Communication

Not peer-reviewed version

# Do Not Fear When Menopause Is Near: The Importance of a Preparatory Time and Space to Face the Consequences before Reaching the Menopause

Manosha Perera * and Irosha Perera

Posted Date: 8 May 2023

doi: 10.20944/preprints202305.0435.v1

Keywords: Omega; Alpha; Menarche; Menopause; Reproductive Health; Preparatory Time

*Communication*

# Do not Fear When Menopause Is Near: The Importance of a Preparatory Time and Space to Face the Consequences before Reaching the Menopause

**Manosha Lakmali Perera [1,*,†] and Irosha Rukmali Perera [2]**

[1] Menzies Health Institute Queensland Australia (Alumnus)
[2] Preventive Oral Health Unit, The National Dental Hospital (Teaching), Colombo, Sri Lanka; Irosha_rukmali@yahoo.com
* Correspondence: manosha_lakmali@yahoo.com

**Abstract:** As a result of scientific technological advancements in medical diagnostics, treatment modalities of non-communicable and communicable diseases, and palliative care approaches, the life expectancy of women is soaring than men across the globe, due to the longer telomere length and other protective factors. The main symptoms of menopause broadly be divided into psychological somatovegetative and urogenital. Neglected menopausal symptoms can lead to debilitating comorbidities which may end up in mortalities. Fortunately, modern treatment and therapeutic formalities based on pharmaceutical preparations, as well as lifestyle-modifications have provided long-lasting relief for the pre-menopausal woman. This can be done as per her preference if she is knowledgeable, resourceful, and cheerful. Menarchae is the " alpha" and menopause is the "omega" phase in the reproductive lifecycle of any woman. Reproductive health is essentially an integral part of women's health. In this 4th industial revolution era information technology and digital science go hand in hand to improve the quality of life of populations across the globe irrespective of their educational and professional status. Health literacy among disadvantageous sub populations increased. Positive attitudes, perception and evidence-informed knowledge on adolesecent girls about not only 'period pains' but menopausal symptoms as an inevitable phase in a woman's reproductive health may make a better sense at the dawn of evidence based medicine even in a low middle income country like Sri Lanka. Hence, this timely communication strengthens by, **Do not fear when menopause is near: The Importance of a Preparatory Time and Space to face the consequences of Menopaus. How to forget the fact that *alpha* and the *omega* are inevitable phases in woman's reproductive health trajectory. Moreover,** the importance of a preparatory time and space well in advance preferably in peri-menopausal time to prevent and control the inevitable health consequences. Moreover, to invest in menopause for a brighter future in the modern personalized medicine era based on global scientific evidence.

**Keywords:** omega; alpha; menarche; menopause; reproductive health; preparatory time

## Introduction

The whole world shrunken into one socio-ecological niche [1] due to the advances in information technology, digital transformation, and the commonality in the basic needs of *Homo sapiens* originated from the *Eve* and *Adam* of the garden of *Eden* as the first and foremost ancestors according to the Holy Bible [2] or evolved according to Darwin's theory [3] in the lithosphere which divided into seven continents based on the plate tectonics [4]. The women undergo two milestones in their reproductive life cycle: the *menarche* and the *menopause* consider 'alpha' and 'omega' respectively [5]. The life course of *oocytes* in a girl starts in the uterus in *oogenesis*, at the first phase of the embryo-foetal life [8]. Whilst the event of *menarch* reveals the onset of the release of a viable oocyte from the ovary termed *ovulation,* followed by monthly periods defined as *menorrhea* [5]. Endocrine health interconnects with the reproductive health through the molecular mechanisms in endocrinology [5.8]. The endocrine axes (prolactin, thyroid, and adrenal) govern the events in the menstruation cycle of a woman [9] thus, feedback mechanisms play a central role, not only in normal physiological but also in psychological functions. The timing of these two milestones is inevitably crucial for a woman's health trajectory

