

Section 11

ABNORMAL MENOPAUSE

- 46. Delayed Menopause
- 47. Early Menopause
- 48. Premature Ovarian Insufficiency
- 49. Surgical Menopause

DELAYED MENOPAUSE

Keywords: Age of delayed menopause, risks, benefits, screening.

46

INTRODUCTION

Determining the average age at natural menopause is challenging due to population heterogeneity, recall bias, and methodological differences across studies. In India, evidence from largely cross-sectional, community-based studies suggests that the mean age at natural menopause is substantially lower than that reported in Western populations. Most Indian studies report a mean menopausal age of 46.5–48 years, with a pooled estimate of approximately 47.5 years.^{1,2} This earlier age has been attributed to a combination of genetic, nutritional, socioeconomic, and health-system factors.³

In contrast, data from the United States consistently report a higher age at menopause. Large longitudinal cohorts estimate the median age at natural menopause (ANM) to be 50–52 years; the Massachusetts Women's Health Study, which followed 2,570 women prospectively, reported a mean age of 51.3 years.^{4,5} Similar findings have been reported across other Western populations. A recent meta-analysis of Asian populations demonstrated considerable geographic variation in menopausal age, with pooled mean estimates ranging from the mid-40s in parts of South Asia to just over 50 years in several Southeast Asian countries. Urban residence was consistently associated with a later age at menopause compared with rural settings, highlighting the influence of lifestyle and environmental factors.⁶ Classic longitudinal data further support this variability. In Treloar's landmark study, the mean age at menopause was 50.7 years, with 95% of women experiencing menopause between 44 and 56 years, reinforcing the concept of a broad normal distribution rather than a fixed biological threshold.⁷

DEFINITION

At present, there is no universally accepted definition of late-onset or delayed menopause, which limits comparability across studies and complicates the interpretation of associated health outcomes, particularly those related to prolonged estrogen exposure and hyperestrogenic states.^{5,8}

Statistically, delayed menopause is defined as menopause occurring 2 standard deviations above the population mean age, corresponding to the upper 5% of the age distribution.⁹ In India, where the estimated mean ANM is approximately 46.6 years, this statistical approach would classify delayed menopause as ≥ 52 years.^{1,3} Given the lower baseline age of menopause in Indian women, menopause occurring at ≥ 52 years may reasonably be considered delayed in the Indian context.^{3,4} Nonetheless, in the absence of validated population-specific cutoffs and to align with the global literature, ≥ 55 years remains the reporting threshold for delayed menopause.^{9,10} Population-based longitudinal studies in Indian women are required to validate appropriate cutoff values and to inform context-specific clinical and research definitions.

PREVALANCE

For India, the most robust nationally representative estimate of delayed (late-onset) natural menopause is derived from the Longitudinal Ageing Study in India (LASI) Wave 1 (2017–2019). Using the conventional definition of delayed menopause as menopause occurring after 55 years, a secondary analysis of LASI-1 data ($n = 25,256$ women with menopausal age information) reported a prevalence of 13.4%. In the same analysis, the prevalence of premature menopause (<40 years) was 7.4%, and early menopause (40–44 years) was 17.5%. As LASI surveys community-dwelling adults aged ≥ 45 years, these estimates represent the strongest population-based data for India; however, the proportion of late menopause may appear higher than clinic-based series due to broader community capture and survivor effects.¹¹

FACTORS ASSOCIATED WITH DELAYED MENOPAUSE

Later ANM has been consistently associated with higher body mass index (BMI), favourable socioeconomic and educational status, and higher parity across diverse populations. A large meta-analysis of Asian studies demonstrated that women with higher BMI and improved socioeconomic indicators tend to experience menopause at a later age.⁶

The relationship between adiposity and menopausal timing is among the most reproducible findings, with several studies showing that higher BMI is independently associated with delayed menopause, likely mediated by increased peripheral aromatisation of androgens to estrogens in adipose tissue.¹²

Lifestyle factors also contribute. Low to moderate alcohol consumption has been associated with a modest delay in the onset of menopause, possibly through its effects on circulating estrogen levels and bone metabolism; however, the magnitude of this association is small and clinically limited.^{13,14} Dietary patterns may influence menopausal timing by affecting ovarian ageing and estradiol levels. Higher intake of fruits and vegetables, antioxidant-rich foods, phytoestrogens (such as soy and whole grains), adequate protein and caloric intake, vitamin E, vitamin D-fortified dairy products, magnesium-rich foods, oily fish, and legumes have been associated with a slightly later age at menopause in observational studies.^{15,16}

Physical activity shows a nuanced relationship with menopausal age. Moderate and sustained recreational physical activity has been associated with delayed menopause, potentially mediated through its effects on BMI and metabolic health.¹⁷⁻¹⁹ In contrast, very high levels of vigorous or energy-deficient exercise may be associated with earlier menopause. Emerging genetic epidemiology data also support a modest causal role of physical activity in delaying menopause.¹⁸ Practices such as yoga, which combine moderate physical activity with stress reduction, have been suggested to delay menopausal onset, although evidence remains limited.²⁰

Familial and genetic factors play a significant role in determining the timing of menopause. Evidence from twin studies demonstrates substantial heritability of age at natural menopause, with women whose mothers or sisters experience later menopause being more likely to have delayed menopause themselves, supporting a strong genetic contribution to ovarian ageing.^{21,22}

Late-onset or persistent polycystic ovary syndrome (PCOS) may be associated with delayed menopause, likely due to a higher initial follicular pool and chronic anovulation, resulting in slower follicular depletion over time.²³ However, data remain limited, and this association should be interpreted cautiously.

Racial and ethnic differences in menopausal timing have been well documented. In the Study of Women's Health Across the Nation (SWAN), Japanese women were observed to have a significantly later mean age at menopause compared with Caucasian and Hispanic women, highlighting the influence of genetic, cultural, and lifestyle factors.²⁴

Certain medical conditions are also associated with delayed menopause. These include estrogen-responsive conditions such as uterine fibroids, as well as rare hormone-secreting tumours of ovarian or adrenal origin. Disorders of the hypothalamic-pituitary axis and metabolic conditions such as diabetes mellitus have been associated with alterations in menopausal timing. Thyroid dysfunction may influence menopausal age in either direction, contributing to both early and delayed menopause, depending on the nature and duration of the disorder.^{25,26}

Exogenous hormonal exposure, including long-term use of combined oral contraceptives or menopausal hormone therapy, can mask the onset of ANM by suppressing ovulation or inducing withdrawal bleeding, thereby delaying its clinical recognition rather than altering the true biological age at menopause.⁵

PATHOPHYSIOLOGY

Emerging evidence suggests that the menopausal transition (MT) represents a systemic, low-grade pro-inflammatory state, closely linked to estrogen withdrawal and disruption of estrogen-regulated neuro-immune pathways. Estrogen functions as a master regulator of immune and neural homeostasis through its actions on estrogen receptor subtypes, primarily estrogen receptor- α (ER- α) and estrogen receptor- β (ER- β). ER- β , in particular, has been shown to play a key role in modulating components of the innate immune response, including regulation of the inflammasome, a critical mediator of inflammatory signalling.²⁷ However, these effects appear to be tissue- and context-dependent.

Estrogen receptors also regulate neuronal mitochondrial function, oxidative stress, and cellular resilience. The decline in estrogen during the menopausal transition (MT) contributes to persistent low-grade inflammation, which may accelerate ovarian follicular depletion and influence the timing of ovarian failure. In women with delayed menopause, this inflammatory cascade and estrogen withdrawal appear to occur later, effectively postponing the onset of ovarian senescence.^{27,28}

Innate immune activation associated with reproductive ageing may also extend beyond the ovary to the central nervous system. Experimental and translational studies suggest that alterations in inflammasome signalling and extracellular vesicle-mediated immune communication may increase brain vulnerability to ischemic injury during

reproductive senescence, highlighting the systemic nature of menopause-related neuro-immune changes.²

ADVANTAGES OF DELAYED MENOPAUSE

Prolonged exposure to endogenous estrogen associated with delayed menopause confers several cardiovascular and skeletal benefits, which together contribute to greater longevity and lower all-cause mortality.

- *Cardiovascular benefits:* Endogenous estrogen exerts multiple cardioprotective actions, including favourable effects on lipid profiles, lower low-density lipoprotein (LDL) cholesterol, higher high-density lipoprotein (HDL) cholesterol, improved fibrinolysis, modulation of the renin–angiotensin system, antioxidant activity, and maintenance of vascular tone and endothelial function.²⁹ Epidemiological studies consistently demonstrate that a later age at natural menopause is associated with lower risks of coronary heart disease, myocardial infarction, and cerebrovascular events.³⁰ Large cohort and pooled analyses indicate that each additional year in age at menopause is associated with a progressive reduction in cardiovascular mortality, estimated at approximately 2% per year, with women experiencing menopause after 52–55 years showing significantly lower rates of cardiovascular death.^{30,31} A long-term Norwegian cohort study with 37 years of follow-up reported longer life expectancy among women with later menopause, largely attributable to reduced cardiovascular mortality.³¹ The authors conclude that ANM is inversely related to all-cause mortality. Recent mechanistic data further support these observations. Women with late-onset menopause demonstrate preservation of vascular endothelial function, mediated by lower mitochondrial reactive oxygen species (mitoROS)–associated oxidative stress and a more favourable circulating lipid metabolite profile, particularly lower triglyceride-derived metabolites. These findings provide biological plausibility for the reduced cardiovascular disease risk observed in women with delayed menopause.³²
- *Skeletal benefits:* Delayed menopause is associated with prolonged maintenance of bone mineral density (BMD) due to extended estrogen exposure. Women with later menopause have higher BMD at the spine and hip, slower rates of postmenopausal bone loss, and a lower lifetime risk of osteoporotic fractures compared with women experiencing early menopause.³³
- *Longevity and overall health:* Through combined cardiovascular and skeletal protection, delayed menopause has been associated with increased life expectancy and reduced all-cause mortality in several population-based studies. Once menopause is established, however, circulating estrogen levels and androgen-to-estrogen ratios in women with delayed menopause become similar to those seen after normally timed menopause, indicating that long-term benefits relate primarily to duration of exposure rather than postmenopausal hormonal differences.

RISKS OF DELAYED MENOPAUSE

The hypothesis that delayed menopause may increase the risk of hormone-dependent cancers is not new. As early as the 1940s, observational studies had noted an association between later age at menopause and increased risk of breast and endometrial cancer. In a seminal report, Blank (1944) observed that late menopause was disproportionately common among women with adenocarcinoma of the uterine fundus and breast cancer, proposing that prolonged estrogenic stimulation over an extended reproductive lifespan contributed to malignant transformation. Although these early observations predated modern molecular biology and epidemiologic methods, they laid the conceptual foundation for subsequent large-scale cohort studies and meta-analyses that have since confirmed the association between delayed menopause and increased risk of estrogen-dependent malignancies. These risks reflect cumulative lifetime estrogen exposure and underscore the importance of individualised risk assessment, weight management, and appropriate cancer screening.³⁴

Hormone-Dependent Cancers

- *Endometrial cancer:* Delayed menopause is a well-established risk factor for endometrial cancer. Prolonged estrogen exposure leads to sustained endometrial proliferation, particularly in the absence of adequate progesterone antagonism. Large meta-analyses demonstrate a dose–response relationship, with increasing age at menopause associated with progressively higher endometrial cancer risk.^{35,36} This risk is further amplified in women with obesity due to increased peripheral aromatisation of androgens to estrogens in adipose tissue.³⁷
- *Ovarian cancer:* Later age at natural menopause has been consistently associated with an increased risk of epithelial ovarian cancer, likely reflecting a greater number of lifetime ovulatory cycles and prolonged estrogenic exposure.³⁸ The risk is higher in women with additional reproductive risk factors such as early menarche, nulliparity, infertility,

or use of ovulation-inducing agents, and may be further modified by genetic susceptibility (BRCA mutations).³⁹

- *Breast cancer:* Delayed menopause increases breast cancer risk by extending the duration of estrogen and progesterone exposure. Epidemiological studies demonstrate that each additional year of reproductive life modestly increases breast cancer risk, and women with late menopause often exhibit higher mammographic breast density, an independent risk factor for breast cancer.^{40,41}
- *Cervical cancer:* While delayed menopause itself is not a direct risk factor for cervical cancer, persistence or reactivation of high-risk human papillomavirus (HPV) infection has been observed in postmenopausal women, particularly beyond 65 years of age. This underscores the importance of continued cervical cancer screening in appropriately selected older women, independent of menopausal timing.⁴²
- *Modifying factors and high-risk phenotypes for cancer:* Women with delayed menopause who also have a high BMI are at particularly increased risk of estrogen-dependent cancers. Maintenance of BMI ≤ 25 kg/m² and waist circumference < 80 cm is therefore recommended, as obesity independently increases estrogen levels and cancer risk.³⁷
- *Genetic and molecular:* Genetic studies have identified hundreds of single-nucleotide polymorphisms associated with age at menopause, many of which involve deoxyribonucleic acid (DNA) repair, immune regulation, and mitochondrial function. These pathways may partially explain the association between delayed menopause and increased cancer risk, although causality remains under investigation.⁴³

Delayed Menopause And Other Gynaecologic Problems

Women with delayed menopause may experience abnormal uterine bleeding, endometrial hyperplasia, or other estrogen-related symptoms during the late reproductive and perimenopausal years, necessitating careful evaluation to exclude pathology.

COUNSELLING

Women with delayed menopause should be advised to seek prompt medical evaluation if they develop abnormal uterine bleeding, including intermenstrual bleeding, heavy menstrual bleeding, or any bleeding occurring after an established period of amenorrhoea. Additional red flags include new-onset or progressive pelvic pain or pressure, a rapid increase in abdominal girth, or detection of an adnexal mass, which may suggest underlying gynecologic pathology. A strong family history of estrogen-dependent malignancies, particularly breast, ovarian, or endometrial cancer, warrants heightened clinical vigilance. Symptoms suggestive of endocrine or pituitary dysfunction, such as persistent headache, visual field disturbances, or galactorrhoea, should prompt further evaluation to exclude hypothalamic–pituitary disease.

SCREENING AND FOLLOW-UP

Asymptomatic women with delayed menopause do not require a routine endometrial biopsy. Screening should be individualised and risk-based rather than determined solely by age. Clinical emphasis should be placed on optimisation of body weight, adherence to age-appropriate breast and cervical cancer screening guidelines, and prompt evaluation of any abnormal uterine bleeding or change in bleeding pattern. Such a targeted approach minimises unnecessary invasive investigations while ensuring early detection of estrogen-dependent pathology.

SYNOPSIS

- Delayed menopause represents a physiological variation characterised by prolonged endogenous estrogen exposure.
- While it confers cardiovascular and skeletal advantages, it is associated with increased risks of estrogen-dependent malignancies.
- Clinical evaluation should focus on excluding endometrial pathology, guided by symptoms and ultrasound findings.
- Asymptomatic women do not require routine invasive testing, and management should prioritise risk stratification, lifestyle optimisation, and vigilant follow-up for red flag symptoms.
- With appropriate surveillance, women with delayed menopause can maintain a good quality of life with favourable mental, bone, and cardiovascular health outcomes.

RESEARCH AGENDA

Longitudinal studies using nationally representative cohorts to determine true prevalence, regional variation, secular trends, and health outcomes associated with delayed menopause.

REFERENCES

1. Singh M. Early age of natural menopause in India, a biological marker for early preventive health programs. *Climacteric J Int Menopause Soc.* 2012 Dec;15(6):581–6. doi: 10.3109/13697137.2011.643514.
2. Prasad JB, Tyagi NK, Verma P. Age at menopause in India: A systematic review. *Diabetes Metab Syndr.* 2021;15(1):373–7. doi: 10.1016/j.dsx.2021.01.013.
3. McKinlay SM, Brambilla DJ, Posner JG. The normal menopause transition. *Maturitas.* 1992 Jan;14(2):103–15. doi: 10.1016/0378-5122(92)90003-m.
4. McKinlay JB, McKinlay SM, Brambilla DJ. Health status and utilization behavior associated with menopause. *Am J Epidemiol.* 1987 Jan;125(1):110–21. doi: 10.1093/oxfordjournals.aje.a114492.
5. Gold EB. The timing of the age at which natural menopause occurs. *Obstet Gynecol Clin North Am.* 2011 Sept;38(3):425–40. doi: 10.1016/j.ogc.2011.05.002.
6. Agrawal PK, Varshney A, Dev S, Garg R, Gautam A, Pursnani N, et al. Menopause Across Asia: A Comprehensive Meta-analysis of Age and Influencing Factors. *J - Life Health.* 2025;16(3):257–66. doi: 10.4103/jmh.jmh_118_25.
7. Treloar AE. Menarche, menopause, and intervening fecundability. *Hum Biol.* 1974 Feb;46(1):89–107.
8. Cancer Genetics Risk Assessment and Counseling (PDQ®) - NCI [Internet]. 2026 [cited 2026 Feb 12]. Available from: <https://www.cancer.gov/publications/pdq/informationsummaries/genetics/risk-assessment-hp-pdq>
9. Meeta M, Digumarti L, Agarwal N, Vaze N, Shah R, Malik S. Clinical Practice Guidelines on Menopause: *An Executive Summary and Recommendations: Indian Menopause Society 2019-2020. *J -Life Health.* 2020;11(2):55–95. doi: 10.4103/jmh.JMH_137_20.
10. Kaufert P, Lock M, McKinlay S, Beyenne Y, Coope J, Davis D, et al. Menopause research: the Korpilampi workshop. *Soc Sci Med.* 1986;22(11):1285–9. doi: 10.1016/0277-9536(86)90196-6.
11. Halder P, Kansal S, Mamgai A, Rathor S, Das A, Garg G. Untimely Menopause, State Wise Prevalence and Determinants: Insights from Longitudinal Aging Study in India (LASI-1). *J Obstet Gynaecol India.* 2025 Apr;75(2):106–14. doi: 10.1007/s13224-024-02094-1.
12. Akahoshi M, Soda M, Nakashima E, Tominaga T, Ichimaru S, Seto S, et al. The effects of body mass index on age at menopause. *Int J Obes Relat Metab Disord J Int Assoc Study Obes.* 2002 July;26(7):961–8. doi: 10.1038/sj.ijo.0802039.
13. Torgerson DJ, Thomas RE, Campbell MK, Reid DM. Alcohol consumption and age of maternal menopause are associated with menopause onset. *Maturitas.* 1997 Jan;26(1):21–5. doi: 10.1016/s0378-5122(96)01075-4.
14. Taneri PE, Kieffe-de Jong JC, Bramer WM, Daan NMP, Franco OH, Muka T. Association of alcohol consumption with the onset of natural menopause: a systematic review and meta-analysis. *Hum Reprod Update.* 2016 June;22(4):516–28. doi: 10.1093/humupd/dmw013.
15. Nagata C, Wada K, Nakamura K, Tamai Y, Tsuji M, Shimizu H. Associations of physical activity and diet with the onset of menopause in Japanese women. *Menopause.* 2012 Jan;19(1):75–81. doi: 10.1097/gme.0b013e3182243737.
16. Sapre S, Thakur R. Lifestyle and dietary factors determine age at natural menopause. *J -Life Health.* 2014 Jan;5(1):3–5. doi: 10.4103/0976-7800.127779.
17. Morris DH, Jones ME, Schoemaker MJ, McFadden E, Ashworth A, Swerdlow AJ. Body mass index, exercise, and other lifestyle factors in relation to age at natural menopause: analyses from the breakthrough generations study. *Am J Epidemiol.* 2012 May 15;175(10):998–1005. doi: 10.1093/aje/kwr447.
18. Emaus A, Dieli-Conwright C, Xu X, Lacey JV, Ingles SA, Reynolds P, et al. Increased long-term recreational physical activity is associated with older age at natural menopause among heavy smokers: the California Teachers Study. *Menopause.* 2013 Mar;20(3):282–90. doi: 10.1097/GME.0b013e318266ce3d4.
19. Sun X. Physical activity associated with age at menopause: A Mendelian randomization study. *Medicine (Baltimore).* 2025 Feb 7;104(6):e41514. doi: 10.1097/MD.00000000000041514.
20. Joshi S, Khandwe R, Bapat D, Deshmukh U. Effect of yoga on menopausal symptoms. *Menopause Int.* 2011 Sept;17(3):78–81. doi: 10.1258/mi.2011.011020.
21. Treloar SA, Do KA, Martin NG. Genetic influences on the age at menopause. *Lancet.* 1998 Oct 3;352(9134):1084–5. doi: 10.1016/S0140-6736(05)79753-1.
22. Murabito JM, Yang Q, Fox C, Wilson PWF, Cupples LA. Heritability of age at natural menopause in the Framingham Heart Study. *J Clin Endocrinol Metab.* 2005 June;90(6):3427–30. doi: 10.1210/jc.2005-0181.
23. Tehrani FR, Solaymani-Dodaran M, Hedayati M, Azizi F. Is polycystic ovary syndrome an exception for reproductive aging? *Hum Reprod.* 2010 July;25(7):1775–81. doi: 10.1093/humrep/deq088.
24. Gold EB, Bromberger J, Crawford S, Samuels S, Greendale GA, Harlow SD, et al. Factors associated with age at natural menopause in a multiethnic sample of midlife women. *Am J Epidemiol.* 2001 May 1;153(9):865–74. doi: 10.1093/aje/153.9.865.
25. Flake GP, Andersen J, Dixon D. Etiology and pathogenesis of uterine leiomyomas: a review. *Environ Health Perspect.* 2003 June;111(8):1037–54. doi: 10.1289/ehp.5787.
26. Popat VB, Calis KA, Vanderhoof VH, Cizza G, Reynolds JC, Sebring N, et al. Bone mineral density in estrogen-deficient young women. *J Clin Endocrinol Metab.* 2009 July;94(7):2277–83. doi: 10.1210/jc.2008-1878.
27. McCarthy M, Raval AP. The peri-menopause in a woman's life: a systemic inflammatory phase that enables later neurodegenerative disease. *J Neuroinflammation.* 2020 Oct 23;17(1):317. doi: 10.1186/s12974-020-01998-9.
28. Raval AP, Martinez CC, Mejias NH, de Rivero Vaccari JP. Sexual dimorphism in inflammasome-containing extracellular vesicles and the regulation of innate immunity in the brain of reproductive senescent females. *Neurochem Int.* 2019 July;127:29–37. doi: 10.1016/j.neuint.2018.11.018.
29. Rosano GMC, Vitale C, Fini M. Cardiovascular aspects of menopausal hormone replacement therapy. *Climacteric J Int Menopause Soc.* 2009;12 Suppl 1:41–6. doi: 10.1080/13697130903012306.
30. Zhu D, Chung HF, Dobson AJ, Pandeya N, Giles GG, Bruinsma F, et al. Age at natural menopause and risk of incident cardiovascular disease: a pooled analysis of individual patient data. *Lancet Public Health.* 2019 Nov;4(11):e553–64. doi: 10.1016/S2468-2667(19)30155-0.

31. Jacobsen BK, Heuch I, Kvåle G. Age at natural menopause and all-cause mortality: a 37-year follow-up of 19,731 Norwegian women. *Am J Epidemiol*. 2003 May 15;157(10):923–9. doi: 10.1093/aje/kwg066.
32. Darvish S, Murray KO, Ludwig KR, Avalani KH, Craighead DH, Freeberg KA, et al. Preservation of Vascular Endothelial Function in Late-Onset Postmenopausal Women. *Circ Res*. 2025 Feb 28;136(5):455–69. doi: 10.1161/CIRCRESAHA.124.325639.
33. van Der Voort DJM, van Der Weijer PHM, Barentsen R. Early menopause: increased fracture risk at older age. *Osteoporos Int J Establ Result Coop Eur Found Osteoporos Natl Osteoporos Found USA*. 2003 July;14(6):525–30. doi: 10.1007/s00198-003-1408-1.
34. Blank F. Late Menopause and Cancer of the Breast. 1944 [cited 2026 Feb 12]; Available from: <https://kb.osu.edu/bitstreams/17c2d063-c437-51d7-b857-fbbfd473c44/download>
35. Wu Y, Sun W, Liu H, Zhang D. Age at Menopause and Risk of Developing Endometrial Cancer: A Meta-Analysis. *BioMed Res Int*. 2019;2019:8584130. doi: 10.1155/2019/8584130.
36. Ryoko K, Motoki I. Reproductive Factors and Endometrial Cancer Risk Among Women - PubMed [Internet]. [cited 2026 Feb 12]. Available from: <https://pubmed.ncbi.nlm.nih.gov/37669051/>
37. Reeves GK, Pirie K, Beral V, Green J, Spencer E, Bull D, et al. Cancer incidence and mortality in relation to body mass index in the Million Women Study: cohort study. *BMJ*. 2007 Dec 1;335(7630):1134. doi: 10.1136/bmj.39367.495995.AE.
38. Moorman PG, Calingaert B, Palmieri RT, Iversen ES, Bentley RC, Halabi S, et al. Hormonal risk factors for ovarian cancer in premenopausal and postmenopausal women. *Am J Epidemiol*. 2008 May 1;167(9):1059–69. doi: 10.1093/aje/kwn006.
39. Tung KH, Goodman MT, Wu AH, McDuffie K, Wilkens LR, Kolonel LN, et al. Reproductive factors and epithelial ovarian cancer risk by histologic type: a multiethnic case-control study. *Am J Epidemiol*. 2003 Oct 1;158(7):629–38. doi: 10.1093/aje/kwg177.
40. Collaborative Group on Hormonal Factors in Breast Cancer. Menarche, menopause, and breast cancer risk: individual participant meta-analysis, including 118 964 women with breast cancer from 117 epidemiological studies. *Lancet Oncol*. 2012 Nov;13(11):1141–51. doi: 10.1016/S1470-2045(12)70425-4.
41. Boyd NF, Guo H, Martin LJ, Sun L, Stone J, Fishell E, et al. Mammographic density and the risk and detection of breast cancer. *N Engl J Med*. 2007 Jan 18;356(3):227–36. doi: 10.1056/NEJMoa062790.
42. Shen Y, Xia J, Li H, Xu Y, Xu S. Human papillomavirus infection rate, distribution characteristics, and risk of age in pre- and postmenopausal women. *BMC Womens Health*. 2021 Feb 25;21(1):80. doi: 10.1186/s12905-021-01217-4.
43. Ruth KS, Day FR, Hussain J, Martínez-Marchal A, Aiken CE, Azad A, et al. Genetic insights into biological mechanisms governing human ovarian ageing. *Nature*. 2021 Aug;596(7872):393–7. doi: 10.1038/s41586-021-03779-7.

EARLY MENOPAUSE

Keywords: Early menopause, definition, diagnostic challenges, risks, benefits, management



INTRODUCTION

Menopause is a natural biological milestone of ageing, most commonly occurring between ages 45 and 55, with a global average around 50–52 years. The World Health Organisation recognises this age range as typical for natural menopause, while also acknowledging substantial regional and individual variation driven by genetic, ethnic, socioeconomic, nutritional, and lifestyle factors.¹ Population-based data demonstrate marked international differences in the mean age at menopause. According to World Population Review (2025), the average age of menopause is highest in Northern and Western Europe and Oceania, 52.7 years in Norway, 51.7 years in Spain, and 51.5 years in New Zealand and lowest in several low- and middle-income regions, including Turkey and Egypt (47 years) and India (46.5 years).² These variations underscore the importance of contextualising menopause-related definitions and clinical thresholds within regional demographic patterns.

DEFINITION

Early menopause (EM) is defined as the permanent cessation of ovarian function occurring between ages 40 and 45. This terminology was introduced by the International Menopause Society and subsequently endorsed by the North American Menopause Society and the European Menopause and Andropause Society to distinguish EM from premature ovarian insufficiency (POI) and menopause occurring at the average age.^{3–5} In the Indian context, epidemiological studies frequently use a statistical cutoff of < 42 years to define EM; however, for clinical practice and international harmonisation, a threshold of < 45 years is recommended and retained in contemporary guidelines.

The diagnosis of EM is frequently delayed and may be associated with significant emotional and psychological distress, particularly among women with ongoing fertility aspirations. EM is a continuum between POI and age at natural menopause (ANM), rather than as a discrete pathological entity.⁶ The medical implications for health indicate that EM needs medical attention.

Diagnosis is often straightforward when a clear iatrogenic cause, such as bilateral oophorectomy, chemotherapy, or pelvic radiotherapy, is present. In contrast, spontaneous EM poses diagnostic challenges. Women may present with secondary amenorrhoea, vasomotor symptoms (VMS), or both, prompting the need for biochemical confirmation. In certain situations, such as hysterectomy with ovarian conservation or use of long-acting progestogen contraception, diagnosis relies primarily on symptomatology and hormonal assessment rather than menstrual history. Currently, there are no universally accepted diagnostic criteria for early menopause following cancer treatment, where ovarian function may be transient, fluctuating, or partially preserved.⁶

EPIDEMIOLOGY

EM is relatively common, affecting approximately 8% of women in high-income countries and around 12% of women globally, with menopause occurring between 40 and 44 years of age.^{6,7} In India, the prevalence of EM is substantially higher. Analyses from the National Family Health Survey (NFHS) and other population-based studies report prevalence estimates ranging from 16% to over 20%, reflecting both biological and social determinants.^{8,9} Recent data suggest a modest decline in prevalence from approximately 21–24% in earlier decades to 16–17% in more recent cohorts, possibly related to improvements in nutrition, healthcare access, and socioeconomic conditions.¹⁰

Limitations: include that most available data on EM are cross-sectional and rely on self-reported age at menopause, which introduces recall bias. The distinction between natural and surgically induced menopause is inconsistent, although recent NFHS-5-based analyses have attempted to address this limitation. Significant regional and state-level heterogeneity exists within India, highlighting the need for more granular data. Longitudinal Indian studies examining long-term outcomes, particularly bone health, cardiovascular disease, and cognitive ageing, are limited.

FACTORS ASSOCIATED WITH EARLY MENOPAUSE

ANM is strongly influenced by genetic factors, with family history among the most consistent predictors. Retrospective and cohort studies report a six- to eight-fold increased risk of menopause before 45 years among women with a maternal history of EM or POI.¹¹⁻¹³ Consequently, screening for early ovarian ageing is likely to be most effective when targeted to high-risk groups, particularly women with a positive family history.¹⁴ Non-genetic and acquired factors also play a significant role. Iatrogenic causes include chemotherapy, pelvic radiotherapy, salpingectomy, uterine artery embolisation, and other pelvic surgeries, all of which may compromise ovarian reserve.^{15,16} Pelvic infections, tubal disease, severe endometriosis, and heavy smoking have been associated with earlier menopause through direct or indirect ovarian damage.¹⁷⁻¹⁹

Sociodemographic factors influence menopausal timing. Earlier menopause has been reported among women of Black, Latina, and Asian ethnicity compared with White populations. Lower educational attainment and lower socioeconomic status are consistently associated with earlier age at menopause, reflecting broader health and nutrition inequities.^{20,21} Lifestyle factors are modifiable contributors. Cigarette smoking is associated with menopause occurring 1–2 years earlier, likely due to the toxic effects of polycyclic aromatic hydrocarbons on ovarian follicles.^{22,23} Higher alcohol intake and chronic psychosocial stress have also been linked to earlier menopause in some populations.^{24,25}

Reproductive factors are important modifiers. Nulliparity, lower parity, and non-use of oral contraceptives are associated with increased risk of early menopause. In pooled analyses from the InterLACE consortium, nulliparous women were twice as likely to develop POI and had a 30% higher risk of EM compared with women with two or more children.²⁶ Early life and in-utero exposures may influence ovarian ageing. Lower birth weight and prenatal exposure to diethylstilbestrol have been associated with an increased risk of early natural menopause, supporting a developmental origins hypothesis.²⁷

Environmental and medical factors such as low body mass index, chronic weight loss, high-altitude residence, treatment for childhood cancer, epilepsy, and long-term psychotropic medication use have also been associated with earlier menopausal onset.^{28,29}

PATHOPHYSIOLOGY

The timing of menopause reflects the rate of ovarian follicle depletion and ovulatory activity. In women at risk of EM, accelerated oocyte loss and early decline in inhibin secretion lead to a compensatory rise in follicle-stimulating hormone (FSH) levels. Genetic variations, including estrogen receptor polymorphisms, may further modulate ovarian ageing and advance the timing of menopause.³⁰

EFFECTS OF EARLY MENOPAUSE

Women with EM or POI have a substantially increased risk of adverse long-term health outcomes, including cardiovascular disease (CVD), type 2 diabetes mellitus, osteoporosis, fractures, neurocognitive decline, and all-cause mortality.³¹⁻⁴⁰ ANM is increasingly recognised as a biomarker of biological ageing and future health risk.⁴¹ EM is associated with increased risks of all-cause mortality, CVD, psychiatric disorders, osteoporosis, psychosexual dysfunction, and mood disturbances, while conferring a reduced risk of hormone-dependent breast cancer. Timely lifestyle interventions and appropriate menopausal hormone therapy (MHT) may mitigate many adverse outcomes.

BONE AND MUSCULOSKELETAL HEALTH

Early estrogen deficiency results in accelerated bone loss, particularly in the first years after menopause, leading to higher lifetime risks of osteoporosis and fragility fractures.^{37,38} Longitudinal data demonstrate increased fracture risk, higher osteoporosis prevalence, and greater need for anti-osteoporosis therapy among women with EM, although treatment rates remain suboptimal.³⁹ Emerging evidence also links EM and POI to reduced muscle mass, strength, and performance, suggesting an increased risk of sarcopenia.⁴²⁻⁴⁴

NEUROLOGICAL AND COGNITIVE OUTCOMES

Bilateral oophorectomy before the ANM is associated with an approximately two-fold increased risk of cognitive impairment or dementia and Alzheimer's disease (AD) and with a greater risk at younger ages of estrogen deprivation.⁴⁵⁻⁴⁷ Importantly, initiation of estrogen therapy soon after oophorectomy and continuation until at least

the average ANM appears to mitigate this risk.⁴⁸ In contrast, the risk of Parkinsonism is increased following premenopausal oophorectomy and does not appear to be attenuated by estrogen therapy.⁴⁹

MORTALITY

EM is associated with reduced life expectancy and increased all-cause and cause-specific mortality, particularly from cardiovascular causes.³² Population-based cohorts consistently demonstrate higher mortality among women experiencing menopause before 45 years compared with those reaching menopause at the average age of 40.

CARDIOVASCULAR AND METABOLIC HEALTH

Earlier age at menopause is consistently associated with higher risks of coronary heart disease, stroke, and cardiovascular mortality, with risk increasing in a near-linear fashion for each year decrease in menopausal age.³¹⁻³³ Women with menopause before 45 years have a 1.3–2-fold higher risk of non-fatal cardiovascular events before age 60 compared with those reaching menopause at 50–51 years.⁴⁰ Data from the Multi-Ethnic Study of Atherosclerosis demonstrate that women who underwent menopause before 45 years had a 66% higher risk of incident heart failure compared with those experiencing menopause at later ages, with an approximately 4% reduction in risk for each additional year of delay in menopause.⁵⁰ Similarly, EM independently predicts future coronary heart disease and stroke.³³ Both natural and surgically induced early menopause confer increased cardiovascular risk, with risk being greatest following early bilateral salpingo-oophorectomy.⁵¹

EM is also associated with a higher risk of type 2 diabetes, independent of conventional cardiometabolic risk factors.^{35,36}

RISK OF CANCER

In contrast, EM is associated with a reduced risk of estrogen-sensitive malignancies. Women experiencing menopause before 45 years have a 27% lower risk of breast cancer and a 33% lower risk in those with POI, reflecting reduced lifetime estrogen exposure.⁵² Menarche and menopause may influence breast cancer risk through mechanisms beyond simply extending reproductive lifespan. Ovarian hormones play a stronger role in estrogen receptor-positive cancers than in receptor-negative ones, and are more strongly linked to lobular than ductal tumours.⁵³

Beyond cardiometabolic and oncologic outcomes, women with EM may experience difficulties adapting to changes in self-image, sexual dysfunction, and loss of fertility related to premature estrogen deprivation.

SYMPTOMS OF EARLY MENOPAUSE

The clinical manifestations of EM are similar to those of menopause at the average age. Symptoms are heterogeneous and may vary in severity, duration, and impact on quality of life.

DIAGNOSIS

There is currently no validated biomarker that reliably predicts the onset of early menopause. Diagnosis remains clinical and is based on 12 months of amenorrhoea in women aged 40–45 years, after exclusion of other causes. Clinical features of estrogen deficiency may include skin dryness, frontal hair thinning, hirsutism, and vulvovaginal atrophy. Vaginal cytology may show an increased vaginal pH and a reduced maturation index.

LABORATORY AND IMAGING EVALUATION

Initial Investigations as clinically indicated

- *Serum FSH*: Levels > 40 IU/L on two occasions at least four weeks apart support the diagnosis
- *TSH (Thyroid Stimulating Hormone)*: To exclude thyroid dysfunction that may mimic menopausal symptoms
- *Cardiovascular risk assessment*: Lipid profile, glucose status, blood pressure
- *Bone health*: Bone Mineral Density (BMD) testing when clinically indicated
- *Anti-Müllerian hormone (AMH)*: Ultrasensitive assays are under investigation for the prediction of menopausal timing, but are not currently recommended for routine diagnosis
- *Inhibin B*: Levels decline with ovarian failure but have limited clinical utility

- *Pelvic ultrasonography:* Reduced ovarian volume and antral follicle count are supportive findings but not diagnostic
- *Exclusion of Other Causes:* Pregnancy, polycystic ovary syndrome, low body weight, excessive exercise, eating disorders, and medication-induced menstrual disturbances should be excluded.

LIFE STYLE MANAGEMENT

MANAGEMENT

Women with EM should receive structured counselling regarding the short- and long-term health implications, including cardiovascular, skeletal, cognitive, sexual, and psychological outcomes. Shared decision-making is essential, with agreement on individualised goals of care to enable informed choices regarding lifestyle measures, menopausal hormone therapy, and long-term surveillance. All women with EM should receive counselling on lifestyle measures aimed at reducing long-term cardiometabolic and skeletal risk.³¹ This includes optimising diet, maintaining a healthy body weight, engaging in regular weight-bearing and muscle-strengthening exercise, smoking cessation, moderating alcohol intake, and adequate intake of calcium and vitamin D. These interventions are essential but not sufficient alone to counteract the adverse effects of prolonged estrogen deficiency. Psychological support and referral to a psychologist or sex therapist may be beneficial for selected women.³¹

HORMONE THERAPY

In the absence of contraindications, systemic estrogen replacement is recommended until at least the average ANM (50–52 years) to reduce the adverse effects of prolonged estrogen deficiency.³¹ A 2012, a study found that VMS increased for about 3 months after risk-reducing salpingo-oophorectomy, and then remains stable over the next year. Hormone therapy (HT) lessens these symptoms and may improve quality of life, but does not restore them to pre-oophorectomy levels.⁵⁴ The choice of terminology, menopausal hormone therapy (MHT) versus hormone replacement therapy (HRT), remains debated in the context of EM, pending more robust data clarifying the long-term consequences and optimal framing of estrogen replacement in this population. Most international guidelines, including those from the North American Menopause Society, International Menopause Society, British Menopause Society, and Global Consensus panels, advise offering MHT to women with EM who do not have contraindications.^{3,55-57}

MHT is preferred over combined oral contraceptives for long-term management in EM, as serious adverse effects of oral contraceptives increase with age, whereas MHT provides physiologic estrogen replacement at lower doses. Higher estrogen doses may be required in some women with EM or POI to approximate premenopausal estradiol concentrations, particularly in younger women or those with persistent symptoms.

BENEFITS AND LIMITATIONS OF MENOPAUSAL HORMONE THERAPY IN EARLY

MENOPAUSE

MHT is highly effective for treating VMS and genitourinary symptoms and is associated with preserved bone mineral density and reduced fracture risk.^{1,2,8} It may also attenuate cardiovascular and neurocognitive consequences of early estrogen deprivation, particularly when initiated soon after menopause.^{6,29} However, evidence supporting the prevention of all long-term outcomes remains incomplete. There are no randomised controlled trials of MHT specifically in women with EM or POI, and observational data suggest cardiovascular benefit may be greater following surgical EM than spontaneous EM.⁹ Evidence regarding breast cancer risk in this population is also limited.⁵² EM necessitates a proactive approach to bone health. BMD assessment is recommended in women experiencing menopause before the age of 45 years, given the increased risk of spine and hip fractures before the age of 70 years.³⁴ EM should also be considered an important factor in cardiovascular risk stratification. These women may require closer monitoring of cardiovascular risk factors and earlier preventive interventions in routine clinical practice.²⁹

PSYCHOLOGICAL AND REPRODUCTIVE COUNSELLING

Women with EM, particularly those with POI or bilateral salpingo-oophorectomy, may experience significant psychological distress related to loss of fertility, altered self-image, sexual dysfunction, and concerns about long-term health. Psychological support and referral to a mental health professional or sex therapist should be offered when indicated.

