Eleonora Garibaldi

Manual therapy to alleviate symptoms of anxiety and depression in menopause

Metropolia University of Applied Sciences

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Abstract

Author	Eleonora Garibaldi
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Menopause represents a significant transition in a woman's life and is often associated with symptoms such as anxiety and depression due to hormonal changes, particularly the decline in estrogen. This hormonal drop influences neurotransmitters like serotonin and dopamine, which are crucial for mood regulation, potentially leading to a reduction in quality of life.
The purpose of this thesis was to explore the effectiveness of manual therapies in alleviating menopausal symptoms—specifically anxiety and depression—as potential alternatives or complements to hormone replacement therapy.
The aim was to support the development of non-pharmacological approaches and to encourage future research in this area. A scoping review was conducted according to PRISMA-ScR guidelines. Scientific articles published between 2009 and 2024 were selected from four databases—PubMed, Cochrane Library, ScienceDirect and Wiley Online Library—using the PICo framework. After applying inclusion criteria, eight relevant studies were analyzed and thematically categorized. Two main themes emerged: the types of manual therapies used to address anxiety and depression in menopausal women and the mechanisms through which these therapies exert their effects.
The results indicated that tissue massage, deep tissue massage, foot reflexology and craniofacial massage can reduce anxiety and depression. These techniques modulate the autonomic nervous system, regulate hormone and neurotransmitter levels and influence the hypothalamic-pituitary-adrenal (HPA) axis. These articles have highlighted how these manual therapies improve parasympathetic tone, reduce sympathetic hyperactivit and potentially improve cerebrospinal fluid circulation.
The results suggest that some manual therapies may offer a valuable non-invasive option to improve emotional well-being in menopausal women. This thesis lays the foundation for future research and the development of standardized clinical protocols.

Keywords	Manual Therapy, Osteopathic Manipulation, Chiropractic Manipulation, Physiotherapy Manipulation, CAM, Massage ,Menopausal Women, Anxiety, Depression, Menopausal Symptoms, Menopause, Alternative therapy ,Osteopathy, Deep Massage, Tissue massage, Hormone Balance

Contents

1 Introduction

Menopause is a significant transition in a woman's life, characterized by the cessation of ovarian function and a significant drop in levels of estrogen, progesterone and neuro-transmitters (Yu 2022).The increase in the average lifespan of women, currently around 85 years, has led the World Health Organization (WHO) to investigate all aspects of premenopause, menopause and postmenopause (Oksuzyan, 2008). The numbers of menopausal and post-menopausal women are significant: approximately 25 million women enter menopause every year, a number expected to rise to 1.2 billion by 2030 (Sherman, 2005). During menopause, the decrease in estrogen and neurotransmitters, such as serotonin and dopamine which regulate mood, causes mood swings and symptoms such as anxiety and depression (Santoro, 2016) , sleep difficulties, social isolation, problems with daily productivity (Moe, 2004) with a consequent worsening of the quality of life (Tepper, 2015). Many women seek solutions to mitigate the effects and promote their well-being (Freeman, 2007). Scientific literature can provide us with the opportunity to explore different approaches, including manual therapy and understand if and how manual therapy can be helpful. Manual therapy may represent an effective approach for these symptoms, resulting in support for women's physical and mental well-being (van der Hulst et al., 2020) and general well-being (Fleming et al., 2021).
Knowledge of the data reported in the literature can help women, manual therapists, osteopaths and doctors to make more informed choices about the therapies to adopt to reduce the symptoms of anxiety and depression, with the aim of helping women in this phase of their lives, so that they can lead a healthy and fulfilling life (Mecpherson & Quinton, 2022).

The purpose of this thesis is to investigate which manual therapies and how manual therapies can alleviate the symptoms of anxiety and depression. The aim is to support new therapeutic options in addition to or as an alternative to hormone replacement therapy (HRT) and to take into consideration future research in this area.

2.Background

The menopausal transition is marked by complex neuroendocrine changes that affect not only the reproductive system but also multiple physiological and psychological domains. A progressive decline in ovarian follicular activity leads to fluctuating levels of estradiol, progesterone and other hormones, disrupting the hypothalamic-pituitary-gonadian axis / HPG (Burger et al., 2007). Estrogen plays a modulatory role on key neurotransmitters, including serotonin, dopamine and norepinephrine, which help regulate affect, motivation and arousal (Bethea et al., 2002; Rubinow & Schmidt, 2006).These hormonal alterations have systemic consequences, especially on brain structures involved in mood regulation, such as the amygdala, hippocampus and prefrontal cortex (Barth et al., 2015).

2.1 Menopause

Menopause is defined as the permanent cessation of menstruation, occurring on average around the age of 51, due to the exhaustion of ovarian follicular activity (Greendale et al., 2019). This transition occurs progressively and is divided into three phases: premenopause, menopause and postmenopause. The hormonal decline associated with this process leads to significant physiological and psychological changes with an increased prevalence of anxiety and depressive symptoms (Maki et al., 2019).

Menopause is a natural biological process that marks the end of a woman's reproductive years. It usually occurs when a woman reaches her 40s or 50s, although the exact timing can vary. World Health Organization (WHO) definition of spontaneous menopause is cessation of menstrual cycles, problems resulting from loss of follicular function and diagnosed retrospectively after 12 consecutive months of amenorrhea ,for which no other physiological or pathological cause has been identified. For a better understanding of menopause and reproductive changes in women, there is a nomenclature of the various stages of reproductive age, updated in 2011 by the workshop Stages of Reproductive Aging +10 (McKinlay, 2008).Menopause is a gradual and complex process, rather than a sudden event, accompanied by various factors and symptoms (McKinlay, 2008), see Figure.1 Stages of Reproductive Aging +10 Workshop.

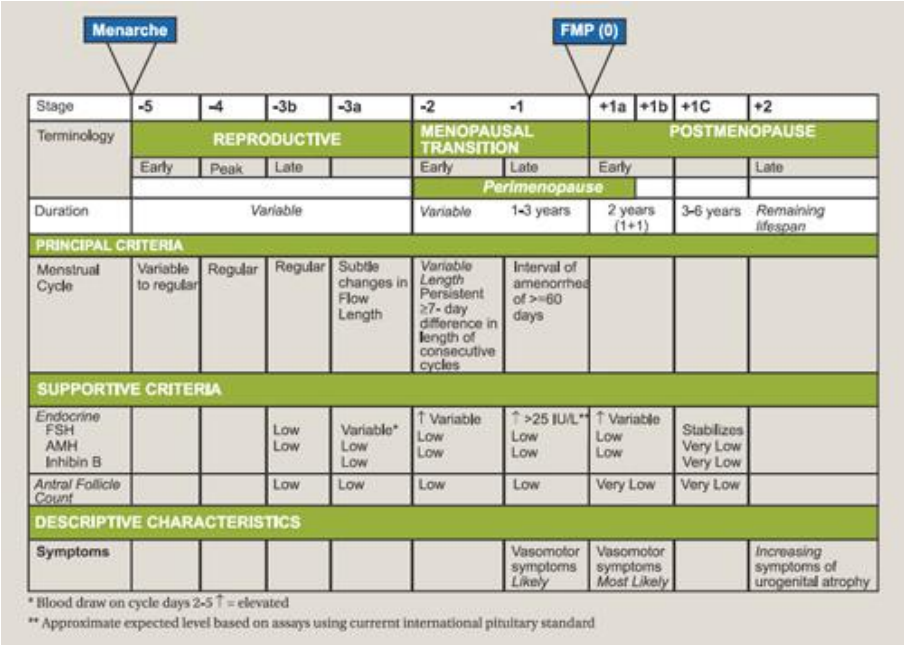

Figure 1. Stages of Reproductive Aging +10 Workshop (McKinlay, 2008).

