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# IMPACT OF MENOPAUSAL HORMONE THERAPY AND PHYSICAL ACTIVITY ON THE INCIDENCE OF DEPRESSION IN WOMEN DURING MENOPAUSAL TRANSITION

Nadia Rahma Putri

***Correspondence**: nadiarahmanrp@gmail.com*
Department of Midwifery, Faculty of Medicine, University of Brawijaya, Malang, Indonesia

**REVIEW** **OPEN ACCESS**

**ABSTRACT**

**Introduction** – Menopausal women will experience symptoms as a result of changes that occur in their bodies, both due to aging and hormonal changes. Changes in estrogen levels during menopause are associated with a wide variety of problems that arise both physically and psychologically. These problems, if not appropriately addressed, will cause a decrease in quality of life that can encourage menopausal women to experience depression. The use of hormone therapy is reported to be effective for reducing menopausal symptoms. In addition to providing therapy, doing physical activity is beneficial for reducing symptoms of depression during the menopausal transition. This paper aims to discuss the impact of women's use of hormone therapy and physical activity during the menopausal transition on the incidence of depression.
**Methods** – This article uses the literature review method. The article used is an original research article in English and was published within the last 5 years (2019-2023). The electronic databases used are Google Scholar, Pubmed, BMC Journal, and Sciencedirect.
**Results –** Hormone therapy given during the menopausal transition can increase the risk of depression. The amount of hormone therapy obtained does not affect the incidence of depression; the use of estrogen hormone therapy and its combination of>1 year and hormone therapy given systemically will increase the incidence.
**Discuss –** Postmenopausal women who use hormone therapy will be at higher risk for depression. Low physical activity will pose a higher risk for depression, especially in postmenopausal women.
**Conclusion –** The use of hormone therapy or hormone replacement therapy during the menopausal transition period can cause an increase in depression and depressive symptoms. Physical activity can help reduce symptoms of depression. In addition, physical activity can also help relieve menopausal symptoms that occur during the transition period.

**Keywords:** depression, hormone replacement therapy, menopause.

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## INTRODUCTION

Women with increasing age will experience a decrease to loss of function of the ovarian follicles, which can cause permanent absence of menstruation, which is usually called menopause. Menopause can occur naturally (on average, it will begin at the age of 45 – 55 years) and can occur due to a medical intervention (for example, pelvic radiation therapy that can cause menopause).[1] Before the cessation of menstruation, women will experience a transition process that begins with irregular menstrual cycles, increased follicle-stimulating hormone (FSH), decreased levels of estradiol and progesterone, and the appearance of various symptoms. The hypothalamic-pituitary axis will decrease in sensitivity to positive and negative estrogen feedback during this time.[1,2]

Hormonal changes that occur will cause symptoms from various aspects that will usually be felt by 80% of women. These aspects can be both physical and psychological. Physical symptoms that often appear such as hot flashes, headaches, fatigue, difficulty sleeping, vaginal dryness, dyspareunia, and mood changes.[2,3] Meanwhile, psychological symptoms that often appear can include anxiety, difficulty socializing, and hypochondriasis.[4] Adaptation is necessary during this transitional period. How women cope with complaints that arise, as already mentioned, will determine the level of well-being in carrying out life during menopause. For

women who cannot adapt, there will be a decrease in quality of life, which can lead to depression.[3,4]

Depression as well as depressive symptoms, increase in women in the menopausal phase.[2] During the transition phase, perceived depressive symptoms can increase 1.5 – 3.0 times.[5] Depressive symptoms are found to have fluctuating levels during each phase of menopause. In perimenopause, symptoms will increase compared to premenopause, then will be milder in postmenopause.[6] Many factors are behind the increase in symptoms felt, such as surgery during menopause, history of depression, adverse events during life, physical discomfort, and emotional changes (can be caused by health problems due to aging, financial problems, and culture) during menopause.[7–9]

Depression can also be triggered by biological aspects such as estrogen and follicle-stimulating hormone levels that change during menopause.[5] During the transition period, estrogen hormone levels will decrease until a deficiency occurs. Estrogen has a protective effect on nerve tissue. The hormone will interact with γ-aminobutyric acid (GABA), which will affect the regulation of mood changes in the brain. In addition, estrogen with minimal levels will cause less serotonin in the brain. Serotonin is associated with mood changes such as in depressive conditions.[7,10]