SYNOPSIS

- EM refers to menopause occurring between 40 and 45 years, distinct from premature ovarian insufficiency and menopause at the average age.
- EM is associated with increased risks of cardiovascular disease, type 2 diabetes, osteoporosis and fractures, sarcopenia, neurocognitive decline, and all-cause mortality, with a higher risk following surgically induced menopause.
- EM confers a reduced risk of estrogen-dependent cancers (breast, endometrial, ovarian), but this does not offset the overall increase in cardiometabolic, skeletal, and mortality risks.
- Diagnosis is clinical, supported by biochemical testing; no validated biomarker reliably predicts early menopause.
- Care should be proactive and life-course oriented, incorporating lifestyle optimisation, psychological and fertility counselling, and long-term bone and cardiovascular surveillance.
- In the absence of contraindications, MHT is recommended until at least the average age of natural menopause.
- Findings from older postmenopausal women should not be extrapolated to EM; despite strong observational data, randomised evidence remains limited.

RESEARCH AGENDA

Establish prospective cohorts of Indian women to evaluate long-term cardiovascular, skeletal, cognitive, and mortality outcomes following EM.

REFERENCES

1. World Population Review. Average Age of Menopause by Country. 2025. Available from: <https://worldpopulationreview.com/country-rankings/age-of-menopause-by-country> (Accessed 7 February 2026).
2. Jaff NG, Crowther NJ. Menopause in low and middle-income countries – an untold story. *Climacteric*. 2025;28(3):217–9. <https://doi.org/10.1080/13697137.2025.2513140>
3. Baber RJ, Panay N, Fenton A, IMS Writing Group. 2016 IMS Recommendations on women's midlife health and menopause hormone therapy. *Climacteric*. 2016;19(2):109–50. <https://doi.org/10.3109/13697137.2015.1129166>
4. The 2022 hormone therapy position statement of The North American Menopause Society. *Menopause*. 2022;29(7):767–94. <https://doi.org/10.1097/gme.0000000000002028>
5. European Menopause and Andropause Society. EMAS position statements on menopause terminology and management. *Maturitas*. 2019;2022 updates. Available from: <https://www.sciencedirect.com/special-issue/10FXTFDFOSW>
6. Mishra GD, Davies MC, Hillman S, Chung HF, Roy S, Maclaran K, et al. Optimising health after early menopause. *Lancet*. 2024;403(10430):958–68. [https://doi.org/10.1016/S0140-6736\(23\)02800-3](https://doi.org/10.1016/S0140-6736(23)02800-3)
7. Mishra GD, Chung HF, Cano A, et al. Age at natural menopause and associated factors. *Hum Reprod Update*. 2019;25(4):469–86. <https://doi.org/10.1093/humupd/dmz008>
8. Meher T, Sahoo H. Premature menopause among women in India: Evidence from National Family Health Survey-IV. *J Obstet Gynaecol Res*. 2021;47(12):4426–39. <https://doi.org/10.1111/jog.15041>
9. Pallikadavath S, Ogollah R, Singh A, Dean T, Dewey A, Stones W. Natural menopause among women below 50 years in India. *Indian J Med Res*. 2016;144(3):366–77. <https://doi.org/10.4103/0971-5916.198676>
10. Kundu S, Acharya SS. Exploring the triggers of premature and early menopause in India: a comprehensive analysis based on National Family Health Survey, 2019–2021. *Sci Rep*. 2024;14(1):3040. <https://doi.org/10.1038/s41598-024-53536-9>
11. van Noord PAH, Dubas JS, Dorland M, Boersma H, te Velde ER. Age at natural menopause in a population-based screening cohort: the role of menarche, fecundity, and lifestyle factors. *Fertil Steril*. 1997;68(1):95–102. [https://doi.org/10.1016/s0015-0282\(97\)81482-3](https://doi.org/10.1016/s0015-0282(97)81482-3)
12. Cresswell JL, Egger P, Fall CHD, Osmond C, Fraser RB, Barker DJP. Is the age of menopause determined in-utero? *Early Hum Dev*. 1997;49(2):143–8. [https://doi.org/10.1016/s0378-3782\(97\)00028-5](https://doi.org/10.1016/s0378-3782(97)00028-5)
13. Treloar SA, Do KA, Martin NG. Genetic influences on the age at menopause. *Lancet*. 1998;352(9134):1084–5. [https://doi.org/10.1016/s0140-6736\(05\)79753-1](https://doi.org/10.1016/s0140-6736(05)79753-1)
14. Mishra GD, Chung HF, Cano A, Chedraui P, Goulis DG, Lopes P, et al. EMAS position statement: Predictors of premature and early natural menopause. *Maturitas*. 2019;123:82–8. <https://doi.org/10.1016/j.maturitas.2019.03.008>
15. Lass A, Ellenbogen A, Croucher C, Trew G, Margara R, Becattini C, et al. Effect of salpingectomy on ovarian response to superovulation in an in vitro fertilization-embryo transfer program. *Fertil Steril*. 1998;70(6):1035–8. [https://doi.org/10.1016/s0015-0282\(98\)00357-4](https://doi.org/10.1016/s0015-0282(98)00357-4)

16. Tulandi T, Sammour A, Valenti D, Child TJ, Seti L, Tan SL. Ovarian reserve after uterine artery embolization for leiomyomata. *Fertil Steril*. 2002;78(1):197–8. [https://doi.org/10.1016/s0015-0282\(02\)03164-3](https://doi.org/10.1016/s0015-0282(02)03164-3)
17. Keay SD, Liversedge NH, Jenkins JM. Could ovarian infection impair ovarian response to gonadotrophin stimulation? *BJOG*. 1998;105(3):252–4. <https://doi.org/10.1111/j.1471-0528.1998.tb10082.x>
18. Barnhart K, Dunsmoor-Su R, Coutifaris C. Effect of endometriosis on in vitro fertilization. *Fertil Steril*. 2002;77(6):1148–55. [https://doi.org/10.1016/s0015-0282\(02\)03112-6](https://doi.org/10.1016/s0015-0282(02)03112-6)
19. Feichtinger W, Papalambrou K, Poehl M, Krischker U, Neumann K. Smoking and In Vitro Fertilization: A Meta-Analysis. *J Assist Reprod Genet*. 1997;14(10):596–9. <https://doi.org/10.1023/a:1022584802711>
20. Gold EB. The Timing of the Age at Which Natural Menopause Occurs. *Obstet Gynecol Clin North Am*. 2011;38(3):425–40. <https://doi.org/10.1016/j.ogc.2011.05.002>
21. Gold EB, Bromberger J, Crawford S, et al. Factors Associated with Age at Natural Menopause in a Multiethnic Sample of Midlife Women. *Am J Epidemiol*. 2001;153(9):865–74. <https://doi.org/10.1093/aje/153.9.865>
22. Augood C, Duckitt K, Templeton AA. Smoking and female infertility: a systematic review and meta-analysis. *Hum Reprod*. 1998;13(6):1532–9. <https://doi.org/10.1093/humrep/13.6.1532>
23. Mishra A, Khan SA, Jadhav K, Mehrotra N. Inhaling Risk: Smoking Impact on Male and Female Reproductive Health. *Biosci Biotech Res Asia*. 2025;22(1):23–35. <https://doi.org/10.13005/bbra/3338>
24. Peycheva D, Sullivan A, Hardy R, Bryson A, Conti G, Ploubidis G. Risk factors for natural menopause before the age of 45: evidence from two British population-based birth cohort studies. *BMC Womens Health*. 2022;22(1):438. <https://doi.org/10.1186/s12905-022-02021-4>
25. Bromberger JT, Meyer PM, Kravitz HM, Sommer B, Cordal A, Powell L, et al. Psychologic Distress and Natural Menopause: A Multiethnic Community Study. *Am J Public Health*. 2001;91(9):1435–42. <https://doi.org/10.2105/ajph.91.9.1435>
26. Mishra GD, Pandeya N, Dobson AJ, Chung HF, Anderson D, Kuh D, et al. Early menarche, nulliparity and the risk for premature and early natural menopause. *Hum Reprod*. 2017;32(3):679–86. <https://doi.org/10.1093/humrep/dew350>
27. Langton CR, Whitcomb BW, Purdue-Smithe AC, Sievert LL, Hankinson SE, Manson JE, et al. Association of In Utero Exposures With Risk of Early Natural Menopause. *Am J Epidemiol*. 2022;191(5):775–86. <https://doi.org/10.1093/aje/>
28. Kapoor AK, Kapoor S. The effects of high altitude on age at menarche and menopause. *Int J Biometeorol*. 1986;30(1):21–6. <https://doi.org/10.1007/bf02192054>
29. Beall CM. Ages at menopause and menarche in a high altitude Himalayan population. *Contributions to Nepalese Studies, Centre for Nepal and Asian Studies (CNAS), Tribhuvan University (TU), Kathmandu, Nepal*. Volume 9, Number 1 & 2, December 1981/June 1982 (Poush 2038/Ashad 2039).
30. Weel AE, Uitterlinden AG, Westendorp IC, Burger H, Schuit SC, Hofman A, Helmerhorst TJ, van Leeuwen JP, Pols HA. Estrogen receptor polymorphism predicts the onset of natural and surgical menopause. *J Clin Endocrinol Metab*. 1999 Sep;84(9):3146–50. doi: 10.1210/jcem.84.9.5981. PMID: 10487678.
31. Faubion SS, Kuhle CL, Shuster LT, Rocca WA. Long-term health consequences of premature or early menopause and considerations for management. *Climacteric*. 2015;18(4):483–91. <https://doi.org/10.3109/13697137.2015.1020484>
32. Muka T, Oliver-Williams C, Kunutsor S, Laven JSE, Fauser BCJM, Chowdhury R, et al. Association of Age at Onset of Menopause and Time Since Onset of Menopause With Cardiovascular Outcomes, Intermediate Vascular Traits, and All-Cause Mortality. *JAMA Cardiol*. 2016;1(7):767–76. <https://doi.org/10.1001/jamacardio.2016.2415>
33. Wellons M, Ouyang P, Schreiner PJ, Herrington DM, Vaidya D. Early menopause predicts future coronary heart disease and stroke. *Menopause*. 2012;19(10):1081–7. <https://doi.org/10.1097/gme.0b013e3182517bd0>
34. Wang J, Chen Y. Age at menopause and risk of ischaemic stroke: a systematic review and meta-analysis. *Eur J Prev Cardiol*. 2024;31(13):1595–605. <https://doi.org/10.1093/eurjpc/zwae156>
35. Anagnostis P, Christou K, Artzouchaltzi AM, Gkekas NK, Kosmidou N, Siolos P, et al. Early menopause and premature ovarian insufficiency are associated with increased risk of type 2 diabetes: a systematic review and meta-analysis. *Eur J Endocrinol*. 2019;180(1):41–50. <https://doi.org/10.1530/EJE-18-0602>
36. Sekhar TV, Medarametla S, Rahman A, Adapa SS. Early Menopause in Type 2 Diabetes - A Study from a South Indian Tertiary Care Centre. *J Clin Diagn Res*. 2015;9(10):OC08–10. <https://doi.org/10.7860/JCDR/2015/14181.6628>
37. Jones AR, Enticott J, Ebeling PR, Mishra GD, Teede HT, Vincent AJ. Bone health in women with premature ovarian insufficiency/early menopause: a 23-year longitudinal analysis. *Hum Reprod*. 2024;39(5):1013–22. <https://doi.org/10.1093/humrep/deae037>
38. Francucci CM, Romagni P, Camilletti A, Fisaletti P, Amoroso L, Cenci G, et al. Effect of natural early menopause on bone mineral density. *Maturitas*. 2008;59(4):323–8. <https://doi.org/10.1016/j.maturitas.2008.03.008>
39. Svejme O, Ahlberg HG, Nilsson JÅ, Karlsson MK. Early menopause and risk of osteoporosis, fracture and mortality: a 34-year prospective observational study in 390 women. *BJOG*. 2012 Jun;119(7):810–6. doi: 10.1111/j.1471-0528.2012.03324.x. Epub 2012 Apr 25. PMID: 22531019.
40. Xu Z, Chung HF, Dobson AJ, Wilson LF, Hickey M, Mishra GD. Menopause, hysterectomy, menopausal hormone therapy and cause-specific mortality: cohort study of UK Biobank participants. *Hum Reprod*. 2022;37(9):2175–85. <https://doi.org/10.1093/humrep/deac137>
41. Singh M. Early age of natural menopause in India, a biological marker for early preventive health programs. *Climacteric*. 2012;15(6):581–6. <https://doi.org/10.3109/13697137.2011.643514>
42. Divaris E, Anagnostis P, Gkekas NK, Kouidi E, Goulis DG. Early menopause and premature ovarian insufficiency may increase the risk of sarcopenia: A systematic review and meta-analysis. *Maturitas*. 2023;175:107782. <https://doi.org/10.1016/j.maturitas.2023.05.006>
43. Li S, Ma L, Huang H, Lou Z, Qi T, Huang Y, et al. Loss of muscle mass in women with premature ovarian insufficiency as compared with healthy controls. *Menopause*. 2022;30(2):122–7. <https://doi.org/10.1097/gme.0000000000002120>
44. Kalra S, Shaikh I, Shende S, Kapoor N, Unnikrishnan A, Sharma O, et al. An Indian Consensus on Sarcopenia: Epidemiology, Etiology, Clinical Impact, Screening, and Therapeutic Approaches. *Int J Gen Med*. 2025;18:1731–45. <https://doi.org/10.2147/ijgm.s510412>
45. Rocca WA, Bower JH, Maraganore DM, Ahlskog JE, Grossardt BR, de Andrade M, et al. Increased risk of cognitive impairment or dementia in women who underwent oophorectomy before menopause. *Neurology*. 2007;69(11):1074–83. <https://doi.org/10.1212/01.wnl.0000276984.19542.e6>

46. Bove R, Secor E, Chibnik LB, Barnes LL, Schneider JA, Bennett DA, et al. Age at surgical menopause influences cognitive decline and Alzheimer pathology in older women. *Neurology*. 2014;82(3):222–9. <https://doi.org/10.1212/wnl.0000000000000033>
47. Rocca WA, Shuster LT, Grossardt BR, Maraganore DM, Gostout BS, Geda YE, et al. Long-Term Effects of Bilateral Oophorectomy on Brain Aging: Unanswered Questions from the Mayo Clinic Cohort Study of Oophorectomy and Aging. *Womens Health (Lond)*. 2009;5(1):39–48. <https://doi.org/10.2217/17455057.5.1.39>
48. Rocca WA, Grossardt BR, Shuster LT. Oophorectomy, menopause, estrogen treatment, and cognitive aging: clinical evidence for a window of opportunity. *Brain Res*. 2011 Mar 16;1379:188–98. doi: 10.1016/j.brainres.2010.10.031. Epub 2010 Oct 18. PMID: 20965156; PMCID: PMC3046246.
49. Rocca WA, Bower JH, Maraganore DM, Ahlskog JE, Grossardt BR, de Andrade M, et al. Increased risk of parkinsonism in women who underwent oophorectomy before menopause. *Neurology*. 2008;70(3):200–9. <https://doi.org/10.1212/01.wnl.0000280573.30975>.
50. Ebong IA, Watson KE, Goff DC, Bluemke DA, Srikanthan P, Horwich T, et al. Age at menopause and incident heart failure. *Menopause*. 2014;21(6):585–91. <https://doi.org/10.1097/gme.0000000000000138>
51. Parker WH, Broder MS, Liu Z, Shoupe D, Farquhar C, Berek JS. Ovarian conservation at the time of hysterectomy for benign disease. *Obstet Gynecol*. 2005;106(2):219–26. doi: 10.1097/01.AOG.0000167394.38215.56.
52. Monninkhof EM, van der Schouw YT, Peeters PH. Early age at menopause and breast cancer: are leaner women more protected? A prospective analysis of the Dutch DOM cohort. *Breast Cancer Res Treat*. 1999 Jun;55(3):285–91. doi: 10.1023/a:1006277207963. PMID: 10517172.
53. Menarche, menopause, and breast cancer risk: individual participant meta-analysis, including 118,964 women with breast cancer from 117 epidemiological studies. *Lancet Oncol*. 2012;13(11):1141–51. [https://doi.org/10.1016/s1470-2045\(12\)70425-4](https://doi.org/10.1016/s1470-2045(12)70425-4)
54. Hickey M, Moss KM, Krejany EO, Wrede CD, Brand A, Kirk J, et al. What happens after menopause? (WHAM): A prospective controlled study of vasomotor symptoms and menopause-related quality of life 12 months after premenopausal risk-reducing salpingo-oophorectomy. *Gynecol Oncol*. 2021;163(1):148–54. <https://doi.org/10.1016/j.ygyno.2021.07.029>
55. The 2012 Hormone Therapy Position Statement of The North American Menopause Society. *Menopause*. 2012;19(3):257–71. <https://doi.org/10.1097/gme.0b013e31824b970a>
56. de Villiers TJ, Gass MLS, Haines CJ, Hall JE, Lobo RA, Pierroz DD, et al. Global Consensus Statement on Menopausal Hormone Therapy. *Climacteric*. 2013;16(2):203–4. <https://doi.org/10.3109/13697137.2013.771520>
57. Meeta M, Digumarti L, Agarwal N, Vaze N, Shah R, Malik S. Clinical practice guidelines on menopause: An executive summary and recommendations: Indian Menopause Society 2019–2020. *J Mid-life Health*. 2020;11(2):55–69. https://doi.org/10.4103/jmh.jmh_137_20

PREMATURE OVARIAN INSUFFICIENCY

48

Keywords: premature menopause, premature ovarian insufficiency, hormone therapy, cardiometabolic health, bone health, fertility, oocyte donation

INTRODUCTION

Menopause marks the culmination of ovarian ageing. Age-related progressive loss of ovarian follicles leads to menstrual irregularity; reduced oocyte quality leads to declining fertility and eventual cessation of menses. Reduced ovarian feedback causes rising follicle-stimulating hormone (FSH) levels, while the diminishing antral follicle pool is reflected by declining anti-Müllerian hormone (AMH) levels. Wide individual variation in ovarian ageing accounts for the broad range in age at natural menopause.¹ Premature Ovarian Insufficiency (POI) is characterised by a continuum of impaired ovarian function before the age of 40 years, resulting in hypoestrogenism and amenorrhoea.²

POI has wide-ranging physical and psychological consequences, affecting bone, cardiovascular, cognitive, and reproductive health, often with delayed diagnosis.^{3,4} Hormone replacement therapy (HRT) is essential to relieve symptoms and protect long-term health and should be continued until the average age of natural menopause.³

TERMINOLOGY

POI is characterised by a premature decline in normal ovarian hormone production, leading to elevated gonadotropin levels and a state of hypergonadotropic hypogonadism. Premature ovarian failure and primary ovarian failure are terms that are no longer recommended because they carry negative connotations and are biologically inaccurate. POI is the preferred term to describe ovarian dysfunction resulting from a primary defect at the ovarian level, with loss of function occurring earlier than expected for age.⁵ Moreover, insufficiency is favoured over failure because ovarian function can be intermittent and unpredictable, with spontaneous ovulation and pregnancy occurring in 5–10% of women, sometimes many years after diagnosis.⁶

Ovarian failure may present before puberty, after puberty, or following iatrogenic interventions. Prepubertal onset results in absent pubertal development and primary amenorrhoea, whereas postpubertal onset presents with secondary amenorrhoea before 40 years of age. Iatrogenic ovarian insufficiency occurs following gonadotoxic therapies or bilateral oophorectomy. All forms are characterised by amenorrhoea with hypergonadotropic hypoestrogenism.^{7,8}

DEFINITION AND DIAGNOSIS

POI is statistically defined as the onset of ovarian insufficiency occurring more than two standard deviations below the mean age of natural menopause in a given population. In Western populations, where the mean age of natural menopause is approximately 50–51 years, this corresponds to a cut-off age of 40 years.⁸ In India, the reported mean age of natural menopause is lower at approximately 46 years,⁹ which would theoretically suggest a lower statistical cut-off, corresponding to <38 years. However, robust population-based data to define population-specific thresholds are lacking. Therefore, Indian guidelines and expert consensus continue to define POI as occurring before age 40, ensuring clinical consistency and alignment with international standards.⁹

The 2025 updated European Society of Human Reproduction and Embryology (ESHRE) guideline defines premature ovarian insufficiency as disordered menstrual cycles, such as spontaneous amenorrhoea or oligomenorrhoea of ≥ 4 months in women aged <40 years, together with an elevated follicle-stimulating hormone (FSH) concentration >25 IU/L on any day of the cycle. A diagnosis can be made based on a single elevated FSH level. Repeat FSH testing after 4–6 weeks is required only if the diagnosis remains uncertain.⁸ Estradiol levels are supportive but not required for diagnosis. Anti-müllerian hormone (AMH) should not be used as a primary diagnostic test.

POI represents a spectrum of ovarian dysfunction ranging from occult to overt disease. While presentations may occur before or after puberty and may be spontaneous or iatrogenic, contemporary guidelines no longer classify POI into formal subtypes based on age at onset. The STRAW+10 model of reproductive ageing does not accommodate women with POI since the course of reproductive ageing is highly variable in such women.¹⁰

Phases of Primary Ovarian Insufficiency

Natural POI may evolve through a menopause transition (MT) like a continuum characterised by progressively impaired and disordered ovarian function. Recognition of early stages is important for fertility counselling, timely diagnosis, timely hormone therapy (HT), prevention of long-term sequelae and differentiation from diminished ovarian reserve and normal reproductive ageing.^{6,11} The evolution of POI can be viewed as a continuum, progressing from occult POI to overt POI.

Occult Premature Ovarian Insufficiency

Refers to impaired ovarian responsiveness to endogenous or exogenous gonadotropin stimulation despite regular ovulatory menstrual cycles. Fertility may be reduced even in the presence of normal cycle regularity. Evaluation may include early follicular phase (day-2/3) FSH and estradiol, AMH, and antral follicle count (AFC) on transvaginal ultrasound (TVS). An elevated day-3 FSH (typically >10–15 IU/L, assay-dependent), particularly when accompanied by elevated estradiol (>80 pg/mL), suggests compromised ovarian reserve and has historically been used to identify occult ovarian insufficiency.^{12,13} However, AMH and AFC are now considered more sensitive and reproducible markers of early ovarian dysfunction.¹⁴

Overt Premature Ovarian Insufficiency

Is characterised by irregular menses or amenorrhoea, persistently elevated gonadotropins, hypoestrogenism, and markedly reduced fertility in women younger than 40 years. Diagnosis requires elevated serum FSH > 25 IU on at least one occasion.⁸

Distinction from Diminished Ovarian Reserve (DOR)

Diminished ovarian reserve is a term used in the evaluation of infertility, referring to a reduced quantity or quality of oocytes as indicated by abnormal ovarian reserve tests (low AMH, low AFC) and/or a poor response to ovarian stimulation. Unlike POI, DOR can occur at any reproductive age, ovarian endocrine function may be preserved, and spontaneous conception remains possible.^{14,15}

POTENTIAL PREDICTORS OF PREMATURE OVARIAN INSUFFICIENCY

Identification of potential predictors of POI is important for early recognition of women at risk, timely fertility counselling and preservation, and prevention of long-term sequelae through appropriate monitoring and early intervention, despite the absence of a reliable population-level screening test.

History of genetic abnormalities: family history of premature or early menopause, autoimmune disorders, early menarche, nulliparity, cigarette smoking (with a clear dose–response relationship), low body mass index (BMI)/underweight status, prior ovarian or pelvic surgery, and exposure to gonadotoxic therapies.

Role of AMH: It is currently considered the most sensitive biochemical marker of diminished ovarian reserve, with improved reliability following the introduction of standardised automated assays.¹⁵ AMH is useful for assessing and predicting ovarian damage following iatrogenic insults, such as chemotherapy for breast cancer.¹⁶

TVS and AFC: TVS of ovarian volume and AFC, which are typically reduced in POI and generally correlate with AMH, reflect the functional rather than true ovarian reserve; in skilled hands, AFC predicts ovarian response as accurately as AMH, although AMH is often the more reproducible predictor in assisted reproduction.¹⁵

EPIDEMIOLOGY

In 2017, data from the InterLACE consortium (N=51,450) across Europe, Australia, and Japan reported that approximately 2% of women experience POI, and 7.6% experience EM. Early menarche (≤ 11 years) and nulliparity were independently associated with increased risk, with the highest risk observed when both factors coexisted, highlighting the influence of reproductive factors on ovarian ageing.¹⁷ A 2019 meta-analysis by Golezar S, et al. calculated the pooled prevalence of POI and EM as 3.7% (95% confidence interval: 3.1, 4.3) and 12.2% (95% confidence interval: 10.5, 14), respectively. The prevalence of POI was higher in countries with a medium or low Human Development Index. The global prevalence trend did not change over time.¹⁸ A 2023 systematic review and meta-analysis reported a global overall prevalence of POI among women of 3.5%. The highest prevalence of POI was 11.3% in North America, followed by South America (5.4%). In a developing country, the prevalence was 5.3%, higher

than 3.1% in a developed country. The trend in POI prevalence over the past 20 years was upward (although $p > 0.05$).¹⁹ A 2025 cross-sectional study that analysed data for 55 low-middle-income countries (LMICs) from the Demographic and Health Surveys (2013–2023) found that premature menopause ranged from 1.58% in the Eastern Mediterranean to 6.87% in Southern Africa, while early menopause ranged from 4.92% to 15.21% in the Americas. Overall, LMICs exhibit higher rates of POI and EM than high-income countries, highlighting the need for a global health approach to menopause due to its associated long-term health risks, particularly cardiovascular disease (CVD).²⁰

Population-based Indian data from the National Family Health Surveys (NFHS 3–5) show that the prevalence of POI is 1.5%–3% among women, while EM affects 8%–16%, with a national mean age at menopause of 46 years.^{21–23} When surgical menopause is included, state-level data suggest an overall POI (natural + induced) prevalence of 8.7% in Telangana and 8.2% in Andhra Pradesh and only 0.7% in Kerala.^{22–24} Low literacy, poor socioeconomic status, smoking, and adverse dietary patterns (including frequent consumption of fried or ultra-processed foods) and early age at menarche have been identified as factors associated with an earlier age at menopause.²¹

In a 2024 analysis in Scientific Reports, Kundu and Acharya observed a clear downward trend in both POI and EM in India over the past few decades. POI was most common in 1998–1999, affecting about 3.4% of women, declined to 2.76% by 2005–2006, remained relatively stable over the subsequent five years, and then fell further to 2.23% in the most recent NFHS-5 cycle (2019–2021). EM showed a similar pattern, with prevalence around 21% in the 1990s, a transient rise to 24% in 2005–2006, followed by a steady decline to 17.5% and subsequently to 16% in recent years. These findings suggest a gradual reduction in the proportion of Indian women experiencing POI and EM over time, probably reflecting broader improvements in social, nutritional, and reproductive health indicators, although the underlying causes were not directly examined in the study.²¹

Large-scale data from the National Family Health Survey-5 (NFHS-5) indicate that POI affects 5% of rural and 3% of urban Indian women, with substantial variation across states.²⁴ Key risk factors include surgical menopause, lower educational status, rural residence, female sterilisation, poorer socioeconomic status, and health insurance coverage. Women with the lowest education levels experience POI at rates nearly seven times higher than those with the highest education, a disparity largely due to early hysterectomy. Women from lower socio-economic backgrounds may undergo surgical interventions earlier, reflecting a lack of awareness of alternative treatments and over-reliance on surgical management. These findings highlight the urgent need for public health strategies to promote reproductive health education, improve access to conservative management, and carefully evaluate surgical indications to prevent POI and its long-term health consequences.²⁴ Analysis of data from Longitudinal Ageing Study in India (LASI-1) (N=25,256) revealed that 7.4% experienced POI, and 17.5% had EM.²⁵ These patterns were more pronounced in several southern states of the country. POI and EM were associated with area of residence (higher prevalence in rural areas), educational status (greater prevalence among women with higher education), working status (more common in currently working women), and alcohol consumption. The substantial burden of untimely menopause represents an important public health concern and highlights the need for targeted attention and region-specific interventions.²⁵

AETIOLOGY OF PREMATURE OVARIAN INSUFFICIENCY

POI may be spontaneous or induced.

SPONTANEOUS PREMATURE OVARIAN INSUFFICIENCY

Spontaneous POI accounts for the majority of cases, with the aetiology remaining idiopathic in approximately 70–90% of women.^{6,8} Although traditionally considered idiopathic, advances in molecular genetics have demonstrated that ovarian function depends on a complex network of pathways regulating folliculogenesis, oocyte survival, and steroidogenesis. POI is characterised by a strong familial and heterogeneous genetic background.^{26,27} Increasing attention has been focused on mutations in single genes that regulate follicle development and maturation, which may play a role in the pathogenesis of POI.²⁶

Genetic causes: X-chromosome abnormalities include deletions, inversions, duplications, balanced translocations, Turner syndrome (45, X and mosaics), Triple X syndrome (47, XXX), and fragile X mental retardation 1 (FMR1) premutation carrier status.^{6,26} Genetic syndromes associated with POI include ataxia telangiectasia, Fanconi anaemia, and premature aging syndromes such as Bloom and Werner syndromes, reflecting defects in deoxyribonucleic acid (DNA) repair and genome maintenance.^{27,28} Enzyme deficiencies implicated in POI include galactosaemia (GALT deficiency), 17 α -hydroxylase deficiency, and aromatase deficiency, which impair normal ovarian steroidogenesis and follicular survival.^{6,26}

Autoimmune causes: Autoimmune ovarian damage is reported in 4–30% of women with spontaneous POI, with autoantibodies and lymphocytic oophoritis documented in women with concomitant autoimmune diseases.^{29,30} In women with 46, XX spontaneous POI, serum adrenal cortex autoantibodies are strongly associated with histologically confirmed autoimmune oophoritis.³¹ POI commonly occurs in association with autoimmune thyroid disease (Graves's and Hashimoto's), primary adrenal insufficiency (Addison's disease), autoimmune polyglandular syndromes types I and II, and type 1 diabetes mellitus. Associations with non-endocrine autoimmune disorders, including systemic lupus erythematosus, pernicious anaemia, and myasthenia gravis, have also been described.^{29,30} The most clinically significant autoimmune association of POI is adrenal insufficiency. Evidence of adrenal autoimmunity and autoimmune oophoritis is found in approximately 2.5–20% of women with POI, while 10–20% of women with Addison's disease develop POI.

Infectious causes: Although uncommon, POI has been reported following viral and bacterial infections like mumps, cytomegalovirus, varicella, shigella, HIV and tuberculosis, and parasitic infections like malaria.^{6,32} In most cases, ovarian function recovers after the infection resolves. An infectious aetiology should be considered if symptoms follow a potential infectious exposure, such as travel or sick contact.³²

INDUCED PREMATURE OVARIAN INSUFFICIENCY

Iatrogenic causes

POI may occur following bilateral salpingo-oophorectomy in premenopausal women. Even after hysterectomy with ovarian conservation, menopause may occur approximately 3–4 years earlier than the expected age.³³ Ovarian failure can also result from ovarian surgery due to inadvertent loss of ovarian tissue or disruption of ovarian blood supply, including after uterine artery embolisation. Women undergoing hysterectomy were at nearly a twofold increased risk for POI as compared with women with intact uteri (hazard ratio [HR] 1.92, 95% confidence interval [CI] 1.29–2.86).³⁴

In 2007, a community-based study in rural Andhra Pradesh reported a mean age at hysterectomy of 28.5 years, with 60% of procedures performed before age 30. A substantial proportion of women underwent concomitant bilateral salpingo-oophorectomy, resulting in abrupt surgical menopause. Postoperative follow-up and hormone replacement therapy (HRT) were not provided, exposing young women to prolonged estrogen deficiency and its long-term health consequences.³⁵ Consequently, surgical menopause constituted a significant contributor to the burden of POI in India. More recent data, however, suggest a declining trend in hysterectomy rates and overall prevalence of POI.²¹

Gonadotoxic chemotherapy, particularly alkylating agents and anthracyclines, is a well-established cause of POI, and the risk is strongly influenced by the type of agent used, cumulative dose, treatment duration, and the woman's age at exposure, reflecting the age-related decline in the ovarian follicle pool.³⁶ The impact of radiotherapy on fertility depends on patient age, radiation dose to the ovaries and uterus, irradiation field (pelvic, abdominal, or hypothalamic–pituitary), and concurrent treatments. Ovarian follicles are highly radiosensitive; a dose as low as 2 Gy reduces the primordial follicle pool by 50%.³⁷

Iatrogenic factors, such as prolonged gonadotropin-releasing hormone (GnRH) agonist therapy, lead to reversible suppression of gonadotropin secretion and ovarian activity and are not associated with permanent POI. Although repeated ovulation induction and assisted reproductive treatments (ART) have been hypothesised to accelerate follicular depletion, available clinical and guideline-based evidence does not support a causal association with POI.^{8,38}

Environmental factors

Exposure to environmental toxins and endocrine-disrupting chemicals has been implicated in accelerated ovarian ageing and POI. Polycyclic aromatic hydrocarbons in cigarette smoke and endocrine disruptors such as phthalates and bisphenol-A have been associated with impaired ovarian reserve and earlier menopause.³⁹ Indoor air pollution, from sources such as smoke and pollutants, significantly increases the risk of early menopause among Indian women. Urban women are more affected by pollution, whereas indoor smoking impacts both urban and rural women.⁴⁰

DOES ETHNICITY OR EPIGENETICS MATTER?

Ovarian ageing appears to be influenced by genetic, environmental, and ethnic factors. Comparative studies have shown that Indian women have lower AMH levels despite being younger than age-matched European women, suggesting an accelerated decline in ovarian reserve and earlier reproductive ageing.⁴¹ Population data also indicate a younger median age at menopause among Indian women compared with white American women. Genetic factors

such as variations in FMR1 genotypes and mutations in NOBOX, a gene essential for early folliculogenesis, further support ethnic and genetic contributions to ovarian reserve dynamics.^{4,2} Emerging evidence suggests that ovarian ageing trajectories may begin in utero, as the primordial follicle pool is fixed at birth and susceptible to adverse influences such as poor nutrition and oxidative stress, potentially predisposing to early menopause.¹

There is increasing evidence that epigenetic ageing may begin as early as a few weeks post-conception in foetal tissues. It has been hypothesised that this process may start in utero. In an unpublished observational study (Sudha Sane, 2010; personal communication, courtesy: Rama Vaidya), histological examination of ovaries from stillborns with intrauterine growth restriction demonstrated ballooning degeneration of oocytes and a reduced total oocyte count compared with normal newborn ovaries (Figures 1 and 2). As the germ cell pool is fixed at birth and no postnatal proliferation occurs, such early depletion or damage may predispose to accelerated ovarian ageing and early menopause. These observations support the hypothesis that inadequate intrauterine nourishment and increased oxidative stress may have a detrimental effect on oocyte quantity and quality.

Figure 1. Normal oocytes in new born ovaries

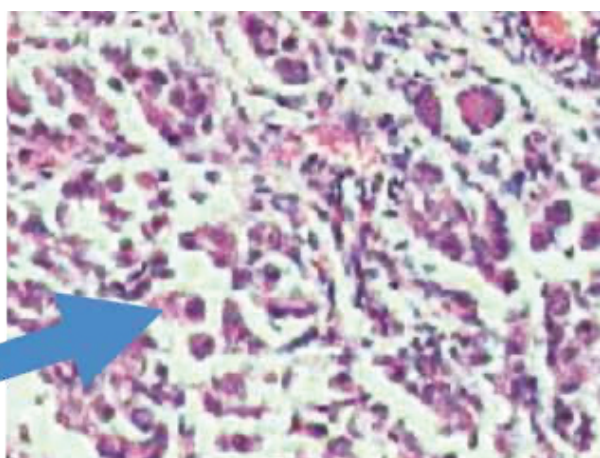
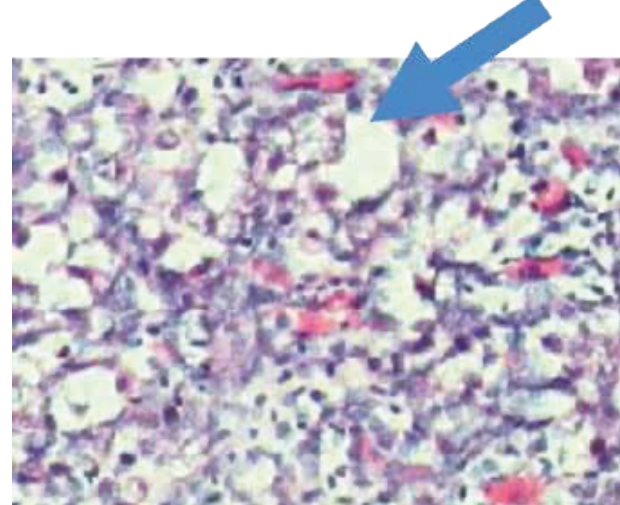


Figure 2. Ballooning degeneration of oocytes



CLINICAL FEATURES

The clinical presentation of POI can be highly variable and can be classified broadly as menstrual symptoms, menopausal symptoms, and long-term consequences.

MENSTRUAL DISTURBANCES

Irregular, usually prolonged, cycles are often the earliest manifestation of POI. Early menarche has been associated with an increased risk of subsequent POI.¹⁷ The initial presentation commonly includes menstrual irregularity or oligomenorrhea, progressing to secondary amenorrhoea. Health care professionals (HCPs) should be aware of the possibility of POI in young women presenting with menstrual irregularity. Approximately 15–20% of women with POI present with primary amenorrhoea, reflecting early-onset ovarian failure due to depletion or dysfunction of the follicle pool.⁶ This is most commonly associated with genetic or developmental abnormalities, including Turner syndrome and other X-chromosome defects, gonadal dysgenesis, or enzymatic/steroidogenic defects. Affected women may exhibit absent or incomplete pubertal development or, when ovarian failure occurs after initial estrogen exposure, normal pubertal development followed by primary amenorrhoea. Amenorrhoea following discontinuation of oral contraceptives may unmask previously unrecognised, underlying POI.⁶

MENOPAUSAL SYMPTOMS

Menopausal symptoms may or may not be present. They may occur intermittently in spontaneous POI due to erratic release of hormones. Patients who have an iatrogenic POI may experience an acute onset of symptoms. Menopausal symptoms are usually more severe in POI than after natural age at menopause.² Estrogen deficiency symptoms in POI

include vasomotor symptoms, genitourinary syndrome, sleep disturbances, psychological symptoms like irritability, anxiety, depression, and mood swings, and joint and muscular discomfort.

ASSOCIATIONS AND LONG-TERM CONSEQUENCES OF POI

An Australian cohort study (N=11258) found that women with POI had twice the odds of experiencing chronic conditions and multimorbidity (defined as 2 or more chronic conditions) by age 60, compared with women who experienced menopause at age 50–51 years.⁴³ In a large prospective cohort of postmenopausal women from the Canadian Longitudinal Study on Aging (N=12,339), women with POI had 2.5-fold higher odds of multimorbidity (adjusted OR 2.0; 95% CI 1.5–2.5), nearly double the prevalence of severe multimorbidity (defined as 3 or more chronic conditions), and increased risks of ischaemic heart disease, gastric ulcers, and osteoporosis.⁴⁴ This trend persists even after adjusting for significant risk factors for multimorbidity. In a meta-analysis of 20 cohort studies (n = 921,517), POI and EM were associated with increased risks of type 2 diabetes (T2DM), hyperlipidaemia, coronary heart disease, stroke, and overall cardiovascular events compared with menopause after age 45 years.⁴⁵

Long-term consequences of POI include the following:

- *Cognitive impairment:* POI can lead to accelerated cognitive impairment, memory issues, concentration problems, and increased risk of dementia. In a recent meta-analysis, women with POI had an increased risk of dementia (OR 1.18; 95% CI 1.15–1.21; I² = 0%), predominantly in cohort studies and those including natural menopause.⁴⁶ In a study by Rocca et al., premenopausal women who underwent bilateral oophorectomy before age 43 years had an increased risk of Parkinsonism.⁴⁷

Cardiovascular risk: Deficiency of endogenous estrogen increases the risk of CVD due to impaired endothelial function and an abnormal lipid profile (increased triglycerides, cholesterol, and LDL-C). Meta-analyses and observational studies have concluded that POI and EM are associated with an increased risk of incident ischaemic heart disease (IHD) and overall CVD.^{45,48,49}

Impact on bone health: POI is associated with abnormal bone micro-architecture and reduced bone mineral density.⁸ Early estrogen deficiency may result in reduced peak bone mass, accelerated bone loss, and an increased risk of osteopenia, osteoporosis, and fragility fractures.^{50,51}

Type 2 diabetes mellitus and POI - POI is associated with early onset insulin resistance, increased visceral adiposity, dyslipidemia, and impaired glucose metabolism, all of which predispose to type 2 diabetes (T2DM) at younger ages than expected in the general population.⁵² A meta-analysis of 13 studies (N = 191,762) including 21,664 cases of T2DM found that both POI and EM were significantly associated with an increased risk of type 2 diabetes (POI: OR 1.50; EM: OR 1.15 vs menopause at 45–55 years), establishing POI and EM as independent risk markers for future T2DM.⁵³ In India, the co-occurrence of POI and T2DM represents a significant emerging challenge of multimorbidity. Given that T2DM tends to present at a younger age and progress more aggressively in Indian populations, the diagnosis of POI should prompt proactive metabolic surveillance and long-term cardiometabolic risk assessment.