Women can enter the phase of life called menopause in different ways ,in a spontaneous manner, where there is a gradual and physiological deprivation of hormones and a non-spontaneous one (Zhu, 2019). The latter can have different causes, a surgical procedure with the removal of both ovaries, or environmental factors such as exposure to toxins, chemicals, also genetics, poor diet, execssive consumption of alcohol or tobacco (Cooper, 2007), chronic stress (Woods, 2005).

Surgical menopause occurs when ovarian function ceases abruptly due to oophorectomy, either alone or in combination with hysterectomy (Santoro, 2016). Unlike natural menopause, which is gradual, surgical menopause leads to a sudden drop in estrogen and progesterone levels, often resulting in more severe symptoms, including heightened anxiety and depressive episodes (Soares, 2016). This sudden hormonal decline has been linked to an increased risk of osteoporosis, cardiovascular disease, and cognitive decline (Vermeer et al., 2018). In addition, the intensity of symptoms is also linked to the lifestyle that women lead (Arnot, 2021).

2.2 Hormonal changes during menopause

Estrogen is one of the hormones produced by the female gonads and is responsible for regulating the female reproductive system. It is produced mainly in the ovaries, until menopause, in conjunction with the adrenal glands and fat cells, which continue to secrete them throughout life, although in small quantities (Burger, 2002) which is why estrogen levels decrease during women's lives but do not disappear completely.

Women of childbearing age generally have estrogen levels between 15 and 350 pg/mL, which fluctuate during the menstrual cycle between ovulation and menstruation. During menopause, estrogen levels decrease to <10 pg/mL. The hormonal changes that occur during menopause can have a significant impact on a woman's physical and emotional well-being (Wieczorek, 2023), but not only , these hormones have effects and repercussions on different aspects such as bone health: on bone, estrogens help maintain bone density by inhibiting the activity of bone-destroying cells (osteoclasts). Without sufficient estrogen, bones can weaken and become more susceptible to fractures, resulting in conditions such as osteoporosis (Kosla, 2012). On reproductive tissues, estrogens are essential for maintaining reproductive tissues and functions, including the menstrual cycle, uterine health and vaginal lubrication. Estrogen deficiency can lead to symptoms such as irregular periods, vaginal dryness and an increased risk of urinary tract infections (Bride, 2010). On cardiovascular health: estrogen has cardioprotective effects, including improving blood vessel function, regulating cholesterol levels and reducing inflammation. Estrogen deprivation may contribute to an increased risk of heart disease, stroke and other cardiovascular conditions (Sohrabji, 2019). On metabolism: estrogen affects glucose and lipid metabolism. Its deprivation may contribute to changes in body composition, insulin sensitivity and lipid profiles, potentially increasing the risk of metabolic disorders such as type 2 diabetes and dyslipidemia (Monteiro, 2014). On skin health: estrogen plays a role in maintaining skin elasticity, hydration and collagen production. Its deprivation can lead to changes in skin texture, including dryness, thinning and increased wrinkles (Thornton, 2013).
On body temperature regulation: estrogen helps regulate body temperature, its drop can contribute to symptoms such as hot flashes and night sweats during menopause (Moe, 2004). On mood regulation: estrogen influences the production and activity of neurotransmitters such as serotonin and dopamine, which are involved in mood regulation. Its deprivation can contribute to mood swings, irritability, anxiety and even

depression (Renczes, 2020). On cognitive function: estrogen receptors are present in areas of the brain involved in memory, attention and cognitive function. Its deprivation can affect cognitive abilities, including memory, concentration, and processing speed (Tao, 2020). On stress response: estrogen can modulate the stress response system, including the hypothalamic-pituitary-adrenal (HPA) axis. Its deprivation can impact how the body responds to stress, potentially exacerbating stress-related symptoms and conditions (Con, 2023).

2.3 Mood disorders

Mood disorders are a category of psychopathological conditions characterized by significant and prolonged alterations in emotional state, which affect daily functioning, relationships and quality of life. According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), they mainly include major depression and bipolar disorder, but also milder forms such as dysthymia (American Psychiatric Association, 2013). Symptoms of mood disorders also include anxiety and depression. Since women, especially in the context of menopause, may experience symptoms that overlap or resemble both disorders, it is important to clearly distinguish between them (Hunter, 1995).

Although they can often coexist and share some symptomatic manifestations, anxiety and depression are two distinct mental conditions. The prevalence of these disorders in menopausal women is significant: it is estimated that about 25% of them present symptoms of anxiety (Huang et al., 2023).

2.3.1 Anxiety

Anxiety is a mood disorder characterized by feelings of worry, fear and apprehension about the future (American Psychiatric Association, 2013). Anxiety can manifest itself in several forms, including generalized anxiety disorder, panic disorder and social phobia (Kessler et al., 2005) . Also it can manifest anxiety with symptoms such as tachycardia, sweating and trembling (Kessler et al., 2003). Menopause poses unique challenges to women's physical and mental health. Even though is not a problem for everyone going through menopause, the risk of mood changes and symptoms of depression and anxiety is higher in women, even in those without a background history of depression

or anxiety. Researches show that in the population aged 45 to 55, a higher percentage of female patients than male patients report anxiety (Pappa ,2020).

The prevalence of anxiety symptoms in middle-aged women is substantial; an estimated 51% of women aged 40–55 report feeling tense/nervous or irritable (Bromberger, 2013). Other global research shows that mood disorders affect 9.5% of women and 5.8% of men, with the prevalence rate of anxiety ranging from 1.9% to 5.1% in the general middle-aged population (Huang, 2023). Anxiety can also affect behavior and quality of life, causing anxious women to isolate themselves from friends and family, feel unable to go to work or avoid certain places (Batista de Freida, 2023). Individuals with anxiety may experience excessive rumination and difficulty controlling their anxious thoughts, resulting in emotional distress. Women with anxiety disorders may experience increased sensitivity to stressors and may have difficulty managing uncertainty or perceived threats (Smith, 2020).The reason why women suffer more from anxiety seems to be the combination of biological and social factors, which influence (Hantsoo,2017). Women may be more likely to experience stressors that contribute to anxiety disorders. Coping with lifestyles that are more prone to rumination and worry or with biological predispositions such as anxiety sensitivity and hormonal fluctuations, can favor the spread of anxiety disorders. In addition, there may be other factors that increase the likelihood of developing anxiety disorders, including genetics, long-term painful health conditions, traumatic events such as abuse, domestic violence, drugs, alcohol, economic or housing problems, unemployment, work stress, loneliness or difficult family and personal relationships (Nolen-Hoeksema S. 2024).

