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Are there differences in symptoms experienced by midlife climacteric women with and without metabolic syndrome? A scoping review

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Abstract

Introduction: Midlife climacteric women with metabolic syndrome are at high risk for experiencing a complex array of symptoms. The aim of this scoping review was to identify the prevalence, types, and clustering of symptoms in midlife climacteric women with metabolic syndrome and to compare them to symptoms of midlife climacteric women without metabolic syndrome.

Methods: A three-step search method was used according to Joanna Briggs Institute methodology. Eligibility criteria of participants, concept, context, and types of evidence were selected in alignment with the review questions. Seven databases (PubMed, Embase, Web of Science, CINAHL, PsycINFO, ProQuest Dissertation & Theses, OpenGrey) were searched using search terms with no language or date restrictions. Title and abstract screening, full-text review, data charting, and data synthesis were conducted by two independent researchers based on the eligibility criteria.

Results: The search yielded 3813 studies after removing duplicates with 48 full-text papers assessed for eligibility. A total of eight studies were reviewed and analyzed which reported the prevalence and types of symptoms individually or grouped based on each body system. Midlife climacteric women with metabolic syndrome experience a wide prevalence of individual and grouped urogenital, vasomotor, psychological, sleep, and somatic symptoms. Mental exhaustion had the highest prevalence (84.4%) among the individual symptoms, and urogenital symptoms had the highest prevalence (81.3%) among the grouped symptoms. There were mixed findings on symptoms between midlife climacteric women with metabolic syndrome and without metabolic syndrome. No studies focused on symptom clusters.

Conclusion: Our findings will serve as a knowledge basis for understanding symptoms experienced by midlife climacteric women with metabolic syndrome. This new knowledge can assist clinicians in effectively assessing and managing their symptoms in clinical settings and inform future development of targeted symptom management interventions.

Keywords

menopause, midlife, symptoms, Syndrome X, women's health

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Introduction

Impacting an estimated quarter of the world's population, metabolic syndrome has become a global public health problem due to its association with type 2 diabetes, cardiovascular disease, and cancer.[1,2] Metabolic syndrome is a cluster of metabolic abnormalities and requires at least three metabolic abnormalities to co-occur for its clinical

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diagnosis.[3] These metabolic abnormalities include elevated waist circumference, elevated triglyceride levels, reduced high-density lipoprotein (HDL), elevated blood pressure, and elevated blood glucose.[2] Women have a higher prevalence than men due to hormonal changes associated with menopause that lead to metabolic disturbances.[4,5]

To date, symptoms associated with metabolic syndrome have been examined. Clinical diagnostic criteria of metabolic syndrome such as central obesity, hypertension, insulin resistance, and atherogenic dyslipidemia facilitate aging and inflammation in midlife women and result in a unique set of symptoms.[6] These symptoms include pain, sleep disturbance, sexual dysfunction, and altered mood.[6–10] In addition, having metabolic syndrome may lead to a psychological burden, which can negatively influence a healthy lifestyle and develop symptoms related to lifestyle such as feeling of loneliness.[11,12] A cross-sectional cohort study found that people with metabolic syndrome are more likely to suffer from neck pain compared to healthy people.[10] In addition, the diagnosis of metabolic syndrome has been significantly associated with a higher prevalence of sexual dysfunction.[13] As such, midlife women with metabolic syndrome experience a complex array of symptoms that leads to significant symptom burden and impaired health-related quality of life.[6,8,9,14]

There are three main stages of menopause that include pre-menopause, peri-menopause, and post-menopause.[15] Peri-menopause refers to a period of time when a woman experiences irregularity in the menstrual cycles of at least 7 days from fluctuating hormonal levels or skips a menstrual cycle.[15,16] When a woman does not have menses for more than 12 consecutive months, they enter into post-menopause. Peri-menopause and post-menopause are also referred to as the climacteric which is a period of time from the decline to end in ovarian activity and function.[17] Hormonal changes, such as a decrease in estrogen, and changes in menstrual cycles start during peri-menopause and continue through post-menopause.[16] A climacteric woman has shown to experience significantly more menopausal symptoms such as hot flashes, night sweats, sleep disturbances, and altered mood than a woman in pre-menopause.[18,19] These troublesome symptoms often last more than a decade which results in impaired health-related quality of life.[20–23]

Midlife refers to a period of life between age 40 and 65 years in which a complex interaction of biological, psychological, and social factors exists and affects the overall well-being of women.[24,25] This is when women begin to experience biochemical changes with aging and psychological distress with social role changes.[25] Compared to other life stages, midlife is a vulnerable period of time when women begin to experience adverse changes in lipid and endocrine profiles that accelerate with peri-menopause.[26]

When the two conditions of metabolic syndrome and climacteric co-occur, midlife climacteric women with metabolic syndrome are placed at a higher risk for significant symptom burden.[20,22] This may be due to the combined effects of symptoms associated with metabolic syndrome and climacteric, respectively. To date, there are studies that systematically reviewed only certain types of symptoms (i.e. vasomotor symptoms) experienced by midlife climacteric women with metabolic syndrome.[27] Yet, none of the studies have provided a broad review of their symptoms and how their symptoms may differ from midlife climacteric women without metabolic syndrome.[20,22] A comprehensive understanding of symptoms experienced by midlife climacteric women with metabolic syndrome is critical because when these symptoms are underdiagnosed or undertreated, they may have a negative impact on patient outcomes such as quality of life, functional ability, and health outcomes.[28,29] Furthermore, findings from this scoping review will serve as a knowledge basis to inform future development of targeted symptom management interventions.[28,29]

An initial search of PROSPERO, Open Science Framework (OSF), Cochrane Database of Systematic Reviews, and the Joanna Briggs Institute (JBI) Database of Systematic Reviews and Implementation Reports indicated that there are neither systematic reviews nor scoping reviews, published or in progress, on this topic. A scoping review synthesizes research evidence and aims to map the existing literature pertaining to a research question.[30] A scoping review was selected for this study because there is a critical need for examining the extent of research on the symptom experience in midlife climacteric women with metabolic syndrome and to identify gaps for future research.[30,31] Therefore, the objective of this scoping review is to systematically review the current literature and to answer the following research questions.

RQ1. What are the types and prevalence of symptoms experienced by midlife climacteric women with metabolic syndrome?

RQ2. Do differences exist in the types and/or prevalence of symptoms between midlife climacteric women with metabolic syndrome and midlife climacteric women without metabolic syndrome?

RQ3. Do the symptoms occur in clusters in midlife climacteric women with metabolic syndrome?

Methods

The JBI Scoping Review methodology served as a guide for this scoping review.[32,33] An a priori scoping review protocol was utilized which provides a detailed plan for the scoping review and decreases the risk of reporting bias.[32,33] In addition, we adhered to the Preferred Reporting Items

for Systematic reviews and Meta-Analyses extension for Scoping Reviews for the development of this article (PRISMA-ScR).[34] The project was registered with OSF (Registration DOI: 10.17605/OSF.IO/8NV67).