Psychological impact: POI has a substantial negative impact on emotional well-being and overall quality of life (QoL). Affected women have an increased risk of depression and anxiety, along with disturbances in body image, reduced self-esteem, and lower life satisfaction, largely related to early estrogen deficiency and infertility-related distress.^{54,55}

Infertility is one of the most distressing aspects of POI. Women with POI have very low chances of spontaneous conception (<5%) and face significant reproductive challenges due to premature depletion or dysfunction of ovarian follicles. Although occasional spontaneous ovulation & pregnancy can occur, the overall likelihood of achieving pregnancy without assisted reproductive technologies is markedly reduced compared with age-matched women with normal ovarian function.^{6,8}

Sexual dysfunction: POI can adversely affect sexual health. A meta-analysis found a poorer overall sexual function in POI, including reduced desire, arousal, lubrication, satisfaction, and increased dyspareunia. These effects persist even with systemic HRT and are caused by hypoestrogenism, genitourinary changes, and psychological factors, all contributing to diminished sexual wellbeing and quality of life in POI.⁵⁶

Long-term morbidity and mortality are increased in POI. A meta-analysis showed that POI women had a higher risk of death from all causes and from ischaemic heart disease, when compared with women of normal age at natural menopause (ANM).⁵⁷ There is a reduced life expectancy and risk of premature death.

DIAGNOSTIC WORKUP

It is crucial that the diagnosis of POI is accurate and made in a timely manner. Unfortunately, the diagnosis and, therefore, the effective management of POI are often delayed.

HISTORY

A thorough history should include personal and family history, age of the patient, details of menstrual history, age at menarche, menstrual pattern, and last menses. Obstetric history, any previous uterine/ovarian surgery, cancer therapy, thyroid or endocrine organ therapy, eating disorders, inherited disorders like Turner's syndrome, and history of any medications should be noted. The following are considered predictors of POI and EM : family history of POI or EM, being a twin or triplet, genetic abnormalities, early menarche, nulliparity or low parity, cigarette smoking (with a strong dose-response effect), and being underweight.⁵⁸

EXAMINATION

A full workup includes height, weight, BMI, secondary sexual characteristics, and gynaecological examination. Specific features of Turner's syndrome, like short stature, elbow, nail deformity, hearing/vision problems, scoliosis, and cardiovascular abnormalities, should be looked for.

INVESTIGATIONS

Serum Follicle-Stimulating Hormone, Anti-Mullerian Hormone, and Estradiol

Diagnosis of POI can be made in women less than 40 years of age with irregular menses and FSH values in the postmenopausal range. According to the 2024 ESHRE guidelines, diagnostic criteria include spontaneous amenorrhoea or an irregular menstrual cycle for at least 4 months, and an elevated FSH level > 25 IU/L. FSH assessment should be repeated after 4-6 weeks if diagnostic uncertainty persists. FSH testing for the diagnosis of POI does not have to be on a specific day of the menstrual cycle.⁸ The Indian Menopause Society aligns with the ESHRE 2024 guideline and accepts a serum FSH > 25 IU/L for the diagnosis of POI in women under 40 years with oligo- or amenorrhoea.⁵⁹ The British Menopause Society Consensus statement 2024, defines POI as oligo/amenorrhoea of > 4 months' duration associated with elevated FSH > 40 IU/L, on at least two occasions, measured 4-6 weeks apart, in women under the age of 40.³ The International Menopause Society also considers the diagnostic limit as > 40 IU/L.⁶⁰ while the National Institute for Health and Care Excellence (NICE) guideline suggests > 30 IU/L.⁶¹ Serum FSH values can be misleading in women with spontaneous POI who may still have intermittent ovarian function, as they can be in the normal range.

AMH reflects ovarian reserve and provides an estimate of the number of remaining oocytes. AMH levels rise during puberty, peak in the mid-twenties, and then steadily decline with age, becoming very low or undetectable around menopause.⁶² According to ESHRE, AMH should not be used as the primary diagnostic test for primary ovarian insufficiency, as low levels alone are not diagnostic. However, AMH testing may be helpful when FSH results are inconclusive, provided results are interpreted in the appropriate clinical context.⁸ AMH levels are low in women with symptomatic POI, consistent with a reduced primordial follicle pool. Although not recommended for population screening, AMH may be useful in identifying women at risk of developing POI, allowing timely counselling regarding fertility potential and consideration of fertility preservation, particularly in women with occult POI or autoimmune ovarian failure. Unlike FSH, AMH shows minimal cycle-to-cycle variation, making it a useful marker of declining fertility rather than a standalone diagnostic test.

Diagnosing POI based on serum estradiol concentrations is not recommended. However, a low estradiol concentration indicates hypoestrogenism and, in combination with an elevated FSH concentration, provides additional confirmation of the POI diagnosis.⁸

Pelvic Ultrasound

Baseline transvaginal sonography is useful in evaluating women with suspected POI to assess uterine size, ovarian volume, and AFC.⁶⁰ Common findings include reduced ovarian volume, low or absent antral follicles (AFC < 5), and a thin endometrium (< 4 mm), reflecting hypoestrogenism. While supportive, ultrasonographic findings are not diagnostic and should be interpreted in conjunction with clinical and hormonal assessment.

Investigations for general health

Should include a baseline assessment of insulin resistance using glycated haemoglobin (HbA1c), a lipid profile for early detection of cardiovascular disease, and a dual-energy X-ray absorptiometry (DXA) scan to assess bone mineral density at diagnosis and quantify lifetime fracture risk.⁶⁰

Investigations to rule out other causes of amenorrhoea

Should include a pregnancy test, serum prolactin to rule out hyperprolactinemia, and thyroid-stimulating hormone (TSH) to rule out thyroid disease.⁹

Second-line investigations

After the diagnosis of POI is confirmed, second-line investigations include:

- *Karyotyping and FMR-1 premutation analysis* - A karyotype is considered mandatory to detect the aetiology of POI. Karyotyping is the gold standard to assess chromosomal abnormalities. Turner syndrome (XO) is the commonest chromosomal abnormality in POI and occurs in 1 in 2500 births. The commonest genetic abnormality in POI involves a pre-mutation in the fragile X mental retardation 1 gene (FMR1). It is carried in 1 in 250 women. The patient should be referred for further genetic counselling and investigations if a positive phenotype is detected.⁵⁸
- *Screening for autoimmune diseases*: Anti-21-hydroxylase, anti-thyroid peroxidase, and anti-thyroglobulin antibodies should be tested; if positive, the patient should be referred to an endocrinologist.⁶⁰

MANAGEMENT OF PREMATURE OVARIAN INSUFFICIENCY

Management of primary ovarian insufficiency requires a multidisciplinary, holistic approach addressing endocrine, emotional, reproductive, genetic, and psychological health.

COUNSELLING AND PSYCHOLOGICAL SUPPORT

The diagnosis of POI can have life-changing consequences for both the patient and her family, especially due to the potential loss of fertility if childbearing is not complete. The clinician should be considerate and disclose the diagnosis sensitively. The patient may require psychological support in managing her diagnosis, and professional counsellors or psychologists may play a role. Non-hormonal therapy, like SSRI, SNRI, in select patients, could be helpful. Sexual function should be discussed with women with POI, and they should be offered psychosexual counselling.⁵⁶ Support groups such as the International Premature Ovarian Failure Association [www.pofsupport.org] and the Daisy Network Premature Menopause Support Group [www.daisynetwork.org.uk] are valuable adjuncts. All management options should be discussed, and women should be encouraged to participate in decision-making.

LIFESTYLE MODIFICATION

A healthy lifestyle, including adequate physical activity and maintaining a normal body weight, should be encouraged. Weight-bearing exercises are essential for bone health. A balanced diet with the recommended intake of calcium and vitamin D should be ensured. Supplementation of calcium and vitamin D may be required in women with inadequate vitamin D status and/or calcium intake and may be of value in women with low BMD.⁸ Coffee, alcohol, and smoking should be avoided.

HORMONE REPLACEMENT THERAPY

Although the new terminology is MHT, in the context of women with POI, it is still called HRT or HT. In women with POI, physiological replacement of estrogen (and progesterone) is essential for their health, and the controversies that surround the use of HRT in postmenopausal women do not apply.⁶³ HRT is strongly recommended for women with POI until the usual age of natural menopause as primary prevention to reduce the risk of long-term morbidity and mortality, regardless of the presence or absence of estrogen deficiency symptoms.⁸

HRT or a combined oral contraceptive pill (COC) should be started as early as possible after the diagnosis is confirmed (unless contraindicated).^{9,58} Standard (medium or high) doses of HT should be prescribed. The woman should be counselled about the short-term symptom control for vasomotor and genito-urinary symptoms, and the long-term goals of therapy to reduce the risk of osteoporosis, and possibly CVD, cognitive impairment, and dementia.⁸ HT must

be continued until at least the age of natural menopause with periodic re-evaluation. HRT has not been found to increase the risk of breast cancer before the age of natural menopause.⁸

The importance of HT in POI is multifaceted;⁵⁸ it effectively reduces vasomotor and urogenital symptoms, can improve mood and cognitive function, and can reduce musculoskeletal pain. HT promotes the development of secondary sexual characteristics, including uterine growth, in prepubertal girls with primary amenorrhoea. It creates a favourable hormonal environment for embryo implantation and may increase the chances of a natural pregnancy. It helps minimise long-term risks associated with POI, such as osteoporosis and CVD.

Hormone Replacement Therapy Options

When prescribing HRT, the patient's preference for route, regimen, and method of administration of each component and contraceptive needs must be taken into consideration.⁸

Estrogen

17 β -estradiol (E2) is preferred to ethinylestradiol or conjugated equine estrogens for estrogen replacement.⁸ Higher doses of 17 β -estradiol 2-4 mg/day, or transdermal estradiol 75-100 mg/day, or estrogel 3-4 pumps are recommended.⁶³ There is no proven ideal E2 level, but the aim of therapy should be for 68-136 pg/mL, the physiological mid-follicular levels. Despite adequate systemic HRT, women with POI may experience genitourinary symptoms (GSM). Local estrogen therapy (LET) may be given to improve genitourinary and sexual symptoms, in addition to systemic HRT. Lubricants are useful for the treatment of vaginal discomfort and dyspareunia for women not using HRT.⁸

Micronised Progesterone / Dydrogesterone / Levonorgestrel Intrauterine Device^{3 64}

In non-hysterectomised women on estrogen therapy, progesterone can be administered as a cyclical regimen of 200-300 mg micronised progesterone (MP) / 10-20 mg of Dydrogesterone (DYD) for at least 12-14 days per month or a continuous regimen of 100-200 mg or 5-10 mg per day, depending on E2 dose.

Combined Ethinyl Estradiol / Progesterone contraceptive pills

Combined COC may be used in women who also need contraception until the expected age of natural menopause, unless there are contraindications. If a COC is chosen, a continuous or extended regimen is recommended to ensure uninterrupted estrogen exposure and help prevent bone loss.⁸ Effect of HT in improving bone health and cardiovascular risk may be more beneficial compared to OCPs.³

Testosterone

For women with low libido, especially after oophorectomy, testosterone gels/implants can be prescribed. Down-titration of 1% male products may be required due to a lack of licensed female formulations.³ It may not be available in all countries.

Hormone Replacement Therapy for the Management of Premature Ovarian Insufficiency - special issues⁸

- In Turner's syndrome, HRT should be offered throughout the normal reproductive lifespan.
- Fibroids are not necessarily a contraindication for HRT use.
- In obese and overweight women, transdermal E2 is the preferred route.
- Hypertension is not a contraindication for HRT use. Transdermal E2 is the preferred route.
- In women with severe endometriosis requiring oophorectomy, combined HRT should be used even after hysterectomy to avoid reactivation of endometriotic implants and endometrioid carcinoma.
- Migraine is not necessarily a contraindication for HRT use. The transdermal route of estrogen is recommended starting with a low dose.
- Women with prior venous thromboembolism (VTE) should be co-managed with a haematologist if considering HRT. Transdermal E2 is the preferred route.

- HRT is contraindicated in breast cancer survivors but may be considered in women with breast cancer susceptibility gene (BRCA) mutations (BRCA1 or BRCA2) who have not had breast cancer, following individualised risk assessment.

FOLLOW-UP AND MONITORING

An annual clinical review should be done, with monitoring of weight, blood pressure, and smoking status.⁸ The dose of HT should be adjusted according to symptom control. Lipid profile, HbA1c, and thyroid test should be done annually. Adrenal and other preventive health care tests should be done at regular intervals. DXA frequency should be according to low or high risk (2–5 yearly).

FERTILITY MANAGEMENT IN PREMATURE OVARIAN INSUFFICIENCY

Infertility in POI is due to ovulatory failure, endocrine dysfunction, and markedly reduced ovarian reserve. Despite reduced reserve, 5–10% of women with POI may conceive spontaneously, often with a prolonged time to pregnancy, but the majority of them require assisted reproductive techniques (ART). Early fertility counselling and consideration of fertility preservation are essential.⁶

Reproductive counselling should include discussion of all options, including remaining child-free, foster care, adoption, donor oocytes, or donor embryos. Genetic counselling and medical genetics consultation are indicated when a hereditary aetiology is suspected.

Challenges with Assisted Reproductive Technology in Premature Ovarian Insufficiency

Women with POI are poor responders to stimulation and often meet the European Society of Human Reproduction and Embryology (ESHRE) Bologna criteria for poor responders, which requires at least two out of three of the following: maternal age > 40 years, prior poor ovarian responder (≤ 3 oocytes with conventional stimulation protocol, abnormal ovarian reserve test (AFC < 5 – 7 follicles, AMH < 0.5–1.1 ng/ml). Poor responders constitute approximately 9–24% of women undergoing in vitro fertilisation (IVF).⁶⁵

In POI, diminished ovarian reserve and oocyte quality, partly related to increased oxidative stress, result in low fertilisation rates, poor embryo development, implantation failure, and higher miscarriage rates. Despite multiple stimulation strategies, treatment outcomes remain limited. While in vitro fertilisation (IVF) with oocyte or embryo cryopreservation using vitrification is an established option with acceptable outcomes in selected patients, ovarian tissue cryopreservation is an emerging strategy. Ovarian tissue cryopreservation with autologous transplantation and in vitro activation has been successful in selected cases, including restoration of endocrine function and fertility.^{66,67} Overall, ART in women with POI remains challenging, with limited success using autologous oocytes.

REVERSAL OF PREMATURE OVARIAN INSUFFICIENCY - EMERGING THERAPIES

Several adjuvant therapies have been explored to improve oocyte yield and quality in women with POI or diminished ovarian reserve, but evidence remains limited and inconsistent, and none of them is considered standard of care.

Platelet-Rich Plasma (PRP)

PRP is an autologous concentrate rich in growth factors and cytokines.⁶⁸ Preclinical studies demonstrate that PRP promotes angiogenesis, modulates inflammation, and supports cell proliferation.⁶⁹ In animal models of POI, intra-ovarian PRP has been shown to reduce follicular atresia, enhance ovarian angiogenesis, and restore ovulation.⁷⁰ Limited human pilot studies suggest possible improvement in hormone profiles, menstrual cyclicity, and oocyte yield. However, PRP remains experimental, with no standardised protocols for preparation, dose, timing, or long-term safety, and robust randomised controlled trials are lacking.⁷¹

Stem Cell and Exosome Therapy

Mesenchymal stem cells (MSCs), derived from sources such as bone marrow, umbilical cord, or adipose tissue, have shown protective effects against germ-cell apoptosis and DNA damage in chemotherapy-induced POI animal models, with partial restoration of ovarian function.^{72–74}

Despite these promising findings, MSC therapy carries theoretical risks including tumourigenicity, immune reactions, and chromosomal instability, and therefore remains investigational.⁷² Exosome-based therapy has emerged as a

potential alternative, aiming to harness paracrine effects without the risks associated with cell transplantation. MSC-derived exosomes containing microRNAs have demonstrated anti-apoptotic and pro-angiogenic effects in preclinical POI models.^{74,75} However, human clinical data are currently insufficient to support routine clinical application.

Other Experimental Approaches

- *Androgen supplementation (DHEA/Testosterone)*: DHEA and transdermal testosterone aim to increase intra-ovarian androgen levels, thereby supporting early folliculogenesis and granulosa cell function. Some studies report increased oocyte yield and modest improvement in in vitro fertilisation (IVF) outcomes in poor responders, but results are heterogeneous and benefits are not universal.⁷⁶ A meta-analysis of 17 randomised controlled trials (RCTs) (n = 1,496) in poor ovarian responders found that pre-treatment with DHEA or testosterone may improve live birth or ongoing pregnancy rates. DHEA was associated with higher live birth/ongoing pregnancy rates (OR 1.88, 95% CI 1.30–2.71), and testosterone with higher live birth rates (OR 2.60, 95% CI 1.30–5.20). However, these benefits were no longer statistically significant after excluding trials at high risk of bias.⁷⁷ No differences were observed in miscarriage or multiple pregnancy rates, and current evidence is insufficient to support routine androgen use or confirm safety.
- *Growth hormone (GH)* - GH may improve oocyte competence by supporting granulosa cell function and oocyte maturation. Small trials suggest possible improvement in live birth rates, but robust evidence is lacking.⁷⁸
- *Antioxidants (melatonin, CoQ10, vitamins C and E)* - Adjunctive therapies such as melatonin, coenzyme Q10, and vitamins C and E are under investigation but currently lack high-quality clinical evidence to support widespread use. These agents target oxidative stress and mitochondrial dysfunction associated with ovarian ageing.

At present, PRP, stem cell, and exosome therapies should be considered experimental and offered only within research settings or ethically approved protocols.^{68,71,72,75} Established fertility options for women with POI remain oocyte or embryo donation, fertility preservation prior to gonadotoxic therapy, and adoption.

HORMONE REPLACEMENT THERAPY AFTER STEM CELL TRANSPLANTATION

Women with POI after SCT should receive physiological-dose HRT until the usual age of menopause, with careful individual risk assessment, particularly for secondary malignancy. Estrogen–progestogen therapy effectively relieves vasomotor, urogenital, and psychological symptoms. In allogeneic SCT, graft-versus-host disease may impair oral hormone absorption, so close monitoring and non-oral routes may be required.

OVARIAN TRANSPLANTATION

Refer to Chapter 37.

MODIFIABLE FACTORS IN PREMATURE OVARIAN INSUFFICIENCY

Several clinical, lifestyle, and treatment-related factors have been identified where intervention may help preserve ovarian function or mitigate the impact of POI.

Gynaecological Surgical Practices

Ovarian damage may occur following pelvic or ovarian surgery due to loss of ovarian tissue or disruption of ovarian blood supply. Conservative surgical techniques, ovarian-sparing approaches, and meticulous haemostasis should be employed whenever possible to reduce iatrogenic ovarian injury.^{33,79,80}

Lifestyle Factors

A balanced, antioxidant-rich diet supports general reproductive health but cannot reverse POI. Cigarette smoking is a well-established, dose-dependent risk factor for accelerated ovarian follicle depletion and earlier menopause. Smoking cessation should be actively encouraged as part of POI prevention strategies.⁸¹

Modification of Treatment Regimens for Malignant and Chronic Diseases

In women undergoing gonadotoxic treatments such as chemotherapy or radiotherapy, fertility preserving strategies should be considered prior to treatment initiation to reduce the risk of POI. These include gonadal shielding during pelvic irradiation, ovarian transposition (oophoropexy) before radiotherapy, and temporary ovarian suppression

using GnRH analogues during chemotherapy. Established fertility preservation options include cryopreservation of oocytes, embryos, or ovarian tissue, which should be discussed as part of pre-treatment counselling.⁸²

Genetic Counselling and Risk Stratification

Genetic counselling is recommended for women at risk of POI, particularly those with a family history of early menopause or known genetic disorders. Identification of high-risk genetic variants may allow anticipatory guidance, fertility planning, and early intervention.

SYNOPSIS

- POI affects approximately 2–4% of women globally and 1.5–3% of Indian women, while early menopause (40–45 years) is more common. Aetiology is heterogeneous and includes idiopathic causes, genetic abnormalities (such as Turner syndrome, FMR1 premutation), autoimmune disease, infections, and iatrogenic factors such as surgery, chemotherapy, and radiotherapy. Environmental toxins and lifestyle factors may accelerate ovarian ageing.
- Clinically, POI presents with menstrual irregularity or amenorrhoea, menopausal symptoms, infertility, and long-term risks including osteoporosis, cardiovascular disease, cognitive decline, psychological distress, sexual dysfunction, and increased mortality. Ovarian activity may be intermittent, and spontaneous pregnancy, though rare, can occur.
- Diagnosis is based on oligo/amenorrhoea ≥ 4 months in women < 40 years with elevated FSH (> 25 IU/L per ESHRE 2024). AMH is supportive but not diagnostic. Evaluation includes excluding secondary causes, assessing bone and cardiovascular health, and performing targeted genetic and autoimmune testing.
- Management requires timely diagnosis, empathetic counselling, psychological support, and lifestyle optimisation. Hormone replacement therapy is the cornerstone of care and should be initiated early and continued until the average age of natural menopause to relieve symptoms and prevent long-term morbidity. Risks associated with postmenopausal HRT do not apply to POI. Fertility counselling is essential, with oocyte/embryo donation remaining the most effective reproductive option. Emerging therapies (PRP, stem cells, androgens) remain experimental.
- POI is a multisystem condition with major reproductive and long-term health implications, requiring individualised, multidisciplinary, and long-term care.

RESEARCH AGENDA

Develop reliable, low-cost strategies (clinical + biochemical) for earlier detection of POI before irreversible follicular loss occurs.

REFERENCES

1. Broekmans FJ, Soules MR, Fauser BC. Ovarian aging: mechanisms and clinical consequences. *Endocrine reviews*. 2009 Aug; 30(5): 465-93. doi: 10.1210/er.2009-0006.
2. Lambrinoudaki I, Paschou SA, Lumsden MA, Faubion S, Makrakis E, Kalantaridou S, et al. Premature ovarian insufficiency: A toolkit for the primary care physician. *Maturitas*. 2021 May; 147: 53-63. doi: 10.1016/j.maturitas.2020.11.004.
3. British Menopause Society. Consensus statement on premature ovarian insufficiency (POI). April 2024. Available from: <https://thebms.org.uk/publications/consensus> Accessed: 12 Mar 2026
4. Faubion SS, Kuhle CL, Shuster LT, Rocca WA. Long-term health consequences of premature or early menopause and considerations for management. *Climacteric: the journal of the International Menopause Society*. 2015; 18(4): 483-91. doi: 10.3109/13697137.2015.1020484.
5. Welt CK. Primary ovarian insufficiency: a more accurate term for premature ovarian failure. *Clinical endocrinology*. 2008 Apr; 68(4): 499-509. doi: 10.1111/j.1365-2265.2007.03073.x.
6. Nelson LM. Clinical practice. Primary ovarian insufficiency. *The New England journal of medicine*. 2009 Feb 5; 360(6): 606-14. doi: 10.1056/NEJMcp0808697.
7. Stuenkel CA, Davis SR, Gompel A, Lumsden MA, Murad MH, Pinkerton JV, et al. Treatment of Symptoms of the Menopause: An Endocrine Society Clinical Practice Guideline. *The Journal of clinical endocrinology and metabolism*. 2015 Nov; 100(11): 3975-4011. doi: 10.1210/jc.2015-2236.
8. Panay N, Anderson RA, Bennie A, Cedars M, Davies M, Ee C, et al. Evidence-based guideline: premature ovarian insufficiency(†)(‡). *Climacteric: the journal of the International Menopause Society*. 2024 Dec; 27(6): 510-520. doi: 10.1080/13697137.2024.2423213.
9. Meeta M, Digumarti L, Agarwal N, Vaze N, Shah R, Malik S. Clinical Practice Guidelines on Menopause: *An Executive Summary and Recommendations: Indian Menopause Society 2019-2020. *Journal of mid-life health*. 2020 Apr-Jun; 11(2): 55-95. doi: 10.4103/jmh.JMH_137_20.

10. Harlow SD, Gass M, Hall JE, Lobo R, Maki P, Rebar RW, et al. Executive summary of the Stages of Reproductive Aging Workshop + 10: addressing the unfinished agenda of staging reproductive aging. *Menopause* (New York, N.Y.). 2012 Apr; 19(4): 387-95. doi: 10.1097/gme.0b013e31824d8f40.
11. Webber L, Davies M, Anderson R, Bartlett J, Braat D, Cartwright B, et al. ESHRE Guideline: management of women with premature ovarian insufficiency. *Human reproduction* (Oxford, England). 2016 May; 31(5): 926-37. doi: 10.1093/humrep/dew027.
12. Scott RT Jr, Hofmann GE. Prognostic assessment of ovarian reserve. *Fertility and sterility*. 1995 Jan; 63(1): 1-11. PMID: 7805895.
13. Scott RT Jr, Elkind-Hirsch KE, Styne-Gross A, Miller KA, Frattarelli JL. The predictive value for in vitro fertility delivery rates is greatly impacted by the method used to select the threshold between normal and elevated basal follicle-stimulating hormone. *Fertility and sterility*. 2008 Apr; 89(4): 868-78. doi: 10.1016/j.fertnstert.2007.03.100.
14. Broer SL, Broekmans FJ, Laven JS, Fauser BC. Anti-Müllerian hormone: ovarian reserve testing and its potential clinical implications. *Human reproduction update*. 2014 Sep-Oct; 20(5): 688-701. doi: 10.1093/humupd/dmu020.
15. Testing and interpreting measures of ovarian reserve: a committee opinion. *Fertility and sterility*. 2020 Dec; 114(6): 1151-1157. doi: 10.1016/j.fertnstert.2020.09.134.
16. Anderson RA, Cameron DA. Pretreatment serum anti-müllerian hormone predicts long-term ovarian function and bone mass after chemotherapy for early breast cancer. *The Journal of clinical endocrinology and metabolism*. 2011 May; 96(5): 1336-43. doi: 10.1210/jc.2010-2582.
17. Mishra GD, Pandeya N, Dobson AJ, Chung HF, Anderson D, Kuh D, et al. Early menarche, nulliparity and the risk for premature and early natural menopause. *Human reproduction* (Oxford, England). 2017 Mar 1; 32(3): 679-686. doi: 10.1093/humrep/dew350.
18. Golezar S, Ramezani Tehrani F, Khazaei S, Ebadi A, Keshavarz Z. The global prevalence of primary ovarian insufficiency and early menopause: a meta-analysis. *Climacteric: the journal of the International Menopause Society*. 2019 Aug; 22(4): 403-411. doi: 10.1080/13697137.2019.1574738.
19. Li M, Zhu Y, Wei J, Chen L, Chen S, Lai D. The global prevalence of premature ovarian insufficiency: a systematic review and meta-analysis. *Climacteric: the journal of the*
20. International Menopause Society. 2023 Apr; 26(2): 95-102. doi: 10.1080/13697137.2022.2153033.
21. Ross S, Juárez SP. Variations in the prevalence of premature and early menopause in low and middle-income regions: a cross-sectional study. *Climacteric: the journal of the International Menopause Society*. 2025 Jun; 28(3): 360-364. doi: 10.1080/13697137.2025.2500561.
22. Kundu S, Acharya SS. Exploring the triggers of premature and early menopause in India: a comprehensive analysis based on National Family Health Survey, 2019-2021. *Scientific reports*. 2024 Feb 6; 14(1): 3040. doi: 10.1038/s41598-024-53536-9.
23. Singh A GDL. Premature menopause among women in India: Evidence from NFHS-4. In: *Proceedings of the International Population Conference 2021*. Hyderabad
24. Meher T, Sahoo H. Premature menopause among women in India: Evidence from National Family Health Survey-IV. *J Obstet Gynaecol Res*. 2021 Dec; 47(12): 4426-4439. doi: 10.1111/jog.15041. Epub 2021 Sep 27. PMID: 34580955.
25. Babbar K, Singh V, Sivakami M. Rising premature menopause and variations by education level in India. *Scientific reports*. 2024 Aug 6; 14(1): 18238. doi: 10.1038/s41598-024-67730-2.
26. Halder P, Kansal S, Mamgai A, Rathor S, Das A, Garg G. Untimely Menopause, State Wise Prevalence and Determinants: Insights from Longitudinal Aging Study in India (LASI-1). *Journal of obstetrics and gynaecology of India*. 2025 Apr; 75(2): 106-114. doi: 10.1007/s13224-024-02094-1.
27. Qin Y, Jiao X, Simpson JL, Chen ZJ. Genetics of primary ovarian insufficiency: new developments and opportunities. *Human reproduction update*. 2015 Nov-Dec; 21(6): 787-808. doi: 10.1093/humupd/dmv036.
28. França MM, Mendonça BB. Genetics of ovarian insufficiency and defects of folliculogenesis. *Best practice & research. Clinical endocrinology & metabolism*. 2022 Jan; 36(1): 101594. doi: 10.1016/j.beem.2021.101594.
29. Tucker EJ, Grover SR, Bachelot A, Touraine P, Sinclair AH. Premature Ovarian Insufficiency: New Perspectives on Genetic Cause and Phenotypic Spectrum. *Endocrine reviews*. 2016 Dec; 37(6): 609-635. doi: 10.1210/er.2016-1047.
30. Kirshenbaum M, Orvieto R. Premature ovarian insufficiency (POI) and autoimmunity-an update appraisal. *Journal of assisted reproduction and genetics*. 2019 Nov; 36(11): 2207-2215. doi: 10.1007/s10815-019-01572-0.
31. Szeliga A, Calik-Ksepka A, Maciejewska-Jeske M, Grymowicz M, Smolarczyk K, Kostrzak A, et al. Autoimmune Diseases in Patients with Premature Ovarian Insufficiency-Our Current State of Knowledge. *International journal of molecular sciences*. 2021 Mar 5; 22(5): doi: 10.3390/ijms22052594.
32. Bakalov VK, Anasti JN, Calis KA, Vanderhoof VH, Premkumar A, Chen S, et al. Autoimmune oophoritis as a mechanism of follicular dysfunction in women with 46,XX spontaneous premature ovarian failure. *Fertility and sterility*. 2005 Oct; 84(4): 958-65. doi: 10.1016/j.fertnstert.2005.04.060.
33. Torrealday S, Kodaman P, Pal L. Premature Ovarian Insufficiency - an update on recent advances in understanding and management. *F1000Research*. 2017; 6: 2069. doi: 10.12688/f1000research.11948.1.
34. Farquhar CM, Sadler L, Harvey SA, Stewart AW. The association of hysterectomy and menopause: a prospective cohort study. *BJOG: an international journal of obstetrics and gynaecology*. 2005 Jul; 112(7): 956-62. doi: 10.1111/j.1471-0528.2005.00696.x.
35. Moorman PG, Myers ER, Schildkraut JM, Iversen ES, Wang F, Warren N. Effect of hysterectomy with ovarian preservation on ovarian function. *Obstetrics and gynecology*. 2011 Dec; 118(6): 1271-1279. doi: 10.1097/AOG.0b013e318236fd12.
36. Vinjamuri P. Medical Ethics: A case study of Hysterectomy in Andhra Pradesh. 2010 [Internet]. Available from: <https://www.semanticscholar.org/paper/Medical-Ethics-%3A-A-case-study-of-Hysterectomy-in-Vinjamuri/>
37. Overbeek A, van den Berg MH, van Leeuwen FE, Kaspers GJ, Lambalk CB, van Dulmen-den Broeder E. Chemotherapy-related late adverse effects on ovarian function in female survivors of childhood and young adult cancer: A systematic review. *Cancer treatment reviews*. 2017 Feb; 53: 10-24. doi: 10.1016/j.ctrv.2016.11.006.
38. Wallace WH, Anderson RA, Irvine DS. Fertility preservation for young patients with cancer: who is at risk and what can be offered?. *The Lancet. Oncology*. 2005 Apr; 6(4): 209-18. doi: 10.1016/S1470-2045(05)70092-9.
39. Whang J, Ahn C, Kim S, Seok E, Yang Y, Han G, et al. Effects of Repeated Ovarian Stimulation on Ovarian Function and Aging in Mice. *Development & reproduction*. 2021 Dec; 25(4): 213-223. doi: 10.12717/DR.2021.25.4.213.
40. Grindler NM, Allsworth JE, Macones GA, Kannan K, Roehl KA, Cooper AR. Persistent organic pollutants and early menopause in U.S. women. *PloS one*. 2015; 10(1): e0116057. doi: 10.1371/journal.pone.0116057.

41. Halder P, Soni A, Seth A, Vijayakumar D, Das A, Sankhyan S, et al. Association of early menopause with indoor air pollution: A multilevel modelling analysis of the nationally representative cross-sectional study in India. *Journal of family medicine and primary care*. 2025 Jan; 14(1): 173-183. doi: 10.4103/jfmpc.jfmpc_1046_24.
42. Iglesias C, Banker M, Mahajan N, Herrero L, Meseguer M, Garcia-Velasco JA. Ethnicity as a determinant of ovarian reserve: differences in ovarian aging between Spanish and Indian women. *Fertility and sterility*. 2014 Jul; 102(1): 244-9. doi: 10.1016/j.fertnstert.2014.03.050.
43. Xu X, Jones M, Mishra GD. Age at natural menopause and development of chronic conditions and multimorbidity: results from an Australian prospective cohort. *Human reproduction (Oxford, England)*. 2020 Jan 1; 35(1): 203-211. doi: 10.1093/humrep/dez259.
44. Kirubarajan A, Sohail N, Mayhew A, Griffith LE, Raina P, Shea AK. The association between primary ovarian insufficiency and increased multimorbidity in a large prospective cohort (Canadian Longitudinal Study on Aging). *Fertility and sterility*. 2025 Feb; 123(2): 289-299. doi: 10.1016/j.fertnstert.2024.08.345.
45. Liu J, Jin X, Liu W, Chen W, Wang L, Feng Z, et al. The risk of long-term cardiometabolic disease in women with premature or early menopause: A systematic review and meta-analysis. *Frontiers in cardiovascular medicine*. 2023; 10: 1131251. doi: 10.3389/fcvm.2023.1131251.
46. Karamitrou EK, Anagnostis P, Vaitis K, Athanasiadis L, Goulis DG. Early menopause and premature ovarian insufficiency are associated with increased risk of dementia: A systematic review and meta-analysis of observational studies. *Maturitas*. 2023 Oct; 176: 107792. doi: 10.1016/j.maturitas.2023.107792.
47. Rocca WA, Smith CY, Gazzuola Rocca L, Savica R, Mielke MM. Association of Premenopausal Bilateral Oophorectomy With Parkinsonism and Parkinson Disease. *JAMA network open*. 2022 Oct 3; 5(10): e2238663. doi: 10.1001/jamanetworkopen.2022.38663.
48. Zhu D, Chung HF, Dobson AJ, Pandeya N, Giles GG, Bruinsma F, et al. Age at natural menopause and risk of incident cardiovascular disease: a pooled analysis of individual patient data. *The Lancet. Public health*. 2019 Nov; 4(11): e553-e564. doi: 10.1016/S2468-2667(19)30155-0.
49. Roeters van Lennep JE, Heida KY, Bots ML, Hoek A. Cardiovascular disease risk in women with premature ovarian insufficiency: A systematic review and meta-analysis. *European journal of preventive cardiology*. 2016 Jan; 23(2): 178-86. doi: 10.1177/2047487314556004.
50. Jiang M, Gao Y, Hou H, Guo J, Li W, Qin T, et al. Bone mineral density in patients with primary ovarian insufficiency: A systematic review and Meta-Analysis. *European journal of obstetrics, gynecology, and reproductive biology*. 2024 Apr; 295: 219-227. doi: 10.1016/j.ejogrb.2024.02.013.
51. Csehely S, Kun A, Orbán E, Katona T, Orosz M, Herman T, et al. Prevalence of Impaired Bone Health in Premature Ovarian Insufficiency and Early Menopause and the Impact of Time to Diagnosis. *Journal of clinical medicine*. 2025 Jun 13; 14(12): doi: 10.3390/jcm14124210.
52. Robeva R, Elenkova A, Kirilov G, Zacharieva S. Metabolic Risk in Patients with a Diminished Ovarian Reserve and Premature Ovarian Insufficiency. *Journal of clinical medicine*. 2024 Aug 28; 13(17): doi: 10.3390/jcm13175105.
53. Anagnostis P, Christou K, Artzouchaltzi AM, Gkekakos NK, Kosmidou N, Siolos P, et al. Early menopause and premature ovarian insufficiency are associated with increased risk of type 2 diabetes: a systematic review and meta-analysis. *European journal of endocrinology*. 2019 Jan 1; 180(1): 41-50. doi: 10.1530/EJE-18-0602.
54. Tian Y, Zhang X, Xin Z, Li CR, Zhang F, Deng H, et al. Premature Ovarian Insufficiency Is Associated with Increased Risk of Depression, Anxiety, and Poor Life Quality: A Systematic Review and Meta-analysis. *Alpha psychiatry*. 2024 Mar; 25(2): 132-141. doi: 10.5152/alphapsychiatry.2024.231501.
55. Schmidt PJ, Luff JA, Haq NA, Vanderhoof VH, Koziol DE, Calis KA, et al. Depression in women with spontaneous 46,XX primary ovarian insufficiency. *The Journal of clinical endocrinology and metabolism*. 2011 Feb; 96(2): E278-87. doi: 10.1210/jc.2010-0613.
56. van Zwol-Janssens C, Pastoor H, Laven JSE, Louwers YV, Jiskoot G. Sexual function in women with premature ovarian insufficiency (POI): Systematic review and meta-analysis. *Maturitas*. 2024 Jun; 184: 107994. doi: 10.1016/j.maturitas.2024.107994.
57. Tao XY, Zuo AZ, Wang JQ, Tao FB. Effect of primary ovarian insufficiency and early natural menopause on mortality: a meta-analysis. *Climacteric : the journal of the International Menopause Society*. 2016; 19(1): 27-36. doi: 10.3109/13697137.2015.1094784.
58. Mishra GD, Chung HF, Cano A, Chedraui P, Goulis DG, Lopes P, et al. EMAS position statement: Predictors of premature and early natural menopause. *Maturitas*. 2019 May; 123: 82-88. doi: 10.1016/j.maturitas.2019.03.008.
59. Meeta M, Anuradha M, Ashraf AB, Aggarwal K, Digumarti L, Singh T. Clinical Practice Guidelines for Menopause: *An Executive Summary and Recommendations: Indian Menopause Society 2026. *J Midlife Health [Internet]*. 2026;17(Suppl 1). Available from: https://journals.lww.com/jomh/fulltext/2026/02001/clinical_practice_guidelines_for_menopause__an.5.aspx
60. Panay N, Anderson RA, Nappi RE, Vincent AJ, Vujovic S, Webber L, et al. Premature ovarian insufficiency: an International Menopause Society White Paper. *Climacteric : the journal of the International Menopause Society*. 2020 Oct; 23(5): 426-446. doi: 10.1080/13697137.2020.1804547.
61. National Institute for Health and Care Excellence (NICE). Menopause: identification and management. London: NICE; 2024 Nov 7. PMID: 31940155
62. La Marca A, Sighinolfi G, Radi D, Argento C, Baraldi E, Arsenio AC, et al. Anti-Müllerian hormone (AMH) as a predictive marker in assisted reproductive technology (ART). *Human reproduction update*. 2010 Mar-Apr; 16(2): 113-30. doi: 10.1093/humupd/dmp036.
63. Webber L, Anderson RA, Davies M, Janse F, Vermeulen N. HRT for women with premature ovarian insufficiency: a comprehensive review. *Human reproduction open*. 2017; 2017(2): hox007. doi: 10.1093/hropen/hox007.
64. Baber RJ, Panay N, Fenton A. 2016 IMS Recommendations on women's midlife health and menopause hormone therapy. *Climacteric : the journal of the International Menopause Society*. 2016 Apr; 19(2): 109-50. doi: 10.3109/13697137.2015.1129166.
65. Ferraretti AP, La Marca A, Fauser BC, Tarlatzis B, Nargund G, Gianaroli L. ESHRE consensus on the definition of 'poor response' to ovarian stimulation for in vitro fertilisation: the Bologna criteria. *Human reproduction (Oxford, England)*. 2011 Jul; 26(7): 1616-24. doi: 10.1093/humrep/der092.
66. Silber SJ, Grudzinskas G, Gosden RG. Successful pregnancy after microsurgical transplantation of an intact ovary. *The New England journal of medicine*. 2008 Dec 11; 359(24): 2617-8. doi: 10.1056/NEJMc0804321.
67. Practice Committee of American Society for Reproductive Medicine, Practice Committee of Society for Assisted Reproductive Technology. Ovarian tissue and oocyte cryopreservation. *Fertil Steril*. 2008 Nov; 90(5 Suppl):S241-6. doi: 10.1016/j.fertnstert.2008.08.039 PubMed PMID: 19007638..
68. Atkinson L, Martin F, Sturmey RG. Intraovarian injection of platelet-rich plasma in assisted reproduction: too much too soon?. *Human reproduction (Oxford, England)*. 2021 Jun 18; 36(7): 1737-1750. doi: 10.1093/humrep/deab106.

