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Hormone replacement therapy in menopausal women diagnosed with metabolic syndrome.

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ABSTRACT

Introduction: Hormone replacement therapy (HRT) has been widely used in the management of menopausal symptoms and has significant effects on metabolism and cardiovascular risk.
The aim of this study was to analyze, through an integrative review, the effects of HRT in postmenopausal women diagnosed with metabolic syndrome or its components.
Methodology: A search was conducted in the PubMed, Virtual Health Library (BVS), and CAPES Periodicals Portal databases, covering studies published between 2021 and 2026.
Results: Sixteen articles that met the eligibility criteria were included in this review. The results showed that HRT is associated with improved metabolic profile, including reduced insulin resistance, improved glycemic control, increased high-density lipoprotein (HDL) and reduced low-density lipoprotein (LDL), as well as decreased visceral adiposity. These effects are attributed to the action of estrogens in regulating metabolic homeostasis, with a direct impact on insulin sensitivity and lipid metabolism. It was also observed that the route of administration influences the outcomes, with the transdermal route being associated with less hepatic impact and a better inflammatory profile compared to the oral route. Furthermore, HRT demonstrated potential to reduce cardiovascular risk by acting on factors directly related to metabolic syndrome. It is concluded that hormone replacement therapy plays a relevant role in metabolic and cardiovascular modulation in postmenopausal women, and its indication should be individualized.

Descriptors: Menopause. Hormone replacement therapy. Metabolic syndrome. Quality of life.

1 INTRODUCTION

Menopause is a natural physiological process in women, characterized by the cessation of menstrual cycles. Permanent amenorrhea is the cessation of menstrual cycles after 12 consecutive months of amenorrhea, resulting from the depletion of ovarian function. It is characterized by substantial changes in the patterns. Estrogenic and progestogenic hormones with unfavorable physiological manifestations. The decline Estrogen triggers a series of metabolic changes in the body, as it plays a role. essential in regulating glucose and lipid metabolism, and may lead to an increase in Insulin resistance, fat accumulation in the abdominal region, and cardiovascular disease.

Natural menopause is considered premature if it occurs before the age of 40 and early if it occurs between the ages of 40 and 40. 40 and 45 years of age. Therefore, many women will spend about 40% of their lives in the post-menopause (Silva et al., 2024).

Metabolic syndrome (MS) is a cluster of risk factors that is becoming more prevalent. with the hormonal decline of menopause. These changes also contribute to a metabolic profile.

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which increases the risk of cardiovascular disease and type II diabetes. Surgical menopause is potentially associated with a higher incidence of metabolic syndrome compared to Natural menopause, due to the abrupt drop in estrogen and progesterone levels. This syndrome It is characterized by a combination of metabolic dysfunctions, glucose intolerance, and low levels. high-density lipoprotein cholesterol (HDL-C), high levels of triglycerides (TGs), Obesity and hypertension. Furthermore, it is associated with a high risk of cardiovascular disease. (CVD). According to the criteria of the *National Cholesterol Education Program Adult Treatment Panel III* (NCEP ATPIII), the diagnosis of metabolic syndrome can be established by the presence of at least three of the components mentioned above (Ou, Ying-Ju et al., 2023).

Epidemiological data show that, in Brazil, approximately 20.8% of postpartum women Menopausal women present with metabolic syndrome. Globally, the World Health Organization (WHO) recognizes metabolic syndrome as one of the leading causes of female mortality after menopause, the which makes the condition relevant to the study, as it highlights the need for preventive strategies. and therapies that include not only hormone replacement therapy, but also lifestyle changes. and multidisciplinary support in women's health care (WHO, 2025).