 doi:10.20944/preprints202305.0435.v1



throughout her life span [5]. The global mean age at menarche ranges from 13 to 16 years old in the current generation [10,11]. However, many prepubertal girls reach menarche at the age of 12 years [10,11]. Menopause is the permanent cessation of menstruation resulting in the loss of ovarian follicle development and fluctuation of sex hormones especially estrogen in the climacteric and perimenopausal period. The 'omega' phase confirms physiologically by the 12-month amenorrhea phase not associated with pathological causes or the use of hormonal contraception [12].The median global age of menopause varies from 42.1 to 53.0 yrs [13]. Nevertheless, reproduction is possible for women in their early fifties with satisfactory general health if they prevented ovulation by taking oral contraceptives as a primordial preventive measure against unplanned fertilizations. Early and late timing of menopause as well as menarch of the reproductive attributed to behavioural and health risks [5] especially in high risk populations due to marked health inquallities, inequities and disparities. The menarche and menopause ages display individuality and population specificity [7] depending on the hereditary and exposures to environmental factors across the life course [5,6]. Hence, hormonal exposures [14], greater maternal weight gain, lack of physical excises and gestational diabetes [15], breastfeeding [16], obesity, smoked tobacco use, secondhand smoke exposure, and socioeconomic status (SES) appeared as pre disposing or risk factors associated with the timing of menarche and menopause in several epidemiological studies based on women's reproductive health. It has been hypothesized that the genetic variants in, for example, Bcl-2 and Bax; epigenetic alterations, including DNA methylation and histone modifications influence the selective survival of oocytes over the lifecurse [5]. Furthermore, psychological stress has been hypothesized to accelerate the onset of menarche [17] and childhood stress has been assumed to decrease the age of menopause because of a higher rate of follicular atresia [18]. However, these hypotheses and assumptions need to confirm by longitudinal studies with large sample sizes controlling for confounders carefully. Moreover, the association between age at menarche and age at menopause seems vague and inconclusive thus, further research work is much warranted [5].

The life expectancy of global women soars more than men [19] due to longer telomere and several other protective factors [20]. The burden of menopausal syndrome is mainly due to the bothersome and embarrassing vasomotor symptoms, problems related to changes in urogenital epithelium, and those impaired cognitive functions [19,20]. Healthy lifestyle modifications with the body and mind concept pave the way for a perimenopausal woman to invest in a brighter menopausal future if the woman prepares for it well in advance. In this light, the current review emphasizes the importance of a preparatory time and space to become knowledgeable and resourceful in the prevention and control of menopausal health consequences which make a negative impact on the quality of life (QOL) of a post-menopausal woman whether a Professor Emeritus or non-schooling great granny irrespective of their anthropological data and socio-demographic profiles.

**Health consequences and distressing symptoms associated with the menopause**

By 2050, the world's women aged 50 years and older will project a total of 1.6 billion, up from 1 billion in 2020 [22]. Furthermore, about 1.2 billion universal women will be non-reproductive in the menopausal and postmenopausal stages in 2030, with 47 million new entrants each year [23]. The menopausal age of Sri Lankan women varies between 49 and 51 years [24,25]. Moreover, the perimenopause period ranges from 2-8 yrs before commencing the menopause [26,27]. Distressing symptoms associated with menopause broadly be divided into physical, physiological, and psychological entities [28]. Perhaps, the most common climacteric physiological symptoms in around 75% of global women are vasomotor symptoms (VMS), including hot flushes or flashes, night sweats, and insomnia or sleep disturbance [28]. Among them, insomnia aggravates neurological symptoms and behavioral disorders. Whereas, psychological symptoms comprise memory loss, irritability, poor concentration, and loss of confidence [28]. In contrast, genitourinary syndrome of menopause (GSM), palpitations, headaches, bone/joint/muscle pain, asthenia, tiredness, breast tenderness, skin thinning, and scanty hair consider as physical symptoms associated with menopausal syndrome [28]. Moreover, GSM with changes in the bladder, vulva, and vagina due to vulvovaginal atrophy affects almost half of postmenopausal women. Symptoms of vaginal dryness, vaginal irritation, itching

