WISELEAF SCIENTIFIC VENTURES



CHAPTER-5
MENOPAUSE TO HEALTHY AGING: HORMONAL TRANSITION, POLYPHARMACY AND PRECISION PHARMACOTHERAPY IN WOMEN

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Abstract

Menopause is a key physiological phase of a woman's life, made of several aspects like reduced ovarian hormonal levels and increased vulnerability to diverse health issues, such as osteoporosis, heart diseases, metabolic disorders, and alteration in mental health. While progressing towards healthy aging, the right medication management is necessary to fulfil evolving health requirements without causing risk of effects. Postmenopausal women undergoing polypharmacy are more prone to experience adverse drug reactions and interactions as well as a bigger chance of inappropriate prescribing and reduced medication adherence. The chapter discusses hormonal changes in menopause as well as their potential consequences in terms of onset of diseases and issues of medication management throughout the process of aging. It also speaks about the application of hormone replacement therapy, non-hormonal treatment options, preventive medication strategy, and regular medication reviews. Moreover, precision pharmacotherapy provides possibilities to customize treatment by incorporating genetic factors, hormonal status, comorbidities, lifestyle habits, and personal preferences of the

patients. New trends such as pharmacogenomics, artificial intelligence-supported decisions, and individualized risk assessment may enhance medication safety and effectiveness. Interdisciplinary health care, deprescribing, and the evidence-based approach to prescribing may enable quality treatment decisions and contribute to patient retention and promotion of good health in the long term.

Keywords: Healthy aging, Menopause, Pharmacogenomics, Polypharmacy, Precision pharmacotherapy.

1. Introduction

Menopause is the natural stage of transition in a woman's life that involves the end of monthly menstruation as a result of the decrease in the ovarian activity and the decreased production of estrogen. The process occurs in women aged 45 to 55 years thus being regarded as the end of their reproductive cycle. The process triggers hormonal, physiological, and metabolic changes that may have an impact on various organ systems. Though menopause is a normal life stage, it also results in the changes that may lead to health problems requiring medical assistance.

The decline of the levels of estrogen and progesterone is one of the main causes of the appearance of symptoms of menopause such as hot flashes, night sweats, mood changes, sleeping problems, dryness in the vagina, and decreased sexual health. The lack of estrogen also influences bone metabolism, heart and vascular processes, glucose metabolism, lipid metabolism, as well as the processes happening in the nervous system, which may lead to such diseases as postmenopausal osteoporosis, cardiovascular diseases, disorders of metabolism, and numerous age-related health issues. The duration and severity of menopausal symptoms are different for every woman depending on hormones, genetics, environment, and lifestyle [1].

Clinical care during menopause may involve possible hormonal or non-hormonal approaches. Hormone replacement therapy (HRT) is a viable option for females suffering from moderate to severe symptoms of menopause especially including disorders related to vasomotor and genitourinary functions. Nevertheless, the selection of a method of treatment needs an in-depth analysis of personal medical condition and problems including medical history, contraindications, adverse effects, and risks. Along with hormonal medication, other kinds of

treatment may include non-hormonal treatment, changes of the lifestyle, correction of the nutrition, and preventive medicine [2].

As women transfer to older age the presence of various chronic illnesses becomes more evident hence the number of medications to take raises thus causing polypharmacy, interactions of the medicines, and side effects. The influence of the age on pharmacokinetics and pharmacodynamics can be taken into consideration while trying to solve the issue of drug absorption, distribution, metabolism, or elimination from the body and response to the treatment. Hence it is important to use rational medications, conduct regular medication reviews, and apply the strategies of deprescribing in order to make the treatment of patients safer and more effective [3].

Innovations in precision medicine, pharmacogenomics, and artificial intelligence create possibilities for personalization of treatment choices for menopausal and elderly women. The combination of hormonal condition, genetic differences, comorbidities, previous medication use, and the individual responses to therapies can increase the efficiency and safety of pharmacological treatment. Thus, it is crucial to have a deep understanding of menopause-related physiology, clinical features, pharmacological treatment, and drug safety in order to promote healthy aging and maintain functional autonomy [4].

2. Perimenopause and Menopause

Menopause is a natural process that occurs in women when they reach the end of their reproductive life. It occurs as a result of natural changes in women's bodies which lead to the decreased functioning of the ovaries and decreased production of hormones which affected reproductive functioning. The process of menopause has many biological and psychological changes among women. In the course of this transition, perimenopause starts. Perimenopause is a time of irregularities in menstruation and related symptoms. The knowledge of all stages of menopause, clinical features, epidemiological patterns, and health consequences is vital for effective clinical management of menopause. Proper diagnosis of changes which occur during menopause and appropriate treatment is possible for alleviation of unpleasant symptoms during this period [5].

2.1 Definition, Stages, and Epidemiology of Menopause

The term menopause indicates the ultimate termination of menses due to declining ovarian follicular function. It can be diagnosed after the event, in a retrospective fashion, when a woman has experienced a 12-month period of amenorrhea with no other conceivable dental pathology. Usually, natural menopause happens between the years of 45 and 55, with the mean age at which it occurs around 51 years. The period of menopause is divided into three stages: perimenopause, menopause, and postmenopause. Perimenopause is marked by changes in the levels of various hormones produced by the ovaries and irregularity in menstrual cycles. In contrast, menopause is characterized by the last menstrual period, which is followed by postmenopause. Menopause may occur either earlier than 40 years or at the beginning of the 40's. The epidemiology of menopause differs according to geographical, genetic, nutrition, socio-economic, and lifestyle factors. It is important to understand these stages of menopause in order to refer women to medical evaluation and preventive care that they may need [6].

2.2 Perimenopause and Its Clinical Manifestations

Perimenopause is defined as the transition before menopause that results in the decline of the ovarian follicles, resulting in changes in ovulation and variations in the level of female hormones. With the changes in the ovulation and hormone production, there may be changes in the menstrual cycle, which includes irregular periods. In this phase, the concentrations of the follicle-stimulating hormone may rise because of reduced responsiveness of the ovaries to hormones, and the estrogen levels may change from the constant values to the variations before the stable decrease in its levels. It is important to mention that the women may experience some of the following symptoms such as heat flashes, increased sweating, some disturbances during sleep, mood swings, feelings of stress or nervousness, fatigue, and a lack of concentration. It is necessary to note that even if the women have all of the above-mentioned symptoms, they may vary concerning their strength and duration since it may significantly differ from woman to woman. The knowledge of the symptoms will help a woman improve her life and receive appropriate recommendations from physicians [7].

2.3 Health Implications of the Menopausal Transition

The menopause brings many physiological changes which can affect one's long-term health and give rise to certain chronic diseases. The decline in the levels of estrogen leads to increased bone resorption, which is responsible for lower bone density and higher osteoporosis risks. Changes can also take place in lipid metabolism, blood circulation, and body fat distribution resulting in an unfavorable profile regarding the chances of developing cardiovascular diseases. Increased fat in the abdomen area as well as reduced sensitivity to insulin greatly impact insulin regulation as well as metabolic processes in one's body. Hormonal changes might balance thermoregulation, ability to sleep, stabilize mood, and train the brain. Changes in sexual sphere include dryness of the vagina, increased desire to urinate, and recurrent problems with urinary tract infections. The effects can vary based on the age of the patient, whether there are hereditary predispositions, and lifestyle. Treating and preventing the complications of menopause involves regular checkups, diagnostics, diet, physical activity, and medication [8].

3. Hormonal Transition and Estrogen Decline

Menopause transition is characterized by changes in ovarian hormones, especially the drop in estrogen and progesterone concentrations. This change is caused by depletion of ovarian follicles and diminished ovarian responses to stimulation from gonadotropins. Estrogen is responsible for regulation of reproductive functions and stimulation of many systems such as the skeletal, cardiovascular, nervous, and urinary systems. Thus, its decrease causes various menopause symptoms as well as long-term implications for health and well-being. Understanding of the endocrine mechanisms, functions of estrogen receptors, and consequences of hormone shortages is important for the assessment of menopausal health and for finding ways to treat it [9].

3.1 Physiological and Endocrine Changes During Menopause

The menopausal transition is marked by a decline in ovarian function as a result of a gradual depletion of ovarian follicles. The effective number of non-active follicles decreases, leading to the diminished response of ovaries to follicle-stimulating hormone (FSH). This means that the frequency of follicular development and ovulation may decline. Nonetheless, FSH levels in the blood increase while those of inhibin B decrease owing to the decrease of inhibin B

produced by ovaries during their developmental phase. Moreover, LH levels may increase due to the regulation of ovary feedback mechanism being broken **(Figure 1)**. The fluctuation of estrogen can be observed before it decreases considerably afterward. It is important to note that progesterone production decreases since ovulation becomes rare and finally disappears. All the changes in hormonal secretion disturb the functioning of the hypothalamus–pituitary–ovary axis and lead to the problems with the menstrual cycle, hot flashes, the problems with sleeping, and mood swings among women. Additionally, in postmenopause the changes in the production of adrenal androgens and peripheral estrogen conversion take place. All the mentioned physiological changes are important reasons for the experiences associated with menopause [10].

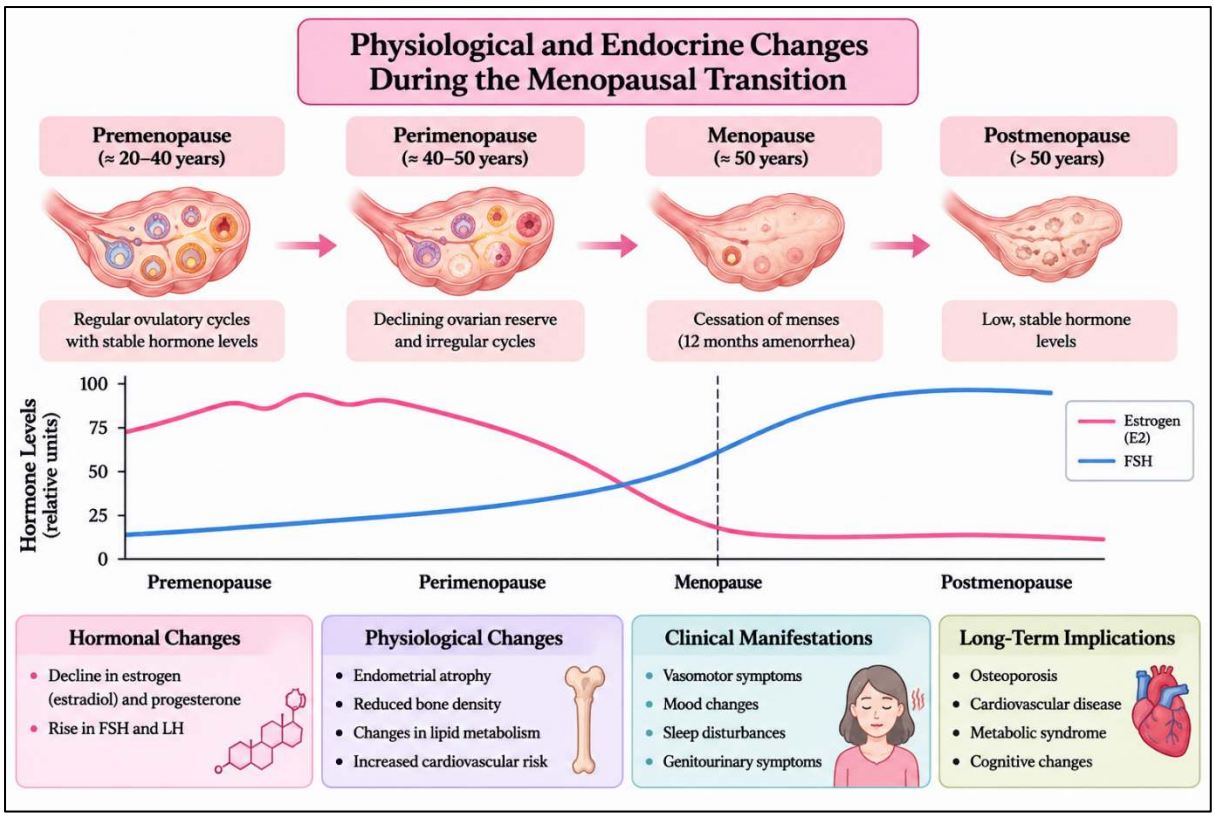

Figure 1. Physiological and Endocrine Changes During the Menopausal Transition image

