Available online on 15.11.2021 at <http://jddtonline.info>

Journal of Drug Delivery and Therapeutics

Open Access to Pharmaceutical and Medical Research

Copyright © 2021 The Author(s): This is an open-access article distributed under the terms of the CC BY-NC 4.0 which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use provided the original author and source are credited



Open Access Full Text Article



Review Article

Menopause Induced Depression, Anxiety, Quality of Life, Lack of Sleep in Women: An Overview

Ragasudha A¹, Minnu Skaria^{1*}, Sambath Kumar R²

¹Department of Pharmacy Practice, J.K.K. Nattraja college of Pharmacy, Kumarapalayam – 638 183, Tamilnadu, India

²Department of Pharmaceutics, J.K.K. Nattraja college of Pharmacy, Kumarapalayam – 638 183, Tamilnadu, India

Article Info:



Article History:

Received 16 September 2021
Reviewed 29 October 2021
Accepted 08 November 2021
Published 15 November 2021

Cite this article as:

Ragasudha A, Minnu S, Sambath Kumar R, Menopause Induced Depression, Anxiety, Quality of Life, Lack of Sleep in Women: An Overview, Journal of Drug Delivery and Therapeutics. 2021; 11(6):319-323

DOI: <http://dx.doi.org/10.22270/jddt.v11i6.5169>

*Address for Correspondence:

Minnu Skaria, Department of Pharmacy Practice, J.K.K. Nattraja college of Pharmacy, Kumarapalayam – 638 183, Tamilnadu, India

Abstract

Background: Menopause occurs between the ages of 40 and 50, and marks the end of a woman's menstrual cycle. A period of time during which a woman does not have a monthly cycle for more than 12 months is known as post-menopause. Women may suffer challenges in their daily lives during this period, such as depression, anxiety, and sleep loss, all of which can have a negative impact on their quality of life. A decrease in hormone production, such as estrogen and progesterone, can cause menopause. To treat psychological difficulties in menopausal women, drugs such as vortioxetine and paroxetine, as well as selective serotonin reuptake inhibitors (SSRI) and anti-depressants, were advised.

Objective: To evaluate the effects in women how menopause inducing depression, anxiety, quality of life and lack of sleep.

Methodology: The recent studies related to the aim of the review were undertaken through a literature search to evaluate the effects in women how menopause inducing depression, anxiety, quality of life and lack of sleep.

Conclusion: Menopause, post-menopause, and peri-menopause are age-related causes in women who are going through the menstrual cycle. There is no need for medication during this time, but in severe cases, medications such as selective serotonin reuptake inhibitors (SSRI) and antidepressants should be administered and also for vaginal dryness and irritation Ospemifene is suggested. Many more clinical researches on the benefits of menopausal complications will be needed in the future.

Keywords: Menopause, post- menopause, depression, estrogen, progesterone

INTRODUCTION:

Menopause is a life stage in which a woman experiences physical, psychological, and social changes, all of which have an impact on her quality of life. More than 25 million women worldwide experienced menopause in the 1990s, and this number is predicted to triple by 2020 and beyond¹. Post-menopause is a period of time that begins about 12 months following a woman's last menstrual period and is marked by a certain sex hormone profile². By 2030, it is anticipated that 1.2 billion women will be postmenopausal, amounting to 47 million women every year^{3, 4}. The reduction in female hormone production by the ovaries causes the transition from the reproductive to the non-reproductive stage. Although menopause is a physiologically related ailment, it is clear that the resulting physical and emotional changes have a significant impact on women's lives.

Depression, anxiety, poor quality of life, and sleep deprivation are all common health problems among women in their forties and fifties. An Australian study indicated that women in the peri-menopausal and postmenopausal phases had a higher risk of more severe depressive symptoms than women in the premenopausal period without a history of depression⁵⁻⁹. Depression causes inflammation and suppresses proper immunological responses. Depression

affects a person's mental and physical health^{10,11}, as well as their quality of life (QoL)^{12, 13}. Depression is connected to a host of functional difficulties as well as significant decreases in a variety of QoL categories; including social functioning.¹⁴ Sadness and anxiety are more common in women in their peri-menopausal and postmenopausal periods². Depressive disorders are also on the rise at an alarming rate. Women have around double the lifetime risk of major depression as men, with about 5% of women experiencing major depression, and depression is expected to be the world's second leading cause of disability by 2020.¹⁵ Higher rates of depression and obesity, according to studies, lower quality of life and raise the risk of illness and early death^{16, 17}

