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Musculoskeletal Manifestations of Perimenopause: A Systematic Review and Meta-Analysis of 93,021 Women

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Background: The prevalence and characterization of specific types of musculoskeletal (MSK) conditions associated with menopausal transition remains unclear and is often underreported. Our objectives were twofold: (1) to systematically review, and conduct meta-analysis whenever appropriate, to compare the prevalence of MSK symptoms across the different stages of menopause and (2) to characterize the specific MSK conditions associated with transition to menopause.

Methods: We searched Medline, EMBASE, CENTRAL, and PubMed from inception to May 2024. Articles were eligible for inclusion if they included perimenopausal women and reported any primary data on MSK symptoms or pathology. The outcomes we aimed to find included muscle and joint pain, back pain, and the prevalence of various MSK conditions. A pairwise meta-analysis was performed using a DerSimonian-Laird random-effects model for all comparative data, and subgroup analyses were used to explore heterogeneity.

Results: After screening 5,556 relevant records, 37 observational studies across 22 countries enrolling 93,021 women were included in the quantitative analysis. Four in 10 women experienced muscle or joint pain during the premenopausal phase (40% [95% confidence interval {CI}: 32%-49%]). Whereas over half of perimenopausal women (57% [95% CI: 48%-65%]) and postmenopausal women (59% [95% CI: 50%-67%]) experienced muscle or joint pain, representing a 1.35-fold increased risk (risk ratio [RR] 1.35, 95% CI: 1.25-1.46, $p < 0.001$, $I^2 = 88.6\%$; absolute risk difference 130 more per 1,000 [95% CI: 93-171]) and a 1.40-fold increased risk (RR 1.40, 95% CI: 1.28-1.53, $p < 0.001$, $I^2 = 95.0\%$; absolute risk difference 148 more per 1,000 [95% CI: 104-197]) on pairwise comparison with premenopausal women, respectively. Geographic study location nor measurement scale explained the considerable heterogeneity in the pooled analyses. There was underreporting of specific MSK conditions beyond the generic descriptors of muscle and/or joint pain.

Conclusion: Women transitioning to menopause appear to be at increased risk of developing muscle or joint pain. However, as these findings are based on observational studies, specific causes of MSK pain are underreported, and there is significant heterogeneity. Further high-quality research is needed to confirm and clarify this association.

Level of Evidence: Diagnostic Level IV. See Instructions for Authors for a complete description of levels of evidence.

Conception and design of the study: All authors. Acquisition of data: C. Kruse, J. Dworsky-Fried, A. Sardar, G. Hacker. Analysis and interpretation of data: All authors. Drafting and revision of the manuscript: All authors. Approval of the final version of the manuscript: All authors. Agreement to be accountable for all aspects of the work: All authors.

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Background

Musculoskeletal (MSK) conditions leading to debilitating pain are highly prevalent, affecting a significant proportion of the adult population globally[1-3]. Studies have consistently shown that women are at a significantly higher risk of developing MSK pain in comparison with men[2-6]. MSK symptoms commonly arise in midlife, and some evidence suggests they may be linked to the menopausal transition and the associated decrease in estrogens[5,7,8]. Several animal studies have demonstrated that reduced estrogen levels adversely affect the synovium and joint cartilage[9-11]. However, this relationship remains uncertain, as age itself is a competing risk factor in this patient population[8].

The STRAW criteria provide a standardized framework for reproductive aging, which can be divided into 3 main stages: the premenopause stage, the menopausal transition or perimenopause, and postmenopause. Each stage is further characterized by menstrual cycle patterns and supported by hormonal changes, offering a clinically useful guide for defining the onset and progression of menopause[12]. Perimenopausal women appear to experience joint pain and stiffness to a greater extent than premenopausal women[13-15]. However, MSK symptoms related to perimenopause are often underrecognized and underreported. For example, well-recognized guidelines for managing menopausal symptoms focus on vasomotor, genitourinary, mood, sleep, and sexual symptoms, but do not address MSK issues[16-18]. Furthermore, recently published reviews on menopausal symptoms have not included MSK symptoms, demonstrating the scarcity of focused research in this area[19,20]. Many women presenting with MSK pain never receive a clear diagnosis, making it difficult to treat from the perspective of clinicians[8,13].

The perimenopausal transition appears to be a crucial time period when many women first develop MSK pain, and some studies suggest that declining estrogen levels may contribute to inflammation in MSK tissues[21-23]. A longitudinal cohort study of 609 women in an urban Chinese community demonstrated that both the prevalence and severity of muscle and joint pain increased as women progressed through menopausal stages[24]. A prospective investigation from the Seattle Midlife Women's Health Study reported a significant increase in back pain during the menopausal transition, whereas joint pain appeared to increase primarily with age rather than menopause-related factors, further complicating the relationship between age, menopause, and MSK symptoms[25]. Beyond this, high-quality longitudinal studies are scarce, and research in this area remains limited. The aim of this systematic review and meta-analysis was to compare the prevalence of MSK pain across the different stages of menopause and characterize the associated MSK conditions.

Methods

This systematic review and meta-analysis is reported in accordance with Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) (Appendices 1-2)[26]. The study protocol was registered on Prospective Register of Systematic Reviews (PROSPERO) (CRD42024613054). Local ethics review board approval was not required.

Search Strategy

The following databases covering the period from database inception through May 2024 were searched: Medline, EMBASE, CENTRAL, and PubMed. The search strategy was developed in consultation with a research librarian and modified for each database accordingly (complete search strategy available in Appendix 3). The references of studies meeting inclusion criteria as well as previous pertinent systematic reviews were searched manually to ensure that all relevant articles were included.

Eligibility Criteria

Articles were eligible for inclusion if they included perimenopausal women and reported any primary data on MSK symptoms. Perimenopause was defined by the STRAW criteria[12] and classified as premenopausal, perimenopausal, and postmenopausal. Randomized controlled trials, comparative cohort studies, case-control studies, and surveys were all eligible for inclusion. Articles written in all languages were considered for inclusion. Studies were excluded if they did not differentiate the menopausal state in keeping with the STRAW criteria. Women who had undergone surgical menopause were excluded from data analysis to ensure the review focused solely on the natural menopausal transition, as surgical menopause may involve different physiological mechanisms and symptom profiles[27].

Outcomes Assessed

The main outcomes we assessed were the prevalence of muscle or joint pain, back pain, and any defined MSK pathology. In studies that differentiated between severity of pain (i.e., mild, moderate, and severe), patients experiencing moderate and severe pain were included in the muscle or joint pain outcome. Questionnaires, including the standardized Menopause Rating Scale, Menopause-Specific Quality-of-Life Questionnaire, Kupperman Menopausal Index, Greene Climacteric Scale, and de novo questionnaires were used to assess pain symptoms. Data on specific MSK conditions were collected when reported.

Data Extraction

Three reviewers independently screened the systematically searched titles and abstracts using a standardized, pilot-tested form on covidence. Discrepancies that occurred at the title and abstract screening phases were included in the full-text screening stage. At the full-text screening stage, discrepancies were resolved by a fourth reviewer. Three reviewers independently and in duplicate conducted data extraction into a data collection form designed a priori and pilot tested on Microsoft Excel. The extracted data included study characteristics (e.g., author, year of publication, and study design), patient demographics (e.g., age, menopausal status, and body mass index), and outcomes (e.g., muscle and joint pain, back pain, and MSK conditions).

Quality Assessment

Three reviewers assessed the quality of these studies independently using the critical appraisal checklist specifically designed

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for cross-sectional studies from the 2020 Reviewers' Manual published by the Joanna Briggs Institute.

Statistical Analysis

All statistical analyses were performed on STATA version 18 (StataCorp). A restricted maximum likelihood random-effects model was used to generate the pooled proportion of each outcome along with their respective 95% confidence intervals (CI) for noncomparative data. A logit-transformed proportion was estimated as the effect size. A pairwise meta-analysis was performed using a DerSimonian-Laird random-effects model for all comparative data. Pooled effect estimates for binary outcomes were estimated by calculating the risk ratio (RR) along with their respective 95% CIs. Mean and standard deviation (SD) were estimated for studies that only report median and interquartile range using the method described by Wan et al.[28]. Missing SD data were calculated according to the prognostic method[29]. Assessment of between-study heterogeneity was performed using the inconsistency (I^2) statistic. An I^2 greater than 40% was considered to represent considerable heterogeneity[30]. Bias in meta-analyzed outcomes was assessed with funnel plots[31]. A leave-one-out sensitivity analysis was performed. Subgroup analysis was determined a priori and performed for the primary outcome of muscle or joint pain on the basis of (1) pain scale used, (2) geographic location of corresponding author, (3) pain severity, and (4) mean age of study cohort (i.e., greater than or equal to 50 vs. less than 50).

Results

Study Characteristics

Database and registry searches identified 5,556 relevant records. After excluding 24 duplicates, 5,532 independent records were available for screening. Title and abstract screening excluded 5,380 records. After the assessment of 152 full texts for eligibility, there were 37 studies that reported the outcomes of interest that could be included in the quantitative analysis. A PRISMA flow diagram is demonstrated in Figure 1.

Pooled study characteristics are reported in Table I. Individual study characteristics are reported in Supplemental Tables 1-2. Included studies were published from 1993 to 2024. The majority of studies (35 of 37) were cross-sectional studies, with the other 2 studies being prospective cohort studies. In terms of geographic location of the included studies, 12 studies were from East Asia[15,32-42], 8 studies from South Asia[43-50], 4 studies from West Asia[51-54], 4 studies from Southeast Asia[55-58], 4 studies from Europe[59-62], 3 studies from North America[63-65], and 1 study from both South America[66] and Africa[67], totaling 22 different countries (Fig. 2). There were 26,789 patients who were categorized as premenopausal, 24,326 patients who were perimenopausal and 41,906 patients who were postmenopausal.

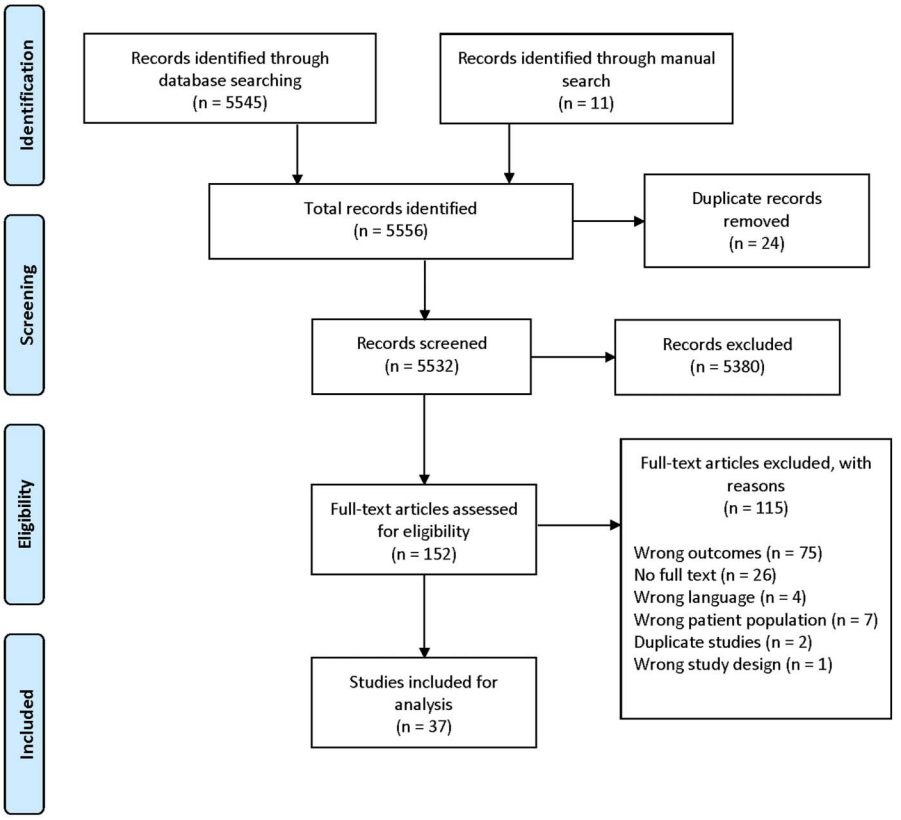

Fig. 1

PRISMA diagram—transparent reporting of systematic reviews and meta-analysis flow diagram outlining the search strategy results from initial search to included studies.