Eligibility criteria

Eligibility criteria were selected in alignment with the review questions. The criteria categories included participants, concept, and context as well as types of evidence.[35] Details of the criteria are presented below.

Participants. Participants included midlife women with metabolic syndrome. Metabolic syndrome is defined as having three or more of the following conditions: elevated waist circumference, elevated triglyceride, reduced HDL, elevated blood pressure, and elevated blood glucose.[2] Midlife women aged 40 to 65 years were included.[24] Studies of mixed population of age were included as long as there was a sub-analysis with midlife women. For the second aim, studies that provided a comparison of the types and/or symptoms between midlife women with and without metabolic syndrome were included.

Concepts. The concepts included symptom(s) and symptom cluster(s). Symptom is defined as the subjective expression of physical or mental disturbances experienced by the patient.[29,36] Symptom cluster is defined as a group of two or more co-occurring symptoms that are associated with each other.[29,36] Therefore, studies that explored the types (category of symptoms) and/or prevalence of symptoms experienced by midlife women with metabolic syndrome in peri-menopause and post-menopause were identified. In addition, studies that identified symptom clusters in this population were also included.

Context. This scoping review considered studies that included the context of climacteric that includes peri-menopause (early and late peri-menopause) and/or post-menopause.[17]

Types of evidence. Study designs considered included quantitative, qualitative, and mixed methods study designs. In addition, case studies, systematic reviews, conference and abstract papers, and dissertations were included in this scoping review. Exclusion criteria consisted of editorials, letters to the editor, commentaries, and literature reviews without systematic approach due to their potential for bias and animal-only studies due to lack of data relevance during the searching.

The search

Information sources. The databases searched included PubMed (MEDLINE), Embase (Elsevier), Web of Science (Clarivate), CINAHL (EBSCO), and PsycINFO (EBSCOHost). Sources of unpublished studies and gray literature included ProQuest Dissertation & Theses, and OpenGrey.

Search strategy. The search strategy aimed to find both published and unpublished primary studies, including gray literature. A three-step search strategy was conducted. First, there was an initial exploratory search of PubMed (MEDLINE) and CINAHL (EBSCO) to identify relevant articles on the topic. With the help of a medical research librarian (L.L.), an analysis of keywords included in the title and abstracts of relevant articles as well as index terms was conducted to finalize a search strategy within PubMed (MEDLINE). Table 1 details the search strategy used for PubMed (MEDLINE). Second, the finalized PubMed (MEDLINE) search strategy was translated into each included database using the appropriate syntax and index terms for that database to search for relevant articles. The search was not limited by language or date. Search hedges or database filters were used to remove publication types such as editorials, letters, case reports, and comment as was appropriate for each database. The search was conducted on 2 February 2021 and found a total of 6462 citations. Complete reproducible search strategies, including date ranges and search filters, for all databases are detailed in Appendix 1. Third, the reference lists of the final included articles were reviewed, and citation tracking in Web of Science and Scopus was used to identify relevant studies for full-text review but none were added.

Selection of evidence sources. After the search, all identified studies were uploaded into Covidence (Veritas Health Innovation, Melbourne, Australia), a software system for managing systematic reviews and duplicates were removed by the software. A final set of 3813 citations was left to be screened in the title/abstract phase. A pilot screening was conducted for a random sample of 30 articles in order to test the predetermined inclusion and exclusion and to train the screeners. Two independent reviewers then screened the titles and abstracts against the finalized inclusion/exclusion criteria. For the full-text screening stage, papers were also reviewed in detail by two independent reviewers and were excluded if they did not meet the inclusion criteria. Any conflicts between the two independent reviewers were resolved through discussion at each stage of the selection process. For papers not published in English that met the inclusion criteria during the title/abstract screening, the abstracts were reviewed for usable data. However, we chose not to have these papers translated due to restrictions in funding and they were excluded at the full-text screening phase. The results of the search are presented in PRISMA-ScR flow diagram.[34]

Data charting. We used a modified JBI data extraction tool (JBI SUMARI, Adelaide, Australia) for data charting. Two

Table 1. Search strategy for PubMed (MEDLINE).

1	"Metabolic Syndrome"[Mesh] OR "Abdominal obesity metabolic syndrome" [Supplementary Concept] OR "Metabolic syndrome"[tw] OR "Metabolic Syndromes"[tw] OR "Insulin Resistance Syndrome X"[tw] OR "Metabolic X Syndrome"[tw] OR "Dysmetabolic Syndrome X"[tw] OR "Reaven Syndrome"[tw] OR "Metabolic Cardiovascular Syndrome"[tw] OR "Syndrome X"[tw]	61,460
2	"Menopause"[Mesh] OR "Postmenopause"[Mesh] OR "Perimenopause"[Mesh] OR Menopause[tw] OR perimenopause[tw] OR "peri menopause"[tw] OR "post menopause"[tw] OR "postmenopause"[tw] OR Postmenopausal[tw] OR "Post menopausal"[tw] OR menopausal[tw] OR perimenopausal[tw] OR "peri menopausal"[tw] OR Menopauses[tw] OR "Climacteric"[Mesh] OR Climacterics[tw] OR climacterium[tw]	114,305
4	#1 AND #2	1527
5	NOT (Editorial[pt] OR Letter[pt] OR Case Reports[pt] OR Comment[pt]) NOT (animals[mh] NOT humans[mh])	1429

Included dates: 1966 and selected coverage of literature prior to that period to 2 February 2021.

independent reviewers charted and reviewed the data. The data included study characteristics such as name of author(s), year of publication, study location, study design, and symptom rating instrument. In addition, we charted population characteristics (demographic and clinical characteristics), concept (types and/or prevalence of symptoms defined as the reported frequency/percentage of population experiencing symptoms, comparison of symptoms between metabolic syndrome and without metabolic syndrome group, presence of symptom clusters), context (climacteric stage), and key study findings related to the scoping review questions.[37,38] Any conflicts between the two independent reviewers were resolved through discussion during charting.

Data synthesis. Data were analyzed using the charted data according to each review question, and the results were discussed with two independent reviewers. Data were presented in a tabular format aligning with the questions. A narrative summary accompanies the tables and aligns the results with the review questions.

Results

Study inclusion

Database searches yielded 6462 articles with 2649 duplicate articles removed, thereby leaving 3813 articles for title and abstract screening. After title and abstract screening, the full texts of the 48 articles were assessed in accordance to inclusion criteria with 39 articles were excluded. As a result, a total of nine articles initially met inclusion for this scoping review. See Figure 1 for the PRISMA-ScR flow diagram of search results.