69. Choi BH, Zhu SJ, Kim BY, Huh JY, Lee SH, Jung JH. Effect of platelet-rich plasma (PRP) concentration on the viability and proliferation of alveolar bone cells: an in vitro study. *International journal of oral and maxillofacial surgery*. 2005 Jun; 34(4): 420-4. doi: 10.1016/j.ijom.2004.10.018.
70. Ahmadian S, Sheshpari S, Pazhang M, Bedate AM, Beheshti R, Abbasi MM, et al. Intra-ovarian injection of platelet-rich plasma into ovarian tissue promoted rejuvenation in the rat model of premature ovarian insufficiency and restored ovulation rate via angiogenesis modulation. *Reproductive biology and endocrinology : RB&E*. 2020 Aug 5; 18(1): 78. doi: 10.1186/s12958-020-00638-4.
71. Sfakianoudis K, Simopoulou M, Grigoriadis S, Pantou A, Tsioulou P, Maziotis E, et al. Reactivating Ovarian Function through Autologous Platelet-Rich Plasma Intraovarian Infusion: Pilot Data on Premature Ovarian Insufficiency, Perimenopausal, Menopausal, and Poor Responder Women. *Journal of clinical medicine*. 2020 Jun 10; 9(6): doi: 10.3390/jcm9061809.
72. Huang Y, Zhu M, Liu Z, Hu R, Li F, Song Y, et al. Bone marrow mesenchymal stem cells in premature ovarian failure: Mechanisms and prospects. *Frontiers in immunology*. 2022; 13: 997808. doi: 10.3389/fimmu.2022.997808.
73. Kilic S, Pinarli F, Ozogul C, Tasdemir N, Naz Sarac G, Delibasi T. Protection from cyclophosphamide-induced ovarian damage with bone marrow-derived mesenchymal stem cells during puberty. *Gynecological endocrinology : the official journal of the International Society of Gynecological Endocrinology*. 2014 Feb; 30(2): 135-40. doi: 10.3109/09513590.2013.860127.
74. Qu Q, Liu L, Cui Y, Liu H, Yi J, Bing W, et al. miR-126-3p containing exosomes derived from human umbilical cord mesenchymal stem cells promote angiogenesis and attenuate ovarian granulosa cell apoptosis in a preclinical rat model of premature ovarian failure. *Stem cell research & therapy*. 2022 Jul 26; 13(1): 352. doi: 10.1186/s13287-022-03056-y.
75. Elahi N, Ai J, Makoolati Z. A Review on Treatment of Premature Ovarian Insufficiency: Characteristics, Limitations, and Challenges of Stem Cell versus ExosomeTherapy. *Veterinary medicine international*. 2023; 2023: 5760011. doi: 10.1155/2023/5760011.
76. Qin JC, Fan L, Qin AP. The effect of dehydroepiandrosterone (DHEA) supplementation on women with diminished ovarian reserve (DOR) in IVF cycle: Evidence from a meta-analysis. *Journal of gynecology obstetrics and human reproduction*. 2017 Jan; 46(1): 1-7. doi: 10.1016/j.jgyn.2016.01.002.
77. Naik S, Lepine S, Nagels HE, Siristatidis CS, Kroon B, McDowell S. Androgens (dehydroepiandrosterone or testosterone) for women undergoing assisted reproduction. *The Cochrane database of systematic reviews*. 2024 Jun 5; 6(6): CD009749. doi: 10.1002/14651858.CD009749.pub3.
78. Yang P, Wu R, Zhang H. The effect of growth hormone supplementation in poor ovarian responders undergoing IVF or intracytoplasmic sperm injection (ICSI): a meta-analysis of randomised controlled trials. *Reproductive biology and endocrinology : RB&E*. 2020 Jul 29; 18(1): 76. doi: 10.1186/s12958-020-00632-w.
79. Raffi F, Metwally M, Amer S. The impact of excision of ovarian endometrioma on ovarian reserve: a systematic review and meta-analysis. *The Journal of clinical endocrinology and metabolism*. 2012 Sep; 97(9): 3146-54. doi: 10.1210/jc.2012-1558.
80. Somigliana E, Berlanda N, Benaglia L, Viganò P, Vercellini P, Fedele L. Surgical excision of endometriomas and ovarian reserve: a systematic review on serum antimüllerian hormone level modifications. *Fertility and sterility*. 2012 Dec; 98(6): 1531-8. doi: 10.1016/j.fertnstert.2012.08.009.
81. Whitcomb BW, Purdue-Smithe AC, Szegda KL, Boutot ME, Hankinson SE, Manson JE, et al. Cigarette Smoking and Risk of Early Natural Menopause. *American journal of epidemiology*. 2018 Apr 1; 187(4): 696-704. doi: 10.1093/aje/kwx292.
82. Oktay K, Harvey BE, Partridge AH, Quinn GP, Reinecke J, Taylor HS, et al. Fertility Preservation in Patients With Cancer: ASCO Clinical Practice Guideline Update. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. 2018 Jul 1; 36(19): 1994-2001. doi: 10.1200/JCO.2018.78.1914.

SURGICAL MENOPAUSE

Keywords: Consequences, diagnosis, management, therapeutic, and prophylactic oophorectomy

49

INTRODUCTION

Surgical menopause is an important public health issue. In India, public awareness of health issues varies widely. Hysterectomy, with or without oophorectomy for benign lesions, is the most common major surgical procedure among women of reproductive and perimenopausal age. In practice, surgical menopause is the removal of the ovaries. In many cases, accurate surgical records may not be available to clearly distinguish between hysterectomy alone and hysterectomy with unilateral or bilateral oophorectomy (BO). Surgical menopause is characterised by an abrupt and profound decline in estrogen levels, unlike the gradual hormonal changes seen in natural menopause. As a result, menopausal symptoms appear suddenly, are more intense, and are often more severe. The health consequences of surgical menopause extend beyond immediate symptoms and may contribute to increased morbidity from chronic conditions such as cardiovascular disease (CVD), osteoporosis, and metabolic disorders. The severity and range of symptoms vary widely among women and are primarily related to estrogen deficiency. Early recognition and appropriate management of postmenopausal symptoms by an alert and knowledgeable physician can significantly improve the quality of life of women undergoing surgical menopause.

DEFINITION

Surgical menopause refers to the sudden and permanent cessation of ovarian function following bilateral oophorectomy, with or without removal of the uterus, resulting in an abrupt endocrine-deficient state of menopause, particularly affecting estrogen, progesterone and ovarian androgens.¹ Loss of ovarian function causes an abrupt decline in estrogen levels, precipitating menopausal symptoms and related complications. The onset, severity, and spectrum of short-term symptoms vary considerably between individuals.² Surgical menopause results from BO, bilateral salpingo-oophorectomy (BSO), total hysterectomy with BSO, or compromise of ovarian blood supply during pelvic surgery, and may also follow extensive oncologic procedures such as abdominoperineal resection or total pelvic exenteration.³ The common symptoms include vasomotor symptoms (VMS) such as hot flushes and night sweats, psychological disturbances including low mood, impaired concentration, and insomnia, dementia, vaginal dryness, and cutaneous changes such as thinning and reduced skin elasticity. Sexual dysfunction often worsens following surgical menopause, reflecting both estrogen deficiency and the effects of ageing.⁴

PREMATURE OVARIAN FAILURE FOLLOWING HYSTERECTOMY

Ovarian conservation at the time of hysterectomy has long been recommended to avoid abrupt estrogen deprivation; however, growing evidence indicates that hysterectomy itself is associated with an increased risk of premature ovarian insufficiency (POI).⁵ Even when the ovaries are preserved, ovarian failure occurs on average approximately four years earlier than the age of natural menopause. The incidence of ovarian failure after hysterectomy is reported to range between 25% and 50%, typically manifesting within 2–5 years following surgery, although it may occur at any time postoperatively.^{5,6} Total hysterectomy appears to induce ovarian dysfunction through complex pathophysiological mechanisms involving hormonal disruption, impaired ovarian blood flow, and a reduction in follicular reserve. A comprehensive meta-analysis of 14 studies including 1,457 premenopausal women demonstrated significant postoperative ovarian changes, with reductions in anti-Müllerian hormone (AMH) and inhibin B, accompanied by increases in follicle-stimulating hormone (FSH) and luteinizing hormone.^{6,7}

These findings support proposed mechanisms, including disruption of the ovarian vascular supply, reduced stromal perfusion, and accelerated follicular depletion. Overall, the evidence consistently indicates a nearly twofold increased risk of ovarian failure following hysterectomy, particularly in women over 40 years of age, underscoring the importance of careful preoperative counselling regarding potential long-term ovarian consequences when hysterectomy is considered in premenopausal women.⁵

DIFFERENCE BETWEEN NATURAL AND SURGICAL MENOPAUSE

In natural menopause, the ovarian follicles that produce estradiol have stopped producing estradiol, but the ovaries can continue to produce testosterone and androstenedione for many years after menopause; these androgens are converted to estrogens peripherally when gonadal hormone production is absent in surgical menopause.⁸ In premenopausal women, BO causes an abrupt fall in estrogen levels to about 80% below follicular phase levels within 24 hours, with a 30% reduction in plasma testosterone levels, lower than those seen after natural menopause. In postmenopausal women, estrogen levels remain unchanged, but testosterone levels fall significantly. The postmenopausal ovary remains hormonally active, contributing about 50% of circulating testosterone and 30% of androstenedione.^{9,10}

CONSEQUENCES OF SURGICAL MENOPAUSE

Women who undergo premenopausal BO experience increased long-term morbidity compared with women who retain their ovaries. In observational studies summarised by Parker et al., women who underwent BO before menopause showed higher risks of congestive heart failure, stroke, fractures, Parkinsonism, cognitive impairment, dementia, anxiety, and depression compared with controls.¹¹ Evidence from large cohorts, including the Nurses' Health Study, also demonstrates a small but significant increase in all-cause mortality, particularly among women who underwent BO before age 45 and did not use estrogen therapy.¹² Young age at menopause was associated with increased risks of all-cause mortality. A later menopause age was associated with a longer lifespan.¹³

Vasomotor, Neuropsychiatric, and Somatic Symptoms

After surgical menopause in perimenopausal women, VMS typically occur abruptly due to the sudden loss of ovarian estrogen production, with about half of women experiencing symptoms soon after surgery and most developing them within several weeks. In many women, these symptoms resolve spontaneously, with a large proportion improving by 6 months and the majority by 5 years as the body adapts to a post-ovariectomy hormonal state.¹⁴ In a random sample survey, conducted by Rocca WA et al, women who had surgical menopause had a higher prevalence of hot flashes, hypoactive sexual desire, vaginal dryness, depression, migraine, headache, and atypical symptoms.¹⁵

A recent longitudinal study in breast cancer genes (BRCA) mutation carriers showed that premenopausal BSO was associated with increased menopausal symptoms, including VMS, and reduced sexual functioning at 3.5 years follow-up, especially in women who were premenopausal at the time of surgery; hormone replacement therapy (HRT) reduced but did not fully eliminate these effects.¹⁶ Women who retain their ovaries at the time of hysterectomy also develop climacteric symptoms, but these commonly occur prematurely, 2–5 years earlier than expected, compared with women without hysterectomy.¹⁷ Studies show that VMS and other menopausal complaints (including vaginal dryness, sexual dysfunction, and psychological symptoms) are often more frequent and/or severe in women after surgical menopause compared to natural menopause because of the abrupt estrogen decline.^{14,18}

Surgical Menopause And Psychological Well-being And Sexuality

Multiple systematic reviews and meta-analyses show that total hysterectomy for benign conditions is not consistently associated with significant changes in overall sexual function when examined as a group. There is substantial heterogeneity across studies, leading to wide variation in individual outcomes.¹⁹ Some women report improvements in pain and sexual enjoyment when pre-existing symptoms like heavy bleeding or pelvic pain are relieved by surgery. Evidence does not conclusively show a universal decline in libido or orgasm solely due to hysterectomy itself. Retrospective studies have reported mixed results, with some women reporting decreased libido and others reporting unchanged or increased libido post-hysterectomy. Dyspareunia and vaginal dryness may improve if preoperative pathology (endometriosis, fibroids) was contributing to pain, but can also persist or emerge postoperatively in some women.²⁰ Some long-term cohort data indicate that specific aspects, such as arousal and orgasm frequency, may be lower after BSO, though hormone levels (testosterone/estradiol) may not show significant differences.¹⁸

Unnecessary BSO should be avoided in women undergoing hysterectomy solely for benign disease if preservation of ovarian hormonal function is possible.¹⁹ Estrogen therapy (systemic and/or local vaginal formulations) is effective for treating genitourinary symptoms of menopause and can improve vaginal lubrication and discomfort. Though not every study included sexual function outcomes, estrogen is clinically recommended to help with vaginal atrophy and dryness, contributing to pain.²¹

Testosterone plays a role in sexual motivation and desire in women. A systematic review and the few available randomised controlled trials suggest that testosterone may improve overall sexual functioning and sexual desire after surgical menopause or BSO.²¹ The evidence base for testosterone in women is smaller and less robust than for estrogen, and decisions should be individualised.

Surgical Menopause And Cardiovascular Risk

Early BO is associated with an increased risk of cardiovascular mortality and disease. In a long-term cohort study from Olmsted County, women who underwent BO before age 45 years had a significantly higher risk of cardiovascular mortality compared with matched controls. This increased risk was particularly evident in women not treated with estrogen through age 45, whereas estrogen treatment appeared to attenuate the risk.²² A recent systematic review and meta-analysis incorporating more than 2.4 million participants reported that BO is associated with a marginally increased risk of CVD and a significantly higher risk of heart failure. Importantly, the increased risk was observed only when oophorectomy was performed at premenopausal ages.²³ Additional evidence indicates that BO is associated with greater progression of subclinical atherosclerosis (carotid intima-media thickness) than natural menopause.²⁴ Several reviews and observational analyses link early surgical menopause with increased CVD rates compared to natural menopause, likely due to earlier loss of estrogen's cardioprotective effects.²⁵ Estrogen therapy initiated after premenopausal oophorectomy may partially mitigate risk, but the cardiovascular benefit depends on the timing and duration of hormone therapy.²²

Surgical Menopause, Bone Mineral Density, and Fracture

Early menopause (EM), whether natural or surgical, is consistently associated with lower bone mineral density (BMD) later in life. Estrogen plays a central role in maintaining skeletal integrity by reducing osteoclast activity and supporting osteoblast activity. When ovarian estrogen production ceases abruptly, as in surgical menopause, there is a rapid increase in bone turnover, resulting in a net loss of bone mass. This results from the removal of estrogen's inhibitory effects on osteoclastogenesis and support for osteoblast survival. Early estrogen deficiency is associated with lower BMD later in life and increased fracture risk.²⁶

After surgical menopause, bone loss occurs rapidly, particularly in the first few years after estrogen loss. Some cohort analyses show up to 20 % loss of BMD in the first 18 months after BO, and a high prevalence of osteopenia/osteoporosis in women undergoing BSO before age 50, especially without HT.²

A systematic review and meta-analysis of surgical menopause and bone outcomes found that surgical menopause is associated with significantly lower BMD at the lumbar spine and femoral neck compared with age-matched premenopausal women.²⁷

In a 34-year prospective observational study, 390 women aged 48 were followed into old age. Women with early natural menopause (before age 47) had significantly higher rates of osteoporosis, fragility fractures, and mortality compared with those who experienced menopause at age 47 or later and HT causes a decrease in fractures.²⁸

In the large Rotterdam Study cohort, early menopause (≤ 45 years) was an independent risk factor for incident vertebral fractures in older women, reinforcing that earlier estrogen deficiency predicts greater fracture risk.²⁹

Surgical Menopause and Cognitive Issues

A systematic review and meta-analysis of 11 studies found that surgical menopause was associated with faster cognitive decline, especially for verbal memory, semantic memory, and processing speed. Early surgical menopause (≤ 45 years) was linked to a higher risk of dementia compared with women without oophorectomy.³⁰

Large longitudinal cohort analyses have repeatedly shown that BO before menopause is associated with increased risk of cognitive impairment or dementia later in life, and that younger age at surgery correlates with greater risk.³¹

Observational evidence suggests natural menopause alone does not cause major short-term cognitive decline, whereas surgical menopause, with abrupt loss of ovarian hormones, is more likely to be associated with cognitive changes.³²

HT taken soon after BO and continued through at least age 50 years was associated with reduced risk of long-term cognitive impairment or dementia, supporting a "window of opportunity" for potential benefit.³³

There may be short-term benefits of estrogen therapy when initiated around the time of surgical menopause,

especially for specific memory outcomes. However, the evidence base is small and inconsistent, and HT is not approved for cognitive protection.³²

Surgical Menopause and Type 2 Diabetes

Evidence from the EPIC-InterAct study indicates that EM is associated with an increased risk of type 2 diabetes mellitus (T2DM). Women who experienced menopause before age 40 had a 32 % higher risk of developing T2DM compared with those who entered menopause at ages 50–54. Additionally, shorter reproductive lifespan was independently associated with increased diabetes risk after adjustment for lifestyle and metabolic risk factors.³⁴

Early natural menopause and surgical menopause are consistently associated with an increased risk of T2DM across large prospective cohorts and meta-analyses. The risk appears independent of metabolic factors, as estrogen's protective effects on glucose homeostasis are lost.³⁵

CHARACTERISTICS OF SURGICAL MENOPAUSE THAT DIFFERENTIATE IT FROM NATURAL MENOPAUSE

- Surgical menopause differs from natural menopause in several key ways. It results from the abrupt cessation of ovarian hormone production, usually after bilateral oophorectomy, whereas natural menopause occurs gradually over several years and is characterised by fluctuating hormone levels.³⁶
- Consequently, women undergoing surgical menopause often experience more severe VMS and GSM than women with natural menopause.³⁷ Surgical menopause also occurs at a younger age, exposing women to longer-term estrogen deficiency and increasing their risk for osteoporosis, CVD, cognitive decline, and metabolic disorders.³⁸
- Additionally, the sudden hormonal change, combined with recovery from surgery or underlying disease, often requires significant psychological and physical adjustment.³⁶
- Natural menopause is diagnosed retrospectively after 12 consecutive months of amenorrhea in women over 45, without another pathological cause.³⁹
- Routine measurement of FSH or estradiol is generally not recommended because hormonal levels fluctuate widely during the menopausal transition.³⁷
- In contrast, surgical menopause is diagnosed immediately following BO, as ovarian hormone production ceases abruptly, and biochemical confirmation is usually unnecessary.⁴⁰

DIAGNOSIS OF MENOPAUSE WITH HYSTERECTOMY WITHOUT BILATERAL OOPHORECTOMY

Diagnosing menopause in women who have undergone a hysterectomy with ovarian conservation is more challenging than in women with intact uteri, as the hallmark criterion of 12 months of amenorrhoea is no longer observable.³⁹

In these women, clinicians rely on a combination of clinical symptoms, including vasomotor disturbances, vaginal dryness, sleep disruption, and mood changes, along with biochemical markers to confirm ovarian failure. Measurement of FSH on at least two occasions, several weeks apart, is commonly used, with levels exceeding 30–40 IU/L suggesting menopausal status. Estradiol levels can provide additional confirmation.³⁷

AMH may reflect residual ovarian reserve, but it is not routinely recommended in clinical practice. Women over 50 years with appropriate symptoms and hormonal patterns are likely postmenopausal. Guidelines from the North American Menopause Society emphasise the combined use of symptom assessment and biochemical evaluation to diagnose menopause in hysterectomised women, while NICE recommends hormonal testing before considering HT in the absence of menstruation.^{37,40}

This approach ensures accurate diagnosis, informs appropriate management, and mitigates long-term risks associated with estrogen decline, such as osteoporosis, cardiovascular disease, and cognitive decline.

INITIATION OF HORMONE THERAPY FOR PATIENTS WHO HAVE HAD BILATERAL OOPHORECTOMY

The primary goals of therapy in surgical menopause are symptom relief, preventing long-term complications, and improving quality of life. HT is strongly recommended for most women experiencing surgical menopause, particularly if performed before the age of 50, unless contraindications exist, because it effectively alleviates VMS and genitourinary syndrome (GSM) and reduces long-term estrogen-deficiency-related morbidity.³⁷

Therapy should generally be initiated as soon as possible after surgery to mimic the physiologic exposure of endogenous hormones and optimise bone and cardiovascular protection at least until the natural age of menopause. For women with an intact uterus, combined estrogen-progestogen therapy is indicated to prevent endometrial hyperplasia, while estrogen-only therapy is appropriate for women without a uterus. The type, dose, and route of estrogen should be tailored to the patient. The transdermal route provides more stable plasma estradiol levels compared to oral formulations, avoids the hepatic first-pass metabolism, and is associated with a lower risk of venous thromboembolism.⁴¹

The lowest effective dose should be used, and therapy should be individualised based on age, time since oophorectomy, comorbidities, and patient preferences. Regular monitoring for symptom control, adverse effects, and risk factors (cardiovascular, thromboembolic, or breast cancer risk) is recommended throughout treatment. HT should be weaned gradually when discontinuing, rather than stopping abruptly, to minimise symptom recurrence. Initiating HT promptly after surgical menopause not only improves quality of life but also mitigates many long-term health consequences of premature estrogen deficiency.^{37,38}

In women with surgical menopause who continue to experience loss of libido, lethargy, depression, or reduced sexual satisfaction despite adequate estrogen therapy, testosterone supplementation may be considered.³⁷ Tibolone may be used as an alternative for symptom management in surgically induced menopause, particularly in women with contraindications to conventional estrogen therapy. Tibolone improves vasomotor symptoms, sexual function, and bone density, but is not recommended for women at high risk of stroke or breast cancer.³⁷

Local vaginal estrogen is effective for urogenital symptoms such as vaginal dryness, dyspareunia, and recurrent urinary tract infections. Systemic absorption is minimal, making it safe for most women, including those who may have contraindications to systemic HT.³⁷

GUIDELINES & RECOMMENDATIONS ON OVARIAN PRESERVATION & OOPHORECTOMY

General Principles of Ovarian Preservation

For women undergoing hysterectomy for benign disease, current evidence and expert opinion favour ovarian conservation, particularly in those who are premenopausal and at average risk for ovarian cancer. Conservation until at least age 65 has been associated with improved long-term survival in decision modelling studies for women without high cancer risk. This approach should be accompanied by informed consent that balances cancer risk with non-oncologic health outcomes.⁴²

Age and Risk Stratification

For women under 45–50 years, ovarian conservation is generally recommended for average-risk women due to significant benefits for cardiovascular, bone, and metabolic health. For women older than 50 or nearing natural menopause, the benefits of conservation versus removal may be more balanced and informed by individual risk profiles. Overall, decisions should be individualised taking into account patient age, cancer risk, comorbidities, and hormone replacement therapy eligibility.⁴³

High Genetic Risk (Risk Reducing Salpingo Oophorectomy (RRSO))

Women with hereditary cancer syndromes such as BRCA1/2 or a strong family history of ovarian/breast cancer are recommended to undergo risk-reducing bilateral salpingo-oophorectomy (RRBSO) after completing childbearing to substantially lower cancer risk. Guidelines emphasise preoperative counselling, including genetics, and careful perioperative planning for hormone management. Post RRSO, HT is recommended until the average age of natural menopause (51 years) in women without a personal history of breast cancer to mitigate risks of premature estrogen loss.⁴⁴

Ovarian preservation in oncologic contexts

- *Early-stage endometrial cancer:* Ovarian preservation may be considered in carefully selected premenopausal patients with low-grade tumours and no evidence of ovarian or extra-uterine disease, after thorough evaluation.⁴⁵
- *Cervical cancer:* Certain subtypes and early tumours may permit ovarian conservation per multidisciplinary oncology guidelines. International Federation of Gynaecology and Obstetrics (FIGO) stage IB1–IB2 node-negative cervical cancer with squamous cell carcinoma or HPV-associated adenocarcinoma may be candidates for ovarian conservation.⁴⁶
- *Ovarian cancer:* The European Society for Medical Oncology–European Society of Gynaecological Oncology (ESMO-ESGO) consensus recommendations state that fertility-sparing surgery (BSO and complete surgical staging) can be performed in all stage IA and IC1 patients with low-risk ovarian carcinomas. Ovarian preservation for invasive epithelial ovarian cancers is not recommended at a higher stage than FIGO I.⁴⁷
- *Borderline ovarian tumours:* Unilateral preservation may be appropriate depending on fertility desires and tumour pathology. Decisions are made based on stage, histology, age, fertility goals, and genetic risk.⁴⁸

Counselling and Shared Decision Making

Across guideline sources, a shared decision-making process is emphasised. Clinicians and patients should discuss the long-term non-cancer health effects of oophorectomy alongside the low absolute risk of ovarian cancer in average-risk women, and tailor the approach accordingly, rather than defaulting to routine ovarian removal with hysterectomy.⁴²

SYNOPSIS

- Hysterectomy should be performed only when necessary; conservative, uterus-sparing surgery is preferred.
- Oophorectomy under age 45 should generally be avoided unless there is a high risk of ovarian cancer.
- Meticulous surgical technique is essential to preserve the ovarian blood supply.
- HT should be started promptly after bilateral oophorectomy unless contraindicated.
- In women with retained ovaries, HT is initiated only if symptoms or biochemical evidence of estrogen deficiency appear.
- Vaginal estrogen can treat urogenital symptoms with minimal systemic exposure.
- Testosterone or tibolone may be considered in select women with persistent symptoms.
- Surgical menopause causes rapid bone loss; HT mitigates osteoporosis and other estrogen-deficiency risks.
- HT selection depends on uterine status: unopposed estrogen if uterus removed; combined therapy or tibolone if uterus intact or history of endometriosis.
- Informed consent and shared decision-making improve compliance and satisfaction.
- Ovarian removal should not be done routinely; only high-risk women benefit from prophylactic oophorectomy.
- The risk of ovarian malignancy is low in average-risk women; the benefits of preservation often outweigh the risks.

RESEARCH AGENDA

AI-based prediction models to identify women at high risk of post-surgical complications or estrogen deficiency symptoms.

REFERENCES

1. C Pillay O, Manyonda I. The surgical menopause. *Best Pract Res Clin Obstet Gynaecol.* 2022 May;81:111–8. doi: 10.1016/j.bpobgyn.2022.03.001.
2. Secoşan C, Balint O, Pirtea L, Grigoraş D, Bălulescu L, Ilina R. Surgically Induced Menopause-A Practical Review of Literature. *Medicina (Mex).* 2019 Aug 14;55(8):482. doi: 10.3390/medicina55080482.

3. Duration of menopausal vasomotor symptoms over the menopause transition. *JAMA Intern Med.* 2015 Apr;175(4):531–9. doi: 10.1001/jamainternmed.2014.8063.
4. Rocca WA, Grossardt BR, Shuster LT. Oophorectomy, estrogen, and dementia: a 2014 update. *Mol Cell Endocrinol.* 2014 May 25;389(1–2):7–12. doi: 10.1016/j.mce.2014.01.020.
5. Moorman PG, Myers ER, Schildkraut JM, Iversen ES, Wang F, Warren N. Effect of hysterectomy with ovarian preservation on ovarian function. *Obstet Gynecol.* 2011 Dec;118(6):1271–9. doi: 10.1097/AOG.0b013e318236fd12.
6. Huang Y, Wu M, Wu C, Zhu Q, Wu T, Zhu X, et al. Effect of hysterectomy on ovarian function: a systematic review and meta-analysis. *J Ovarian Res.* 2023 Feb 9;16(1):35. doi:10.1186/s13048-023-01117-1.
7. Terry MB, Daly MB, Phillips KA, Ma X, Zeinomar N, Loece N, et al. Risk-Reducing Oophorectomy and Breast Cancer Risk Across the Spectrum of Familial Risk. *J Natl Cancer Inst.* 2019 Mar 1;111(3):331–4. doi: 10.1093/jnci/djy182.
8. Hughes CL, Wall LL, Creasman WT. Reproductive hormone levels in gynecologic oncology patients undergoing surgical castration after spontaneous menopause. *Gynecol Oncol.* 1991 Jan;40(1):42–5. doi: 10.1016/0090-8258(91)90083-h.
9. Korse CM, Bonfrer JMG, van Beurden M, Verheijen RHM, Rookus MA. Estradiol and testosterone levels are lower after oophorectomy than after natural menopause. *Tumour Biol J Int Soc Oncodevelopmental Biol Med.* 2009;30(1):37–42. doi: 10.1159/000199449.
10. Wu X, Lin Y, Long Y, Yi Q. Changes of hormone levels for postmenopausal women after bilateral oophorectomy: A meta-analysis. *Medicine (Baltimore).* 2025 Aug 8;104(32):e43726. doi: 10.1097/MD.00000000000043726.
11. Parker WH, Jacoby V, Shoupe D, Rocca W. Effect of bilateral oophorectomy on women's long-term health. *Womens Health.* 2009 Sept;5(5):565–76. doi: 10.2217/whe.09.42.
12. Parker WH, Feskanich D, Broder MS, Chang E, Shoupe D, Farquhar CM, et al. Long-term mortality associated with oophorectomy compared with ovarian conservation in the nurses' health study. *Obstet Gynecol.* 2013 Apr;121(4):709–16. doi: 10.1097/AOG.0b013e3182864350.
13. Xing Z, Kirby RS. Age at natural or surgical menopause, all-cause mortality, and lifespan among postmenopausal women in the United States. *Menopause.* 2024 Mar 1;31(3):176–85. doi: 10.1097/GME.00000000000002314.
14. Ozdemir S, Celik C, Gökemli H, Kiyici A, Kaya B. Compared effects of surgical and natural menopause on climacteric symptoms, osteoporosis, and metabolic syndrome. *Int J Gynaecol Obstet Off Organ Int Fed Gynaecol Obstet [Internet].* 2009 July [cited 2026 Feb 6];106(1). doi: 10.1016/j.ijgo.2009.03.016. Available from: <https://pubmed.ncbi.nlm.nih.gov/19394614/>
15. A. Rocca W, R Grossardt B. Long-term risk of depressive and anxiety symptoms after early bilateral oophorectomy - PubMed [Internet]. [cited 2026 Feb 6]. doi: 10.1097/gme.0b013e318174f155. Available from: <https://pubmed.ncbi.nlm.nih.gov/18724263/>
16. Hall E, Finch A, Jacobson M, Rosen B, Metcalfe K, Sun P, et al. Effects of bilateral salpingo-oophorectomy on menopausal symptoms and sexual functioning among women with a BRCA1 or BRCA2 mutation. *Gynecol Oncol.* 2019 Jan;152(1):145–50. doi: 10.1016/j.ygyno.2018.10.040.
17. Oldenhave A, Jaszmann LJ, Everaerd WT, Haspels AA. Hysterectomized women with ovarian conservation report more severe climacteric complaints than do normal climacteric women of similar age. *Am J Obstet Gynecol.* 1993 Mar;168(3 Pt 1):765–71. doi: 10.1016/s0002-9378(12)90816-9.
18. Zimmerman J, Brännström M, Bergdahl C, Aziz A, Hermansson J. Long-Term Follow Up of Sexual Function and Steroid Levels in Women after Perimenopausal Hysterectomy with or without Concomitant Oophorectomy. *J Clin Med.* 2023 July 28;12(15):4976. doi: 10.3390/jcm12154976.
19. Dedden SJ, Werner MA, Steinweg J, Lissenberg-Witte BI, Huirne JAF, Geomini PMAJ, et al. Hysterectomy and sexual function: a systematic review and meta-analysis. *J Sex Med.* 2023 Mar 31;20(4):447–66. doi: 10.1093/jsxmed/qdac051.
20. Rhodes JC, Kjerulff KH, Langenberg PW, Guzinski GM. Hysterectomy and sexual functioning. *JAMA.* 1999 Nov 24;282(20):1934–41. doi: 10.1001/jama.282.20.1934.
21. Stuursma A, Lanjouw L, Idema DL, de Bock GH, Mourits MJE. Surgical Menopause and Bilateral Oophorectomy: Effect of Estrogen-Progesterone and Testosterone Replacement Therapy on Psychological Well-being and Sexual Functioning; A Systematic Literature Review. *J Sex Med.* 2022 Dec;19(12):1778–89. doi: 10.1016/j.jsxm.2022.08.191.
22. Rivera CM, Grossardt BR, Rhodes DJ, Brown RD, Roger VL, Melton LJ, et al. Increased cardiovascular mortality after early bilateral oophorectomy. *Menopause.* 2009;16(1):15–23. doi: 10.1097/gme.0b013e31818888f7.
23. Attachaipanich T, Attachaipanich S, Kaewboot K. Cardiovascular outcomes of bilateral oophorectomy: A systematic review and meta-analysis. *Indian Heart J.* 2025;77(6):424–31. doi: 10.1016/j.ihj.2025.08.001.
24. Chen JJ, Shoupe D, Karim R, Stanczyk FZ, Kono N, Sriprasert I, et al. The association of hysterectomy with or without ovarian conservation with subclinical atherosclerosis progression in healthy postmenopausal women. *Menopause.* 2023 July 1;30(7):692–702. doi: 10.1097/GME.0000000000002192.
25. Lobo RA. Surgical menopause and cardiovascular risks. *Menopause.* 2007;14(3 Pt 2):562–6. doi: 10.1097/gme.0b013e318038d333.
26. Gallagher JC. Effect of early menopause on bone mineral density and fractures. *Menopause.* 2007;14(3 Pt 2):567–71. doi: 10.1097/gme.0b013e31804c793d.
27. Fakkert IE, Teixeira N, Abma EM, Slart R, Mourits M, de Bock GH. Bone mineral density and fractures after surgical menopause: systematic review and meta-analysis. *BJOG Int J Obstet Gynaecol.* 2017 Sept;124(10):1525–35. doi: 10.1111/1471-0528.14703.
28. Svejme O, Ahlberg HG, Nilsson JÅ, Karlsson MK. Early menopause and risk of osteoporosis, fracture and mortality: a 34-year prospective observational study in 390 women. *BJOG Int J Obstet Gynaecol.* 2012 June;119(7):810–6. doi: 10.1111/j.1471-0528.2012.03324.x.
29. van der Klift M, de Laet CEDH, McCloskey EV, Johnell O, Kanis JA, Hofman A, et al. Risk factors for incident vertebral fractures in men and women: the Rotterdam Study. *J Bone Miner Res Off J Am Soc Bone Miner Res.* 2004 July;19(7):1172–80. doi: 10.1359/JBMR.040215.
30. Georgakis MK, Beskou-Kontou T, Theodoridis I, Skalkidou A, Petridou ET. Surgical menopause in association with cognitive function and risk of dementia: A systematic review and meta-analysis. *Psychoneuroendocrinology.* 2019 Aug;106:9–19. doi: 10.1016/j.psyneuen.2019.03.013.
31. Rocca WA, Lohse CM, Smith CY, Fields JA, Machulda MM, Mielke MM. Association of Premenopausal Bilateral Oophorectomy With Cognitive Performance and Risk of Mild Cognitive Impairment. *JAMA Netw Open.* 2021 Nov 1;4(11):e2131448. doi:10.1001/jamanetworkopen.2021.31448.
32. Henderson VW, Sherwin BB. Surgical versus natural menopause: cognitive issues. *Menopause.* 2007;14(3 Pt 2):572–9. doi: 10.1097/gme.0b013e31803df49c.
33. Zhang G, Devo P, O'Leary VB, Ovsepian SV. Ageing perspective on cognitive outcomes from reproductive hormone adjustments. *Heliyon.* 2023 Aug;9(8):e19050. doi: 10.1016/j.heliyon.2023.e19050.

34. Brand JS, van der Schouw YT, Onland-Moret NC, Sharp SJ, Ong KK, Khaw KT, et al. Age at menopause, reproductive life span, and type 2 diabetes risk: results from the EPIC-InterAct study. *Diabetes Care*. 2013 Apr;36(4):1012–9. doi: 10.2337/dc12-1020.
35. Yazdkhasti M, Keshavarz M, Khoei EM, Hosseini A, ESmaeilzadeh S, Pebdani MA, et al. The Effect of Support Group Method on Quality of Life in Post-menopausal Women. *Iran J Public Health*. 2012 Nov 1;41(11):78–84.
36. Rocca WA, Mielke MM, Gazzuola Rocca L, Stewart EA. Premature or early bilateral oophorectomy: a 2021 update. *Climacteric J Int Menopause Soc*. 2021 Oct;24(5):466–73. doi: 10.1080/13697137.2021.1893686.
37. Faubion SS, Crandall CJ. The 2022 hormone therapy position statement of The North American Menopause Society. *Menopause*. 2022 July;29(7):767. doi: 10.1097/GME.0000000000002028.
38. Shuster LT, Rhodes DJ, Gostout BS, Grossardt BR, Rocca WA. Premature menopause or early menopause: long-term health consequences. *Maturitas*. 2010 Feb;65(2):161–6. doi: 10.1016/j.maturitas.2009.08.003.
39. Harlow SD, Gass M, Hall JE, Lobo R, Maki P, Rebar RW, et al. Executive summary of the Stages of Reproductive Aging Workshop + 10: addressing the unfinished agenda of staging reproductive aging. *J Clin Endocrinol Metab*. 2012 Apr;97(4):1159–68. doi: 10.1210/jc.2011-3362.
40. Lumsden MA, Davies M, Sarri G, Guideline Development Group for Menopause: Diagnosis and Management (NICE Clinical Guideline No. 23). Diagnosis and Management of Menopause: The National Institute of Health and Care Excellence (NICE) Guideline. *JAMA Intern Med*. 2016 Aug 1;176(8):1205–6. doi: 10.1001/jamainternmed.2016.2761.
41. Rossouw JE, Anderson GL, Prentice RL, LaCroix AZ, Kooperberg C, Stefanick ML, 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 July 17;288(3):321–33. doi: 10.1001/jama.288.3.321.
42. Parker WH, Broder MS, Chang E, Feskanich D, Farquhar C, Liu Z, et al. Ovarian conservation at the time of hysterectomy and long-term health outcomes in the nurses' health study. *Obstet Gynecol*. 2009 May;113(5):1027–37. doi: 10.1097/AOG.0b013e3181a11c64.
43. Giannakaki AG, Giannakaki MN, Nikolettos K, Pagkaki C, Tsikouras P. The Optimal Age for Oophorectomy in Women with Benign Conditions: A Narrative Review. *J Pers Med*. 2025 Apr 19;15(4):158. doi: 10.3390/jpm15040158.
44. Ovarian cancer: identifying and managing familial and genetic risk [Internet]. London: National Institute for Health and Care Excellence (NICE); 2024 [cited 2026 Feb 6]. (National Institute for Health and Care Excellence: Clinical Guidelines). Available from: <http://www.ncbi.nlm.nih.gov/books/NBK604286/>
45. Colombo N, Creutzberg C, Amant F, Bosse T, González-Martín A, Ledermann J, et al. ESMO-ESGO-ESTRO Consensus Conference on Endometrial Cancer: diagnosis, treatment and follow-up. *Ann Oncol Off J Eur Soc Med Oncol*. 2016 Jan;27(1):16–41. doi: 10.1093/annonc/mdv484.
46. Bizzarri N, Pavone M, Loverro M, Querleu D, Fagotti A, Scambia G. Ovarian preservation in gynecologic oncology: current indications and techniques. *Curr Opin Oncol*. 2023 Sept 1;35(5):401–11. doi: 10.1097/CCO.0000000000000969.
47. Colombo N, Sessa C, du Bois A, Ledermann J, McCluggage WG, McNeish I, et al. ESMO-ESGO consensus conference recommendations on ovarian cancer: pathology and molecular biology, early and advanced stages, borderline tumours and recurrent disease†. *Ann Oncol Off J Eur Soc Med Oncol*. 2019 May 1;30(5):672–705. doi: 10.1093/annonc/mdz062.
48. Westermann T, Karabeg E, Heitz F, Traut A, Plett H, Moubarak M, et al. Role of fertility-sparing surgery and further prognostic factors in borderline tumors of the ovary. *Int J Gynecol Cancer Off J Int Gynecol Cancer Soc*. 2024 June 3;34(6):898–905. doi: 10.1136/ijgc-2023-005214.