2.3. 2 Depression

Depression is a mood disorder characterized by feelings of sadness, hopelessness, and loss of interest in daily activities (American Psychiatric Association, 2013). Depression can manifest itself in several forms, including major depression, minor depression and postpartum depression (Kessler et al., 2003). Depression, also referred to as major depressive disorder (MDD), it is a prevalent and disabling mood disorder characterized by persistent low mood, loss of interest or pleasure (anhedonia), cognitive impairments, and a variety of somatic symptoms that significantly impair an individual's ability to function in daily life (American Psychiatric Association, 2013). According to the World Health Organization (2023), depression affects more than 280 million people globally and it is a leading cause of disability worldwide.

The core symptoms include sustained sadness, feelings of worthlessness or excessive guilt, diminished concentration, recurrent thoughts of death or suicide, fatigue and alterations in sleep and appetite (Miller, 2018). In addition to psychological and behavioral manifestations depression is also associated with biological alterations, including dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis, inflammatory processes, and imbalances in monoamine neurotransmitters such as serotonin, dopamine, and norepinephrine (Dean & Keshavan, 2017).

In women, depression frequently emerges or worsens during periods of hormonal fluctuation, such as the menopausal transition. This period is marked by declining estrogen levels, which influence the regulation of stress response systems and brain areas involved in emotion and cognition. Estrogen withdrawal has been associated with increased vulnerability to depressive episodes (Soares, 2014; Albert, 2019).

Differences between Depression and Anxiety : Depression and anxiety are two distinct mood disorders, that can present similar symptoms (Hirschfeld, 2001). However, there are some key differences: depression is characterized by a feeling of sadness and hopelessness, while anxiety is characterized by a feeling of worry and fear (American Psychiatric Association, 2013). Also, depression can manifest itself with symptoms such as loss of appetite, difficulty sleeping and fatigue, while anxiety can manifest itself with symptoms such as rapid heartbeat, sweating and trembling (Kessler et al., 2003).

2.4 Possible Treatments for Symptoms of Anxiety and Depression

The goal of interventions during menopause is to alleviate the symptoms associated with it, particularly for women who experience a worsening of quality of life. There are multiple treatment possibilities, which can be used alone or in combination depending on the patient’s needs, preferences and clinical condition.
Management of menopausal symptoms may include several therapeutic options. Hormone replacement therapy (HRT) has been shown to be effective in reducing vasomotor symptoms and improving sleep quality and mood (Soares, 2013). However, it is important to note that hormone replacement therapy (HRT) is not suitable for all

women and its use should be evaluated individually according to current clinical guidelines (The North American Menopause Society, 2022).

Psychological interventions, such as cognitive behavioral therapy (CBT) and mindfulness-based stress reduction (MBSR), have been studied for their effectiveness in managing mood disorders (Hofmann et al., 2010; Khoury et al., 2013). CBT can help women manage negative thoughts and improve coping strategies, while MBSR can reduce stress and improve emotional regulation. (Hunter & Smith, 2015; Carmody & Baer, 2008). Pharmacological treatment with selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) can be used to control moderate to severe mood symptoms (Nelson et al., 2006). These medications can help reduce depressive and anxiety symptoms, improving the quality of life of postmenopausal women. Regular exercise and a balanced diet can help improve mood and reduce anxiety (Elavsky & McAuley, 2007; Kritz-Silverstein et al., 2008). Complementary and alternative medicine, such as acupuncture and yoga, and manipulative therapies can also have positive effects on vasomotor and emotional symptoms (MacPherson et al., 2013; Cramer et al., 2012).

2.4.1 Manual therapy

Manual therapy and in particular osteopathic manipulative treatment (OMT), has gained increasing attention as a non-pharmacological and non-hormonal intervention. Manual approaches are proposed to act on both somatic dysfunctions and the autonomic nervous system, modulating the hypothalamic-pituitary-adrenal (HPA) axis, which is often hyperactivated in menopausal women experiencing anxiety and depression (Licciardone et al., 2010). Several studies have highlighted the role of OMT in reducing sympathetic overactivity, improving sleep quality and enhancing emotional balance (Fleming et al., 2021). Specific osteopathic techniques focusing on the craniosacral system, the diaphragm, the thoracic spine and the pelvic floor have been described to influence neurovegetative regulation and hormonal homeostasis (Bruno et al., 2020).

Manual therapy can be defined as the application of precise and directed manual force to the body in order to improve mobility in restricted areas, such as joints, connective tissues or skeletal muscles (Korr, 2012, p. 12). This definition emphasizes the

importance of both the precision and specificity of the force applied, as well as the therapeutic objective of enhancing mobility and reducing functional limitations.

According to the Advanced Practice Description of Orthopedic Manual Physical Therapy (2019), manual therapy is a clinical approach that uses specific manual techniques, including mobilization and manipulation. The primary goals include modulating pain, increasing range of motion (ROM), reducing or eliminating soft tissue inflammation, inducing relaxation, enhancing the repair and extensibility of contractile and non-contractile tissues, improving stability, facilitating movement and restoring function.

Traditional systems of manual therapy (TMT), which include physiotherapy, osteopathy, chiropractic and soft tissue therapy, have all contributed to the development of manual therapy as a discipline. Manual therapy (MT) has been described as the deliberate application of externally generated force to body tissues, typically through the hands, with therapeutic intent. It encompasses a wide range of touch-based interventions such as thrust manipulation, joint mobilization, soft-tissue mobilization and neurodynamic techniques (Kerry et al., 2024). Importantly, manipulative and body-based therapies are recognized as one of the five core domains of complementary and integrative health by the National Center for Complementary and Integrative Health (NCCIH). During the 2017 NCCIH congress, complementary and alternative medicine (CAM) therapies were classified into five categories:

1. Whole Medical Systems: Comprehensive systems of theory and practice, often with historical and cultural roots, such as Ayurveda, homeopathy, naturopathy and Traditional Chinese Medicine ,(NCCIH, 2017).

2. Mind–Body Interventions: Techniques that use the mind to influence physical health, including biofeedback, guided imagery, hypnotherapy, meditation and relaxation techniques.

3. Biologically-Based Therapies: Treatments that use substances found in nature, such as botanical medicine, dietary supplements and nutrition-based therapies.

4. Manipulative and Body-Based Methods: Therapies involving physical manipulation of the body, including chiropractic care, osteopathic manipulative treatment, cupping therapy, massage therapy, reflexology and moxibustion.

5. Energy Therapies: Interventions based on the use of biofields or supposed energy fields surrounding the body, including acupuncture, therapeutic touch, magnetism, Qi Gong, Tai Chi, and Reiki (NCCIH, 2017) , see Figure.2 CAM Domains (Petrie,K.J.2008).