TABLE I Pooled Study Characteristics

Study Characteristic	No. of Studies (n = 37)
Geographic location	
East Asia	12 (32.4)
Southeast Asia	4 (10.8)
South Asia	8 (21.6)
West Asia	4 (8.1)
Africa	1 (10.8)
Europe	4 (10.8)
South America	1 (2.7)
North America	3 (8.1)
Study design	
Cross sectional	35 (94.6)
Prospective cohort	2 (5.4)
No. of included patients	
<1,000	19 (51.4)
1,000-1,999	10 (27.0)
2,000-4,999	4 (10.8)
≥5,000	4 (10.8)
Mean patient age	
<50	20 (54.1)
≥50	14 (37.8)
NR	3 (8.1)
Outcomes	
Muscle and joint pain	25 (67.6)
Joint pain	11 (29.7)
Muscle pain	1 (2.7)
Back pain	11 (29.7)
Measurement scales	
MRS	9 (24.3)
MENQOL	6 (16.2)
Kupperman Index	5 (13.5)
Greene Climacteric Scale	2 (5.4)
De novo questionnaire	15 (40.5)

MENQOL = Menopause-Specific Quality-of-Life Questionnaire, MRS = Menopause Rating Scale, and n = number of studies.

Muscle and Joint Pain

The prevalence of muscle or joint symptoms was 40% (95% CI: 32%-49%) in premenopausal women, 57% (95% CI: 48%-65%) in perimenopausal women, and 59% (95% CI: 50%-67%) in postmenopausal women (Figs. 3-A, 3-B, and 3-C). Pairwise meta-analysis (N = 28 studies, 43,715 patients) demonstrated a significantly increased risk of muscle or joint pain among perimenopausal compared with premenopausal women (RR 1.35, 95% CI: 1.25-1.46, $p < 0.001$; absolute risk difference 130 more per 1,000 [95% CI: 93-171]; $I^2 = 88.6\%$) (Fig. 4). There were no observed subgroup interactions according to measurement scale ($p = 0.84$), geographic study location ($p = 0.06$), or pain severity ($p = 0.25$) (Supplemental Figure 1-3).

Pairwise meta-analysis (N = 28 studies, 57,696 patients) demonstrated there was a significantly increased risk of muscle or joint pain among postmenopausal compared with premenopausal women (RR 1.40, 95% CI: 1.28-1.53, $p < 0.001$; absolute risk difference 148 more per 1,000 [95% CI: 104-197]; $I^2 = 95.0\%$) (Fig. 5). There was no observed subgroup interaction ($p = 0.57$) according to measurement scale (Supplemental Figure 4). We identified one subgroup interaction by geographic study location ($p < 0.001$) and severity of pain (Supplemental Figures 5 and 6). The subgroup analysis by mean cohort age (i.e., greater than or equal to 50 vs. less than 50) did not demonstrate a significant interaction between studies with a mean patient age greater than 50 or less than 50 (Supplemental Figure 7-9).

Pairwise meta-analysis (N = 35 studies, 66,232 patients) that compared the prevalence of muscle or joint pain between perimenopausal and postmenopausal women demonstrated no difference between the 2 groups (RR 0.97, 95% CI: 0.92-1.01, $p = 0.16$; absolute risk difference 16 fewer per 1,000 [95% CI: 143 fewer to 5 more]; $I^2 = 85.7\%$) (Fig. 6). We identified subgroup interactions according to measurement scale ($p < 0.001$), geographic location, and pain severity (Supplemental Figures 10-12). A summary of all effect estimates for overall analyses and subgroup analyses is reported in Table II.

Back Pain

The overall prevalence of back pain from the pooled data was 42% (95% CI: 26%-60%; 8 studies) in premenopausal women, 57% (95% CI: 44%-69%; 10 studies) in perimenopausal women, and 59% (95% CI: 45%-71%; 10 studies) in postmenopausal women. Pairwise meta-analysis (N = 8 studies, 15,821 patients) demonstrated a 1.15-fold increased risk of back pain in the perimenopausal compared with premenopausal women (RR 1.15, 95% CI: 1.06-1.24, $p < 0.001$, $I^2 = 59.8\%$) (Supplemental Figure 13). Pairwise meta-analysis (8 studies, 20,565 patients) demonstrated a 1.2-fold increased risk of back pain among postmenopausal compared with premenopausal women (RR 1.20, 95% CI: 1.11-1.30, $p < 0.001$, $I^2 = 66.9\%$) (Supplemental Figure 14).

Prevalence of MSK Conditions in Perimenopausal Women

A single study reported the prevalence of specific MSK conditions in perimenopausal women. This study by Yoon et al. evaluated the causes of perimenopausal arthralgia in the shoulder[68]. The prevalence of adhesive capsulitis, synovitis, rotator cuff disorder, arthritis, and other shoulder pathologies was compared between perimenopausal (n = 197) and premenopausal (n = 113) women. Adhesive capsulitis was the most common diagnosis (35% and 32%, respectively), but there was no significant difference between groups. The second most common diagnosis was shoulder synovitis, and a significantly higher prevalence (25.1%) was observed in the perimenopausal group when compared with premenopausal women (6.2%).

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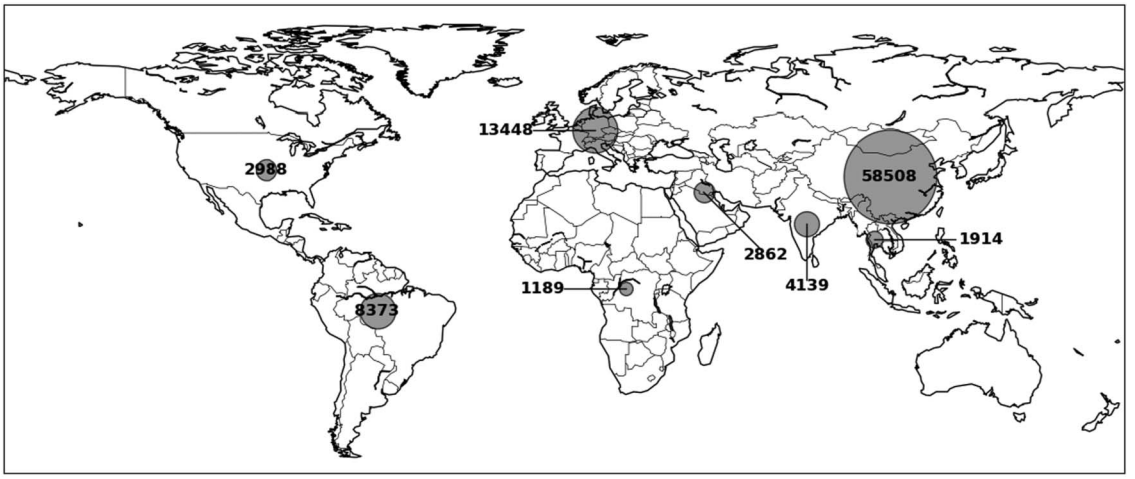

Fig. 2

Geographic distribution of number of included patients in data synthesis (North America: n = 3,096; South America: n = 8,373; Europe: n = 12,384; Africa: n = 1,189; West Asia: n = 2,862; South Asia: n = 5,013; Southeast Asia: n = 1,914; East Asia: n = 58,653). *n corresponds to the number of patients.