Section 12

MISCELLANEOUS

- 50. Imaging at Menopause
- 51. Medicolegal Aspects and Menopause
- 52. Travel at Menopause
- 53. Healthcare Insurance for Elderly Women
- 54. Economics of Menopause Management
- 55. Disease Specific Pharmacotherapy and Interaction with Hormones
- 56. Artificial Intelligence, Apps and Social Media

IMAGING AT MENOPAUSE

Keywords: Ultrasound, endometrium, myometrium, adenexa, pelvic floor, urethra, bladder

50

INTRODUCTION

Menopause represents a critical transition in a woman's life, marked by hormonal, metabolic, and structural changes in the reproductive system. In Indian women, menopause often occurs earlier than in Western populations, and healthcare-seeking behaviour is frequently delayed due to sociocultural factors, lack of awareness, and limited access to specialist care. As a result, imaging plays a pivotal role in the early identification of gynaecological pathology, particularly endometrial and ovarian malignancies.¹

Ultrasonography, especially transvaginal ultrasound (TVS), is the cornerstone of imaging in menopausal and postmenopausal women. Recent advances, including 3D imaging, Doppler analysis, and the integration of artificial intelligence (AI), have significantly increased the diagnostic accuracy of TVS in endometrial assessment.² The integration of Doppler studies and three-dimensional power Doppler (3D-PD) significantly enhances diagnostic accuracy by providing information on vascular patterns and resistance indices, aiding differentiation between benign and malignant conditions.^{3,4} Ultrasound is the first-line imaging modality for evaluation of the postmenopausal pelvis owing to its safety, accessibility, affordability, and repeatability. A combined approach using transabdominal ultrasound for general pelvic assessment and TVS for detailed evaluation is recommended.⁵

PRECAUTIONS DURING TRANSVAGINAL ULTRASOUND IN POSTMENOPAUSAL WOMEN

TVS in postmenopausal women requires particular care because of the hypoestrogenic genitourinary syndrome of menopause (GSM).⁶ These alterations predispose women to discomfort, mucosal irritation, and minor trauma during probe insertion. Therefore, a patient-centred approach is essential. Adequate pre-procedural counselling helps reduce anxiety-related pelvic floor tension, which itself can exacerbate pain. A generous application of water-based lubricant over the probe cover and at the introitus is recommended to minimise friction. Gentle, slow insertion of the probe along the posterior vaginal wall, with avoidance of excessive pressure, is critical, particularly in women with vaginal stenosis or severe atrophy. If significant pain persists, alternative approaches such as transabdominal or transperineal ultrasound should be considered. In symptomatic women with marked atrophic changes, pre-treatment with topical vaginal estrogen has been shown to improve mucosal integrity and reduce discomfort during instrumentation. Thus, careful technique and awareness of menopausal anatomical changes are fundamental to ensuring both diagnostic adequacy and patient safety.

In women with significant vaginal atrophy, marked introital narrowing, dyspareunia, vulvodynia, or severe anxiety-related pelvic floor spasm, application of 2% lidocaine (xylocaine) jelly at the introitus 3–5 minutes prior to probe insertion may reduce discomfort.⁷

SCANNING PROTOCOL

A standardised scanning protocol should be adopted to ensure that pelvic ultrasound examinations are systematic, comprehensive, and reproducible. A structured approach enhances consistency between studies and improves the detection of clinically significant abnormalities. A recommended sequence for transvaginal pelvic ultrasonography begins with evaluation of the vagina upon probe insertion, followed by assessment of the bladder. The uterus and cervix are then examined, with detailed evaluation of the endometrium, including measurement and characterisation. Subsequent assessment includes the right ovary and adnexa, followed by the left ovary and adnexa. The pouch of Douglas and uterosacral ligaments should be inspected for free fluid, nodularity, or masses. Examination of the rectum may be performed where indicated, and, when clinically appropriate, evaluation of the kidneys and ureters should be included to exclude hydronephrosis or associated urinary tract pathology. This systematic protocol ensures a thorough and complete pelvic assessment.⁸ In postmenopausal women, expected findings include: reduced uterine size; thin, regular endometrium; and small ovaries, often difficult to visualise. Any deviation from these expected involutional changes should prompt further scrutiny.⁸ Refer to Figure 1

ADVANCED ULTRASOUND TECHNIQUES

Three-dimensional (3D) ultrasound combined with power Doppler (PD) represents an important advancement over conventional two-dimensional TVS (2D TVS) in the evaluation of endometrial pathology. Unlike 2D imaging, 3D ultrasound enables endometrial volume assessment and allows quantitative analysis of vascularity through indices such as the vascularisation index (VI), flow index (FI), and vascularisation flow index (VFI). Multiple studies have demonstrated that lesions suggestive of endometrial malignancy are associated with increased endometrial thickness and volume and significantly higher 3D power Doppler vascular indices compared with benign conditions. Diagnostic models that combine endometrial thickness with 3D vascular parameters achieve very high diagnostic accuracy, with reported area under the curve (AUC) values ranging from 0.88 to 0.98.

FI appears particularly useful when endometrial thickness is ≥ 5 mm, whereas VI may be more predictive when thickness is < 5 mm. The technique is especially valuable in cases with borderline endometrial thickness (3–15 mm) or when focal intrauterine lesions are suspected, as it enhances risk stratification and may help reduce unnecessary biopsies. However, variability in cut-off values, operator dependence, differences in machine settings, and limited external validation restrict universal application. Therefore, although 3D power Doppler adds significant discriminatory value, histopathological assessment remains the definitive diagnostic standard.^{3,9,10}

Limitations: 3D parameters and cut-offs vary across studies (different VOCAL settings, operator dependence). External validation is limited despite promising internal AUCs. This requires specialised equipment and training. Local validation is advised before substituting for histology.

Role of Doppler Studies

Doppler ultrasound provides functional information that complements grayscale imaging and improves diagnostic confidence. Uterine artery Doppler of a prospective cross-sectional cohort of 60 postmenopausal women with bleeding and 23 malignant cases found that malignant cases had lower resistance index (RI), pulsatility index (PI), and peak systolic velocity (PSV) than benign cases. Optimal uterine artery thresholds for predicting endometrial cancer were an $RI \leq 0.73$: AUC 0.85, Sensitivity 91.3%, Specificity 83.3%; $PI \leq 1.42$: AUC 0.88, Sensitivity 91.3%, Specificity 83.3% - $ET > 12.5$ mm: AUC 0.89, Sensitivity 93.8%, Specificity 77.8%. Combined uterine artery Doppler and ET provided the best discrimination.¹¹

Limitations

- Colour Doppler indices and power Doppler studies, although initially encouraging, show variable performance across studies.
- Doppler thresholds and indices vary with equipment, settings, and operator technique.
- Many Doppler cut-offs come from moderate-sized single-centre studies and require external validation.
- No single Doppler index alone reliably excludes malignancy.
- Doppler performs best when used in multiparametric models alongside ET, volume, and clinical risk factors.
- Use of standardised Doppler terminology, as recommended by the International Endometrial Tumour Analysis (IETA) group, is encouraged.⁴

SALINE INFUSION SONOHYSTEROGRAPHY

Transvaginal saline infusion sonohysterography (SIS) after a saline infusion improves the detection rate of focal abnormalities.¹²

Indications

- Better detection of focal intracavitary lesions, such as polyps, submucous fibroids, when TVS is inconclusive, or ET is thickened.
- SIS is comparable to hysteroscopy for detecting focal lesions.
- Cannot reliably distinguish benign from malignant focal lesions alone.

- Difficulties with distension during SIS may raise suspicion of malignancy.
- SIS and 3D techniques further enhance ultrasound-histopathology correlation and more reliably differentiate between patients who need endometrial sampling and those who could be offered prudent expectant management.
- Both 2D SIS and 3D SIS, as per the availability, should be considered alternatives to diagnostic hysteroscopy when intracavitary pathology is suspected in women with abnormal uterine bleeding.¹³

ENDOMETRIUM

Technique of Endometrial Assessment

Technique: Endometrial thickness (ET) should be measured on a true mid-sagittal transvaginal image, from one basal layer to the other, excluding intracavitary fluid.^{5,8} Refer to figure 2

Systematic evaluation includes

- Use a standardised midsagittal midline approach to ensure accurate and reproducible measurements.
- Measure the maximum anteroposterior (AP) thickness of the endometrium at its widest point.
- Record the double-layer thickness, including both anterior and posterior endometrial layers.
- If intracavitary fluid is present, measure each endometrial layer separately and sum the two measurements; the fluid itself should not be included in the total thickness.⁸
- Clearly document any inability to adequately visualise the endometrium, as this may necessitate further evaluation.⁸
- Assess and describe the endometrial echogenicity (homogeneous, heterogeneous, or trilaminar pattern).
- Note the presence of cystic spaces, focal irregularities, or intracavitary masses, which may suggest pathology such as endometrial polyps.
- When focal lesions or abnormal vascularity are suspected, apply colour or power Doppler imaging with an appropriately low pulse repetition frequency (0.3-0.5 kHz) to evaluate vascular patterns.
- When the endometrium cannot be reliably visualised due to obesity, fibroids, adenomyosis, uterine position, or prior surgery, this limitation must be clearly stated, as meaningful exclusion of pathology may not be possible, and alternative evaluation may be required.^{14,15}

Normal Endometrium at Menopause

The endometrium atrophies during menopause and becomes thinner in the absence of estrogen-induced epithelial stimulation.⁸ This appears on ultrasound as a “pencil-line” of echogenicity, representing the thickness of the tissues between the two sides of the atrophic basal endometrium.^{8,15}

Endometrial Thickness: Refer to Table 1

Effect of Hormone Therapy on Endometrial Thickness

Hormone therapy (HT) typically increases endometrial thickness by about 1–1.5 mm with continuous estrogen or estrogen/progesterone therapy and by about 3 mm with sequential therapy.^{16,17} Women undergoing sequential therapy also show greater monthly variation in endometrial thickness, with the thinnest endometrium occurring after progesterone withdrawal.¹⁸ Changes in endometrial thickness are not significantly different from those of the non-HT group in patients taking tibolone. Endometrial thickness with tibolone closely mimics the naturally atrophic postmenopausal state.¹⁸ In asymptomatic women on HT, routine serial ultrasound is not universally recommended.¹⁹ However, an endometrial thickness greater than 4–5 mm in the presence of unscheduled bleeding typically prompts further assessment with biopsy or hysteroscopy.^{14,20} Thus, the interpretation of endometrial thickness in HT users must consider the specific hormonal regimen, the timing of imaging, and the clinical presentation.

Effect of Antihypertensive Medications

Endometrial thickness is frequently greater in asymptomatic, hypertensive postmenopausal women receiving antihypertensive drugs than in untreated hypertensive and normotensive patients: 6.2 mm, 4.3 mm, and 3.6 mm, respectively.²¹

DIAGNOSIS OF FOCAL ENDOMETRIAL LESIONS AT MENOPAUSE

Focal endometrial lesions, including polyps, submucosal fibroids, and focal hyperplasia or carcinoma, are an important cause of postmenopausal bleeding. Accurate diagnosis is essential to differentiate benign from malignant pathology. TVS is the first-line investigation. It allows measurement of endometrial thickness and may suggest focal abnormalities; however, its sensitivity for detecting focal lesions is limited, especially when the endometrium appears diffusely thickened.¹⁵ SIS significantly improves diagnostic accuracy by distending the uterine cavity, enabling clear visualisation of intracavitary lesions such as polyps and submucosal fibroids. It is more sensitive and specific than TVUS alone for detecting focal pathology.²²

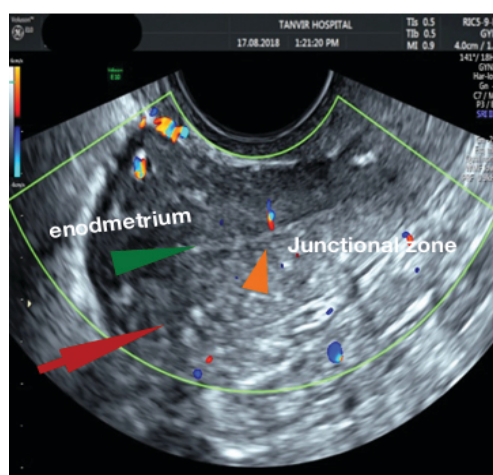


Figure 1. A mid-sagittal transvaginal image of the uterus in a 75-year-old postmenopausal woman. Green -thin endometrium; orange-junctional Zone(JZ). The red arrow indicates Mönckeberg's calcification of arcuate arteries.



Figure 2: Fluid in the cavity - the sum of the thickness of both layers of the endometrium is measured, excluding the fluid in the cavity in a 75 yr old postmenopausal woman



Figure 3. Tamoxifen induced endometrial hyperplasia and irregular cystic changes, with subendometrial cysts, no colour in a 52-year-old woman with a history of breast cancer.

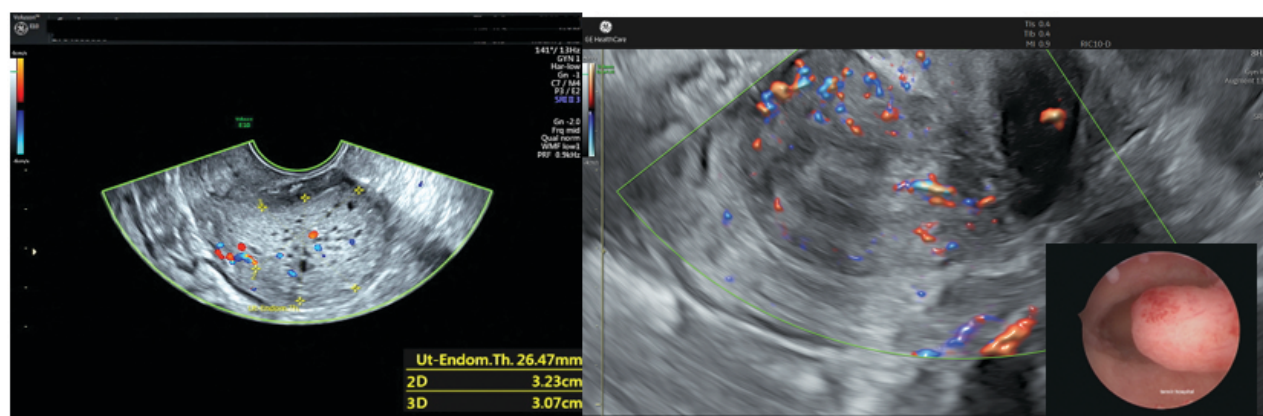


Figure 4.A and 4 B Thick endometrium - 3A Cystic endometrial polyp in an 80-year-old woman with a feeding vessel, JZ seen. 3B -Polyp with a feeding vessel and hysteroscopy picture

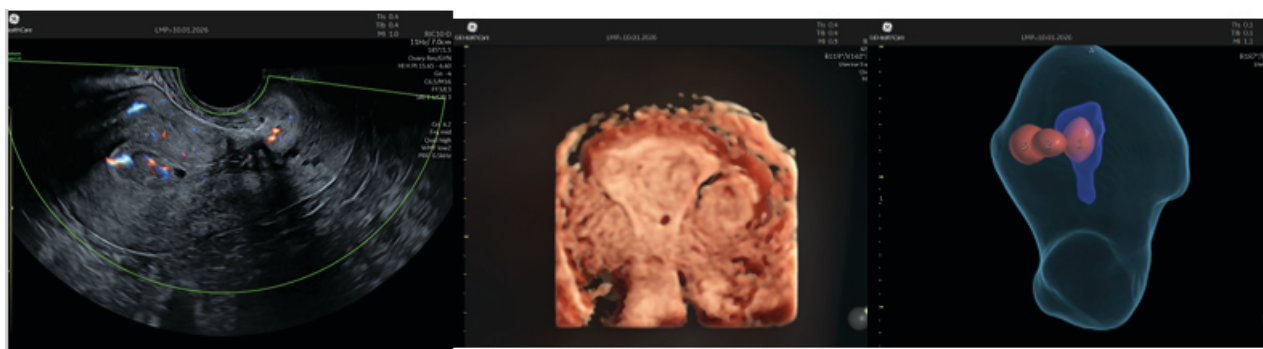


Figure 5: A Submucosal Fibroid type 0 in a post menopausal woman with a rim flow, regular. 4 B-in 3D. 4C-fibroid Mapping

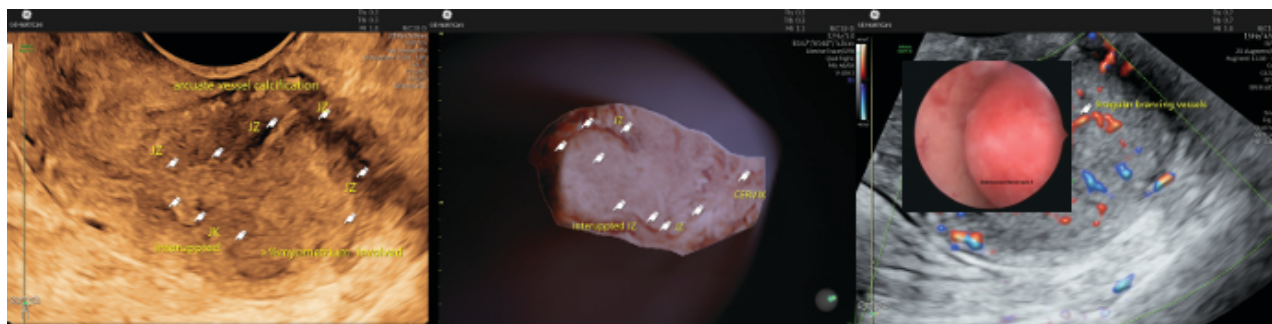


Figure 6. Endometrial cancer. Thick, irregular, high colour score with multiple dense, irregular branching vessels; the junctional zone is interrupted in the anterior wall; a hysteroscopy view

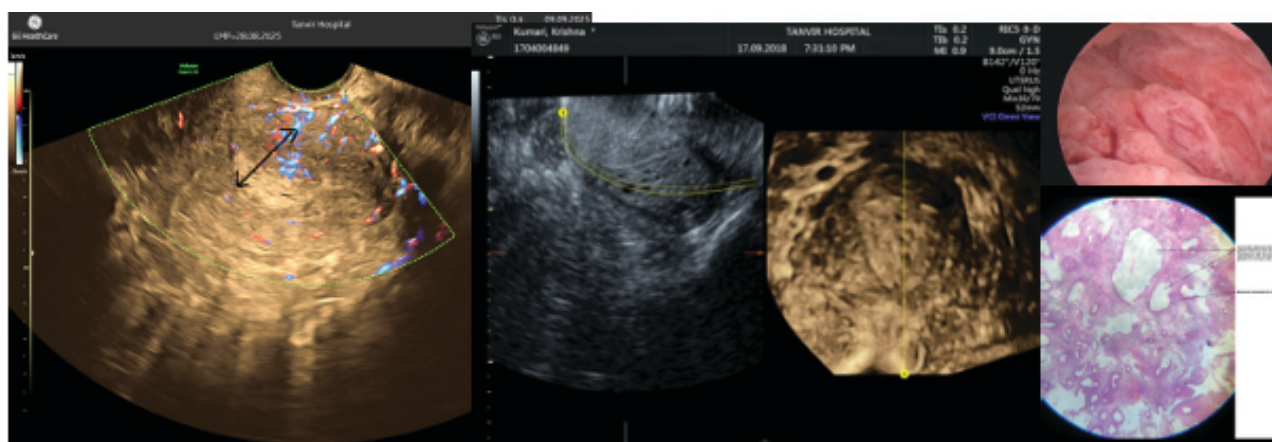


Figure 7. Benign endometrial hyperplasia - hyperechogenic, with cystic spaces, regular JZ, multifocal linear vessels, colour score 2 crossing the junctional zone, in a postmenopausal woman. Hysteroscopy and histopathology report

POSTMENOPAUSAL BLEEDING

Postmenopausal bleeding (PMB) is the most important symptom requiring evaluation. Atrophic endometrium is prone to superficial ulceration and is the most common cause of postmenopausal bleeding.⁵ However, because 80% of endometrial cancer occurs in postmenopausal women and because these patients usually present with vaginal bleeding, endometrial assessment is essential.^{22,23} TVS should include double-layer endometrial thickness (ET) measured as the maximum anteroposterior thickness of the double endometrial echo in the long axis (sagittal). Assess morphology by the echotexture (homogeneous vs. heterogeneous), focal or cystic areas, regularity of the endometrial-myometrial junction, and endocavitary fluid. Power Doppler mapping to evaluate the endometrial and sub-endometrial vascular pattern.⁵ 3D TVS is adjunctive and only provides moderate accuracy in assessing endometrial volume and focal abnormalities, but shows no consistent advantage over standard two-dimensional TVS for predicting EC.²³

In women presenting with PMB and no other high-risk factors, a TVS with an ET threshold between 3 and 5 mm provides a high negative predictive value for endometrial malignancy. However, assessment should include endometrial morphology, Doppler findings, and individual risk factors.^{5,15,20,23} Women presenting with a first episode of PMB who have any of the following risk factors should undergo both TVS and endometrial sampling: obesity, diabetes, hypertension, tamoxifen use, increasing years since menopause, history of polyps, smoking, family history of EC, poor image definition, focal echogenicity, diffuse heterogeneity, or persistent bleeding.⁵

Low-risk women (ET $\leq 3-4$ mm, clearly defined homogeneous echo pattern, normal morphology and colour Doppler, and good image quality) whose bleeding has ceased may be managed conservatively with shared decision-making and repeat TVS or biopsy only if bleeding recurs.^{14,25,26}

An endometrial thickness of > 4 mm warrants further evaluation with endometrial sampling or hysteroscopy.^{5,14,15} For patients with an inadequately visualised endometrium on ultrasonography, sampling is advisable, given a similar cancer diagnosis rate to those with a clearly thickened endometrium, as reported in the 2025 study.²⁷ Persistent or recurrent bleeding requires evaluation irrespective of endometrial thickness, as high-grade endometrial carcinomas may occasionally present with a thin endometrium.⁵ An Indian tertiary centre study (n=50) reported TVS sensitivity of 85% and specificity of 89% versus histology, confirming the reliability of TVS in resource-limited settings.²⁸

ASYMPTOMATIC POSTMENOPAUSAL WOMEN WITH ENDOMETRIAL THICKNESS

Incidental detection of a thickened endometrium in women without bleeding should be interpreted cautiously. Incidentally detected ET > 4 mm in asymptomatic women does not routinely require investigation.⁵ There is currently no clear ET threshold that can predict the risk of malignant transformation.²⁰ Many reviews recommend ET < 4 mm as low risk and suggest endometrial sampling for ET ≥ 4 mm only in symptomatic or high-risk women, while asymptomatic thickened endometrium should be individualised.²⁰ Evidence suggests that global endometrial thickness < 11 mm in asymptomatic postmenopausal women is rarely associated with malignancy and does not require invasive evaluation in the absence of additional risk factors.^{14,15,20,29-32} The decision to biopsy if the ET is between 3/4 and 11 mm should depend on the patient's individual risk factors, endometrial morphology, and power Doppler findings.^{5,31}

Endometrial thickness ≥ 11 mm, focal thickening, or abnormal morphology should prompt further evaluation.^{20,29} As a woman's age increases, her risk of cancer increases at each endometrial thickness measurement. For example, using an 8 mm threshold, the risk of cancer associated with a thick endometrium increases from 4.1% at age 50 to 9.3% at age 79.²⁰ Given the high prevalence of metabolic risk factors in Indian women, individual risk assessment is essential.

Table 1: Updated Consensus Norms for Endometrial Thickness in Postmenopausal Women

Section	Clinical Scenario	Endometrial Thickness	Recommendation	Evidence Level
Symptomatic (PMB)				
	PMB, no HT	≤ 4 mm	Reassuring; expectant management	High (multiple large cohorts)
	PMB, no HT	> 4 mm	Requires endometrial sampling	High
	PMB, with HT (continuous)	≤ 5 mm	Generally reassuring	Moderate
	PMB, with HT (sequential)	≤ 7 mm	Generally reassuring	Moderate
Asymptomatic				
	Asymptomatic, no HT	< 4 mm	No routine investigation	High
	Asymptomatic, no HT	4–10 mm	Individualised based on risk factors	Moderate
	Asymptomatic, no HT	≥ 11 mm	Consider further evaluation	Moderate

Special Populations				
	Tamoxifen use (symptomatic)	individualise	Requires hysteroscopy/biopsy	Moderate
	Tamoxifen use (asymptomatic)	Any thickness	Symptom-driven evaluation	Moderate
	Obesity/diabetes /metabolic syndrome	Lower threshold	Consider ET > 3–4 mm for sampling	Low-Moderate

PMB: Postmenopausal bleeding; HT: Hormone therapy; ET: Endometrial thickness

SPECIAL SITUATIONS

Tamoxifen-Associated Endometrial Changes

In women on tamoxifen with PMB, the ET cut-off of 5 mm yielded 97% sensitivity but low specificity (35%), indicating a high false-positive rate. This means that while a negative test (ET < 5 mm) is reassuring, a positive scan requires hysteroscopy or biopsy for a definitive diagnosis.³³ Ultrasound findings on women with tamoxifen commonly include endometrial thickening, cystic changes, and polyps. Refer to Figure 2. Tamoxifen exerts a partial estrogen agonist effect on the endometrium, often producing a heterogeneous appearance with subendometrial cystic spaces. Importantly, tamoxifen significantly reduces the specificity of conventional ET thresholds, as sonographic thickening does not reliably correlate with underlying pathology in this group. Consequently, ET measurements alone are considered unreliable indicators of disease risk in tamoxifen users. Refer to the figure 3. Clinical management should therefore be guided primarily by symptoms and detailed morphological assessment rather than thickness values alone. In symptomatic women, particularly those presenting with postmenopausal bleeding and suspicious imaging features, further evaluation with hysteroscopy and/or endometrial biopsy is recommended. In contrast, asymptomatic women on tamoxifen generally do not require routine ultrasound screening beyond.^{34,35}

KEY MORPHOLOGICAL FEATURES REQUIRING FURTHER EVALUATION

Endometrial thickness should not be interpreted in isolation; morphological assessment is essential.^{5,20}

- Heterogeneous or inhomogeneous echotexture increases suspicion for underlying pathology.
- Focal or asymmetric thickening is more concerning than uniform thickening.
- Irregular or interrupted endomyometrial junction suggests possible invasive or atypical processes.
- Polypoid intracavitary lesions warrant targeted assessment.
- Intracavitary fluid associated with irregular or thickened endometrium is suspicious.
- Focal or diffuse increased echogenicity is associated with a higher likelihood of pathological findings.
- Endometrial sampling is indicated when suspicious morphological features are present, even if the thickness is below the standard cutoff value.
- Expectant management may be considered in a low-risk woman with a homogeneous endometrium ≤ 4 mm, provided there are no focal abnormalities or concerning clinical features.
- This emphasises that qualitative sonographic features may outweigh absolute thickness measurements in clinical decision-making.

Malignant vs Benign Signatures^{5,15}

- *Endometrial carcinoma*: Increased and irregular vascularity with low resistance flow.
- *Benign conditions, such as atrophy*: minimal or absent flow.

- *Endometrial polyps* often demonstrate a single feeding vessel. Refer to Figure 4
- Type 0 fibroid with a peripheral rim flow. Refer to figure 5

FEATURES OF ENDOMETRIAL PATHOLOGIES

Endometrial Cancer

Endometrial cancer is the most common gynaecological malignancy in postmenopausal women. Ultrasound features suggestive of endometrial cancer include: Refer to figure 4

- The endometrium is typically >4-5 mm in symptomatic women.
- Heterogeneous echotexture.
- Irregular endomyometrial junction.
- Increased vascularity with low resistance indices ($RI \leq 0.73$, $PI \leq 1.42$).
- Myometrial invasion, loss of the subendometrial halo.
- Higher 3D vascular indices (VI, FI, VFI).

Endometrial polyps appear as:

- Focal endometrial thickening.
- Well-defined echogenic lesions.
- Often with a feeding vessel on Doppler.
- May contain cystic spaces.

Polyps are common in postmenopausal women and are usually benign, but malignant transformation can occur, particularly in larger polyps (>1.5 cm).

Endometrial Hyperplasia

Endometrial hyperplasia shows: Refer to figure 7

- Diffuse or focal endometrial thickening.
- Heterogeneous echotexture.
- Cystic changes may be present.
- Increased vascularity may be seen.

Differentiation from endometrial cancer on ultrasound alone is often not possible, requiring histological diagnosis.

MYOMETRIUM ASSESSMENT

Technique: The myometrium should be evaluated on sagittal and transverse transvaginal images for symmetry, echotexture, focal lesions, and integrity of the endomyometrial junction.

Systematic evaluation includes

- Assessment of myometrial echotexture (homogeneous versus heterogeneous).
- Identification of focal lesions, such as leiomyomas, with documentation of size, number, location (submucosal, intramural, subserosal), and margins
- Evaluation of the junctional zone (when visible), particularly in suspected adenomyosis.
- Application of colour or power Doppler to assess the vascularity of focal masses or areas of asymmetry.
- Measurement and comparison of anterior and posterior myometrial wall thickness.
- Vascular calcifications typically appear as linear or punctate echogenic foci along the arcuate or radial arteries within the myometrium, often producing posterior acoustic shadowing.

Any rapid increase in uterine size, newly detected mass, irregular margins, or abnormal vascularity should raise suspicion for malignant transformation. Persistent or enlarging fibroids after menopause warrant careful evaluation, as most leiomyomas regress with declining estrogen levels. Suspicious features suggestive of uterine sarcoma include rapid growth, heterogeneous echotexture with cystic degeneration, irregular borders, and increased central vascularity.

Vascular calcifications are generally benign and are frequently associated with systemic vascular conditions such as hypertension, diabetes mellitus, and atherosclerosis.^{36,37}

Physiological calcifications are usually small, symmetrical, and confined to vascular walls without associated uterine enlargement or mass formation. They do not cause symptoms and require no specific intervention.³⁸ Abnormal calcifications should be suspected when they are associated with focal myometrial masses, distortion of uterine architecture, rapid enlargement, or abnormal vascularity. Coarse or irregular calcifications are commonly seen in degenerating leiomyomas, particularly in postmenopausal women.³ Rarely, calcifications may occur in association with uterine sarcoma or chronic inflammatory conditions, and such cases warrant further evaluation with Doppler ultrasound, magnetic resonance imaging (MRI), or histopathological assessment.^{37,38}

CERVICAL ASSESSMENT

Technique: The cervix should be examined on mid-sagittal and transverse transvaginal images, assessing size, contour, stromal echogenicity, endocervical canal, and vascularity.

Systematic evaluation:

Evaluation includes assessing the cervix in both sagittal and transverse planes, with attention to size, contour, echotexture, and the integrity of the endocervical canal. Normally, the postmenopausal cervix appears small, homogeneous, and relatively hypovascular due to hypoestrogenic changes.

- Cervical length and symmetry
- Endocervical canal thickness and patency
- Presence of focal masses or nodules
- Cystic lesions such as Nabothian cysts
- Stromal heterogeneity
- Increased or abnormal vascularity on Doppler

Clinical Implications

Cervical carcinoma: Small cervical carcinomas may not be reliably detected by ultrasound, particularly in early stages. Suspicious findings include an irregular hypoechoic mass, distortion of cervical architecture, disruption of the stromal ring, and increased central vascularity with low-resistance flow. Ultrasound complements but does not replace cytological or histopathological diagnosis.

The risk of cervical cancer may be relatively higher in women presenting with PMB and a thin endometrium, as the source of bleeding in such cases is less likely to originate from the endometrial cavity.

In South East Asia, cervical cancer represents a more common cause of PMB than endometrial cancer, with reported prevalence rates ranging from 5% to 13% among women presenting with PMB. Small cervical carcinomas may not be reliably detected by transvaginal sonography.^{39,40}

VAGINAL ASSESSMENT^{5,8}

Technique: The vaginal walls should be inspected during probe insertion in sagittal and transverse planes for thickness, symmetry, focal lesions, and abnormal vascularity.

Systematic evaluation:

Ultrasound has a limited but adjunctive role in the evaluation of vaginal thickness in postmenopausal women. Vaginal evaluation in postmenopausal women is performed primarily through clinical examination. During TVS, the vagina is assessed upon probe insertion before advancing toward the cervix and uterus.

- Evaluation of vaginal wall thickness and uniformity
- Identification of focal masses or nodular lesions
- Assessment for cystic structures, such as Gartner duct cysts
- Detection of fluid collections or haematocolpos (rare in menopause)
- Doppler assessment of suspicious masses for abnormal vascularity

OVARIAN ASSESSMENT^{5,8}

Technique: Each ovary should be identified in longitudinal and transverse planes, measured in three orthogonal dimensions, and assessed for morphology, volume, and vascularity using colour or power Doppler.

In postmenopausal women, normal ovaries are typically small, homogeneous, and relatively avascular on ultrasound examination. Any visualised ovary in this population warrants careful assessment, as ovarian volume decreases after menopause and persistent enlargement may be abnormal. Ultrasound remains the primary imaging modality for evaluating adnexal masses and identifying features suspicious for malignancy.

Technique of Ovarian Assessment

Identification of the Ovary

- Locate the ovary in relation to the internal iliac vessels and lateral to the uterus.
- Gentle probe manipulation and slow sweeping movements improve detection.
- Apply slight abdominal pressure if needed to bring the ovary into view.

Assessment of Ovarian Size and Volume

- Measure three orthogonal diameters (length × width × height).
- Calculate ovarian volume using the prolate ellipsoid formula: Length × Width × Height × 0.523.
- Postmenopausal ovaries are typically small, often < 2–3 cm in maximum diameter.
- Any enlargement warrants careful evaluation.

Morphological Evaluation

- Assess ovarian contour (smooth vs irregular).
- Evaluate internal echotexture (homogeneous vs complex).
- Identify cystic or solid components.
- Look for septations, papillary projections, mural nodules, or wall thickening.

Doppler Assessment

- Apply colour or power Doppler to assess vascularity.
- Normal postmenopausal ovaries show minimal or absent flow.
- Central vascularity, increased flow, or low resistance indices may raise suspicion for malignancy.

Evaluation of Adnexa and Surrounding Structures

- Examine the fallopian tubes and adnexal region for masses.
- Assess the pouch of Douglas for free fluid.
- Note the bilaterality of any lesions.

Documentation

- Record ovarian visibility or non-visualisation (non-visualisation is common and usually benign in low-risk women).

- Document size, morphology, vascularity, and any associated findings.
- Apply standardised risk stratification tools, such as the International Ovarian Tumour Analysis (IOTA)⁴¹ Simple Rules and the Assessment of Different Neoplasias in the adnexa
- (ADNEX) model, when adnexal masses are detected.⁴²

A structured and methodical approach is essential in menopausal ovarian assessment, as subtle abnormalities may represent early malignancy, while many findings, such as small simple cysts are benign and suitable for conservative management.

Ovarian Mass Evaluation: Imaging Features and Clinical Approach

Sonographic characteristics associated with ovarian cancer include solid or complex masses, thick septations greater than 3 mm, papillary projections, bilaterality, and the presence of ascites. On Doppler evaluation, malignant lesions often demonstrate increased central vascularity with low resistance flow indices, reflecting tumour neovascularisation. Risk stratification should be performed using standardised, validated models such as the IOTA Simple Rules and the ADNEX model, which improve diagnostic accuracy and guide clinical management.

Simple ovarian cysts are relatively common in postmenopausal women and are usually benign. Asymptomatic simple cysts measuring less than 5 cm with no suspicious features can be managed conservatively with interval follow-up. However, cysts measuring 5 cm or greater, enlarging cysts, or those demonstrating complex or suspicious features require further evaluation, including consideration of serum tumour markers and referral for specialist assessment.

Importantly, routine population screening for ovarian cancer in average-risk women is not currently recommended, as large trials have not demonstrated a clear mortality benefit. Evaluation should therefore be individualised, with particular attention to women at increased genetic risk, such as those with Breast Cancer gene (BRCA) mutations or strong family history, who may require specialised surveillance or risk-reducing strategies.

ASSESSMENT OF THE URETHRA AND BLADDER

Technique: The urethra should be evaluated using transvaginal or transperineal ultrasound in the midsagittal plane at rest and during Valsalva, assessing urethral length, mobility, sphincter integrity, and periurethral structures.

Urethral Assessment

Urethral evaluation is primarily clinical but may be supplemented by transvaginal or transperineal ultrasound. Sonographically, the urethra appears as a hypoechoic tubular structure anterior to the vaginal wall. In menopausal women, thinning of periurethral tissues and reduced vascularity may be observed. Transperineal ultrasound allows dynamic assessment during the Valsalva manoeuvre, helping evaluate bladder neck descent and urethral mobility.

Clinical Conditions Identified by Urethral Ultrasound:

- Urethral hypermobility in stress urinary incontinence
- Intrinsic sphincter deficiency
- Urethral diverticula
- Periurethral masses.

Bladder Assessment

Technique: The bladder should be assessed transabdominally when adequately distended to evaluate wall thickness, contour, intraluminal lesions, and post-void residual volume using three orthogonal measurements.

Bladder evaluation during pelvic ultrasound includes a systematic assessment of bladder wall thickness, contour, intraluminal lesions, trabeculation, and post-void residual (PVR) urine volume. The bladder should be adequately distended during assessment, as under filling may falsely increase apparent wall thickness. In a properly distended bladder, normal wall thickness is generally ≤ 3 mm, while measurements exceeding 5 mm in a non-distended bladder may be considered abnormal.^{43,44} Smooth contour and anechoic lumen are expected findings; focal wall thickening, irregularity, or intravesical masses warrant further evaluation to exclude neoplasia or inflammatory pathology. Bladder wall trabeculation appears as irregular thickening of the muscular wall and is commonly associated with chronic bladder outlet obstruction or longstanding detrusor overactivity. Persistent trabeculation may suggest chronic outlet obstruction or longstanding detrusor overactivity.⁴⁵

Measurement of post-void residual urine volume (PVR) is particularly important in menopausal women presenting with voiding dysfunction, recurrent urinary tract infections, or suspected bladder outlet obstruction. PVR is measured using transabdominal ultrasound immediately after voiding. Three orthogonal bladder diameters, height (superoinferior), width (transverse), and depth (anteroposterior), are obtained, and bladder volume is calculated using the prolate ellipsoid formula ($\text{Height} \times \text{Width} \times \text{Depth} \times 0.52$). A PVR of less than 50 mL is generally considered normal, whereas a volume greater than 100 mL is typically abnormal and may indicate incomplete bladder emptying.^{44,47}

PELVIC FLOOR ULTRASOUND AT MENOPAUSE

Transperineal or translabial ultrasound is most commonly used, allowing visualisation of the bladder neck, urethra, vagina, rectum, and levator ani muscles in both resting and dynamic states. In menopausal women presenting with lower urinary tract symptoms or pelvic pressure, pelvic floor ultrasound provides important anatomical information and complements clinical examination and urodynamic studies.

Pelvic floor ultrasound does not replace clinical examination but enhances diagnostic accuracy, objectivity, and preoperative evaluation. Its advantages include real-time dynamic assessment, reproducibility, and absence of radiation exposure. Pelvic floor ultrasound is a useful adjunct for bladder neck descent and urethral hypermobility in women with urinary incontinence, detects occult levator ani defects associated with prolapse, and defines the specific compartment involved in pelvic organ descent. This enhances diagnostic precision, refines surgical planning, and aids in selecting appropriate management strategies. Additionally, in women with prior prolapse or anti-incontinence surgery, ultrasound enables assessment of mesh position, sling integrity, and postoperative complications.⁷

ROLE OF OTHER IMAGING MODALITIES

Magnetic resonance imaging (MRI) : is an important second-line modality for evaluating pelvic pathology in postmenopausal women, particularly when ultrasound findings are inconclusive or detailed tissue characterisation is required. It is the imaging modality of choice for local staging of endometrial carcinoma, as it accurately assesses the depth of myometrial invasion and cervical stromal involvement, which are key prognostic factors and guide management decisions.^{47,48} MRI also plays a crucial role in evaluating indeterminate adnexal masses and differentiating adenomyosis from leiomyomas, owing to its superior soft-tissue contrast and multiplanar imaging capabilities.⁴⁹ The addition of diffusion-weighted imaging (DWI) further enhances lesion detection and improves differentiation between benign and malignant pathology.⁴⁷

Computed tomography (CT) has a limited role in the primary diagnosis of gynaecological conditions due to its relatively poor soft-tissue resolution; however, it is invaluable in the assessment of advanced disease, including the detection of distant metastases, lymphadenopathy, and peritoneal, omental, bowel, and urinary tract involvement.^{48,50} Although CT is less sensitive than MRI for local pelvic staging, it remains essential for comprehensive abdominopelvic evaluation and preoperative planning in patients with suspected extra-pelvic spread.^{48,50}

EMERGING TECHNOLOGIES AND ARTIFICIAL INTELLIGENCE

Recent advances in gynaecological imaging have enhanced the diagnostic performance of TVS, particularly in endometrial assessment. Developments in three-dimensional (3D) ultrasound, high-resolution Doppler techniques, and AI-assisted image analysis have improved characterisation of endometrial morphology and vascular patterns. Contemporary reviews highlight that integrating 3D volumetric assessment with Doppler-derived vascular indices has increased diagnostic accuracy in distinguishing benign from malignant endometrial pathology.^{51,52}

Artificial Intelligence and Machine Learning

AI and machine learning (ML) applications in gynaecological ultrasound are increasingly focused on predictive modelling and risk stratification. Automated segmentation of endometrial volume, extraction of radiomic features, and quantification of vascular indices (VI, FI, VFI) are being incorporated into predictive algorithms. These models are often combined with clinical risk factors such as age, BMI, bleeding pattern, and comorbidities to improve the prediction of malignancy risk. Recent multicentre studies have demonstrated that AI-assisted models for endometrial cancer risk stratification can achieve AUC values ranging from approximately 0.88 to 0.98, comparable to or exceeding expert interpretation.⁵³⁻⁵⁵

In addition, deep learning techniques are being explored for automated classification of adnexal masses and

endometrial lesions, potentially reducing operator dependence and interobserver variability. AI-driven systems may also support standardised reporting and real-time decision support during ultrasound acquisition.