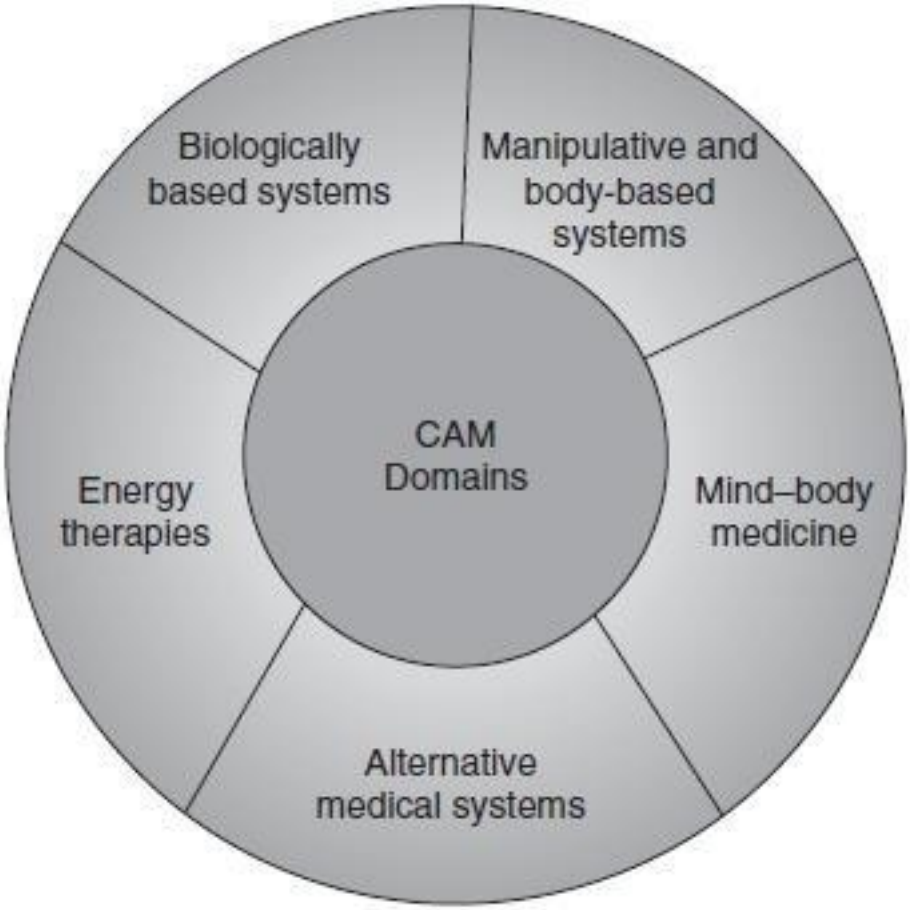

Figure 2. CAM Domains (Petrie,K.J.2008).

This type of treatments are considered unconventional medicine, but is also called traditional medicine, in fact the World Health Organization has long called unconventional medicine "Traditional Medicine" in respect of the countries in which these forms of healing have long been a heritage permanent culture: think of China and India (Hsia, 2012).

3.Purpose and aim

The purpose of this thesis is to describe what type of manual therapies have been used to alleviate symptom of anxiety and depression and how manual therapies have an effects on the symptoms.

The aim of this thesis is to support new treatment options in addition to or as an alternative to HRT, to take into consideration future investigations on this regard.

Research questions:

1. What kind of manual therapies have been used to treat anxiety and depression symptoms in menopause ?
2. How manual therapies can alleviate the anxiety and depression symptoms?

4.Method

The steps will be use in the scoping review are : the search strategy, data selection, critical appraisal and data analysis.

4.1 Scoping review

A scoping review (SR) is a second-level study that synthesizes other studies (Stoll, 2020). The goal of scoping reviews is to collect and synthesize the available scientific evidence on a given topic in a comprehensive, transparent and reproducible way (Pollock, 2024). Unlike a systematic review, a scoping review does not aim to produce a critical synthesis or a definitive answer to a specific research question, but rather to provide an overview or mapping of the existing evidence (Munn , 2018).

A scoping review can be defined as a method of summarizing knowledge in a comprehensive way, in order to identify priorities for future research (Colquhoun , 2014). This type of review can include different types of studies, including randomized clinical trials (RCTs), observational studies, qualitative studies and others, which is why it was chosen in this thesis (Levac , 2010). However, a scoping review is not limited to a simple synthesis of existing literature, but represents an analytical process that evaluates and interprets relevant sources to build a coherent understanding of the research area (Rewhorn, 2016).

4.2 Search strategy

To ensure methodological rigor in conducting a scoping review, it is essential to develop a thorough search strategy that allows for a comprehensive and systematic

analysis of the available literature on the topic (Bramer, 2018). This involves establishing clear eligibility criteria, using multiple sources of evidence and adopting an iterative search strategy to refine and broaden the scope of relevant studies (Arksey 2005). Transparency and reproducibility in the search process are critical to ensuring that scoping reviews provide a reliable synthesis of the literature (Levac et al., 2010). Adherence to these methodological guidelines improves the validity and applicability of findings, strengthening the scoping review as a robust tool for mapping existing research and identifying knowledge gaps.

The Population Intervention Context (PICo) model provides a structured approach to defining search terms, ensuring clarity and reproducibility in identifying relevant studies (Schardt, 2007), which is why it was adopted. Since the aim is to conduct a thorough review of what types of manual therapies can alleviate anxiety and depression in menopausal women and how, the search terms used are: for the population menopausal women , for intervention manual therapy ,osteopathic manipulation, massage, deep massage, chiropractic manipulation, physiotherapy manipulation, CAM and for the context anxiety and depression . In the search strategy, therefore, synonyms were highlighted, which increases the sensitivity of retrieval and minimizes the risk of missing relevant studies due to terminological differences between disciplines and databases (Rethlefsen, 202), see Table.1 PICo.

Table.1 PICo.

	PICo
P (Population)	Women in Menopause
I (Intervention)	Manual Therapy, Osteopathic Manipulation, Chiropractic Manipulation, Physiotherapy Manipulation, Osteopathy, CAM, Massage, Deep Massage, Tissue massage, Menopausal Women Symptoms, Anxiety, Depression, Menopausal Symptoms, Hormones Balance, Alternative therapy
Co (Context)	Anxiety/Depression

The use of synonyms ensured that studies using different nomenclature or indexing terms were retrieved, thus improving the comprehensiveness and reliability of the review (Gusenbauer, 2020).

Searching multiple databases minimizes the risk of selection bias and ensures a broader scope of evidence (Bramer 2017). The literature search was conducted using multiple scientific databases, chosen based on their relevance and coverage of peer-reviewed research in the field of interest.

The databases chosen were the following: PubMed, which represents one of the main sources of literature in the scientific field and includes a large number of articles indexed in MEDLINE (Lu, 2011), Wiley Online Library was selected because it allows the comparison of scientific studies published in authoritative journals, ensuring the reliability of the sources (Wiley, 2020), The Cochrane Library is a database specialized in systematic reviews and clinical trials and is recognized as one of the most reliable sources, thanks to its standardized review protocols (Lefebvre et al., 2019), ScienceDirect was chosen for its ability to access a wide range of full-text articles, offering interdisciplinary publications and critical reviews that may not be indexed in other databases (Elsevier, 2020), see Table.2 Search terms and database.

Table .2 Search terms and database.

Database	Search terms
PUBMED COCHRANE LIBRARY SCIENCE DIRECT WILEY ONLINE LIBRARY	Manual Therapy, Osteopathic Manipulation, Chiropractic Manipulation, Physiotherapy Manipulation, Osteopathy, CAM, Massage, Deep Massage, Tissue massage, Menopausal Women Symptoms, Anxiety, Depression, Menopausal Symptoms, Hormones Balance, Alternative therapy

4.3 Data selection

The data selection process was conducted in accordance with the methodological guidelines outlined in the Cochrane Handbook for Systematic Reviews of Interventions (Higgins, 2022) and the PRISMA scoping review protocol (Tricco, 2018). The definition of inclusion and exclusion criteria represents an essential and fundamental step in conducting a scoping review, as it guarantees methodological coherence and transparency in the study selection process (Peters et al., 2020; Tricco et al., 2018). These criteria allow the field of investigation to be systematically circumscribed, ensuring that the collected literature is relevant to the research question and the

objectives of the study (Arksey ; O'Malley, 2005). Furthermore, the rigorous application of predefined criteria helps to minimize bias, improve the reproducibility of the work and facilitate the understanding of the selection process by readers (Peters et al., 2020).