Antidepressants' efficacy on anxiety and depressive symptoms, as well as vasomotor and cognitive symptoms, especially Selective Serotonin Reuptake Inhibitors (SSRIs) and Serotonin and Norepinephrine Reuptake Inhibitors (SNRIs). In the menopausal phase, the development of depression and anxiety symptoms is typically 1.8 and 2.0 times higher than in the premenopausal period^{18, 19}. Depression and anxiety symptoms affect 18 percent to 41.8 percent of perimenopausal and postmenopausal women, respectively and 7 percent to 25% of postmenopausal women¹⁷⁻²². Estrogen's neuromodulator of the serotonergic and noradrenergic systems as a source of

amine dysregulation Cognitive symptoms, such as loss of attention and memory, are sometimes mentioned; estrogens. Estrogens modulate synaptic plasticity and neuroprotection and their chronic insufficiency lowers neuronal repair capacity, dendritic spine number and neurotransmitter synthesis, deposit and release ²³⁻²⁵.

MENOPAUSE:

Menopause is the period of a woman's life when her menstrual cycle comes to an end. As a result, the reproductive hormone naturally declines. Menopause is a natural and biological process that is associated with the lack of a menstrual period for duration of 12 months. It can happen between the ages of 40 and 50. Approximately 1% of women reach menopause before the age of 40, whereas 5% of women reach menopause between the ages of 40 and 45. Perimenopausal period transition is the term for this procedure.

The perimenopausal period is the time around a menopause transition; it varies among different in women it mostly begins before the four years of menopause. Only a few women start their perimenopausal transition 10 years before their menopause. This period is characterized by an irregular menstrual period this may skip a month and then return or may skip for several months and then the regular cycle starts for a few months. During this period the menstrual flow may also get heavier or even lighter.

Causes:

- Natural decline of reproductive hormone like estrogen and progesterone
- Hysterectomy- surgical procedure to remove uterus
- Primary ovary insufficiency
- Removal of the ovaries i.e. bilateral oophorectomy surgery

- Cancer chemotherapy and radiation therapy can also lead to an induced menopause- during this therapy this may cause early menopause because this treatments are toxic to ovaries.
- Premature ovarian condition is also characterized by an early occurrence of menopause before the age of 40; this may be related to some autoimmune disease or gene.
- Hypothyroidism can cause symptoms of menopause

Signs and symptoms:

Hot flashes or night sweats (36 – 87%), sleep problems (40– 60%), Mood symptoms (15 – 78%), Weight gain (60 – 70%), Muscle and/or joint pain (48 – 72%), Palpitation(44-50%), Headache (32 – 71%), Memory impairment (41-44%), Genitourinary symptoms (25–30%), Sexual dysfunction (20 – 30%).

