Open Access

SCHOLARENA

Journal of Orthopaedics and Bone Research

REVIEW ARTICLE

ISSN: 2643-9956

Musculoskeletal Symptoms in Menopause

Amelia Dickinson, Laura Casey, Aishwarya Ghosh and Shamim Umarji*

St George's University Hospitals NHS Foundation Trust, London, United Kingdom

***Corresponding Author:** Shamim Umarji, St George's University Hospitals NHS Foundation Trust, London, United Kingdom, E-mail: s.umarji@nhs.net

Citation: Amelia Dickinson, Laura Casey, Aishwarya Ghosh and Shamim Umarji (2024) Musculoskeletal Symptoms in the Menopause, J Orthop Bone Res 5: 103

Introduction

Women represent 51% of the population, yet there is a gap in knowledge regarding musculoskeletal symptoms and how they affect menopausal women. Menopausal (and perimenopausal) women will present to healthcare professionals with symptoms of aching and painful joints, as well as the other more familiar menopausal symptoms. There are no specific guidelines on the musculoskeletal care of menopausal women. This gap presents an opportunity to improve overall musculoskeletal health of women, and in turn have a positive impact on society given the important roles fulfilled by women in the workforce, as well as being caregivers for families and in communities. The aim of this paper is to consider how musculoskeletal symptoms impact perimenopausal and menopausal women, covering prevalence, risk factors, physiological mechanisms and management strategies.

Menopause is a natural biological process that marks the end of reproductive years in women and is accompanied by numerous physiological changes [1]. While it is commonly associated with symptoms such as hot flushes, night sweats and mood changes, musculoskeletal symptoms are often overlooked despite being experienced by more than 50% of menopausal women globally [2]. The aim of this literature review is to explore the musculoskeletal symptoms women experience during menopause and to gain a better understanding of these physiological mechanisms. Furthermore, we aim to provide some guidance for healthcare professionals on musculoskeletal manifestations in menopause and when clinically, further treatment or investigation is required.

Musculoskeletal Presentations of the Menopause

Arthralgia and arthritis

It is likely that hormonal changes around the menopause modulate disease and can act as triggers for the development of certain conditions. 50% of menopausal women will experience arthralgia or arthritis. The group of symptoms affecting joints and tendons have been linked to the decline in sex hormones. Joint synovium and cartilage interaction with oestrogen is well documented.- Menopause is associated with a higher prevalence of joint pain and stiffness in the knee, hand, shoulder and back [3,4,5] with a systematic review in 2020 reporting a linear increase in incidence from premenopausal to the peri- and postmenopausal periods [6].

Identifying causes of joint pain or arthralgia can be difficult to ascertain in this age as it coincides with other pathological processes such as osteoarthritis. There is mounting evidence that the systemic decline of circulating sex hormones (oestrogen and progesterone) in menopause significantly impacts established pain processing pathways as well as immune cell and chondrocyte activity, resulting in arthralgia and associated symptoms [7].

Women of menopausal age are twice as likely as men to suffer painful osteoarthritic hands resulting in pain and dysfunction. There remains an unmet need for effective drug therapy for pain or disease modification. There is growing interest in the hypothesis that addressing oestrogen deficiency with HRT could improve or prevent hand osteoarthritis [8]

Carpal Tunnel Syndrome

It is important to diagnose and exclude readily treatable conditions like nerve entrapments, tendinopathies, degenerative joints etc. A good example is carpal tunnel syndrome (CTS). Carpal Tunnel syndrome is one of the commonest nerve entrapment disorders affecting the hand characterised by symptoms of numbness, tingling, pain and dysfunction. CTS affects more women than men (especially those aged 45-54), and can be caused by a variety of factors but the hormonal fluctuations associated with the perimenopause and menopause can put women at greater risk of developing the condition. The relationship between CTS and menopause is not well understood. There is some evidence that Hormone Replacement Therapy (HRT) improves symptoms of CTS although this requires further research [9].