3.2 Estrogen and Progesterone Decline: Receptors and Functions

Estrogen and progesterone are important hormones in reproduction and they participate in regulating aspects of menstruation, reproductive organs, bone formation, the cardiovascular system, and the functioning of the nervous system. Estradiol is the main kind of estrogen circulating in the body during a woman's reproductive period, as it is produced by the ovaries. After menopause, hormone production from the ovaries is reduced and estrone which comes from the conversion of androgens produced by the adrenal glands into fat, becomes the main type of hormone circulating in the body. In addition, the concentration of progesterone goes down as ovulation and the production of the yellow body stops. Estrogen is able to exert its impact through particular receptors known as estrogen receptors α (ERα) and β (ERβ) and they are responsible for controlling transcription of genes and signaling of cells in different tissues. The two types of receptors are found in all reproductive tissues, bones, heart, brain, and the other tissues. The progesterone hormone is able to act through receptors of progesterone hormone affecting the endometrium and different metabolic processes [11].

3.3 Effects of Estrogen Deficiency on Multiple Organ Systems

The lack of estrogen after menopause affects many physiological systems as estrogen receptors are present throughout the body. In the skeletal system, decreased production of estrogen leads to increased activities of osteoclasts that cause bone tissue resorption thus leading to a decrease in bone density and higher chances of fractures **(Table 1)**. Alongside, cardiovascular related changes occur, including vascular endothelia function impairment, lipid metabolism, as well as vascular stiffness thus resulting in a higher cardiovascular risk. If talking about the central nervous system, reduction of the estrogen level can influence neurotransmitters metabolism, thermoregulation, mood, and cognitive processes. Genitourinary organs are also affected which brings structural and functional changes such as loss of vaginal epithelium thickness and lubrication, pH imbalance as well as urinary symptoms. In addition, lack of estrogen causes changes in fat distribution in the body with the accumulation of fatty tissues in the abdomen as well as low sensitivity to insulin. Moreover, there are changes of collagen level in the skin and also changes in connective tissue functioning thus making the skin lose elasticity and integrity [12].

Table 1. Effects of Estrogen Deficiency on Different Organ Systems

Organ system	Physiological changes associated with estrogen deficiency	Clinical consequences
Skeletal system	Increased bone resorption and reduced bone mineral density	Osteoporosis and increased fracture risk
Cardiovascular system	Endothelial dysfunction and increased arterial stiffness	Increased cardiovascular risk
Central nervous system	Alterations in neurotransmitter activity and neuronal signaling	Mood changes and cognitive symptoms
Genitourinary system	Vaginal epithelial thinning and reduced lubrication	Vaginal dryness, dyspareunia, and urinary symptoms
Metabolic system	Changes in fat distribution and insulin sensitivity	Abdominal obesity and metabolic disturbances
Skin and connective tissue	Reduced collagen production and skin elasticity	Skin dryness and reduced skin firmness
Musculoskeletal system	Changes in muscle mass and physical function	Reduced muscle strength and physical performance

4. Menopausal Symptoms and Their Pharmacological Management

Menopause is accompanied by multiple symptoms which can be physical, emotional, or genitourinary but they are caused by decrease in hormone production from the ovaries. Symptoms differ in intensity, time of occurrence and variety. Symptoms can lead to serious consequences on the quality of life and daily activities. Typical symptoms include hot flushes, mood swings, cognitive problems, sleeplessness, dryness, and difficulties with urination. Treatment of symptoms can include hormonal therapy, medications with no hormones, and methods of localized treatment. The choice depends on the severity of symptoms, medical

history, contraindications, preferences of the patient, and other potential risks of the treatment [13].

4.1 Vasomotor Symptoms, Mood Changes, and Cognitive Symptoms

Vasomotor symptoms are one of the common signs of menopause that occur in the form of hot flashes and night sweats. These symptoms are believed to be caused by the changes in hypothalamus thermoregulation due to reduced estrogen levels. The processes caused by these changes limit the thermoneutral zone, so even slight rises in core body temperature lead to peripheral vasodilation and sweating. Some women suffer from other symptoms like rapid heartbeat and flushing while experiencing the hot flashes. The night sweats that also occur during the menopausal period are said to have a negative impact on sleep. It is believed that hormonal changes in this period may annoy the neurotransmitter systems, associated with the regulation of mood, which may lead to anxiety, irritability, and mood swings. Some women may also experience memory problems, and the ability to concentrate. Hormone therapy is believed to be effective in reducing vasomotor symptoms, whereas some non-hormonal drugs such as antidepressants can be used too [14].

4.2 Sleep Disturbances and Genitourinary Symptoms

Sleep disorders along with urinary tract issues are frequently reported by women going through menopause and these issues may last long after menopause ends. Hormonal problems associated with menopause that led to rising temperatures are primarily responsible for various sleep disorders including night sweats, numerous awakenings at night and insomnia. Poor sleep at night may lead to problems with performances during the days. Urinary disorders occur mostly because hormonal problems lead to changes in the structure of the vagina and urinary tract. There are various symptoms of genitourinary syndrome of menopause including a dry vagina, discomfort, pains during sexual intercourses, constant need to go to the toilet and high frequency of urination. Treatment includes vaginal moisturizers, lubricants, low doses of vaginal estrogen as well as other local therapies. Sleep disorders may be managed with the help of CBT, correct sleep routine and using some drugs [15].

4.3 Hormonal and Non-Hormonal Treatment Approaches

The management of menopausal symptoms is carried out through pharmacological therapy, which includes hormonal and non-hormonal strategies based on the patient's situation and the risk factors involved. Menopausal hormone therapy remains the most effective method of treating disturbing vasomotor symptoms and can be useful in some cases of genitourinary symptoms. Systemic estrogen can be provided orally or transdermally. It should be noted that those women who have their uterus need to also take progestogen for the prevention of hyperplasia that can occur because of estrogen. In cases of chronic genitourinary symptoms, local estrogen is administered. Non-hormonal options that can be utilized in treating vasomotor symptoms include SSRIs, SNRIs, gabapentin, and fezolinetant, which also act in different ways. In some cases, oxybutynin could be used as well. Also, vaginal moisturizers or lubricants can be used together with hormone therapy. The treatment is chosen depending on the symptom severity, contraindications, the presence of cardiovascular and thromboembolic disorders, food preferences, and side effects [16].

5. Menopausal Hormone Therapy

Menopausal hormone therapy (MHT) is a key pharmacological method for treating moderate to severe menopausal symptoms due to decreasing ovarian hormone production. It consists mainly of using estrogen alone or together with a progestogen in order to restore the hormone's activity and alleviate the symptoms. MHT has been proven particularly effective in treating vasomotor symptoms (e.g., hot flashes and sweating at night) and preventing bone loss in eligible women. The formulation of the treatment, its route of administration, and prescription dosage will depend upon individual clinic's needs. Nonetheless, the therapy requires careful consideration of the advantages, contraindications, side effects, and long-term risks. Individualized therapy and close clinical follow-ups are essential for the successful results of the treatment [17].

5.1 Types, Formulations, and Routes of Administration

Hormonal treatment for menopause comes in various forms that can work either systemically or locally. The various kinds of estrogen products that are used are 17β-estradiol and conjugated equine estrogens. Some of the more commonly used progestogens include micronized

progesterone and synthetic progestins **(Table 2)**. Such methods of administering estrogen can be through oral preparation, patches, gels, sprays, and other local treatments that can give systemic effect. There is also the choice of using a transdermal application that canThus, such, local therapy may use creams, tablets, devices, and rings to deal with specific genitourinary problems. There is also a methodology of using the progestogens orally or vaginally, depending on the type of treatment required. The choice of treatment method will depend on several factors which include how severe the symptoms are, what the patient prefers, what the doctor has planned, and what risks are involved in the treatment [18].

Table 2. Classification of Menopausal Hormone Therapy: Formulations, Routes, and Characteristics

Type of hormone therapy	Common formulations	Route of administration	Clinical characteristics
Estrogen-only therapy	Estradiol, conjugated estrogens	Oral, transdermal, vaginal	Used primarily in women without a uterus, depending on clinical circumstances
Estrogen–progestogen therapy	Estradiol with micronized progesterone or progestins	Oral, transdermal	Provides endometrial protection in women with an intact uterus
Transdermal estrogen therapy	Estradiol patches, gels, sprays	Transdermal	Avoids gastrointestinal absorption and hepatic first-pass metabolism
Local vaginal estrogen therapy	Estradiol tablets, creams, vaginal rings	Vaginal	Primarily used for genitourinary symptoms

Tissue-selective estrogen complex	Conjugated estrogens with bazedoxifene	Oral	Combines estrogenic effects with selective estrogen receptor modulation
Progestogen-only therapy	Micronized progesterone and other progestogens	Oral or other formulation-dependent routes	Used in selected clinical situations; not a substitute for estrogen therapy for all menopausal symptoms

5.2 Clinical Benefits, Indications, and Individualized Treatment

Menopausal hormone therapy has a number of advantages, especially for women with troublesome vasomotor symptoms and genitourinary symptoms because of estrogen deficiency. It is reportedly the best treatment option for hot flashes and night sweats and can profile sleep quality when disturbances are represented by vasomotor symptoms. Systemic estrogen therapy in addition can prevent loss of bones and risk of fractures during the process of treatment. Vaginal estrogen, when introduced at low doses, might provide good effects in treating vaginal dryness, irritation, and certain urinary symptoms in women with genitourinary syndrome of menopause. Generally, the treatment is evaluated more positively in healthy symptomatic women younger than 60\+ years or in women who might experience menopause a little bit earlier in their life. In order to perform therapy, factors such as age, menopausal status, symptom severity, uterine status, medical history, and personal preferences should be considered [19].