 doi:10.20944/preprints202305.0435.v1



elasticity, dyspareunia, urinary urgency, dysuria, and recurrent urinary tract infections will deteriorate with time from the menopausal transition if left untreated [28]. Osteoporosis, heart disease, diabetes, obesity, osteoarthritis, and cognitive decline are other diseases associated with untreated menopausal syndrome [28]. In 2019, Rathnayake and colleagues [26] evaluated pre and post-menopausal symptoms using the menopause rating scale under three subscales: psychological symptoms, somatovegetative symptoms, and urogenital symptoms in women aged 30-60 yrs in the Galle district, Sri Lanka [26]. The mean (SD) ages of pre and postmenopausal women were 46.1(3.7) and 55.8(3.8) respectively. Accordingly, in premenopausal women, the most frequently reported menopausal symptoms were mental exhaustion (49.5%), joint and muscular discomforts (48.5%), and irritability (41.3%) [26]. However, physical and mental exhaustion (53%), irritability (48.2%), depressive mood (43.4%), and hot fushes (42.2%) were most frequently reported in the postmenopausal women [26].

The skin is the largest target organ of estrogens, androgens, and cortisol hormones. Unfortunately, the skin and hair with noticeable menopausal effects often receive less attention than other menopausal symptoms. Dryness and pruritus, thinning and atrophy, pigmentation, wrinkles and sagging, poor wound healing, and reduced vascularity consider common mucosal and skin menopausal symptoms. Moreover the menopausal symptoms affecting hair include scanty hair growth, diffuse effluvium due to follicular rarefication and/or androgenetic alopecia altered hair quality and structure, and increased unwanted hair growth on facial areas [28]. This array of menopausal symptoms, especially the vasomotor and sexual symptoms, are associated with poor quality of sexual life (QOL) in married women [29,30]. About 80% of women experience cessation of severe menopausal symptoms after 5 yrs of confirmation of menopause or continuing further as mild symptoms. Nevertheless, 20% of menopausal women may have symptoms for up to 10 years or longer [26]. Health economic wise, the neglected perimenopausal symptoms could affect the gross domestic production (GDP) negatively, though nobody has surveyed it so far.

**Menopausal hormone therapy (MHT) or Hormone replacement therapy (HRT)**

There have been many speculations about the symptoms that appear before (climacteric and perimenopausal), during (menopausal), and, after the onset of menopause (early post-menopausal) in the reproductive life cycle of a woman [32,33]. Women typically begin the shift from a reproductive state to a non-reproductive state of complete termination of ovulation due to the depletion of ova during their mid-to-late 40s while, declining of the sex hormones estrogen, androgens, and glucocorticoids [32–35]. Traveling, and engaging in recreational activities are common among English-speaking pensionable menopausal Sri Lankan ladies who represent an elite cohort of Sri Lankan women equated with their Western counterparts in developed countries with good QOL. The major consequences of menopause are related primarily to estrogen and progesterone deficiency [32–36]. The destructive menopausal syndrome negatively affects the QOL of menopausal women and is easily treatable by an artificial supply of deficient hormones as medication. This notion justifies the need and the basic principle of Menopausal hormone therapy (MHT) or Hormone replacement therapy (HRT) [36–40]. It is the most effective pharmacological treatment modality in Western Medicine and abides by the state of the art of internationally accepted post-reproductive health guidelines to reduce bothersome issues of vasomotor symptoms and cognitive dysfunction in perimenopausal, menopausal, and post-menopausal women. The hormone therapy (HT), oral and transdermal administration of estrogen-progestin and estrogen-alone hormone therapy (HT) [37] conditionally to the past medical history (PMH) or risk profile and individual preference is widely recommended at present [36,37]. Temporal administration in appropriate doses is beneficial not only for the protective effects against cardiovascular diseases but also for bone loss [36] which may end up as a hip fracture due to a domestic fall in a post-menopausal lady who is in her late seventies. Promising new data on the direct effect of estradiol on the arterial wall and recent serum lipid results obtained during percutaneous administration of estradiol in postmenopausal women concluded that similar outcomes of cardioprotection could be obtained from both peroral and percutaneous administration [36].