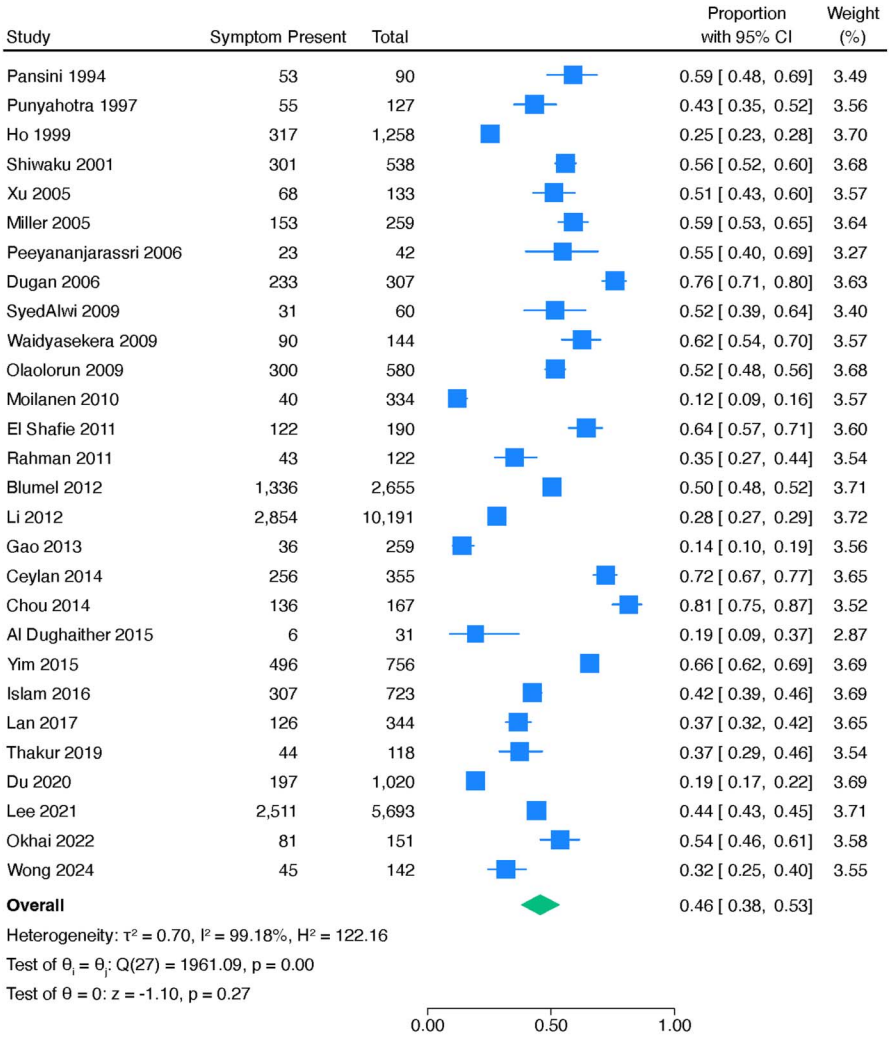

Fig. 3-A

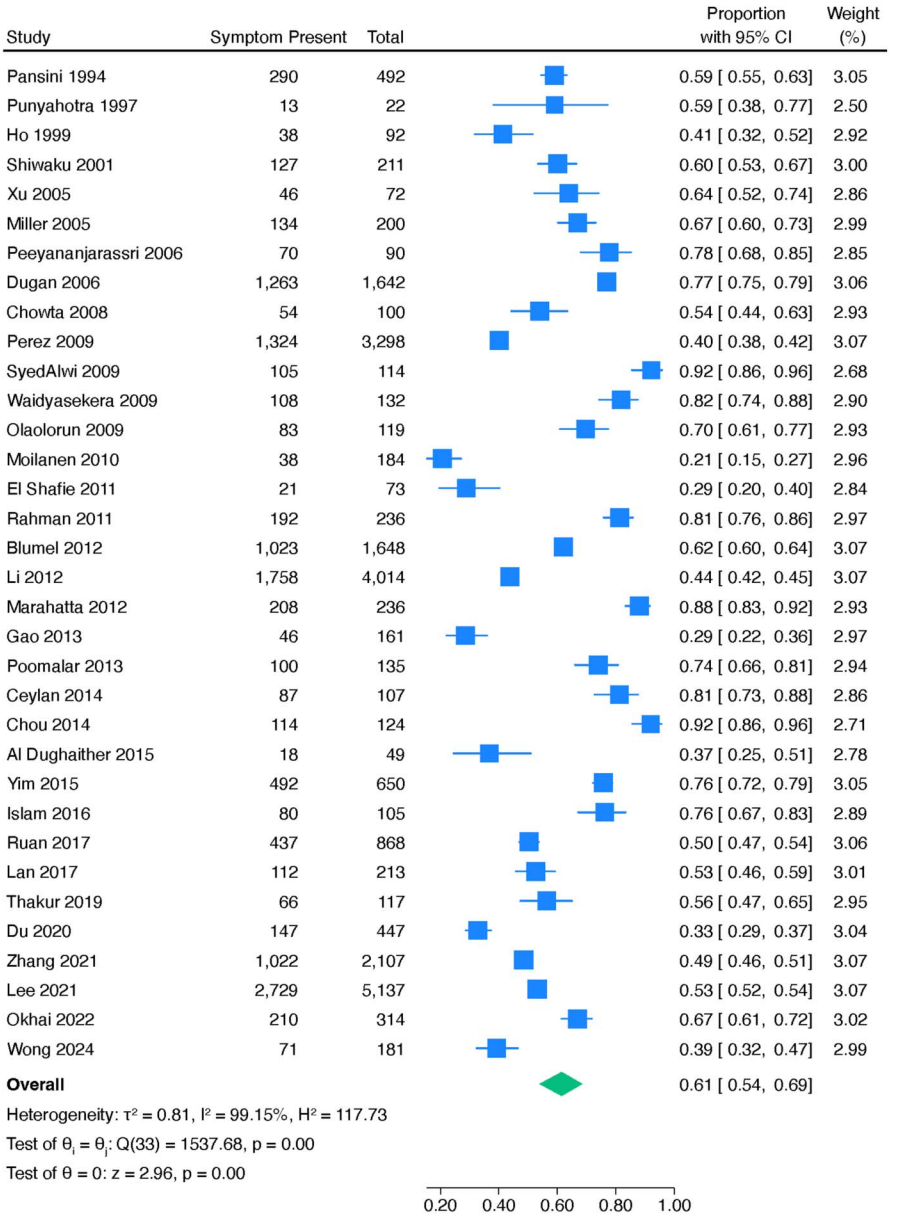
Study
Symptom Present
Total
Proportion with 95% CI
Weight (%)
Pansini 1994 290 492 0.59 [0.55, 0.63] 3.05
Punyahotra 1997 13 22 0.59 [0.38, 0.77] 2.50
Ho 1999 38 92 0.41 [0.32, 0.52] 2.92
Shiwaku 2001 127 211 0.60 [0.53, 0.67] 3.00
Xu 2005 46 72 0.64 [0.52, 0.74] 2.86
Miller 2005 134 200 0.67 [0.60, 0.73] 2.99
Peeyananjarassri 2006 70 90 0.78 [0.68, 0.85] 2.85
Dugan 2006 1,263 1,642 0.77 [0.75, 0.79] 3.06
Chowta 2008 54 100 0.54 [0.44, 0.63] 2.93
Perez 2009 1,324 3,298 0.40 [0.38, 0.42] 3.07
SyedAlwi 2009 105 114 0.92 [0.86, 0.96] 2.68
Waidyasekera 2009 108 132 0.82 [0.74, 0.88] 2.90
Olaolorun 2009 83 119 0.70 [0.61, 0.77] 2.93
Moilanen 2010 38 184 0.21 [0.15, 0.27] 2.96
El Shafie 2011 21 73 0.29 [0.20, 0.40] 2.84
Rahman 2011 192 236 0.81 [0.76, 0.86] 2.97
Blumel 2012 1,023 1,648 0.62 [0.60, 0.64] 3.07
Li 2012 1,758 4,014 0.44 [0.42, 0.45] 3.07
Marahatta 2012 208 236 0.88 [0.83, 0.92] 2.93
Gao 2013 46 161 0.29 [0.22, 0.36] 2.97
Poomalar 2013 100 135 0.74 [0.66, 0.81] 2.94
Ceylan 2014 87 107 0.81 [0.73, 0.88] 2.86
Chou 2014 114 124 0.92 [0.86, 0.96] 2.71
Al Dughaither 2015 18 49 0.37 [0.25, 0.51] 2.78
Yim 2015 492 650 0.76 [0.72, 0.79] 3.05
Islam 2016 80 105 0.76 [0.67, 0.83] 2.89
Ruan 2017 437 868 0.50 [0.47, 0.54] 3.06
Lan 2017 112 213 0.53 [0.46, 0.59] 3.01
Thakur 2019 66 117 0.56 [0.47, 0.65] 2.95
Du 2020 147 447 0.33 [0.29, 0.37] 3.04
Zhang 2021 1,022 2,107 0.49 [0.46, 0.51] 3.07
Lee 2021 2,729 5,137 0.53 [0.52, 0.54] 3.07
Okhai 2022 210 314 0.67 [0.61, 0.72] 3.02
Wong 2024 71 181 0.39 [0.32, 0.47] 2.99
Overall 0.61 [0.54, 0.69]
Heterogeneity: τ^2 = 0.81, I^2 = 99.15%, H^2 = 117.73
Test of $\theta_i = \theta_j$: Q(33) = 1537.68, p = 0.00
Test of θ = 0: z = 2.96, p = 0.00
0.20
0.40
0.60
0.80
1.00
Random-effects REML model

Fig. 3-B

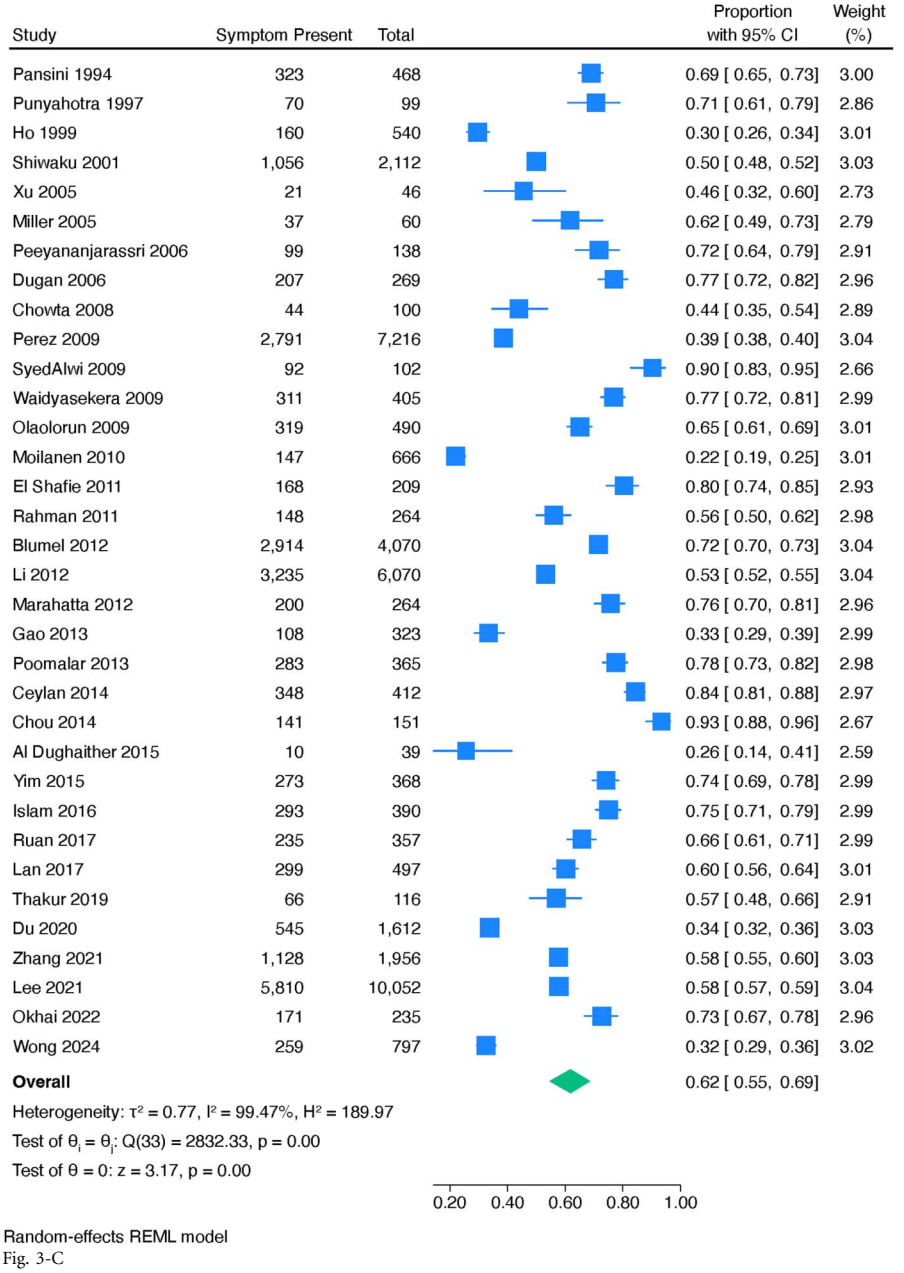

Fig. 3 Single-arm meta-analysis of proportions of musculoskeletal symptoms in (**Fig. 3-A**) premenopausal women, (**Fig. 3-B**) perimenopausal women, and (**Fig. 3-C**) postmenopausal women.

Discussion

Our systematic review of 37 studies and 93,421 women suggests that women experiencing perimenopause have increased risk of muscle and joint pain when compared with premenopausal women. The MSK symptoms identified during perimenopause, however, did not increase significantly in the postmenopausal stage, indicating a potential inflection point at menopause transition. The specific causes or diagnoses associated with MSK symptoms were poorly reported. Common orthopaedic conditions such as osteoarthritis (OA), tendinopathies, synovitis, or bursitis were rarely specified, and their inclusion would have provided more insight into how these symptoms might be better managed.