Hormone replacement therapy (HRT) has proven to be an effective alternative for relieving symptoms. of climacteric symptoms and for the modulation of these metabolic changes. Recent studies Studies show that estrogen plays a protective role in the lipid profile, reducing LDL levels. and increasing HDL cholesterol, as well as improving insulin sensitivity. The therapeutic choice should It should be individualized, considering age, the presence of cardiovascular risk factors, and medical history. of cancer, for example, in addition to the routes of administration, as a common practice to mitigate the Discomfort of symptoms and an important strategy in treatment. The first line of treatment is the use of systemic estrogens, orally or transdermally, with a need for progestogen in those who has a uterus. (Santos et al., 2023 and Oliveira & Moura, 2024).

They are the basis of HRT for treating moderate to severe vasomotor symptoms and preventing blood loss. bone marrow cancer screening when initiated within the window of opportunity (up to 10 years after menopause or <60 years of age, in women without contraindications). On the other hand, initiating HRT in women over 60 years of age and after more A 10-year delay in menopause can increase the risk of cardiovascular disease. Venous thromboembolism and stroke. In these circumstances, it is not recommended. Initiating hormone therapy is generally recommended (Oliveira et al., 2024). This study aims to analyze the effects hormone replacement therapy in menopausal women diagnosed with metabolic syndrome, considering its metabolic and cardiovascular impacts, as well as its impact on quality of life, with based on published scientific evidence.

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2 METHODOLOGY

This study is characterized as an integrative literature review. The survey
The bibliographic review was conducted between January and May 2026, through a structured search in PubMed databases, Virtual Health Library (VHL) and CAPES Periodicals Portal, including articles published in the last 5 years, with no language restriction.

The search strategy was developed using the Health Sciences Descriptors (DeCS). using the terms “Menopause”, combined with “Hormone Replacement Therapy”, “Metabolic The terms "Syndrome" and "Quality of life" are associated using the Boolean operator AND. The strategies were adapted to the specific characteristics of each database.

Original studies, available in full, that investigated women in postgraduate studies were included. menopause, whether of natural or surgical origin, undergoing hormone replacement therapy, using estrogen alone or in combination with progestogens, regardless of the route of administration. administration. Studies that addressed metabolic syndrome or its administration were considered eligible. isolated components, such as insulin resistance, changes in lipid profile, abdominal obesity, blood pressure and glucose metabolism, provided they presented a quantitative approach and measurable results, including clinical trials, cohort studies, case-control studies, and studies analytical cross-sections.

Studies that included premenopausal or perimenopausal women without [specific criteria] were excluded. separate analysis of the data, as well as those that investigated phytoestrogens exclusively, Alternative therapies or supplements were excluded. Literature reviews and reviews were also excluded. Systematics, meta-analyses, editorials, letters, opinions, case reports, and series with small samples. Additionally, studies that did not present clear quantitative data were disregarded. were not available in full, had insufficiently described methodology, or were highly... Risk of bias, as well as duplicates identified between the databases.

For the search of scientific articles, structured searches were performed. In PubMed, it was... The following search was performed: "Menopause" AND "Hormone Replacement Therapy" AND "Metabolic Syndrome", with research of articles published in the last 5 years, in humans, in full text/free. Full text. Total: 15 articles.

The following search was performed in the Virtual Health Library (VHL): "Menopause" AND "Hormone Replacement Therapy" AND "Quality of life", searching for articles published in the last 5 years, in Portuguese, English, and Spanish, with access to the full text. Study types: factors of risk, observational study, systematic review, controlled clinical trial, prevalence study, Qualitative research. Total: 23 articles.