 doi:10.20944/preprints202305.0435.v1



**Complementary and alternative medicine (CAM) for menopausal women**

Menopausal hormone therapy (MHT) or Hormone replacement therapy (HRT) is not suitable for each woman as there is an increased risk of stroke, venous thromboembolism, gallbladder disease, and breast and ovarian cancer [41–43]. This situation essentially guided the scientific community of native physicians and mind therapists to fndout alternative and complementary answers respectively to treat menopausal women suffering from the menopausal syndrome. As a result, CAM re-emerged as a better option with modern medical technological advancements for menopausal sufferers on all continents. Nearly 51% of women in the recent past stood on CAM. Furthermore, about 60% perceive it as better than HRT for menopausal symptoms [41]. Antidepressants and psychoactive agents effective as non-hormonal alternatives for vasomotor symptoms [44,45] in menopausal women who are also hormone-dependent cancer survivors. Moreover, Gabapentin and pregabalin are anticonvulsant drugs capable of decreasing the frequency of HFs by binding to calcium channels in the hypothalamus and, accordingly, better modulating thermoregulatory activity [46]. Selective serotonin reuptake inhibitors (SSRIs) and selective serotonin-norepinephrine reuptake inhibitors (SNRIs) are two examples of antidepressants [46–48] to treat vasomotor symptoms. The USA used them for a shorter period to relieve bothersome and embarrassing vasomotor symptoms. In 2012, Aidelsburger and colleagues assessed the efficacy and the cost-effectiveness of alternative methods for women with post-menopausal symptoms in Germany. However, they did not conclude their findings by making recommendations due to the lack of published medical literature. [48].

Women (irrespective of their stage of the reproductive health) make up half of the global workforce [19,49]. Professional never married women in administrative and technical positions prioritize their carrier life than the personal life [19] even with their bothersome and embarrassing menopausal symptoms. The menopausal syndrome should not retard the efficiency not only of a school teacher or a University Lecturer in her carrier routine but also the duty of a grandma to take care of grandchildren letting her daughter or daughter in law to remain in the workforce after due full pay, half pay and no-pay maternity leave in the government service of Sri Lanka. In this situation, complementary and alternative medicine (CAM) may provide a better option for Sri Lankan women who also make up approximately 80% of global menopausal women who suffer from the menopausal syndrome. CAM centers on the physical, physiological, and spiritual well-being of a woman. According to Johnson et al [49], CAM interventions for menopausal syndrome be broadly divided into two categories:

Mind body practices:

1.1 Hypnosis, cognitive behavioral therapy [CBT], relaxation, biofeedback and relaxation training , Mindfulness-Based Stress Reduction (MBSR) and yoga [49].

1.2 Aromatherapy, Herbal Products, Vitamins, and Supplements : Black Cohosh (Cimicifuga racemosa), Wild Yam (Diascorea), Dong Quai (Angelica sinensis), Maca (Lepidium meyenii), Pollen Extract, Evening Primrose Oil (Oenothera biennis), Phytoestrogens and Vitamin E [49].

1 Whole System Alternative Medicinal Approache: Reflexology, Homeopathy, Acupuncture and Traditional Chinese and East Asian Medicine [49].

Essentially, post-reproductive health is an integral part of women's health. Intregating and implementing complementary and alternative medicine (CAM) in women's health gidelines and protocols locally, regionally and internationally may be challenging. Considerable progress in reducing maternal and perinatal mortality and morbidity was an achieving goal even in a low-middle income country (LMIC) like Sri Lanka. The same success would be achieved in menopausal medicine to improve the QOL for ordinary women who also victims of treatable menopausal syndrome. CAM generate new concepts on well being of menopausal women depending on their compliance with treatment options, if they are knowledgable. It seems the Well Woman Clinics (WWC) established in Sri Lanka in 1996 based on CAM concept [19]. At present, there are about 1,000 clinic centres across the island. In addition to life style modifications and habit interventions, WWC- screens women aged 35 and 45 years for specific non communicable diseases, common female cancers and post

 doi:10.20944/preprints202305.0435.v1



reproductive health issues including menopause [19]. At the WWC, women of 35 and 45 years of age are made aware of symptoms of menopause. Whenever necessary, women that attend WWC with menopausal symptoms are referred for specialized services [19]. Lifestyle modifications highlight the importance of a plant-based diet, refraining from poly saturated fatty acids. Habit intervention in regular physical and intellectual activities prevents non-communicable diseases in menopausal women with obesity, a sedentary lifestyle, depression, and lack of coping skills due to life course risk factors [49,50].