Osteoporosis

Osteoporosis is a systemic skeletal disease characterized by low bone mineral density or BMD (defined by WHO criteria as a T-score less or equal to 2.5 and micro-architectural deterioration of bone tissue resulting in fragility fractures [10]. Whilst bone mineral density declines with age, the fall in oestrogen during menopause removes an inhibitory effect on osteoclasts, resulting in greater bone resorption than formation and accelerating the rate of osteoporosis development. During the menopausal transition period, the average reduction in BMD is about 10% with approximately half of affected women losing as much as 20% in the perimenopause period. The National Osteoporosis Foundation [11], estimates that menopausal women are 3 times more likely to have osteoporosis when compared to men and have a lifetime risk of fractures twice that of a man the same age [12].

Other contributing risk factors for osteoporosis include low body mass index, parental history of hip fracture, smoking, alcohol intake, oral glucocorticoid therapy rheumatoid arthritis and diabetes mellitus (both types I and II). There are also secondary causes of inflammatory bowel disease and endocrine disorders [10]

The greatest risk associated with osteoporosis is osteoporotic fractures, most commonly in the spine, the hip, or the distal radius. Osteoporotic fractures can begin in the perimenopause period with the first peak of fragility fractures being fractures of the distal radius starting at age 50 years, followed by vertebral fractures at age 60–75 years and hip fractures beginning in the late 70s. [13] Not only do these fractures impact on a patient's quality of life, they also accrue large financial costs to any health service, accounting for 2.4% of annual healthcare spending in the UK [10]. Therefore, awareness and subsequent prevention of osteoporosis and associated fragility fractures is key to reducing its global financial and social burden. The British Orthopaedic Association has published guidance regarding Fracture Liaison Services (FLS) which provide secondary prevention for fragility fractures (defined as a low energy fracture sustained from a standing height) [14]. A patient presenting with one fragility fracture (eg wrist fracture) is at high risk of sustaining a secondary fragility fracture (eg hip fracture) in the first 2 years after the initial injury. Therefore, there is an opportunity to prevent the latter by ensuring bone health is optimised (checking bone, hormonal blood profiles, DEXA scanning, treatment of osteoporosis and osteopenia, lifestyle changes, possible Hormone Replacement Therapy, smoking cessation, reduction in alcohol and exercise)

Sarcopenia

Sarcopenia is the progressive and generalised age-related loss of skeletal muscle mass. Its progression can be influenced by both genetic and lifestyle risk factors. For the diagnosis of sarcopenia, the European Working Group on Sarcopenia for Older People (EWGSOP) recommends using the presence of both low muscle mass and low muscle function (strength or performance) [15]. A recent study highlighted that the muscle degeneration during the menopause transition is due to decreased proliferation of muscle

satellite cells, increased inflammatory markers and altered sex hormones. In particular this has been linked to a change in oestrogen levels. Oestrogen is known to stimulate satellite cell proliferation, thus when oestrogen levels decrease throughout the menopause there is a reduction in satellite proliferation, and therefore decreased muscle mass [16]. Muscle loss has been estimated between 1-2% in women after the age of 50 years. A recent study from the Korean National Health and Nutrition Examination Surveys 2009-2011 reviewed data of approximately 30,000 individuals, in postmenopausal women looking at the prevalence of sarcopenia, obesity, and sarcopenic obesity with radiographic knee osteoarthritis (OA). They categorized participants into four groups based on body composition: either sarcopenic (appendicular skeletal muscle < 23%) or not, either obese (body mass index ≥ 25.0 kg/m2) or not. The results conveyed there was a higher incidence of osteoarthritis in patients with sarcopenia with coexistence of obesity [17]. Furthermore, a study looking at the same data highlighted how postmenopausal women with sarcopenia (low muscle mass) had a higher incidence of fractures at various sites when compared to postmenopausal women without low muscle mass (relative risk [RR], 1.64; odds ratio [OR], 1.62; 95% confidence interval [CI], 1.06-2.48; P = 0.027) [18]. Moreover, oestrogen regulates the function of muscle fibres by binding to E2-specific receptors, thereby directly regulating muscle metabolism [19]. Overall, muscle weight and strength decrease in menopausal women, and it has been elicited that a reduction in oestrogen and its receptors can cause muscle loss and muscle atrophy [20]. Maintaining skeletal muscle function is important for health and longevity. Therefore, based on the beneficial effects of oestrogen on skeletal muscle, it is important to consider the role of oestrogen in sarcopenia and in menopausal women.

