

## EDITORIAL

1. Editor, The Peruvian Journal of Gynecology and Obstetrics. ORCID iD: <https://orcid.org/0000-0002-3168-6717>. Scopus Author ID: 34971781600

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**Correspondence:**

✉ [jpachecoperu@yahoo.com](mailto:jpachecoperu@yahoo.com)

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# New guidelines, and a new hypertensive population

## How to select women for menopausal hormone therapy

José Pacheco-Romero, MD, PhD; MSc, FACOG<sup>1</sup>

The 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults published in November 2017<sup>(1)</sup> designates new categories of blood pressure in adults: Normal <120/<80 mmHg, Elevated Blood Pressure 120-129/<80 mm Hg, stage 1 Hypertension 130-139/80-89 mm Hg, stage 2 Hypertension >140/>90 mm Hg.

A previous report based on blood pressure readings in 19.1 million adults pooled from 1 479 studies found that the global age-standardized prevalence of raised blood pressure was 24.1% (21.4–27.1) in men and 20.1% (17.8–22.5) in women in 2015<sup>(2)</sup>. The Peruvian Tornasol II study on Risk Factors for Cardiovascular Diseases reported in 2011 a prevalence of 27.3% for arterial hypertension<sup>(3)</sup>, showing an increase compared to the previous value of 23.7% in 2006<sup>(4)</sup>.

We still do not know how these new BP values will influence the diagnosis of preeclampsia. There are no academic pronouncements yet. This has motivated a letter to the Editor that we publish in this issue. The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure recommended in 2003 that subjects with a systolic blood pressure of 120-139 mmHg or a diastolic blood pressure of 80-89 mmHg should be considered prehypertensive and would require lifestyle modifications in order to prevent cardiovascular disease<sup>(5)</sup>. Patients with prehypertension are at high risk of progressing to hypertension. In November 2013, the new guidelines of hypertension in pregnancy published by the Task Force of Hypertension in Pregnancy and the American College of Obstetricians and Gynecologists – ACOG concluded that preeclampsia can be diagnosed even in the absence of proteinuria. In this case, preeclampsia diagnosis is considered when hypertension is associated with low platelets, altered liver function, renal failure, pulmonary edema or appearance of cerebral or visual disturbances in the pregnant woman<sup>(6)</sup>.

The Editors of The Peruvian Journal in Gynecology and Obstetrics have found it appropriate to publish a symposium on the new categories of blood pressure in adults, where specialists will express their points of view.

The Peruvian Journal of Gynecology and Obstetrics presents in this issue the symposium “Therapeutic Management of the Climacteric and Menopause, Recent Evidences”. There is still confusion among doctors and patients regarding the benefits and risks of hormonal replacement therapy in the menopause, as a result of the findings of the Women’s Health Initiative study<sup>(7)</sup>. New revisions of the WHI study and further clinical experience seem to be settling the issue, as presented in the symposium.



The North American Menopause Society 2017 Position Statement presents hormone therapy (HT) as the most effective treatment for vasomotor symptoms (VMS) and the genitourinary syndrome of menopause (GSM). HT has also been shown to prevent bone loss and fracture<sup>(8)</sup>. Treatment should be individualized to identify the most appropriate HT type, dose, formulation, route of administration, and treatment time, using the best available evidence to maximize benefits and minimize risks, with periodic reevaluation of the benefits and risks of continuing or discontinuing HT.

In Latin America, menopause has been found to occur at age 49.4 + 5.5<sup>(9)</sup>, about one year later than in Peruvian women<sup>(10)</sup>. In both studies, high altitude would reduce the age of menopause. In a study of immigrants in Madrid, the median estimated age at natural menopause was 52.0 years (51.2–53.0) for Spanish women and 50.5 years (49.9–51.2) for immigrant Latin-American women<sup>(11)</sup>. In the Tracking cohort of the Canadian Longitudinal Study of Aging, which included 7 719 women aged 40 or more, the median age at natural menopause (ANM) was 51 years. Having no partner, having a low household income and low education levels, being a current and former smoker, and having cardiovascular disease were all associated with an earlier ANM. Meanwhile, current employment, alcohol consumption, and obesity were associated with a later ANM<sup>(12)</sup>. This means other factors aside from age, genetics and hormones are associated with early or late menopause.