Based on the purpose and research questions of this thesis, the criteria used are as follows.

- Inclusion criteria. Menopausal women, with articles published in the last 15 years (from 2009 to 2024) to ensure the topicality and clinical relevance of the evidence collected (Tricco et al., 2018). Document type, only English peer-reviewed scientific articles which offer an adequate level of scientific rigor. Accessibility, only open access articles, to ensure transparency, accessibility and replicability of the work done by other researchers.

- Exclusion criteria. Women of childbearing age, pre-menopausal or post-menopausal. Books, abstracts, thesis and articles not subjected to peer review, studies that do not report anxiety or depression as primary or secondary symptoms relevant within the investigation. Non-English articles published before 2009 or after 2024. These are all excluded from this data collection ,see Table.3 Inclusion and exclusion criteria.

Table. 3 Inclusion and exclusion criteria.

Criteria	Inclusion	Exclusion
Population	Women in menopause	Women of reproductive age, pre-menopausal or post-menopausal
Symptoms to consider	Presence of anxiety and depression, even if associate with other conditions	Absence of anxiety and depression
Publication date	Articles published between 2009 and 2024	Articles published before or after 2009 and 2024
Type of document	Peer-reviewed scientific articles	Books, theses, abstract, non-peer-reviewed and duplicate articles
Accessibility	Open access articles	Articles not freely available or paid for
Language	Articles published in English	Articles published in languages other than English
Screening process	Articles selected based on title, abstract and full-text review	Articles excluded if clearly irrelevant based on title or abstract

Accuracy in the documentation of the selection phases is an essential element to guarantee the quality and reliability of the results (Lockwood, 2019). In a first phase, all the articles whose title was not relevant to the objective of the review were excluded. Successively, an analysis of the abstract was conducted to verify the presence of the main inclusion criteria (menopausal population and presence of anxiety and/or depression). Finally, in order to confirm their suitability with respect to the defined criteria and the research questions, all potentially relevant articles were examined in full-text. Any duplicates were discarded.

This approach is recommended in the definition of the scope of the review methodology to ensure accuracy and consistency in the selection of sources (Peters et al., 2020; Tricco et al., 2018).

The initial screening identified 1,327 articles, divided as follows: PubMed 649, Wiley Online Library 366, Cochrane Library 12, ScienceDirect 300. After removing duplicates (15 articles removed), the total number of articles is 1,312. After screening the titles and abstracts, the number of articles was reduced to 16, as 1279 articles were discarded for the titles and 17 for the abstracts, for a total of 1296 articles removed. Subsequently the 16 articles were read and then, 3 were selected for the text and 13 were eliminated. Since the number of selected studies was insufficient for a scoping review, manual search was performed using the bibliography of the previously selected texts, for a total of 84 articles. Applying the same selection process: 75 articles were excluded, 63 based on the title and 12 based on the abstract, 9 articles were subjected to full-text review, of which 4 were excluded, while 5 were included. Therefore, the final number of articles included in the scoping review was 8 studies. The entire selection process was conducted according to the PRISMA guidelines for scoping reviews (Tricco, 2018), see Figure.3 Prisma flow diagram.

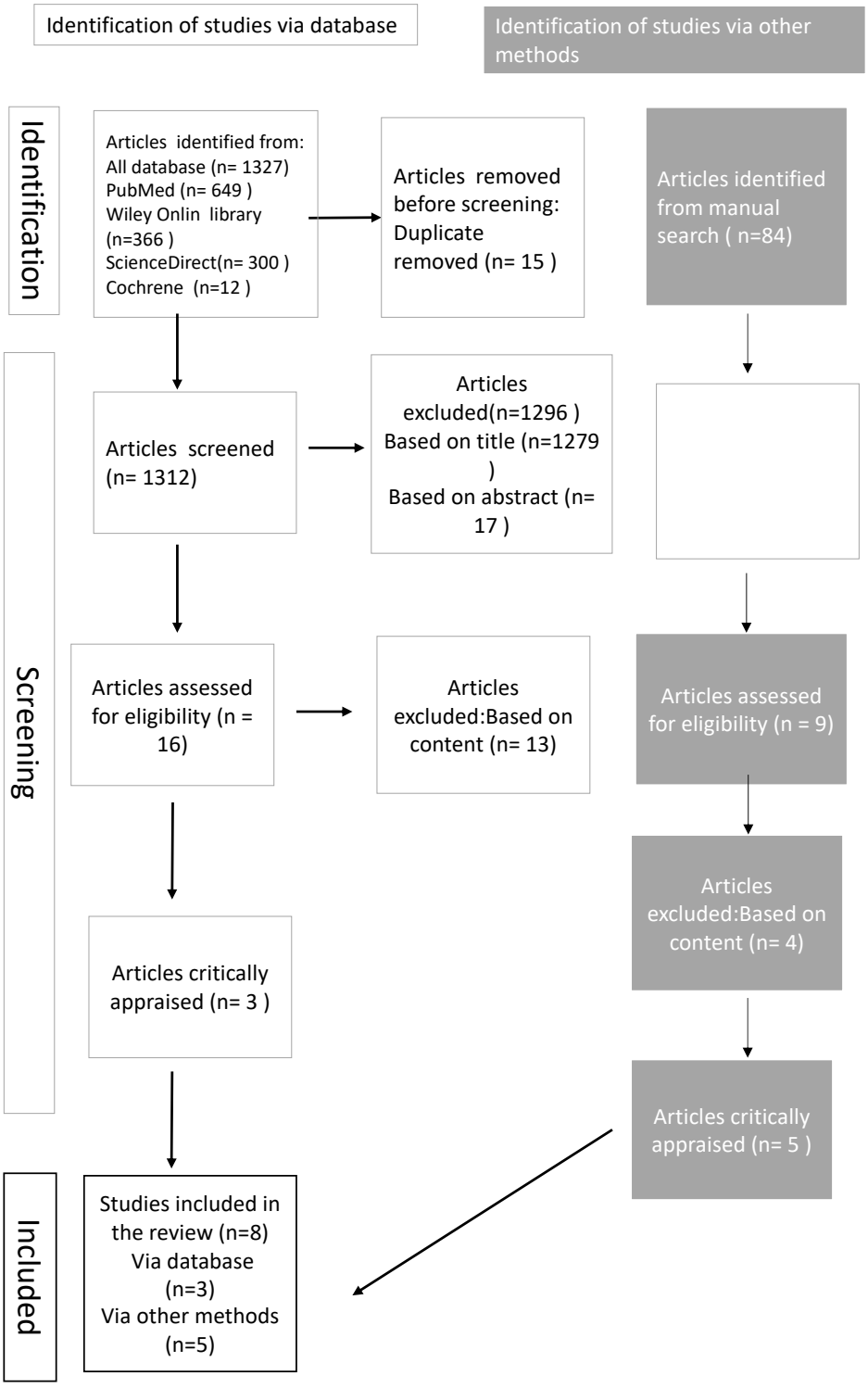

Figure 3. Prisma flow diagram.