5.3 Risks, Contraindications, and Safety Considerations

While hormones used during the menopause are effective against various symptoms, such treatments must always be weighed for associated risks and individual circumstances. Systemic hormone therapy may carry the risk of venous thromboembolism, stroke, and gall bladder problems. The associated risks change depending on the various forms of and methods for administering hormones, dosages, age, and medical history of the person. Estrogen-only systemic treatment is generally given to patients who have had a hysterectomy. Systemic use of estrogen in women with an intact uterus requires additional use of progesterone to prevent

endometrial hyperplasia and cancer. Important contraindications include unexplained vaginal bleeding and active or past cancers such as breast cancer, history of venous thromboembolism, stroke, heart attack or current liver disease which should be evaluated by doctors. The most commonly experienced side effects are breast tenderness, bloating, headaches, nausea, and irregular bleeding patterns. Practitioners should measure each patient's individual risk of having cardiovascular or thromboembolic problems, cancer history, blood pressure and experience with this method of treatment [20].

6. Osteoporosis and Musculoskeletal Health

In postmenopausal women, osteoporosis and complications related to the osteoarticular system are significant health issues mainly caused by decreased levels of estrogen hormone. Estrogen is necessary for bone remodeling via regulation of osteoblasts and osteoclasts activity. Lack of estrogen leads to increased bone resorption; thus, bone mineral density decreases, the bone microstructure deteriorates, and the likelihood of fractures arises. In some cases, other symptoms may appear in the postmenopausal women, such as joint pain, weakness of the muscular system, and limited physical functioning. Therefore, proper diagnosis of the condition, assessment of the fracture risk, and prevention are essential to keep the bones healthy. Treatment of the issue includes pharmacotherapy, sufficient calcium and vitamin D intake, regular activity, fall prevention measures, and monitoring of the patient condition [21].

6.1 Estrogen Deficiency and Pathophysiology of Postmenopausal Osteoporosis

The deficiency of estrogen is one of the significant factors that contribute to the acceleration of bone loss after menopause. Estrogen acts on normal physiological processes by maintaining bone integrity through guiding the balance between the two physiological processes, bone formation and bone resorption **(Figure 2)**. Estrogen does this through inhibition of excessive osteoclast functions and even by preserving osteoblast activity, thus maintaining normal bone remodelling. During postmenopause, the lack of estrogen increases the concentration of RANKL and the induction of the development of osteoclasts. This has been shown to lead to an increased process of bone resorption and a decrease in bone mineral density. It should be noted that the negative ratio between bone formation and resorption especially affects spongiosa, which leads to fragility of the skeleton. Usually, postmenopausal osteoporosis

affects vertebrae, hip, and distal radius. The contributing factors include age, lack of calcium intake, vitamin D deficit, lack of physical activity, smoking, and genetic predisposition. It is necessary to understand these processes so that people with higher risk can be identified and treated on time through proper measures [22].

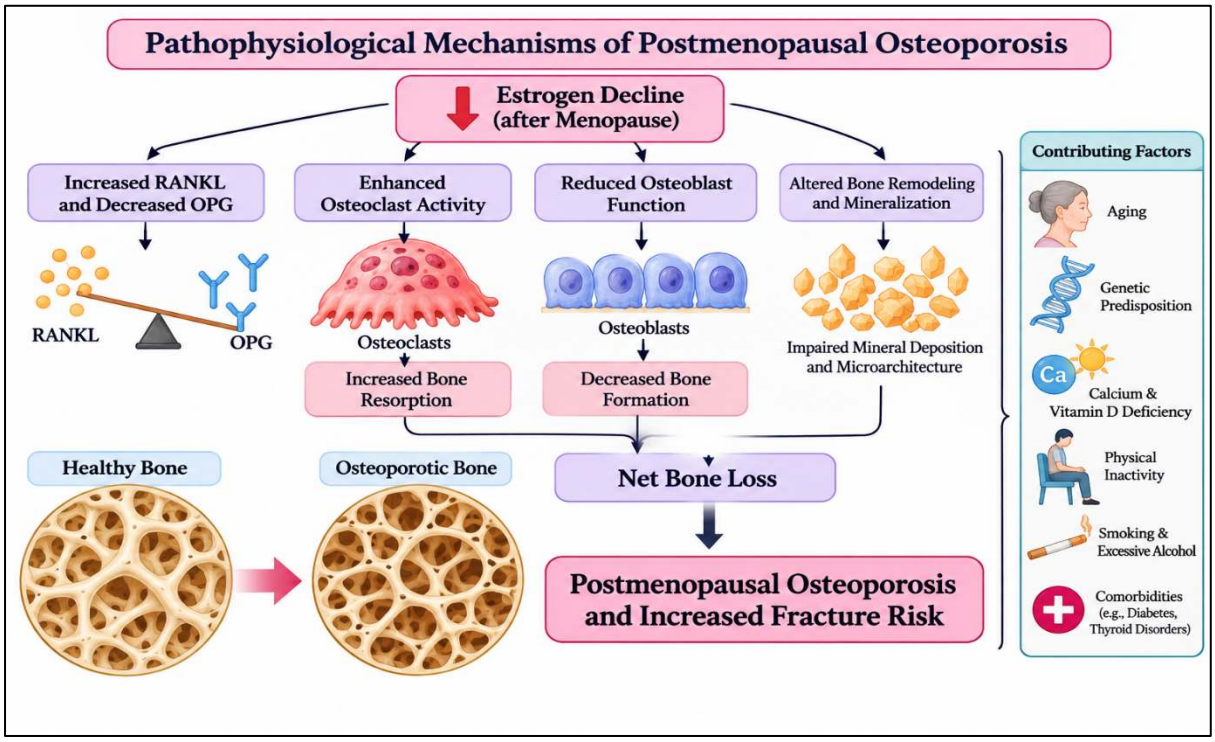

Figure 2. Pathophysiological Mechanisms of Postmenopausal Osteoporosis

6.2 Screening, Diagnosis, and Fracture Risk Assessment

It is very important to screen a person to diagnose osteoporosis early in order to avoid skeletal breakdowns and subsequent disabilities among postmenopausal women. Dual-energy X-ray absorptiometry (DXA) is what doctors use to check bone density in the lumbar spine and hip area. Results of the procedure are expressed as T-scores, where a score that equals less than -2.5 qualifies as osteoporosis in postmenopausal women. Scores from -1 to -2.5 mean that a person suffers from poor bone density or osteopenia disease. Using tools such as the Fracture Risk Assessment Tool (FRAX), a person's risk of having major osteoporotic and hip fractures during the next 10 years can also be approximated based on clinical risk factors, with or without taking into account femoral neck bone density. At this moment, risk factors include advanced age, previous fragility fractures, family history of hip fracture, low body weight, smoking, and

prolonged usage of glucocorticoids. The evaluation process, apart from the bone density exam, can include blood tests of calcium and vitamin D as well as renal functions to identify other causes of bone density decline [23].

6.3 Pharmacological and Non-Pharmacological Management

The treatment of postmenopausal osteoporosis comprises the use of drugs combined with adjustments in lifestyle and dietary approaches. Among the antiresorptive agents which are usually used first, one can find bisphosphonates (alendronate, risedronate, and zoledronic acid) which stop the process of bone destruction caused by the osteoclasts. Denosumab is another kind of drug which acts on the osteoclast formation and activity and represents a monoclonal antibody which influences RANKL. Another option for some postmenopausal patients includes selective estrogen receptor modulators. One can also consider anabolic agents (teriparatide, abaloparatide, and romosozumab) when the fracture risk is very high. When treating patients, it is also crucial to make sure that calcium and Vitamin D usage is constant, whereas the importance of weight-bearing exercises is significant for bone maintenance. Moreover, it is important to give up smoking, drink alcohol in moderation and take measures to reduce the risk of falling down [24].

7. Cardiovascular and Metabolic Disorders

Menopause and aging are also linked to cardiovascular and metabolic diseases as significant health risks. The decrease in estrogen concentration contributes to changes in the lipid metabolism process, endothelial function of blood vessels, insulin metabolism, and the general distribution of body fat. As a result, there will be an increase in abdominal obesity, dyslipidemias, hypertensive disease, and disturbance of glucose metabolism in postmenopausal women that leads to a higher probability of developing cardiovascular diseases, metabolic syndrome, and diabetes mellitus type 2. However, there are other factors in this case like genetic influences, sedentary rest lifestyle, unhealthy eating habits, and previously existing diseases. Thus, it is important to detect the risk of cardiovascular and metabolic diseases in time and screen the patients regularly [25].

7.1 Menopause-Associated Cardiovascular and Vascular Changes

Estrogen is crucial for cardiovascular health because it affects the functioning of the vascular endothelium, blood cholesterol levels, and flexibility of blood vessels. With lower estrogen levels, endothelial functioning is impaired and less nitric oxide is produced during menopause and this may hinder normal blood vessel dilation. Blood vessel function can also change due to influences of smooth muscles of blood vessels and their stiffness **(Figure 3)**. Furthermore, lack of estrogen will lead to changes in the inflammatory processes in the blood, oxidative stress, and metabolic processes in vascular tissues. All these variations increase the risk of cardiovascular disease. Menopause is usually accompanied by an increased level of low-density lipoproteins and changes in high-density lipoproteins concentration. But there are many factors which affect cardiovascular health such as age, smoking, diabetes, hypertension, and family history. Regular cardio health evaluation helps to prevent possible complications [26].

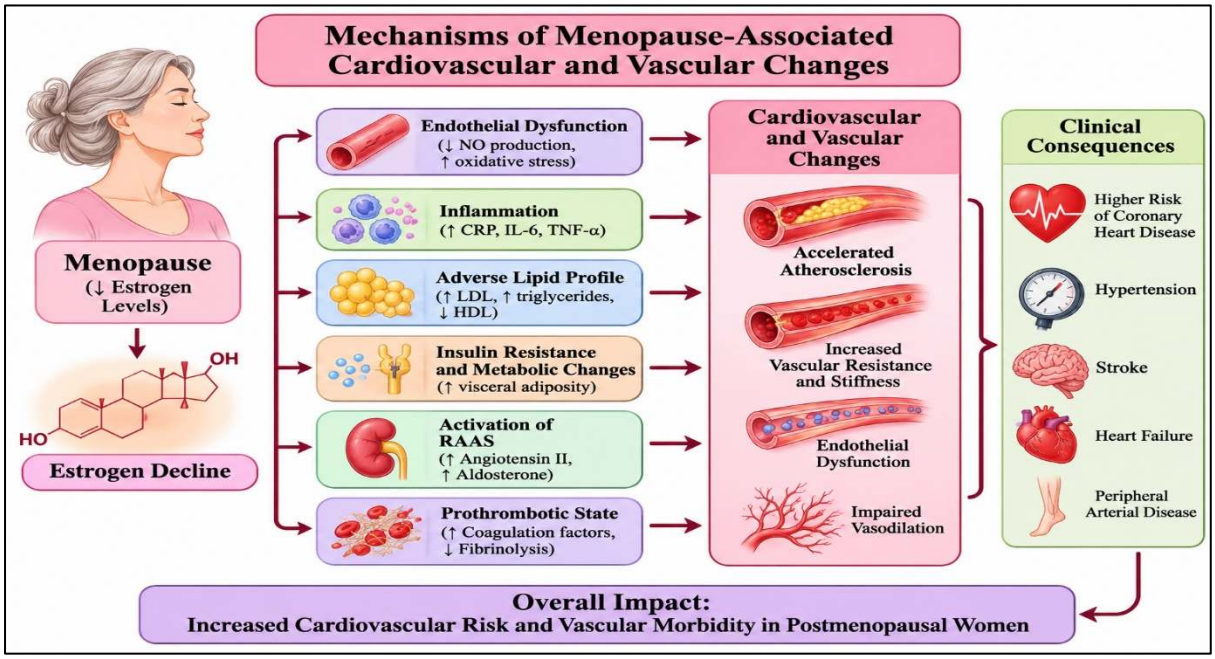

Figure 3. Mechanisms of Menopause-Associated Cardiovascular and Vascular Changes

7.2 Dyslipidemia, Abdominal Obesity, and Metabolic Syndrome

Menopause usually happens at the time of metabolism changes in lipids and body fat, which can result in metabolic syndrome. With reduced estrogen, fat accumulates in the abdominal space and the central adiposity grows. These changes can occur without the significant increase