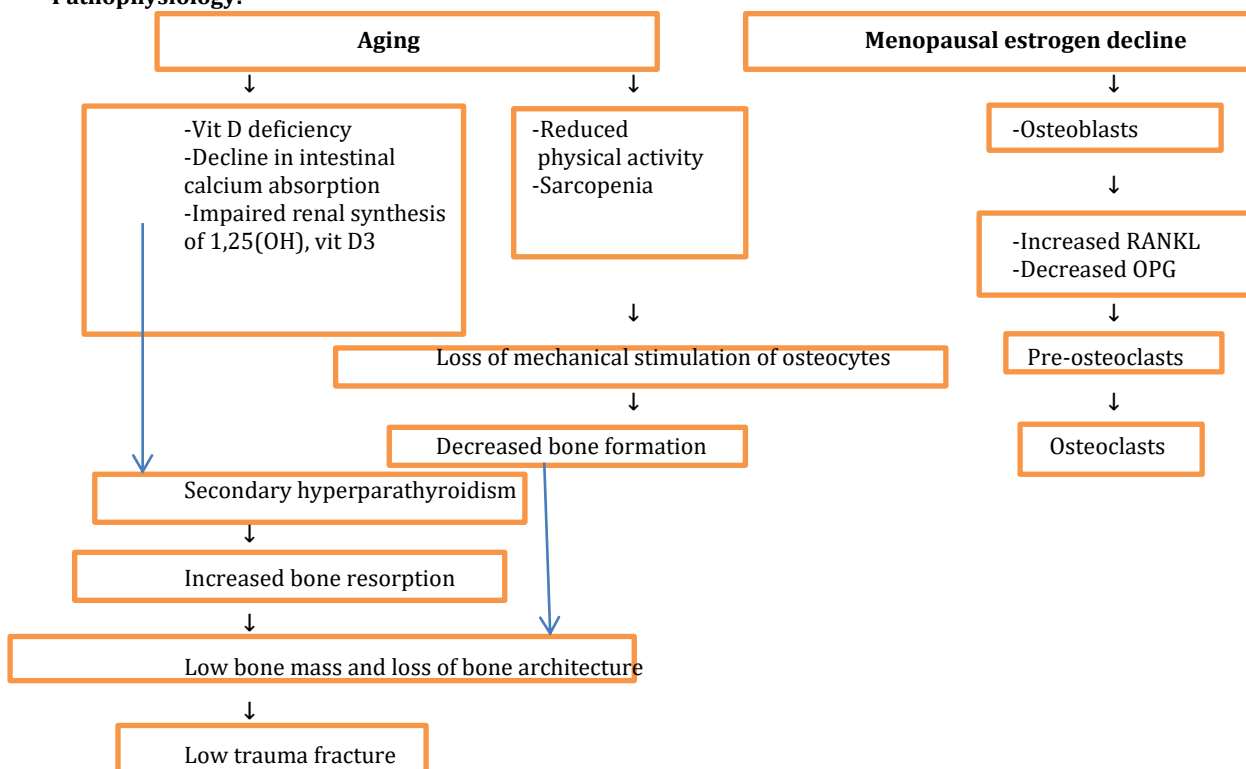
Complication:

Vasomotor symptoms, urogenital atrophy, osteoporosis, cardiovascular illnesses, breast and skin atrophy, cancer, decreased cognitive function and increased sexual issues are all effects of estrogen deficiency during menopause ^{26, 27}.

Diagnosis:

- History collection- Menopause is usually considered complete after 1 year of amenorrhea.
- FSH- follicle stimulating hormones: the FSH helps to control the menstrual cycle and the production of eggs by the ovaries. An elevated FSH blood level of 30 ml or higher combined with 12 consecutive months of no menstrual flow is usually a confirmation of menopause.
- TSH- Thyroid stimulating hormone.

Pathophysiology:



*RANKL- Receptor activator for nuclear factor k B ligand *OPG- Osteoprotegerin

Depression due to menopause

Antidepressants (ADs) are routinely recommended to women who suffer from depression and are successful in treating it. In recent decades, the prevalence of Alzheimer's disease has quadrupled, with 22.8 percent of women aged 40–59 reporting current usage²⁸. Anti-inflammatory properties of ADs^{29, 30} may help to reduce the impact of depression on breast cancer risk. However, the most generally used family of AD drugs, selective serotonin reuptake inhibitors (SSRIs), may raise circulating prolactin levels^{31–33}, which may increase the risk of breast cancer^{34–36}. Two prospective studies suggest a 50–75 percent increased risk of breast cancer related with Alzheimer's disease or SSRI usage in particular^{37, 38}, but other studies found no link^{39–41}.

Women are more prone to suffer from depression, which affects quality of life and can lead to suicide in some cases⁴². An Australian study indicated that women in the perimenopausal and postmenopausal stages had a higher risk of severe depressive symptoms than those in the premenopausal stage without a history of depression⁵. Depressive disorders in postmenopausal women are characterized by sadness, tearfulness, irritability, emotional fragility, and poor attention⁴³.