A bidirectional association between vasomotor symptoms and depressive symptoms has been reported in sixteen articles involving a total of 10 008 participants, obtained from a search in multiple databases from 1961 until July 31, 2016, and a manual search of reference lists of identified articles<sup>(13)</sup>. In a sample of Spanish elderly people, the prevalence of depressive symptoms was 19.7%<sup>(14)</sup>. In European populations, the prevalence of depressive disorder in people older than 65 years was 12.3%, ranging from 8.8% in Iceland to 23.6% in Munich, based on multicenter studies (9 health centers) that used the Geriatric Mental Scale (GMS) AGE-CAT<sup>(15)</sup>. In Japan, 13% of subjects aged 65 years or more fulfilled the criteria for depression symptoms<sup>(16)</sup>. In Lima, Peru, 62.1% of institutionalized older

adults showed depression symptoms<sup>(17)</sup>. In Callao, Peru, the prevalence of depression in older adults detected in a psychiatric clinic was 9.37% and increased to 43% in patients with diabetes mellitus<sup>(18)</sup>. The study in the Peruvian Andes found differences in the prevalence rates of depression in both quechua and not quechua population groups (17.6% vs. 15.6%)<sup>(19)</sup>. The North American Menopause Society considers that women who had a severe form of premenstrual syndrome in their youth may have more severe mood swings during perimenopause. Also, women with a history of clinical depression seem to be particularly vulnerable to recurrent clinical depression during menopause<sup>(20)</sup>. Thus, it is important to check for depression symptoms in menopausal women presenting with neurovegetative symptoms, in order to refer them to the specialist before any menopausal treatment.

The WHI study focused on strategies to reduce heart disease, breast and colorectal cancer, and fractures in postmenopausal women<sup>(7)</sup>. The beneficial role of estrogen in the vascular system may be due, in part, to a reduction in peripheral vascular resistance. In menopausal women with endothelial dysfunction, menopausal transition is associated with increased carotid arterial stiffness and epicardial fat thickness, independent of age<sup>(21)</sup>. Therefore, arterial ageing is a prominent factor that reduces the vasodilating action of estrogenic compounds<sup>(22)</sup>. But which comes first, the estrogenic deprivation or the arterial stiffness? Emerging research suggests the importance of arterial stiffness already in pediatric populations<sup>(23)</sup>. This arterial stiffness is reportedly greater in children/adolescents with obesity compared with controls<sup>(24)</sup>. Epicardial fat thickness is linked to obesity, carotid subclinical atherosclerosis, and cardiac geometry parameters, and may be a useful tool for cardiovascular risk stratification in children and adolescents<sup>(25)</sup>. Consequently, atherosclerosis in women may start at an early age or early adulthood and not necessarily only in the adult and at menopause. This would be the case for women with obesity, history of intrauterine fetal growth, preterm birth, kidney disease, or born to mothers with preeclampsia. These confounders are not considered in the studies of menopause and decisions for estrogen therapy.



Regarding osteoporosis and exercise, individuals with greater cognitive ability in early life are more likely to engage in healthy behaviors (e.g., leisure time physical activity) in adulthood, which in turn are associated with greater bone mass density later in life<sup>(26)</sup>. Strategies like physical exercise, vitamin D, and calcium intake had limited effect when used as single interventions; furthermore, vitamin D and calcium may potentially cause an increase in cardiovascular events<sup>(27)</sup>.

With respect to the association of nutrition and longer life expectancy, improved diet quality was consistently associated with a decreased risk of death among 47 994 women in the Nurses' Health Study and 25 745 men in the Health Professionals Follow-up Study from 1998 through 2010<sup>(28)</sup>. Among 0.5 million Chinese women aged 30 to 79 years from 10 diverse regions across China, history of breastfeeding was associated with a 10% lower risk of cardiovascular disease in later life; this association was stronger among those with a longer duration of breastfeeding<sup>(29)</sup>. In another study of 1.93 million adults without cardiovascular disease at baseline, light to moderate alcohol use was associated with a reduced risk of death compared to no alcohol consumption at all. Heavy drinking may increase the risk of death<sup>(30)</sup>. Weight gain accompanied by an increased tendency for central fat distribution is common among women in midlife. Central obesity results in several adverse metabolic consequences, including dysglycemia, dyslipidemia, hypertension and cardiovascular disease, cancer, arthritis, mood disorders, and sexual dysfunction. Despite its favorable influence on body fat distribution, menopausal hormone therapy cannot be recommended as a treatment for central obesity in middle-aged women<sup>(31)</sup>. In summary, healthy nutrition across the lifespan, exercise, avoidance of central obesity, breastfeeding, and moderate alcohol use seem to be associated with a longer life expectancy. Menopausal hormone therapy is not recommended as a treatment for central obesity.

Tibolone is considered an alternative to estrogens in hormone menopause therapy. A study of more than 900 000 Danish women aged 50 to 79, followed for 9.8 years on average, reported that 4 513 were diagnosed with ovarian cancer and 6 202 with endometrial cancer, in particular serous ovarian tumors and type 1

endometrial cancer. Because the associations are stronger with increasing durations of use, and for hormone-sensitive tumors, the results seem indicative of causality<sup>(32)</sup>. This finding should be considered when we choose to use tibolone for estrogen substitution.

To conclude, our suggestion is that before indicating HRT to a menopausal woman, we should determine her present and past physical and mental status, her medical history, and put in the balance what will be gained from estrogen administration. The NAMS recommendations must be taken into account. It is possible that this therapy will become more convenient when the pharmaceutical laboratories obtain an estrogenic product that more closely resembles natural human estrogen.

José C. Pacheco-Romero, MD, PhD, MSc, FACOG  
Editor

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