of the overall body weight. Lipid abnormalities correspond to the presence of increased levels of total cholesterol, low-density lipoprotein, and triglycerides, which is not desirable from the metabolic point of view **(Table 3)**. The decreased sensitivity of insulin and the increase of visceral fat can promote inflammation and lead to metabolic dysregulation. Metabolic syndrome itself has a combination of symptoms such as central obesity, increased blood pressure, increased triglycerides, decreased level of high-density lipoprotein cholesterol, and impaired glucose metabolism. Occurrence of several metabolism problems increases the chance of getting heart problems and diabetes type II. Treatment consists of nutrition adjustment, physical exercises, control of body weight, and proper medication of particular risk factors. Regular monitoring of cholesterol level, waist, blood pressure, and glucose level contributes to the early detection of possible complications [27].

Table 3. Metabolic and Cardiovascular Risk Factors Associated with Menopause

Risk factor	Menopause-associated changes	Potential health implications	Recommended clinical assessment
Dyslipidemia	Increased LDL cholesterol and changes in HDL and triglyceride levels	Atherosclerotic cardiovascular disease	Lipid profile
Abdominal obesity	Increased visceral fat accumulation	Cardiometabolic risk and insulin resistance	Waist circumference and BMI
Insulin resistance	Reduced insulin sensitivity	Increased risk of type 2 diabetes mellitus	Fasting glucose and HbA1c
Hypertension	Increased arterial stiffness and changes in vascular regulation	Cardiovascular and cerebrovascular complications	Blood pressure measurement

Metabolic syndrome	Clustering of abdominal obesity, dyslipidemia, hypertension, and hyperglycemia	Increased cardiometabolic risk	Comprehensive metabolic assessment
Endothelial dysfunction	Reduced vascular responsiveness and impaired endothelial function	Vascular dysfunction and atherosclerosis	Clinical cardiovascular risk assessment

7.3 Hypertension, Diabetes Mellitus, and Pharmacological Management

Hypertension and type 2 diabetes are significant cardiometabolic diseases that may become more common in postmenopause. Alterations in blood vessel function, rigidity of vessels, change in fat distribution in the body, and change in sensitivity to insulin can lead to increased blood pressure and decreased ability to regulate glucose. To treat hypertension, antihypertensives are widely used. There are different types of those medicines and the choice between them depends on the clinical picture. Managing diabetes includes lifestyle changes and medications that lower blood sugar levels. Different SGLT2 inhibitors and GLP-1 RAs can also be used since they are known to reduce the risk of cardiovascular diseases. While making a choice, one should pay attention to kidney function, risk of cardiovascular diseases, weight, side effects, and interaction with other medications. To improve the effectiveness of treatment, it is necessary to obtain regular results regarding blood pressure, glycated hemoglobin, and kidney functioning [28].

8. Central Nervous System and Cognitive Health

The changes in several physiological and functional aspects of the central nervous system during the menopausal transition can be attributed to decreasing estrogen levels in the body. Estrogen is known to have an effect on a number of processes including the activities of neurons, regulation of neurotransmitters, brain circulation, synaptic plasticity, and memory functions. Erratic hormone levels may lead to some psychoneurological complaints, such as mood swings, anxiety, and sleeping difficulties. Memory problems, such as forgetfulness and

weakened concentration skills may be common among women of postmenopausal age, yet they do not indicate the presence of the progressive disease. Aging, cardiovascular factors, and psychological stress, among others, can affect memory [29].

8.1 Estrogen and Its Effects on Brain Function

Estrogen is essential for normal brain function by acting on the neuronal signaling and neurotransmitters and synaptic plasticity. Estrogen receptors such as ERα and ERβ are located in various parts of the brain including the hippocampus, hypothalamus, and cerebral cortex which are responsible for such brain functions as learning, memory, and emotional states. The neurotransmitter systems modified by estrogen include serotonin, dopamine, acetylcholine, and glutamate. Besides, the neuroprotective role of estrogen is reflected through its positive impact on neuronal function, mitochondria, anti-oxidative system, and blood flow to the brain. The decrease in the level of estrogen during menopause may result in changes of the mentioned processes and lead to cognitive complaints, moods, and sleep disturbances. However, the connection between estrogen deficiency and long-term effects is intricate due to factors like age, genetics, metabolic health, and other lifestyle components. The knowledge of the neurological functions of estrogen is crucial for understanding cognitive changes that occur during menopause [30].

8.2 Mood Disorders, Anxiety, Depression, and Cognitive Changes

A large number of women suffer from mood changes and cognitive dysfunctions during menopause. Changes in levels of estrogen can affect the system of neurotransmitters responsible for regulating mood. Some women during this period report irritability, anxiety, excessive emotional sensitivity, lack of motivation, and depressive moods. Factors affecting the probability of developing mood disorders may be connected to the patient's history of mental disorders, sleep quality, stress level, and sensitivity to hormonal changes. Patients suffering from cognitive problems often have memory issues, concentration problems, lack of attention, and difficulties with verbal memory. Most of the symptoms are only temporary and do not mean that the patients suffer from neurodegenerative disorders. If the symptoms are both hard and persistent, they need to be assessed by a health care specialist in order to find the

psychogenic causes of the issue. Help may include psychotherapy in the form of behavioral therapy, lifestyle changes, and medication [31].

8.3 Neurodegenerative Disorders and Pharmacological Management

Neurodegenerative disorders refer to the progressive degeneration of neurons and effects on cognitive abilities, memory, behavior, and activities. Alzheimer's disease and Parkinson's disease are important disorders linked with age advancement. Unlike menopause and estrogen deficiency which have been investigated for their relationship to aging neurologically, the role of hormonal changes due to menopause in neurodegeneration is not sufficiently studied. Moreover, age, the predisposition to diseases, cardiovascular disorders, metabolic pathologies, way of life, and other aspects determine neurologically related risks. The issue of treatment depends on the concrete neurologic disorder and its clinical picture. Thus, treatment of Alzheimer's disease utilizes cholinesterase-inhibiting medications - donepezil, rivastigmine, and galantamine, while memantine is used for selected patients. Levodopa combined with carbidopa and other medicines is the standard treatment for Parkinson's disease. The treatment is directed mainly towards symptom elimination but does not provide a cure. Apart from that, regular monitoring of cognitive activity, using medications, and other aspects are required for effective treatment for all patients [32].

9. Sleep Disorders During Menopause

Sleep disorders often occur during menopause and can have significant impacts on an individual's physical as well as emotional health and overall functioning. The hormonal fluctuations that characterize menopause, especially the falling levels of hormones like estrogen and progesterone, have effects on thermoregulation, circadian rhythms, and the mechanism regulating sleep. Some common complaints regarding sleep include difficulty falling asleep, having frequent awakenings during sleep, waking up very early in the morning, and having nonrestorative sleep. One of the major physical problems that contribute to sleep fragmentation are hot flashes and symptoms related to the regulation of body temperature. Also, some psychological issues like stress, anxiety, depression, etc. have been reported to intensify sleep disorders [33].

9.1 Hormonal Regulation of Sleep and Menopause-Related Changes

Sleep control is a multifaceted process that might comprise interactions between hormone actions, biological clock, neurotransmitters, and also thermoregulation. Estrogens act upon several pathways in the brain, which regulate the sleep-wake cycle; it is known that they can influence serotonin and acetylcholine signaling. Furthermore, progesterone and its derivative allopregnanolone play a role in activating GABA-A receptors and thus promoting inhibition in the process of signaling. It is claimed that the menopausal transition period is characterized by the drop of hormone levels that could alter sleep regulation. Moreover, changes to the levels of melatonin secretion due to aging may influence the biorhythms of an individual. As a result of these physiological changes, individuals may experience difficulties falling asleep, waking up during the night, and achieving deep sleep. The individual factors, such as hormonal sensitivity, mental health, individual lifestyle, and possible illness also contribute to the general sleep quality. Therefore, knowing the physiological processes that contribute to sleep problems during menopause would help find the reasons for sleep disorders during this period and elaborate suitable therapies [34].

9.2 Insomnia, Sleep Fragmentation, and Vasomotor Symptoms

Insomnia is commonly experienced by many women during menopause as it is a disorder in sleep characterized by difficulty either in falling asleep, sustaining sleep, and achieving restorative sleep even when you have adequate opportunity to rest. Sleep fragmentation is defined as multiple awakenings interrupting the sleep cycle and affects the overall sleep continuity of the individual. Most of the time, vasomotor symptoms such as hot flashes and night sweats are responsible for this kind of interrupting the sleeping pattern. Abrupt changes in the thermoregulatory activity may lead to flushing, sweating, and feelings of discomfort that make the person wake up many times during the night. Psychological issues such as anxiety, depression, and stress also add to the sleep disorder situation. There are other conditions that can cause sleeping problems, such as sleep apnea, restless legs syndrome, chronic pain, or urinary frequency. The consequence of insomnia could be constant fatigue during the day, irritability, concentration issues, or the decline of the quality of life in total [35].

9.3 Pharmacological and Non-Pharmacological Management

In order to manage sleep disturbances during menopause, it is important to target the possible causes of the problem and then choose the most suitable medical or other treatments. CBT-I, or cognitive behavioral therapy for insomnia, is one of the methods that works really well for chronic insomnia. This treatment includes several approaches, such as sleep restriction, stimulus control, relaxation techniques, and cognitive restructuring. Patients can also improve their sleep quality if they stick to sleep hygiene practices, do regular physical exercises, follow consistent sleeping regime, sleep in comfortable environment, etc. In cases when sleep disturbances are due to some uncomfortable vasomotor symptoms, menopausal hormone therapy is very effective and the method can be used in selected situations. In addition to that, some non-hormonal medications can also be useful because they help with sleeping well at night. There are other techniques for treating insomnia, but it is also necessary to measure risks and benefits of their use [36].