4.4 Critical Appraisal

Even though critical appraisal in a literature review is not always mandatory, even if highly recommended to ensure the reliability and validity of the results (Snyder, 2019), it remains essential to understand the methodological quality of the included studies and to ensure that the conclusions of the review are based on solid and relevant evidence (Munn, 2018). Critical appraisal helps to identify gaps in the research, assess the methodological rigor of the studies and highlight any biases, which could influence the final conclusions of the scoping review (Peters, 2015).

The aim of critical appraisal is to determine the quality, validity and possible biases, in order to highlight the strengths and weaknesses of the studies (Grant, 2009). It is conducted using tools and checklists that offer a standardized and transparent approach to data analysis. It is important to know the type of research method adopted in the selected articles. This awareness allows choosing the most suitable checklist among those available and in the case of this thesis those of the Joanna Briggs Institute (JBI) in order to guarantee an accurate and comparable critical appraisal that contributes to the transparency of the literature review (Jordam 2019) see Table. 4 JBI Cheklist.

Table. 4 JBI Cheklist.

No	Articles title /Author	Method	JBI cheklist	Score
1	Massage Therapy to Relieve Menopausal Symptoms: A Systematic Review of RCTs (Listiana et al 2022)	Systematic review of RCTs /Quantitative	Systematic Reviews and Research Syntheses	18/22
2	Efficacy of Complementary and Alternative Therapies for the Management of Psychological Symptoms of Menopause: A Systematic Review of RCTs (Mehrnoush et al.2021)	Systematic review of RCTs /Quantitative	Systematic Reviews and Research Syntheses	20/22
3	Prevalence of CAM Use by Menopausal Women: A Systematic Review of Survey Studies (Posadski et al 2013)	Systematic review of RCTs /Quantitative	Systematic Reviews and Research Syntheses	18/22

4	The Beneficial Effects of Therapeutic Cranio-Facial Massage on Quality of Life, Mental Health and Menopausal Symptoms and Body Image: A RCT (Espi-Lopez et al 2020)	RCT /Quantitative	Randomized Controlled Trials	18/20
5	The Effects of Foot Reflexology on Depression During Menopause (Mahdavipour et al 2019)	RCT /Quantitative	Randomized Controlled Trials	18/20
6	The use of Complementary and Alternative Medicine by Women Experiencing Menopausal Symptoms (Cardini et al 2010)	Observational study /Survey study	Analytical Cross-Sectional Studies	11/16
7	Menopause symptoms in women and its relation with using complementary and alternative medicines: A survey in southeast Iran (Dehgan,2022)	Observational study /Survey study	Analytical Cross-Sectional Studies	11/16
8	"I Am Hot, Irritable and Feeling Low; What Alternatives Do I Have Besides Hormone Replacement Therapy?"(Sulaiha et al 2010)	Literature review /Qualitative	Qualitative Research	14/20

The critical evaluation of the eight studies included in the scoping review, for this thesis, highlighted the methodological strengths and weaknesses that affect the solidity of the evidence that emerged. The heterogeneity in study designs, manual intervention techniques and psychological symptom measurement tools constitutes an element of complexity that limits the possibility of direct comparison between the results. Three systematic reviews of RCTs have good methodological quality, two articles Mehrnoush et al., 2021 and Listiana et al., 2022 present good methodological quality , respectively 18/22 and 20/22 in the JBI checklist. Both provide a positive overall picture of the efficacy of CAM in the treatment of psychological symptoms in menopause, but differ in inclusion criteria, definition of symptoms and type of interventions analyzed. Furthermore, the absence of a quantitative meta-analysis and the lack of uniformity in outcome criteria reduce the strength of their conclusions. Finally, the third article, the

study by Posadzki et al. 2013, represents an important point of connection between the perceived efficacy and the spread of CAM use. However, it focuses mainly on epidemiological aspects, without a direct evaluation of clinical outcomes.

Two randomized controlled trials (RCTs) focus on specific interventions: craniofacial massage, foot reflexology, and general manual treatments. In particular, the study by Espí-López et al. 2020, shows a significant reduction in anxiety and an improvement in body image, but with a limited sample and without follow-up. The study by Mahdavipour et al. 2019, although methodologically valid, has geographical and cultural bias. One literature review Sulaiha et al., use a qualitative design and a poorly structured narrative tool, with interesting but less generalizable results.

Two cross-sectional observational studies (Cardini et al., 2010 and Dehghan et al., 2022) provide an insight into the spontaneous use of CAM by menopausal women. The JBI score shows good clarity in data collection, but a poor ability to directly correlate the use of manual therapies to the reduction of symptoms of anxiety and depression, as these are descriptive and non-interventional studies..

In summary, although most of the studies present a satisfactory methodological quality, the diversity of approaches, the small sample size, the absence of shared protocols and the lack of long-term follow-up represent significant limitations. However, the convergence of results towards a positive effect of manual therapies on anxiety and depression symptoms in menopause suggests that these interventions deserve further well-designed, multicenter, and adequately powered clinical research.

4.5 Data analysis

The data were analyzed using a thematic system because thematic analysis allows for the identification and classification of recurring patterns in the data, facilitating an in-depth understanding of a phenomenon (Braun, 2006) and is particularly useful in literature reviews, where synthesizing fragmented knowledge from different studies is sought. The thematic system can be applied to a wide range of data without requiring a rigid structure (Nowell, 2017), making it suitable for a literature review that integrates heterogeneous studies as in this case. Thematic analysis allows for the critical interpretation of the literature, going beyond a simple synthesis of the data (Terry 2017). The thematic structure adopted in this study facilitates a systematic evaluation of the availa-

ble evidence, organizing the findings into distinct but interrelated themes. In accordance with the thematic system and research questions the themes are: types of manual therapies and mechanisms of action of manual therapies, for anxiety and depression in menopausal women.

The first theme explores the different manual therapies highlighted in the selected articles. The second examines the physiological and neurobiology pathways through which manual therapies exert their therapeutic effects, see Table. 5 Themes.

Table. 5 Themes

Research question	Themes
What kind of manual therapies have been used to treat anxiety and depression symptoms in menopause ?	Types of manual therapies for anxiety and depression in menopausal women
How manual therapies can alleviate the anxiety and depression symptoms?	Mechanisms of action of manual therapies on symptoms of anxiety and depression in menopausal women

5. Results

This scoping review analyzed eight studies investigating the effectiveness of manual therapies in treating symptoms of anxiety and depression in postmenopausal women. Two main themes emerged from the literature review: the types of manual therapies used to alleviate symptoms of anxiety and depression in menopausal women and the mechanisms by which these therapies influence these symptoms. Each theme will be explored in detail below, supported by the evidence gathered.

The results of this scoping review confirm that manual therapies, such as therapeutic massage, craniofacial massage, foot reflexology and osteopathic or chiropractic manipulations, can play a significant role in reducing symptoms of anxiety and depression in menopausal women. These effects appear to be associated with changes in neuroendocrine regulation, modulation of the autonomic nervous system (ANS) and improved body perception and general well-being.

5.1 Results on the type of manual therapies

The studies included in this review investigated different types of manual therapies used to support the management of anxiety and depression in menopausal women. The interventions can be grouped according to the specific manual techniques applied and the body areas targeted.

