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COMMENTARY

Executive Summary: Treatment of Osteoporosis and Osteoarthritis in the Oldest Old

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Abstract
This is the executive summary of a work by the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases (ESCEO) (Nicholas Fuggle et al. in Drugs, 2024).

Key Points

1. Anti-resorptive and bone-forming agents effectively manage osteoporosis in the oldest old.
2. Cost-effectiveness studies highlight that osteoporosis drugs reduce fractures and expenses.
3. Further studies assessing safety and efficacy of new chemical entities aimed at the management of musculoskeletal disorders should include enough older patients who, until now, have been dramatically under-represented in previous trials.

1 Pharmacological Interventions

1.1 Osteoporosis Treatments

The principal pharmacological interventions for osteoporosis in the oldest old are primarily antiresorptive medications and bone-forming agents [1]. Bisphosphonates, such as alendronate and zoledronate, are anti-resorptive drugs commonly prescribed to reduce bone loss and prevent fractures [2]. Denosumab, as observed in the trial leading to its use, i.e. the FREEDOM trial [3] that included a significant proportion of older people and showed an important reduction in the risk of vertebral fracture, is commonly used in real practice, particularly in the primary care setting and often without the knowledge of potential rebound bone loss and fracture upon discontinuation [4].

While they are effective in reducing the risk of vertebral and hip fractures in younger seniors, their safety profile in the oldest old is less certain owing to potential side effects, including gastrointestinal and renal complications [5]. Bone-forming agents, such as teriparatide and abaloparatide, stimulate new bone formation and are considered for patients with severe osteoporosis [6]. Romosozumab, an antisclerostin antibody, has shown promising results in reducing fracture risk, similar to that of parathyroid hormone (PTH) analogues, but poses a potentially higher risk of cardiovascular events, necessitating careful selection and monitoring, particularly in this age group, which is at increased cardiovascular risk [7].

The members of the ESCEO Working Group are mentioned in Acknowledgments section.

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1.2 Osteoarthritis Treatments

Management of osteoarthritis in the oldest old typically includes a combination of symptomatic slow-acting drugs for osteoarthritis (SYSADOAs), paracetamol and NSAIDs [8]. SYSADOAs, such as prescription glucosamine and chondroitin, are included in some guidelines, providing pain relief and improving joint function with minimal adverse effects [8]. In contrast, NSAIDs, though effective for short-term pain relief, carry serious risks for gastrointestinal, renal and cardiovascular complications, particularly in the oldest old [9]. Consequently, clinicians often face challenges in balancing the need for pain relief with the heightened risk of adverse events in this demographic, highlighting the need for more research focused on the safety of these drugs in older populations.

At the same time, it is important to observe that for both osteoporosis and osteoarthritis, the number of older people included in the intervention studies made thus far is extremely limited.

2 Non-pharmacological Interventions

2.1 Exercise and Physical Therapy

Physical activity remains a cornerstone of osteoarthritis and osteoporosis management, offering multiple benefits beyond joint health, including improved balance, muscle strength, and mental wellbeing [10]. Exercise regimens for the oldest old are often tailored to address common age-related limitations, such as reduced balance and muscular strength. Resistance training, for instance, can improve muscle mass and reduce the risk of falls, while balance exercises, such as tai chi, have been shown to decrease fall risk and improve functional mobility [11]. Despite these benefits, many older adults face barriers to regular exercise, including physical limitations and a lack of access to structured programs. Multidisciplinary approaches involving physical therapists can help personalise exercise plans to overcome these barriers.

2.2 Nutritional Support

Nutrition plays a critical role in the management of both osteoporosis and osteoarthritis, particularly in the oldest old, who may face challenges in maintaining adequate nutrient intake [12]. Calcium and vitamin D are essential for bone health, and protein is vital for muscle maintenance, which can prevent frailty and reduce falls risk. Emerging evidence suggests that diets rich in anti-inflammatory foods, such as the Mediterranean diet, may offer benefits for joint health and pain reduction in patients with osteoarthritis [13]. However, these findings require further validation in the oldest old, and dietary recommendations must be personalised to address the nutritional deficiencies commonly observed in this age group.

3 Health Economics

Osteoporotic fractures, particularly hip fractures, are associated with significant healthcare expenses, including surgical treatment, rehabilitation and in some cases, long-term care or loss of independence [14]. Given the high incidence of fractures in the oldest old, cost-effectiveness studies generally support the use of osteoporosis medications, as these treatments often prevent costly fractures and reduce overall healthcare spending.

Osteoarthritis management in older adults, including pharmacological and non-pharmacological interventions, has been found to be cost-effective, although studies specific to the demographic aged $\geq$ 80 years are limited. Expanding these analyses to include the oldest old will better inform resource allocation and ensure that interventions are economically sustainable as the aging population grows [15].

4 Conclusions

While osteoporosis and osteoarthritis are highly prevalent among the oldest old, clinical guidelines for managing these conditions in this population are often extrapolated from studies involving younger cohorts or from post hoc subgroup analyses of pivotal trials. The Working Group indicates that further studies assessing safety and efficacy of new chemical entities aimed at the management of musculoskeletal disorders should include a sufficient number of older patients who, until now, have been dramatically under-represented in previous trials. Physiological changes, such as altered pharmacokinetics and higher rates of multimorbidity, require age-specific considerations for treatment safety and efficacy. The limited inclusion of individuals over 80 years old in clinical trials necessitates a reliance on real-world data, but these data are often insufficient to support comprehensive guidelines. To address this evidence gap, there is an urgent need for research that specifically evaluates the risks, benefits, and cost-effectiveness of interventions for osteoporosis and osteoarthritis in the oldest old. Addressing these needs can improve patient outcomes, reduce healthcare costs, and enhance quality of life for this growing population, aligning clinical care with the realities of aging.

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