Characteristics of included studies

Study characteristics of all included studies in this review are presented in Table 2.[39–47] Among a total of nine articles, seven were cross-sectional design with one prospective cohort study and one systematic review. The systematic review conducted in the Netherlands by van Dijk et al.[47] has been excluded from data analysis because it included only one study related to our questions,[41] which was already included for review, thereby leaving eight articles. All included studies were published between 2009 and 2020, and were conducted outside the United States. A variety of symptom rating instruments were used to measure the symptoms with Female Sexual Function Index as the most commonly used instrument.[39,40,43,44] Midlife women in all of the studies were in post-menopause and only one study included women in both peri-menopause and post-menopause.

The type and prevalence of symptoms

Urogenital symptoms, vasomotor symptoms, psychological symptoms, sleep symptoms, and somatic symptoms were consistently observed in midlife climacteric women with metabolic syndrome.[39–46] Urogenital symptoms were the most frequently assessed, while sleep and somatic symptoms were the least frequently assessed. Some of the studies reported aggregated symptoms based on a specific body system, whereas other studies focused on specific individual symptoms. To account for such difference, symptoms were categorized into either grouped symptoms or individual symptoms to allow for a better comparison across the studies. Refer to Table 3 for further details.

Urogenital symptoms: grouped symptoms. More than half of the articles (75%) discussed urogenital symptoms experienced by midlife climacteric women with metabolic syndrome.[39,41,42,44] These urogenital symptoms were categorized into grouped urinary symptoms, which is a constellation of difficulty in urinating, increased need to urinate, and bladder incontinence, and sexual symptoms, which is a constellation of change in sexual desire, arousal, lubrication, satisfaction, orgasm, and pain during sexual intercourse. Among all the grouped symptoms, urogenital symptoms had the highest prevalence. The prevalence of grouped urinary symptoms was 67.2% which was reported in only one study,[41] while the prevalence of grouped sexual symptoms ranged from 46.0% to 81.3%.[39,41,42,44]

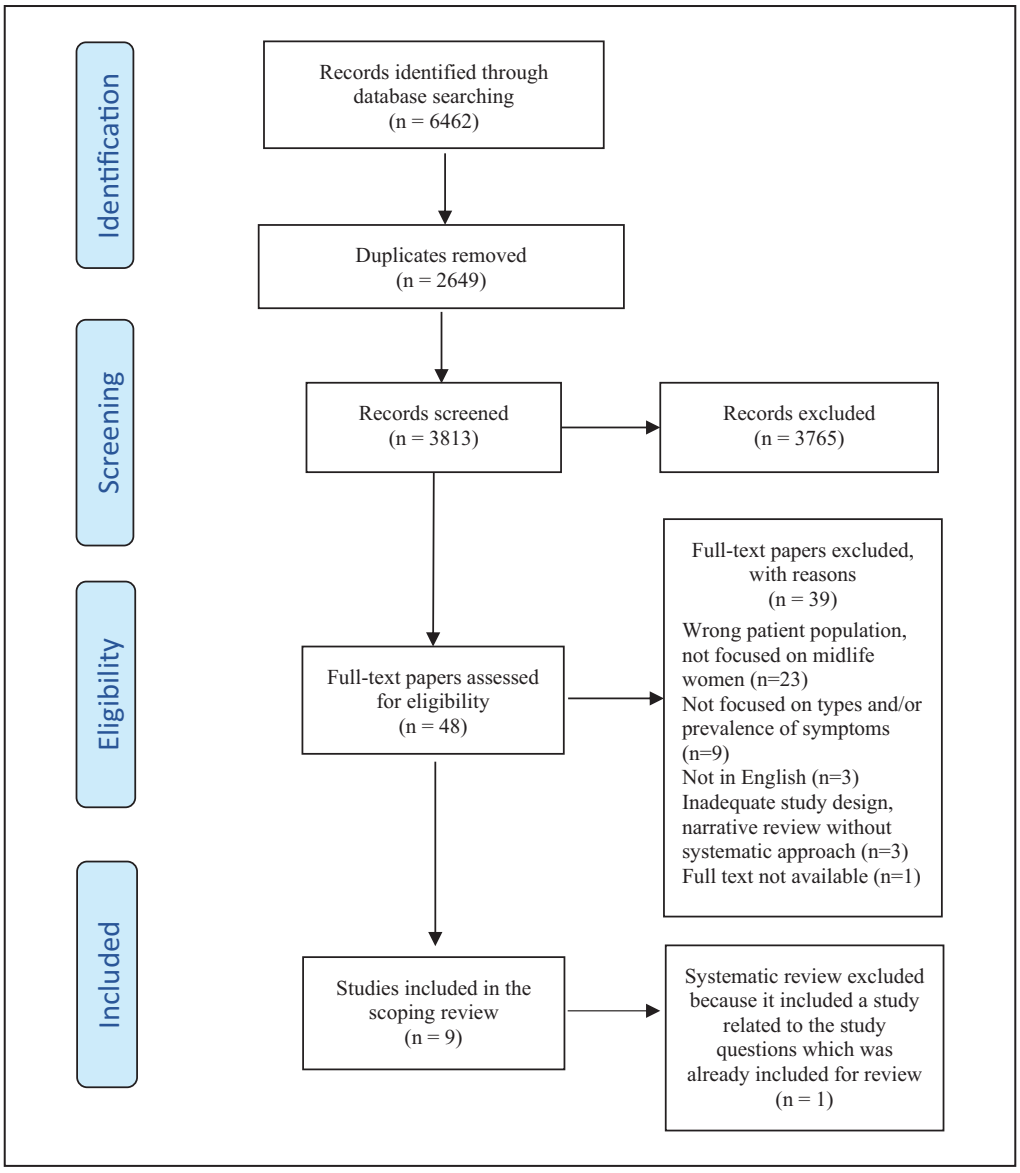

Figure 1. Search results, and study selection and inclusion process.

Urogenital symptoms: individual symptoms. Among the six studies on grouped urogenital symptoms, three studies also focused on reporting individual sexual symptoms.[40,41,43] One study discussed the prevalence of individual sexual symptoms in midlife climacteric women with metabolic syndrome, while two studies included those only in post-menopause.[40,41,43] Some of the most frequently reported individual sexual symptoms were vaginal dryness (62.5%), change in sexual desire (44.7%), and decreased sexual lubrication (13.8%–44.7%).[40,41,43] None of these studies included individual urinary symptoms experienced in this population.

Vasomotor symptoms: grouped symptoms. Vasomotor symptoms and their prevalence were identified for midlife women with metabolic syndrome in post-menopause in three studies.[41,45,46] These grouped vasomotor symptoms included hot flash, sweating, and night sweats. The overall reported prevalence of grouped vasomotor symptoms ranged from 65.4% to 75.0%.[41,45,46] In addition, the number of clinical diagnostic components of metabolic syndrome had a significant linear association with the prevalence of vasomotor symptoms.[45] For example, there was a 65.4% prevalence with three diagnostic components satisfied and it increased to 68.3% when four diagnostic components were satisfied.[45]

Vasomotor symptoms: individual symptoms. There were no studies that focused on individual vasomotor symptoms and their prevalence.