Our review has several strengths including sample size and rigorous systematic review methodology. Moreover, we comprehensively tried to explain between study heterogeneity. There are also several limitations. Most of the included studies were cross-sectional, making it difficult to infer causality. There is a notable lack of prospective or longitudinal research that could better clarify causal relationships. Nonetheless, the available data provide valuable insights into prevalence. A majority of the pooled data were collected through self-reporting, introducing a

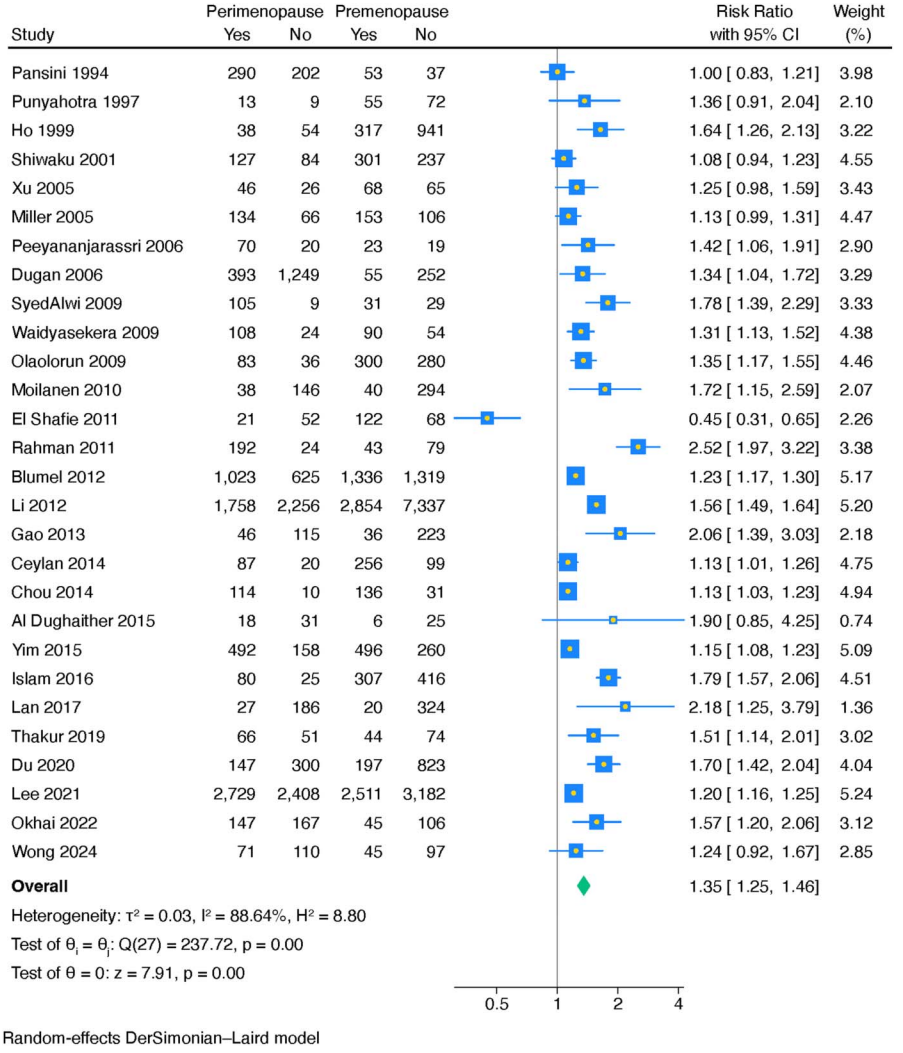

Fig. 4

Pairwise meta-analysis comparing the prevalence of muscle or joint pain in premenopausal women with perimenopausal women.

risk of misclassification bias regarding menopausal state[69]. Given that data were self-reported and collected across multiple countries, cultural factors are likely to influence how pain is perceived and reported. To address this, we performed a subgroup analysis by geographic location of the study population, which only partially accounted for the between-study heterogeneity. Furthermore, most of the included studies investigated were not designed with MSK symptoms as a key primary outcome measure; rather, they included all types of symptoms. Therefore, underreporting of MSK symptoms and specific causes is a potential risk. Our findings, therefore, may represent an underestimate of the magnitude of the effect. The symptom scales used were not designed to assess MSK pain and lacked details on localization, functional impact, and correlation with clinical or imaging findings. Future prospective studies using more specific tools are needed to clarify the etiology of MSK pain in this population. Finally, lack of reported baseline demographics across studies precluded meta-regression including potential confounding variables, such as age stratified by menopausal status and hormone therapy, which may influence the prevalence of MSK symptoms.

Our results add to the growing body of evidence demonstrating an association between MSK pain and the onset of menopause[9,70,71]. A similar review by Lu et al. (n = 14 studies) also demonstrated an increased prevalence of muscle and joint pain in perimenopausal women[13]. Our review included 23 additional (N = 74,423 women) published studies reporting MSK symptoms in perimenopausal women. Lu et al. reported that postmenopausal women were at a higher risk of moderate to severe MSK symptoms than perimenopausal women. Our findings, however, suggest no difference in MSK symptom severity between the perimenopausal and postmenopausal phases with a precise 95% CI [RR 0.97, 95% CI: 0.92-1.01]. In addition, a primary aim of our review was to better characterize the etiology of MSK symptoms in perimenopausal women. Despite MSK symptoms being common in perimenopause, one of the main findings of our review was a glaring lack of reporting on specific MSK conditions.

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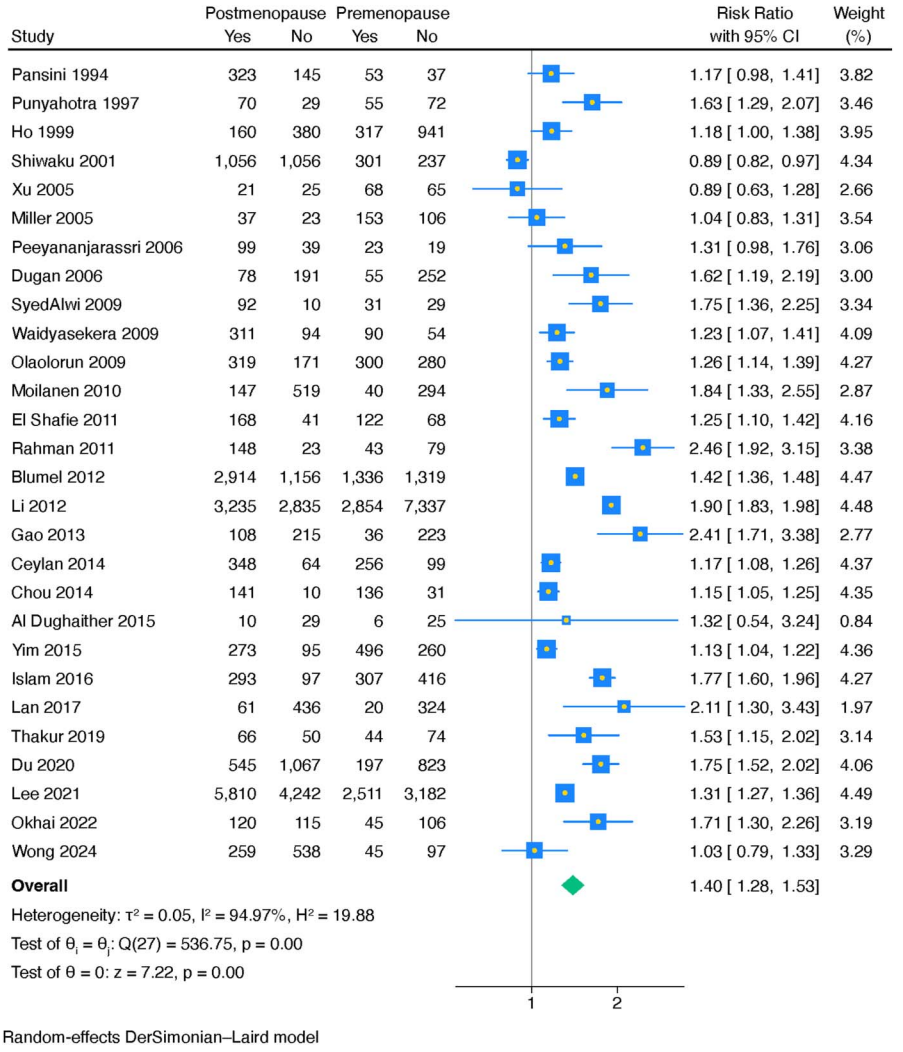

Fig. 5

Pairwise meta-analysis comparing the prevalence of muscle or joint pain in premenopausal women with postmenopausal women.

Altogether, there is evidence suggesting a high prevalence of MSK symptoms in perimenopausal women. The scientific rationale for these symptoms has implicated estrogen deficiency[8]. There have been multiple proposed theories to explain how estrogen deficiency can contribute to these MSK symptoms in this population[8]. Estrogen receptors are found on a range of human immune cells[72]. High estrogen levels produce an anti-inflammatory state[8,73]. Similarly, there is some evidence to suggest that low estrogen levels can contribute to a proinflammatory state and could influence the development of OA[73].

There are estrogen receptors found in all joint tissues, including articular cartilage, subchondral bone, and synovium[74]. Findings from animal studies suggest that female hormones have an important influence on inflammation-induced cartilage breakdown[10,11]. A clinical study by Lou et al. investigated the association between menopause and severity of knee joint cartilage degeneration using magnetic resonance imaging in 860 healthy women and, after removing the effects of age, showed that the severity of cartilage degeneration increased significantly from premenopausal to perimenopausal state and then to postmenopausal state[75]. Women have a significantly higher prevalence of OA in comparison with men and account for more than 60% of OA cases globally[76,77]. Radiographic studies of knee cartilage loss show that women experience faster deterioration than men, with the gap becoming more pronounced after the age of 50, potentially implicating the decline in estrogen[9,78-80]. However, observational studies have yet to provide conclusive evidence regarding the potential mechanism of estrogen and the development of OA in women[81,82]. Although age is an important confounding factor, some authors suggest that arthralgia related to menopausal estrogen changes is often misdiagnosed as age-related OA[9]. Recognizing the effects of declining estradiol on bone and cartilage is important, and many authors have highlighted the need for higher quality studies in this area[9,82,83].

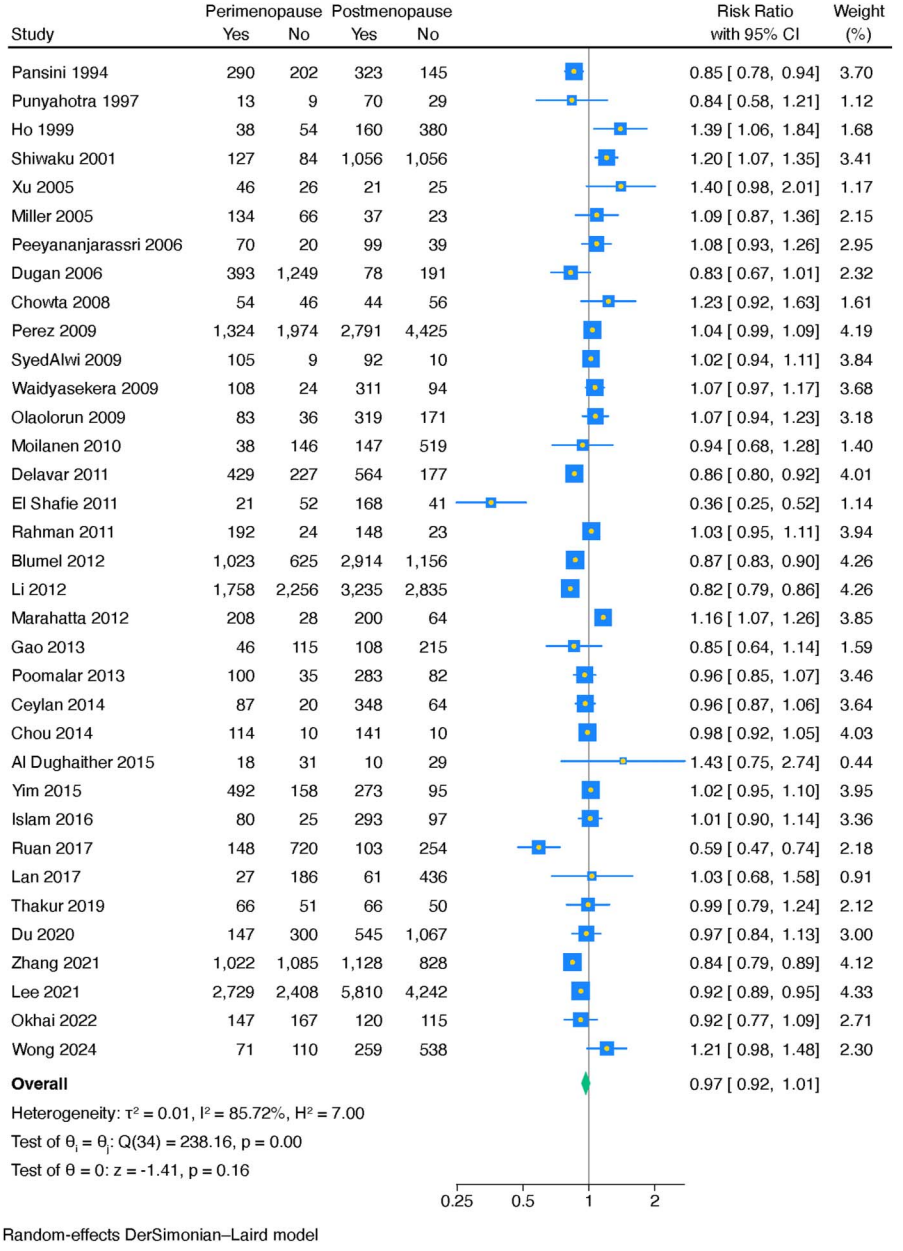

Fig. 6

Pairwise meta-analysis comparing the prevalence of muscle or joint pain in perimenopausal women with postmenopausal women.