Treatment to reduce complaints that occur during menopause can be in the form of the use of hormone therapy or hormone replacement therapy. This therapy is available in the form of estrogen or in combination with progesterone (if the uterus is still present).[11] In the concept of estrogen replacement in hormone therapy, it is necessary to pay attention to its use both in administered doses, contraindications, as well as the period in its use. Vasomotor symptoms, mood changes, and depressive symptoms are reported to improve when given this therapy. Mood-related symptoms are 60 to 80% improved.[12]

Menopause causes reduced physical activity due to symptoms felt by women. This can contribute to the risk of depression during menopause. Physical activity such as exercise will help release endorphins from the brain to reduce depression.[7] High-intensity activity in perimenopause and moderate and high intensity in postmenopause are useful for reducing the incidence of depression.[3,13]

This article will discuss the effects of the use of hormone therapy and women's physical activity during the menopausal phase and its relation to the incidence of depression experienced by menopausal women.

# METHOD

This article will discuss the effect of hormone therapy and physical activity on the incidence of depression in women during the menopausal phase using the literature review method. The literature used is articles published within the last 5 years (2019-2023), uses English, is original research, and the subject of research is human. Articles on the subject of animal research and review are not included in this literature review. Article search using electronic databases in the form of Google Scholar, Pubmed, BMC Journal, and Sciencedirect. The article search method used uses a combination of keywords in the form of: (menopausal hormone therapy or hormone therapy or hormone replacement therapy) and (depression or depressive disorder or depressive symptoms) and (menopause); (physical activity) and (depression or depressive disorder or depressive symptoms) and (menopause); (menopausal hormone therapy or hormone therapy or hormone replacement therapy) and (physical activity) and (depression or depressive disorder or depressive symptoms) and (menopause).

# RESULT

### Hormone Therapy and Depression in the Menopausal Transition

Changes in sex hormone levels during the transition predispose to the incidence of depression. This can be linked to estrogen levels that play a role in mood regulation. The perimenopausal and early postmenopausal periods are associated with increased depressive symptoms and the occurrence of major depressive disorder. So far, the treatment of menopausal complaints can be overcome with hormone therapy, but its benefits to the incidence of menopausal depression.[14,15]

A cohort study was conducted by Shea et al. on women ages 45 to 64 to determine the relationship between hormone therapy and depression during the menopausal transition. Results showed that early menopause and the use of hormone therapy were risk factors for depression in women (OR: 1,19; OR: 1.20). This study did not see any relationship between the duration of hormone therapy use and depressive symptoms that occurred.[14]

Another cohort study by Wium-Andersen et al. used women from age 45 to look at the use of hormone therapy (including the amount consumed, type of hormone therapy, and type of administration) on the incidence of depression. The results of the study show that users of hormone therapy are more at risk than those who do not use it for depression. The amount of hormone therapy used did not affect depression. The incidence will increase with the use of estrogen-type therapy or its combination with progesterone after the first year. The risk of depression will also increase with the systemic use of hormone therapy compared to local administration.[15]

Kim et al.'s research shows a greater risk of depression in the use of hormone therapy than in postmenopausal women. Longer-term use of hormone therapy is found in women with depression.[16]