Table 2. Study characteristics.

Reference	Location	Study design	Symptom rating instrument	Population	Population characteristics	Climacteric stage
da Silva et al.[39]	Brazil	Cross-sectional design	Female Sexual Function Index	$N = 291$ post-menopausal women in total $N = 153$ with metabolic syndrome (52.6%) $N = 138$ without metabolic syndrome (47.4%)	Aged between 40 and 65 years Mean age: 54.4 ± 6 years; Race: White (58.2%), Brown (26.1%), and Black (15.7%) Mean age: 53.4 ± 4.8 years, $p = 0.118$; Race: White (58.0%), Brown (24.6%), and Black (17.4%), $p = 0.908$	Post-menopause
Kim et al.[40]	South Korea	Cross-sectional design	Female Sexual Function Index	$N = 773$ menopausal women $N = 94$ (12.2%) with metabolic syndrome $N = 679$ (87.8%) without metabolic syndrome	Aged 40–65 years (median: 48 years) Median age: 50 (47–55) years, comorbidity of hypertension and hypercholesterolemia (32.98%, 24.47%) Median age: 48 (45–51) years, $p < 0.001$**; comorbidity of hypertension and hypercholesterolemia (4.27%, 3.39%), $p < 0.001$**	Pre-menopause,[a] peri-menopause, post-menopause
Lee et al.[41]	South Korea	Cross-sectional design	Menopause Rating Scale	$N = 183$ post-menopausal women $N = 64$ (35.0%) with metabolic syndrome $N = 119$ (65.0%) without metabolic syndrome	NS Mean age: 56.1 ± 6.8 years, Years since menopause: 6.8 ± 4.2 years Mean age: 54.2 ± 4.9 years, $p = 0.020$**; Years since menopause: 5.3 ± 4.2 years, $p = 0.026$**	Post-menopause
Llaneza et al.[42]	Spain	Prospective cohort study	Cervantes Scale	$N = 110$ insulin resistant post-menopausal women $N = 56$ (50.9%) with metabolic syndrome $N = 54$ (49.1%) without metabolic syndrome	Aged between 50 and 65 years NS NS	Post-menopause
Martelli et al.[43]	Italy	Cross-sectional design	Female Sexual Function Index, Female Sexual Distress Scale	$N = 208$ post-menopausal women with metabolic syndrome $N = 103$ (49.5%) with metabolic syndrome $N = 105$ (50.5%) without metabolic syndrome	Aged between 50 and 65 years Mean age: 57.7 ± 4.9 years, Years of menopause: 8.2 ± 5.9 years Mean age: 56.5 ± 5 years, $p = 0.08$; Years of menopause: 7.2 ± 5.5 years, $p = 0.22$	Post-menopause
Otunctemur et al.[44]	Turkey	Prospective cross-sectional design	Female Sexual Function Index	$N = 400$ women with metabolic syndrome $N = 200$ pre-menopause and post-menopause with metabolic syndrome $N = 200$ pre-menopause and post-menopause without metabolic syndrome	NS Mean age: 48.52 ± 8.16 years, Diagnosis of hypertension: 62% Mean age: 48.81 ± 8.31 years, $p = 0.52$; Diagnosis of hypertension: 42.5%, $p < 0.001$[a]	Pre-menopause,[a] post-menopause
Ryu et al.[45]	South Korea	Cross-sectional design	Menopause Rating Scale	$N = 1906$ Korean post-menopausal women $N = 370$ (19.4%) with metabolic syndrome	Aged between 45 and 65 years NS	Post-menopause
Sayan et al.[46]	Turkey	Cross-sectional design	Study-designed questionnaire	NR $N = 200$ post-menopausal women $N = 48$ (24.0%) with metabolic syndrome $N = 152$ (76.0%) without metabolic syndrome	Mean age: 51.9 ± 5.65 years, Menopause age: 46.8 ± 5.2 years NS NS	Post-menopause
van Dijk et al.[47]	The Netherlands	Systematic review	Menopause Rating Scale	$N = 1$ study by Lee et al.[41] focused on the association between vasomotor symptoms and metabolic syndrome	NA	Post-menopause

NS: not specified; NA: not applicable; NR: not reported.
[a]Not included in this analysis.
**Statistically significant, $p < 0.05$.

Table 3. Prevalence of symptoms.

Reference	Reported symptoms	Prevalence of symptoms	Prevalence of severe symptoms
Urogenital symptoms			
da Silva et al.[39]	HSDD: sexual desire, arousal, lubrication, orgasm, satisfaction, pain	Grouped symptom: HSDD (61.4%) Individual symptom: NA	NA
Kim et al.[40]	Impaired sexual function (sexual desire, arousal, lubrication, orgasm, satisfaction, pain)	Grouped symptom: NA Individual symptom: Impaired sexual desire (44.7%) Impaired arousal (29.8%) Impaired lubrication (13.8%) Impaired orgasm (20.2%) Impaired satisfaction (19.1%) Pain during intercourse (11.7%)	NA
Lee et al.[41]	Sexual problem (change in sexual desire, change in sexual activity, and satisfaction), bladder problem (difficulty in urinating, increased need to urinate, bladder incontinence), vaginal dryness	Grouped symptom: Sexual problem (81.3%) Bladder problem (67.2%) Individual symptom: Vaginal dryness (62.5%)	NA
Llaneza et al.[42]	Sexual problem (sexual desire, arousal, orgasm, satisfaction, lubrication, pain)	Grouped symptom: Low–medium level of sexual problem (46.4%) High level of sexual problems (46.4%) Individual symptom: NA	Grouped symptom: Severe sexual problem (1.8%) Individual symptom: NA
Martelli et al.[43]	Sexual dysfunction (sexual desire, arousal, lubrication, orgasm, satisfaction, pain during intercourse)	Grouped symptom: NA Individual symptom: Decreased sexual desire (44.7%) Decreased arousal (37%) Decreased lubrication (44.7%) Decreased orgasm (39.8%) Decreased satisfaction (36.9%) Pain during intercourse (40.8%)	NA
Otunctemur et al.[44]	Female sexual dysfunction (sexual desire, arousal, lubrication, orgasm, satisfaction, pain)	Grouped symptom: Female sexual dysfunction (46%) Individual symptom: NA	NA
Vasomotor symptoms			
Lee et al.[41]	Hot flashes, sweating	Grouped symptom: Hot flashes and sweating (75.0%) Individual symptom: NA	NA

(Continued)

Table 3. (Continued)