Susceptibility to depression is linked to some women's greater susceptibility to hormonal changes during this time. Co-morbidities, sleep issues, and stressful life events, all of which are unrelated to the menopausal transition, play a significant influence. Ethnicity, culture, tradition, prior history of depression, body mass index, degree of education, and marital status, on the other hand, are all linked to postmenopausal depression^{44, 45}. Longitudinal studies demonstrate that the risk of depressive symptoms increases with age in women. It rises from 1.30 to 1.55 times during the early stages of menopausal transition. Depression risk is 1.71–2.89 times higher in the postmenopausal period than in the premenopausal period^{46, 19, and 47}. As a result, the risk of developing Major Depressive Disorder (MDD) in the postmenopausal period increases by two to four times. This, however, only applies to women who have a history of mental health issues¹⁸.

Quality of life affecting in menopause

Menopause has an impact on one's quality of life. Menopause is a stage in a woman's life that has physical, psychological, and social consequences that affect her quality of life. QoL in postmenopausal women is influenced by symptoms experienced during menopause and socio-demographic variables^{48, 49}. The principal consequences of menopause are linked to a lack of estrogen. Vasomotor symptoms, urogenital atrophy, osteoporosis, cardiovascular disease, cancer, impaired cognitive function, and sexual issues are among the key health concerns of postmenopausal women⁵⁰. Hormonal changes that begin during the menopausal transition cause physiological changes and a variety of additional symptoms.

As a result, women commonly experience hot flashes, insomnia, weight gain and bloating, mood swings, irregular menstruation, breast pain, depression, and headaches. These symptoms could be worrisome, especially since they occur at a time when women are expected to play key roles in society, the home, and the job⁵¹. Women's quality of life is deteriorated as a result of menopause-related illnesses^{51, 52}.

Anti-depressants used for menopause

Antidepressants are prescribed for women going through menopause. The efficacy of antidepressants, particularly

selective serotonin reuptake inhibitors and serotonin and norepinephrine reuptake inhibitors, on anxiety and depressive symptoms, as well as vasomotor and cognitive symptoms, has been extensively established in the literature. Paroxetine, the first non-hormone medication for vasomotor symptoms approved by the Food and Drug Administration in 2013, has proven to be the most effective antidepressant for treating vasomotor and cognitive symptoms in postmenopausal transition. Vortioxetine was also licensed by the FDA in 2013 for the treatment of depressive disorders. Vortioxetine is a serotonin modulator and stimulant that has been shown to improve mood and cognitive symptoms. Vortioxetine appears to have a better tolerance profile than the other SSRIs, particularly for side effects that menopausal women find difficult to bear, such as libido loss, weight gain, and withdrawal symptoms.

Menopause affecting sleep:

In comparison to premenopausal years, sleep disturbances are more common during the menopausal transition⁵³. Vasomotor symptoms, night sweats, exhaustion, mood swings, irritability, headache, palpitation, and sleep disturbances are typically associated with estrogen and progesterone levels declining throughout menopause^{54, 55}. These symptoms might range from mild to severe and incapacitating. Women's sleep difficulties are one of the most common health issues throughout menopause. Difficulty falling asleep, fractioned sleep, night-time awakening, inability to resume sleep, issues waking up, lethargy, and daytime sleepiness are among the disorders^{56, 57}.

CONCLUSION:

Menopause, post-menopause, and peri-menopause are age-related causes in women who are going through the menstrual cycle. These conditions can impair women's daily lives, producing mental distress, anxiety, irritability, mood swings, lack of sleep, and poor quality of life. There is no need for medication during this time, but in severe cases, medications such as selective serotonin reuptake inhibitors (SSRI) and antidepressants should be administered and also for vaginal dryness and irritation Ospemifene is suggested. The challenges of causing menopause in women will be addressed in this study. Many more clinical researches on the benefits of menopausal compilations will be needed in the future.

ACKNOWLEDGEMENT:

We would like to express our thanks to the head, Department of Pharmacy Practice and our Department staffs to their valuable suggestions and recommendations.

CONFLICT OF INTEREST

There are no conflicts of interest to declare.

FUNDING SOURCES

There is no funding sources, what so ever, for this study.