Summary of Physiological Musculoskeletal changes in Menopause

Bone Loss

Oestrogen plays a crucial role in maintaining bone health mostly by inhibiting osteoclasts and promoting osteoblasts. However, during menopause, oestrogen levels decline, resulting in increased bone resorption relative to bone formation. Resulting in conditions such as osteoporosis as already discussed [21].

Connective Tissue Changes

Oestrogen has multiple effects on connective tissue. Firstly, it stimulates the synthesis of collagen by binding to fibroblasts and activates transcription factors that lead to increased collagen production. Oestrogen also inhibits the matrix metalloproteinases (MMPs) which break down collagen, and it also inhibits the production of tissue inhibitors of metalloproteinases (TIMPs), which further protect collagen from degradation. This balance between MMPs and TIMPs helps maintain the integrity and strength of connective tissue which is lost during/after menopause. Oestrogen also influences angiogenesis which is essential for connective tissue repair and maintenance. Oestrogen does this by promoting VEGF and stimulating endothelial cell proliferation. Furthermore, oestrogen is protective against cell apoptosis and senescence by suppressing apoptotic pathway thus preserving connective tissue cells [22, 23].

Muscle Mass and Strength

Although with aging it is known that muscle mass and strength will decrease, menopause can further exacerbate this due to the hormonal physiological changes. A recent study revealed that oestrogen deficiency (secondary to menopause) alters the microRNA signalling (regulates key steps in cell death pathway) in skeletal muscle which can activate the signalling cascades leading to loss of muscle mass and therefore strength [24].

Metabolic Changes

Menopause is associated with changes in adipose tissue as well as altered lipid profile and the onset of insulin resistance, studies have highlighted this is due to a shift from predominantly oestrogenic state to an androgenic state due to increased levels of bioa-

vailable testosterone in menopause [25]. Increased testosterone levels can induce fat accumulation in the preadipocytes of visceral fat [26]. These metabolic changes in menopause significantly increase the risk of cardiometabolic diseases, such as obesity, type 2 diabetes, cardiovascular diseases, non-alcoholic liver disease /metabolic associated fatty liver disease, and metabolic syndrome [27, 28, 29]. The increase in adipose tissue secondary to these metabolic changes can also lead to an increase in body fat and fat redistribution. Excess body weight can increase the mechanical load on the musculoskeletal system furthermore leading to joint stress and musculoskeletal symptoms [30].

Inflammatory Changes

Oestrogen has multiple anti-inflammatory effects that help regulate our immune system therefore when it declines during menopause it can lead to an increased inflammatory response. Oestrogen reduces the production of cytokines such as tumour necrosis factor-alpha (TNF-α), interleukin-1 beta (IL-1β), and interleukin-6 (IL-6). Oestrogen also enhances the production of anti-inflammatory cytokines like interleukin-10 (IL-10) [31]. Thus, the decline in oestrogen levels during menopause can lead to an imbalance in the immune response, promoting inflammation. As discussed above menopause is associated with increase in weight and adipose tissue. During menopause, the decrease in oestrogen can disrupt this balance, leading to increased secretion of pro-inflammatory adipokines and promoting inflammation [32]. Oestrogen also scavenges free radicals and inhibits the production of reactive oxygen species (ROS). Therefore, when oestrogen levels decline during menopause, there is a decrease in the antioxidant capacity, which can lead to increased oxidative stress and overall inflammation [33].

Summary of Risk factors and Associations

Weight

Increased weight leads to higher stress on joints, particularly weight-bearing joints such as knees and hips leading to joint pain and stiffness. During menopause the increase in adipose tissue can also lead to inflammation that can contribute to MSK symptoms [34].

Age

Menopause typically occurs in women around the age of 50. Menopause is related to a decline in bone density and muscle mass as discussed above, increasing the risk of musculoskeletal symptoms such as osteoporosis [35].

Previous musculoskeletal conditions

Patients who suffer from conditions such as osteoarthritis, osteoporosis, fibromyalgia, carpal tunnel syndrome, TMJ, muscular tension and myofascial pain are at higher risk of developing musculoskeletal conditions during menopause. This is mostly due to the hormonal changes exacerbating already present conditions due to the physiological changes such as above [36].