Reference	Reported symptoms	Prevalence of symptoms	Prevalence of severe symptoms
Ryu et al.[45]	Hot flashes, sweating, night sweats	Grouped symptom: Number of diagnostic components of metabolic syndrome and presence of vasomotor symptoms, $p = 0.001$** 0: 53.6%[a] 1: 56.8%[a] 2: 57.1%[a] 3: 65.4% 4: 68.3% 5: 65.4% Individual symptom: NA	Grouped symptom: Number of diagnostic components of metabolic syndrome and severity of vasomotor symptoms, $p = 0.093$ 0: 23.0%[a] 1: 24.9%[a] 2: 21.5%[a] 3: 28.8% 4: 27.7% 5: 38.5% Individual symptom: NA
Sayan et al.[46]	Hot flashes, sweating, night sweats	Grouped symptom: Hot flashes, sweating, night sweats (70.9%) Individual symptom: NA	Grouped symptom: No severity of hot flashes, sweating, night sweats (29.2%) Moderate severity of hot flashes, sweating, night sweats (2.1%) Severe severity of hot flashes, sweating, night sweats (68.8%) Individual symptom: NA
Psychological symptoms			
Lee et al.[41]	Mental exhaustion, irritability, depressive mood, anxiety	Grouped symptom: NA Individual symptom: Mental exhaustion (84.4%) Irritability (51.6%) Depressive mood (50.0%) Anxiety (50.0%)	NA
Llaneza et al.[42]	Psychological domain (depression, anxiety, irritability)	Grouped symptom: Low–medium level of psychological symptoms (71.4%) High level of psychological symptoms (10.7%) Individual symptom: NA	Grouped symptom: Severe psychological symptoms (8.9%) Individual symptom: NA
Sleep symptoms			
Lee et al.[41]	Sleeping problem (difficulty falling asleep, difficulty staying asleep, early morning awakenings)	Grouped symptom: Sleeping problem (57.8%) Individual symptom: NA	NA
Somatic symptoms			
Lee et al.[41]	Muscle and joint discomfort, heart discomfort	Grouped symptom: NA Individual symptom: Heart discomfort (59.4%) Muscle and joint discomfort (76.6%)	NA

HSDD: hypoactive sexual dysfunction disorder; NA: not applicable.
[a]Not included in this analysis.
**Statistically significant, $p < 0.05$.

Psychological symptoms: grouped symptoms. One study reported the prevalence of their grouped psychological symptoms which is a combination of depression, anxiety, and irritability.[42] This study reported that 71.4% of midlife women with metabolic syndrome in post-menopause suffer from low–medium level of psychological symptoms and 10.7% from a high level of psychological symptoms. Low–medium level symptoms refer to psychological symptom scores between –1 SD and +1 SD below or over the reference score and high level between +1 SD and +2 SD over the reference score on the Cervantes Scale.[42] Among them, 8.9% were experiencing a severe degree of psychological symptoms who had psychological symptom scores +2 SD or over than the reference score.[42]

Psychological symptoms: individual symptoms. The prevalence of individual symptoms of psychological symptoms was discussed in one study, which included mental exhaustion, irritability, depressive mood, and anxiety.[41] Among them, mental exhaustion (84.4%) was the most commonly reported, while other individual psychological symptoms such as irritability, depressive mood, and anxiety had a reported prevalence rate between 50.0% and 51.6%.[41]

Sleep symptoms: grouped symptoms. One study discussed the grouped sleep symptoms experienced by midlife women with metabolic syndrome in post-menopause.[41] These grouped sleep symptoms were a combination of difficulty falling asleep, difficulty staying asleep, and early morning awakenings.[41] More than half (57.8%) of midlife women with metabolic syndrome in post-menopause reported these sleep symptoms.[41]

Sleep symptoms: individual symptoms. There were no studies that focused on individual sleep symptoms and their prevalence.

Somatic symptoms: grouped symptoms. None of the studies have discussed the prevalence of grouped somatic symptoms experienced by midlife climacteric women with metabolic syndrome.

Somatic symptoms: individual symptoms. One study reported that midlife women with metabolic syndrome in post-menopause experienced a wide array of individual somatic symptoms such as muscle and joint discomfort, and heart discomfort.[41] The most commonly reported individual somatic symptom was the muscle and joint discomfort (76.6%).[41]

Metabolic syndrome versus without metabolic syndrome group

Comparison in types and/or prevalence of symptoms between midlife climacteric women with metabolic syndrome and without metabolic syndrome is shown in Table 4. These symptoms included grouped and/or individual urogenital symptoms, vasomotor symptoms, psychological symptoms, sleep symptoms, and somatic symptoms.

Urogenital symptoms: grouped symptoms. Among the six studies, five studies compared the grouped urogenital symptoms between midlife women with metabolic syndrome group and without metabolic syndrome group in post-menopause.[39,41–44] For the grouped urogenital symptoms, all of the studies found a higher prevalence of grouped urogenital symptoms in the metabolic syndrome group compared to the without metabolic syndrome group, but statistical significance was only reached in four studies.[39,42–44] In contrast, one study yielded a contradictory finding that a low–medium level of grouped sexual problems was more prevalent in the without metabolic syndrome group (57.4% vs 46.4%, $p > 0.05$) even though a high level of grouped sexual problems was more prevalent in the metabolic syndrome group (46.4% vs 27.8%, $p = 0.044$).[42]

Urogenital symptoms: individual symptoms. Three studies focused on comparing the individual urogenital symptoms between the two groups.[40,41,43] While the three studies reported majority of urogenital symptoms to be more prevalent in the metabolic syndrome group, statistical significance was reached in only study.[43]

Vasomotor symptoms: grouped symptoms. Two studies have compared the prevalence of grouped vasomotor symptoms between midlife women with and without metabolic syndrome in post-menopause.[41,46] These grouped vasomotor symptoms included hot flashes, night sweats, and cold sweats. Among them, one study found that the grouped vasomotor symptoms of hot flashes and sweating (75%) were more prevalent in the metabolic syndrome group than the without metabolic syndrome group (60.1%) which was statistically significant, $p = 0.034$.[41] In contrast, a study by Sayan et al.[46] reported mixed findings based on the severity of grouped vasomotor symptoms between the two groups.

Vasomotor symptoms: individual symptoms. There were no studies that compared the individual vasomotor symptoms and their prevalence between midlife climacteric women with and without metabolic syndrome.

Psychological symptoms: grouped symptoms. One study compared the prevalence of grouped psychological symptoms that included depression, anxiety, and irritability in midlife women with metabolic syndrome and without metabolic syndrome in post-menopause.[42] The without metabolic syndrome group experienced more low–medium level of

Table 4. Metabolic syndrome versus without metabolic syndrome group.