REFERENCES:

1. World Health Organization: Research on Menopause. Report on World Health Organization Scientific Group. Technical Report Series 670. Geneva: World Health Organization; 1981. Available from: <http://www.apps.who.int/iris/handle/1065/41526>. [Last accessed on 2018 May 20].
2. Harlow SD, Gass M, Hall JE, Lobo R, Maki P, Rebar RW, Sherman S, Sluss PM, de Villiers TJ, STRAW + 10 Collaborative Group. Executive summary of the Stages of Reproductive Aging Workshop + 10: Addressing the unfinished agenda of staging

- reproductive aging: *Fertil Steril*, 2012; 19(4):387-95. <https://doi.org/10.1097/gme.0b013e31824d8f40>
3. Schneider HPG, Birkhäuser M, Quality of life in climacteric women: *Climacteric*, 2017; 20(3):187-194. <https://doi.org/10.1080/13697137.2017.1279599>
 4. Tang R, Luo M, Li J, Peng Y, Wang Y, Liu B, Liu G, Wang Y, Lin S, Chen R, Symptoms of anxiety and depression among Chinese women transitioning through menopause: Findings from a prospective community-based cohort study: *Fertil Steril*, 2019; 112(6):1160-1171. <https://doi.org/10.1016/j.fertnstert.2019.08.005>
 5. Mulhall S, Andel R, Anstey K.J, Variation in symptoms of depression and anxiety in midlife women by menopausal status: *Maturitas*, 2018; 108(3):7-12. <https://doi.org/10.1016/j.maturitas.2017.11.005>
 6. Ader R, Cohen N, Felten D. Psychoneuroimmunology: interactions between the nervous system and the immune system: *Lancet*, 1995; 345(8942):99-103. [https://doi.org/10.1016/S0140-6736\(95\)90066-7](https://doi.org/10.1016/S0140-6736(95)90066-7)
 7. Dowlati Y, Herrmann N, Swardfager W, Liu H, Sham L, Reim EK, et al., A meta-analysis of cytokines in major depression: *Biol Psychiatry*, 2010; 67(5):446-57. <https://doi.org/10.1016/j.biopsych.2009.09.033>
 8. Liu Y, Ho RC, Mak A. Interleukin (IL)-6, tumour necrosis factor alpha (TNF-alpha) and soluble interleukin-2 receptors (sIL-2R) are elevated in patients with major depressive disorder: a meta-analysis and meta-regression: *J Affect Disord*. 2012; 139(3):230-9. <https://doi.org/10.1016/j.jad.2011.08.003>
 9. Ma Y, Balasubramanian R, Pagoto SL, Schneider KL, Hebert JR, Phillips LS, et al., Relations of Depressive Symptoms and Antidepressant Use to Body Mass Index and Selected Biomarkers for Diabetes and Cardiovascular Disease: *Am J Public Health*. 2013; 108(3): e34-e43. <https://doi.org/10.2105/AJPH.2013.301394>
 10. Prince M, Patel V, Saxena S, Maj M, Maselko J, Phillips M.R, Rahman A, No health without mental health: *Lancet*, 2007, 370(9590):859-877. [https://doi.org/10.1016/S0140-6736\(07\)61238-0](https://doi.org/10.1016/S0140-6736(07)61238-0)
 11. Luppá M, Sikorski C, Luck T, Ehreke L, Konnopka A, Wiese B, Weyerer S, König H.H, Riedel-Heller S.G, Age- and gender-specific prevalence of depression in latest-life-systematic review and meta-analysis: *J. Affect. Disord*, 2012, 136:212-221. <https://doi.org/10.1016/j.jad.2010.11.033>
 12. Kessler RC, Bromet EJ, The epidemiology of depression across cultures: *Annu. Rev. Public Health*, 2013; 34: 119-138. <https://doi.org/10.1146/annurev-publhealth-031912-114409>
 13. Ferrari AJ, Charlson FJ, Norman RE, Patten SB, Freedman G, Murray CJ, Vos T, Whiteford H.A, Burden of depressive disorders by country, sex, age, and year: Findings from the global burden of disease study 2010: *PLoS Med*, 2013; 10(11): e1001547. <https://doi.org/10.1371/journal.pmed.1001547>
 14. Ravindran AV, Matheson K, Griffiths J, Merali Z, Anisman H, Stress, coping, uplifts, and quality of life in subtypes of depression: A conceptual frame and emerging data: *J. Affect. Disord*. 2002; 71(1-3):121-130. [https://doi.org/10.1016/S0165-0327\(01\)00389-5](https://doi.org/10.1016/S0165-0327(01)00389-5)
 15. Lopez AD, Mathers CD, Ezzati M, Jamison DT, & Murray CJ, Global and regional burden of disease and risk factors, 2001: systematic analysis of population health data: *Lancet*, 2006; 367(9524):1747-1757. [https://doi.org/10.1016/S0140-6736\(06\)68770-9](https://doi.org/10.1016/S0140-6736(06)68770-9)