Lifestyle factors

Leading a sedentary lifestyle can result in a lack of physical activity and prolonged periods of inactivity furthermore resulting in muscle weakness, joint stiffness, and decreased bone density. Regular exercise and physical activity can help maintain musculoskeletal health. Other lifestyle factors such as smoking, drinking alcohol (both associated with decreased bone density and increased risk of fractures) and nutritional deficiencies (such as inadequate intake of vitamin D and calcium) are also factors associated with increased musculoskeletal symptoms in menopause [37,38].

Risk factors are subject to significant geographical variation within the United Kingdom. For example, the prevalence of smoking ranges from 1.8% in Kensington to 21.4% in Blackpool [39]

Genetic factors

Genetic predispositions to osteoporosis (studies on osteoporosis demonstrated that genetic factors are responsible for about 60–85% of variability of bone mineral density), osteoarthritis, connective tissue disorders and genetic variability in hormone metabolism like oestrogen are all associated with increased musculoskeletal symptoms in menopause [40].

Combining risk factors including some of the characteristics discussed above affecting women from different ethnicities or races, there will be some aggregative effects. For example, post-menopausal white and South Asian women are at particular risk of osteoporosis though highest fragility fracture rates are found in white women. Management strategies for bone health should consider all risk factors, and their aggregative effects.

Ethnic Differences in Menopause

Incidence and prevalence of symptoms vary across ethnicities, geographic locations and individual characteristics [1]. The United Kingdom is a multi-ethnic society and in 2018, 13.8 % of the UK population had an ethnic minority background [41].

Menopause can manifest differently in certain ethnic minority groups. For example, the mean age of menopause in Afro--Caribbean women is 49.6 years with a longer menopause transition [42]. South-East Asian (Chinese and Japanese) women may not complain of severe vasomotor symptoms, and they have lower bone mineral density but are still a lower risk of osteoporotic fractures compared to Caucasian women. Women living in South Asian countries (India, Pakistan) have an earlier menopause at a mean age of 46.7 years [43]. compared to women in Western countries (average age 51 years). This can increase the risk of long-term conditions like cardiovascular disease or osteoporosis.

A survey of 734 women in China between the ages of 35 and 64 showed a significantly higher prevalence of musculoskeletal symptoms in postmenopausal women compared to premenopausal women with a peak in prevalence at early post-menopause [3]. This is evidenced in a prospective longitudinal study conducted by the Melbourne Women's Mid-life Health Project, who found that postmenopausal women were more than twice as likely to experience aches and stiff joints when compared to the premenopausal group [4]. These results continue to reverberate internationally with a Japanese study of 1,969 women found to have moderate and severe joint pain most frequently at perimenopause (36.4%), followed by early post-menopause (33.9%), late post-menopause (31.2%) and least likely in pre-menopause (25%). They also found a significant association between increasing severity of joint pain with estradiol levels less than 25 and FSH greater than 40 [5].

The menopause transition in ethnic minorities is poorly understood and there is a gap in service provision. The influence of race, culture and ethnicity on attitudes towards menopause and treatment are complex and there is opportunity to address this health inequality.

Management

Joint Pain and Stiffness

Hormone replacement therapy (HRT) is the most widely used treatment for menopause related vasomotor symptoms however the evidence is currently limited on its effectiveness for menopause related musculoskeletal symptoms. Evidence from one of the Women's Health Initiative (WHI) largest randomised control trials (RCT), found that a statistically significant 47% of women receiving combined oestrogen and progesterone, reported improved joint pain and stiffness when compared to 38% in the placebo group. Moreover, those treated with HRT had a lower incidence of new joint pain or stiffness and general or lower back pain and aches [44].

Although, the majority of reported studies demonstrate the beneficial effects of hormone replacement on arthralgia, there are concerns of symptom resurgence on withdrawal or cessation of HRT. There is emerging evidence that musculoskeletal symptoms could be associated with a lack of natural ovarian hormone production following a period of HRT use. In another large Women's Health Initiative cross sectional survey, those who stopped HRT were twice as likely than the control group to report pain or stiffness symptoms at 8-12 months following cessation (adjusted odds ratio [AOR], 2.16; 95% confidence interval [CI], 1.95-2.40) [45]. Brunner et al [46] also found that postmenopausal women who were treated with Conjugated Equine Oestrogens (CEE) had a 5% lower rate of joint pain/stiffness than with placebo but significantly more women in the CEE group (5.4%) compared to the placebo group, reported joint pain/stiffness after stopping treatment.