10. Genitourinary Health and Sexual Well-Being

Genitourinary health along with sexual wellbeing in females becomes one of the prime issues of women's health. With decreasing levels of estrogen, the vaginal, vulvar, urethral, and bladder organs undergo changes on both structural and functional levels, leading to discomfort and painful intercourse and causing decreased urination and increased susceptibility to urinary tract infections. All described symptoms are known as the genitourinary syndrome of menopause (GSM). Hormonal fluctuations can also affect different aspects of sexuality of a woman and cause problems related to sexual desire, arousal, and comfort. The described symptoms can disturb intimate relations, feelings, and general quality of life [37].

10.1 Genitourinary Syndrome of Menopause and Clinical Manifestations

Genitourinary syndrome of menopause is a long-lasting disorder caused by decreased estrogen activity in the genital tract. The lack of estrogen results in the thinning of the vaginal epithelium, less elasticity, less lubrication, and change in the vaginal pH. Changes like this may reduce the defense mechanisms of the vagina and increase its sensitivity to harmful irritants and discomfort. Common symptoms include dryness, itching, burning, vulvar irritation, painful intercourse, and bleeding after sex **(Figure 4)**. As for the urinary symptoms, there are possible

occurrences of urgency, frequency, painful urination, and urinary tract infection. Contrary to some vasomotor symptoms, the genitourinary symptoms might remain in the future or progress if the treatment is not provided timely. The diagnosis is based on history, symptoms, and physical examination where applicable. Other conditions must be ruled out during the evaluation such as infections and skin conditions [38].

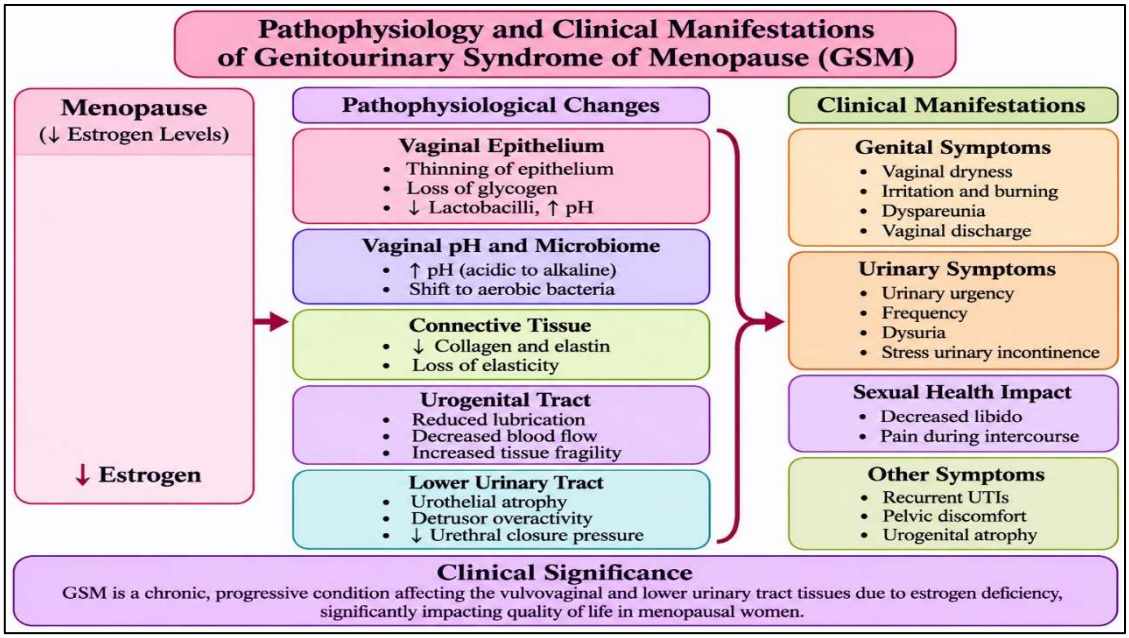

Figure 4. Pathophysiology and Clinical Manifestations of Genitourinary Syndrome of Menopause

10.2 Local Estrogen Therapy and Non-Hormonal Treatment Approaches

The treatment of genitourinary syndrome of menopause emphasizes alleviating symptoms, enhancing the health of tissues, and ensuring comfort of the genitourinary system. Treatment with low-dose estrogen is effective for women with moderate to severe symptoms. Low-dose estrogen can be administered in form of vaginal applications; i.e., creams, tablets, inserts, and rings. Estrogen is proven to improve tissue thickness, lubrication, elasticity, and functioning even while producing less systemic impact. The non-hormonal treatment options available include the use of vaginal moisture products which provide long-term hydration, and lubricants which help to lower friction during sex. In some patients, dry vagina treatment may include dehydroepiandrosterone (DHEA) used vaginally and oral ospemifene. Pelvic floor exercises may assist women with some urinary symptoms. Choice of treatment depends on severity of

the condition, medical history, contraindications, and preference of a patient. Patients with history of estrogen-related cancer should always consult specialists before commencing a hormonal treatment. Regular follow-ups enable to monitor the progress of the treatment as well as patients' tolerance level and further treatment [39].

10.3 Sexual Health, Quality of Life, and Patient Counseling

Hormonal changes due to menopause could affect sexual health through varying factors, including the reduction of lubrication in the vagina, change in sensitivity of genital tissues, lowered sexual appetite, and issues arising from sexual intercourse. Vaginal dryness and difficulty during sexual intercourse could lessen pleasure during intimacy and make individuals opt out of having sexual relations altogether. There are also those psychological aspects of oneself such as anxiety, depression, alterations in self-image, and relations with others in the context of sleeping disorders that could influence one's sexual health. These issues can lead to a low quality of life overall. Counseling has a key role to play in addressing the problems facing a woman on the way to a successful sexual life post-menopause. Women must be taught to talk about their symptoms openly with healthcare professionals without any shame before being informed about the kinds of therapy that are available. Vaginal moisturizers and lubricants, pelvic floor exercises and proper local treatment could help improve sexual pleasure after menopause [40].

11. Polypharmacy in Postmenopausal Women

Polypharmacy is regarded as a serious healthcare problem faced by postmenopausal women especially with age progression and the rise of chronic diseases. The term polypharmacy normally connotes the simultaneous use of several medications (usually five or more), although the meaning of this term differs based on the context. As a result, postmenopausal women can be prescribed treatments for hypertension, diabetes, heart diseases, osteoporosis, sleep problems and other age-related disorders. The increasing pressure of the use of drugs leads to drug-drug interactions, negative side effects of drugs, medical mistakes and poor adherence. Age-related changes in the way medications are metabolized and excreted make the situation with drugs even worse. The solution of this problem lies in systematic medication reviews,

justified prescriptive practices, information work with patients, and appropriate application of the principles of deprescribing.

11.1 Prevalence, Contributing Factors, and Medication Burden

Polypharmacy has become prevalent among women undergoing menopause due to the presence of several chronic illnesses and health disorders caused by old age. The prevalence of polypharmacy differs among populations depending on population traits, the healthcare context, the disease burden level, and the prescribing practices adopted. The most important health problems that contribute to polypharmacy cases include hypertension, diabetes, dyslipidemia, osteoporosis, cardiovascular diseases, and chronic musculoskeletal disorders. Many of the women suffering from a variety of health conditions take medications prescribed by different health professionals, which increases the chances of prescription duplications and unnecessary medication consumption. Besides, the patients tend to self-medicate, take medications over the counter, use herbal remedies, and get multiple prescriptions without regular monitoring of medications. Hormonal treatment and medications used to treat sleep disorders can complicate things even further for the patients. Such composition of medications causes the risks of side effects, medicine interactions, falls, and hospitalizations. Thus, it is important to assess whether a patient really needs a medicine, how long they have been taking it, and what the possible side effects can be.

11.2 Potentially Inappropriate Medications and Adverse Drug Reactions

Inappropriate medications refer to drugs for which potential risks could surpass benefits based on a patient's condition or age. Post-menopausal women, for instance, are often particularly prone to complications from medication, owing to a variety of causes, including physiological changes in age, simultaneous consumption of several drugs, and different reasons. Some medications need to be used cautiously among older people, including some types of sedative-hypnotics, drugs with anticholinergic activity, non-steroidal anti-inflammatory drugs, and some administration forms of steroids inhibiting the action of the proton pump. Medications bad consequences, including falls, issues connected to cognitive activities, as well as bleeding from gastrointestinal organs, kidney-related problems, and other consequences. Generally, bad drug effects cause changes in drug clearance, overdose, and altered response to medication. The use

of evaluation tools, such as Beer's criteria, and STOPP/START criteria, may help specialists identify cases of the wrong prescription. The need for drug assessment on a regular basis is undeniable.

11.3 Medication Adherence and Patient Safety

Adherence to medication is crucial for effective control of the disease and prevention of complications among postmenopausal women undergoing prolonged pharmaceutical therapy. Nevertheless, the increased number of medications can cause problems with following complex schedules especially among those with several chronic diseases. The factors which may lead to poor adherence are forgetfulness, the price of medications, possible side effects, misconceptions about treatment administration, and concerns about long-term use of medications. Also, visual impairment, cognitive changes, and difficulties with the containers may prevent taking medications correctly. Poor adherence may result in uncontrolled hypertension, hyperglycemia, increased fracture risk, and unnecessary hospitalizations. Improvement of patients' safety may include medication reconciliation, easier schedules, proper advice, and monitoring. Moreover, pill organizers, medication reminder apps, and medication lists may be used to help with proper medication intake while clinical pharmacists take part in recognizing barriers to adherence, explaining possible side effects, and encouraging rational process of medication use [41].

12. Drug–Drug Interactions and Medication Safety

In the case of postmenopausal women, the effect of drug-drug interactions is significant and should be taken into consideration, especially in patients treated with several medications for chronic diseases. Subsequent uptake of different medicines can lead to changes in their absorption, distribution, metabolism, elimination, and effects, which may result in complications with therapy or could potentially bring harm to patients. Hormonal treatments, medications controlling blood pressure, antidiabetic drugs, antidepressants, anticoagulants, and medications for osteoporosis therapy could be applied simultaneously, which would increase the possibility of crucial interactions. In addition, various age-related physiological transformations could result in consequences for the use of medicines due to the slower functioning of the kidneys and the liver. If a patient enters therapy without proper medication

reconciliation, interaction screening, and careful monitoring, their chances to achieve their therapeutic goals are greatly reduced.

12.1 Common Drug–Drug Interactions in Menopausal Women

Postmenopausal women can often be prescribed drugs for heart diseases, diabetes, osteoporosis, mood disorders, and symptoms of menopause. This situation provides chances for drug interactions that may come from pharmacokinetics (drug absorption, metabolism, and elimination) or pharmacodynamics (result of combined drugs effects). For instance, using different types of antihypertensive medicines can lead to hypotension. In addition, a combination of blood thinner medication and non-steroid anti-inflammatory drugs can increase risks of bleeding. Antidepressants can cause serotonin syndrome when mixed with other drugs that affect serotonin. Calcium itself can be responsible for drug absorption blockages for some drugs like levothyroxine and certain antibiotics. Herbs and some over-the-counter medications can also influence the process of drug metabolism. It's necessary to consider all prescribed medications, minerals, and vitamins in order to prevent any side effects. It is worth mentioning that medicines should have proper dosage, timing, and clinical follow-up for achieving adequate results.