Reference	Symptom	Metabolic syndrome group	Non-metabolic syndrome group	*p* value
Urogenital symptoms				
da Silva et al.[39]	Grouped symptom			
	Hypoactive sexual disorder	61.4%	42.8%	0.001**
Kim et al.[40]	Individual symptom			
	Impaired sexual desire	44.7%	39.3%	0.369
	Impaired sexual arousal	29.8%	33.7%	0.485
	Impaired sexual lubrication	13.8%	11.0%	0.391
	Impaired sexual orgasm	20.2%	19.6%	0.890
	Impaired sexual satisfaction	19.1%	13.3%	0.151
	Pain during intercourse	11.7%	7.1%	0.143
Lee et al.[41]	Grouped symptom			
	Sexual problem	81.3%	73.1%	0.147
	Bladder problem	67.2%	58.0%	0.145
	Individual symptom			
	Vaginal dryness	62.5%	58.8%	0.373
Llaneza et al.[42]	Grouped symptom			
	Low–medium level of sexual problems	46.4%	57.4%	>0.05
	High level of sexual problems	46.4%	27.8%	0.044**
Martelli et al.[43]	Grouped symptom			
	Sexual dysfunction	37.9%	19.0%	0.003**
	Individual symptom			
	Impaired sexual desire	44.7%	34.1%	0.002**
	Impaired sexual arousal	37.0%	17.1%	0.004**
	Impaired sexual lubrication	44.7%	17.1%	<0.0005**
	Impaired sexual orgasm	39.8%	19.0%	0.002**
	Impaired sexual satisfaction	36.9%	15.2%	<0.0005**
	Pain during intercourse	40.8%	16.2%	<0.0005**
Otunctemur et al.[44]	Grouped symptom			
	Female sexual dysfunction	46.0%	34.0%	<0.05**
Vasomotor symptoms				
Lee et al.[41]	Grouped symptom			
	Hot flashes, sweating	75.0%	60.1%	0.034**
Sayan et al.[46]	Grouped symptom			
	No severity of hot flashes, sweating, night sweat	29.2%	15.8%	0.037**
	Moderate severity of hot flashes, sweating, night sweat	2.1%	10.5%	0.026**
	Severe severity of hot flashes, sweating, night sweat	68.8%	73.7%	0.164
Psychological symptoms				
Lee et al.[41]	Individual symptom			
	Depressive mood	50.0%	63.9%	0.049**
	Irritability	51.6%	54.6%	0.405
	Anxiety	50.0%	42.9%	0.221
	Mental exhaustion	84.4%	86.6%	0.422
Llaneza et al.[42]	Grouped symptom			
	Low–medium level of psychological problems	71.4%	74.1%	>0.05
	High level of psychological problems	10.7%	9.3%	>0.05
Sleep symptoms				
Lee et al.[41]	Grouped symptom			
	Sleeping problem	57.8%	61.3%	0.378
Somatic symptoms				
Lee et al.[41]	Individual symptom			
	Heart discomfort	59.4%	58.0%	0.491
	Muscle and joint problem	76.6%	72.2%	0.328

**Statistically significant, $p < 0.05$.

grouped psychological problems while the metabolic syndrome group experienced more high level of grouped psychological problems, but the difference was not statistically significant.[42]

Psychological symptoms: individual symptoms. One study compared the prevalence of individual psychological symptoms between midlife women with metabolic syndrome and without metabolic syndrome in post-menopause.[41] The without metabolic syndrome group experienced higher prevalence in depressive mood (50% vs 63.9%; $p=0.049$), irritability (51.6% vs 54.6%; $p=0.405$), and mental exhaustion (84.4% vs 86.6%; $p=0.422$).[41] In contrast, the metabolic syndrome group reported a higher prevalence in only anxiety (50.0% vs 42.9%, $p=0.221$).[41]

Sleep symptoms: grouped symptoms. While it did not reach significance, one study reported that the without metabolic syndrome group frequently experienced grouped sleep symptoms, which is a constellation of difficulty falling asleep, staying asleep, and early morning awakenings.[41]

Sleep symptoms: individual symptoms. There were no studies that compared the individual sleep symptoms and their prevalence between midlife climacteric women with and without metabolic syndrome.

Somatic symptoms: grouped symptoms. None of the included studies compared the grouped somatic symptoms and their prevalence between midlife climacteric women with and without metabolic syndrome.

Somatic symptoms: individual symptoms. One study by Lee et al.[41] focused on the prevalence of individual somatic symptoms that included muscle and joint discomfort and heart discomfort. All of the individual somatic symptoms were higher in the metabolic syndrome group than without metabolic syndrome group but was not statistically significant.[41]

Presence of symptom clusters

There were no studies that reported the presence of symptom clusters in midlife climacteric women with metabolic syndrome.

Synthesis of results

This scoping review included a total of eight studies in the analysis on the topic of symptoms experienced by midlife climacteric women with metabolic syndrome.[39–46]

Symptoms. The included studies reported that these midlife climacteric women with metabolic syndrome experience urogenital, vasomotor, psychological, sleep, and somatic symptoms with a wide range of prevalence. Their overall symptom experience yielded different and mixed findings when comparing midlife climacteric women with and without metabolic syndrome. However, none of the studies have focused on symptom clusters in this population.[39–46]

Symptom rating instrument. Many symptom rating instruments with established validity and reliability were used to measure the prevalence and severity of symptoms in midlife climacteric women with metabolic syndrome. These symptom rating instruments included Female Sexual Function Index, Menopause Rating Scale, Cervantes Scale, Female Sexual Distress Scale, and study-designed questionnaire.[39–46] The most commonly used symptom rating instrument was the Female Sexual Function Index, followed by the Menopause Rating Scale.

Discussion

To the best of our knowledge, this is the first study to review the current literature to understand the types and prevalence of symptoms and symptom clusters experienced by midlife climacteric women with metabolic syndrome and to compare them to midlife climacteric women without metabolic syndrome.

The grouped urogenital symptoms had the highest prevalence among all other grouped symptoms in midlife climacteric women with metabolic syndrome.[39–46] In regard to individual symptoms, the most commonly occurring symptom was mental exhaustion (84.4%).[41] It is interesting to note that mental exhaustion had the highest prevalence among all the individual symptoms while psychological symptoms did not have the highest prevalence among other grouped symptoms. As such, the authors of the included studies used different symptom classifications to examine their prevalence with some using grouped symptoms that included multiple individual symptoms while others focused on an individual symptom.[39–46] This may be due to different symptom rating tools used in the studies. For example, Menopausal Rating Scale tool examines broad symptom experience in menopausal women,[41,45] whereas Female Sexual Function Index tool asks specific sexual problems that include change in sexual desire and lubrication.[39,40,43,44] While both symptom rating tools may measure the same concept of symptoms, one of them measures sexual symptoms as a grouped symptom category and the other measures specific and individual types of sexual symptoms. Without consistent classification of symptoms, this may impact the overall study findings and make it difficult to compare symptom prevalence across the studies.