 16. Kozela, M. et al. The association of depressive symptoms with cardiovascular and all-cause mortality in Central and Eastern Europe: prospective results of the HAPIEE study: *Eur. J. Prev. Cardiol*, 2016; 23(17):1839-1847. <https://doi.org/10.1177/2047487316649493>
 17. Christensen GT, Maartensson S & Osler M, The association between depression and mortality-a comparison of survey-and register-based measures of depression: *J. Affect. Disord*, 2017; 210:111-114. <https://doi.org/10.1016/j.jad.2016.12.024>
 18. Tangen T, Mykletun A. Depression and anxiety through the climacteric period: an epidemiological study (HUNT-II): *J Psychosom Obstet Gynaecol*, 2008 <https://doi.org/10.1080/01674820701733945>
 - 29(2):125-31. Epub 2008/05/20. <https://doi.org/10.1080/01674820701733945> PMID: 18484441.
 19. Tang R, Luo M, Li J, Peng Y, Wang Y, Liu B, et al. Symptoms of anxiety and depression among Chinese women transitioning through menopause: findings from a prospective community-based cohort study: *Fertil Steril*. 2019 <https://doi.org/10.1016/j.fertnstert.2019.08.005>
 - 112(6):1160-71. Epub 2019/12/18. <https://doi.org/10.1016/j.fertnstert.2019.08.005> PMID: 31843093. <https://doi.org/10.1016/j.fertnstert.2019.08.005>
 20. Timur S, Sahin NH. The prevalence of depression symptoms and influencing factors among perimenopausal and postmenopausal women: *Menopause*, 2010 <https://doi.org/10.1097/gme.0b013e3181cf8997>
 - 17(3):545-51. Epub 2010/04/20. <https://doi.org/10.1097/gme.0b013e3181cf8997> PMID: 20400922.
 21. Unsal A, Tozun M, Ayranci U. Prevalence of depression among postmenopausal women and related characteristics: *Climacteric*, 2011 <https://doi.org/10.3109/13697137.2010.510912>
 - 14(2):244-51. Epub 2010/10/23. <https://doi.org/10.3109/13697137.2010.510912> PMID: 20964551.
 22. Bromberger JT, Assmann SF, Avis NE, Schocken M, Kravitz HM, Cordal A. Persistent mood symptoms in a multiethnic community cohort of pre- and perimenopausal women: *Am J Epidemiol*, 2003 <https://doi.org/10.1093/aje/kwg155>
 - 158 (4):347-56. Epub 2003/08/14. <https://doi.org/10.1093/aje/kwg155> PMID: 12915500. <https://doi.org/10.1093/aje/kwg155>
 23. Zeng LN, Yang Y, Feng Y, Cui X, Wang R, Hall BJ, et al. The prevalence of depression in menopausal women in China: A meta-analysis of observational studies: *J Affect Disord*, 2019; 256:337-43. <https://doi.org/10.1016/j.jad.2019.06.017>
 - Epub 2019/06/17. <https://doi.org/10.1016/j.jad.2019.06.017> PMID: 31202988. <https://doi.org/10.1016/j.jad.2019.06.017>
 24. Shively CA, Laber-Laird K, Anton RF. Behavior and physiology of social stress and depression in female cynomolgus monkeys: *Biol Psychiatry*. 1997; 41(8):871-882. [https://doi.org/10.1016/S0006-3223\(96\)00185-0](https://doi.org/10.1016/S0006-3223(96)00185-0)
 25. Shively CA, Williams JK, Laber-Laird K, Anton RF. Depression and coronary artery atherosclerosis and reactivity in female cynomolgus monkeys: *Psychosom Med*, 2002; 64(5):699-706. <https://doi.org/10.1097/00006842-200209000-00001>
 26. Shively CA, Register TC, Friedman DP, Morgan TM, Thompson J, Lanier T. Social stress associated depression in adult female cynomolgus monkeys (*Macaca fascicularis*): *Biol Psychol*. 2005; 69(1):67-84. <https://doi.org/10.1016/j.biopsycho.2004.11.006>
 27. Berek JS. Berek & Novak's gynecology. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins 16th ed; 2019.
 28. Gumuşay M, Erbil N. Alternative methods in the management of menopausal symptoms. *Middle Black Sea J Health Sci*, 2016; 2(2):20-5. <https://doi.org/10.19127/mbsjohs.20236>
 29. Pratt, LA., Brody, DJ. Depression in the U S household population, 2009-2012. Hyattsville, MD: National Center for Health Statistics; 2014. NCHS Data Brief, no 172
 30. Kenis G, Maes M. Effects of antidepressants on the production of cytokines: *Int J Neuropsychopharmacol*, 2002; 5(4):401-12. <https://doi.org/10.1017/S1461145702003164>