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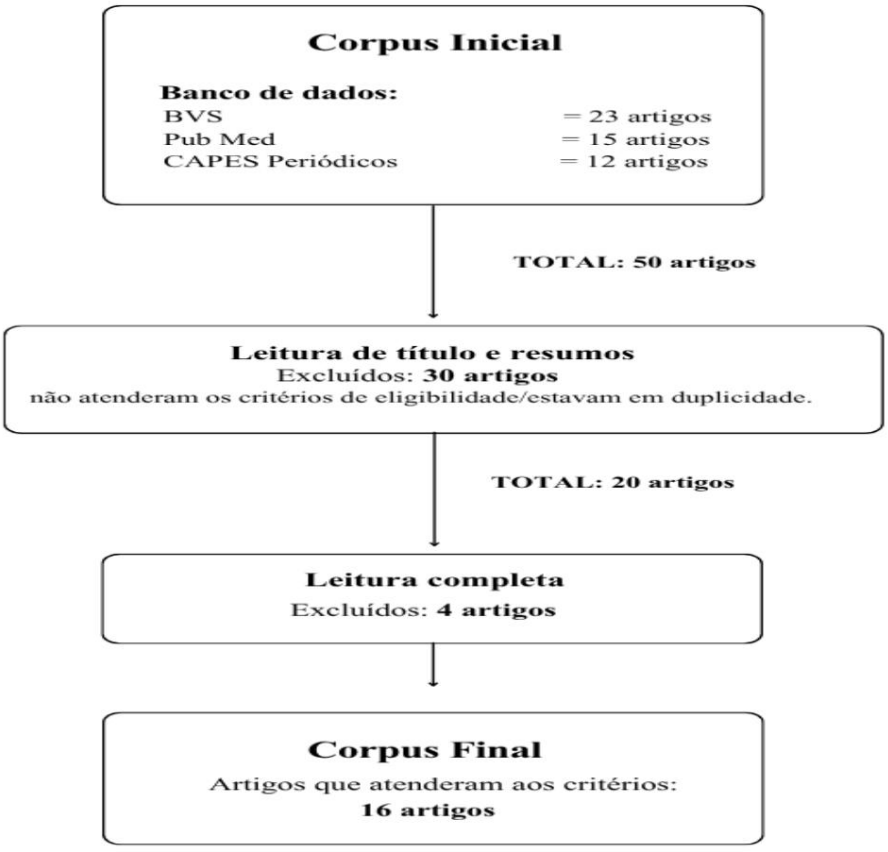
The following search was performed in CAPES Periodicals: "Menopause" AND "Hormone" "Replacement Therapy" AND "Metabolic Syndrome", searching open articles and peer-reviewed articles. peer-reviewed articles published in the last 5 years. TOTAL: 12 articles

3 RESULTS

The selected studies were published in the last 5 years (2021 to 2026), with a predominance of observational designs and clinical trials, encompassing postmenopausal women. undergoing hormone replacement therapy (HRT).

The search was conducted in the PubMed database (15 studies), Virtual Health Library (VHL) (23 articles) and the CAPES Periodicals Portal (12 articles) resulted in the identification of 50 articles. After screening of Of the titles and abstracts, 30 studies were excluded for not meeting the eligibility criteria or for... There were duplicates, leaving 20 studies to be read in full. In the end, 16 articles met all the requirements. The established criteria were included in the integrative review, as shown in Figure 1.

Figure 1. Flowchart of article selection included in the integrative review, 2026.



Source of figure 1: author's own work, 2026.

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Table 1 presents a summary of the main characteristics of the selected studies. considering the title, authors, year of publication, objectives, and main results.