Limitations and Future Directions

Despite promising results, current evidence is derived predominantly from single-centre or limited multicentre cohorts, often with retrospective designs. External validation, prospective trials, and standardisation of image acquisition protocols remain necessary before widespread clinical implementation. There is also a need for uniform reporting systems and regulatory oversight to ensure reproducibility, transparency, and clinical safety. Thus, while AI represents a significant advancement in gynaecological imaging, routine integration into everyday practice awaits further validation and standardisation.

SYNOPSIS

- TVS, complemented by Doppler evaluation and emerging three-dimensional (3D) power Doppler techniques, remains the cornerstone of imaging in menopausal and postmenopausal women.
- In the Indian context, a judicious, structured imaging approach incorporating evidence-based protocols facilitates early diagnosis while minimising unnecessary invasive procedures.
- Integration of validated endometrial thickness cutoff values, detailed morphological assessment, Doppler vascular parameters, and selective use of advanced imaging modalities, such as MRI, enhances diagnostic accuracy and optimises patient care in the era of precision medicine.
- Risk stratification incorporating clinical profile, imaging findings, and emerging predictive models supports personalised decision-making in the era of precision medicine.
- Continuous advances in imaging technology and artificial intelligence hold promise for improved standardisation, reproducibility, and early detection of gynaecological pathology in menopausal care.

RESEARCH AGENDA

Prospective Multicentre Validation of an Artificial Intelligence–Integrated 3D Transvaginal Ultrasound Model for Risk Stratification of Endometrial Cancer in Postmenopausal Women.

REFERENCES

1. Saha I, Wankhede S, Thakare S, Narayan G, Sawant AA, Gupta A, et al. Assessing the Role of Transvaginal Sonography in Post-menopausal Bleeding: A Less Invasive Approach to Identify Endometrial Carcinoma. *Cureus*. 2024 Jul; 16(7): e65608. doi: 10.7759/cureus.65608.
2. Deenadayal M. Understanding The Endometrium At Menopause: A Sonologist's View. *Journal of mid-life health*. 2021 Jan-Mar; 12(1): 66-78. doi: 10.4103/0976-7800.313985
3. El-Sharkawy M, El-Mazny A, Ramadan W, Hatem D, Abdel-Hafiz A, Hammam M, et al. Three-dimensional ultrasonography and power Doppler for discrimination between benign and malignant endometrium in premenopausal women with abnormal uterine bleeding. *BMC women's health*. 2016 Mar 16; 16: 18. doi: 10.1186/s12905-016-0297-3.
4. Nguyen PN, Nguyen VT. Endometrial thickness and uterine artery Doppler parameters as soft markers for prediction of endometrial cancer in postmenopausal bleeding women: a cross-sectional study at tertiary referral hospitals from Vietnam. *Obstetrics & gynecology science*. 2022 Sep; 65(5): 430-440. doi: 10.5468/ogs.22053.
5. ACOG Committee Opinion No. 734: The Role of Transvaginal Ultrasonography in Evaluating the Endometrium of Women With Postmenopausal Bleeding. *Obstetrics and gynecology*. 2018 May; 131(5): e124-e129. doi: 10.1097/AOG.0000000000002631
6. Portman DJ, Gass ML. Genitourinary syndrome of menopause: new terminology for vulvovaginal atrophy from the International Society for the Study of Women's Sexual Health and the North American Menopause Society. *Maturitas*. 2014 Nov; 79(3): 349-54. doi: 10.1016/j.maturitas.2014.07.013.
7. Dietz HP. Pelvic floor ultrasound: a review. *American journal of obstetrics and gynecology*. 2010 Apr; 202(4): 321-34. doi: 10.1016/j.ajog.2009.08.018.
8. Seelbach-Göbel B, Rempen A, Kristen P. Transvaginal ultrasound of the endometrium in postmenopause. *Geburtshilfe und Frauenheilkunde*. 1995 Feb; 55(2): 59-64. doi: 10.1055/s-2007-1022776.
9. Lu P, Liao Y, Zhang Z. Value of 3D Ultrasonography with Malignancy Risk Model for Screening for Endometrial Cancer with Postmenopausal Bleeding. *Chinese General Practice*. 2022;25(14):1724-1729, 1740. doi: 10.12114/j.issn.1007-9572.2022.02.018.
10. Wang L, Quan S, Yang X. Ultrasonic prediction model using three-dimensional power doppler for endometrial cancer detection in women with postmenopausal bleeding. *Scientific reports*. 2025 May 26; 15(1): 18302. doi: 10.1038/s41598-025-02067-y.
11. Abdalla S, Abou-Taleb H, Badary DM, Ali WA. Multiparametric transvaginal ultrasound in the diagnosis of endometrial cancer in post-menopausal bleeding: diagnostic performance of a transvaginal algorithm and reproducibility amongst less experienced observers. *The British journal of radiology*. 2021 Mar 1; 94(1119): 20201195. doi: 10.1259/bjr.20201195.

12. Kaveh M, Sadegi K, Salarzaei M, Parooei F. Comparison of diagnostic accuracy of saline infusion sonohysterography, transvaginal sonography, and hysteroscopy in evaluating the endometrial polyps in women with abnormal uterine bleeding: a systematic review and meta-analysis. *Wideochir Inne Tech Maloinwazyjne*. 2020 Sep;15(3):403-415. doi: 10.5114/wiitm.2020.93791. Epub 2020 Mar 19. PMID: 32904526; PMCID: PMC7457193.
13. Nieuwenhuis LL, Hermans FJ, Bij de Vaate AJM, Leeftang MM, Brölmann HA, Hehenkamp WJ, Mol BWJ, Clark TJ, Huirne JA. Three-dimensional saline infusion sonography compared to two-dimensional saline infusion sonography for the diagnosis of focal intracavitary lesions. *Cochrane Database Syst Rev*. 2017 May 5;5(5):CD011126. doi: 10.1002/14651858.CD011126.pub2. PMID: 28472862; PMCID: PMC6481510.
14. Ibrahim AM, Elioba JLR, Ali FA, M. Mohamed M, M. Omar A, J. Osman A, et al. The role of transvaginal ultrasonography in evaluating the endometrium of women with postmenopausal bleeding. *International Journal of Reproduction, Contraception, Obstetrics and Gynecology* 2025;14:2824-8. doi: 10.18203/2320-1770.ijrcog20252373.
15. Goldstein SR. Modern evaluation of the endometrium. *Obstetrics and gynecology*. 2010 Jul; 116(1): 168-176. doi: 10.1097/AOG.0b013e3181dfd557.
16. Chantler IW, Davie MW. Low dose continuous combined hormone replacement therapy: early and late postmenopausal effect on endometrium. *J Ultrasound Med*. 2000 Jan;19(1):33-8. doi: 10.7863/jum.2000.19.1.33. PMID: 10625188.
17. Affinito P, Palomba S, Pellicano M, Sorrentino C, Di Carlo C, Morgera R, Arienzo MP, Nappi C. Ultrasonographic measurement of endometrial thickness during hormonal replacement therapy in postmenopausal women. *Ultrasound Obstet Gynecol*. 1998 May;11(5):343-6. doi: 10.1046/j.1469-0705.1998.11050343.x. PMID: 9644774.
18. Hänggi W, Bersinger N, Altermatt HJ, Birkhäuser MH. Comparison of transvaginal ultrasonography and endometrial biopsy in endometrial surveillance in postmenopausal HRT users. *Maturitas*. 1997 Jun;27(2):133-43. doi: 10.1016/s0378-5122(97)00037-6. PMID: 9255748.
19. Archer DF, McIntyre-Seltman K, Wilborn WW Jr, Dowling EA, Cone F, Creasy GW, et al. Endometrial morphology in asymptomatic postmenopausal women. *American journal of obstetrics and gynecology*. 1991 Aug; 165(2): 317-20; discussion 320-2. doi: 10.1016/0002-9378(91)90084-5.
20. Smith-Bindman R, Kerlikowske K, Feldstein VA, Subak L, Scheidler J, Segal M, et al. Endovaginal ultrasound to exclude endometrial cancer and other endometrial abnormalities. *JAMA*. 1998 Nov 4; 280(17): 1510-7. doi: 10.1001/jama.280.17.1510.
21. Alcázar JL. Endometrial sonographic findings in asymptomatic, hypertensive postmenopausal women. *Journal of clinical ultrasound : JCU*. 2000 May; 28(4): 175-8. PMID: 10751738.
22. de Kroon CD, de Bock GH, Dieben SW, Jansen FW. Saline contrast hysterosonography in abnormal uterine bleeding: a systematic review and meta-analysis. *BJOG*. 2003;110(10):938-47.
23. Xydias EM, Kalantzi S, Tsakos E, Ntanika A, Beis N, Prior M, et al. Comparison of 3D ultrasound, 2D ultrasound and 3D Doppler in the diagnosis of endometrial carcinoma in patients with uterine bleeding: A systematic review and meta-analysis. *Eur J Obstet Gynecol Reprod Biol* 2022;277:42-52.
24. Gupta JK, Chien PF, Voit D, Clark TJ, Khan KS. Ultrasonographic endometrial thickness for diagnosing endometrial pathology in women with postmenopausal bleeding: A meta-analysis. *Acta Obstet Gynecol Scand* 2002;81:799-816
25. Timmermans A, Opmeer BC, Khan KS, Bachmann LM, Epstein E, Clark TJ, et al. Endometrial thickness measurement for detecting endometrial cancer in women with postmenopausal bleeding: A systematic review and meta-analysis. *Obstet Gynecol* 2010;116:160-7.
26. Wong AS-W, Lao TT-H, Cheung CW, Yeung SW, Fan HL, Ng PS, Yuen PM, Sahota DS. Reappraisal of endometrial thickness for the detection of endometrial cancer in postmenopausal bleeding: a retrospective cohort study. *BJOG* 2016;123:439-446.
27. Atkins S, Nolin A, Unnithan S, Myers ER, Kruse DE, Erkanli A, Havrilesky LJ. Analysis of Timely Follow-Up in the Evaluation of Postmenopausal Bleeding. *O G Open*. 2025 Jan 30;2(1):e054. doi: 10.1097/og9.000000000000054. PMID: 41000569; PMCID: PMC12456509.
28. Morampudi SC, Kumar B, Preethi A, Chandrasekhar K, Santosh A P. Diagnostic accuracy of transabdominal and transvaginal ultrasound in assessing endometrial pathologies in women with postmenopausal bleeding: a cross-sectional study. *Int J Anat Radiol Surg*. 2024;13:RO01-RO05.
29. Iqbal A, Murrium SKS, Yaseen M, et al. Ultrasound measurement of endometrial thickness for detecting endometrial malignancy with uterine bleeding in postmenopausal women: a systematic review. *Pak J Med Health Sci*. 2021;15:1461-1465.
30. Li JX, Chan F, Johansson CY. Can a higher endometrial thickness threshold exclude endometrial cancer and atypical hyperplasia in asymptomatic postmenopausal women? A systematic review. *Aust N Z J Obstet Gynaecol* 2022;62:190-7.
31. Li Z, Li L. Risk of malignancies among asymptomatic postmenopausal women with thickened endometrium: A cohort study. *Medicine (Baltimore)* 2019;98:e14464
32. Van Den Bosch T, Verbakel JY, Valentin L, Wynants L, De Cock B, Pascual MA, et al. Typical ultrasound features of various endometrial pathologies described using International Endometrial Tumor Analysis (IETA) terminology in women with abnormal uterine bleeding. *Ultrasound Obstet Gynecol* 2021;57:164-72.
33. Gerber B, Krause A, Müller H, Reimer T, Külz T, Makovitzky J, et al. Effects of Adjuvant Tamoxifen on the Endometrium in Postmenopausal Women With Breast Cancer: A Prospective Long-Term Study Using Transvaginal Ultrasound. *Journal of Clinical Oncology* 2000;18:3464-70. <https://doi.org/10.1200/jco.2000.18.20.3464>.
34. Garuti G, Grossi F, Centinaio G, Sita G, Nalli G, Luerti M. Pretreatment and prospective assessment of endometrium in menopausal women taking tamoxifen for breast cancer. *Eur J Obstet Gynecol Reprod Biol* 2007;132:101-6.
35. Kantarcı S, Karabulut A, Kilis S, Dağlı U, Uçar İ, İnan AH. Endometrial pathology in tamoxifen-treated breast cancer patients: Correlation of endometrial thickness on ultrasound, preoperative sampling, and final pathology. *Anatol J Gen Med Res* 2025;35:178-84. their standard oncological follow-up, unless new clinical concerns arise
36. Akilli R, Kucukgoz Gulec U, Deniz A, Aikimbaev K, Akcabay C, Seydaoglu G. Uterine arcuate artery calcification as a potential marker of cardiovascular risk-a preliminary study. *Menopause (New York, N.Y.)*. 2022 Aug 1; 29(8): 905-910. doi: 10.1097/GME.0000000000001997.
37. Fleischer AC, Andreotti RF, Strachowski LM, et al. Sonography in obstetrics and gynecology: principles and practice. 8th ed. New York: McGraw-Hill; 2018.
38. Occhipinti K, Kutcher R, Rosenblatt R. Sonographic appearance and significance of arcuate artery calcification. *Journal of ultrasound in medicine*. 1991 Feb; 10(2): 97-100. doi: 10.7863/jum.1991.10.2.97.
39. Lee WH, Tan KH, Lee YW. The aetiology of postmenopausal bleeding—a study of 163 consecutive cases in Singapore. *Singapore medical journal*. 1995 Apr; 36(2): 164-8. PMID: 7676260
40. Lin HH, Wu MY, Shyu MK, Chen D, Tsai JL, Hsieh CY. Clinical study of 381 postmenopausal bleeding patients. *Journal of the Formosan Medical Association*. 1993 Mar; 92(3): 241-4. PMID: 810227

41. Timmerman D, Testa AC, Bourne T, et al. Simple ultrasound-based rules for the diagnosis of ovarian cancer. *Ultrasound Obstet Gynecol*. 2008;31(6):681–90.
42. Van Calster B, Van Hoorde K, Valentin L, et al. Evaluating the risk of ovarian cancer before surgery using the ADNEX model. *BMJ*. 2014;349:g5920.
43. Oelke M, Höfner K, Wiese B, Grünewald V, Jonas U. Increase in detrusor wall thickness indicates bladder outlet obstruction (BOO) in men. *World journal of urology*. 2002 Apr; 19(6): 443-52. doi: 10.1007/s00345-001-0238-z.
44. Zafar A, John A, Ali A, Ansar A, Ashfaq N. Sonographic Evaluation of Urinary Bladder Wall Thickness in Healthy Adults. *Pakistan Journal of Health Sciences* 2022;38–41. doi: 10.54393/pjhs.v3i01.42.
45. Ballstaedt L, Leslie SW, Woodbury B. Bladder Post Void Residual Volume. 2025 Jan; PMID: 30969661.
46. Kim SH, Cho JY, Lee HJ, Sung CK, Kim SH. Ultrasound of the Urinary Bladder, Revisited. *Journal of Medical Ultrasound* 2007;15:77–90. doi: 10.1016/s0029-6441(08)60026-0.
47. Sala E, Rockall A, Rangarajan D, Kubik-Huch RA. The role of dynamic contrast-enhanced and diffusion weighted magnetic resonance imaging in the female pelvis. *Eur J Radiol*. 2010 Dec;76(3):367-85. doi: 10.1016/j.ejrad.2010.01.026. PMID: 20810230.
48. Colombo N, Creutzberg C, Amant F, Bosse T, González-Martín A, Ledermann J, et al ESMO-ESGO-ESTRO Endometrial Consensus Conference Working Group. ESMO-ESGO-ESTRO consensus conference on endometrial cancer: Diagnosis, treatment and follow-up. *Radiother Oncol*. 2015 Dec;117(3):559-81. doi: 10.1016/j.radonc.2015.11.013. Epub 2015 Dec 9. PMID: 26683800.
49. Frei KA, Kinkel K, Bonél HM, Lu Y, Zaloudek C, Hricak H. Prediction of deep myometrial invasion in patients with endometrial cancer: clinical utility of contrast-enhanced MR imaging-a meta-analysis and Bayesian analysis. *Radiology*. 2000 Aug;216(2):444-9. doi: 10.1148/radiology.216.2.r00au17444. PMID: 10924568.
50. Practice Bulletin No. 149: Endometrial cancer. *Obstet Gynecol*. 2015 Apr;125(4):1006-1026. doi: 10.1097/01.AOG.0000462977.61229.de. PMID: 25798986.
51. Alcazar JL, Galvan R. Three-dimensional power Doppler ultrasound scanning for the prediction of endometrial cancer in women with postmenopausal bleeding and thickened endometrium. *American journal of obstetrics and gynecology*. 2009 Jan; 200(1): 44.e1-6. doi: 10.1016/j.ajog.2008.08.027.
52. Van den Bosch T. Ultrasound in the diagnosis of endometrial and intracavitary pathology: an update. *Australasian journal of ultrasound in medicine*. 2012 Feb; 15(1): 7-12. doi: 10.1002/j.2205-0140.2012.tb00135.x.
53. Moro F, Ciancia M, Zace D, Vagni M, Tran HE, Giudice MT, et al. Role of artificial intelligence applied to ultrasound in gynecology oncology: A systematic review. *International journal of cancer*. 2024 Nov 15; 155(10): 1832-1845. doi: 10.1002/ijc.35092.
54. Shi J, Kraft P, Rosner BA, Benavente Y, Black A, Brinton LA, et al. Risk prediction models for endometrial cancer: development and validation in an international consortium. *Journal of the National Cancer Institute*. 2023 May 8; 115(5): 552-559. doi: 10.1093/jnci/djad014.
55. Han X, Qiu J. Development and validation of a machine learning-based pathomics nomogram for prognostic prediction in endometrial cancer. *Discover oncology*. 2025 Dec 4; 17(1): 45. doi: 10.1007/s12672-025-04226-z.

MEDICOLEGAL ASPECTS AND MENOPAUSE

Keywords: Informed consent, hormones, medicolegal issues.

51

INTRODUCTION

The millennium has been seen as a time of significant change in the doctor-patient relationship. Until very recently, many patients, male and female, expected not only advice from their doctor but also to be told which treatment would be best for them.¹ This paternalistic approach, however, is rapidly disappearing. Nowadays, early postmenopausal women expect to make decisions about their treatment after being fully informed of all the possible benefits and risks.² Menopause is a physiological transition marking the end of a woman's reproductive life, typically occurring between 45 and 55 years. While primarily a biological and psychological event, menopause also carries important medico-legal implications. These aspects are often underemphasised but remain crucial for safeguarding patient rights, guiding healthcare providers, and ensuring ethical and legal compliance in clinical practice.³ Provision for this requires the doctor to keep abreast of the literature. Patient access to medical information has been revolutionised during the last decade. The availability of the internet, books, magazines, and newspaper articles, which have long been important sources of patient information, has increased significantly.^{4,5} According to surveys, these forms of communication are the primary sources of information for 50% of women seeking advice on menopausal hormone therapy (MHT).⁶

Effective communication of risks and benefits is a cornerstone of ethical and legal practice in menopause management. Clinicians are legally required to ensure that patients understand the potential outcomes of any intervention, including MHT, lifestyle modifications, or alternative therapies. A clear discussion of both benefits and potential adverse effects empowers women to make informed decisions about their health care.⁷ Shared decision-making is central to the medicolegal framework. Respecting a patient's autonomy by incorporating her preferences alongside clinical recommendations demonstrates ethical practice and can reduce the likelihood of litigation. Clinicians must also consider the long-term implications of therapy and discuss uncertainties in the evidence when applicable. Transparent, patient-centred communication not only fosters trust but also safeguards both the patient and the clinician from medicolegal consequences.⁸

Physicians, therefore, have a responsibility to advise patients accurately about both conventional and alternative treatments.⁸ Knowledge of alternative medical literature is becoming essential to maintain professional credibility. Clinicians must communicate information in an unbiased manner, highlighting the benefits and risks of different treatments in line with the patient's concerns. Failure to do so may not only erode patient trust but also expose the clinician to potential medicolegal consequences.⁹ The medico-legal issues surrounding menopause span diagnosis, treatment choices, counselling, the use of MHT, medico-social consequences, occupational concerns and litigation risks. There must be very few areas in medicine today where there is such ambivalence of expression and such divergence of views as on the issues of MHT.¹⁰

INFORMED CONSENT

Informed consent recognises an individual's right to make decisions affecting their well-being. Decision-makers should understand the risks and benefits of their choices.¹¹ In the doctor-patient relationship, the duty to disclose treatment risks lies with the doctor, while the patient retains the right to decide how their body will be treated.¹² Risk involves exposure to the possibility of injury or loss, with two components: the probability of an uncertain event and the resulting injury or disutility. The law requires disclosure of such risks, and a causal link between nondisclosure and injury must exist. Medical informed consent ensures that patients are informed about risks, alternatives, and costs, enabling them to make informed decisions.¹³

Informed consent is more than a signed form; it is a process that verifies the patient's understanding of the treatment, its risks, alternatives, and expected outcomes. Legally, failing to provide adequate information may constitute negligence, while thorough documentation of these discussions provides critical evidence of compliance with professional standards. This is particularly important in menopause care, where interventions such as MHT have

individualised benefit–risk profiles depending on age, comorbidities, and symptom severity.¹⁴ Finally, documentation of the informed consent process, including discussions of risks, benefits, alternatives, and patient questions, is essential. Meticulous records provide evidence that patients were adequately informed and consented voluntarily, thereby meeting legal and ethical obligations in clinical practice. This approach ensures that menopause care is delivered safely, ethically, and in accordance with current medicolegal standards. Refer to Figure 1 for a sample of consent for the prescription of MHT.

PENAL PROVISIONS IN INDIA REQUIRING INFORMED CONSENT

Medical practitioners who violate are liable to be removed from the rolls of the Medical Council of India or the State Medical Council. The Indian Penal Code also makes the offence punishable by fine or imprisonment, depending on the circumstances of each case.

Legal Recognition Of Menopause In Health And Employment

- *Age of Menopause:* Legally, menopause is often presumed to occur at age 50, though it may vary widely. Courts may accept menopausal status as evidence in medico-legal cases involving infertility, disputed paternity, or compensation claims.¹⁴
- *Early or Premature Menopause:* Can influence insurance claims, employment disputes, and compensation for iatrogenic causes like premature ovarian failure following surgery, chemotherapy, or radiation.¹⁵
- *Workplace Rights:* Increasingly, labour laws in some countries, such as the United Kingdom (UK), recognise menopausal symptoms as a factor in workplace discrimination or disability claims under the Equality Act 2010. In India, this is emerging as a policy discussion.¹⁶

Medico-Legal Concerns In Diagnosis

- *Misdiagnosis:* Failure to identify menopause or attributing symptoms (abnormal bleeding) solely to menopause without ruling out malignancy may give rise to allegations of medical negligence.
- *Documentation:* Proper record-keeping of history, examination, and investigations is vital for defending against medicolegal claims.¹⁷
- *Informed consent:* Any intervention (hysterectomy, oophorectomy endometrial biopsy) requires clear documentation of risks, alternatives, and the possible effect on menopausal status.¹⁸ Initiating informed consent for menopausal hormone therapy requires clear documentation of the indication, risks, and alternatives.

MEDICOLEGAL ISSUES SPECIFICALLY ABOUT HORMONE THERAPY

As our patients depend on us to make therapeutic decisions, we need a strategy for MHT. To suit our circumstances and considering the overall effects of such therapy, the following measures are suggested :

- Define the goal for using MHT: symptom control (flushes) or preventive measures (to reduce the risk of osteoporosis-related fractures).
- Assess the feasibility and availability of regular follow-up, and evaluate compliance.
- Identify risks/medical conditions on which MHT may have an adverse effect: coronary heart disease, breast/uterine cancer, liver disease, thromboembolism, and hypertriglyceridemia
- Select the appropriate hormone regimen, such as estrogen alone in women without a uterus and estrogen/progestogen in women with an intact uterus
- Discontinue MHT in the event of an acute coronary event, the development of breast or endometrial cancer, stroke, or thromboembolism¹⁹
- Any pharmacotherapy given for estrogen deficiency syndrome or treatment for menopausal women must legibly specify:
 - Name and dose of the drug

- Duration of the therapy advice and planned
- Indication for initiating treatment
- The patient was counselled about the risks/benefits of therapy, and the details were explained
- Follow-up date
- Results of investigations undertaken prior to initiating
- HT, mammogram, ultrasound, lipid profile
- Informed consent needs to be taken before starting MHT²⁰
- On follow-up visits, it would be advisable to document legibly:
 - The dose and frequency of medication taken, and for how long
 - During use, the regularity and frequency of intake, perceived benefits and problems, and any specific problems were inquired about.
 - Any new circumstances or medical problems that have developed in the woman
 - The reasons for continuing or discontinuing therapy
 - The results of physical examination and monitoring investigations
 - The next advised follow-up visits and monitoring tests
 - Any recent information given to the patient based on new developments regarding the therapy
 - Discussion of alternative, complementary, and supplementary therapies.
- Failure to adequately counsel and document informed consent can result in negligence litigation.
- *Product liability*: Lawsuits have been filed worldwide against pharmaceutical companies for inadequate labelling of the risks of HRT.
- *Monitoring and follow-up*: Regular breast and pelvic examinations, mammography, and endometrial monitoring should be documented to avoid liability claims in the event of adverse outcomes.²¹

Medico-Legal Aspects Of Menopause-Associated Disorders

- *Osteoporosis and fractures*: Failure to assess fracture risk or advise preventive therapy may lead to malpractice claims if a fracture occurs.
- *Cardiovascular health*: Misinterpretation of menopausal symptoms like palpitations and chest pain may delay diagnosis of cardiac disease, raising liability.²²
- *Psychological issues*: Depression, cognitive changes, and sexual dysfunction require sensitive handling. Allegations of negligence may arise if these are ignored or dismissed without evaluation.²³

Ethical And Social-Legal Considerations

- *Autonomy and confidentiality*: Women must be empowered to make informed decisions regarding HRT, contraception in perimenopause, and surgical interventions.
- *Discrimination and stigma*: Social prejudices related to menopause may contribute to workplace discrimination or marital disputes, sometimes reaching legal forums.
- *Research and clinical trials*: Participation of menopausal women in clinical trials must strictly adhere to ethical guidelines (ICMR 2017; Declaration of Helsinki).²⁴

Forensic Implications

- *Age determination*: Menopausal status may be relevant in a medico-legal age dispute, especially when documentary proof is absent.
- *Sexual assault cases*: Postmenopausal women may show different physical signs of sexual violence

- compared to younger women. Documentation must be meticulous to withstand legal scrutiny.
- *Medico-legal autopsy*: Postmortem findings may require correlation with menopausal status in cases of hormone therapy, cardiovascular deaths, or osteoporosis-related fractures.²⁴

ETHICAL PRINCIPLES IN THE CONDUCT OF MENOPAUSE RESEARCH

The same ethical principles that apply to biomedical research in general also govern research on menopause. The principles of respect for persons, beneficence, and justice inform the selection and recruitment of subjects, the process of obtaining informed consent from potential subjects, the assessment of risks and benefits, and the conduct of the research itself.²⁵

INDIAN CONTEXT

- There are no specific Indian laws directly addressing menopause, but medico-legal issues arise under:
 - Consumer Protection Act (2019)- for medical negligence cases.
 - Medical Council of India/NMC Guidelines- regarding ethical practice.
 - Indian Evidence Act (1872) – in cases where menopausal status is relevant to disputes of fertility or sexual function.
 - There is growing advocacy for menopause-friendly workplace policies, but these have yet to be formally legislated in India.²⁶

SYNOPSIS

- Communication is key to maintaining patient trust.
- The benefits and risks of different treatments, tailored to the patient's concerns, should be explained in the local language.
- There must be very few areas in medicine today where there is such ambivalence of expression and diversion of views as on the issues of MHT. Hence, the decision to take MHT has to be left to the woman.
- Informed consent must be obtained before starting MHT.

RESEARCH AGENDA

Influence of written consent on the uptake of HT for management of menopause.

REFERENCES

1. Chipidza FE, Wallwork RS, Stern TA. Impact of the Doctor-Patient Relationship. *Prim Care Companion CNS Disord*. 2015 Oct 22;17(5):10.4088/PCC.15f01840. doi: 10.4088/PCC.15f01840.
2. Whitehead M. The need for continuing education of the prescriber. *Climacteric J Int Menopause Soc*. 2000;3:28–32.
3. McCarthy M, Raval AP. The peri-menopause in a woman's life: a systemic inflammatory phase that enables later neurodegenerative disease. *J Neuroinflammation*. 2020 Dec;17(1):317. doi: 10.1186/s12974-020-01998-9.
4. Slomian J, Bruyère O, Reginster JY, Emonts P. The internet as a source of information used by women after childbirth to meet their need for information: A web-based survey. *Midwifery*. 2017 May;48:46-52. doi: 10.1016/j.midw.2017.03.005. Epub 2017 Mar 14. PMID: 28324809.
5. ACOG Committee Opinion No. 585: Health literacy. *Obstet Gynecol*. 2014 Feb;123(2 Pt 1):380-383. doi: 10.1097/01.AOG.0000443277.06393.32. PMID: 24451675.
6. Meeta M, Guduru S, Tanvir T, Madan A. Awareness of menopause and menopause hormone therapy in India: perspectives of healthcare providers and consumers. *Climacteric*. 2025 May 4;28(3):286–95. doi: 10.1080/13697137.2025.2503876.
7. Fenton A, Panay N. Communicating risk and benefit to patients. *Climacteric*. 2014 Dec;17(6):623–4. doi: 10.3109/13697137.2014.974895.
8. Masic I, Miokovic M, Muhamedagic B. Evidence based medicine–new approaches and challenges. *Acta Inform Medica*. 2008;16(4):219.
9. Aljardi OY, Alalawi S, Aljohani AZ, Humaida AA, Hashim OS, Abdullah AR. Assessment of Knowledge and Communication Regarding Complementary and Alternative Medicine Among Physicians in Madinah City. *Cureus*. 16(5):e61307. doi: 10.7759/cureus.61307.
10. Harper-Harrison G, Carlson K, Shanahan MM. Hormone Replacement Therapy. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 [cited 2026 Feb 4]. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK493191/>

11. Vedder A, Spajić D. Moral autonomy of patients and legal barriers to a possible duty of health related data sharing. *Ethics Inf Technol.* 2023 Mar;25(1):23. doi: 10.1007/s10676-023-09697-8.
12. Kumar A, Mullick P, Prakash S, Bharadwaj A. Consent and the Indian medical practitioner. *Indian J Anaesth.* 2015;59(11):695–700.
13. Dove ES. Confidentiality, public interest, and the human right to science: when can confidential information be used for the benefit of the wider community? *J Law Biosci.* 2023;10(1):lsad013.
14. Huang S, Gongye R, Zou S, Hee JY, Tang K. Menopausal status, age at menopause and risk of all-cause mortality among Chinese women: findings from a 10-year prospective study. *BMJ Public Health.* 2023;1(1).
15. Hernández-Angeles C, Castelo-Branco C. Early menopause: A hazard to a woman's health. *Indian J Med Res.* 2016;143(4):420–7.
- Howe D, Duffy S, O'Shea M, Hawkey A, Wardle J, Gerontakos S, et al. Policies, Guidelines, and Practices
16. Supporting Women's Menstruation, Menstrual Disorders and Menopause at Work: A Critical Global Scoping Review. *Healthcare* 2023, 11, 2945. 2023.
17. Thomas J. Medical records and issues in negligence. *Indian J Urol.* 2009;25(3):384–8.
18. Furness S, Roberts H, Marjoribanks J, Lethaby A. Hormone therapy in postmenopausal women and risk of endometrial hyperplasia. *Cochrane Database Syst Rev.* 2012 Aug 15;2012(8):CD000402. doi: 10.1002/14651858.CD000402.pub4.
19. Gupta R, Guptha S. Strategies for initial management of hypertension. *Indian J Med Res.* 2010 Nov;132(5):531–42.
20. Meeta M, Anuradha M, Ashraf AB, Aggarwal K, Digumarti L, Singh T. Clinical Practice Guidelines for Menopause: *An Executive Summary and Recommendations: Indian Menopause Society 2026. *J Mid-life Health* 2025; 0.
21. Boumil MM, Curfman G. Legal Liability of Generic vs Brand Drug Manufacturers for Inadequate Product Labels. *JAMA.* 2018 Aug 14;320(6):547–8. doi: 10.1001/jama.2018.8408.
22. Ryczkowska K, Adach W, Janikowski K, Banach M, Bielecka-Dabrowa A. Menopause and women's cardiovascular health: is it really an obvious relationship? *Arch Med Sci AMS.* 2022 Dec 10;19(2):458–66. doi: 10.5114/aoms/157308.
23. Berlin L. Liability for Failure to Order Screening Examinations. *Am J Roentgenol.* 2002 Dec;179(6):1401–5. doi: 10.2214/ajr.179.6.1791401.
24. Mendoza-Huertas L, Mendoza N, Godoy-Izquierdo D. Impact of violence against women on quality of life and menopause-related disorders. *Maturitas.* 2024 Feb;180:107899. doi: 10.1016/j.maturitas.2023.107899.
25. Macklin R. Ethical principles in the conduct of menopause research. *Exp Gerontol.* 1994;29(3–4):519–24.
26. Agrawal A. Medical negligence: Indian legal perspective. *Ann Indian Acad Neurol.* 2016;19(Suppl 1):S9–14.

TRAVEL AT MENOPAUSE

Keywords: Safety, travel and disease, immunisations

52

INTRODUCTION

Whether for business or for a holiday, travelling can be as stressful as it is enjoyable. Postmenopausal women need to be cautious when travelling, as they may be experiencing menopausal symptoms and/or age-related medical problems. Ageing alone is an indication that requires special precautions during travel. It is important to provide recommendations on a range of issues affecting travellers, including travel advice for women with sensory and speech impairments.

Women with hearing, visual, or speech impairments can travel safely with appropriate advance planning and communication. Patients should be advised to inform airlines, transport authorities, hotel staff, and co-travellers in advance about their impairment to facilitate necessary assistance during boarding, transit, and emergencies. A clearly written itinerary, destination address, and emergency contact information should be carried at all times. Assistance should be requested proactively during air, bus, or rail travel. Adequate food, water, and essential personal devices (for example, hearing aids, visual aids, communication devices) should be carried to minimise unnecessary movement and delays. Women with visual impairments should seek support for boarding, seating, and emergency exit orientation, and may prefer window seating for spatial orientation. Those with speech impairments should carry written communication cards or notes to convey common needs and instructions. Clear documentation and prior disclosure improve safety, reduce travel-related anxiety, and facilitate timely assistance.

PREPARATION FOR TRAVEL

All travellers should plan their trips. If travelling overseas, a physician's appointment should be made at least one month before travel. Travel insurance should be reviewed before departure. Many health insurance policies cover travel abroad, but if this is not available, inexpensive policies can be obtained for short-term periods. All travellers with health-related problems should carry information from their physician, including a copy of a recent electrocardiogram and a list of current medications. If travelling with inhalers or controlled substances, a letter from the patient's physician is recommended in case customs or security officials ask questions. The passenger's health care provider should also consider vaccination status and the public health aspects of infectious diseases. It is now mandatory for all commercial aircraft to carry an automated external defibrillator.

GENERAL GUIDELINES

Women should be advised to plan travel in advance to avoid rushing and allow sufficient time for safe ambulation. Appropriate assistive devices (cane, walker, or wheelchair) should be used when mobility is limited, and wheelchair assistance should be pre-arranged for long distances at stations and airports. Non-slip, well-fitting footwear and appropriate visual aids (such as spectacles) should be used. Comfortable, well-fitting clothing that does not trail underfoot should be worn to minimise the risk of falling.

Patients should be encouraged to travel light, keep their hands free for support, and avoid rushing while boarding or alighting. Accessible seating (lower berths on trains; aisle or toilet-adjacent seats on buses/aircraft) should be preferred. Back support and seat belts should be used during travel. Prolonged uninterrupted sitting should be avoided to reduce venous congestion. Essential medications should be carried during travel, along with personal identification and emergency medical information. Alighting should be delayed until crowding subsides to minimise the risk of falls and injuries.

Dedicated Myocardial Infarction (MI) Emergency Kit

Emergency Instructions (to be printed in the kit):

- If chest pain/pressure, breathlessness, jaw/arm pain, diaphoresis, or unexplained fatigue occur: stop activity and sit/lie down.
- Chew Aspirin 300–325 mg immediately (if no allergy/active bleeding).

- Take Nitroglycerin 0.4 mg sublingually; repeat every 5 min up to 3 doses if pain persists and SBP 100 mmHg.
- Take Clopidogrel 300 mg stat.
- Take Atorvastatin 80 mg stat.
- Call emergency services immediately

Medico-Legal Concerns In Diagnosis

In well-controlled high blood pressure, travelling or flying is as safe as for any other passenger. While flying, the cabin is pressurised, so a passenger with high blood pressure is not at risk from a health perspective. Uncontrolled blood pressure puts a person at high risk because stressful situations during travel can raise it.

- Keep medicine in a handbag so it can be taken at the right time.
- Keeps a note in the purse/tag indicating what to do if it's taken and what to do if it's found in an adverse situation.
- Always know the warning signs and symptoms of complications that can occur in hypertension.

Specific Travel Recommendations for Cardiovascular Patients

Commercial air travel is generally safe for most patients with stable cardiovascular disease. Patients should carry an adequate supply of all cardiac medications (including an emergency cardiac kit) in hand luggage, along with a written medication list showing doses and timings. Dose schedules should be adjusted appropriately when crossing time zones. A copy of the most recent electrocardiogram (ECG), relevant laboratory reports, and details of recent cardiac procedures should also be carried. Patients with cardiac implantable devices should carry their device identification card and a recent ECG.¹⁻³ Airlines should be informed in advance of any special requirements, such as dietary needs, wheelchair assistance, or in flight oxygen. Seating near the aisle or the restroom may be preferred. Unnecessary ambulation during travel should be minimised, and adequate connection time should be allowed. In-flight supplemental oxygen may be considered for patients with class III–IV angina or baseline hypoxaemia. Patients should carry the emergency contact details of their treating physician(s) and be educated about symptoms that require immediate medical attention.

Cardiovascular Contraindications to Commercial Air Travel

Commercial air travel should be deferred in patients with:

- Uncomplicated myocardial infarction within the preceding 2–3 weeks
- Complicated myocardial infarction within the preceding 6 weeks
- Unstable angina
- Severe or decompensated congestive heart failure
- Uncontrolled hypertension
- Recent coronary artery bypass grafting within 10–14 days of an uncomplicated procedure
- Recent cerebrovascular accident within 2 weeks to allow assessment for complications such as haemorrhagic transformation Uncontrolled ventricular or supraventricular tachyarrhythmias
- Eisenmenger syndrome
- Severe symptomatic valvular heart disease

Deep Vein Thrombosis (DVT) Prevention During Travel

Prolonged immobility during travel may precipitate venous thromboembolism in predisposed individuals through mechanisms described by Virchow's triad. All travellers should be encouraged to:

- Walk in the cabin or aisle at least every 30–60 minutes when feasible
- Prefer aisle seating to allow frequent movement

- Maintain adequate hydration
- Perform ankle and calf muscle exercises while seated
- Use graduated compression stockings
- Keep emergency contact information accessible.⁴⁻⁷

In high-risk individuals, pharmacological thromboprophylaxis (for example, low-dose aspirin or low-molecular - weight heparin) may be considered in consultation with the treating physician. For passengers without identifiable risk factors, regular lower-limb stretching, posture adjustments, and periodic ambulation are recommended to balance mobility with in-flight safety.

Travel Advice for Patients With Diabetes Mellitus

Commercial air travel is generally safe for individuals with well-controlled diabetes mellitus. Patients should carry visible medical identification indicating their diabetic status and written emergency contact details. An adequate supply of insulin, oral antidiabetic medications, glucose-monitoring equipment, and consumables should be carried in hand luggage, with additional backup supplies to account for loss or damage. Insulin should be transported in insulated containers to prevent exposure to extreme temperatures, and a spare glucometer should be carried. A written prescription or medical letter should accompany all medications.^{8,9}

Medication regimens may require adjustment when crossing time zones, and patients should seek pre-travel medical advice regarding dose modification. During road travel, blood glucose should be monitored before driving and every two hours thereafter, and fast-acting carbohydrates should be readily available for hypoglycaemia. During air travel, insulin should be administered after meals are served, and diabetic meals or portable carbohydrate snacks should be arranged. Comfortable, well-fitting footwear is recommended to reduce the risk of foot injury. For long-haul intercontinental travel, dose modification of intermediate- and long-acting insulin may be necessary depending on eastward or westward travel, and should be individualised by the treating physician to prevent hypo- or hyperglycaemia.

