

## THE INFLUENCE OF HORMONE REPLACEMENT THERAPY TO THE LIFE QUALITY OF MENOPAUSAL WOMEN

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### Abstract

According to World Health Organization, there are 25 million women in the world is estimated to reach menopause phase every year. The vasomotor symptoms influence 60% to 80% women who enter menopause phase. Premenopause syndrome is experienced by women in the world, around 70-80% European women, 60% in America, 57% in Malaysia, 18% in China and 10% in Japan and Indonesia. Hormone replacement therapy is a therapy of estrogen hormone to decrease the menopause symptom. The purpose of this Systematic Literature Review preparation is to find evidence based about Hormone Therapy of Menopausal Women in the developed country. There were eight steps of systematic literature review which were used in this review. Those eight steps covered: identifying midwifery problem, problem priority and research question, framework of primary and secondary data, relevant study identification, prism flow diagram, critical assessment, data analysis and data extraction. This systematic literature review was done by finding articles using database such as Pubmed and Pro Quest. the effectiveness of hormone therapy to menopausal women can be seen as follow: women who is given estrogen and medroxyprogesterone have experienced better changes from the menopause sweating symptom ( $p=0,001$ ), sleep problem ( $p<0,001$ ), sore throat ( $p=0,096$ ), and hot flushes ( $<0,001$ ). Vasomotor symptom, urogenital symptom, and sexual dysfunction are menopausal symptom that is mostly experienced by women in before menopause, in menopause phase and after menopause. Hormone therapy is an effective therapy to tackle menopause symptoms. Stopping the hormone therapy may cause significant increase to the heavy menopause symptom, which means therapy hormone has a big role in the life quality of menopausal women.

**Keywords:** Hormone replacement therapy, Menopause symptom and Menopause.

### 1. INTRODUCTION

According to World Health Organization, every year around 25 million women in the world has experienced menopause. WHO also stated that around 467 million women aged 50 years and over spend their lives in a post-menopausal state, and 40% of postmenopausal women live in developing countries with an average age of menopause at the age of 51. WHO estimating the number of women aged 50 years and over is expected to increase from 500 million at present to more than 1 billion by 2030 (Syalfina, 2017). Vasomotor symptoms influences 60% until 80% women that enter menopause phase (Freeman & Sherif, 2007). Pre menopausal syndrome is experienced by many women in almost all over the world, around 70-80% of European women, 60% in America, 57% in Malaysia, 18% in China and 10% in Japan and Indonesia (Sasrawita, 2017). Vasomotor instability (or hotflash), is the main symptom of menopause, including a feeling of heat that is suddenly came along with sweat and inflammation. Vasomotor instability can also be associated with anxiety, palpitations and sleep disorder symptoms. Even though the prevalence of vasomotor symptoms varies across racial and ethnic backgrounds, more than 50% of women report

vasomotor symptoms at some point during menopause (O'Neill & Eden, 2012).

Hormone replacement therapy. This therapy can improve sexual function, reduce insomnia and reduce body heat. Hormone Replacement Therapy (TSH) or currently called hormone therapy is estrogen hormone therapy to reduce menopause symptoms.

## 2. MATERIALS AND METHODS

The author filtered 690 literature from two databases (*Pubmed*, *Sciencedirect*) to be conducted a review. All articles chosen by quantitative research method indexed by *scopus*. The arrangement of this *Systematic Literature Review* was adjusted with steps of *Systematic Literature Review*. The arrangement steps of *systematic literature review* are 1) problems identification, 2) making priority of problems and questions 3) using framework, 4) literature searching using databases, manual searching or grey literature, 5) choosing paper based on inclusion and exclusion criteria, 6) conducting critical appraisal, 7) extract data from the chosen paper, 8) collecting data and mapping for answering questions.

Framework used in this review is PICOC (*Population*, *Exposure/ event*, *Outcomes* and *Study design*).