Table 1. of the articles selected for the article, 2026

Article Title: Objective	Author/Year		Key results
Hormones and women in menopause	SAMPAIO; Medrado; MENEGON, 2021	Critically analyze discourses on the use of hormones. During menopause.	Hormone replacement therapy (HRT) is embedded within a context of the medicalization of menopause, being associated with the maintenance of youth and femininity. The use of this therapy is influenced by sociocultural factors and the pharmaceutical industry, which reinforces the need for an individualized approach.
Quality of life assessment using a questionnaire. WHOQOL-BREF in women during menopause and menopause	JESUS et al., 2023	Assessing the quality of life of women in the climacteric and menopause using the WHOQOL-BREF instrument.	Quality of life was shown to be more associated with behavioral factors, especially the practice of physical activity, with better scores in the physical, psychological, and social domains. The use of HRT is secondary and showed a tendency towards higher average values among the female users.
Association between hormone replacement therapy and sex hormones in postmenopausal women: a systematic review and meta-analysis	LU et al., 2023	Evaluate the effects of HRT in the hormonal profile	Hormone replacement therapy (HRT) improves the hormonal profile and positively influences metabolic parameters.
Impacts of hormone replacement therapy on the metabolic profile of postmenopausal women with metabolic syndrome.	SANTOS, MF et al., 2023	To evaluate the effects of hormone replacement therapy on the metabolic profile in postmenopausal women with metabolic syndrome.	Hormone replacement therapy (HRT) promotes improvements in the metabolic profile, including reduced insulin resistance, improved lipid profile, and decreased inflammatory markers.
Association between Menopause, Postmenopausal Hormone Therapy, and Metabolic Syndrome.	OU, YJ et al., 2023	To investigate the association between menopause and the use of HRT and the occurrence of metabolic syndrome	Menopause is associated with an increased risk of metabolic syndrome, while HRT (Hormone Replacement Therapy) has a protective effect on metabolic parameters.
Hormone replacement therapy in menopause: benefits,	ROCHA et al., 2024	Analyze the benefits, risks, and impacts of HR in	HRT reduces vasomotor symptoms, improves sleep, cognitive function, and symptoms.

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risks and impacts on women's quality of life		quality of life of women in menopause.	urogenital problems, in addition to providing benefits to the skin and sexuality. It assesses risks such as breast cancer and endometrial changes.
Effects of hormone replacement therapy on metabolic syndrome in menopausal women.	SILVA, M. et al., 2024	Evaluate the effects of Hormone replacement therapy (HRT) in metabolic syndrome and different routes of hormone administration.	Hormone replacement therapy (HRT) improves metabolic parameters, with differences between administration routes. The transdermal route is associated with a better metabolic profile and a lower thrombotic risk.
Hormone Replacement Therapy in Menopause: A Comprehensive Review	CYRULIK et al., 2025	Review the effects of TRH	Metabolic and clinical benefits
Cardiovascular risk associated with menopause and menopause hormone therapy: a review and contemporary approach to risk assessment	D'COSTA et al., 2025	Assess cardiovascular risk	HRT may be beneficial depending on the clinical profile.
Legal Considerations in Bioidentical Hormone Replacement Therapy: Anticipating Future Challenges in Medical Liability	DEL DUCA et al., 2025	To analyze the clinical and legal aspects related to the use of bioidentical hormones in hormone replacement therapy.	Bioidentical hormones are presented as an alternative to conventional HRT because they are structurally identical to endogenous hormones. However, they have limitations regarding standardization, quality control, and long-term scientific safety evidence.
The impact of estrogen deficiency on liver metabolism: implications for hormone replacement therapy	DONG et al., 2025	Evaluate liver metabolism	Estrogen deficiency associated with metabolic alterations
Metabolic syndrome, insulin resistance, and menopause: the changes in body structure and the therapeutic approach	GENAZZANI, Alessandro D. et al., 2025	Assess metabolic changes	Increased adiposity and insulin resistance
Metabolic syndrome in menopause	GUMPENY et al., 2025	Assessing the relationship between menopause and metabolic syndrome	Association with insulin resistance and dyslipidemia
Relationship between MASLD and women's health: A review	JANCOVA et al., 2025	Assess the liver-metabolism relationship	Strong association between metabolism and menopause.

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Reconsidering hormone replacement therapy: Current insights on utilization in premenopausal and menopausal women	VYANCHKOVA et al., 2025	Review the use of HRT effective HRT with metabolic impact	
Effect of hormone replacement therapy on liver and cardiometabolic outcomes in peri-menopausal MASLD	HENNEY et al., 2026	Assessing HRT in metabolic outcomes	Hormone replacement therapy (HRT) improves liver and cardiometabolic parameters.