Travel Advice for Women With Sensory and Speech Impairments

Women with hearing, visual, or speech impairments can travel safely with appropriate advance planning and communication. Patients should be advised to inform airlines, transport authorities, hotel staff, and co-travellers in advance about their impairment to facilitate necessary assistance during boarding, transit, and emergencies.¹⁰⁻¹² A clearly written itinerary, destination address, and emergency contact information should be carried at all times. Assistance should be requested proactively during air, bus, or rail travel. Adequate food, water, and essential personal devices (for example, hearing aids, visual aids, communication devices) should be carried to minimise unnecessary movement and delays. Women with visual impairments should seek support with boarding, seating, and emergency exit orientation, and may prefer window seating for spatial orientation. Those with speech impairment should carry written communication cards or notes to convey common needs and instructions. Clear documentation and prior disclosure improve safety, reduce travel-related anxiety, and facilitate timely assistance.

Travel Advice for Women With Cancer or Receiving Chemotherapy

Travel can be undertaken safely by patients with cancer when appropriately planned. A pre-travel consultation with the treating oncologist is essential to determine the optimal timing and fitness for travel. Patients should carry copies of recent medical records, laboratory reports, and their oncologist's contact details. Adequate quantities of all prescribed medications should be carried in hand luggage, with additional backup supplies to account for loss or damage. In their original packaging, with a written medication list that includes generic names.^{13,14}

Patients using oxygen therapy should carry recent oximetry reports and a physician's certificate for oxygen devices or injectable medications. Travel and medical insurance coverage should be verified, particularly for international travel. Identification indicating the diagnosis and emergency contact details is advised. During travel, patients should use safe drinking water, avoid ice and unpasteurised foods, minimise sun exposure due to treatment-related photosensitivity, and plan for adequate rest. Wheelchair assistance and early boarding may be considered. High-altitude travel should be approached with caution, particularly in anaemic patients. Supplemental oxygen should be arranged in advance for those with compromised pulmonary function.

Travel Advice for Women With Arthritis and Osteoporosis

Travel is feasible and beneficial for women with arthritis and osteoporosis when appropriate precautions are taken. Prolonged sitting, luggage handling, transfers, and cramped seating may exacerbate joint stiffness, pain, and fatigue in women with arthritis. Patients should be advised to minimise joint strain by resting adequately, using assistive devices, using comfortable seating, and adhering to general travel safety recommendations.¹⁵⁻¹⁷ Osteoporosis is highly prevalent in older women and is associated with increased fracture risk, particularly of the hip, spine, and wrist. Osteoporosis alone is not a contraindication to travel; however, activities during travel may increase the risk of falls and fragility fractures. Sea travel may pose a higher fall risk due to slippery and uneven surfaces. Air and road travel are generally safe when comfortable seating and fall-prevention measures are ensured. Adherence to general travel safety and fall-prevention guidelines is strongly recommended.

Travel Advice for Patients With Renal Disease

Travel is feasible for patients with chronic kidney disease, including kidney transplant recipients, with appropriate advance planning. Patients should carry adequate quantities of prescribed medications and dialysis-related prescriptions, with surplus supplies to cover unforeseen delays. Dialysis centres and nephrology services at the destination should be identified prior to travel. Dietary requirements, particularly low-sodium diets, should be pre-arranged with airlines or cruise operators when indicated.¹⁸

Travel Advice for Women With Asthma

Travel is generally safe for women with asthma when appropriate preparation is undertaken. Patients should carry their written prescription, asthma action plan, and an adequate supply of both controller and reliever medications in hand luggage, with additional backup supplies. A dedicated asthma travel kit should include inhalers, spacer devices, and a peak flow meter if prescribed; nebulisers should be carried when regularly required. Medications should be protected from extreme temperatures.¹⁹ Pre-travel planning should include identification of nearby medical facilities at the destination. Patients should minimise exposure to temperature extremes, high altitude, and known allergens, and ensure smoke-free, allergen-controlled accommodation. Personal bedding or dust-mite protective covers may be carried when indicated. Adequate rest, stress reduction, and adherence to regular breathing and physical exercise routines are recommended to maintain asthma control during travel.

Air Travel After Surgical Procedures

With the increasing frequency of ambulatory and medical tourism-related surgeries, the appropriate timing of postoperative air travel is essential. General anaesthesia per se is not a contraindication to flying; however, patient stability, pain control, and special medical needs must be assessed prior to travel. Postoperative patients may have increased oxygen demand and reduced oxygen delivery, particularly in the elderly, anaemic, hypovolaemic, or cardiopulmonary-compromised individuals; in such cases, postponing travel or providing in flight supplemental oxygen should be considered.²⁰ Following open abdominal surgery, intestinal gas expansion at cabin altitude increases the risk of suture line disruption, bleeding, and perforation. Air travel should therefore be avoided for 1–2 weeks after open abdominal procedures (minimum 1 week if the bowel lumen is not opened) and for at least 24 hours after a colonoscopy. Laparoscopic abdominal surgery is associated with less ileus, and travel may be considered the next day in the absence of abdominal bloating. Air travel is contraindicated in patients with intracranial air, cerebrospinal fluid leak, or recent neurosurgical procedures with residual intracranial gas due to the risk of increased intracranial pressure and infection from cabin pressure changes.

Motion Sickness, Jet Lag and Altitude Illness

Motion sickness may occur in any mode of travel and can be prevented with appropriate premedication when indicated (for example, hyoscine, ephedrine-based combinations, or other anti-motion sickness agents). Jet lag is common in international travel and results from circadian rhythm disruption due to rapid time zone changes. Severity is influenced by the number of time zones crossed, direction of travel (westward travel is generally better tolerated), environmental stimulation, cumulative sleep deprivation, and individual chronotype. Symptoms include irritability, insomnia, impaired concentration, and fatigue. Preventive strategies include gradually shifting sleep schedules during the pre-travel phase, adequate hydration, avoiding alcohol and carbonated beverages, minimising sleep debt, and allowing flexible schedules after arrival.^{21,22}

Altitude illness occurs after prolonged exposure (> 8 hours) to altitudes above 10,000 ft. Mild symptoms include headache, nausea, fatigue, and dyspnoea, while severe illness may present with vomiting, ataxia, altered mental status, fever, and cyanosis. Travellers ascending to high altitudes should be counselled on recognising symptoms and on graded ascent.

Sun Exposure

Tropical areas are characterised by intense sunlight, high ultraviolet radiation, and dry conditions. For this reason, travellers should use sunscreen with at least SPF 15. Other measures include long-sleeved shirts, cool, loose clothing, ChapStick for dry or cracked lips, and wide-brimmed hats to shield against the sun's intense rays. Sunglasses should also be worn to protect the eyes.²³

Medications and Immunisations for Travellers

Travellers with chronic medical conditions should carry at least two separate supplies of their regular medications, with one supply kept in hand luggage. A spare pair of spectacles should be carried by those who use corrective lenses. Prophylactic antibiotics are not routinely recommended; however, a general antibiotic may be considered for travel to remote areas. Symptomatic medications such as antidiarrhoeals (loperamide), analgesics, antipyretics, antispasmodics, antihistamines, antifungal creams, and short-course oral corticosteroids for patients with chronic respiratory disease may be included in a personal travel kit. Malaria and high-altitude prophylaxis should be prescribed based on the travel destination and individual risk profile. All travellers should have their immunisation status reviewed prior to travel. Routine adult immunisations, including tetanus, measles–rubella, hepatitis B, influenza, and pneumococcal vaccines, should be updated as indicated. Hepatitis B vaccination is essential for travellers involved in healthcare activities. Destination-specific vaccines, including yellow fever, where mandated, should be administered in accordance with national and international travel health guidelines.

Simple In-Travel Stretching and Mobility Exercises

Travellers should be encouraged to maintain an upright seated posture with relaxed shoulders and an engaged core. Periodic shoulder elevation and circumduction, gentle lateral neck tilts and rotations, and upper-limb stretching (forward, lateral, and posterior with scapular retraction) are recommended to reduce stiffness. Hand exercises, including fist clenching and finger abduction, may be performed to improve circulation. Lower-limb mobility should be maintained through ankle rotations and repeated ankle dors flexion–plantar flexion exercises to minimise stiffness and venous stasis.

SYNOPSIS

- Menopause is a natural physiological process in women; however, certain menopause-related symptoms and medical conditions pose special situations that need to be managed to ensure a safe journey.
- Planning the travel and making necessary arrangements can make the journey a memorable one
- The dedicated MI Emergency Kit should include aspirin 300–325 mg for immediate use (if no allergy or bleeding). Nitroglycerin 0.4 mg SL every 5 min (max 3 doses) if Systolic blood pressure (SBP) $\geq$ 100 mmHg. Clopidogrel 300 mg stat. Atorvastatin 80 mg stat.

RESEARCH AGENDA

Travel-Related Health Risks and Preparedness in Peri- and Postmenopausal Indian Women

REFERENCES

1. Fogoros RN. How to Fly Safely With Heart Disease [Internet]. Verywell Health. 2025 [cited 2026 Feb 4]. Available from: <https://www.verywellhealth.com/guidelines-for-flying-with-heart-disease-1746208>
2. Hammad M, Kindya BR, Allard-Ratick MP, Jazbeh S, Eapen D, Wilson Tang WH, et al. Navigating air travel and cardiovascular concerns: Is the sky the limit? Clinical cardiology. 2017 Sep; 40(9): 660-666. <https://doi.org/10.1002/clc.22741>
3. Goldermund D. Air travel considerations after a stroke | STROKE MANUAL [Internet]. [cited 2026 Feb 4]. Available from: <https://www.stroke-manual.com/air-travel-considerations-after-stroke/>
4. Flying: DVT Prophylaxis [Internet]. Canadian Cardiovascular Society. [cited 2026 Feb 4]. Available from: <https://ccs.ca/guideline/drive-and-fly-2003/chapter-10-flying-dvt-prophylaxis/>

5. Bartholomew JR, Evans NS. Travel-related venous thromboembolism. *Vascular medicine* (London, England). 2019 Feb; 24(1): 93-95. <https://doi.org/10.1177/1358863X18818323>
6. Karsanji DJ, Bates SM, Skeith L. The risk and prevention of venous thromboembolism in the pregnant traveller. *Journal of travel medicine*. 2020 Mar 13; 27(2). <https://doi.org/10.1093/jtm/taz091>
7. Watson HG, Baglin TP. Guidelines on travel-related venous thrombosis. *British Journal of Haematology* 2010;152:31-34. <https://doi.org/10.1111/j.1365-2141.2010.08408.x>
8. Traveling with diabetes: Tips for packing, snacking, monitoring, and more | Diet and Nutrition | Prevention | UT Southwestern Medical Center [Internet]. [cited 2026 Feb 4]. Available from: <https://utswmed.org/medblog/diabetes-travel-safety/>
9. Travel and diabetes | Diabetes Australia [Internet]. 2020 [cited 2026 Feb 4]. Available from: <https://www.diabetesaustralia.com.au/living-with-diabetes/travel/>
10. How To Travel with a Hearing Impairment or Deafness – SATH [Internet]. [cited 2026 Feb 4]. Available from: <https://sath.org/how-to-travel-with-a-hearing-impairment-or-deafness/>
11. Travel Tips for the Hearing Impaired | Ascentist [Internet]. Ascentist Healthcare. [cited 2026 Feb 4]. Available from: <https://ascentist.com/resources/patient-health/travel-tipsfor-the-hearing-impaired/>
12. Travel - Hearing Loss Association of America [Internet]. Hearing Loss Association of America -. [cited 2026 Feb 4]. Available from: https://www.hearingloss.org/post_topic/travel/
13. Traveling With Cancer: Safety and Preparation Tips to Know [Internet]. [cited 2026 Feb 4]. Available from: <https://www.cancercenter.com/community/blog/2024/11/traveling-with-cancer>
14. Travel Tips For Patients Chemotherapy | UPMC Hillman Cancer Center [Internet]. [cited 2026 Feb 4]. Available from: <https://hillman.upmc.com/patients/communitysupport/education/miscellaneous/travel-tips-for-patients-chemotherapy>
15. 8 Tips for Pain-Free Travel [Internet]. 2025 [cited 2026 Feb 4]. Available from: <https://www.arthritis.org/health-wellness/healthy-living/daily-living/life-hacks-tips/8-tips-for-pain-free-travel>
16. Alvea A. Travelling with Osteoporosis – Part 2 | Osteoporosis Canada [Internet]. 2021 [cited 2026 Feb 4]. Available from: <https://osteoporosis.ca/oc-blog/travelling-with-osteoporosis-part-2/>
17. Alvea A. Travelling with Osteoporosis – Part 1 | Osteoporosis Canada [Internet]. 2021 [cited 2026 Feb 4]. Available from: <https://osteoporosis.ca/oc-blog/travelling-with-osteoporosis-part-1/>
18. Travel Tips: A Guide for Kidney Patients | National Kidney Foundation [Internet]. National Kidney Foundation. [cited 2026 Feb 4]. Available from: <https://www.kidney.org/kidney-topics/travel-tips-guide-kidney-patients>
19. Traveling with Asthma & Allergies [Internet]. Asthma & Allergy Foundation of America. [cited 2026 Feb 4]. Available from: <https://aafa.org/asthma/living-withasthma/traveling-with-asthma-allergies/>
20. Surgical Conditions [Internet]. 2003. Available from: <https://asma.org/wpcontent/uploads/2025/08/Surgical-Conditions.pdf>
21. Services D of H&H. Jet lag [Internet]. Department of Health & Human Services; [cited 2026 Feb 4]. Available from: <http://www.betterhealth.vic.gov.au/health/healthyliving/jet-lag>
22. Jet Lag: Symptoms, Causes, and Prevention [Internet]. Sleep Foundation. 2021 [cited 2026 Feb 4]. Available from: <https://www.sleepfoundation.org/travel-and-sleep/jet-lag>
23. Fivenson D, Norton SA. Sun Exposure in Travelers [Internet]. Yellow Book. 2025 [cited 2026 Feb 4]. Available from: <https://www.cdc.gov/yellow-book/hcp/environmentalhazards-risks/sun-exposure-in-travelers.html>

HEALTHCARE INSURANCE FOR ELDERLY WOMEN

53

Keywords: Healthcare insurance, types, selection of insurance policy.

INTRODUCTION

Women today are multitasking and often have little or no time to care for themselves. Their effort to support the family financially, socially, and emotionally takes a toll on their health. Stress, pollution, and lifestyle-related factors adversely impact women's well-being. Late childbearing in pursuit of professional goals, along with menopausal transition and subsequent menopause, creates unique health demands.

Menopause is inevitable. How you handle it isn't

To enjoy the menopausal years in a healthy way, both financial and medical health are important. Financial planning involves structuring financial resources to achieve long-term goals, and insurance, both life and health, constitutes an integral part of this process. An insurance policy is a financial instrument that reduces or eliminates the risk of loss of life and property.¹ Under the insurance plan, many people share risk. The individual plan that covers only healthcare costs is called health insurance.

Key Considerations Before Purchasing a Health Insurance Policy

It is essential to obtain clear, written clarification from the insurer on the facilities and terms offered. Confirm whether the policy provides total cashless treatment or involves co-payments, and, if co-payments apply, determine the exact percentage payable by the insured. Enquire whether the policy is effective from day one or subject to an initial waiting period. Carefully review the definition of pre-existing (co-existing) diseases and the applicable waiting periods for their coverage. Obtain a detailed list of policy exclusions, including disease-specific and procedure-related exclusions. Clarify room rent limits, as these can significantly influence out-of-pocket expenses during hospitalisation. Ask about any premium discounts, such as those for long-term policies, no-claim bonuses, or wellness incentives. Importantly, at midlife and beyond, individuals should insist on comprehensive coverage of pre-existing conditions, as health issues are common in the menopausal age group, and restricted coverage may undermine the financial protection intended by the policy.

TYPES OF HEALTH INSURANCE COVERAGE

Cashless Hospitalisation

A facility in which the insured does not pay eligible hospital expenses at discharge, as the insurer settles the bill directly with the hospital after third party transactions (TPA) approval.

Types of cashless hospitalisation:

- *Planned hospitalisation:* Admission known in advance, with pre-authorisation obtained prior to admission.
- *Emergency hospitalisation:* Sudden admission due to an emergency, where approval is sought during or shortly after admission.¹

Medical Reimbursement

In this system, the insured initially bears all treatment costs. After discharge, the policyholder must submit a duly completed form and the required documents for reimbursement. A sum is granted as reimbursement for treatment purposes.¹

How to Make a Claim

Steps to Proceed With a Health Insurance Claim: Two pathways exist.¹

- *Cashless Basis:* For a cashless claim, treatment must be provided only at a network hospital of the TPA servicing your policy. Pre-authorisation is mandatory in accordance with the guidelines set out in the prescribed form. It is advisable to read the policy documents, including the terms and conditions, as soon as you receive them, rather

than waiting for a claim to arise.

- **Reimbursement Basis:** Familiarise yourself with the policy terms and conditions upon receipt of the policy, including the required documents. When a claim arises, notify the provider/insurer as required. After hospitalisation, obtain and keep ready the necessary documents, including the claim form, prescriptions, hospital bills, and the discharge summary, for submission, duly signed and attested by the treating doctor.

Things to Consider

- Medical check-ups may be required before policy issuance, especially at midlife or older age.
- Premiums increase with age, making early purchase more cost-effective.
- Always read the fine print, particularly clauses related to waiting periods, exclusions, room rent limits, and co-payments.
- Online comparison platforms such as PolicyBazaar can help compare premiums and features, but final decisions should be based on policy wording, not advertisements.²

Tips Before Buying Health Insurance

- Check waiting periods for pre-existing conditions and critical illnesses.
- Ensure that nearby hospitals that offer cashless treatment are accessible.
- Purchasing insurance early, ideally between ages 45 and 50, helps secure lower premiums and broader coverage.
- Review insurers' claim settlement ratios published by Insurance Regulatory and Development Authority of India (IRDAI).
- Consider adding suitable riders such as accidental death coverage, a premium waiver if relevant.

HEALTH INSURANCE POLICIES AVAILABLE IN INDIA

Various health insurance policies are available in India.²

- **Star Senior Citizen Red Carpet Policy**
 - Eligibility: 60–75 years (can buy after 45 years with other STAR plans).
 - Coverage: Up to ₹25 lakhs.
 - Pre-existing conditions: Covered after 1 year.
 - Bonus: No pre-medical tests till the age of 60 years.

Star Health Red Carpet Premium Policy

Care Health Insurance : Care Senior

- Entry age: 61 years (but Care Plus/Care plans are now under 60).
- Cashless hospitalisation: At 19,000+ hospitals.
- Annual health check-ups: Free every year.
- **HDFC ERGO – Optima Secure or Energy (if Diabetic)**
- **Niva Bupa (Max Bupa) – Health Companion**
 - Eligibility: 18–65 years.
 - Coverage: ₹2 lakhs – ₹1 crore.
 - Benefits: Covers maternity complications, day-care procedures, and critical illnesses.
- **Ayushman Vay Vandana Card**
 - Under the Ayushman Bharat Pradhan Mantri Jan Arogya Yojana (AB PM-JAY), it provides free health cover of ₹5 lakhs to all senior citizens aged 70 years and above, irrespective of socio-economic status.³

- Registration/Verification: Age verification via Aadhaar. You can register online through the official PM-JAY portal or the UMANG app, or visit a Common Service Centre (CSC) or an LIC branch. Provide Aadhaar for eKYC and verify details via OTP.

Varishtha Mediclaim for Senior Citizens⁴

- Designed to cater to the needs of senior citizens.
- Section 1: Hospitalisation and domiciliary expenses.
- Section 2 (optional): Critical illnesses at extra premium—Coronary artery surgery, cancer, renal failure, stroke, multiple sclerosis, major organ transplant, paralysis, blindness.
- Ambulance charges: Reimbursed up to ₹1,000 per policy year.
- Entry age: 60–80 years.
- Renewal: Up to 90 years; premium of 76–80 band loaded by 10% up to 85 and 20% up to 90 years.
- Medical check-up: Not required if insured uninterruptedly for the previous 3 years under National Insurance or another company; otherwise, medical tests at own cost (blood sugar and urine sugar, blood pressure, echocardiography, eye check-up including retinoscopy).

HOPE – Health of Privileged Elders (Oriental Insurance)⁴

- Public-sector non-life insurance product for citizens aged 60 and above.
- Covers hospitalisation due to 10 specified diseases common among the elderly.
- Sum insured: ₹1–5 lakhs.
- Premium range: ₹4,500–₹29,000 depending on age band and sum insured (new entrants +10%).
- Co-pay: 20% compulsory of the admissible claim; an optional 10–50% co-pay reduces the premium proportionately.
- Cashless payment: Through TPA up to ₹1 lakh.

Critical Illness Insurance

Especially useful for protection against diseases such as cancer, heart disease, and stroke

Top Plans Include:

- HDFC ERGO Critical Illness Insurance: Covers 15–30 major illnesses (one can choose). One-time lump sum on diagnosis.
- ICICI Pru Heart/Cancer Protect: Entry age: 18–65 years; specifically covers breast and cervical cancer, among others; includes a monthly income benefit on diagnosis.
- Aditya Birla Active Secure Critical Illness Plan: Offers both Cancer and Heart plans; an optional hospital cash benefit; and a premium waiver post-diagnosis.

Women-Specific Insurance Plans

Some insurers offer plans tailored for Indian women (some maternity-focused, others offering critical illness/milestone benefits).²

- *HDFC Life Smart Woman Plan*: Unit link insurance plan (ULIP) that covers pregnancy-related complications, childbirth issues, and cancer; career break cover after childbirth.
- *SBI Life Smart Women Advantage*: Combines life insurance and savings; covers major women-specific illnesses; waives future premiums on diagnosis.

Health Insurance Portability

Having health insurance for financial protection during medical emergencies is vital. Even more important is choosing the right plan with adequate coverage. Once you have bought a health insurance policy, you can renew it for life. If you

initially misjudged your needs and made an incorrect choice, you can set it right during policy renewal. IRDAI permits health insurance portability—that is, changing insurance companies or insurance plans while retaining benefits.¹ The prerequisite is to apply for portability 60 days before the expiry of the existing plan, but no later than 30 days before expiry.

Process & Timelines

- Start exploring new plans and providers 3 months before policy expiry to allow sufficient time to find a plan that suits your changing needs.
- Select the plan and coverage you need, then submit the required documents.
- The new service provider will review the information provided, may check with the previous insurer to verify the data's authenticity, and then approve the request for portability.
- The entire process may take up to 15 days.
- Care: Ensure there is no lapse in coverage during the transition.

Advantages of portability

- Extended coverage with better features (some insurers may tailor-make a policy).
- Potentially more affordable premiums; at times, the first premium may be waived off.
- Retention of benefits like no-claim bonus for claim-free periods and carrying forward accrued waiting periods.
- Improved service, including better customer service, easier claim process, and higher claim settlement ratios.
- Better hospital network with upgraded equipment and more extensive facilities.
- Usually, no additional fees are charged; however, cross-check before proceeding.

Disadvantages of portability

- Available only at renewal of the existing policy; not allowed at any time during the policy term.
- Potential for higher premiums when opting for additional benefits from a different insurer.
- Risk of losing benefits if details are not carefully reviewed when shifting existing plans.

Platforms to Compare and Buy in India

- PolicyBazaar.com²
- Coverfox.com²
- Turtlemint.com²

SYNOPSIS

- Health insurance is not just a financial product; it is a shield that protects individuals and families from the uncertainties of medical emergencies.
- In India, where healthcare costs are rising rapidly and lifestyle-related diseases are increasing, the importance of a comprehensive health insurance plan cannot be overstated.
- For women aged 45 and over, the need becomes more pressing, as this stage of life often carries higher risks of chronic conditions, critical illnesses, and age-related health concerns.
- A thoughtfully chosen health policy ensures access to quality healthcare without compromising financial stability.
- With insurers now offering women-specific plans and senior-friendly options, there is a wide range of products to meet diverse needs. The key lies in comparing benefits, understanding waiting periods, checking the hospital network, and opting for add-on riders that enhance protection.
- Health is wealth, and a robust insurance plan is the smartest way to safeguard it for the future.

RESEARCH AGENDA

Adequacy, Awareness and Financial Protection of Health Insurance among Peri- and Postmenopausal Indian Women:
A Multicentric Observational Study.

REFERENCES

1. Insurance Regulatory and Development Authority of India. IRDAI – Home [Internet]. Hyderabad: IRDAI; 2025 [cited 2025 Aug 31]. Available from: <https://irdai.gov.in/home>
2. Government of India. Policyholder.gov.in [Internet]. New Delhi: Department of Financial Services; 2025 [cited 2025 Aug 31]. Available from: <https://policyholder.gov.in>
3. Ministry of Health and Family Welfare, Government of India. Ayushman Bharat – Press Releases [Internet]. New Delhi: MoHFW; 2025 [cited 2025 Aug 31]. Available from: <https://www.mohfw.gov.in>
4. HelpAge India. Senior Citizens Guide: Revised Edition 2016 [Internet]. New Delhi: HelpAge India; 2016 [cited 2025 Aug 31]. Available from: <https://www.helpageindia.org>

ECONOMICS OF MENOPAUSE MANAGEMENT

Keywords: Economics, menopause, healthcare systems, healthcare costs, lifestyle, work productivity, future scope

54

INTRODUCTION

Menopause represents a critical life transition in women. According to the United Nations (UN) World Population Prospects 2024 Revision (medium variant), India had approximately 46 million women aged 45–49 years in 2024 and is projected to have approximately 57 million in 2050, compared with 30 million in 2011.^{1,2}

“Life expectancy is growing, while quality of life is still dormant.”

This statement captures the modern paradox of longevity. Medical and socioeconomic advances have extended human lifespans, yet these extra years are often marked by prolonged periods of poor health, disability, and social isolation. The quote suggests that society has become very effective at preventing death but less successful at fostering overall well-being in the additional years of life gained.³ The emergence of menopause as a health issue is attributed to rapid globalisation, urbanisation, increased awareness, and increased longevity among middle-aged Indian women.⁴ The transition to menopause is complex and multifaceted, significantly affecting women’s biological, emotional, sociocultural and financial health and wellbeing. Menopausal responses vary widely depending on genetics, culture, lifestyle, financial situation, education, behaviour and diet.

“Ageing is natural but requires graceful acceptance.”

Addressing the challenges of menopause with empathy and comprehensive care not only improves women’s health outcomes but also affirms their intrinsic value and the diversity of their roles within society. For women to age with dignity and confidence, they need financial security, family and workplace support, and timely medical care. Medicines play a role not only in easing immediate menopausal symptoms but also in preventing long-term consequences, including osteoporosis, cardiovascular disease, memory loss, urogenital problems, neurological disorders, and cancers. Overall cost of care depends on the healthcare system in place, a woman’s financial situation, and the affordability and accessibility of medicines in her region.

HEALTHCARE SYSTEM IN INDIA

The public healthcare system was initially developed to provide access to healthcare, regardless of socioeconomic status or caste.⁵ Public healthcare is free for every Indian resident.⁶ It is accessible and affordable for a large section of the population, especially the poor and marginalised. Still, it faces issues such as overcrowding, long waiting times, inadequate infrastructure, and a shortage of doctors and support staff, particularly in rural areas. India’s healthcare system is a complex mix of public and private healthcare facilities, both playing crucial roles in addressing the health needs of the vast and diverse population.

Public healthcare system

- The focus is primarily on providing affordable or free basic healthcare services, especially in rural and underserved areas. It mainly consists of three-tier systems.
- *At the Primary Level*, there are Sub-Centres and Primary Health Centres (PHCs) at the village level that provide basic healthcare, immunisation, and preventive services.
- *The Secondary Level* comprises Community Health Centres (CHCs) at the block level and Sub-District hospitals, providing specialised care and inpatient services.
- *The Tertiary Level* mainly comprises District Hospitals, Medical Colleges, and other specialised institutions at the district and state levels, providing advanced and super-specialty care, including research and teaching facilities.

Private healthcare system

Although many private clinics provide outpatient services, the private healthcare sector remains predominantly secondary- and tertiary-care oriented, characterised by hospital-centric, specialist-driven, and procedure-focused

care models. Structured, longitudinal, family-physician-based primary care systems with embedded preventive and life-course health services remain limited, leading to fragmented delivery of midlife and menopausal healthcare. It provides advanced technology, specialised services, and shorter waiting times, attracting both domestic and international patients (medical tourism). However, high costs can make it inaccessible to many, and concerns about transparency in pricing and quality of care persist.

Limitations Of India's Health Care System

The country's health care system, which focuses on women of reproductive age, is ill-equipped to address the challenges posed by perimenopause and menopause.⁷ India's healthcare system faces significant challenges in meeting current population needs, and the rising ageing population is likely to exacerbate these problems. Health facilities are concentrated in specific pockets, particularly in metropolitan cities, while smaller towns lack adequate facilities. This infrastructure gap poses a significant challenge to achieving healthy ageing in India.⁸

Key Challenges Facing The Indian Healthcare System

The Indian healthcare system is a diverse and complex network of public and private sectors that provide a wide range of medical services to India's 1.4 billion inhabitants. Despite significant changes over the years, the system continues to face multiple challenges, including inadequate infrastructure, a shortage of healthcare professionals, urban-rural disparities, limited health insurance coverage, insufficient public healthcare funding, and a fragmented healthcare system. India is grappling with a growing burden of non-communicable diseases (NCDs), which poses a significant challenge to its healthcare system.⁹

ECONOMIC IMPACT OF MENOPAUSE ON INDIAN WOMEN

The economic impact of menopause on Indian women is a multifaceted and often overlooked issue, affecting not only individual women but also their families, employers, and the wider economy of the country. Women primarily suffer through reduced productivity, lost career opportunities, increased healthcare costs, and deepened socioeconomic inequalities. Indian women, on average, experience menopause around 46.2 years, earlier than their Western counterparts, thereby extending the period of living with post-menopausal health consequences.

Impact on workforce and career: Reduced productivity and absenteeism due to various menopausal symptoms, including hot flashes, fatigue, poor concentration due to brain fog, and anxiety, resulting in diminished work performance and increased absenteeism. The menopausal transition often coincides with a stage in a woman's career when she could be advancing to senior leadership roles. Symptoms can prompt women to turn down promotions or even leave the workforce entirely, potentially leading to a loss of experienced talent for employers. Due to gender and age bias, some employers may inaccurately perceive older women as less capable or less productive.

"The menopause penalty" is the term for the significant and lasting economic cost women face due to menopausal symptoms, including a drop in earnings and employment. The phenomenon is comparable to the "motherhood penalty." A menopause diagnosis leads to lasting drops in earnings and jobs, possibly up to 10-20% in the 4th year.¹⁰

Financial And Health Costs

Direct and indirect healthcare costs: Women may face financial burdens from consultations and treatments for menopausal symptoms and associated conditions such as osteoporosis, heart disease, or mental health issues. Every woman's menopause journey is unique, with symptoms varying widely in onset and severity. Financial planning becomes essential for managing these uncertainties. Recognising that menopause can be as financially disruptive as other major life events, women can take proactive steps to safeguard their financial futures. In some partnerships, women may be the primary earners, contributing significantly to household finances. Any disruption to their income during menopause can have widespread effects, potentially straining family finances or even contributing to relationship breakdowns.

Socioeconomic Status: Women from lower socioeconomic backgrounds may experience a greater economic impact due to limited access to healthcare, resources, and support systems. Women with lower levels of education may be more vulnerable to premature menopause and have fewer options for managing symptoms and maintaining financial stability. In some cultures, menopause is a taboo topic, leading to a lack of awareness and support for women experiencing symptoms.

Addressing the Challenges

Addressing menopause in India requires a multifaceted approach that recognises the unique needs of both rural and urban women. By implementing comprehensive policies and expanding healthcare services, a supportive environment can be created for all women navigating this critical life stage.¹¹

Increased Awareness: Raising awareness of menopause and its potential impact on women's health and economic well-being is crucial.

Workplace Support: Employers should implement policies and programmes that support women during the menopause transition, such as providing access to healthcare benefits, offering flexible working arrangements, and fostering a supportive work environment.

Affordable Healthcare: Ensuring access to affordable, high-quality healthcare services for women experiencing menopause is essential.

Financial Planning: Encouraging women to plan for menopause and its potential economic implications is important. Building emergency funds, maximising savings and pension contributions, and utilising available tax incentives are prudent strategies. Planning early can provide a financial cushion, helping women navigate menopause without the added stress of economic instability.

Financial status of women: Traditionally, the health-seeking behaviour of Indian women is influenced by inter-spouse communication; women are not at liberty to report issues considered trivial. Factors such as the non-availability of health facilities, illiteracy and economic deprivation are also responsible for their negative health-seeking behaviour.¹²

Like most cultures across the world, Indian society has deeply entrenched patriarchal norms and values. Patriarchy manifests itself in both the public and private spheres of women's lives in the country, determining their life chances and resulting in their qualitatively inferior status across various socio-economic spheres. Women have been undervalued since time immemorial. Women are still held in low esteem in emerging economies. They typically have little autonomy, living first under their father's control, then their husband's, and finally their son's. Research on women's status has found that the contributions Indian women make to families are often overlooked, and they are instead viewed not only as non-productive but also as an economic burden. Growing female economic and social participation has been a significant development in the current era, but women's gross monthly earnings remain lower than men's. Gender bias persists, and women still bear most of the family's responsibilities, leaving them financially dependent. The country has yet to recognise women's economic potential. Many women refrain from therapy because of fear, misconceptions, a lack of awareness, or financial constraints.¹³ Financial access is expanding significantly. Over 86% of Indian women now have a bank account, mainly due to initiatives such as the Pradhan Mantri Jan Dhan Yojana (PMJDY). However, many of these accounts remain inactive, limiting meaningful financial engagement.

COST OF MENOPAUSE-SPECIFIC MANAGEMENT

Menopause management is associated with high direct and indirect costs. Menopause-specific treatment in India includes hormone therapy (HT), non-hormonal medications, nutraceuticals, anti-osteoporotic medications, and lifestyle modifications, with costs varying by chosen treatment and individual needs. Direct costs include initial and follow-up consultations with physicians, specialist consultations, and traditional pharmacotherapy or complementary and alternative medicine modalities. Indirect costs include laboratory testing (Rs 4000–5000 for an executive health check-up package at corporate hospitals), management of adverse events (variable emergency charges), and loss of productivity at home or at work.

Cost and availability of drugs across the country

*"It is thanks to the efforts of the pharma industry that today India is recognised as the 'pharmacy of the world'"*¹⁴ The Indian pharmaceutical industry is ranked 3rd globally by volume and 14th by value as of early 2025. India is the world's largest producer and supplier of generic drugs (over 60000), accounting for 20% of the global supply. While the entire country is recognised for this, the city of Hyderabad is a major pharmaceutical hub in India, sometimes called the "pharmacy hub of the world" or the "Bulk Drug Capital of India". Despite this, evidence-based medicine is accessible to only a few Indian women. Most menopausal women either go untreated or use unproven alternative therapies.

Drug formulations available in India^{15,16}

Disclaimer :

- This information has been provided solely as a reference for menopause practitioners in the context of the economic aspects of menopause management.
- The list represents a comprehensive compilation based on currently available information at the time of writing.
- The authors do not endorse or promote any specific brand or manufacturer.
- Other brands and generic equivalents may also be available in the Indian market. Prices are approximate and may vary according to manufacturer, location, and time

Oral Estrogen Formulations

Generic Name	Brand Name	Availability	MRP
Estradiol valerate	Progynova (Bayer-Zydus Pharma)	1 mg x 28's	380/-
		2 mg x 28's	634/-
Estradiol valerate	Evadiol (Intas)	2 mg x	430/-
17beta estradiol	Estrabet (Abbott)	Tab 1mg /2 mg x 28's	307/ 684/-
Estradiol valerate	Valest (Walter Busnell)	2 mg x 28's	780/-
Estradiol valerate	Estova (Cipla)	2 mg x 28's	473/-
Conjugate Equine Estrogen	Premarin (Pfizer)	0.3 mgx 28's	987/-
		0.625x 28's	1275/-
	Espause (Glenmark)	0.625x 28's	457/-
	Conjugase (Elder)	0.625x 28's	242/-
	Conjubrook (Healing Pharma)	0.625x 28's	1500/-
Tibolone	Conjumed (West Coast)	0.625x 28's	562/-
	Livial (organon)	2.5 mg x 28's	1777/-
	Sibolone (Serum Institute of India)	2.5 mg x 15's x 2	816/-
	Maxtib (Sun Pharma)	2.5 mg x 14's x 2	544/-
	Tibofem (Cipla)	2.5 mg x 14's x 2	830/-

Oral Progesterone Formulations: Medroxyprogesterone.