31. Pizzi C, Mancini S, Angeloni L, Fontana F, Manzoli L, Costa GM. Effects of selective serotonin reuptake inhibitor therapy on endothelial function and inflammatory markers in patients with coronary heart disease: *Clin Pharmacol Ther*, 2009; 86(5):527-32. <https://doi.org/10.1038/clpt.2009.121>
32. Olsson M, Marcus SC. National patterns in antidepressant medication treatment: *Arch Gen Psychiatry*. 2009; 66(8):848-56. <https://doi.org/10.1001/archgenpsychiatry.2009.81>
33. Balsa JA, Sanchez-Franco F, Pazos F, Lara JI, Lorenzo MJ, Maldonado G, et al. Direct action of serotonin on prolactin, growth hormone, corticotropin and luteinizing hormone release in co-cultures of anterior and posterior pituitary lobes: autocrine and/or paracrine action of vasoactive intestinal peptide: *Neuroendocrinology*, 1998; 68(5):326-33. <https://doi.org/10.1159/000054381>
34. Emiliano AB, Fudge JL. From galactorrhea to osteopenia: rethinking serotonin-prolactin interactions: *Neuropsychopharmacology*, 2004; 29(5):833-46. <https://doi.org/10.1038/sj.npp.1300412>
35. Madhusoodanan S, Parida S, Jimenez C. Hyperprolactinemia associated with psychotropics-a review: *Hum Psychopharmacol*. 2010; 25(4):281-97. <https://doi.org/10.1002/hup.1116>
36. Tworoger SS, Eliassen AH, Rosner B, Sluss P, Hankinson SE. Plasma prolactin concentrations and risk of postmenopausal breast cancer: *Cancer Res*, 2004; 64(18):6814-9. <https://doi.org/10.1158/0008-5472.CAN-04-1870>
37. Tworoger SS, Eliassen AH, Sluss P, Hankinson SE. A prospective study of plasma prolactin concentrations and risk of premenopausal and postmenopausal breast cancer: *J Clin Oncol*, 2007; 25(12):1482-8. <https://doi.org/10.1200/JCO.2006.07.6356>
38. Tworoger SS, Eliassen AH, Zhang X, Qian J, Sluss PM, Rosner BA, et al. A 20-year prospective study of plasma prolactin as a risk marker of breast cancer development: *Cancer Res*, 2013; 73(15):4810-9. <https://doi.org/10.1158/0008-5472.CAN-13-0665>
39. Haukka J, Sankila R, Klaukka T, Lonnqvist J, Niskanen L, Tanskanen A, et al. Incidence of cancer and antidepressant medication: record linkage study: *International Journal of Cancer*, 2010; 126(1):285-96. <https://doi.org/10.1002/ijc.24537>
40. Kato I, Zeleniuch-Jacquotte A, Toniolo PG, Akhmedkhanov A, Koenig K, Shore RE. Psychotropic medication use and risk of hormone-related cancers: the New York University Women's Health Study: *Journal of Public Health Medicine*, 2000; 22(2):155-60. <https://doi.org/10.1093/pubmed/22.2.155>
41. Brown SB, Hankinson SE, Arcaro KF, Qian J, Reeves KW. Depression, Antidepressant Use, and Postmenopausal Breast Cancer Risk: *Cancer Epidemiological Biomarkers Prev*, 2016; 25(1):158-64. <https://doi.org/10.1158/1055-9965.EPI-15-1063>
42. Ashbury JE, Levesque LE, Beck PA, Aronson KJ. A population-based case-control study of Selective Serotonin Reuptake Inhibitors (SSRIs) and breast cancer: the impact of duration of use, cumulative dose and latency: *BioMed Central Medicine*, 2010; 8:90, 1741-7015. <https://doi.org/10.1186/1741-7015-8-90>