Source: Author's own work, 2026.

4. DISCUSSION

The decrease in estrogen levels leads to an increase in gonadotropin levels. which induces ovarian secretion of androgens, as well as decreasing levels of binding globulin of sex hormones. This imbalance increases the level of bioavailable testosterone and can induce fat accumulation in the pre-adipocytes of visceral fat. All these factors increase The incidence of obesity in postmenopausal women is due to hormonal imbalance. Dysfunction of adipocytes generates an inflammatory response, associated with an increase in the population of M1 macrophages in the tissue (Ou, Ying-Ju et al., 2023). Gumpeny et al. (2025) still state that this This condition favors the secretion of pro-inflammatory adipokines, such as TNF-ÿ and IL-6, contributing to a chronic low-grade inflammatory state and the development of insulin resistance.

In parallel, estrogen deficiency is associated with the accumulation of hepatic lipids and... development of metabolically associated fatty liver disease (MASLD), because It disrupts liver metabolism. Studies highlight the role of estrogen in regulating it. Lipid homeostasis, reinforcing the interconnection between menopause, insulin resistance, and dyslipidemia. This scenario significantly contributes to an increased risk of cardiovascular disease, since the The liver plays a central role in the regulation of plasma lipoproteins. (Dong et al., 2025; Jancova et al., 2025; Henney et al., 2026).

With regard to vascular mechanisms, Genazzani et al. (2025) highlight that the reduction Elevated estrogen levels compromise endothelial function, contributing to the onset and progression of disease. of atherosclerosis. In addition, Gumpeny et al. (2025) address menopause as a factor in This is a significant risk factor for the development of metabolic syndrome, emphasizing that conditions such as

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High blood pressure, hyperglycemia, and changes in lipid profile increase the risk of events.
cardiovascular.

Given this scenario, hormone replacement therapy (HRT) emerges as a strategy.
A therapy capable of mitigating the effects of estrogen deficiency. Evidence demonstrates that HRT (Hormone Replacement Therapy)
It improves the hormonal profile and exerts beneficial effects on glucose and lipid metabolism.
including increased insulin sensitivity and reduced visceral fat (Lu et al., 2023; Cyrulik
et al., 2025). Furthermore, hormone therapy with bioidentical hormones can modulate pathways
They reduce inflammation and improve endothelial function, contributing to a reduction in cardiometabolic risk.
(D'Costa et al., 2025; Dong et al., 2026).

Bioidentical hormones are chemical compounds that have exactly the same structure.
molecular structure of human endogenous steroid hormones. They have been presented as a
an alternative to conventional hormone replacement therapy in the management of menopausal symptoms, by
They exhibit identical molecular structure. Their use may be safer and more effective than that of
Non-bioidentical hormones, since these bind to chemical receptors present in the membrane.
of the cells in a manner similar to the connection established by endogenous hormones, replenishing what
deficiency in the body, with the correct dosage indicated individually (Vyanchkova et al., 2025 and Leite et
al.,2024).

However, according to Del Duca et al. (2025), this characteristic contributes to the perception of greater
Safety and "naturalness" among patients, however, while they may offer clinical benefits.
Similar to traditional HRT, its use still requires robust evidence regarding...
therapeutic superiority and long-term safety, due to the significant limitations related to
Standardization and quality control of these hormones, especially when compounded,
which can result in dosage variations and unpredictable effects. In the context of menopause, this
This represents a significant challenge, since hormonal treatment requires precision and
continuous monitoring. The study also emphasizes ethical and legal implications, highlighting that the
Prescribing these compounds requires caution, proper patient education, and informed consent.
informed, due to the absence of consolidated scientific consensus and the potential increase in
Medical responsibility in the face of potential adverse events.