There is also evidence suggesting that sex hormones can influence the properties of soft tissues, such as muscles[21], tendons[22], and ligaments[23]. Estrogens maintain energy homeostasis and promote metabolic health throughout the body, and the decline in estrogens during menopause appears to reduce muscle function[84]. This decline can also lead to changes such as decreased collagen production, reduced tendon and ligament elasticity, and overall weakening of connective tissue, which may increase the risk of inflammation, injury, and tendon pathology[85-88]. Furthermore, an increasing body of evidence suggests that the loss of estrogen during menopause may contribute to the postclimacteric decline in muscle mass. It is estimated that postmenopausal women lose about 0.6% of muscle mass per year if sarcopenia remains untreated[9,89]. Although it is difficult to isolate the exact mechanisms of sex hormones, balanced physiological levels appear to be crucial for regulating inflammation in the body, promoting tendon health, and maintaining physical function[22,87,90].

Owing to the scarcity of studies outlining specific MSK pathologies in perimenopausal women, the evidence regarding any interventions in these patients is also quite limited. The role of Menopausal Hormone Therapy (MHT) in the management of MSK symptoms in women is controversial. A post hoc

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TABLE II Summary of Effect Estimates and Heterogeneity for Each Pairwise Comparison and Subgroup Analysis

Outcome	Interaction p value	Subgroup	No. of Studies	Pairwise Meta-Analysis RR	95% CI	*P*	I^2
Premenopause vs. perimenopause							
Overall MSK symptoms			28	1.35	1.25-1.46	<0.001	88.6
Geographic location subgroup	**0.06**	East Asia	9	1.37	1.21-1.55	<0.001	93.6
		South America	1	1.23	1.17-1.30	<0.001	-
		Europe	3	1.36	0.94-1.96	0.10	80.8
		North America	3	1.19	1.07-1.33	<0.001	0
		Africa	1	1.35	1.17-1.55	<0.001	-
		South Asia	4	1.72	1.33-2.23	<0.001	86.7
		West Asia	3	0.93	0.45-1.93	0.85	91.4
		Southeast Asia	4	1.47	1.24-1.74	<0.001	18.8
Pain scale subgroup	**0.84**	MRS	8	1.27	1.08-1.49	<0.001	89.9
		MENQOL	5	1.41	1.15-1.73	<0.001	90.9
		De Novo	9	1.30	1.17-1.45	<0.001	62.3
		Kupperman	4	1.47	1.16-1.88	<0.001	87.1
		Greene	2	1.35	1.13-1.63	<0.001	1.8
Pain severity	**0.25**	Pain	25	1.34	1.24-1.45	<0.001	89.7
		Moderate-to-severe	3	1.52	1.23-1.89	<0.001	25.0
Premenopause vs. postmenopause							
Overall MSK symptoms			28	1.40	1.28-1.53	<0.001	95.0
Geographic location subgroup	**<0.001**	East Asia	9	1.41	1.17-1.71	<0.001	98.1
		South America	1	1.42	1.36-1.48	<0.001	-
		Europe	3	1.52	1.12-2.06	0.01	76.4
		North America	3	1.15	0.83-1.59	0.40	73.4
		Africa	1	1.26	1.14-1.39	<0.001	-
		South Asia	4	1.68	1.28-2.19	<0.001	89.8
		West Asia	3	1.19	1.12-1.27	<0.001	0.00
		Southeast Asia	4	1.41	1.11-1.78	0.01	70.5
Pain scale subgroup	**0.57**	MRS	8	1.35	1.21-1.52	<0.001	87.3
		MENQOL	5	1.39	1.13-1.70	<0.001	93.2
		De Novo	9	1.37	1.15-1.64	<0.001	91.7
		Kupperman	4	1.66	1.32-2.07	<0.001	88.8
		Greene	2	1.18	0.70-2.00	0.53	81.2
Pain severity	**0.03**	Pain	25	1.37	1.24-1.51	<0.001	95.5
		Moderate-to-severe	3	1.73	1.43-2.09	<0.001	0
Perimenopause vs. postmenopause							
Overall MSK symptoms			35	0.97	0.92-1.01	0.16	85.7
Geographic location subgroup	**<0.001**	East Asia	11	0.94	0.87-1.01	0.10	89.0
		South America	1	0.87	0.83-0.90	<0.001	-
		Europe	4	0.94	0.83-1.07	0.34	77.6
		North America	3	1.05	0.79-1.38	0.74	72.3

continued

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TABLE II (*continued*)

Outcome	Interaction p value	Subgroup	No. of Studies	Pairwise Meta-Analysis RR	95% CI	*P*	I^2
		Africa	1	1.07	0.94-0.123	0.32	—
		South Asia	7	1.05	0.99-1.12	0.09	43.2
		West Asia	4	0.79	0.62-1.01	0.06	89.6
		Southeast Asia	4	1.05	0.96-1.15	0.25	20.6
Pain scale subgroup	**0.03**	MRS	9	0.97	0.88-1.08	0.61	90.7
		MENQOL	6	1.01	0.97-1.05	0.77	0.0
		De Novo	13	0.98	0.91-1.05	0.56	83.0
		Kupperman	5	0.83	0.74-0.93	<0.001	73.6
		Greene	2	1.14	0.82-1.59	0.43	60.6
Pain severity	**0.03**	Pain	31	0.98	0.94-1.03	0.49	86.3
		Moderate-to-severe	4	0.81	0.64-1.01	0.06	73.3

Bolded entries represent statistically significant values ($p < 0.05$). CI = confidence interval, MENQOL = Menopause-Specific Quality-of-Life Questionnaire, MRS = Menopause Rating Scale, MSK = musculoskeletal, and RR, relative risk.

analysis of the landmark women's health initiative randomized controlled trial demonstrated that estrogen use alone resulted in a modest but sustained reduction in the frequency of joint pain[91]. In contrast to these findings, other studies have shown that MHT is associated with a higher risk of knee OA[92,93]. There has been little subsequent research investigating MHT in healthy postmenopausal women, and therefore, its effects are not yet fully understood. Recognizing the effects of declining estradiol on the MSK system is essential for physicians to develop treatment plans that address the underlying cause rather than attributing symptoms solely to age-related degeneration[9].

In summary, our systematic review and meta-analysis identified a potential association between the onset of menopause and the prevalence of muscle and joint symptoms. The risk of developing muscle or joint pain, along with moderate to severe symptoms, appears to increase from premenopause to perimenopause, but were similar between perimenopause and postmenopause, indicating there may be an inflection point at the menopause transition. Because specific diagnoses were not reported, it is difficult to make direct causal inferences or determine the exact contributors to pain in this population, especially given that age is a competing factor. Nonetheless, the findings highlight that MSK pain is a significant concern in perimenopausal women and underscore the urgent need for prospective studies to better characterize and address this issue.

Appendix

eA Supporting material provided by the authors is posted with the online version of this article as a data supplement at jbjs.org (http://links.lww.com/JBJSOA/B66). This content was not copyedited or verified by JBJS. ■

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References

1. Kopec JA, Cibere J, Sayre EC, Li LC, Lacaille D, Esdaile JM. Descriptive epidemiology of musculoskeletal disorders in Canada: data from the global burden of disease study. Osteoarthritis and Cartilage. 2019;27:S259.

2. Urwin M, Symmons D, Allison T, Brammah T, Busby H, Roxby M, Simmons A, Williams G. Estimating the burden of musculoskeletal disorders in the community: the comparative prevalence of symptoms at different anatomical sites, and the relation to social deprivation. Ann Rheum Dis. 1998;57(11):649-55.

3. Fayaz A, Croft P, Langford RM, Donaldson LJ, Jones GT. Prevalence of chronic pain in the UK: a systematic review and meta-analysis of population studies. BMJ Open. 2016;6(6):e010364.

4. Wijnhoven HAH, de Vet HCW, Picavet SJH. Explaining sex differences in chronic musculoskeletal pain in a general population. Pain. 2006;124(1):158-66.

5. Prieto-Alhambra D, Judge A, Javaid MK, Cooper C, Diez-Perez A, Arden NK. Incidence and risk factors for clinically diagnosed knee, hip and hand osteoarthritis: influences of age, gender and osteoarthritis affecting other joints. Ann Rheum Dis. 2014;73(9):1659-64.

6. Wijnhoven HAH, de Vet HCW, Picavet HSJ. Prevalence of musculoskeletal disorders is systematically higher in women than in men. Clin J Pain. 2006;22(8):717-24.

7. Kapur P, Sinha B, Pereira BMJ. Measuring climacteric symptoms and age at natural menopause in an Indian population using the Greene Climacteric Scale. Menopause. 2009;16(2):378-84.

8. Watt FE. Musculoskeletal pain and menopause. Post Reprod Health. 2018; 24(1):34-43.

9. Blumer J. Arthralgia of menopause–a retrospective review. Post Reprod Health. 2023;29(2):95-7.

10. Sniekers YH, Weinans H, Bierma-Zeinstra SM, van Leeuwen JPTM, van Osch GJVM. Animal models for osteoarthritis: the effect of ovariectomy and estrogen treatment–a systematic approach. Osteoarthritis Cartilage. 2008;16(5):533-41.

11. Da Silva JP, Colville-Nash P, Spector TD, Scott DL, Willoughby DA. Inflammation-induced cartilage degradation in female rodents. Protective role of sex hormones. Arthritis Rheum. 1993;36(7):1007-13.

12. Soules MR, Sherman S, Parrott E, Rebar R, Santoro N, Utian W, Woods N. Executive summary: stages of Reproductive Aging Workshop (STRAW). Fertil Steril. 2001;76(5):874-8.

13. Lu CB, Liu PF, Zhou YS, Meng Fc, Qiao Ty, Yang Xj, Li Xy, Xue Q, Xu H, Liu Y, Han Y, Zhang Y. Musculoskeletal pain during the menopausal transition: a systematic review and meta-analysis. Neural Plast. 2020;2020:1-10.

14. Szoeke CE, Cicuttini FM, Guthrie JR, Dennerstein L. The relationship of reports of aches and joint pains to the menopausal transition: a longitudinal study. Climacteric. 2008;11(1):55-62.

15. Ho SC, Chan SG, Yip YB, Cheng A, Yi Q, Chan C. Menopausal symptoms and symptom clustering in Chinese women. Maturitas. 1999;33(3):219-27.

16. Stuenkel CA, Davis SR, Gompel A, Lumsden MA, Murad MH, Pinkerton JV, Santen RJ. Treatment of symptoms of the menopause: an Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2015;100(11):3975-4011.

17. Recommendations|Menopause: Identification and Management|Guidance. NICE. 2015. Available at: https://www.nice.org.uk/guidance/ng23/chapter/recommendations?utm_source=chatgpt.com#managing-symptoms-associated-with-menopause-in-people-aged-40-or-over. Accessed January 26, 2025.

18. Practice bulletin no. 141: management of menopausal symptoms. Obstet Gynecol. 2014;123(1):202-16.

19. Santoro N, Roeca C, Peters BA, Neal-Perry G. The menopause transition: signs, symptoms, and management options. J Clin Endocrinol Metab. 2021; 106(1):1-15.