Table 1. Framework of systematic literature review

	Inclusion	Exclusion
<b>Population</b>	Menopause Women	Menopausal hormonal therapy in women at risk.
<b>Intervention</b>	Hormonal therapy	
<b>Comparison</b>	Non hormonal therapy	
<b>Outcome</b>	Menopausal symptoms	
<b>Context</b>	Developed countries	Developing countries

There were three strategy steps in the search for literature used. The first step was to search on a limited scope on Google Scholar, that allows to analyze the words contained in the title and abstract. The search terminologies included are Treatment, "Hormone Therapy", Hot Flush, menopause symptoms and Menopause. The second step was by using all identified keywords. All of these keywords have been searched at Pubmed, Sciencedirect and Scopus. The third step was a list of references from all identified reports and articles traced for additional study.

Keywords used to find out paper in pubmed was (management) OR treatment) OR "hormone replacement") OR "hormone therapy") AND climacteric) OR premenopause) OR menopause) OR postmenopause AND Europe) AND "last 10 years". Key criteria like title, author, year of article publication, research location, research objectives, methodology, research population, and results or conclusions were significant. In the search for 2 databases and reference lists, there were 690 articles, 19 filtered for relevance. Then a further article filtering was conducted to find out the right and complete reference about the effect of hormone therapy on menopausal women and found 11 articles to be used for Systematic Literature Review. The author filtered the title and abstract of all articles to be used as inclusion criteria. Full text studies were taken and reviewed independently based on those criteria. So, 11 articles were left for the final review.

**Table 2. Extraction Data**

No	Title/Author/Year/Grade	Country	Aim	Method	Data Collection	Participant	Result
1.	The effect of hormone therapy on women's quality of life in the first year of the Estonian Postmenopausal Hormone Therapy Trial. /Veerus Piret, et al/2012/Q1	Estonia	To find out whether women taking hormone therapy in a randomized trial experienced fewer symptoms and a better quality of life after one year of using hormone therapy than women who were not given hormone therapy.	RCT	Women were randomly divided into two groups, given hormone therapy, and not given therapeutic hormones. After one year in the experiment, the sample was given a questionnaire to discuss the symptoms that were felt after the use of HT and non-HT.	1,823 menopausal women took a hormone therapy trial in Estonia and divided into 2 groups, 686 were given hormone therapy, and 673 were not given hormone therapy.	After one year in the trial, women who underwent therapeutic hormones reported fewer hot flashes, insomnia, and sweating in vasomotor symptoms.
2	Hot flushes and reproductive hormone levels during the menopausal transition./Tanveer Dhanoya, et al/ 2015/Q1	United Kingdom	To test specific hormone levels and ethnic differences in relation to hot flushes	Cross Sectional	Data using a questionnaire. The questionnaire contains information on demographics, reproduction and developmental history, menopausal status and symptoms, education and employment status, and migration and medical history. To assess whether you have experienced hot flushes, have you experienced it for the past two weeks, have you ever been disturbed by hot flushes? And how severe.	108 women, Bangladeshi women living in Sylhet, Bangladeshi women living in London, and European women living in London.	A significant relationship was found between AMH, FSH and hot flush through menopause. The relationship found in this study shows that women experience a menopausal transition and experience symptoms, rather than AMH and FSH which are mechanically involved in symptom formation.

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3	Progesterone for hot flush and night sweat treatment – effectiveness for severe vasomotor symptoms and lack of withdrawal rebound./ Jerilynn C. Prior, et al./2012/	Canada	To present the results of two additional results from a recent randomized controlled trial (RCT) of progesterone for vasomotor symptoms.	RCT	Data collection was divided into two groups, groups that experienced severe vasomotor symptoms, and groups who were stopped using progesterone to reduce vasomotor symptoms.	The sample was divided into two groups, vasomotor symptoms randomly selected 29 given progesterone and 17 no. While the group stopped taking HT 17 who Used progesterone and 17 placebo.	This study shows that progesterone effectively treats all cohorts, is also effective for severe vasomotor symptoms. And stopping the use of progesterone can significantly improve vasomotor symptoms.
4	Hot flushes, hormone therapy and alternative treatments: 30 years of experience from Sweden./ L. Lindh- Å strand, et al/2014/	Swedia	To describe the use of hormone therapy and alternative medicine also to study the frequency of hot flushes.	Cross Sectional	The questionnaire was distributed randomly to 2000 women as a result compared to previous studies related to the use of hormone therapy.	2000 women aged 47-56 years living in Ostergotland Country, Sweden.	Women in this study appeared to be more susceptible to using herbal medicines, dietary supplements and alternative treatments than using HT but women with severe vasomotor complaints stated that they would be more likely to use hormone therapy.
5	Menopausal symptom experience before and after stopping estrogen therapy in the Women's Health Initiative randomized, placebo-controlled trial, et al/2010/		To find out vasomotor symptoms and other menopausal symptoms, from before starting estrogen therapy also placebo, 1 year later the therapy was stopped and a reassessment was carried out.	RCT	The study began with an initial assessment before the use of estrogen therapy and non-therapy regarding menopausal symptoms, a reassessment was conducted 1 year later to find out menopausal symptoms after the use of hormone therapy was stopped.	Analysis was carried out on 10,739 postmenopausal women before estrogen and placebo use and 1 year later 3,496 women completed the symptom survey.	The use of estrogen therapy significantly reduces vasomotor symptoms and vaginal dryness in women with early symptoms. And symptoms significantly increase after stopping estrogen therapy compared to non-treatment.