In the modern era of evidence-based medicine, Community Physicians specialized in Reproductive Health, Native Physicians, Neutotinists, Beauty and Mind therapists and Fitness instructors opened up a multidisciplinary approach to treating menopausal women. This approach widens the horizons of the existing knowledge of the health benefits of vegan and Mediterranean food habits [49,50]. The role of phytoestrogen as a harmless natural substitute for the lack of oestrogen in menopausal women is noteworthy to mention. Whole soybean is a classical example of a phytoestrogen-rich member of the family Leguminosae. Perhaps, antioxidants, micronutrients, phytoestrogen, and fibers riched plant-based diets, and fermented food ease troublesome menopausal symptoms [50]. In a randomized controlled trial, the combination of a low-fat vegan diet and whole soybeans was associated with reduced frequency and severity of hot flashes and improved quality of life in vasomotor, psychosocial, physical, and sexual domains in postmenopausal women [50]. During the 12-week study period, the majority of intervention-group participants became free of moderate-to-severe hot flashes. [50].

**The Importance of a preparatory time and space in prevention and management of menopausal syndrome at least 10 yrs ahead of alpha**

An online survey was performed in London, United Kingdom [51] among perimenopausal women (English-speaking older than 40 yrs) to determine their attitudes and knowledge on menopause. Lack of education caused perimenopausal women to suffer unnecessarily in the UK without appropriate medical care [51]. Menopausal education should start at school for adolescent girls to consider it an event in their lives [51]. Mass and social media can be used to educate adolescent girls and perimenopausal women in new trends of addressing menopausal syndrome in the same pacage of prevention of non communicable disease. Menopausal syndrome influences poorer QOL in pre and postmenopausal women [5,19,24,26]. Preparatory time and space for modern perimenopausal women arise as the slogan of Well Woman Clinics (WWC) for harnessing the potential of measures taken by the free-of-charge public health system in Sri Lanka. Investments for better QOL in the latter decade of alpha are crucial for the smooth functioning of a carrier woman. Menopausal age does not limit the carrier prospects of experienced professional academic women. That may be the ideal age of her to enter politics, commencing the service as a Consul General or Ambassador. If she is adventurous, knowledgeable, and resourceful enough she can challenge the menopausal challenges with a great deal of confidence as older wine kept for ripening.

**Conclusion and future direction**

In addition to sufficient preparatory time and space for every woman to face the consequences of the menopausal syndrome, making awareness of healthcare professionals on new trend of addressing the menopausal syndrome emerge as an achievable goal in the passion of personalized medicine. Moreover, the prevention of non-communicable and communicable diseases in perimenopausal women and the management of co-morbidities in post-menopausal women are established as public health obligations irrespective of socio-cultural barriers. Consideration of menopausal syndrome as a preventable non communicable disease gains popularity across the globe in the era of evidence based medicine. Future work on inculcating positive attitudes, perception and evidence-informed knowledge on adolesecent girls about not only 'period pains' but menopausal symptoms as an inevitable phase in a woman's life cycle may make a better sense at the dawn of evidence based medicine even in a low middle income country like Sri Lanka when public health system collapsed due to COVID-19 aftermath, economic recession and depriciation of the Sri Lankan Rupee. **"Do not fear when menopause is near" would be the motto of every woman who is in mid**

**forties if she did not become aging and menopause before reaching mid forties.** Importantly, life course epidemiology of reproductive health appears as a grey are which can accommodate many researchers who would be able to give valuable clues in socio cultural , determinants and risk factors of embryo-foetal life, childhood, adolesecenc, reproductive and post reproductive phases which may influence the aetiology of menopausal syndrome.

**Author Contributions:** M. Perera and I Perera equally contributed to conception, information acquisition, interpretation and writing of this manuscript especially sharing their personal experiences as post menopausal academic professionals.