20. Crandall CJ, Mehta JM, Manson JE. Management of menopausal symptoms: a review. JAMA. 2023;329(5):405-20.

21. Alexander SE, Pollock AC, Lamon S. The effect of sex hormones on skeletal muscle adaptation in females. Eur J Sport Sci. 2022;22(7):1035-45.

22. Hansen M, Kjaer M. Sex hormones and tendon. Adv Exp Med Biol. 2016;920: 139-49.

23. Gilmer G, Crasta N, Tanaka MJ. The effect of sex hormones on joint ligament properties: a systematic review and meta-analysis. Am J Sports Med. 2025;53(11): 2738-48.

24. Huang F, Fan Y, Tang R, Xie Z, Yang L, Ma X, Liang J, Chen R. Musculoskeletal pain among Chinese women during the menopausal transition: findings from a longitudinal cohort study. Pain. 2024;165(11):2644-54.

25. Mitchell ES, Woods NF. Pain symptoms during the menopausal transition and early postmenopause. Climacteric. 2010;13(5):467-78.

26. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Li T, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, Moher D. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. 2021;372: n71.

27. Demir O, Ozalp M, Sal H, Aran T, Osmanağaoğlu MA. The relationship of menopausal symptoms with the type of menopause and lipid levels. Prz Menopauzalny. 2020;19(1):6-10.

28. Wan X, Wang W, Liu J, Tong T. Estimating the sample mean and standard deviation from the sample size, median, range and/or interquartile range. BMC Med Res Methodol. 2014;14(1):135.

29. Weir CJ, Butcher I, Assi V, Lewis SC, Murray GD, Langhorne P, Brady MC. Dealing with missing standard deviation and mean values in meta-analysis of continuous outcomes: a systematic review. BMC Med Res Methodol. 2018;18(1):25.

30. Higgins J, Green S. Identifying and measuring heterogeneity. Cochrane Handbook for Systematic Reviews of Interventions. Version 5.1.0. The Cochrane Collaboration; https://handbook-5-1.cochrane.org/ (2011, Accessed July 20, 2025).

31. Lau J, Ioannidis JPA, Terrin N, Schmid CH, Olkin I. The case of the misleading funnel plot. BMJ. 2006;333(7568):597-600.

32. Ruan X, Cui Y, Du J, Jin F, Mueck AO. Prevalence of climacteric symptoms comparing perimenopausal and postmenopausal Chinese women. J Psychosom Obstet Gynaecol. 2017;38(3):161-9.

33. Zhang L, Ruan X, Cui Y, Gu M, Mueck AO. Menopausal symptoms among Chinese peri- and postmenopausal women: a large prospective single-center cohort study. Gynecol Endocrinol. 2021;37(2):185-9.

34. Chiu HH, Tsao LI, Liu CY, Lu YY, Shih WM, Wang PH. Using a short questionnaire of the perimenopausal fatigue scale to evaluate perimenopausal women prone to fatigue syndrome. Taiwan J Obstet Gynecol. 2021;60(4):734-8.

35. Du L, Xu B, Huang C, Zhu L, He N. Menopausal symptoms and perimenopausal healthcare-seeking behavior in women aged 40-60 years: a community-based cross-sectional survey in Shanghai, China. Int J Environ Res Public Health. 2020;17(8): 2640.

36. Lee PS, Lee CL. Prevalence of symptoms and associated factors across menopause status in Taiwanese women. Menopause. 2021;28(2):182-8.

37. Lan Y, Huang Y, Song Y, Ma L, Chen P, Ying Q, Li W, Cai Y, Zhou J. Prevalence, severity, and associated factors of menopausal symptoms in middle-aged Chinese women: a community-based cross-sectional study in southeast China. Menopause. 2017;24(10):1200-7.

38. Gao HL, Lin SQ, Wei Y, Chen Y, Wu ZL. The effect of age and menopausal status on musculoskeletal symptoms in Chinese women aged 35-64 years. Climacteric. 2013;16(6):639-45.

39. Li L, Wu J, Pu D, Zhao Y, Wan C, Sun L, Shen Ce, Sun W, Yuan Z, Shen Q, He X, Jiang J, Luo N, He Y, Qian Q, Cai P, Zhang M. Factors associated with the age of natural menopause and menopausal symptoms in Chinese women. Maturitas. 2012;73(4):354-60.

40. Yim G, Ahn Y, Chang Y, Ryu S, Lim JY, Kang D, Choi EK, Ahn J, Choi Y, Cho J, Park HY. Prevalence and severity of menopause symptoms and associated factors across menopause status in Korean women. Menopause. 2015;22(10):1108-16.

41. Chou MF, Wun YT, Pang SM. Menopausal symptoms and the menopausal rating scale among midlife Chinese women in Macau, China. Women Health. 2014;54(2): 115-26.

42. Shiwaku K, Yamane Y, Sugimura I, Hayasht M, Nojiri M, Matsushima S, Koyama W. Vasomotor and other menopausal symptoms influenced by menopausal stage and psychosocial factors in Japanese middle-aged women. J Occup Health. 2001; 43(6):356-64.

43. Chalise GD, Shrestha S, Thapa S, Bharati M, Pradhan S, Adhikari B. Health problems experienced by peri-menopausal women and their perception towards menopause. J Nepal Health Res Counc. 2022;20(01):102-7.

44. ChowtaN K, Sebastián J, ChowtaM N. Comparative study of menopausal symptoms in post menopausal and perimenopausal women; 2008. Available at: https://www.semanticscholar.org/paper/Comparative-Study-Of-Menopausal-Symptoms-in-Post-ChowtaN-Sebasti%C3%A1n/a1355c22ebea6b28923e6a3ac5af834fc49ff166. Accessed February 23, 2025.

45. Waidyasekera H, Wijewardena K, Lindmark G, Naessen T. Menopausal symptoms and quality of life during the menopausal transition in Sri Lankan women. Menopause. 2009;16(1):164-70.

46. Islam RM, Bell RJ, Billah B, Hossain MB, Davis SR. Prevalence and severity of vasomotor symptoms and joint pain in women at midlife in Bangladesh: a population-based survey. Menopause. 2016;23(7):731-9.

47. Marahatta RK. Study of menopausal symptoms among peri and postmenopausal women attending NMCTH. Nepal Med Coll J. 2012;14(3):251-5.

48. Poomalar GK, Arounassalame B. The quality of life during and after menopause among rural women. J Clin Diagn Res. 2013;7(1):135-9.

49. Rahman S, Salehin F, Iqbal A. Menopausal symptoms assessment among middle age women in Kushtia, Bangladesh. BMC Res Notes. 2011;4(1):188.

50. Thakur M, Kaur M, Sinha AK. Assessment of menopausal symptoms in different transition phases using the Greene Climacteric Scale among rural women of North India. Ann Hum Biol. 2019;46(1):46-55.

51. Delavar MA, Hajiahmadi M. Age at menopause and measuring symptoms at midlife in a community in Babol, Iran. Menopause. 2011;18(11):1213-8.