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6	Effect esofestrogen and venlafaxineon menopause-related quality of life in healthy postmenopausal women with hot flashes: a placebo controlled randomized trial./ Bette Caan, et al/ 2014	Californi a	To evaluate the effects of RCT low doses of estradiol (E2) or venlafaxine related to quality of life and associated symptoms in healthy premenopausal and postmenopausal women with hot flashes.		Participants completed the questionnaire at the beginning, 4 weeks and 8 weeks, and recorded menopausal symptoms as well as the pattern of vaginal bleeding in the diary every day for 3 weeks before randomization and during the 8- week trial.	339 women, including female African-American women (34.2%). The average age of the study participants was	Effect esofestrogen and venlafaxineon menopause-related quality of life in healthy postmenopausal women with hot flashes: a placebo controlled randomized trial./ Bette Caan, et al/ 2014
7	Vasomotor symptoms usually reappear after cessation of postmenopausal hormone therapy: a Swedish populationYbased study./ Lotta Lindh-A°strand, et al/2009/	Swedia	To find out the extent to which vasomotor symptoms reappear after the cessation of postmenopausal hormone therapy in women who start HT because of hot flashes	Cross Sectional	Using a questionnaire about the attitudes and knowledge of menopausal women and HT data, the incidence of vasomotor symptoms before HT begins, there are vasomotor symptoms, reasons for stopping HT, and others.	The questionnaire was given to 1722 women aged 53 and 54 years.	Most women who have vasomotor symptoms when they start HT report recurrence of symptoms after HT discontinuation (87%), although fewer than usual are reported to be less frequent and disturbing than those before HT.
8	Effects of botanicals and combined hormone therapy on cognition in postmenopausal women./ Pauline M. Maki, et al/2009/	Cicago	To characterize the effects of red clover, black cohosh, and a combination of hormone therapy on cognitive function compared to placebo in women with moderate to severe vasomotor symptoms.	RCT	66 middle-aged women (average age, 53 years), with 35 weeks or more hot flash randomly to receive red clover, black cohosh, estrogen and placebo. Participants complete measurements of other verbal and cognitive memories.	89 women were enrolled in a randomized clinical trial comparing the effects of black cohosh, red clover, and menopausal symptoms in comparison to placebo.	The results show that red clover (phytoestrogen) or black cohosh supplements do not have an effect on cognitive function. CEE / MPA reduces objective hot flash but worsens some aspects of verbal memory.

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9	Vasomotor and sexual symptoms in older Australian women: a cross-sectional study./ Berihun M. Zeleke, et al/2015/	Australia	To determine the prevalence and severity of vasomotor symptoms (VMS) and sexual symptoms in people living in older women, and to explore factors related to vasomotor symptoms.	Cross	The sample was asked to give permission to be contacted by telephone for clarification of important data. All items begin with a yes or no question about the presence of these symptoms over the past 4 weeks.	1,548 women aged 65-79 years.	The factors that were significantly associated with VMS were age, obesity, being a caregiver for others, and bilateral oophorectomy.
10	The use of complementary and alternative medicine by women transitioning through menopause in Germany: Results of a survey of women aged 45—60 years./ K.J. Buhling, et al/ 2013/Q1	German	To describe the prevalence of complementary and alternative medicine (CAM) therapy to eliminate complaints of menopause among German women.	RCT	The questionnaire was sent to 9785 randomly selected women in Germany between the ages of 45 and 60 years.	9785 women aged 45-60 years.	CAM interventions to alleviate menopausal complaints are popular among German women. Respondents reported using CAM either alone or in combination with HRT.