A wide range of prevalence was reported for both grouped symptoms and individual symptoms which may be due to culture or ethnic differences of midlife women.

Symptoms might have been overreported or underreported from six different study locations and the influence of each culture on reporting of their symptoms.[39–46] For example, Asian population tends to hold negative attitude toward climacteric and believes that climacteric symptoms should not be treated.[48,49] Therefore, Asian population is less likely to report vasomotor symptoms than the North American and European populations.[50] In addition, a strong societal stigma exists in the Hispanic community that hinders Hispanics from reporting their symptoms, leading to further problems such as underutilization of mental health services.[51] With the potential influence of culture on symptom reporting, future studies should be conducted with midlife climacteric women with metabolic syndrome located in similar geographical location or in similar culture/ethnicity.

In addition, the symptom experience yielded different and mixed findings between midlife women with and without metabolic syndrome in post-menopause.[39–46] The metabolic syndrome group reported higher prevalence of majority symptoms while the without metabolic syndrome group reported a higher prevalence of certain symptoms such as depressive mood, irritability, mental exhaustion, and low–medium level of vasomotor symptoms.[41,42] This may be a result of differences in demographic and clinical characteristics[52] in the included studies. Midlife climacteric women with metabolic syndrome may vary in their time to menopause which may have affected their overall symptom experience. Time to menopause has been associated with accelerated epigenetic aging which in turn leads to development of severe vasomotor symptoms.[53] While our study aimed to identify characteristics of both groups, they were not reported consistently across the studies. For example, only three studies included information on time to menopause.[41,43,45] Such understanding will help us conceptualize their symptom profile and determine which group is at the highest risk for worse symptom profile. This will allow the clinicians to engage in a more targeted symptom assessment, diagnosis, and management.

While the studies discussed various types of symptoms, none of the studies reported presence of symptom clusters. People with chronic conditions generally present with more than one symptom.[29] For example, a study of chronic kidney disease patients found five symptom clusters that include fluid volume, neuromuscular, gastrointestinal, sexual, and psychological symptom clusters.[54] When symptom clusters are left underdiagnosed or undertreated, they may have a negative impact on patient outcomes.[29] Therefore, it is critical that we understand what types of symptoms constitute a symptom cluster in midlife climacteric women with metabolic syndrome and the nature of clinically significant symptom clusters. Identification of symptom clusters will allow for reduction in symptom burden that may improve their capacity to maintain a good quality of life over time.[29]

Limitations and implications

This is the first study to review current literature on symptoms experienced by midlife climacteric women with metabolic syndrome. Our review has several limitations. First, most of the studies were cross-sectional studies. Therefore, we were not able to understand their trajectory of symptom experience over time. Future research should use a longitudinal approach that will allow us to capture how symptoms may change. Second, different time points (i.e. years since menopause) were used to measure symptoms or these time points were not reported across the studies. It is important to use similar time points to avoid any possible errors such as time-specific differences in their symptom experience. Third, different symptom definitions and measurement tools were used to measure symptoms. A consistent definition and symptom rating tools should be used for a more accurate comparison of symptoms in this population. Fourth, majority of the studies included primarily women in post-menopause. As midlife women's symptom experience may vary based on their menopausal status, it is critical for future research to include women in other menopausal status and to examine whether their symptom experience is different. Last, a methodological decision was made not to conduct a quality appraisal, which may impact interpretation of results. However, this is consistent with scoping review methodology.[33] Future research could consider the addition of quality assessment to increase the reliability and validity of study findings.

Conclusion

The current literature was reviewed to understand the symptoms experienced by midlife climacteric women with metabolic syndrome. Midlife climacteric women with metabolic syndrome experienced grouped and individual urogenital symptoms, vasomotor symptoms, psychological symptoms, sleep symptoms, and somatic symptoms with a wide range of prevalence reported across the eight studies. In addition, their symptom profile was different when compared to the symptom profile of midlife climacteric women without metabolic syndrome, with majority of symptoms to be more prevalent in midlife climacteric women with metabolic syndrome and some mixed findings on the prevalence and severity of certain individual and grouped symptoms. Our findings will serve as a knowledge basis for clinicians to better understand the complex symptom experience in midlife climacteric women with metabolic syndrome and to assist in developing future targeted symptom interventions.

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Author contribution(s)

Se Hee Min: Conceptualization; Data curation; Formal analysis; Funding acquisition; Investigation; Methodology; Project administration; Writing—original draft; Writing—review & editing.
Qing Yang: Conceptualization; Supervision; Writing—review & editing.
Se Won Min: Conceptualization; Formal analysis; Investigation; Writing—review & editing.
Leila Ledbetter: Conceptualization; Data curation; Methodology; Writing—review & editing.
Sharron L Docherty: Conceptualization; Supervision; Writing—review & editing.
Eun-Ok Im: Conceptualization; Supervision; Writing—review & editing.
Sharron Rushton: Conceptualization; Formal analysis; Methodology; Supervision; Writing—review & editing.

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Supplemental material

Supplemental material for this article is available online.

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Appendix 1

Search Strategy for Databases, Search Date: 2 February 2021
Database (including vendor/platform): PubMed (MEDLINE)
Included dates: 1966 and selected coverage of literature prior to that period to 2 February 2021

1	"Metabolic Syndrome"[Mesh] OR "Abdominal obesity metabolic syndrome" [Supplementary Concept] OR "Metabolic syndrome"[tw] OR "Metabolic Syndromes"[tw] OR "Insulin Resistance Syndrome X"[tw] OR "Metabolic X Syndrome"[tw] OR "Dysmetabolic Syndrome X"[tw] OR "Reaven Syndrome"[tw] OR "Metabolic Cardiovascular Syndrome"[tw] OR "Syndrome X"[tw]	61,460
2	"Menopause"[Mesh] OR "Postmenopause"[Mesh] OR "Perimenopause"[Mesh] OR Menopause[tw] OR perimenopause[tw] OR "peri menopause"[tw] OR "post menopause"[tw] OR "postmenopause"[tw] OR Postmenopausal[tw] OR "Post menopausal"[tw] OR menopausal[tw] OR perimenopausal[tw] OR "peri menopausal"[tw] OR Menopauses[tw] OR "Climacteric"[Mesh] OR Climacterics[tw] OR climacterium[tw]	114,305
4	#1 AND #2	1527
5	NOT (Editorial[pt] OR Letter[pt] OR Case Reports[pt] OR Comment[pt]) NOT (animals[mh] NOT humans[mh])	1429

Database (including vendor/platform): Embase (Elsevier)
Included dates: 1947 to 2 February 2021