**Table 1. Characteristics of Study**

| No. | Author Name, Article Title, Year | Research Objectives | Research Design | Research Results |
|---|---|---|---|---|
| 1. | Shea, Alison & Sohel, Nazmul & Gilsing, Anne & Mayhew, Alexandra & Griffith, Lauren & Raina, Parminder, Depression, hormone therapy, and the menopausal transition among women aged 45 to 64 years using Canadian Longitudinal Study on aging baseline data, 2020 | To determine the continuity between hormone therapy use, menopausal status and depressive symptoms in elderly women in Canada | Cross-sectional research | This study evaluated the use of hormone therapy by identifying the initial age of use, the preparation used (estrogen, progesterone, or a combination thereof), and the length of use of hormone therapy. The results obtained in the form of the use of hormone therapy are currently at risk for increasing the incidence of depression. |
| 2. | Wium-Andersen, Marie & Jørgensen, Terese & Halvorsen, Anniken & Hartsteen, Birgitte & Jørgensen, Martin & Osler, Merete, Association of Hormone Therapy With Depression During Menopause in a Cohort of Danish Women, 2022 | To know the use of therapeutic hormones during menopause with the occurrence of depression afterwards | *Nationwide register–based cohort and self-controlled case series study* | The study showed that there was no effect on the amount of hormone used, but on the use of estrogen and its combination after the first year as well as systemic therapy there was an increased incidence of depression |
| 3. | Kim, Hyewon & Jung, Jin Hyung & Han, Kyungdo & Lee, Dong-Yun & Fava, Maurizio & Mischoulon, David & Jeon, Hong Jin, Ages at menarche and menopause, hormone therapy, and the risk of depression. General Hospital Psychiatry, 2023 | To determine the relationship between female reproductive factors and the risk of depression | Retrospective cohort research | The results showed a higher risk in women on hormone therapy at menopause |
| 4. | Liu, X. Y., Peng, S. Z., Pei, M. Y., & Zhang, P., The effects of physical activity on depression and quality of life in Chinese perimenopausal women, 2023 | To determine the impact of physical activity as an intermediary on the relationship of depressive events with quality of life in perimenopausal women in China | Cross-sectional research | The results of this study showed that physical activity factors (duration, intensity, and frequency) influenced quality of life factors except physical in mild depressive conditions; all three factors also have an effect on quality of life except on physical and psychological in moderate depression; Factors of duration and intensity of physical activity have an effect on physical and psychological factors in major depression. |

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|---|---|---|---|---|
| 5. | Huang, Chuanya & Luo, Biru & Wang, Jing & Ao, Yiling & Xiong, Weijun & Liao, Shujuan, Depressive symptoms and physical activity among community-dwelling perimenopausal women: a prospective longitudinal study, 2023 | To determine the longitudinal relationship between depressive symptoms and physical activity in perimenopausal women in China | Multi-center prospective longitudinal research | The correlation between physical activity and depressive symptoms showed no significant results. While the results using a cross-lagged panel model showed depressive symptoms would worsen at lower activity. |
| 6. | Yılmaz, S., Arslan, I., & Yengil Taci, D, The effect of physical activity and depressive mood on menopausal symptoms in postmenopausal women, 2021 | To find out the relationship between menopausal symptoms, physical activity, and depressive symptoms | Cross-sectional research | Lower scores on physical activity will be at risk of experiencing more severe depressive symptoms. |

**Physical Activity and Depression in the Menopausal Transition**

The association of depression with physical activity in women during the menopausal phase is thought to be interrelated, where physical activity is used as a method to reduce menopausal symptoms. A decrease in physical activity will be a cause that contribute to a decrease in quality of life as well as mental health. A cross-sectional study in Shanghai by Liu et al. examined the association of physical activity as an intermediate variable of the relationship between depression and quality of life in a population of perimenopausal women (ages 40 – 60 years). In the study, observed factors of physical activity that mediate the occurrence of depression, the factors observed were frequency, intensity, and duration. While quality of life factors consist of psychological, physical, environmental, and social relationship factors. The results showed that in mild depressive conditions all three physical activity factors had a moderate effect on all quality of life factors except physical factors; in moderate depression all three factors of physical activity have a moderate effect except on the physical and psychological factors of the quality of life; As well as in major depression, the duration and intensity of physical activity affect the physical and psychological factors of perimenopausal women. [17]

Another study related the relationship of physical activity with depressive symptoms at menopause. Huang et al. in China examined the relationship using female subjects aged 45 to 60 years. The results of the study showed that there was no association between depressive symptoms and physical activity in perimenopause from the results of the correlation test. But other results using a cross-lagged panel model showed different things, where depressive symptoms worsened with less physical activity and vice versa.[18]

The previous two studies examined perimenopausal women, with the criteria that women have not stopped menstruating for 1 year. So, this study will investigate the relationship between physical activity and depression in menopausal women. The criterion for postmenopausal women is to have stopped menstruating for at least 1 year.[17–19] In a cross-sectional study, Yilmaz et al. showed that there was a significant difference between physical activity and depression status; the lower the score, the more at risk of experiencing depressive symptoms compared to those with higher scores.[19]