### 3. RESULT AND DISCUSSION

#### Symptoms felt by menopausal women

Research conducted by L. Lindh-Astrand “*Hot flushes, hormone therapy and alternative treatments: 30 years of experience from Sweden.*” From that research in Sweden 70% of women experience hot flushes and one from three of them are interested in using hormonal therapy in their use can reduce these symptoms. (L. Lindh-Astrand, 2014) Research conducted in Buhling, 2013 “*The use of complementary and alternative medicine by women transitioning through menopause in Germany: Results of a survey of women aged 45-60 years.*” from 1.517 of women respondents that experience menopause symptoms, the highest reported were vasomotor symptoms for 71,2%, sleep disorder for 68,5%, easily get emotional for 62,7% and mental fatigue, symptoms that less experienced is bleeding for 42,7%. This research is in line with research conducted by Berihun in 2015, “*Vasomotor and sexual symptoms in older Australian women: a cross- sectional study.*” shows that almost 90% or more menopause women experience vasomotor or urogenital symptoms.

#### a. Vasomotor Symptoms

Amounted 1.452 samples show 1.442 experience *hot flush*, 1.443 experience *night sweats*, and 1.434 experience *sweating*.

#### b. Urogenital symptoms

Amounted 1.362 samples for sexual domain found 1.309 women experience changes in sexual desire, *vaginal dryness* 1.244, and 1.244 that avoids intimacy. (Berihun, 2015)

From all those symptoms not less that affect life quality.

#### Factors that Affect Menopause Symptoms

#### a. Ethnicity

Ethnicity is a significant determinant of women experiencing hot flush. In Europe, natives experience more hot flush compared to migrants ( $p = 0.002$ ), from the study “*Hot flushes and reproductive hormone levels during the menopausal transition.*” many of these are from groups of European ethnic. (Tanveer Dhanoya, 2016.)

#### b. Previous Medical History

Research conducted in Australia “*Vasomotor and sexual symptoms in older Australian women: a cross- sectional study.*” Factors that affect menopause symptom according to Berihun, BMI ( $p=0,07$ ), *bilateral oophorectomy* ( $p=0,68$ ), cancer history ( $p=0,002$ ). (Berihun, 2015)

#### Effect of hormone therapy towards menopause women related to menopause symptom

Piret Veerus in the research “*The Effect of hormone therapy on women’s quality of life in the first year of the Estonian Postmenopausal Hormone Therapy trial.*” shows the effectiveness of hormone therapy in Estonia for menopause women, women that given estrogen and medroxyprogesterone experience changes in menopause symptoms like *sweating* ( $p=0,001$ ), sleep disorder ( $p<0,001$ ), *sore throat* ( $p=0,096$ ), and *hot flushes* ( $<0,001$ ). (Piret Veerus, 2012).

Research of “*Effects of estrogen and venlafaxine on menopause-related quality of life in healthy postmenopausal women with hot flashes: a placebo-controlled randomized trial.*” Conducted by Bette Caan, comparing the use of estrogen and venlafaxine, from the research shows that both have effect and can help to reduce menopausal symptoms, estrogen ( $p=0.001$ ),

venlafaxine ( $p=0.042$ ) even though the use of venlafaxine for improving the life quality for menopausal women does not seem influential in this research. (Bette Caan, 2015)

Robert L Brunner, his finding in *“Menopausal symptom experience before and after stopping estrogen therapy in the Women’s Health Initiative randomized, placebo controlled trial.”* Found that women who started using hormone therapy, after the discontinuation of therapy then compared to those who had not previously used hormone therapy showed an increase in menopausal symptoms ( $p<0,001$ ). (Robert. L, 2010). This research shows the same result with research conducted by Jerilynn *“Progesterone for hot flush and night sweat treatment-effectiveness for severe vasomotor symptoms and lack of withdrawal rebound.”* in 2012, discontinuation of the use of hormone therapy also affects menopausal symptoms suggesting that women who previously used hormone therapy can experience significant menopausal symptoms increase compared to before, from 40% to 78% compared to women who were previously given a placebo there is no significant increase. (Jerilynn C, 2012.)