12.2 Interactions Involving Hormonal, Cardiometabolic, and CNS Medications

Hormone treatment may interact with some drugs taken for cardiovascular, metabolic, and neurological disorders. Preparations containing estrogen may change enzyme activity in the liver, influence blood clotting, and affect the metabolism of certain medications. For instance, estrogen in tablets has been shown to increase the levels of thyroid-binding globulin, which may lead to an amended dosage of levothyroxine for women having thyroid hormone therapy. Apart from that, estrogen may have an influence on sugar level and blood pressure in some patients, which must be monitored in patients with diabetes mellitus or hypertonic disease **(Table 4)**. Some medications stimulating enzymatic activity, such as carbamazepine, phenytoin as well as rifampicin, may increase the metabolism of estrogen and progestogens that may lead to a lower efficiency of the hormonal therapy. The interactions with medications acting on the central nervous system will have their own significance. For instance, the prescription of some

antidepressants may increase the likelihood of developing serotonin syndrome, while the joint use of the sedatives and other drugs may lead to excessive sedation and even falls.

Table 4. Clinically Important Drug–Drug Interactions Involving Hormonal, Cardiometabolic, and CNS Medications

Drug combination	Interaction mechanism	Potential clinical consequence	Clinical management
Estrogen + enzyme-inducing antiepileptics (carbamazepine, phenytoin)	Increased hepatic enzyme activity and estrogen metabolism	Reduced estrogen exposure and potentially reduced therapeutic efficacy	Review symptom control and consider alternative treatment
Estrogen + rifampicin	Induction of hepatic drug-metabolizing enzymes	Reduced systemic estrogen concentrations	Evaluate treatment response and alternative options
Estrogen + warfarin	Potential alteration in anticoagulant response	Changes in INR and anticoagulation control	Monitor INR when initiating or modifying hormone therapy
SSRIs + tramadol	Increased serotonergic activity	Risk of serotonin syndrome	Avoid or carefully monitor the combination
ACE inhibitors + potassium-sparing diuretics	Additive potassium-retaining effects	Hyperkalemia	Monitor serum potassium and renal function

Statins + strong CYP3A4 inhibitors	Reduced statin metabolism and increased drug exposure	Increased risk of myopathy and rhabdomyolysis	Review statin selection and monitor for muscle symptoms
Benzodiazepines + opioids	Additive CNS and respiratory depression	Excessive sedation and respiratory depression	Avoid concomitant use when possible or closely monitor

12.3 Age-Related Pharmacokinetic Changes and Clinical Monitoring

The advance of age causes physiological changes in postmenopausal women that can impact the pharmacokinetic and pharmacodynamic properties of drugs used by them. The decrease in the total volume of water in the body and lean mass of the body, together with the increase in body fat can influence the distribution of hydrophilic and lipophilic drugs. Decreased hepatic blood flow and metabolic capability that accompany age may affect the clearance of drugs from the liver. Similarly, decreased kidney function may result in decreased excretion of drugs through the kidneys, leading to toxicity. Alterations in the sensitivity of the receptors and homeostatic processes may increase the risk of adverse effects of medications including hypotension, sedation, and hypoglycemia. It is necessary to regularly monitor kidney and liver function, blood pressure, glucose, and drug levels in plasma. The dosage of medications should be personalized depending on the state of the organs, and the clinical picture of the patient [42].

13. Deprescribing and Rational Medication Use

Deprescribing refers to a systematic clinical process aimed at stopping or decreasing the use of a drug in cases when drug misuse poses more harm than good or when it is no longer medically required. This concept is of paramount importance to women after menopause, since, due to ageing, multi-morbidity, and polypharmacy, there is a high risk of adverse drug reactions. Prolonged use of medication without regular checks may lead to unnecessary treatment burden and medication problems. Rational drug use is based on the idea of using right drugs, determining right doses and ensuring that the treatment is in line with the medical requirements. Deprescribing must be done via shared decision-making and thorough medical evaluations.

Regular medication reviews and team work ensure better treatment safety and decrease exposure to potentially dangerous drugs and provide health benefits.

13.1 Principles and Importance of Deprescribing

Deprescribing refers to a systematic evaluation of drugs prescribed that may no longer generate substantial clinical advantages, as well as the replacement of these medications with alternative therapy or doses. The main aim of this practice is to make drug therapy more optimally effective and minimize side effects from drug interactions and treatment load. In the case of postmenopausal women, deprescribing is especially important, as they tend to suffer from many chronic illnesses requiring prolonged pharmacological therapy. Some of the key principles of deprescribing are assessment of an indication for each and every drug, evaluation of what therapeutic effects have been obtained and what the risks are in terms of using medications. Those medications applicable to temporary diseases should also be carefully reviewed. It is necessary to make deprescribing as personalized as possible and to involve patients in the process. Some drugs must be tapered gradually in order not to experience withdrawal symptoms or relapses. Monitoring of the treatment process is vital in order to assess its effectiveness and possible complications.

13.2 Identification and Management of Potentially Inappropriate Medications

Recognizing inappropriate medication use is crucial for minimizing medication-related risks for women who have undergone menopause. Inappropriate medications might not have significant effects, be utilized unnecessarily, be prescribed in excessive quantities, or have a negative advantage versus risk ratio. Main areas that must be considered are benzodiazepines, sedative-hypnotics, strong anticholinergic agents, certain non-steroidal anti-inflammatory drugs, and drugs that boost chances of falls or fractures. Investigating the patient's medical biography, diagnoses, renal functions, metabolism, prescription details, and possible drug interactions must take place. Clinical assessment methods like Beers Criteria and STOPP/START criteria can be very helpful in identifying improper prescriptions and unaddressed prescriptions. Once inappropriate medications have been identified, they must be studied to make sure if it is possible to adjust their doses, and/or change or withdraw them from the patient's regimen. Shared-decision making which encompasses dialogue between the

healthcare worker and their patient is a very important thing in order for the patient to realize what is being done and agree to the prescribed treatment. Tracking the course of therapy is very important to record all the effects.

13.3 Structured Deprescribing, Clinical Monitoring, and Pharmacist's Role

Structured deprescribing necessitates a methodical approach to ensure that medications considered unnecessary will be withdrawn safely without hampering adequacy of the management of the conditions. Generally, the process is started with medication reconciliation, and followed by searching for inappropriate medication (s) whenever they are used and by determining its (their) indications, effectiveness, and risk factors. Medications should be sorted according to the level of harm they can cause, the burden of treatment they entail, and availability of replacement medications. Adjustment (or even gradual withdrawal) of bigger doses of drugs like benzodiazepines, antidepressants, and corticosteroids can be obligatory in case of the need to minimize the reactions of withdrawal or reoccurrence of diseases. Informed consent is a very important in case of deprescribing, as patients must know why certain drugs should be removed from their medicinal regimen and which symptoms require medical help. The contribution of clinical pharmacists is also considerable, since they review the medication history of the patients, determine the interactions of drugs and recommend alternative medications. The cooperation of physicians, pharmacists, nurses, and patients helps to develop individualized treatment plans [43].

14. Precision Pharmacotherapy in Menopausal and Aging Women

Precision pharmacotherapy is a personalized method for drug selection and dosage based on genetic make-up, hormonal level, biological changes, accompanying medical conditions, and the way the particular patient responds to the treatment. It is essential for menopausal and elderly women, because the differences in drug metabolism, sensitivity to receptors, and vulnerability to diseases affect treatment efficacy and safety of medications. The standard therapeutic methods fail to account for the individual differences when it comes both to reactions to drugs and predisposition to side effects. The development of pharmacogenetics, molecular diagnostics, artificial intelligence, and personalized medicine creates an opportunity to improve treatment options. The integration of clinical data with genetic and biological

characteristics allows bringing the process of medication selection and dosing to perfection and minimizing drug-related complications.

14.1 Principles of Precision Medicine and Pharmacogenomics

Precision medicine refers to a personalized approach to treatment through the consideration of each person's genetics, lifestyle, and other factors. In pharmacotherapeutics, the main goal of precision medicine is the discovery of factors that determine how individuals respond to medications. Pharmacogenetics is the study of the impact of genetic variation on the efficiency of the use of drugs. Polymorphisms of genes coding cytochrome P450 enzymes, especially of CYP2D6 and CYP2C19 enzymes, may affect the metabolism of a wide range of medications applicable in the treatment of cardiovascular diseases, psychiatric disorders, and other medical conditions. The effect of genetic variability on response to hormonal and non-hormonal treatments is also relevant to menopausal women. Pharmacogenetic tests can be beneficial only if there is sufficient amount of scientific data to back them up.

14.2 Integration of Hormonal Status, Genetics, and Comorbidities

The personalized approach to pharmacotherapy in menopausal women requires consideration of hormonal background, genetic differences, age-related changes in physiology, and pre-existing diseases. The absence of estrogen may have an impact on cardiovascular health, bone metabolism, sugar metabolism, and work of the nervous system, meaning that the required drugs could differ. Differences in genetics, which lead to differences in the rate of metabolism of drugs can lead to different drug exposure. Apart from the above-mentioned reasons, some chronic diseases can also affect medication choice and dose. For example, a patient with a renal impairment may need to correct doses of drugs that are eliminated by kidneys, whereas liver dysfunction may alter the metabolism of some drugs. Special attention should be paid to medications that a person is taking to determine possible drug interactions. The combination of the patient assessment, laboratory and genetic studies, and drug history may result in the creation of a comprehensive plan.

14.3 Individualized Drug Selection, Artificial Intelligence, and Future Applications

Individualized drug selection is the process of selecting specific medications and dosages based upon the clinical, genetic, and physiological characteristics of the particular patient.

Innovations in Artificial Intelligence (AI) and machine learning technologies make it possible to conduct a detailed analysis of the available clinical, genomic, laboratory, and medication information for the purpose of clinical decision support in personalized pharmacotherapy. AI technologies can help the healthcare professionals predict unexpected drug reactions, evaluate potential drug interactions, predict treatment reaction, and provide support for drug dosage optimization **(Figure 5)**. Clinical decision-support system also has the ability to incorporate the patient information into the treatment guidelines to make more effective treatment decisions during drug prescription. The role of mentioned technologies in the psychotherapy of menopausal women is significant due to the fact that they may facilitate customized treatment of osteoporosis, cardiovascular diseases, pathways of metabolic diseases, and the effects of menopause. However, the AI-based recommendations have to be validated clinically and interpreted by specialists, as various limitations exist including incomplete information, algorithmic bias, and privacy issues. In the future, pharmacogenomic testing, electronic health records and predictive analytics may be combined for the purpose of ensuring better treatment decisions in postmenopausal period [44].