Set #		Results
1	"metabolic syndrome x"/exp OR "metabolic syndrome":ti,ab,kw OR "metabolic syndromes":ti,ab,kw OR "insulin resistance syndrome x":ti,ab,kw OR "metabolic x syndrome":ti,ab,kw OR "dysmetabolic syndrome x":ti,ab,kw OR "reaven syndrome":ti,ab,kw OR "metabolic cardiovascular syndrome":ti,ab,kw OR "syndrome x":ti,ab,kw	107,594
2	"menopause"/exp OR "menopause" OR "postmenopause"/exp OR "postmenopause" OR "climacterium"/exp OR menopause:ti,ab,kw OR perimenopause:ti,ab,kw OR "peri menopause":ti,ab,kw OR "post menopause":ti,ab,kw OR "postmenopause":ti,ab,kw OR postmenopausal:ti,ab,kw OR "post menopausal":ti,ab,kw OR menopausal:ti,ab,kw OR perimenopausal:ti,ab,kw OR "peri menopausal":ti,ab,kw OR menopauses:ti,ab,kw OR climacterics:ti,ab,kw OR climacterium:ti,ab,kw	175,909
3	#1 AND #2	2974
4	AND ([article]/lim OR [article in press]/lim OR [data papers]/lim OR [review] OR [short survey]/lim) AND [humans]/lim	1863

Database (including vendor/platform): Web of Science (Clarivate)
Included dates: 1900 to 2 February 2021

Set #		Results
1	TS=("Metabolic syndrome" OR "Metabolic Syndromes" OR "Insulin Resistance Syndrome X" OR "Metabolic X Syndrome" OR "Dysmetabolic Syndrome X" OR "Reaven Syndrome" OR "Metabolic Cardiovascular Syndrome" OR "Metabolic Cardiovascular Syndrome" OR "Syndrome X")	102,126
2	TS=(Menopause OR perimenopause OR "peri menopause" OR "post menopause" OR "postmenopause" OR Postmenopausal OR "Post menopausal" OR menopausal OR perimenopausal OR "peri menopausal" OR Menopauses OR Climacterics OR climacterium)	132,357
3	#1 AND #2	3138
4	AND DT = (Article)	2501

Database (including vendor/platform): CINAHL (EBSCOhost)
Included dates: 1937 to 2 February 2021

Set #		Results
1	(MH "Metabolic Syndrome X+") OR TI ("Metabolic syndrome" OR "Metabolic Syndromes" OR "Insulin Resistance Syndrome X" OR "Metabolic X Syndrome" OR "Dysmetabolic Syndrome X" OR "Reaven Syndrome" OR "Metabolic Cardiovascular Syndrome" OR "Metabolic Cardiovascular Syndrome" OR "Syndrome X") OR AB ("Metabolic syndrome" OR "Metabolic Syndromes" OR "Insulin Resistance Syndrome X" OR "Metabolic X Syndrome" OR "Dysmetabolic Syndrome X" OR "Reaven Syndrome" OR "Metabolic Cardiovascular Syndrome" OR "Metabolic Cardiovascular Syndrome" OR "Syndrome X")	20,572
2	(MH "Menopause+") OR (MH "Climacteric") OR TI (Menopause OR perimenopause OR "peri menopause" OR "post menopause" OR "postmenopause" OR Postmenopausal OR "Post menopausal" OR menopausal OR perimenopausal OR "peri menopausal" OR Menopauses OR Climacterics OR climacterium) OR AB (Menopause OR perimenopause OR "peri menopause" OR "post menopause" OR "postmenopause" OR Postmenopausal OR "Post menopausal" OR menopausal OR perimenopausal OR "peri menopausal" OR Menopauses OR Climacterics OR climacterium)	34,669
3	#1 AND #2	567
4	NOT PT (Book Review OR Case Study OR Commentary OR Editorial OR Letter OR Pamphlet OR Pamphlet Chapter OR Poetry)	545

Database (including vendor/platform): PsycINFO (EBSCOhost)
Included dates: coverage dating back to the 17th and 18th centuries, with extensive coverage from the 1800s to 2 February 2021

Set #		Results
1	DE "Metabolic Syndrome" OR TI ("Metabolic syndrome" OR "Metabolic Syndromes" OR "Insulin Resistance Syndrome X" OR "Metabolic X Syndrome" OR "Dysmetabolic Syndrome X" OR "Reaven Syndrome" OR "Metabolic Cardiovascular Syndrome" OR "Metabolic Cardiovascular Syndrome" OR "Syndrome X") OR AB ("Metabolic syndrome" OR "Metabolic Syndromes" OR "Insulin Resistance Syndrome X" OR "Metabolic X Syndrome" OR "Dysmetabolic Syndrome X" OR "Reaven Syndrome" OR "Metabolic Cardiovascular Syndrome" OR "Metabolic Cardiovascular Syndrome" OR "Syndrome X")	3965
2	DE "Menopause" OR TI (Menopause OR perimenopause OR "peri menopause" OR "post menopause" OR "postmenopause" OR Postmenopausal OR "Post menopausal" OR menopausal OR perimenopausal OR "peri menopausal" OR Menopauses OR Climacterics OR climacterium) OR AB (Menopause OR perimenopause OR "peri menopause" OR "post menopause" OR "postmenopause" OR Postmenopausal OR "Post menopausal" OR menopausal OR perimenopausal OR "peri menopausal" OR Menopauses OR Climacterics OR climacterium)	7042
3	#1 AND #2	72

Database (including vendor/platform): ProQuest Dissertations & Theses
Included dates: 1939 to 2 February 2021

Set #		Results
1	noft("Metabolic syndrome" OR "Metabolic Syndromes" OR "Insulin Resistance Syndrome X" OR "Metabolic X Syndrome" OR "Dysmetabolic Syndrome X" OR "Reaven Syndrome" OR "Metabolic Cardiovascular Syndrome" OR "Metabolic Cardiovascular Syndrome" OR "Syndrome X")	1936
2	noft(Menopause OR perimenopause OR "peri menopause" OR "post menopause" OR "postmenopause" OR Postmenopausal OR "Post menopausal" OR menopausal OR perimenopausal OR "peri menopausal" OR Menopauses OR Climacterics OR climacterium)	4052
3	#1 AND #2	56

Database (including vendor/platform): OpenGrey
Included dates: 1997 to 2 February 2021

Set #		Results
1	("Metabolic syndrome" OR "Metabolic Syndromes" OR "Insulin Resistance Syndrome X" OR "Metabolic X Syndrome" OR "Dysmetabolic Syndrome X" OR "Reaven Syndrome" OR "Metabolic Cardiovascular Syndrome" OR "Metabolic Cardiovascular Syndrome" OR "Syndrome X")	194
2	(Menopause OR perimenopause OR "peri menopause" OR "post menopause" OR "postmenopause" OR Postmenopausal OR "Post menopausal" OR menopausal OR perimenopausal OR "peri menopausal" OR Menopauses OR Climacterics OR climacterium)	570
3	#1 AND #2	4