Therefore, given that HRT may potentially improve but also exacerbate MSK symptoms, it is important to consider and promote conservative measures to alleviate pain using simple analgesia, physical therapy and weight loss [7].

Osteoporosis

The aim of primary prevention is to identify those at risk of and subsequently prevent, osteoporotic fragility fractures. Strategies for primary prevention include reducing modifiable risk factors through dietary and lifestyle changes, and the use of pharmacologic therapy for patients at significant risk of osteoporosis or fracture. The National Osteoporosis Guideline Group (NOGG) advises that a FRAX assessment should be performed in any postmenopausal woman, or man age ≥ 50 years, with a clinical risk factor for fragility fracture, to guide Bone Mineral Density measurement and prompt timely referral and/or drug treatment [10].

Secondary prevention of osteoporotic fragility fractures involves identifying those patients who had fragility fractures and commencing measures to prevent further fragility fractures. The British Orthopaedic Association in its BOAST guidelines states that a Fracture Liaison Service should be available to all hospitals that provide definitive fracture care and should conduct a multifactorial bone health assessment within 3 months of the incident fracture [47].

Pharmacological management options for the prevention of osteoporotic fragility fractures include oral bisphosphonate therapy (the recommended first line agent by the Royal Osteoporosis Society in its Clinical Standards for Fracture Liaison Services), injectable osteoporosis treatments such as intravenous bisphosphonates and denosumab, as well as supplementary Calcium and Vitamin D. They also recommend falls prevention strategies which are of particular importance in the time between commencement of pharmacological treatment and the onset of reduction in fracture risk which can be up to 18 months [48]. There is evidence that whilst HRT reduces the risk of fragility fracture when it is taken the benefit decreases once treatment stops although it may continue for longer in women who take HRT for longer [49].

Table 1: Optimising Musculoskeletal health during the menopause – joining up care

Objective	Areas of focus	Management
Arthralgia, arthritis	Diagnose & Treat concomitant conditions (generalised arthralgia)	Treat Carpal tunnel syndrome, Arthritis, Tendonitis etc as per usual guidancePhysiotherapy
Managing bone health and sarcopenia Prevention of future fragility fractures	Lifestyle changesOptimising Bone Health	Weight lossCessation of smokingExercise inc weight bearingDietary advice inc reduction of alcohol intakeBone profile inc calcium, phosphate, vitamin DHormonal profile inc sex hormones (oestrogen, testosterone) -possible role for HRT
	Imaging (for suspected osteoporosis)	DEXA scanning
Collaboration	Orthopaedic. service	Primary careWomen's Health (?role for HRT)RheumatologistsFracture Liaison Service

Sarcopenia

There are several measures that can be used to help attenuate the risk of developing sarcopenia during the menopause, one of which is improving nutrition. Given that sarcopenia describes a loss of musculature, an important way to maintain and regulate muscle homeostasis is to ensure a healthy volume of protein is present in the diet. Several studies in a recent literature review demonstrate that simply achieving the target recommended daily allowance of protein (usually 0.8-1gr/kg/day) is superior to consuming moderately higher protein, when aiming to maintain lean body mass and muscle strength in postmenopausal women [20]. Furthermore, low vitamin D is highly prevalent in menopause, contributing to a loss of muscle mass and strength and its correction has been associated with a positive effect on muscular mass, particularly in the sarcopenic, obese postmenopausal woman [50]. Finally, a mediterranean diet (rich in Omega-3 polyunsaturated fatty acids or PUFA) has found to be particularly beneficial in addressing oxidative stress, inflammation and insulin resistance that is observed in menopause and hence helps to reduce the extent and rate of muscle catabolism [51].