Deep tissue massage was identified as effective in two studies, which emphasized its role in promoting physical and emotional relief in menopausal women experiencing psychological distress (Listiana et al., 2022; Sulaiha et al., 2010). General therapeutic massage, including relaxation-oriented manual treatments, was reported in several studies as a useful tool for reducing symptoms of anxiety and depression and was among the most frequently applied manual therapies in this population (Mehrnoush et al., 2021; Cardini et al., 2010; Posadzki et al., 2013). Manipulative techniques targeting the musculoskeletal system, such as osteopathic or spinal mobilization, were described as potentially effective in improving psychological balance through manual interaction with structural systems (Dehghan et al., 2022). Craniofacial therapy, focusing on the head, neck, and facial regions, was associated with positive outcomes not only on mood and anxiety but also on sleep quality and body image perception (Espí-López et al., 2020). Foot reflexology was described as a non-invasive manual therapy that can contribute to emotional well-being by stimulating specific areas of the feet, with evidence of improvement in depressive symptoms in menopausal women (Mahdavipour et al., 2019).Overall, the literature supports the idea that a range of manual therapies whether localized, structural, or reflex-based—can serve as valuable non-pharmacological tools to reduce emotional symptoms during menopause (Posadzki et al., 2013; Mehrnoush et al., 2021; Cardini et al., 2010; Dehghan et al., 2022), see Table.6 Results on the type of manual therapies.

Table. 6 Results on the type of manual therapies

No	Articles title	Author	Type of Manual therapy
1	Massage Therapy to Relieve Menopausal Symptoms: A Systematic Review of RCTs	Listiana et al 2022	Deep massage
2	Efficacy of Complementary and Alternative Therapies for the Management of Psychological Symptoms of Menopause: A Systematic Review of RCTs	Mehrnoush et al.2021	Therapeutic massage
3	Prevalence of CAM Use by Menopausal Women: A	Posadski et al 2013	Generic manual therapy

	Systematic Review of Survey Studies		
4	The Beneficial Effects of Therapeutic Cranio-Facial Massage on Quality of Life, Mental Health and Menopausal Symptoms and Body Image: A RCT	Espi-Lopez et al 2020	Craniofacial massage
5	The Effects of Foot Reflexology on Depression During Menopause	Mahdavipour et al 2019	Craniofacial massage
6	The use of Complementary and Alternative Medicine by Women Experiencing Menopausal Symptoms	Cardini et al 2010	Therapeutic massage
7	Menopause symptoms in women and its relation with using complementary and alternative medicines: A survey in southeast Iran	Dehgan,2022	Manipulative therapies
8	"I Am Hot, Irritable and Feeling Low; What Alternatives Do I Have Besides Hormone Replacement Therapy?"	Sulaiha et al 2010	Deep massage

5.2 Results on the mechanism of action

The studies included in this review highlight several physiological and neurobiological mechanisms through which manual therapies may exert their effects on anxiety and depression in menopausal women. These mechanisms primarily involve modulation of the autonomic nervous system, hormonal and neurotransmitter regulation, and improved cerebral circulation. Multiple studies report a consistent reduction in cortisol levels and an increase in parasympathetic tone following manual interventions, which contribute to the alleviation of anxiety and depressive symptoms (Mehrnoush et al., 2021; Sulaiha et al., 2010). Some studies indicate that the increase in serotonin and dopamine production, following manual stimulation, plays a role in mood regulation and emotional resilience (Mahdavipour et al., 2019; Espí-López et al., 2020). Other mechanisms include the activation of the hypothalamic-pituitary-adrenal (HPA) axis, which supports stress regulation and restores neuroendocrine balance (Dehghan et al., 2022). A psychosomatic approach is also emphasized, where manual therapy contributes to mind-body integration through effects on somato-visceral reflexes and psychophysiological feedback systems (Cardini et al., 2010). In particular, craniofacial

techniques have been associated with improved cerebral perfusion, which facilitates better oxygenation and nutrient delivery to brain tissues. This effect may promote neuroplasticity and improve the brain's emotional processing capacity, helping to reduce symptoms of anxiety and depression (Espí-López et al., 2020; Listiana et al., 2022). Overall, manual therapies appear to support the neuroendocrine system by reducing stress hormones and enhancing neurotransmitter levels, thereby contributing to emotional stability and psychological well-being in menopausal women (Mehrnoush et al., 2021; Espí-López et al., 2020; Mahdavipour et al., 2019). see Table.7 Results on the mechanism of action.

Table.7 Results on the mechanism of action

Article Title	Authors	Reported Effects	Mechanism of Action
Massage Therapy to Relieve Menopausal Symptoms: A Systematic Review of RCTs	Listiana et al 2022	Reduction of anxiety and depression, improvement of mood	Reduction of cortisol and activation of the parasympathetic, via neuroendocrine modulation
Efficacy of Complementary and Alternative Therapies for the Management of Psychological Symptoms of Menopause: A Systematic Review of RCTs	Mehrnoush et al.2021	Reduction of anxiety ,depression and cortisol levels	Modulation of the autonomic nervous system. Increased parasympathetic tone, reduced cortisol and increased serotonin
Prevalence of CAM Use by Menopausal Women: A Systematic Review of Survey Studies	Posadski et al 2013	Reduction of depression	Support for psychophysiological. Mind-body integration with effect on somato visceral pathways and on depression
The use of Complementary and Alternative Medicine by Women Experiencing	Cardini et al 2010	Reduction of anxiety and depression symptoms	Neurovegetative balance and reduction of perceived stress and therefore benefits on anxiety Modulation on hormonal axes HPA

Menopausal Symptoms			
Menopause symptoms in women and its relation with using complementary and alternative medicines: A survey in southeast Iran	Dehgan,2022	Improvement of emotional response and perceived anxiety	Autonomic nervous system balance Emotional benefits with stress reduction and consequent anxiety reduction
"I Am Hot, Irritable and Feeling Low; What Alternatives Do I Have Besides Hormone Replacement Therapy?"	Sulaiha et al 2010	Positive effects on anxiety and psychological well-being	Improved general relaxation, parasympathetic stimulation reduced sympathetic activity, benefits on anxiety and depression
The Beneficial Effects of Therapeutic Cranio-Facial Massage on Quality of Life, Mental Health and Menopausal Symptoms and Body Image: A RCT	Espi-Lopez et al 2020)	Reduction of anxiety and depression	Improvement of cerebral perfusion, cerebral oxygenation, regulation of neuroendocrine with positive effects on anxiety and depression
The Effects of Foot Reflexology on Depression During Menopause	Mahdavipour et al 2019	Reduction of depression	Sympathetic stimulation and increased serotonin and dopamine, an increase in positive neurotransmitters that counteract anxiety, depression, and improve mood.

6 Discussion

This scoping review identified eight studies exploring the effectiveness of manual therapies in alleviating symptoms of anxiety and depression among menopausal women. The findings suggest that interventions such as therapeutic massage, foot

reflexology and craniofacial therapy may positively influence emotional regulation through modulation of the autonomic nervous system (ANS), reduction in cortisol levels and stimulation of serotonin and dopamine production (Espí-López et al., 2020; Mahdavipour et al., 2019; Listiana et al., 2022).