52. AlDughaither A, AlMutairy H, AlAteeq M. Menopausal symptoms and quality of life among Saudi women visiting primary care clinics in Riyadh, Saudi Arabia. Int J Womens Health. 2015;7:645-53.
53. Ceylan B, Özerdoğan N. Menopausal symptoms and quality of life in Turkish women in the climacteric period. Climacteric. 2014;17(6):705-12.
54. El Shafie K, Al Farsi Y, Al Zadjali N, Al Adawi S, Al Busaidi Z, Al Shafaee M. Menopausal symptoms among healthy, middle-aged Omani women as assessed with the Menopause Rating Scale. Menopause. 2011;18(10):1113-9.
55. Peeyananjarassri K, Cheewadhanaraks S, Hubbard M, Zoa Manga R, Manocha R, Eden J. Menopausal symptoms in a hospital-based sample of women in southern Thailand. Climacteric. 2006;9(1):23-9.
56. Syed Alwi SAR, Lee PY, Awi I, Mallik PS, Md Haizal MN. The menopausal experience among indigenous women of Sarawak, Malaysia. Climacteric. 2009; 12(6):548-56.
57. Wong BWX, Chan YH, Logan S, Kramer MS, Yong EL. Arthralgia in midlife Singaporean women: the Integrated Women's Health Program (IWHP). Climacteric. 2024;27(2):178-86.
58. Punyahotra S, Dennerstein L, Lehert P. Menopausal experiences of Thai women. Part 1: symptoms and their correlates. Maturitas. 1997;26(1):1-7.
59. Pérez JAM, Garcia FC, Palacios S, Pérez M. Epidemiology of risk factors and symptoms associated with menopause in Spanish women. Maturitas. 2009;62(1): 30-6.
60. Moilanen J, Aalto AM, Hemminki E, Aro AR, Raitanen J, Luoto R. Prevalence of menopause symptoms and their association with lifestyle among Finnish middle-aged women. Maturitas. 2010;67(4):368-74.
61. Okhai H, Sabin C, Haag K, Sherr L, Dhairyawan R, Shephard J, Richard G, Burns F, Post F, Jones R, Gilleece Y, Tariq S. The prevalence and patterns of menopausal symptoms in women living with HIV. AIDS Behav. 2022;26(11):3679-87.
62. Pansini F, Albertazzi P, Bonaccorsi G, Calisesi M, Campobasso C, Zanotti L, Bagni B, Mollica G. The menopausal transition: a dynamic approach to the pathogenesis of neurovegetative complaints. Eur J Obstet Gynecol Reprod Biol. 1994; 57(2):103-9.
63. Dugan SA, Powell LH, Kravitz HM, Everson Rose SA, Karavolos K, Luborsky J. Musculoskeletal pain and menopausal status. Clin J Pain. 2006;22(4):325-31.
64. Xu J, Bartoces M, Neale AV, Dailey RK, Northrup J, Schwartz KL. Natural history of menopause symptoms in primary care patients: a MetroNet study. J Am Board Fam Pract. 2005;18(5):374-82.
65. Miller SA, Santoro N, Lo Y, Howard AA, Arnsten JH, Floris-Moore M, Moskaleva G, Schoenbaum EE. Menopause symptoms in HIV-infected and drug-using women. Menopause. 2005;12(3):348-56.
66. Blümel JE, Chedraui P, Baron G, Belzares E, Bencosme A, Calle A, Danckers L, Espinoza MT, Flores D, Gomez G, Hernandez-Bueno JA, Izaguirre H, Leon-Leon P, Lima S, Mezones-Holguin E, Monterrosa A, Mostajo D, Navarro D, Ojeda E, Onatra W, Royer M, Soto E, Tserotas K, Vallejo MS. Menopausal symptoms appear before the menopause and persist 5 years beyond: a detailed analysis of a multinational study. Climacteric. 2012;15(6):542-51.
67. Olaolorun FM, Lawoyin TO. Experience of menopausal symptoms by women in an urban community in Ibadan, Nigeria. Menopause. 2009;16(4):822-30.
68. Yoon S, Lee DH, Bang J. Perimenopausal arthralgia in the shoulder. Menopause. 2018;25(1):98-101.
69. Shea AK, Buwembo A, Mayhew A, Sohel N, Griffith LE, Raina P. The association between primary ovarian insufficiency and osteoporosis in the Canadian Longitudinal Study on Aging. Menopause. 2021;28(6):693-8.
70. Wright VJ, Schwartzman JD, Itinoche R, Wittstein J. The musculoskeletal syndrome of menopause. Climacteric. 2024;27(5):466-72.
71. Vidal-Neira LF, Neyro JL, Maldonado G, Messina OD, Moreno-Alvarez M, Ríos C. Climacteric and fibromyalgia: a review. Climacteric. 2024;27(5):458-65.
72. Phiel KL, Henderson RA, Adelman SJ, Elloso MM. Differential estrogen receptor gene expression in human peripheral blood mononuclear cell populations. Immunol Lett. 2005;97(1):107-13.
73. Gulati M, Dursun E, Vincent K, Watt FE. The influence of sex hormones on musculoskeletal pain and osteoarthritis. Lancet Rheumatol. 2023;5(4):e225-e238.
74. Lugo L, Villalvilla A, Largo R, Herrero-Beaumont G, Roman-Blas JA. Selective estrogen receptor modulators (SERMs): new alternatives for osteoarthritis? Maturitas. 2014;77(4):380-4.
75. Lou C, Xiang G, Weng Q, Chen Z, Chen D, Wang Q, Zhang D, Zhou B, He D, Chen H. Menopause is associated with articular cartilage degeneration: a clinical study of knee joint in 860 women. Menopause. 2016;23(11):1239-46.
76. Di J, Bai J, Zhang J, Chen J, Hao Y, Bai J, Xiang C. Regional disparities, age-related changes and sex-related differences in knee osteoarthritis. BMC Musculoskelet Disord. 2024;25(1):66.
77. Vos T, Lim SS, Abbafati C, Abbas KM, Abbasi M, Abbasifard M, Abbasi-Kangevari M, Abbastabar H, Abd-Allah F, Abdelalim A, Abdollahi M, Abdollahpour I, Abolhassani H, Aboyans V, Abrams EM, Abreu LG, Abrigo MRM, Abu-Raddad LJ, Abushouk AI, Acebedo A, Ackerman IN, Adabi M, Adamu AA, Adebayo OM, Adekanmbi V, Adelson JD, Adetokunboh OO, Adham D, Afshari M, Afshin A, Agardh EE, Agarwal G, Agesa KM, Aghaali M, Aghamir SMK, Agrawal A, Ahmad T, Ahmadi A, Ahmadi M, Ahmadieh H, Ahmadpour E, Akalu TY, Akinyemi RO, Akinyemiju T, Akombi B, Al-Aly Z, Alam K, Alam N, Alam S, Alam T, Alanzi TM, Albertson SB, Alcalde-Rabanal JE, Alema NM, Ali M, Ali S, Alicandro G, Alijanzadeh M, Alinia C, Alipour V, Aljunid SM, Alla F, Allebeck P, Almasi-Hashiani A, Alonso J, Al-Raddadi RM, Altirkawi KA, Alvis-Guzman N, Alvis-Zakzuk NJ, Amini S, Amini-Rarani M, Aminorroaya A, Amiri F, Amit AML, Amugsi DA, Amul GGH, Anderlini D, Andrei CL, Andrei T, Anjomshoa M, Ansari F, Ansari I, Ansari-Moghaddam A, Antonio CAT, Antony CM, Antriyandarti E, Anvari D, Anwer R, Arabloo J, Arab-Zozani M, Aravkin AY, Ariani F, Ärnlöv J, Aryal KK, Arzani A, Asadi-Aliabadi M, Asadi-Pooya AA, Asghari B, Ashbaugh C, Atnafu DD, Atre SR, Ausloos F, Ausloos M, Ayala Quintanilla BP, Ayano G, Ayanore MA, Aynalem YA, Azari S, Azarian G, Azene ZN, Babaee E, Badawi A, Bagherzadeh M, Bakhshaei MH, Bakhtiari A, Balakrishnan S, Balalla S, Balassyano S, Banach M, Banik PC, Bannick MS, Bante AB, Baraki AG, Barboza MA, Barker-Collo SL, Barthelemy CM, Barua L, Barzegar A, Basu S, Baune BT, Bayati M, Bazmandegan G, Bedi N, Beghi E, Béjot Y, Bello AK, Bender RG, Bennett DA, Bennitt FB, Bensenor IM, Benziger CP, Berhe K, Bernabe E, Bertolacci GJ, Bhageerathy R, Bhala N, Bhandari D, Bhardwaj P, Bhattacharyya K, Bhutta ZA, Bibi S, Biehl MH, Bikbov B, Bin Sayeed MS, Biondi A, Birihane BM, Bisanzio D, Bisignano C, Biswas RK, Bohlouli S, Bohluli M, Bolla SRR, Boloor A, Boon-Dooley AS, Borges G, Borzi AM, Bourne R, Brady OJ, Brauer M, Brayne C, Breitborde NJK, Brenner H, Briant PS, Briggs AM, Briko NI, Britton GB, Bryazka D, Buchbinder R, Bumgarner BR, Busse R, Butt ZA, Caetano dos Santos FL, Cámera LLA, Campos-Nonato IR, Car J, Cárdenas R, Carreras G, Carrero JJ, Carvalho F, Castaldelli-Maia JM, Castañeda-Orjuela CA, Castelpietra G, Castle CD, Castro F, Catalá-López F, Causey K, Cederroth CR, Cercy KM, Cerin E, Chandan JS, Chang AR, Charlson FJ, Chattu VK, Chaturvedi S, Chimed-Ochir O, Chin KL, Cho DY, Christensen H, Chu DT, Chung MT, Cicuttini FM, Ciobanu LG, Cirillo M, Collins EL, Compton K, Conti S, Cortesi PA, Costa VM, Cousin E, Cowden RG, Cowie BC, Cromwell EA, Cross DH, Crowe CS, Cruz JA, Cunningham M, Dahlawi SMA, Damiani G, Dandona L, Dandona R, Darwesh AM, Daryani A, Das JK, Das Gupta R, das Neves J, Dávila-Cervantes CA, Davletov K, De Leo D, Dean FE, DeCleene NK, Deen A, Degenhardt L, Dellavalle RP, Demeke FM, Demsie DG, Denova-Gutiérrez E, Dereje ND, Dervenis N, Desai R, Desalew A, Dessie GA, Dharmaratne SD, Dhungana GP, Dianatinasab M, Diaz D, Dibaji Forooshani ZS, Dingels ZV, Dirac MA, Djalalinia S, Do HT, Dokova K, Dorostkar F, Doshi CP, Doshmangir L, Douiri A, Doxey MC, Driscoll TR, Dunachie SJ, Duncan BB, Duraes AR, Eagan AW, Ebrahimi Kalan M, Edvardsson D, Ehrlich JR, El Nahas N, El Sayed I, El Tantawi M, Elbarazi I, Elgendy IY, Elhabashy HR, El-Jaafary SI, Elyazar IR, Emamian MH, Emmons-Bell S, Erskine HE, Eshrati B, Eskandarieh S, Esmaeilnejad S, Esmaeilzadeh F, Esteghamati A, Estep K, Etemadi A, Etisso AE, Farahmand M, Faraj A, Fareed M, Faridnia R, Farinha CSeS, Farioli A, Faro A, Faruque M, Farzadfar F, Fattahi N, Fazlzadeh M, Feigin VL, Feldman R, Fereshtehnejad SM, Fernandes E, Ferrari AJ, Ferreira ML, Filip I, Fischer F, Fisher JL, Fitzgerald R, Flohr C, Flor LS, Foigt NA, Folayan MO, Force LM, Fornari C, Foroutan M, Fox JT, Freitas M, Fu W, Fukumoto T, Furtado JM, Gad MM, Gakidou E, Galles NC, Gallus S, Gamkrelidze A, Garcia-Basteiro AL, Gardner WM, Geberemariyam BS, Gebrehiwot AM, Gebremedhin KB, Gebreslassie AAAA, Gershberg Hayoon A, Gething PW, Ghadimi M, Ghadiri K, Ghafourifard M, Ghajar A, Ghamari F, Ghashghaee A, Ghiasvand H, Ghith N, Gholamian A, Gilani SA, Gill PS, Gitimoghaddam M, Giussani G, Goli S, Gomez RS, Gopalani SV, Gorini G, Gorman TM, Gottlich HC, Goudarzi H, Goulart AC, Goulart BNG, Grada A, Grivna M, Grosso G, Gubari MIM, Gugnani HC, Guimaraes ALS, Guimarães RA, Guled RA, Guo G, Guo Y, Gupta R, Haagsma JA, Haddock B, Hafezi-Nejad N, Hafiz A, Hagins H, Haile LM, Hall BJ, Halvaei I, Hamadeh RR, Hamagharib Abdullah K, Hamilton EB, Han C, Han H, Hankey GJ, Haro JM, Harvey JD, Hasaballah AI, Hasanzadeh A, Hashemian M, Hassanipour S, Hassankhani H, Havmoeller RJ, Hay RJ, Hay SI, Hayat K, Heidari B, Heidari G, Heidari-Soureshjani R, Hendrie D, Henrikson HJ, Henry NJ, Herteliu C, Heydarpour F, Hird TR, Hoek HW, Hole MK, Holla R, Hoogar P, Hosgood HD, Hosseinzadeh M, Hostiuc M, Hostiuc S, Househ M, Hoy DG, Hsairi M, Hsieh VCr, Hu G, Huda TM, Hugo FN, Huynh CK, Hwang BF, Iannucci VC, Ibitoye SE, Ikuta KS, Ilesanmi OS, Ilic IM, Ilic MD, Inbaraj LR, Ippolito H, Irvani SSN, Islam MM, Islam M, Islam SMS, Islami F, Iso H, Ivers RQ, Iwu CCD, Iyamu IO, Jaafari J, Jacobsen KH, Jadidi-Niaragh F, Jafari H, Jafarinia M, Jahagirdar D, Jahani MA, Jahanmehr N, Jakovljevic M, Jalali A, Jalilian F, James SL, Janjani H, Janodia MD, Jayatilleke AU, Jeemon P, Jenabi E, Jha RP, Jha V, Ji JS, Jia P, John O, John-Akinola YO, Johnson CO, Johnson SC, Jonas JB, Joo T, Joshi A, Jozwiak JJ, Jürisson M, Kabir A, Kabir Z, Kalani H, Kalani R, Kalankesh LR, Kalhor R, Kamiab Z, Kanchan T, Karami Matin B, Karch A, Karim MA, Karimi SE, Kassa GM, Kassebaum NJ, Katikireddi SV, Kawakami N, Kayode GA, Keddie SH, Keller C, Kereselidze M, Khafaie MA, Khalid N, Khan M, Khatab K, Khater MM, Khatib MN, Khayamzadeh M, Khodayari MT, Khundkar R, Kianipour N, Kieling C, Kim D, Kim YE, Kim YJ, Kimokoti RW, Kisa A, Kisa S, Kissimova-Skarbek K, Kivimäki M, Kneib CJ, Knudsen AKS, Kocarnik JM, Kolola T, Kopec JA, Kosen S, Koul PA, Koyanagi A, Kravchenko MA, Krishan K, Krohn KJ, Kuate Defo B, Kucuk Bicer B, Kumar GA, Kumar M, Kumar P, Kumar V, Kumaresh G, Kurmi OP, Kusuma D, Kyu HH, La Vecchia C, Lacey B, Lal DK, Lalloo R, Lam JO, Lami FH, Landires I, Lang JJ, Lansingh VC, Larson SL, Larsson AO, Lasrado S, Lassi ZS, Lau KMM, Lavados PM, Lazarus JV, Ledesma JR, Lee PH, Lee SWH, LeGrand KE, Leigh J, Leonardi M, Lescinsky H, Leung J, Levi M, Lewington S, Li S, Lim LL, Lin C, Lin RT, Linehan C, Linn S, Liu HC, Liu S, Liu Z, Looker KJ, Lopez AD, Lopukhov PD, Lorkowski S, Lotufo PA, Lucas TCD, Lugo A, Lunevicius R, Lyons RA, Ma J, MacLachlan JH, Maddison ER, Maddison R, Madotto F, Mahasha PW, Mai HT, Majeed A, Maled V, Maleki S, Malekzadeh R, Malta DC, Mamun AA, Manafi A, Manafi N, Manguerra H, Mansouri B, Mansournia MA, Mantilla Herrera AM, Maravilla JC,