During the menopausal transition, there is a decline in energy use often due to decrease in physical activity which in turn increases the risk of adiposity and increased body weight which combined contributes to development of sarcopenia. Promotion of an active lifestyle is therefore essential in this group in maintaining muscle mass and strength with studies demonstrating that combination of endurance, strength and balance is key to achieving this [52]

Current literature finds that hormone replacement therapy (HRT) may improve skeletal muscle mass and strength by maintaining regulation of oestrogen receptors on myosin [20]. However, the caveats to its use include factors such as low dosage and increased level of physical activity in the postmenopausal woman, when the effects of hormone replacement therapy appear minimal. The European Menopause and Andropause Society (EMAS) instead suggest using natural hormonal management (such as soy protein and isoflavones) for those who cannot take or tolerate HRT, in preventing osteo-sarcopenia and obesity in post-menopausal groups [53].

Conclusions and Recommendations

Musculoskeletal diseases prevalent in the women can seriously compromise quality of life and their functionality. This review highlights how musculoskeletal symptoms can manifest in menopause. Increasing awareness, as healthcare professionals, can help reduce and improve musculoskeletal symptoms in this cohort of patients. An understanding of the symptoms, risk factors and physiological changes associated with musculoskeletal symptoms in menopause, earlier detection and healthcare intervention can have a positive impact on affected patients. As clinicians, simply being cognisant of musculoskeletal symptoms in the menopause as well as having an awareness of the multiple strategies used to help aid management. Firstly, by focussing on modifiable lifestyle risk factors, such as educating patients on healthy nutrition (encouraging protein and calcium rich foods as well as taking vitamin D supplements), promoting regular aerobic and resistance exercise, recommending smoking cessation and reducing excessive alcohol intake. Secondly, by focusing on ways we can improve oestrogen deficiency. Although HRT is not considered a universal treatment for all menopausal patients with musculoskeletal symptoms, it is important that suitable women are offered it. This can be done by referring patients in primary care or women's health centres for further investigation and care. Other medical pharmaceutical treatments such as selective oestrogen receptor modulators (SERMs), bisphosphonates and calcitonin may also be offered if deemed appropriate [54].

When women present with musculoskeletal symptoms it is important that a holistic approach is considered. There is an opportunity to optimise bone health (bone profile blood tests, measurement of oestradiol and testosterone levels, DEXA scanning, lifestyle and dietary advice etc), manage generalised musculoskeletal symptoms and prevent future fragility fractures. This is particularly important in patients with particular combinations of risk factors including racial and ethnicity related effects.

Improved awareness and collaborating with healthcare partners in primary care as well as women's health experts will provide women with more holistic and equitable healthcare. Addressing musculoskeletal health for menopausal (and perimenopausal). women should be a key component of global women's health strategy.

Conflict of Interest

The authors declare no conflict of interest.

References

1. Monteleone P, Mascagni G, Giannini A, Genazzani AR, Simoncini T (2018) Symptoms of menopause - global prevalence, physiology and implications. Nat Rev Endocrinol. 14: 199-215.

2. Watt FE (2018) Musculoskeletal pain and menopause. Post Reproductive Health. 24: 34-43.

3. Gao HL, Lin SQ, Wei Y, Chen Y, Wu ZL (2018) The effect of age and menopausal status on musculoskeletal symptoms in Chinese women aged 35-64 years. Climacteric. 16: 639-45.

4. Szoeke, C E I et al. (2006) Factors affecting the prevalence of osteoarthritis in healthy middle-aged women: data from the longitudinal Melbourne Women's Midlife Health Project. Bone. 29: 1149-55.

5. Yokota, Megumi et al. (2016) Symptoms and effects of physical factors in Japanese middle-aged women. Menopause. 23: 974-83.

6. Lu CB, Liu PF, Zhou YS, Meng FC, Qiao TY et al. (2020) Musculoskeletal Pain during the Menopausal Transition: A Systematic Review and Meta-Analysis. Neural Plast. 2020: 8842110.

7. Magliano M (2010) Menopausal arthralgia: Fact or fiction. Maturitas, 67: 29-33.

8. Watt FE et al. (2022) Hormone Replacement Therapy (conjugated oestrogens plus bazedoxifene) for post-menopausal women with symptomatic hand osteoarthritis: primary report from the HOPE-e randomised, placebo-controlled feasibility study. Lancet Rheumatol. 4: e725-e7.