**Acknowledgment:** Firstly, I appreciate the cumbersome task of Dr. Gerard Ranasinghe, Fellow of the Royal College of Pathologists (Microbiology Division) Australia for two decades to make me a researcher and a manuscript writer. The support and guidance provided by Sri Lanka Ranjana Sir Sabaratnam Arulkumaran; Professor Emeritus of Obstetrics and Gynaecology, Dr. Anil Jasinghe; former Director General of Health Services, Dr. Sanath Lanerolle; The President of the Menopause Society of Sri Lanka in their messages published on the program and the abstract book of MENOSOC 2019,18th Annual Academic Sessions Menopause Society of Sri Lanka. Lastly, I thank Dr. Himanshu Arora, Associate Professor, University of Queensland, Australia for his untimely support to involve in publications.

**Funding:** No source of funding.

**Conflict of interest**: The authors declare no potential conflicts of interest with respect to the authorship and/or publication of this article.

## Reference

1. Iheanetu, C.U.; Maguire, K.A.; Moricová, V.; Tandlich, R.; Alloggio, S. Utilitarian Qubit, Human Geography, and Pandemic Preparedness in the 21st Century. *Sustainability* **2023**, *15*, 321. https://doi.org/10.3390/su15010321
2. Professor Brian Murdoch, review of *From Eden to Eternity: Creations of Paradise in the Later Middle Ages*, (review no. 1936) 2023,DOI: 10.14296/RiH/2014/1936
3. Boyd, Robert and Peter J. Richerson. Culture and the Evolutionary Process. Chicago: University of Chicago Press 1985
4. Yong-Fei Zheng, Fifty years of plate tectonics, *National Science Review*, Volume 5, Issue 2, March 2018, Page 119, https://doi.org/10.1093/nsr/nwy024
5. Forman MR, Mangini LD, Thelus-Jean R, Hayward MD. Life-course origins of the ages at menarche and menopause. Adolesc Health Med Ther. 2013 Jan 18;4:1-21. doi: 10.2147/AHMT.S15946. PMID: 24600293; PMCID: PMC3912848.
6. Currie C, Ahluwalia N, Godeau E, Nic Gabhainn S, Due P, Currie DB. Is obesity at individual and national level associated with lower age at menarche? Evidence from 34 countries in the Health Behaviour in School-aged Children Study. J Adolesc Health. 2012;50(6):621–626.
7. Parent AS, Teilmann G, Juul A, Skakkebaek NE, Toppari J, Bourguignon JP. The timing of normal puberty and the age limits of sexual precocity: variations around the world, secular trends, and changes after migration. Endocr Rev. 2003;24(5):668–693
8. Omatis, V.; Battipaglia, C.; Genazzani, A.D. Thyroid, Adrenal, PRL Impairments and Ovarian Function. *Endocrines* **2021**, *2*, 212-225. https://doi.org/10.3390/endocrines2030021
9. De Felici M, Klinger FG, Farini D, Scaldaferri ML, Iona S, Lobascio M. Establishment of oocyte population in the fetal ovary: primordial germ cell proliferation and oocyte programmed cell death. Reprod Biomed Online. 2005 Feb;10(2):182-91. doi: 10.1016/s1472-6483(10)60939-x. PMID: 15823221.
10. .Karapanou O, Papadimitriou A. Determinants of menarche. Reprod Biol Endocrinol. 2010;8:115.
11. Hillard PJA. Menstruation in adolescents: what's normal? Medscape J Med. 2008;10(12):295.
12. Soules MR, Sherman S, Parrott E, Rebar R, Santoro N, Utian W, Woods N. Executive summary: Stages of Reproductive Aging Workshop (STRAW). Fertil Steril. 2001 Nov;76(5):874-8. doi: 10.1016/s0015-0282(01)02909-0. PMID: 11704104.
13. Palacios S, Henderson VW, Siseles N, Tan D, Villaseca P. Age of menopause and impact of climacteric symptoms by geographical region, Climacteric 2010; 13(5):419-428