Marks A, Martins-Melo FR, Martopullo I, Masoumi SZ, Massano J, Massenburg BB, Mathur MR, Maulik PK, McAlinden C, McGrath JJ, McKee M, Mehndiratta MM, Mehri F, Mehta KM, Meitei WB, Memiah PTN, Mendoza W, Menezes RG, Mengesha EW, Mengesha MB, Mereke A, Meretoja A, Meretoja TJ, Mestrovic T, Miazgowski B, Miazgowski T, Michalek IM, Mihretie KM, Miller TR, Mills EJ, Mirica A, Mirrakhimov EM, Mirzaei H, Mirzaei M, Mirzaei-Alavijeh M, Misganaw AT, Mithra P, Moazen B, Moghadaszadeh M, Mohamadi E, Mohammad DK, Mohammad Y, Mohammad Gholi Mezerji N, Mohammadian-Hafshejani A, Mohammadifard N, Mohammadpourhodki R, Mohammed S, Mokdad AH, Molokhia M, Momen NC, Monasta L, Mondello S, Mooney MD, Moosazadeh M, Moradi G, Moradi M, Moradi-Lakeh M, Moradzadeh R, Moraga P, Morales L, Morawska L, Moreno Velásquez I, Morgado-da-Costa J, Morrison SD, Mosser JF, Mouodi S, Mousavi SM, Mousavi Khaneghah A, Mueller UO, Munro SB, Muriithi MK, Musa KI, Muthupandian S, Naderi M, Nagarajan AJ, Nagel G, Naghshtabrizi B, Nair S, Nandi AK, Nangia V, Nansseu JR, Nayak VC, Nazari J, Negoi I, Negoi RI, Netsere HBN, Ngunjiri JW, Nguyen CT, Nguyen J, Nguyen M, Nguyen M, Nichols E, Nigatu D, Nigatu YT, Nikbakhsh R, Nixon MR, Nnaji CA, Nomura S, Norrving B, Noubiap JJ, Nowak C, Nunez-Samudio V, Oţoiu A, Oancea B, Odell CM, Ogbo FA, Oh IH, Okunga EW, Oladnabi M, Olagunju AT, Olusanya BO, Olusanya JO, Oluwasanu MM, Omar Bali A, Omer MO, Ong KL, Onwujekwe OE, Orji AU, Orpana HM, Ortiz A, Ostroff SM, Otstavnov N, Otstavnov SS, Øverland S, Owolabi MO, P A M, Padubidri JR, Pakhare AP, Palladino R, Pana A, Panda-Jonas S, Pandey A, Park EK, Parmar PGK, Pasupula DK, Patel SK, Paternina-Caicedo AJ, Pathak A, Pathak M, Patten SB, Patton GC, Paudel D, Pazoki Toroudi H, Peden AE, Pennini A, Pepito VCF, Peprah EK, Pereira A, Pereira DM, Perico N, Pham HQ, Phillips MR, Pigott DM, Pilgrim T, Pilz TM, Pirsaheb M, Plana-Ripoll O, Plass D, Pokhrel KN, Polibin RV, Polinder S, Polkinghorne KR, Postma MJ, Pourjafar H, Pourmalek F, Pourmirza Kalhori R, Pourshams A, Poznańska A, Prada SI, Prakash V, Pribadi DRA, Pupillo E, Quazi Syed Z, Rabiee M, Rabiee N, Radfar A, Rafiee A, Rafiei A, Raggi A, Rahimi-Movaghar A, Rahman MA, Rajabpour-Sanati A, Rajati F, Ramezanzadeh K, Ranabhat CL, Rao PC, Rao SJ, Rasella D, Rastogi P, Rathi P, Rawaf DL, Rawaf S, Rawal L, Razo C, Redford SB, Reiner RC Jr, Reinig N, Reitsma MB, Remuzzi G, Renjith V, Renzaho AMN, Resnikoff S, Rezaei N, Rezai Ms, Rezapour A, Rhinehart PA, Riahi SM, Ribeiro ALP, Ribeiro DC, Ribeiro D, Rickard J, Roberts NLS, Roberts S, Robinson SR, Roever L, Rolfe S, Ronfani L, Roshandel G, Roth GA, Rubagotti E, Rumisha SF, Sabour S, Sachdev PS, Saddik B, Sadeghi E, Sadeghi M, Saeidi S, Safi S, Safiri S, Sagar R, Sahebkar A, Sahraian MA, Sajadi SM, Salahshoor MR, Salamati P, Salehi Zahabi S, Salem H, Salem MRR, Salimzadeh H, Salomon JA, Salz I, Samad Z, Samy AM, Sanabria J, Santomauro DF, Santos IS, Santos JV, Santric-Milicevic MM, Saraswathy SYI, Sarmiento-Suárez R, Sarrafzadegan N, Sartorius B, Sarveazad A, Sathian B, Sathish T, Sattin D, Sbarra AN, Schaeffer LE, Schiavolin S, Schmidt MI, Schutte AE, Schwebel DC, Schwendicke F, Senbeta AM, Senthilkumaran S, Sepanlou SG, Shackelford KA, Shadid J, Shahabi S, Shaheen AA, Shaikh MA, Shalash AS, Shams-Beyranvand M, Shamsizadeh M, Shannawaz M, Sharafi K, Sharara F, Sheena BS, Sheikhtaheri A, Shetty RS, Shibuya K, Shiferaw WS, Shigematsu M, Shin JI, Shiri R, Shirkoohi R, Shrime MG, Shuval K, Siabani S, Sigfusdottir ID, Sigurvinsdottir R, Silva JP, Simpson KE, Singh A, Singh JA, Skiadaresi E, Skou ST, Skryabin VY, Sobngwi E, Sokhan A, Soltani S, Sorensen RJD, Soriano JB, Sorrie MB, Soyiri IN, Sreeramareddy CT, Stanaway JD, Stark BA, Ştefan SC, Stein C, Steiner C, Steiner TJ, Stokes MA, Stovner LJ, Stubbs JL, Sudaryanto A, Sufiyan MB, Sulo G, Sultan I, Sykes BL, Sylte DO, Szócska M, Tabarés-Seisdedos R, Tabb KM, Tadakamadla SK, Taherkhani A, Tajdini M, Takahashi K, Taveira N, Teagle WL, Teame H, Tehrani-Banihashemi A, Teklehaimanot BF, Terrason S, Tessema ZT, Thankappan KR, Thomson AM, Tohidinik HR, Tonelli M, Topor-Madry R, Torre AE, Touvier M, Tovani-Palone MRR, Tran BX, Travillian R, Troeger CE, Truelsen TC, Tsai AC, Tsatsakis A, Tudor Car L, Tyrovolas S, Uddin R, Ullah S, Undurraga EA, Unnikrishnan B, Vacante M, Vakilian A, Valdez PR, Varughese S, Vasankari TJ, Vasseghian Y, Venketasubramanian N, Violante FS, Vlassov V, Vollset SE, Vongpradith A, Vukovic A, Vukovic R, Waheed Y, Walters MK, Wang J, Wang Y, Wang YP, Ward JL, Watson A, Wei J, Weintraub RG, Weiss DJ, Weiss J, Westerman R, Whisnant JL, Whiteford HA, Wiangkham T, Wiens KE, Wijeratne T, Wilner LB, Wilson S, Wojtyniak B, Wolfe CDA, Wool EE, Wu AM, Wulf Hanson S, Wunrow HY, Xu G, Xu R, Yadgir S, Yahyazadeh Jabbari SH, Yamagishi K, Yaminfirooz M, Yano Y, Yaya S, Yazdi-Feyzabadi V, Yearwood JA, Yeheyis TY, Yeshitila YG, Yip P, Yonemoto N, Yoon SJ, Yoosefi Lebni J, Younis MZ, Younker TP, Yousefi Z, Yousefifard M, Yousefinezhadi T, Yousuf AY, Yu C, Yusefzadeh H, Zahirian Moghadam T, Zaki L, Zaman SB, Zamani M, Zamanian M, Zandian H, Zangeneh A, Zastrozhin MS, Zewdie KA, Zhang Y, Zhang ZJ, Zhao JT, Zhao Y, Zheng P, Zhou M, Ziapour A, Zimsen SRM, Naghavi M, Murray CJL. Global burden of 369 diseases and injuries in 204 countries and territories, 1990-2019: a systematic analysis for the Global Burden of Disease Study 2019. Lancet. 2020;396(10258):1204-22.

78. Boyan BD, Hart DA, Enoka RM, Nicolella DP, Resnick E, Berkley KJ, Sluka KA, Kwoh CK, Tosi LL, O'Connor MI, Coutts RD, Kohrt WM. Hormonal modulation of connective tissue homeostasis and sex differences in risk for osteoarthritis of the knee. Biol Sex Differ. 2013;4(1):3.

79. Cui A, Li H, Wang D, Zhong J, Chen Y, Lu H. Global, regional prevalence, incidence and risk factors of knee osteoarthritis in population-based studies. EClinicalMedicine. 2020;29-30:100587.

80. Ding C, Cicuttini F, Blizzard L, Scott F, Jones G. A longitudinal study of the effect of sex and age on rate of change in knee cartilage volume in adults. Rheumatology (Oxford). 2006;46(2):273-9.

81. Cirillo DJ, Wallace RB, Wu L, Yood RA. Effect of hormone therapy on risk of hip and knee joint replacement in the Women's Health Initiative. Arthritis Rheum. 2006; 54(10):3194-204.

82. Dennison EM. Osteoarthritis: the importance of hormonal status in midlife women. Maturitas. 2022;165:8-11.

83. Watt FE. Hand osteoarthritis, menopause and menopausal hormone therapy. Maturitas. 2016;83:13-8.

84. Camon C, Garratt M, Correa SM. Exploring the effects of estrogen deficiency and aging on organismal homeostasis during menopause. Nat Aging. 2024;4(12):1731-44.

85. Maffulli N, Waterston SW, Squair J, Reaper J, Douglas S. Changing incidence of Achilles tendon rupture in Scotland: a 15-year study. Clin J Sport Med. 1999;9(3): 157-60.

86. Cook JL, Khan KM, Kiss ZS, Griffiths L. Patellar tendinopathy in junior basketball players: a controlled clinical and ultrasonographic study of 268 patellar tendons in players aged 14-18 years. Scand J Med Sci Sports. 2000; 10(4):216-20.

87. Leblanc DR, Schneider M, Angele P, Vollmer G, Docheva D. The effect of estrogen on tendon and ligament metabolism and function. J Steroid Biochem Mol Biol. 2017;172:106-16.

88. Chidi-Ogbolu N, Baar K. Effect of estrogen on musculoskeletal performance and injury risk. Front Physiol. 2019;9:1834.

89. Maltais ML, Desroches J, Dionne IJ. Changes in muscle mass and strength after menopause. J Musculoskelet Neuronal Interact. 2009;9(4):186-97.

90. Shivers KY, Amador N, Abrams L, Hunter D, Jenab S, Quiñones-Jenab V. Estrogen alters baseline and inflammatory-induced cytokine levels independent from hypothalamic–pituitary–adrenal axis activity. Cytokine. 2015;72(2):121-9.

91. Chlebowski RT, Cirillo DJ, Eaton CB, Stefanick ML, Pettinger M, Carbone LD, Johnson KC, Simon MS, Woods NF, Wactawski-Wende J. Estrogen alone and joint symptoms in the Women's Health Initiative randomized trial. Menopause. 2013; 20(6):600-8.

92. Hou WY, Zhu CY, Gu YF, Zhu L, Zhou ZX. Association of hormone replacement therapy and the risk of knee osteoarthritis: a meta-analysis. Medicine (Baltimore). 2022;101(51):e32466.

93. Zhou M, Chen J, Wang D, Zhu C, Wang Y, Chen W. Combined effects of reproductive and hormone factors and obesity on the prevalence of knee osteoarthritis and knee pain among middle-aged or older Chinese women: a cross-sectional study. BMC Public Health. 2018;18(1):1192.