However, the effects of HRT are not homogeneous and depend on multiple factors, including
The route of administration of hormones. The oral route, widely used, is associated with the effect of
First-pass metabolism, which can result in increased hepatic protein synthesis.
such as coagulation factors and triglycerides, which can increase the risk of thromboembolism in
certain populations. In contrast, the transdermal route avoids initial hepatic metabolism,
promoting a more stable release of estrogen into the systemic circulation and less impact on

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Inflammatory and metabolic markers (Cho et al., 2023; Vyanchkova et al., 2025).

In this sense, studies indicate that transdermal administration presents a metabolic profile.
more favorable in women with higher cardiovascular risk or with metabolic syndrome
established, since it is associated with a smaller increase in triglyceride levels and less
Interference with coagulation. That being said, the choice of administration route should consider
Individual patient characteristics, including age and time elapsed since the onset of menopause.
and the presence of comorbidities, which reinforces the importance of a therapeutic approach.
individualized (Xia et al., 2025).

The results presented by Silva et al. (2024) show that the impact of therapy
Hormone replacement therapy (HRT) in menopausal women manifests itself comprehensively in both
The benefits are not merely related to metabolic aspects as well as the overall health of patients.
physiological benefits also improve women's quality of life by reducing symptoms.
vasomotor symptoms, improved psychological well-being, and greater physical and emotional balance, which
It promotes the maintenance of daily activities and social interactions. The authors emphasize that HRT (Hormone Replacement Therapy)
It is associated with a reduction in irritability, anxiety, and depressive symptoms, frequently.
reported during menopause. The hormonal modulation promoted by the therapy favors balance.
neuroendocrine system, which is reflected positively in mood and mental health. In this way, not only
It minimizes the clinical manifestations of menopause, but also promotes significant benefits to...
quality of life.

The study by Jesus et al. (2023) indicates that the quality of life of women in menopause and
Menopause is influenced by multiple factors, most notably the practice of
Physical activity and the use of hormone replacement therapy (HRT). A trend was observed towards
The best averages are found among therapy users who regularly engage in physical activity.
In this way, the research shows that non-pharmacological interventions, especially physical activity, are effective.
Regular therapy plays a central role in promoting well-being at this stage, suggesting that HRT may...
to act as a complementary resource for improving the overall health conditions of these women.

According to Rocha et al. (2024), HRT acts primarily in reducing symptoms.
vasomotor symptoms, such as hot flashes and night sweats, can decrease their frequency by up to 75%.
and its intensity up to 87%. Furthermore, the therapy promotes improved sleep and cognitive function.
and psychological well-being, essential factors for maintaining overall health during the
perimenopause and menopause. Other benefits include improvement of vulvovaginal atrophy, with
Increased lubrication and elasticity, which positively impacts sexual function and reduces
associated discomforts. The author also advocates for replacement, especially via local injections.
contributing to the restoration of vaginal lubrication during sexual intercourse. As a result,

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There is a positive impact on sexual life and interpersonal relationships, in addition to improved self-esteem and... emotional well-being of patients.

In contrast, the studies by Sampaio, Medrado and Menegon (2021) present a A critical approach to HRT, highlighting that its prescription goes beyond mere necessity. strictly clinical and is strongly influenced by social and cultural constructs about female aging. The authors argue that HRT is often presented as A solution for the imbalance caused by menopause, which reinforces the medicalization of this process. In this sense, menopause is treated as a pathological condition that requires... intervention, which contributes to the increased use of hormones as a way to restore an ideal. of a young and functional body.

Furthermore, they emphasize that TRH is embedded in a context strongly influenced by the industry. pharmaceutical and biomedical discourses that associate femininity with youth and active sexuality. and to attractiveness. Therefore, HRT not only acts on the biological body, but also on the construction of Subjectivities shape social expectations about how women should age. The study Sampaio, Medrado and Menegon (2021) points out that not all women present symptoms. Significant factors in menopause, and what cultural, social, and individual factors influence this. experience, contributing to a critical reflection on the use of HRT.