14. Gluckman PD, Lillycrop KA, Vickers MH, et al. Metabolic plasticity during mammalian development is directionally dependent on early nutritional status. Proc Natl Acad Sci U S A. 2007;104(31): 12796–12800
15. Colbert LH, Graubard BI, Michels KB, Willett WC, Forman MR. Physical activity during pregnancy and age at menarche of the daughter. Cancer Epidemiol Biomarkers Prev. 2008;17(10): 2656–2662
16. Otero UB, Chor D, Carvalho MS, Faerstein E, Lopes Cde S, Werneck GL. Association between socioeconomic position in earlier and later life and age at natural menopause: Estudo Pró-Saúde, Brazil. Womens Health (Lond Engl). 2011;7(6):719–727.
17. Al-Sahab B, Adair L, Hamadeh MJ, Ardern CI, Tamim H. Impact of breastfeeding duration on age at menarche. Am J Epidemiol. 2011;173(9):971–977.
18. Hardy R, Kuh D. Social and environmental conditions across the life course and age at menopause in a British birth cohort study. BJOG. 2005;112(3):346–354.
19. Silva P, Moonesinghe L. Menopause in Sri Lankan context. Sri Lanka Journal of Menopause. 2020;2(1):34–5. DOI: http://doi.org/10.4038/sljom.v2i1.36
20. Lansdorp PM. Sex differences in telomere length, lifespan, and embryonic dyskerin levels. Aging Cell. 2022 May;21(5):e13614. doi: 10.1111/acel.13614. Epub 2022 Apr 20. PMID: 35441417; PMCID: PMC9124296.
21. Hoga L, Rodolpho J, Gonçalves B, et al. Women's experience of menopause: a systematic review of qualitative evidence. JBI Database System Rev Implement Rep 2015; 13(8): 250–337.
22. United Nations Population Division. World population prospects 2019. New York: United Nations Population Division; 2020. Available from: https://population.un.org/wpp/ DataQuery
23. Hill K. The demography of menopause. Maturitas. 1996;23: 113-127.
24. Waidyasekera H, Wijewardena k, Lindmark G, Naessen T. Menopausal symptoms and quality of life during the menopausal transition in Sri Lankan women. Menopause 2009; 16(1):164–170
25. Goonaratna C, Fonseka P, Wijeywardene K. Perimenopausal symptoms in Sri Lankan women. Ceylon Medical Journal 1999; 44(2):63–69
26. Rathnayake N, Lenora J, Alwis G, Lekamwasam S. Prevalence and Severity of Menopausal Symptoms and the Quality of Life in Middle-aged Women: A Study from Sri Lanka. Nurs Res Pract. 2019;2019:2081507. doi: 10.1155/2019/2081507. PMID: 31354992; PMCID: PMC6632501
27. Research on the menopause in the 1990s. Report of a WHO scientific group. World Health Organ Tech Rep Ser. 1996;866: 1–107.
28. Brambilla DJ, McKinlay SM. A prospective study of factors affecting age at menopause. J Clin Epidemiol. 1989;42(11): 1031–1039.
29. C. C. Zouboulis, U. Blume-Peytavi, M. Kosmadaki, E. Roó, D. Vexiau-Robert, D. Kerob & S. R. Goldstein. Skin, hair and beyond: the impact of menopause, Climacteric, 2022 ; 25:5, 434-442.
30. Calleja-Agius J, Brincat MP. The urogenital system and the menopause. Climacteric. 2015;18(Suppl 1):18–22.
31. Santoro N, Komi J. Prevalence and impact of vaginal symptoms among postmenopausal women. J Sex Med. 2009;6(8): 2133–2142
32. Hale G, Burger H. Hormonal changes and biomarkers in late reproductive age, menopausal transition, and menopause. Best Practice & Research Clinical Obstetrics and Gynaecology. 2009; 23:7–23. [PubMed: 19046657]
33. Hoyt LT, Falconi AM. Puberty and perimenopause: reproductive transitions and their implications for women's health. Soc Sci Med.2015;132:103-12. doi: 10.1016/j.socscimed.2015.03.031
34. Slominski A, Zbytek B, Nikolakis G, et al. Steroidogenesis in the skin: implications for local immune functions. J Steroid Biochem Mol Biol. 2013;137:107–123.
35. Su HI, Freeman EW. Hormone changes associated with the menopausal transition. Minerva Ginecol. 2009;61(6):483–489
36. Schneider, HPG & Birkhäuser, M. Quality of life in climacteric women, Climacteric, 2017; 20:3, 187-194, DOI: 10.1080/13697137.2017.1279599
37. Dalal PK, Agarwal M. Postmenopausal syndrome. Indian J Psychiatry. Jul;57(Suppl 2):S222-32. 2015; doi: 10.4103/0019-5545.161483.
38. Kaunitz AM, Manson JE. Management of Menopausal Symptoms. Obstet Gynecol. 2015 Oct;126(4):859-876. doi: 10.1097/AOG.0000000000001058.
39. Birkhäuser MH, Haenggi W. Benefits of different routes of administration. Int J Fertil Menopausal Stud. 1994;39 Suppl 1:11-9. PMID: 8199636.
40. Richard J. Santen, D. Craig Allred, Stacy P. Ardoin, David F. Archer, Norman Boyd, Glenn D. Braunstein, Henry G. Burger, Graham A. Colditz, Susan R. Davis, Marco Gambacciani, Barbara A. Gower, Victor W. Henderson, Wael N. Jarjour, Richard H. Karas, Michael Kleerekoper, Roger A. Lobo, JoAnn E. Manson, Jo Marsden, Kathryn A. Martin, Lisa Martin, JoAnn V. Pinkerton, David R. Rubinow, Helena Teede, Diane M. Thiboutot, Wulf H. Utian, Postmenopausal Hormone Therapy: An Endocrine Society Scientific