43. Ashbury JE, Levesque LE, Beck PA, Aronson KJ. Selective Serotonin Reuptake Inhibitor (SSRI) Antidepressants, Prolactin and Breast Cancer: *Front Oncol*, 2012; 2:177. <https://doi.org/10.3389/fonc.2012.00177>
44. Zimny M, Starczewska M, Szkup M, Karakiewicz-Krawczyk K, Grochans E, Sipak-Szmigiel O. Analysis of the Impact of Type 2 Diabetes on the Psychosocial Functioning and Quality of Life of Perimenopausal Women: *International Journal of Environmental Research and Public Health*, 2020; 17(12):4349. <https://doi.org/10.3390/ijerph17124349>
45. Azizi M, Fooladi E, Masoumi M, Orimi TG, Elyasi F, Davis SR. Depressive symptoms and their risk factors in midlife women in the Middle East: A systematic review: *Climacteric*, 2018; 21(1):13-21. <https://doi.org/10.1080/13697137.2017.1406908>
46. Sassarini, D.J. Depression in midlife women: *Maturitas*, 2016; 94:149-154. <https://doi.org/10.1016/j.maturitas.2016.09.004>
47. Mauas V, Kopala-Sibley DC, Zuroff DC. Depressive symptoms in the transition to menopause: The roles of irritability, personality vulnerability, and self-regulation: *Archives of Womens Mental Health*, 2014; 17(4):279-289. <https://doi.org/10.1007/s00737-014-0434-7>
48. Colvin A, Richardson GA, Cyranowski JM, Youk A, Bromberger JT. The role of family history of depression and menopausal transition in the development of major depression in midlife women: Study of women's health across the nation Mental Health study (SWAN MHS): *Depress Anxiety*, 2017; 34(9):826-835. <https://doi.org/10.1002/da.22651>
49. Schneider H, Birkhäuser M. Quality of life in climacteric women: *Climacteric*, 2017; 20(3):187-94. <https://doi.org/10.1080/13697137.2017.1279599>
50. Gobbens RJ, Remmen R. The effects of socio demographic factors on quality of life among people aged 50 years or older are not unequivocal: Comparing SF-12, WHOQOL-BREF, and WHOQOL-OLD: *Clinical Interventions in Aging*, 2019; 14:231-9. <https://doi.org/10.2147/CIA.S189560>
51. Berek JS. Berek & Novak's Gynecology. 16th ed. Philadelphia: Lippincott Williams & Wilkins (LWW); 2019.
52. Monteleone P, Mascagni G, Giannini A, Genazzani AR, Simoncini T. Symptoms of menopause-global prevalence, physiology and implications: *Nature Reviews Endocrinology*, 2018; 14(4):199-215. <https://doi.org/10.1038/nrendo.2017.180>
53. Ozcan H. Healthy life style behaviors and quality of life at menopause: *International Journal of Caring Sciences*, 2019; 12(1):492-500.
54. Landis CA and Moe KE. Sleep and menopause: *Nursing Clinics of North America*, 2004; 39(1):97-115. <https://doi.org/10.1016/j.cnur.2003.11.006>
55. Luoto R. Hot flushes and quality of life during menopause: *BioMed Central Women's Health*, 2009; 9:13. <https://doi.org/10.1186/1472-6874-9-13>
56. Kalleinen N, Polo O, Himanen SL, Joutsen A, Urrila AS, Polo-Kantola P. Sleep deprivation and hormone therapy in postmenopausal women: *Sleep Medicine*, 2006; 7(5):436-447. <https://doi.org/10.1016/j.sleep.2006.02.004>
57. Freedman R. Hot flashes: behavioral treatments, mechanisms, and relation to sleep: *The American Journal of Medicine*, 2005; 118(12):124-130. <https://doi.org/10.1016/j.amjmed.2005.09.046>