Women's Health Initiative clinical trials: interaction of calcium and vitamin D with hormone therapy. Menopause. Menopause. 2014 Feb;21(2):116–23.

36. Jackson RD, LaCroix AZ, Gass M, Wallace RB, Robbins J, Lewis CE, et al. Calcium plus Vitamin D Supplementation and the Risk of Fractures. New England Journal of Medicine. 2006 Feb 16;354(7):669– 83.

37. Grant AM, Avenell A, Campbell MK, et al. Oral vitamin D3 and calcium for secondary prevention of low-trauma fractures in elderly people (Randomised Evaluation of Calcium Or vitamin D, RECORD): a randomised placebo-controlled trial. Lancet [Internet]. 2005 May 1 [cited 2024 Apr 27];365(9471):1621–8. Available from: https://pubmed.ncbi.nlm.nih.gov/15885294/

Dr. Mohammed Mubarak Mohammed Ahmed , (2024). Role of Bone Supplement(Ca, Vit D) In Elderly Fragility Fracture. *MAR Orthopedics & Trauma (2024) 6:2*

Dr. Mohammed Mubarak Mohammed Ahmed, MAR Orthopedics & Trauma (2024) 6:2 Page 14 of 14

38. Porthouse J, Cockayne S, King C, Saxon L, Steele E, Aspray T, et al. Randomised controlled trial of calcium and supplementation with cholecalciferol (vitamin D 3) for prevention of fractures in primary care. BMJ British medical journal [Internet]. 2005 Apr 28 [cited 2024 Apr 27];330(7498):1003–3. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC557150/

39. Salovaara K, Tuppurainen M, Kärkkäinen M, Rikkonen T, Sandini L, Sirola J, et al. Effect of vitamin D3 and calcium on fracture risk in 65- to 71-year-old women: A population-based 3-year randomized, controlled trial-the OSTPRE-FPS. Journal of Bone and Mineral Research [Internet]. 2010 Jan 29 [cited 2020 Jan 16];25(7):1487–95. Available from: https://onlinelibrary.wiley.com/doi/full/10.1002/jbmr.48

40. Reid IR, Mason B, Horne A, Ames R, Reid HE, Bava U, et al. Randomized controlled trial of calcium in healthy older women. The American Journal of Medicine [Internet]. 2006 Sep 1;119(9):777–85. Available from: https://pubmed.ncbi.nlm.nih.gov/16945613/

41. Prince RL, Devine A, Dhaliwal SS, Dick IM. Effects of Calcium Supplementation on Clinical Fracture and Bone Structure. Archives of Internal Medicine. 2006 Apr 24;166(8):869.

42. Reid IR, Bolland MJ. Controversies in medicine: the role of calcium and vitamin D supplements in adults. Medical Journal of Australia [Internet]. 2019 Nov;211(10):468–73. Available from: https://www.mja.com.au/system/files/issues/211_10/mja250393.pdf

43. Reid IR, Bristow SM, Bolland MJ. Cardiovascular Complications of Calcium Supplements. Journal of Cellular Biochemistry. 2015 Jan 29;116(4):494–501.

44. Malihi Z, Wu Z, Lawes CMM, Scragg R. Adverse events from large dose vitamin D supplementation taken for one year or longer. The Journal of Steroid Biochemistry and Molecular Biology [Internet]. 2019 Apr 1;188:29–37. Available from: https://pubmed.ncbi.nlm.nih.gov/30529281/

45. Marcinowska-Suchowierska E, Kupisz-Urbańska M, Łukaszkiewicz J, Płudowski P, Jones G. Vitamin D Toxicity–A Clinical Perspective. Frontiers in Endocrinology [Internet]. 2018 Sep 20;9(550). Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6158375/.