9. Hall GM, Spector TD, Studd JW (1992) BMJ, 304: 382.

10. Gregson CL, Armstrong DJ, Bowden J, Cooper C, Edwards J (2002) UK clinical guideline for the prevention and treatment of osteoporosis. Arch Osteoporos. 17: 58.

11. Nguyen ND, Ahlborg HG, Center JR, Eisman JA, Nguyen TV (2007) Residual lifetime risk of fractures in women and men. J Bone Miner Res. 22: 781-8.

12. Cawthon PM (2011) Gender differences in osteoporosis and fractures. Clin Orthop Relat Res. 469: 1900–5.

13. Ji MX, Yu Q (2015) Primary osteoporosis in postmenopausal women. Chronic Dis Transl Med. 1: 9-13.

14. British Orthopaedic Association, (2014) BOAST - Fracture Liaison Services.

15. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T (2010)European Working Group on Sarcopenia in Older People. Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older

People. Age Ageing. 39: 412-23.

16. Geraci A, Calvani R, Ferri E, Marzetti E, Arosio B, Cesari M (2021) Sarcopenia and Menopause: The Role of Estradiol. Front Endocrinol (Lausanne). 12: 682012.

17. Kim HI, Ahn SH, Kim Y, Lee JE, Choi E, Seo SK (2022) Effects of sarcopenia and sarcopenic obesity on joint pain and degenerative osteoarthritis in postmenopausal women. Sci Rep. 12: 13543.

18. Lee Y, Je S, Kim HR, Lee JK, Choi E et al. (2023) Association between Fractures and Low Muscle Mass in Korean Menopausal Women: Data from Korean National Health and Nutrition Survey (2010-2011). J Menopausal Med. 29: 66-72.

19. Glass DJ (2010) PI3 kinase regulation of skeletal muscle hypertrophy and atrophy. Curr Top Microbiol Immunol. 346: 267-78.

20. Buckinx F, Aubertin-Leheudre M (2022) Sarcopenia in Menopausal Women: Current Perspectives. Int J Womens Health. 14: 805-19.

21. Almeida M, Laurent MR, Dubois V, Claessens F, O'Brien CA (2017) Estrogens and Androgens in Skeletal Physiology and Pathophysiology. Physiol Rev. 97: 135-187.

22. Thornton MJ (2003) Estrogens and aging skin. Dermatoendocrinol. 5: 264-70.

23. Lee YJ, Lee EB, Kwon YE, Lee JJ, Cho WS, Kim HA, Song YW (2003) Effect of estrogen on the expression of matrix metalloproteinase (MMP)-1, MMP-3, and MMP-13 and tissue inhibitor of metalloproternase-1 in osteoarthritis chondrocytes. Rheumatol Int. 23: 282-8.

24. Karvinen S, Juppi HK, Le G, Cabelka CA, Mader TL et al. (2020) Estradiol deficiency and skeletal muscle apoptosis: Possible contribution of microRNAs. Exp Gerontol. 147: 111267.

25. Khalfa A, Tiali A, Zemour L, Fatah A, Mekki K (2017) Prevalence of metabolic syndrome and its association with lifestyle and cardiovascular biomarkers among postmenopausal women in western Algeria. Int J Gynaecol Obstet. 138: 201-6.

26. Guthrie JR, Dennerstein L, Taffe JR, Ebeling PR, Randolph JF, Burger HG, Wark JD (2003) Central abdominal fat and endogenous hormones during the menopausal transition. Fertil Steril. 79: 1335-40.

27. Yang M, Jiang L, Yao NN (2022) Management of cardiovascular disease in women with premature ovarian insufficiency: critical quality appraisal of clinical guidelines and algorithm development. Menopause. 29: 189-99.

28. Canning KL, Brown RE, Jamnik VK, Kuk JL (2014) Relationship between obesity and obesity-related morbidities weakens with aging. J Gerontol A Biol Sci Med Sci. 69: 87-92.

29. Yang YL, Chee W, Im EO (2019) Type 2 Diabetes and Musculoskeletal Symptoms Among Midlife Women. Diabetes Educ. 45: 520-8.

30. Davis SR, Castelo-Branco C, Chedraui P, Lumsden MA, Nappi RE, Shah D, et al. (2012) Writing Group of the International Menopause Society for World Menopause Day 2012. Understanding weight gain at menopause. Climacteric. 15: 419-29.