# DISCUSS

The transition of menopause in women will make women take some unwanted events, such as menopause symptoms that are present in complaints of physical and psychological problems. Physical complaints will usually be paid more attention to than psychological complaints. Mental health issues are more often underestimated and overlooked in women. In a study conducted in Bangladesh, women in the menopausal transition experienced depressive symptoms as much as 34.2% higher in perimenopause due to complaints that occurred during that time.[20]

**Hormone Therapy and Depression in the Menopausal Transition**

Menopausal symptoms that occur during the transition period will interfere with a woman's daily life. Vasomotor disorders and sleep problems are the symptoms that make most women come to consult a doctor and can develop into depression during menopause.[20] Some women will be given hormone therapy to overcome these symptoms. Hormone therapy given can contain estrogen, progesterone, a combination of estrogen and progesterone, tibolone (TIB), and tissue selective estrogen complex (TSEC). The use of each preparation adjusts the medical condition of the woman.[21]

In the period of menopause, the number of oocytes decreases, and the ovarian follicles stop their activity, resulting in hormonal changes. A decrease in estrogen occurs during this time.[2] Estrogen plays a role in mood regulation, and its influence on the neurotransmission of serotonin and noradrenaline will trigger the occurrence of female depressive symptoms. In addition, estrogen has properties as an antidepressant that can improve mood.[22]

The use of hormone therapy at menopause is more effective in reducing vasomotor symptoms than therapy using other preparations. The use of therapy in a short time can improve symptoms of depression and mood. Progesterone preparations are reported to have detrimental effects to improve this.[12] The use of exogenous estrogen therapy has a worse influence in postmenopausal than in perimenopausal. This can be because, in perimenopause, endogenous estrogen levels are unstable, and exogenous estrogen administration reacts to stabilize them rather than to increase levels of the hormone.[23] Exogenous estrogen exposure in postmenopausal women, associated with the use of hormone therapy and oral contraceptives for more than 1 year, increases the risk of menopausal depression.[16]

Estrogen is believed to have a powerful effect on modulating neurotransmitters, which can function as antidepressants and stimulate the brain to produce serotonin.[23] However, other things need to be considered, such as progesterone levels, which also change during menopause. The hormone is associated with the regulation of brain-derived neurotrophic factor (BDNF) in neurotrophins, where decreased BDNF levels will contribute to depression.[16]

Shea et al. revealed that this increase in depression can be related to vasomotor symptoms, which are not studied, that are felt so that women use the therapy, and this will be related to the time of use.[14] This is corroborated in the study of Wium-Andersen et al.. Women who use hormone therapy with estrogen preparations or combinations after the first year have a higher risk of depression, but not with the amount used.[15]

The risk of depression increases in women taking hormone therapy in the postmenopausal period. This can be due to unknown indications for use at the time, gynecological problems can aggravate the occurrence of depression so that it will make different results. Women with previous depressive symptoms were then given hormone therapy so that the results obtained depressed women after giving therapy.[16]

**Physical Activity and Depression in the Menopausal Transition**

Perimenopausal women will have a reduced activity level, but symptoms of depression will increase during this time. Depression in perimenopausal women can be reduced by physical activity. Many factors affect physical activity, such as family income, age, chronic health problems, marital status, and negative things that can affect the occurrence of depression.[17,18]

Physical activity such as exercise performed at menopause can be a solution to reduce symptoms of depression by changing women's daily habits. This is proven to be effective for overcoming physical and psychological disorders that occur during menopause. The secretion of endorphins, estriol, and testosterone hormones will increase, which reduces anxiety, depression, and stress.[24]

Depression was shown to be lower in women who did resistance and aerobic exercise outdoors than indoors. In addition, walking activities with moderate intensity can reduce symptoms of depression.[25]

## CONCLUSION

The use of hormone therapy in women during the menopausal transition can increase the risk of depression. Further research is needed because, in previous studies, no one has observed anything related to the hormone content in the therapy given and differences in depression in different hormone therapies. Physical activity can help reduce the risk of depression or the onset of depressive symptoms. Problems related to aging can limit menopausal women from doing physical activity..

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