Statement, *The Journal of Clinical Endocrinology & Metabolism*, Volume 95, Issue 7_supplement_1, 1 July 2010, Pages s1–s66, https://doi.org/10.1210/jc.2009-2509

41. Posadzki P, Lee MS, Moon TW, Choi TY, Park TY, Ernst E. Prevalence of complementary and alternative medicine (CAM) use by menopausal women: a systematic review of surveys. Maturitas. 2013;75:34-43
42. Rossouw JE, Anderson GL, Prentice RL, et al. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative randomized controlled trial. JAMA. 2002;288:321-333.
43. Ma J, Drieling R, Stafford RS. US women desire greater professional guidance on hormone and alternative therapies for menopause symptom management. Menopause. 2006;13:506-516
44. Non-hormonal strategies for managing menopausal symptoms in cancer survivors: an update ecancer 2019, 13:909; https://doi.org/10.3332/ecancer.2019.909
45. American College of Obstetricians and Gynaecologists .ACOG practice bulletin No. 141: management of menopausal symptoms Obstet Gynecol, 2014. 123(1) 202–216 https://doi.org/10.1097/01.AOG.0000441353.20693.78 PMID: 24463691
46. Hayes LP, Carroll DG, and Kelley KW .Use of gabapentin for the management of natural or surgical menopausal hot flashes Ann Pharmacother 2011, 45, 388–394 https://doi.org/10.1345/aph.1P366 PMID: 21343402
47. Sassarini J, Fox H, and Ferrell W, et al .Hot flushes, vascular reactivity and the role of the $\alpha$-adrenergic system Climacteric 2012; 15 332–338 https://doi.org/10.3109/13697137.2011.636847 PMID: 2220878
48. Aidelsburger P, Schauer S, Grabein K, Wasem J. Alternative methods for the treatment of post-menopausal troubles. GMS Health Technol Assess. 2012; 8:Doc03.doi: 10.3205/hta000101. Epub 2012 May 7. PMID: 22690252; PMCID: PMC3356850.
49. Johnson A, Roberts L, Elkins G. Complementary and Alternative Medicine for Menopause. *J Evid Based Integr Med*. 2019; 24:2515690X19829380. doi:10.1177/2515690X19829380.
50. Barnard ND, Kahleova H, Holtz DN, Del Aguila F, Neola M, Crosby LM, Holubkov R. The Women's Study for the Alleviation of Vasomotor Symptoms (WAVS): a randomized, controlled trial of a plant-based diet and whole soybeans for postmenopausal women. Menopause. 2021 Jul 12;28(10):1150-1156.
51. Harper JC, Phillips S, Biswakarma R, Yasmin E, Saridogan E, Radhakrishnan S, C Davies M, Talaulikar V. An online survey of perimenopausal women to determine their attitudes and knowledge of the menopause. Womens Health (Lond). 2022 Jan-Dec;18:17455057221106890. doi: 10.1177/17455057221106890. PMID: 35758176; PMCID: PMC9244939