6.1 Interpretation of Results and Comparison with Existing Literature

The results align with previous literature demonstrating that manual therapies can influence the hypothalamic-pituitary-adrenal (HPA) axis, reducing sympathetic hyperactivity and enhancing stress resilience (Licciardone et al., 2010; Bruno et al., 2020). Psychological benefits are often accompanied by improved sleep quality and body image, which are key components of well-being during the menopausal transition (Hernandez-Reif et al., 2000). Notably, this review highlights emerging evidence on the effectiveness of craniofacial massage, a relatively understudied technique, which shows promise in enhancing emotional stability and self-perception. However, variability in study designs, sample sizes and sociocultural settings necessitates cautious interpretation (Dehghan et al., 2022; Mahdavipour et al., 2019).

6.2 Clinical Implications

Manual therapies may serve as complementary or alternative strategies to hormone replacement therapy (HRT), especially for women who are unable or unwilling to pursue pharmacological treatment. Within a person-centered care framework, these non-invasive and holistic interventions address both physical symptoms and emotional distress (MacPherson et al. 2017). For osteopaths, this represents an opportunity to integrate neuroendocrine knowledge with hands-on therapeutic techniques, supporting ANS regulation and hormonal adaptation during menopause (Bruno et al., 2020; Korr, 2012). These findings advocate for greater inclusion of manual therapies in integrative care models targeting women’s mental health.

6.3 Methodological Limitations

Several limitations affect the generalizability of the findings. The included studies varied widely in methodology, ranging from randomized controlled trials to observational designs and reviews, which hinders direct comparison and synthesis (Munn et al., 2018; Peters et al., 2020). Many studies featured small sample sizes, lacked long-term follow-up, or were conducted in limited geographical contexts such as Iran, Indonesia or Spain, thereby reducing external validity (Dehghan et al., 2022; Nasiri et al., 2020). Inconsistent reporting of adverse events and a lack of standardization in manual therapy protocols are additional limitations. Furthermore, potential confounding factors—such as patients' pre-existing preference for complementary medicine—were often not addressed (Gohari & Hosseini, 2021; Abbaspoor et al., 2021). Lastly, the data analysis was performed by a single author, without a second reviewer to independently assess study selection or thematic synthesis, which could introduce interpretive bias (Armstrong et al., 2011). However, adherence to rigorous frameworks, such as the PRISMA-ScR and the Joanna Briggs Institute methodology, aimed to mitigate these risks (Tricco et al., 2018; Peters et al., 2020).

6.4 Ethical Considerations and Validity

This study did not involve human participants or the collection of primary data and therefore did not require formal ethical approval. Nonetheless, it was conducted in accordance with the ethical guidelines set by Metropolia University of Applied Sciences (Metropolia, 2023). Peer-reviewed articles were selected using clear inclusion and exclusion criteria, ensuring credibility and replicability of the data collection process. To enhance academic rigor, artificial intelligence tools such as ChatGPT and Meta AI were used to support language refinement and bibliographic organization. However, all critical evaluations and interpretations were the sole responsibility of the author.

The author brings extensive clinical expertise in osteopathy, especially in women's health, but she had to familiarize herself with academic research terminology. Several pilot searches were performed to refine the search strategy and optimize the Boolean combinations. This preparatory work contributed to a conceptually grounded and methodologically transparent review.

6.5 Conclusion

This scoping review highlights the potential role of manual therapies—such as therapeutic massage, craniofacial massage and foot reflexology—as effective non-pharmacological interventions for the management of anxiety and depression symptoms in menopausal women. These approaches appear to act through the modulation of the autonomic nervous system and neuroendocrine pathways, promoting emotional regulation, stress reduction and improved bodily awareness. Despite the encouraging results, current evidence remains limited by methodological heterogeneity, small sample sizes and a lack of long-term follow-up. Nevertheless, the findings point toward a promising direction in the field of integrative care for menopausal women. Manual therapies offer accessible, low-risk options that support active engagement in self-care and may complement or provide alternatives to conventional treatment approaches. Their inclusion in holistic and personalized care models reflects a growing recognition of the importance of body-based interventions in addressing mental health challenges during menopause. Expanding scientific knowledge in this area will not only strengthen clinical decision-making but also contribute to improving the overall quality of life for women in this transitional phase. The integration of manual therapies into multidisciplinary strategies may represent a valuable advancement in promoting well-being in a population often underserved in traditional health care.

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Appendix 1

Article Title	Authors	Country of the study	Methodology/Research Design	Results	JBI as-sess-ment score
Massage Therapy to Relieve Menopausal Symptoms: A Systematic Review of RCTs	Listiana et al 2022	United States, South Korea, Iran	Quantitative /Systematic review of RCTs	Deep massage: reduction of anxiety and depression, via neuroendocrine modulation, improvement of mood. Reduction of cortisol and activation of the parasympathetic.	18/22

Efficacy of Complementary and Alternative Therapies for the Management of Psychological Symptoms of Menopause: A Systematic Review of RCTs	Mehrnoush et al.2021	United States, United Kingdom, Australia	Quantitative/ Systematic Reviews and Research Syntheses	Therapeutic massage: increased parasympathetic tone, reduced cortisol and increased serotonin. Modulation of the autonomic nervous system, reduction of anxiety and depression	20/22
Prevalence of CAM Use by Menopausal Women: A Systematic Review of Survey Studies	Posadski et al 2013	United States, Canada, Australia	Quantitative/ Systematic Reviews and Research Syntheses	Generic manual therapy: effectiveness on psychological disorders, including anxiety and depression. Mind-body integration with effect on the somato-visceral pathway and support for psychophysiological regulation.	18/22
The use of Complementary and Alternative Medicine by Women Experiencing Menopausal Symptoms	Cardini et al 2010	United States	Quantitative/ Observational study /Analytical Cross-Sectional Studies	Therapeutic massage: neurovegetative balance and reduction of perceived stress, modulation of the HPA hormonal axis and therefore benefits on anxiety.	11/16
Menopause symptoms in women and its relation with using complementary and alternative medicines: A survey in southeast Iran	Dehgan,2022	Iran	Quantitative/ Observational study /Analytical Cross-Sectional Studies	Manipulative therapies: reduction of perceived anxiety and improvement of emotional response, reduction of stress and consequent reduction of anxiety, balance of the autonomic nervous system	11/16
"I Am Hot, Irritable and Feeling Low; What Alternatives Do	Sulaiha et al 2010	Malaysia	Qualitative/Literature review	Deep massage: Parasympathetic stimulation with improved general relaxation, reduction	14/20

I Have Besides Hormone Replacement Therapy?"				of sympathetic activity. Positive effects on anxiety and psychological well-being.	
The Beneficial Effects of Therapeutic Cranio-Facial Massage on Quality of Life, Mental Health and Menopausal Symptoms and Body Image: A RCT	Espi-Lopez et al 2020	Spain	Quantitative/Randomized Controlled Trials	Craniofacial massage: Improved cerebral perfusion and neuroendocrine regulation, Improved cerebral oxygenation, Reduced anxiety and depression	18/20
The Effects of Foot Reflexology on Depression During Menopause	Mahdavipour et al 2019)	Turkey	Quantitative/Randomized Controlled Trials	Foot reflexology: sympathetic stimulation and increase in serotonin and dopamine, which have an effect on counteracting anxiety, depression and improving mood.	18/20