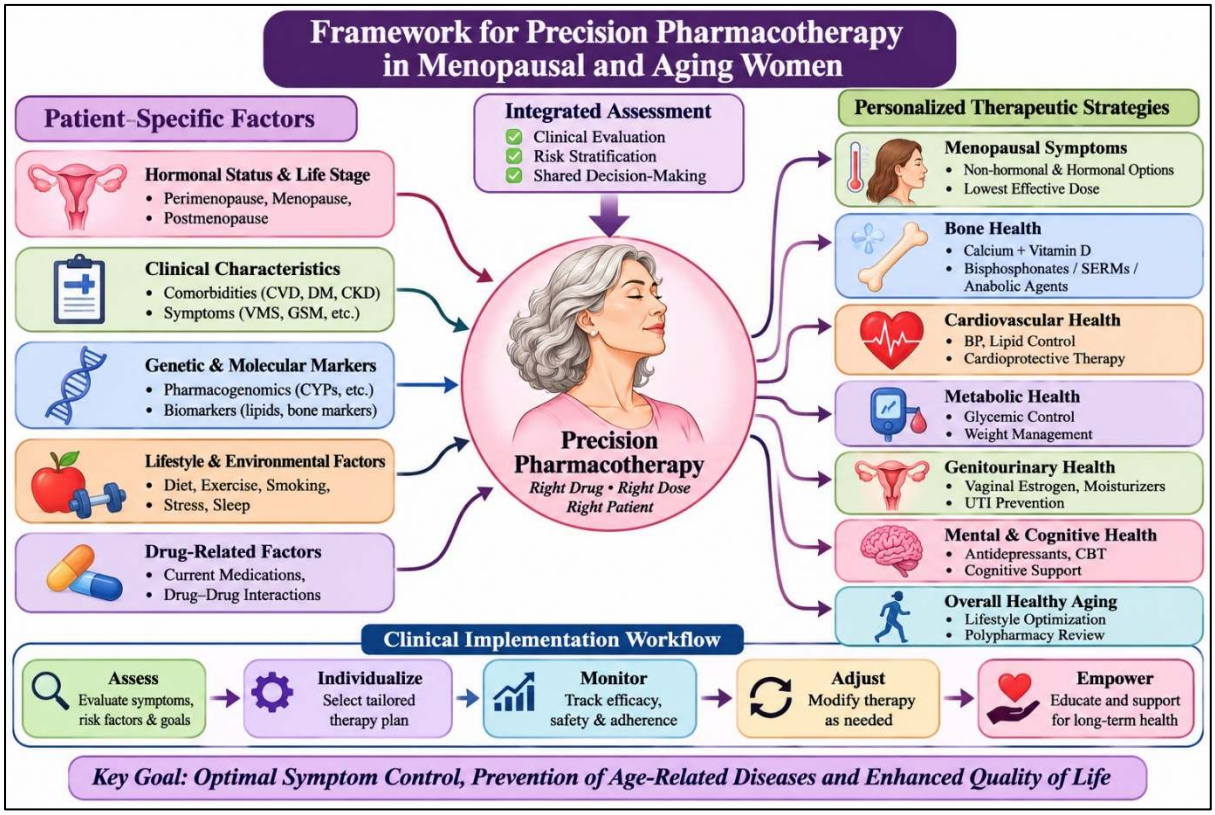

Figure 5. Framework for Precision Pharmacotherapy in Menopausal and Aging Women

15. Strategies for Promoting Healthy Aging

To age healthily after menopause means to look after all aspects of health in order to reduce risks of developing chronic diseases and complications related to increasing age. Reduced levels of estrogen and aging themselves affect the condition of bones, cardiovascular system, metabolic processes, nervous system, and genitourinary system. Thus, it is necessary to pay attention to preventive medicine and health management during post-menopausal stage. Some measures include regular check-ups and examinations, healthy diet, physical activity, sleep, and lifestyle changes. If medication is applied, it has to be prescribed taking into account the needs of particular patient. Educational activities directed at individuals, mental health, and social activity of these patients should be included in the practice of doctors for the purpose of increasing effectiveness of therapy and improvement of patients' quality of life.

15.1 Preventive Healthcare and Early Risk Assessment

The role of preventive healthcare in minimizing chronic disease burden and maintaining long-term health of postmenopausal women is considerable. Health evaluations on a regular basis allow for risk factor identification of various conditions such as osteoporosis, cardiovascular diseases, diabetes, hypertension and other age-related diseases. The result of testing for bone density by means of dual-energy X-ray absorptiometry may depend on the age and fracture risk of the patient. Cardiovascular testing consists of measurement of blood pressure, evaluation of lipid profile, body weight, and defining all clinical risk factors. Tests done to reveal diabetes by determining either the level of fasting blood glucose or glycated hemoglobin may help find the cases of glucose dysfunction. Cancer tests (including the ones for breast and cervical cancers) also depend on the age of the patient and her risk factor information. Also, mental health assessment, assessment of sleeping habits, eating habits, and medication must be performed. If the abnormalities are found, lifestyle modifications and pharmacological intervention may take place. Health education and follow-up visits are necessary for preventive care realization and to facilitate aging process.

15.2 Nutrition, Physical Activity, and Management of Age-Related Health Risks

Pathological aging can be avoided through proper nutrition and exercise for women who have completed menopause. In order to keep bones intact and muscles working, the right amount of protein, calcium, vitamin D, and fruits (vegetables as well) should be consumed on a regular basis. Calcium and vitamin D are responsible for proper skeletal development of bones and prevention of nutrient shortage due to osteoporosis. Of course, regular lifting of weights and exercises that require walking reduces osteoporosis chances, as well as improves body functions. Weight exercises are also an important factor for body's physical condition, helping control the weight and the level of blood pressure. Not smoking, drinking not more than one or two drinks per day, drinking enough water may also improve the state of health. The changes made to one's lifestyle should match current physical abilities and health status of a person.

15.3 Medication Optimization, Mental Well-Being, and Quality of Life

There are two crucial aspects of health care included in comprehensive care strategy for postmenopausal women. The common aging-related health problems become complex,

demanding the usage of a number of medications, leading to the increased risk of polypharmacy, adverse drug reactions, and drug interactions. Implementation of regular medication reconciliation, proper prescribing, and deprescribing, if required, help with the improvement of safety and compliance of treatment. Clinical pharmacists may provide support contributing to medication optimization through patient counseling, determination of medication-related problems, and monitoring of treatment outcomes. Psychological well-being should not be neglected because the significant changes in the level of hormones, problems with sleeping, changing social standing, and chronic medical conditions may be the reason for anxiety, depression, and emotional distress. Psychological counseling, support from the social environment, regular physical exercise, and engaging in meaningful activities may improve emotional health. Good sleeping and mental activity will help maintain overall well-being [45].

16. Current Challenges and Future Perspectives

Menopausal healthcare development is boosted by advancements in clinical pharmacology, hormone research, personalized medicine, and preventive health care. Despite the growing public knowledge of menopause, there still remain certain issues that hinder the proper diagnosis, treatment, and management of menopausal symptoms and diseases associated with it. For instance, uniqueness of the symptoms for each patient, lack of available access to specialists who can treat problems of menopausal patients, worries about utilizing hormone therapy for treatment purposes, and not enough clinical studies of women may adversely affect the results of treatment. Furthermore, matching proper medicines become a problem because of polypharmacy, age-related physiological changes, and patients who have several comorbid conditions. In order to resolve the mentioned problems, it is possible to use disease-oriented therapeutic approaches and make use of developments in pharmacogenomics, AI, and precision medicine.

16.1 Gaps in Sex-Specific Clinical Research

Sex and gender responsive research is crucial to clarify the differences in the development of diseases, drug therapy and metabolism, and adverse medical effects in women and men. However, women have been underrepresented in many studies including those with older population or in the presence of major chronic diseases. The hormonal changes during the

reproductive life, pregnancy and menopause result in biological differences, having significant impact on the clinical outcomes. There is a lack of the data on effectiveness of medicines for menopausal women due to the limited availability of pharmacokinetics and pharmacodynamics information. Further research is needed to evaluate the impact of estrogen deficiency on drug metabolizing enzymes, transporters, receptors and responses to medications. More research is needed to analyze the long-term effectiveness of hormonal and non-hormonal treatment for women of different ethnic backgrounds and age. The implementation of the reaserch results in clinical practice with special focus on involvement of postmenopausal women and their data analysis across the study population will provide the opportunity to improve performance of doctors and provide safer and more effective treatment.

16.2 Barriers to Safe and Effective Menopausal Care

There are many clinical, social, and health-related barriers that may restrict the accessibility of safe and effective menopausal assistance. Lack of information on menopausal symptoms, insufficient education for patients on menopause and unnecessarily strong social stigma are obstacles that prevent women from receiving timely medical help. Differences in how symptoms manifest themselves and lacking specialists can postpone the diagnosis and treatment of those patients. Furthermore, fear of future complications from menopause hormone therapy may become a reason for avoidance of therapy even in cases where it can be clinically useful. Financial difficulties, insufficient health systems, and different access to health care only deepen the problem of unequal access to the menopausal health care. Polypharmacy and various chronic illnesses lead to additional issues with the choice of medicines, as well as monitoring possible drug interactions and treatment. To cope with these barriers, it is necessary to improve the education of health professionals and provide patient-oriented consultations, evidence-based prescriptions, and easy access to preventive services. Thus, the work of different specialists should be better coordinated with the help of medical and clinical pharmacists, doctors, nurses, etc.

16.3 Emerging Therapies and Future Directions in Precision Women's Healthcare

Emerging medicinal methods are broadening the scope for personalized treatment of menopausal symptoms and health problems associated with older age. One of these methods

is using non-hormonal therapies that utilize certain physiological pathways such as neurokinin-3 receptor antagonists (fezolinetant being one of them). The evolution of select estrogen receptor modulators, tissue-selective estrogen complexes, and local hormonal preparations may contribute even more to the therapeutic options of certain types of applications. The use of pharmacogenomic analysis as well as precision medicine techniques may allow us to detect individual differences that affect drug metabolism, efficiency, and toxicity. Moreover, artificial intelligence and machine learning systems may help with clinical decision-making by screening medications for interactions, predicting possible side effects, and personalizing the dosage of drugs. At the same time, technologies associated with telemedicine seem to be paramount in monitoring patients and increasing their involvement in the treatment process. Future studies should be directed at safety and efficiency of long-lasting therapies, pharmacological responses belonging to different sexes, as well as equitable access to personalized medicine [46].

17. Conclusion

Menopause is a natural biological event that causes a change in hormones, physiology, metabolism, and psychology, which will impact women's health in the process of aging. The reduction of the amount of estrogen and progesterone has a number of clinical outcomes such as vasomotor symptoms, sleep disorders, psychological symptoms, problems with the genitourinary tract, and gradual loss of bone tissue. Also, menopause may influence cardiovascular health as well as glucose metabolism, cognitive aspects, and the quality of life in general. Therefore, it is important to study physiological mechanisms and consequences of menopause.

The use of medication helps to cope with the symptoms of menopause and avoid some age-related problems. Hormonal therapy in menopause treatment is still efficient in case of bothersome vasomotor symptoms and helps to increases the chances of avoiding such a common problem as bone loss in selected women. There are also possibilities of using non-hormonal drugs, treatments of osteoporosis, therapies for cardiovascular diseases, treatments of metabolism, as well as local treatment of the genitourinary tract depending on the patients'

clinical needs. However, it is necessary to take into account the patients' previous diseases, contraindications, possible side effects, and interactions between drugs.