31. McCarthy M, Raval AP (2020) The peri-menopause in a woman's life: a systemic inflammatory phase that enables later neurodegenerative disease. J Neuroinflammation. 17: 317.

32. Kuryłowicz A (2023) Estrogens in Adipose Tissue Physiology and Obesity-Related Dysfunction. Biomedicines. 11: 690.

33. Tian H, Gao Z, Wang G, Li H, Zheng J (2016) Estrogen potentiates reactive oxygen species (ROS) tolerance to initiate carcinogenesis and promote cancer malignant transformation. Tumour Biol. 37: 141-50.

34. King LK, March L, Anandacoomarasamy A (2013) Obesity & osteoarthritis. Indian J Med Res. 138: 185-93.

35. Kanis JA, Cooper C, Rizzoli R, Reginster JY (2019) Scientific Advisory Board of the European Society for Clinical and Economic Aspects of Osteoporosis (ESCEO) and the Committees of Scientific Advisors and National Societies of the International Osteoporosis Foundation (IOF). European guidance for the diagnosis and management of osteoporosis in postmenopausal women. Osteoporos Int. 30: 3-44.

36. Khadilkar SS (2019) Musculoskeletal Disorders and Menopause. J Obstet Gynaecol India. 69: 99-103.

37. Park JH, Moon JH, Kim HJ, Kong MH, Oh YH (2020) Sedentary Lifestyle: Overview of Updated Evidence of Potential Health Risks. Korean J Fam Med. 41: 365-73.

38. Turner RT, Sibonga JD (2001) Effects of alcohol use and estrogen on bone. Alcohol Res Health. 25: 276-81.

39. Women's health strategy for England 2022 https://www.gov.uk

40. Marini F, Brandi ML (2010) Genetic determinants of osteoporosis: common bases to cardiovascular diseases? Int J Hypertens. 2010: 394579.

41. https://diversityuk.org/diversity-in-the-uk/ (Accessed 20th March 2023)

42. Palmer JR, Rosenberg L, Wise LA, Horton NJ, Adams-Campbell LL (2003) Onset of natural menopause in African American women. Am J Public Health. 93: 299-306.

43. Kriplani A, Banerjee K (2005) An overview of age of onset of menopause in northern India. Maturitas. 52: 199-204.

44. Barnabei VM, Cochrane BB, Aragaki AK, Nygaard I, Williams RS (2005) Women's Health Initiative Investigators. Menopausal symptoms and treatment-related effects of estrogen and progestin in the Women's Health Initiative. Obstetrics and Gynaecology, 105: 1063–73.

45. Ockene JK, Barad DH, Cochrane BB, Larson JC, Gass M, et al. (2005) Symptom experience after discontinuing use of estrogen plus progestin. JAMA. 294: 183-93.

46. Brunner RL, Aragaki A, Barnabei V, Cochrane BB, Gass M, et al. (2010) Menopausal symptom experience before and after stopping estrogen therapy in the Women's Health Initiative randomized, placebo-controlled trial. Menopause. 17: 946-54.

47. British Orthopaedic Association (2014) BOAST-Fracture Liaison Services.

48. Royal Osteoprosis Society (2019) Effective secondary prevention of fragility fractures

49. NICE (2019) Menopause: Diagnosis and management.

50. Petroni ML, Caletti MT, Dalle Grave R, Bazzocchi A, Aparisi Gómez MP, Marchesini G (2019) Prevention and Treatment of Sarcopenic Obesity in Women. Nutrients. 11: 1302.

51. Silva TR, Oppermann K, Reis FM, et al. (2021) Nutrition in menopausal women: a narrative review. Nutrients. 13: 2149.

52. Mishra N, Mishra VN, Devanshi (2011) Exercise beyond menopause: Dos and Don'ts. J Midlife Health. 2: 51-6.

53. Mintziori G, Lambrinoudaki I, Goulis DG, et al. (2015) EMAS position statement: non-hormonal management of menopausal vasomotor symptoms. Maturitas. 81: 410-13.

54. An KC (2016) Selective Estrogen Receptor Modulators. Asian Spine J. 10: 787-91.