However, all studies were categorical and highlighted important controversies surrounding the topic. regarding the use of HRT, especially concerning its indiscriminate prescription. Thus, the generalization of Hormone therapy as a universal solution is being questioned, and an individualized approach is being advocated. For each patient. HRT should be prescribed individually, considering the risks. Associated conditions, such as breast cancer and endometrial changes, make monitoring essential. Continuous clinical practice is necessary to ensure the safety and effectiveness of the treatment.

FINAL CONSIDERATIONS

This integrative review demonstrated that hormone replacement therapy exerts effects Relevant positive findings regarding the components of metabolic syndrome in menopausal women. Findings demonstrate that HRT is associated with improved glucose metabolism and a reduction in... insulin resistance, favorable modulation of the lipid profile, and reduction of visceral adiposity. factors directly involved in the pathophysiology of metabolic syndrome, diabetes, and other diseases Cardiovascular benefits. In addition to improvements in psychological and sexual aspects and quality of life.

It was also observed that the route of administration of hormone therapy influences the outcomes. Metabolic: the transdermal route is associated with a better inflammatory profile and less impact.

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The oral route has more pronounced effects on hepatic metabolism, while the oral route has more pronounced effects on lipid metabolism.

The great medical responsibility involved in prescribing the use of bioidentical hormones was noted. Regarding HRT, there are still no robust studies on its long-term use and quality control. Manipulating these hormones is difficult.

It is also worth highlighting that the improvement in metabolic parameters promoted by HRT contributes directly related to reducing the risk of events such as atherosclerosis, coronary artery disease and Acute myocardial infarction. Estrogenic action improves endothelial function and enhances its potential. Cardioprotective, especially when initiated in the early stages of menopause. Therefore, HRT It can act not only in relieving menopausal symptoms, but also as a relevant strategy. for modulating cardiometabolic risk.

The *Food and Drug Administration* (FDA) announced in November 2025, in the United States United States of America, which will remove the maximum warnings (“black box warnings”) from dozens of hormones used in hormone replacement therapy for menopausal symptoms, introduced more than 20 years, based on the 2002 "Women's Health Initiative" (WHI) study, which indicated an increase in risk of cardiovascular disease and breast cancer. The new FDA assessment concluded that, when Initiated in women under 60 years of age or up to 10 years after the onset of menopause, the therapy Hormonal therapy is safe and effective for menopausal symptoms, in addition to providing other benefits. In Brazil, The Brazilian Federation of Gynecology and Obstetrics Associations (FEBRASGO) affirms progress. in accessing hormone therapy when indicated.

In light of the above, it is evident that HRT represents a promising therapeutic approach. in the management of metabolic syndrome in menopausal women, in addition to alleviating the symptoms. associated, acting on pathophysiological mechanisms closely related to hypoestrogenism. However, the heterogeneity of available studies regarding the pathways of The administration, the doses used, and the profile of the populations investigated still limit the consolidation. of universally established clinical protocols, signaling the need for clinical trials. Larger randomized controlled trials with prolonged follow-up and more complex methodological designs. rigorous. Future research should also explore the impact of different hormonal formulations, including bioidentical estrogens and new-generation progestogens, on inflammatory markers, adipokines, gut microbiota, and potential neoplasms, broadening the understanding of the effects systemic aspects of this therapy.

In this scenario, the biomedical professional emerges as a uniquely relevant professional, contributing both for the laboratory analysis of biochemical and hormonal parameters that support the diagnosis. and therapeutic monitoring as well as the scientific production that underpins clinical practices safe and evidence-based, reaffirming their indispensable role in promoting health.

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females in all stages of menopause.

It is of utmost importance to emphasize the need for individualized therapy, considering clinical characteristics, risk profile, age, and time since menopause, in order to maximize the benefits and minimize potential harm. Therefore, it can be concluded that HRT can play a role. relevant in the prevention and management of metabolic and cardiovascular changes in post-Menopausal women, provided that it is used judiciously, individually, and based on evidence. scientific.

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