Polypharmacy and multimorbidity are significant obstacles in the field of postmenopausal health care, which points to the necessity of rational prescribing, reconciliation of medications and appropriate methods of deprescribing. Clinical pharmacists have an important role to play in recognizing drug therapy-related problems, optimization of pharmacotherapy and compliance with medications instruction as well as increasing patient safety by means of constant monitoring and consulting. At the same time, changes in pharmacogenomics, and precision medicine offer possible solutions that allow to arrange therapy that is the most effective and causes minimal risks for patients.

In conclusion, it is obvious that the effective management of various problems arising during menopause requires a well-coordinated approach that brings together preventive medicine, pharmacological treatment based on evidence, changes in lifestyle, dietary help, psychological enhancement, and thorough clinical observation. Strengthening research in various fields dealing with pen, drug treatment and making personalized medicine more accessible is necessary for overcoming problems existing in dealing with menopause issues. A patient-oriented approach is an opportunity to support vitality and healthy life.

References

1. García-Nicolás M, Jarrín-Orozco MP, Romo-Vaquero M, Martínez-Nortes ME, Ávila-Gálvez MÁ, Espín JC. Dietary (poly) phenols, the gut-brain axis, and menopause: a perspective on an overlooked biological crossroad. Food & Function. 2026 May 12;17(9):3854-70.
2. Guo ZQ. Precision pharmacology in menopause: advances, challenges, and future innovations for personalized management. Frontiers in Reproductive Health. 2025 Nov 13;7:1694240.
3. Haga SB. Menopause-associated gut microbiome remodeling and pharmacomicrobiomics: emerging mechanisms influencing drug response. Frontiers in Microbiomes. 2026 Sep 15;5:1953547.

4. Yanachkova V, Lebanova H, Stoev S. Menopausal Hormone Therapy in Clinically Vulnerable Women: A Narrative Review of Guidelines and Real-World Evidence. Medicina. 2026 Apr 8;62(4):712.
5. Duralde ER, Sobel TH, Manson JE. Management of perimenopausal and menopausal symptoms. Bmj. 2023 Aug 8;382.
6. Gatenby C, Simpson P. Menopause: Physiology, definitions, and symptoms. Best Practice & Research Clinical Endocrinology & Metabolism. 2024 Jan 1;38(1):101855.
7. Crandall CJ, Mehta JM, Manson JE. Management of menopausal symptoms: a review. Jama. 2023 Feb 7;329(5):405-20.
8. Cunningham AC, Hewings-Martin Y, Wickham AP, Prentice C, Payne JL, Zhaunova L. Perimenopause symptoms, severity, and healthcare seeking in women in the US. npj Women's Health. 2025 Feb 25;3(1):12.
9. Patel P, Patil S, Kaur N. Estrogen and metabolism: Navigating hormonal transitions from perimenopause to postmenopause. Journal of Mid-life Health. 2025 Sep 5;16(3):247.
10. Motlani V, Motlani G, Pamnani S, Sahu A, Acharya N. Endocrine changes in postmenopausal women: a comprehensive view. Cureus. 2023 Dec 29;15(12):e51287.
11. Yang JL, Hodara E, Sriprasert I, Shoupe D, Stanczyk FZ. Estrogen deficiency in the menopause and the role of hormone therapy: integrating the findings of basic science research with clinical trials. Menopause (New York, NY). 2024 Jul 30;31(10):926.
12. Lobato VA, Minari TP, Pisani LP. Perimenopause and metabolic vulnerability: hormones, body composition and lifestyle changes. Climacteric. 2026 Aug 21:1-6.
13. Davis SR, Pinkerton J, Santoro N, Simoncini T. Menopause—Biology, consequences, supportive care, and therapeutic options. Cell. 2023 Sep 14;186(19):4038-58.
14. Comparetto C, Borruto F. Treatments and management of menopausal symptoms: current status and future challenges. OBM Geriatrics. 2023 Sep;7(3):1-47.
15. Djapardy V, Panay N. Alternative and non-hormonal treatments to symptoms of menopause. Best Practice & Research Clinical Obstetrics & Gynaecology. 2022 May 1;81:45-60.

16. Pan M, Zhou J, Pan X, Wang J, Qi Q, Wang L. Drugs for the treatment of postmenopausal symptoms: Hormonal and non-hormonal therapy. Life Sciences. 2023 Jan 1;312:121255.
17. Cho L, Kaunitz AM, Faubion SS, Hayes SN, Lau ES, Pristera N, Scott N, Shifren JL, Shufelt CL, Stuenkel CA, Lindley KJ. Rethinking menopausal hormone therapy: for whom, what, when, and how long?. Circulation. 2023 Feb 14;147(7):597-610.
18. Madsen TE, Sobel T, Negash S, Shrout Allen T, Stefanick ML, Manson JE, Allison M. A review of hormone and non-hormonal therapy options for the treatment of menopause. International journal of women's health. 2023 Dec 31:825-36
19. Makary MA, Nguyen CP, Høeg TB, Tidmarsh GF. Updated labeling for menopausal hormone therapy. JaMa. 2026 Jan 13;335(2):117-8.
20. Levy B, Simon JA. A contemporary view of menopausal hormone therapy. Obstetrics & Gynecology. 2024 Jul 1;144(1):12-23.
21. Walker MD, Shane E. Postmenopausal osteoporosis. New England Journal of Medicine. 2023 Nov 23;389(21):1979-91.
22. Wright VJ, Schwartzman JD, Itinoche R, Wittstein J. The musculoskeletal syndrome of menopause. Climacteric. 2024 Sep 2;27(5):466-72.
23. Lu L, Tian L. Postmenopausal osteoporosis coexisting with sarcopenia: the role and mechanisms of estrogen. Journal of endocrinology. 2023 Sep 1;259(1).
24. Liang H, Chen S, Shi M, Xu J, Zhao C, Yang B, Zheng S, Tan J. Global epidemiology and burden of osteoporosis among postmenopausal women: insights from the Global Burden of Disease Study 2021. npj Aging. 2025 Sep 1;11(1):78.
25. Jeong HG, Park H. Metabolic disorders in menopause. Metabolites. 2022 Oct 8;12(10):954.
26. Ryczkowska K, Adach W, Janikowski K, Banach M, Bielecka-Dabrowa A. Menopause and women's cardiovascular health: is it really an obvious relationship?. Archives of medical science: AMS. 2022 Dec 10;19(2):458.
27. Nappi RE, Chedraui P, Lambrinoudaki I, Simoncini T. Menopause: a cardiometabolic transition. The lancet Diabetes & endocrinology. 2022 Jun 1;10(6):442-56.

28. Motlani V, Motlani G, Pamnani S, Sahu A, Acharya N. Endocrine changes in postmenopausal women: a comprehensive view. Cureus. 2023 Dec 29;15(12):e51287.
29. Mervosh N, Devi G. Estrogen, menopause, and Alzheimer's disease: understanding the link to cognitive decline in women. Frontiers in molecular biosciences. 2025 Jun 30;12:1634302.
30. Schwarz KG, Vicencio SC, Inestrosa NC, Villaseca P, Del Rio R. Autonomic nervous system dysfunction throughout menopausal transition: A potential mechanism underpinning cardiovascular and cognitive alterations during female ageing. The Journal of Physiology. 2024 Jan;602(2):263-80.
31. Guerrero-González C, Cueto-Ureña C, Cantón-Habas V, Ramírez-Expósito MJ, Martínez-Martos JM. Healthy aging in menopause: prevention of cognitive decline, depression and dementia through physical exercise. Physiologia. 2024 Mar;4(1):115-38.
32. Cho JM, Lee J, Ahn EM, Bae J. Beyond hot flashes: The role of estrogen receptors in menopausal mental health and cognitive decline. Brain Sciences. 2025 Sep 16;15(9):1003.
33. Tandon VR, Sharma S, Mahajan A, Mahajan A, Tandon A. Menopause and sleep disorders. Journal of mid-life health. 2022 May 2;13(1):26.
34. Maki PM, Panay N, Simon JA. Sleep disturbance associated with the menopause. Menopause. 2024 Aug 1;31(8):724-33.
35. Troìa L, Garassino M, Volpicelli AI, Fornara A, Libretti A, Surico D, Remorgida V. Sleep disturbance and perimenopause: a narrative review. Journal of clinical medicine. 2025 Jan;14(5):1479.
36. Salari N, Hasheminezhad R, Hosseinian-Far A, Rasoulpoor S, Assefi M, Nankali S, Nankali A, Mohammadi M. Global prevalence of sleep disorders during menopause: a meta-analysis. Sleep and Breathing. 2023 Oct;27(5):1883-97.
37. Nappi RE, Cucinella L. Menopause and sexual health: hormones, aging or both?. Clinical Obstetrics and Gynecology. 2025 Mar 1;68(1):44-50.

38. Wasnik VB, Acharya N, Mohammad S. Genitourinary syndrome of menopause: a narrative review focusing on its effects on the sexual health and quality of life of women. Cureus. 2023 Nov 2;15(11).
39. Barbagallo F, Cucinella L, Tiranini L, Chedraui P, Calogero AE, Nappi RE. Obesity and sexual health: focus on postmenopausal women. Climacteric. 2024 Mar 3;27(2):122-36.
40. Kasano JP, Crespo HF, Arias RA, Alamo I. Genitourinary syndrome in menopause: Impact of vaginal symptoms. Turkish Journal of Obstetrics and Gynecology. 2023 Mar 10;20(1):38.
41. García-Nicolás M, Jarrín-Orozco MP, Romo-Vaquero M, Martínez-Nortes ME, Ávila-Gálvez MÁ, Espín JC. Dietary (poly) phenols, the gut-brain axis, and menopause: a perspective on an overlooked biological crossroad. Food & Function. 2026 May 12;17(9):3854-70.
42. Gil-Ibáñez B, Aznar AL, Barretina-Ginesta MP, Quer N, Ramirez PT. Hormone replacement therapy in gynecologic cancer survivors: bridging the gap between evidence and clinical practice. International Journal of Gynecological Cancer. 2026 Aug 3:104881.
43. Jepsen DB, Bergen ES, Pan J, van Poelgeest E, Osman A, Burghle A, Ryg J, Thompson W, Lundby C. Recommendations on deprescribing of bisphosphonates in osteoporosis guidelines: a systematic review. European geriatric medicine. 2023 Aug;14(4):747-60.
44. Guo ZQ. Precision pharmacology in menopause: advances, challenges, and future innovations for personalized management. Frontiers in Reproductive Health. 2025 Nov 13;7:1694240.
45. Godoy-Izquierdo D, de Teresa C, Mendoza N. Exercise for peri-and postmenopausal women: Recommendations from synergistic alliances of women's medicine and health psychology for the promotion of an active lifestyle. Maturitas. 2024 Jul 1;185:107924.
46. Lin F, Ma L, Sheng Z. Health disorders in menopausal women: microbiome alterations, associated problems, and possible treatments. BioMedical Engineering OnLine. 2025 Jul 7;24(1):84.