In the research conducted by Pauline M *“Effects of botanicals and combined hormone therapy on cognition in postmenopausal women.”* None of botany treatment has an impact on cognitive size. Compared to placebo, CEE / MPA causes a bigger reduction ( $P = 0,057$ ) in the analysis that was not adjusted but achieve significance ( $P = 0.02$ ) after adjusted to vasomotor symptoms. None of the botanical treatments showed changes in verbal memory that different from the placebo group ( $Ps9\ 0.28$ ), even after hot flash is reduced. In the secondary results, CEE / MPA causes a decrease in recall and an increase in letter fluency. Only CEE / MPA significantly reduces objective hot flash. (Pauline M, 2009)

From 242 of hormon therapy users in the research *“Vasomotor symptoms usually reapper after discontinuation of postmenopausal hormone therapy: Swedish population-based study.”*, 165 (69%) women state that they have vasomotor symptoms before starting HT. Vasomotor symptoms recur after HT discontinuation in 143 (87%) from these 165 women. (Lotta Lindh, 2009)

Research conducted by Lucy Abraham *“Menopause-specific quality of life across varying menopausal populations with conjugated estrogens/bazedoxifene.”* found a significant improvement in menopausal symptoms compared with placebo that found with CE / BZA doses in the vasomotor MENQOL domain ( $-0.61$  to  $-2.23$  for 3-24 months) and total scores ( $-0.24$  to  $-0.94$ ) in VMS / VVA population is general and symptomatic. (Lucy Abraham 2014.)

Vasomotor instability that occurs in menopausal women is a result of decreased estrogen levels which can have a negative impact on quality of life and is often the main symptom of menopause that causes women to find treatment (Avisetal., 2009; Burleson, Todd, & Trevathan, 2010; Hesselal., 2012). Menopause-specific Quality of Life (MENQOL) according to Abraham, is divided into some symptoms:

- 1) *Vasomotor Functioning*
- 2) *Psychosocial functiong*
- 3) *Physical function*
- 4) *Sexual function*

Vasomotor symptoms are symptoms with the highest prevalence that mostly experienced by menopausal women. *Hot flush, night sweating and sweats* symptoms with a significant percentage compared to other menopausal symptoms. Many factors influence the occurrence of menopause, one of which is ethnic or culture. European and American women have more estrogen than Asian women. When menopause occurs, estrogen in European and American women decreases



dramatically compared to Asian women with moderate estrogen levels. The decrease in estrogen levels often causes symptoms that greatly disrupt the life activities of women (Sholichah & Anjarwati.).

In addition, the health problems that occur in menopausal women because of the lack of estrogen hormone, the treatment is also by giving estrogen replacement hormones, known as Estrogen Replacement Therapy or Estrogen Replacement Therapy (ERT). Because administration of estrogen is usually combined with the giving of hormone progesterone, it is known as Hormone Replacement Therapy (TPH) or Hormone Replacement Therapy (TSH) or Hormone Replacement Therapy (HRT).

The use of hormone therapy has a clear effect in relieving vasomotor and urogenital complaints related to menopause. Estrogen in TSH can relieve those complaints, even better than the use of antidepressant and phytoestrogen.

#### 4. CONCLUSION

According to the *systematic literature review*, it was concluded that vasomotor symptom, urogenital symptom, and sexual dysfunction are menopausal symptoms that experienced by many women before, at menopause, or after menopause. Some factors that influence menopausal symptoms are culture or ethnicity also medical history such as cancer history, and *IMT/BMI*. Hormone therapy is a therapy that is quite effective in handling with menopausal symptoms. The use of hormone therapy can cause a significant increase in menopausal symptoms that are quite severe, meaning that hormone therapy has a significant contribution to the life quality of menopausal women. Thus, hormone therapy can improve the life quality of women in their menopause phase.

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