Generic Name	Brand Name	Availability	MRP
Medroxyprogesterone	Provera (Pfizer)	2.5 mg x 10's	25/-
	Meprate (Serum Institute)	2.5 mg x 10's	58/-
	Deviry (Elder)	2.5 mg x 10's	14/-

Oral Progesterone Formulations: Norethisterone

Generic Name	Brand Name	Availability	MRP
Norethisterone	Primolut N (Zydus Cadila)	5 mg x 10's	58/-
	Regestrone (Torrent)	5 mg x 10's	58/-
	Sysron N (Systopic)	5 mg x 10's	52/-
	Norlut N (Cipla)	5 mg x 10's	58/-
	Cycloreg (Jagsonpal)	5 mg x 10's	56/-

Oral Progesterone Formulations: Micronized Progesterone

Generic Name	Brand Name	Availability	MRP
Micronized Progesterone	Susten (Sun Pharma)	100 mg x 10's	195/-
	Naturogest (Cipla)	100 mg x 10's	232/-
	Gestifit (Alembic)	100 mg x 10's	180/-
	Microgest (Walter Busnell)	100 mg x 10's	208/-

Oral Progesterone Formulations: Dydrogesterone

Generic Name	Brand Name	Availability	MRP
Dydrogesterone	Duphaston	10 mg x 10's	902/-
	Jigest (Sanzyme)	10 mg x 10's	213/-
	Dydropreg (Torrent)	10 mg x 10's	714/-
	Dydroboon (Mankind)	10 mg x 10's	668/-

Testosterone formulations for use in women are not available in India. Transdermal Estrogen Formulations

Estradiol transdermal gel (TDG)	Estogel gel (Intas Pharma)	0.06%w/w x 80 gms	1213/-
	Estrabet gel (Abbott)	0.06%w/w x 80 gms	1205/-
	Prostium E (Pharmanova)	0.06%w/w x 80 gms	879/-

Local Estrogen Formulations

Generic Name	Brand Name	Formulations	MRP
Conjugated equine estrogen	Premarin vaginal cream (Pfizer)	0.625 mg x 14 gms	536/-
Estriol	Evalon vaginal cream (Torrent)	1 mg x 15 gms	525/-

Non-oral Progesterone Formulations (vaginal, injectable and intrauterine)

Generic Name	Brand Name	Formulations	MRP
Progesterone Vaginal Gel	Momtime Gel (Gynogen)	8% w/w, 10 x 1 prefilled applicator	220/-
	Crinon Gel (Merke)	8% w/w x 1	206/-
	Susten gel (Sun Pharma)	8% w/w x 1	148/-
	Gestone vaginal gel (Ferring)	8% w/w x 1	183/-
Progesterone soft gelatin capsule for Vaginal/Rectal/Oral use	Susten 100 (Sun Pharma)	Progesterone natural micronized 100 mg x 10's	194/-
Medroxy progesterone acetate injection	Inj. Depoprovera (Pfizer)	150 mg/1 ml	290/-
Levonorgestrel-Releasing Intrauterine System (LNG-IUS)	Mirena (Bayer Zydus)	52 mg x 20 mcg levonorgestrel	4103/-
	Eloira (Pregna)	52 mg x 20 mcg levonorgestrel	3785/-

Fixed Dose Combination Packs of Estrogen & Progesterone

Generic Name	Brand Name	Formulations	MRP
Estradiol + Dydrogesterone	Femostan Conti 1/5 (Abbott)	1mg estradiol + 5 mg Dydrogesterone x 28's [continuous combined]	1226/-
	Femostan 1/10 (Abbott)	1mg estradiol + 10 mg Dydrogesterone x 28's [sequential]	1328/-
	Dydrogest 1/10 (Zydus)	1mg estradiol + 10 mg Dydrogesterone x 28's [sequential]	1312/-
	Femostan 2/10 (Abbott)	2 mg estradiol + 10 mg Dydrogesterone x 28's [sequential]	1412/-
	Dydrogest 2/10 (Zydus)	2 mg estradiol + 10 mg Dydrogesterone x 28's [sequential]	1406/-
Estradiol hemihydrate + Progesterone	MemUp (Jagsonpal)	Estradiol hemihydrate 1 mg + Progesterone 100 mg x 10's (bioidentical hormone)	455/-

Nonhormone Prescription Therapies

Generic Name	Brand Name	Formulations	MRP
Venlafaxine	Venlor (Cipla)	75 mg x 10's	65/-
	Velor (Organic Lab)	75 mg x 10's	80/-
	Ventab XL (Intas)	37.5, 75 mg	74/-, 145/-
Desvenlafaxine	Ventab DXT ER (Intas)	25, 50, 100 mg x 10's	110/-, 213/-, 403/-
Paroxetine	Paxidep CR (Sun)	12.5, 25, 37.5 mg x 10's	202/-, 266/-, 337/-
	Xet (Zydus Cadila)	12.5, 25, 37.5 mg x 10's	275/-, 354/-, 427/-
	Pexep (Intas)	12.5, 25 mg x 15's 37.5 mg x 10's	339/-, 492/- 442/-
Fluoxetine	Fludac (Cadila)	10 mg, 20 mg x 10's	35/-, 64/-
	Flunil (Intas)	10 mg, 20 mg x 10's	35/-, 43/-
	Prodep (Sun)	10 mg, 20 mg x 10's	35/-, 43/-
Duloxetine	Duzela (Sun Pharma)	20 mg, 30 mg x 10's	142/-, 196/-
	Dulot (Lupin)	20 mg, 30 mg x 10's	166/-, 271/-
Escitalopram	Nexito (Sun Pharma)	5, 10 mg x 15's 15, 20 mg x 10's	80/-, 144/- 150/-, 154/-
	Feliz-S (Torrent)	5, 10, 15, 20 mg x 10's	53/-, 96/-, 136/-, 151/-
Gabapentin	Gabantin (Sun)	100, 300 mg x 10's	97/-, 234/-
	Gabapin (Intas)	100, 300 mg x 15's	154/-, 392/-
Oxybutynin	Oxyspas (Cipla)	2.5, 5 mg x 10's	134/-, 248/-

Vaginal moisturisers and lubricants

Generic Name	Brand Name	Formulations	MRP
Vaginal moisturiser-hyaluronic acid (0.05%) based	Pelvik gel (Zuventus)	50 gm	332/-
Vaginal lubricants	K-Y lubricating jelly (Reckitt Benckiser)	82 gms	324/-
	Lubic jelly (Neon)	50 gms	321/-

Medications for Osteoporosis Available in India Oral Formulations

Generic Name	Brand Name	Formulations	MRP
Raloxifene	Ralista (Cipla)	60 mg x 10's	126/-
	Fiona (Dr Reddys)	60 mg x 10's	120/-
	Ralosto (Abbott)	60 mg x 10's	94/-
	Bonbay (Novartis)	60 mg x 10's	89/-
Alendronate	Osteofos 70 (Cipla)	70 mg x 4 tabs in 1 strip	322/-
	Alenfos 70 (Mi-Dose)		173/-
Risedronate	Gemfos (Alkem)	35 mg x 4 tabs in 1 strip	421/-
	Risofos (Cipla)	35 mg x 4 tabs in 1 strip	293/-
Ibandronic acid	Flurish (Dr Reddy's)	150 mg x 1 tab	353/-
	GemiDro (Alkem)	150 mg x 1 tab	443/-

Medications for Osteoporosis: Combination kits

Generic Name	Brand Name	Formulations	MRP
Alendronate + Calcium + Vit D3	Ostonat Kit (Natco)	70 mg + 500 mg + 250 iu Tabs 4+24	165/-
	T score kit	70 mg + 500 mg + 250 iu Tabs 4+24	165/-
Risedronate + Calcium + Vit D3	Risofos Kit (Cipla)	35 mg + 250 mg + 400 iu Tabs 4+24	120/-
	Resica Kit (Aristo)	35 mg + 500 mg + 500 iu Tabs 4+24	60/-
Ibandronate + Calcium + Vit D3	Goldcal Kit (Ronyd Healthcare)	150 mg + 250 mg + 0.25 mcg Tabs 1 + 30	346/-
	Idrofos Kit (Sun Pharma)	150 mg + 250 mg + 0.25 mcg Tabs 1 + 30	450/-

Medications for Osteoporosis: Injectables & Nasal Spray

Generic Name	Brand Name	Formulations	MRP
Zoledronic acid Infusion	Zolephos (Abbott)	5 mg/100 ml	3993/-
	Aclasta (Novartis)	5 mg/100 ml	19211/-
	Natzold (Natco)	5 mg/100 ml	2990/-

Teriparatide Injection Prefilled syringe	Terifrac (Intas)	20 mcg/day 28 days' supply 600 mcg	6186/-
	Zotide (Cipla)	20 mcg/day 28 days' supply 600 mcg	6806/-
	Bonista (Sun Pharma)	20 mcg/day 28 days' supply 600 mcg	7922/-
Denosumab Injection	Inj. Olimab (Intas)	60 mg x 1 ml prefilled syringe	14990/-
	Densucor (Torrent)	60 mg x 1 ml prefilled syringe	7,000/-
Salmon calcitonin Nasal Spray	Ostospray (Sun Pharma)	60 mg x 1 ml prefilled syringe	8085/-
	Rockbon C (Abbott)	200 iu 3.7 ml nasal solution	1724/-
	Miacalcic (Novartis)	200 iu 2 ml nasal solution	1496/-

Newer Drugs for Osteoporosis

Generic Name	Brand Name	Formulations	MRP
Romosozumab monthly x 12 doses	Inj Eveniy (Dr Reddy's) Humanised monoclonal antibody to Sclerostin	210 mg SC monthly	24000/-

Alternative & Complementary medications for Menopausal Symptoms and Osteoporosis

Generic Name	Brand Name	Formulations	MRP
Isoflavones + Antioxidants + Essential micronutrients	Menoflave (Zydus Cadila)	40 mg x 10's	141/-
	Isoflave CR (Raptakos Brett)	60 mg x 10's	340/-
	Isovon (Alembic)	60 mg x 10's	100/-
	Celol XT (Emcure)	60 mg x 10's	290/-
	Calciflavon plus (Meyer)	60 mg x 15's	491/-
	Shelcal Iso (Torrent)	60 mg x 15's	431/-
	Menoease (Pharmed)	75 mg x 10's	333/-
	Calcimax Iso (Meyer)	100 mg x 15's	384/-
	Menopace Iso (Vitabiotics)	100 mg x 30's	653/-
Black Cohosh	Evepearl MP (Nicholas Piramal)	10's	99/-
Red Clover	Trexgenics Red clover extract (Trexgen Pharma)	500 mg x 60's	800/-
Evening Primrose oil	Primosa softgel caps (Uni Medicare)	500 mg x 15's	372/-
	Simrose softgel caps (Serum Institute)	500 mg x 15's	238/-
Ginseng + Ginkobiloba	Full-24 (Emcure)	10's	282/-
	Goldcare (Meyer)	6's	74/-
Lycopene + Multivitamins & Multiminerals	Lycored softgel caps (Jagsonpal)	10's	171/-
	Lycamax (Demorbus India)	10's	204/-
Fermented soy derivate (DT56a)+ Flaxseed+ Vitamin B6	Femarelle Recharge Capsule (Maneesh Pharma)	60's	1953/-
Rhapontic rhubarb extract	Estroease (Lupin)	10's	579/-

Indian Menopause Society Initiatives & Recommendations:

The Indian Menopause Society (IMS) has taken the initiative to support middle-aged women by promoting and establishing Menopause Clinics in its 51+ societies (2025). The aim is to provide a multidisciplinary, holistic approach to the care of elderly women, encompassing both medical and non-medical care under one roof. The IMS has formulated guidelines to guide its more than 6,500 (2025) members and others in initiating and running them.¹⁷

Recommendations to Government

1. Develop integrated healthcare policies that specifically address menopause as part of women's life-course health needs, with dedicated budgetary allocations.
2. Expanding insurance coverage for women's health needs, including menopause-related care.
3. Strengthening healthcare infrastructure in smaller cities and rural areas to improve access to menopause care.
5. Establish public-private partnerships to improve access to menopause care.
5. Use digital health technology-based interventions to improve access to menopause education and care
6. Create economic incentives for employers to implement menopause-supportive workplace policies, such as tax benefits or recognition programmes.

Government of India Initiatives and Key Programs: The Government of India has launched multiple initiatives to strengthen the healthcare system, focusing on infrastructure development, cost reduction, and improved accessibility. These include Ayushman Bharat, the National Health Mission, digital health initiatives, public-private partnerships, and reforms in medical education to expand the healthcare workforce.

Key programmes introduced by the Government of India include the Atal Vayo Abhyuday Yojana (AVYAY), the National Programme for Health Care of the Elderly (NPHCE), the SACRED Portal, Tax Benefits, Vayo Shreshtha Samman, and the Maintenance and Welfare of Parents and Senior Citizens (MWPSA) Act.

While these initiatives collectively strengthen geriatric care, financial security, and social protection for India's ageing population, they remain largely gender-neutral and overlook the unique needs of midlife and older women. Despite umbrella programmes for senior citizens, a significant gap persists in addressing the specific health needs of women during the menopausal transition and post-menopause, a critical life stage that remains underrepresented in policy frameworks.¹⁸ Bridging this gap is a pressing need.

Special Note from the Parliament (India)

**Government of India Ministry of Women and Child Development Lok Sabha,
Unstarred Question No. 1072 (Answered on 08 December 2023)**

Subject: Menopause Policy

Shri Ravikumar D. sought clarification from the Ministry of Women and Child Development regarding: (a) Whether the Ministry is considering introducing a menopause policy for women employees in the public and private sectors;

(b) The details of the policy;

(c) Whether such a policy is proposed to be rolled out within the next year;

(d) If not, the expected timeline for its introduction; and

(e) Existing provisions to enhance awareness of women's health issues, such as menopause, in government and private offices.

Official Response: The Hon'ble Minister of Women and Child Development, Smt. Smriti Zubin Irani stated that menopause is a normal physiological consequence of ageing, generally occurring between 45 and 55 years of age, and is defined by the cessation of menstruation for one year in the absence of other causes. While many women experience minimal or no symptoms, a significant proportion experience moderate to severe symptoms. Given that women spend a substantial portion of their lives in the post-menopausal phase, menopause represents an important public health consideration.

The Ministry further clarified that the National Health Mission (NHM) aims to ensure universal access to equitable, affordable, and quality healthcare services responsive to population needs, which implicitly includes health concerns related to menopause.

At present, there is no formal menopause policy for women employees in either the government or private sectors in India. The formulation of such a policy would require extensive stakeholder consultations, expert inputs, and robust research evidence on the physical and mental health impacts of menopause on working women. Meanwhile, awareness regarding women's health issues, including menopause, is promoted through various Government of India schemes, public health programmes, mass media campaigns, and community-based initiatives such as street plays (*nukkad natak*).

Cost-Effectiveness Of Menopause Management In India

A lack of comprehensive studies limits a complete cost-effectiveness analysis of menopause management in India. Still, research suggests that investing in awareness, lifestyle changes, and subsidised, risk-appropriate therapies is highly cost-effective. Menopause management could significantly improve quality of life and reduce the long-term economic burden associated with health issues such as osteoporosis and cardiovascular disease.

Lifestyle interventions, including adequate exercise and a diet rich in calcium, fibre, and phyto-oestrogens, have a high-value impact with little to no cost. Initiatives promoting yoga and meditation, along with lifestyle changes such as diet and exercise modifications, are universally accessible and low-cost options for all Indian women, regardless of socioeconomic status or location. HT is a cost-effective treatment for symptomatic women in the early postmenopausal years, particularly for severe symptoms such as hot flushes and urogenital issues. Employers and governments are increasingly recognising that supporting menopausal employees, such as through flexible working arrangements, dedicated menopause policies, gender equality and diversity training, and environmental changes, such as improved ventilation, can help retain skilled women for longer.

Evidence Gaps In Menopause Research in India

Major national surveys, such as the National Family Health Survey (NFHS)¹⁹ and the Longitudinal Ageing Study in India (LASI)²⁰, address menopause only tangentially, leaving a gap in understanding women's physical, emotional, and social health needs during this important life stage. Consequently, significant gaps remain in evidence related to the prevalence, symptom burden, healthcare access, and management practices for menopausal women in India. Expanding the scope of future research to include dedicated menopause-related indicators and longitudinal assessments would provide valuable insights into the health and well-being of midlife women. Such data are essential for informing evidence-based policies, clinical guidelines, and resource allocation aimed at improving menopause care. There is a need to conduct, robust cost-effectiveness analyses of different menopause management in the Indian healthcare.

SYNOPSIS

- Menopause has a significant economic impact on Indian women, affecting their productivity, career progression, and financial well-being.
- For many, menopause is not just a natural transition but can be as disruptive as any other major illness requiring treatment, with direct and indirect costs. The economics of menopause depend on the health care system, the woman financial status, and the price and availability of drugs across the country.
- By raising awareness among menopausal women, promoting gender equality, and offering workplace support and affordable healthcare, the country can retain experienced women's talent.
- Women need drug support for not only the control of immediate symptoms but also for the prevention or treatment of long-term consequences of menopause.

RESEARCH AGENDA

Longitudinal studies examining the economic impact of menopause on women's healthcare expenditure, productivity, and long-term financial outcomes

REFERENCES

1. Pallikadavath S, Ogollah R, Singh A, Dean T, Dewey A, Stones W. Natural menopause among women below 50 years in India. *Indian Journal of Medical Research* 2016;144:366-77. <https://doi.org/10.4103/0971-5916.198676>

2. Dewangan KK, Pattanaik S, Patnaik L, Sahu T. Prevalence of Morbidities among Peri-Menopausal and Postmenopausal Women in Selected Urban Slums of Eastern India. *International Journal of Current Research and Review* 2020;12:55–60. <https://doi.org/10.31782/ijcrr.2020.12188>
3. Chakraborty R. India menopause policy women. *The Hindu*. 2025 May 6. <https://www.thehindu.com/society/india-menopause-policy-women>
4. Sengupta A. The emergence of the menopause in India. *Climacteric* 2003;6:92–5. <https://doi.org/10.1080/cmt.6.2.92.95>
5. Chokshi M, Patil B, Khanna R, Neogi SB, Sharma J, Paul VK, et al. Health systems in India. *Journal of Perinatology* 2016;36:S9–12. <https://doi.org/10.1038/jp.2016.184>
6. A Pathway to Universal Healthcare in India. *IPS News*. 2020 Jul 5. <http://www.ipsnews.net/2020/07/pathway-universal-healthcare-india/>
7. Kundu S, Acharya SS. Exploring the triggers of premature and early menopause in India: a comprehensive analysis based on National Family Health Survey, 2019–2021. *Scientific Reports* 2024;14. <https://doi.org/10.1038/s41598-024-53536-9>
8. Hemalatha SA, Sarif N, Barman P. ASSESSING ADEQUACY OF HEALTH FACILITIES FOR OLDER ADULTS IN INDIAN CITIES. *Innovation in Aging* 2023;7:949–949. <https://doi.org/10.1093/geroni/igad104.3048>
9. Kumar A. The Transformation of The Indian Healthcare System. *Cureus* 2023. <https://doi.org/10.7759/cureus.39079>
10. Conti G, Ginja R, Persson P, Willage B. The menopause “penalty.” *The IFS*; 2025. <https://doi.org/10.1920/wp.ifs.2025.1025>
11. Rajput NH. Menopause: a midlife crisis for women in India. *BMJ Global Health* 2025;10:e017863. <https://doi.org/10.1136/bmjgh-2024-017863>
12. Kapur P. Empowering the Indian woman. New Delhi: Publications Division, Ministry of Information and Broadcasting, Government of India; 2001. ISBN 978-8123009728.
13. Rizvi M. Patriarchy: the Indian experience. 2010 Jan. <http://works.bepress.com/mubashshir/19>
14. Modi N. Prime Minister interacts with leaders of pharma industry. Press Information Bureau, Government of India. 2024 Aug 22. <https://www.narendramodi.in/prime-minister-narendra-modi-interacts-with-leaders-of-pharma-in-dustry-555053>
15. 1mg. Pharmaceutical database. 2025. <https://www.1mg.com>
16. PharmEasy. Healthcare platform. 2025. <https://pharmeasy.in>
17. Meeta M, Digumarti L, Agarwal N, Vaze N, Shah R, Malik S. Clinical Practice Guidelines on Menopause: An Executive Summary and Recommendations: Indian Menopause Society 2019-2020. *J Midlife Health*. 2020 Apr-Jun;11(2):55-95. doi: 10.4103/jmh.JMH_137_20. Epub 2020 Aug 10. PMID: 33281418; PMCID: PMC7688016.
18. Shukla S. Advancing the agenda for women’s health in India. International Center for Research on Women (ICRW). 2024 May 9. <https://www.icrw.org>

DISEASE-SPECIFIC PHARMACOTHERAPY AND INTERACTION WITH HORMONES



Keywords: Pharmacotherapy, medical eligibility criteria, menopause hormone therapy, drug interactions

INTRODUCTION

Women requiring menopausal hormone therapy (MHT) are often taking medications for pre-existing chronic medical conditions such as hypertension, thyroid disorders, diabetes, dyslipidaemia, rheumatoid arthritis, depression and epilepsy. Many may also be taking common supplements such as vitamins, omega-3 fatty acids and calcium, or other medications, and may be addicted to alcohol and smoking. Hence, decision-making becomes more complex when addressing a symptomatic woman who also presents with one or more chronic medical conditions that may influence the risk associated with MHT use, thereby altering the risk-benefit balance.¹ Pharmacokinetic interactions may occur when several medications are administered together.² Understanding the interactions between MHT and other medications, as well as the influence of menopausal hormonal changes on these interactions, is of great clinical importance.

DISEASE-SPECIFIC PHARMACOTHERAPY

The management of postmenopausal women requires the integration of disease-specific pharmacotherapy, where treatment decisions are influenced not only by menopausal symptoms but also by coexisting medical conditions. Many drugs prescribed for these comorbidities may cause adverse effects that complicate symptom control and overall care. A thorough understanding of these side effects is therefore essential, as they can interact with menopausal physiology and significantly affect both quality of life and treatment adherence. This section focuses on the side effects and contraindications of common medications and is not intended as a therapeutic guide; the mechanism of action, specific indications, and doses are not included.

HYPERTENSION

The common antihypertensive drug classes, along with the drugs, their common adverse effects and contraindications, are listed in Table 1.

Table 1: Antihypertensives, side-effects and contraindications^{3,4}

Drug Class	Names	Side-effects	Contraindications
Thiazide diuretics	Hydrochlorothiazide Chlorthalidone	Hyponatremia, hypokalemia, hyperuricemia, hyperlipidemia, increased glucose levels, and dizziness Chlorthalidone can cause sexual dysfunction and sleep disturbances	Anuria, sulfa allergy

ACE-inhibitors	Enalapril, ramipril, lisinopril	Dry cough (more frequent in women), angioedema, hyperkalemia	Pregnancy, history of angioedema, bilateral renal artery stenosis (RAS)
Angiotensin Receptor Blockers (ARBs)	Losartan, Valsartan, Olmesartan	Hyperkalemia, dizziness, headache Olmesartan induced enteropathy	Pregnancy, bilateral RAS
Dihydropyridine Calcium Channel Blockers (DHP CCBs)⁵	Amlodipine, Nifedipine, Nicardipine, Felodipine, Isradipine	Peripheral edema (more common in women), flushing, headache, palpitations, reflex tachycardia	Known hyper-sensitivity, severe hypotension, cardio-genic shock, unstable angina, severe aortic stenosis, liver failure
Non-Dihydro-pyridine Calcium Channel Blockers (Non-DHP CCBs)⁵	Diltiazem, Verapamil	Constipation, bradycardia, fatigue, dizziness, hypotension, AV block, sinus bradycardia	Severe aortic stenosis, HFrEF, second or third degree AV blockade, systolic BP < 90mmHG, and sick sinus syndrome
Beta Blockers	Metoprolol, Bisoprolol, Atenolol	Fatigue, bradycardia, sexual dysfunction, depression, cold limbs	Severe asthma, bradycardia, 2nd/3rd degree heart block

Additional Considerations In Midlife Women

Women are more prone to adverse drug reactions from antihypertensives, such as thiazide-induced hyponatraemia and CCB-related peripheral oedema, than men.⁶ ACE inhibitor-induced cough and angioedema are approximately twice as common in women as in men.⁷ Polypharmacy and cumulative side-effects are common in elderly women and may contribute to non-compliance, especially with symptoms such as urinary incontinence and dizziness.⁸ Beta blockers may cause a greater drop in heart rate and blood pressure in women at the same dose, and require careful titration.⁹

DIABETES

The different classes of drugs used for treatment of Type 2 diabetes mellitus (T2DM) along with the drugs, common adverse effects and contraindications are listed in Table 2. The different types of Insulin and their adverse effects are listed in Table 3.

Table 2: Antidiabetic drugs, side-effects, and contraindications^{10,11}

Drug Class	Names	Side-effects	Contraindications
Biguanides	Metformin	Nausea, vomiting, diarrhea, chest discomfort, flushing, palpitation, headache, chills, dizziness, taste disorder, nail disease, skin rash, Vit. B12 defi., rarely lactic acidosis (< 1%) which can be life-threatening, precipitated by severe renal failure (eGFR < 30 ml/min/1.73 m ²)	Hypersensitivity to the drug, severe renal impairment (eGFR < 30 mL/min), metabolic acidosis including diabetic ketoacidosis

Sulfonylureas	Glibenclamide Gliclazide, Glipizide, Glyburide, Glimepiride	Hypoglycemia, weight gain, nausea	Hypersensitivity to the drug or sulfonamide derivatives, type 1 DM, diabetic ketoacidosis, avoid in elderly with renal impairment, risk of prolonged hypoglycemia
Meglitinides	Repaglinide, Nateglinide	Hypoglycemia, weight gain, headache, upper respiratory tract infection, and cardiovascular ischemia.	Hypersensitivity to drug, type 1 DM, diabetic ketoacidosis, and severe liver dysfunction. Repaglinide is safer than metformin and sulfonylureas in chronic kidney disease. ¹²
Hydrochlorothiazide (TZDs)	Pioglitazone, Rosiglitazone	Weight gain, edema, heart failure exacerbation, fracture risk, hypoglycaemia, headache, myalgia, sinusitis, and pharyngitis.	Heart failure (NYHA Class III/IV), bladder cancer (pioglitazone), liver failure, history of macroscopic hematuria, and pregnancy.
Alpha-Glucosidase inhibitors	Acarbose, Miglitol, Voglibose	Flatulence that tends to decrease with time, diarrhea, abdominal pain, and increased serum transaminases.	Hypersensitivity to acarbose, diabetic ketoacidosis, cirrhosis, inflammatory bowel disease, ulcers of the intestine, partial intestinal obstruction
Sodium-dependent glucose transporter-2 inhibitors (SGLT-2i)	Empagliflozin, dapagliflozin	Genital infections, urinary tract infections, nausea, dehydration, hypotension, hypovolemia, increased urine output, influenza, fracture, hyper-phosphatemia, diabetic ketoacidosis, dyslipidemia, and renal impairment.	History of serious hypersensitivity to the drug, end-stage renal disease (ESRD), and patients on dialysis, recurrent urinary/genital infections, ketoacidosis risk
Dipeptidyl peptidase-4 inhibitors (DPP-4i)	Sitagliptin, Saxagliptin Linagliptin	Hypoglycemia, gastro- intestinal symptoms, headache, acute pancreatitis (rare) naso-pharyngitis, acute renal failure, peripheral edema, headache, urinary tract infection, lympho-cytopenia, increased uric acid.	History of pancreatitis, renal impairment (dose adjustment needed)
Glucagon-like peptide-1 receptor agonists (GLP-1RA)	Liraglutide, Exenatide Dulaglutide	Nausea, vomiting, weight loss, injection site reactions, pancreatitis (rare)	Personal/family history of medullary thyroid carcinoma, pancreatitis

Additional Considerations In Midlife Women

Metformin is a very safe drug, but renal function monitoring is crucial (stop metformin if creatinine >1.4 mg/dL in females). Long-term use may cause vitamin B12 deficiency, anaemia, and neuropathy (with increased risk in the elderly), warranting monitoring.¹¹ Heart failure risk increases with thiazolidinediones; caution is advised.¹³ Hypoglycaemia risk is higher with sulfonylureas; dose adjustments are needed as renal function declines.¹⁴ TZDs should be avoided in women with osteoporosis and increased fracture risk.¹⁵

While insulin-related adverse effects such as hypoglycaemia, weight gain, and injection-site reactions are consistent across formulations, midlife and menopausal women require careful dose and side-effect management due to hormonal influences on insulin sensitivity and overlapping symptom profiles.¹⁶ Long-acting and ultra-long-acting insulins may offer more stable glycemic control with lower hypoglycemia risk.¹⁷ Vasomotor symptoms such as hot flashes, night sweats, cold sweats and palpitations can potentially mask hypoglycemic events in midlife women.

Table 3: Types of Insulin and side-effects¹⁸

Insulin type	Common side-effects
Rapid-acting (Lispro, Aspart)	Hypoglycemia (sweating, trembling, dizziness, headache and confusion), injection site reactions
Short-acting (regular insulin)	Hypoglycemia, weight gain, injection site reactions
Intermediate-acting (NPH)	Hypoglycemia (especially nocturnal), weight gain, local reactions like pain at the injection site and lipodystrophy
Long-acting [Basal] (glargine, detemir)	Hypoglycemia (less nocturnal), weight gain, injection site reactions
Ultra-long-acting (degludec)	Hypoglycemia (rare), weight gain
Inhaled insulin (Afrezza)	Cough, throat irritation, hypoglycemia

DYSLIPIDEMIA

The different classes of drugs used for the treatment of dyslipidaemia, along with the drugs, common adverse effects and contraindications, are listed in Table 4.

Table 4: Lipid-lowering drugs, side-effects and contraindications^{19,20}

Drug Class	Names	Side-effects	Contraindications
Statins	Atorvastatin, Simvastatin, Rosuvastatin, Pravastatin, Pitavastatin	Myalgia, myopathy, rhabdomyolysis, elevated liver enzymes, headache, GI disturbances, increased diabetes risk	Active liver disease, pregnancy, breastfeeding,
Fibrates	Finofibrate, Gemfibrozil	GI disturbances, gallstones, myopathy, liver enzyme elevations	Severe renal or hepatic dysfunction, gallbladder disease
Niacin		Flushing, pruritus, GI upset, hepatotoxicity, uric acid elevation, hyperglycaemia,	Active liver disease, active peptic ulcer, severe gout
Bile Acid Sequestrants	Cholestyramine, Colesevelam	Constipation, GI upset, interference with absorption of other drugs/vitamins	Bowel obstruction, severe hypertriglyceridemia
Ezetimibe		Headache, mild GI upset, elevated liver enzymes (rare when monotherapy)	Severe liver disease, con-comitant use with statin in active hepatic impairment

PCSK9 Inhibitors	Evolocumab, Alirocumab	Injection site reactions, nasopharyngitis, muscle pain, flu-like symptoms	Hypersensitivity to drug/ component
Omega-3 Fatty Acids		Dyspepsia, fishy aftertaste, GI disturbance	Caution with allergy to fish or shellfish. Purified or non-fish-derived (algal) preparations are preferred.

Grapefruit juice, rarely consumed in India, can significantly increase blood levels of CYP3A4-metabolised statins, especially simvastatin and lovastatin. Concomitant use of large amounts of grapefruit juice and simvastatin should be avoided, or the dose of simvastatin should be greatly reduced.²¹

OBESITY

The different classes of anti-obesity medications, along with the drugs, common adverse effects and contraindications are listed in Table 5.

Table 5: Anti-obesity drugs, side-effects and contraindications^{22,23}

Names	Side-effects	Contraindications
Orlistat	Oily rectal leakage, abdominal distress and pain, flatulence with discharge, fecal urgency, steatorrhea, fecal incontinence, increased defecation	Chronic malabsorption syndrome, cholestasis, pregnancy
Phentermine/Topiramate	Elevation in heart rate, mood and sleep disorders, cognitive impairment, metabolic acidosis, paresthesia, dry mouth	Glaucoma, hyperthyroidism, during or within 14 days of MAO inhibitors use, hypersensitivity to sympathomimetic amines, pregnancy
Naltrexone/B upropion	Nausea, constipation, headache, vomiting, dizziness, insomnia, dry mouth, diarrhea, sleep disorder	Chronic opioid use, acute opioid withdrawal, uncontrolled hypertension, seizure disorder, bulimia or anorexia nervosa, sudden withdrawal of alcohol, benzodia-zepines, barbiturates, and antiseizure drugs; concomitant use of MAOIs, patient receiving linezolid or IV methylene blue, pregnancy
Liraglutide	Increased heart rate, hypoglycemia, constipation, diarrhea, nausea, vomiting, headache	Medullary thyroid cancer, Multiple Endocrine Neoplasia Syndrome type 2 (MEN2), pancreatitis, pregnancy, hypersensitivity to drug
Semaglutide	Nausea, vomiting, constipation, abdominal pain, diarrhea, headache, fatigue, hypoglycemia	Medullary thyroid cancer, MEN2, pregnancy, pancreatitis, hypersensitivity to drug
Setmelanotide	Injection site reactions, hyper-pigmentation, nausea, headache, diarrhea, vomiting, abdominal pain	none
Tirzepatide	Nausea, diarrhea, decreased appetite, vomiting, dyspepsia, constipation, abdominal pain	Medullary thyroid carcinoma or MEN 2 syndrome, known serious hypersensitivity to tirzepatide

THYROID DISORDERS

Thyroid hormone replacement and anti-thyroid medications, their side-effects and contraindications are listed in Table 6.

Table 6: Thyroid medications, side-effects and contraindications²⁴⁻²⁷

Drug Class	Names	Side-effects	Contraindications
Thyroid hormone replacement	Levothyroxine	Palpitations, tachycardia, insomnia, sweating, weight loss, anxiety	Untreated adrenal insufficiency, acute myocardial infarction
Anti-thyroid medications	Methimazole	Rash, pruritus, GI upset, agranulocytosis (rare), hepatotoxicity	Pregnancy (first trimester), breastfeeding
	Propylthiouracil	Rash, arthralgia, hepatotoxicity, agranulocytosis (rare)	Pregnancy (except first trimester), breastfeeding
Adjunctive use	Beta blockers	Fatigue, bradycardia, hypotension, exacerbation of asthma	Severe bradycardia, asthma, heart block

ANTICOAGULANTS AND ANTIPLATELET AGENTS

Anticoagulants and antiplatelet medications, together called blood thinners, are listed in Table 7 along with their common side effects and contraindications.

Table 7: Blood thinners, side-effects and contraindications²⁸

Drug Class	Names	Side-effects	Contraindications
Vitamin K Antagonists	Warfarin	Bleeding, bruising, nosebleeds, GI bleed, skin necrosis, purple toe syndrome	Pregnancy (especially first trimester), active bleeding, severe hypertension, recent surgery
Heparins	Unfractionated Heparin, LMWH	Bleeding, injection site reactions, heparin-induced thrombocytopenia (HIT), osteoporosis (long-term)	Active bleeding, severe thrombocytopenia, history of HIT
Direct Thrombin Inhibitors	Dabigatran	Bleeding, dyspepsia, GI discomfort, anemia	Active bleeding, mechanical heart valves, severe renal impairment
Direct Factor Xa Inhibitors	Rivaroxaban, Apixaban, Edoxaban, Betrixaban	Bleeding, anemia, nausea, elevated liver enzymes	Active bleeding, severe liver disease, pregnancy
Antiplatelets ²⁹	Aspirin, Clopidogrel, Ticagrelor, Prasugrel	Bleeding, bruising, GI upset, rash, dyspnea	Active bleeding, allergy to drug, recent stroke, peptic ulcer

ANTI-SEIZURE MEDICATIONS (ASM)

Anti-epileptics, now called anti-seizure medications, are listed in Table 8 with their side-effects and contraindications.

Table 8: Anti-seizure medications, side-effects and contraindications³⁰

ASM Class	Drugs	Side-effects	Contraindications/Precautions
Hydantoins	Phenytoin	Sedation, ataxia, visual disturbance, rash, gingival hyperplasia, folic acid deficiency, bone loss, hepatotoxicity	Hypersensitivity, liver impairment, pregnancy, heart block
Carboxamides	Carbamazepine, Oxcarbazepine	Drowsiness, gastrointestinal (GI) upset, blurred vision, rash (SJ syndrome), hyponatremia, blood dyscrasias, hepatic dysfunction	History of marrow depression, severe hepatic impairment, hypersensitivity, HLA-B*1502 allele
Succinimides	Ethosuximide	GI upset, dizziness, rash, headache, blood dyscrasias	Severe liver/renal impairment, porphyria
Valproates	Sodium valproate, Divalproex	Weight gain, GI upset, tremor, hair loss, hepato-toxicity, teratogenicity, thrombocytopenia	Liver dysfunction, pregnancy, mitochondrial/urea disorders
Benzodiazepines	Clobazam, Clonazepam	Sedation, muscle weakness, cognitive effects, addiction risk, depression	Severe hepatic impairment, history of addiction, respiratory depression
Barbiturates	Phenobarbital	Sedation, cognitive impairment, rash, osteopenia, dependence	Severe hepatic impairment, porphyria, respiratory depression
Gaba derivatives	Gabapentin, Pregabalin	Drowsiness, dizziness, weight gain, peripheral edema	Severe renal impairment, hypersensitivity
Triazines	Lamotrigine	Rash (Steven Johnson Syndrome), headache, dizziness, blurred vision	Caution with valproate, hypersensitivity/ h/o rash
Pyrrolidines	Levetiracetam	Drowsiness, agitation, mood changes, headache	Renal impairment, hypersensitivity

SUPPLEMENTS

Dietary supplements are widely recommended to improve bone health, alleviate menopausal symptoms, and support cardiometabolic function in midlife women; however, rigorous assessment of their appropriateness, potential drug interactions, and adverse effects is essential for clinical decision-making. Current evidence does not show a clinically significant increase in bleeding risk with omega-3 fatty acids, even in patients on antiplatelet or anticoagulant therapy; therefore, routine discontinuation before surgery is not supported by available data.^{31,32}

Common dietary supplements, micronutrients, and vitamins are listed in Table 9, along with their side effects and contraindications.

Table 9: Common supplements, side effects and contraindications^{33,34}

Drug Class	Side-effects	Contraindications
Calcium	GI upset, bloating, constipation	Hypercalcemia, severe renal impairment
Vitamin D	Hypercalcemia, nausea, headache, vomiting (if excess)	Hypercalcemia, vitamin D hypersensitivity
Magnesium	Diarrhea, abdominal cramps, nausea (high dose)	Severe renal failure
Multivitamins	Nausea, GI upset, constipation, allergic reaction, vitamin toxicity (excess)	Allergy to ingredients, risk of toxicity with excess intake
Isoflavones/Soy	GI upset, constipation, diarrhea, allergic reactions	Soy allergy, thyroid dysfunction, hormone-sensitive cancers
Black cohosh ³⁵	GI upset, rash, liver enzyme elevation, headache	Liver disease, pregnancy, history of hormone-Sensitive cancer
Red clover	GI upset, rash, bleeding (with anticoagulants), estrogenic effects	Avoid in hormone-sensitive cancers (breast, endometrial, ovarian cancer) and active liver disease, pregnancy, breast feeding, ³⁶ Caution with concomitant use with anticoagulants /anti-platelet agents, ³⁷ MHT/ OCPs, discontinuation 1–2 weeks before surgery
Ginseng ³⁸	headache, hypertension, diarrhea, sleeplessness, skin rash, and vaginal bleeding ³⁹	Avoid in patients on anti-coagulants or narrow-therapeutic-index drugs, pregnancy and breastfeeding, uncontrolled hypertension, bleeding disorders or peri-operative settings, and in hormone-sensitive conditions due to possible estrogenic activity. ^{38,39}
Omega-3 fatty acids	Fishy aftertaste, GI discomfort, mild increase in bleeding risk at high dose	Hypersensitivity

MHT IN CO-MORBID CONDITIONS AND DRUG INTERACTIONS

The decision to initiate hormone therapy (HT) in a woman should be based on a thorough evaluation of menopausal symptoms, individual risk-benefit analysis, presence of other pre-existing diseases and personal preferences.⁴⁰ Regular monitoring and dose adjustments may be required to avoid drug-drug interactions in women with medical conditions.

Eligibility Criteria For Pharmacological Interactions With MHT

Establishing evidence-based eligibility criteria for pharmacological interactions with MHT is important, due to the existing confusion about its suitability in women with comorbidities, particularly regarding safety concerns such as increased adverse effects, reduced therapeutic efficacy, or other undesirable outcomes.²

Decisions on combining HT with other treatments are guided by evidence on the bidirectional effects between disease and MHT, known drug–drug interactions, and the clinical strength of recommendation for co-administration. These eligibility criteria are classified into four categories, which aid clinical decision-making for women receiving other classes of drugs for comorbid conditions. They are as follows:²

- *Category 1:* There is strong published evidence that using both treatments together is preferred or is considered safe. These treatments are frequently used together with no known risks or reasons to expect harm.

- *Category 2:* There is no strong published evidence, but using both treatments together is allowed because either no harmful interaction is known, or any anticipated risk is minor and the benefit justifies treatment, or a simple change in dosage can solve any problems.
- *Category 3:* Other treatment options should be considered first, but concomitant use may be allowed if the potential benefits outweigh the anticipated risks of the interaction. This also applies if the other medicine carries some risk when used with HT, but its use may still be reasonable.
- *Category 4:* Concomitant use only if there is a very clear justification. There may be evidence against using the treatments together, or there is no good reason to use both at the same time. The combination could cause harmful effects or may not be advised for the underlying disease.

The most common pharmacological agents prescribed to postmenopausal women with medical conditions are described in the context of four types of hormone therapy: EPT (combined estrogen-progestogen, oral and transdermal), ET (estrogens only, oral, transdermal, and vaginal), and Tibolone.

Hypertension

Before prescribing MHT to a woman with hypertension, her overall risk of cardiovascular disease should be evaluated.¹ The effect of MHT on blood pressure varies by formulation, particularly the type of estrogen used and the route of therapy. In the Women's Health Initiative study, conjugated equine estrogens (CEE), with or without medroxyprogesterone acetate (MPA), increased systolic blood pressure (SBP) compared with placebo.⁴¹ In a meta-analysis of 8 studies (N=1,718), oral CEE plus progestogen was associated with increased systolic blood pressure; however, oral or transdermal 17 β -estradiol (E2) plus progestogen, E2 alone, and tibolone did not show any significant effect.⁴²

No formulation significantly affected diastolic blood pressure. Oral estrogen therapy (ET) may affect blood pressure regulation in some women, likely due to individual sensitivity, and dose adjustment of anti-hypertensives may be required (Category 2).² It is important to reassess blood pressure and confirm that it is well controlled after modifying the dose.² Transdermal estrogen, by avoiding the first-pass metabolism through the liver, has a neutral effect on blood pressure, making it a preferred option in women with hypertension and risk factors like obesity.⁴³ Tibolone neither affects the systolic BP nor the diastolic BP,⁴⁴ but in some patients with unique individual differences, tibolone may affect blood pressure control and dose adjustment, and periodic monitoring may be needed (Category 2).^{2,44}

In a Chinese study of postmenopausal women, higher progesterone levels were associated with lower diastolic and mean arterial blood pressure, but this relationship was not observed in premenopausal women.⁴⁵ Micronised progesterone and dydrogesterone appear to have the safest cardiovascular profile, including effects related to blood pressure and vascular risk.⁴⁶

Drospirenone (DRSP), a progestin with anti-mineralocorticoid properties, when given with E2 has been shown to significantly lower both systolic and diastolic blood pressure in early menopausal women with stage 1 hypertension in clinical studies.⁴⁷ It has a potassium-sparing effect that counteracts hydrochlorothiazide (HCTZ) induced potassium loss.⁴⁸ The addition of DRSP/E2 to existing antihypertensive therapy with HCTZ reduces both systolic and diastolic blood pressure in hypertensive postmenopausal women (Category 1-2).⁴⁸ For antihypertensives, transdermal ET, transdermal EPT and vaginal HT are assigned Category 1.²

Diabetes

ET enhances insulin sensitivity by upregulating insulin receptor expression, preserving pancreatic β -cell function, promoting insulin secretion, reducing pro-inflammatory cytokines like TNF- α and IL-6, and preventing apoptosis.^{1,49,50}

The beneficial effects of MHT on glycaemic control appear to be more pronounced with oral estrogen, particularly CEE, compared with transdermal formulations. This difference is largely due to hepatic first-pass metabolism with oral therapy, which influences glucose homeostasis and insulin sensitivity.¹ In the results from the WHI trial during a 5.6-year follow-up, diabetes occurred less frequently in women receiving HT (0.625 mg CEE+2.5 mg MPA) than in those receiving placebo (3.5% vs 4.2%; hazard ratio 0.79), and this reduction was largely independent of changes in body weight and waist circumference.⁵¹ Pooled data from 107 trials showed that HT reduces abdominal fat by about 7%, improves homeostatic model assessment of insulin resistance (HOMA-IR) by approximately 13%, and lowers the risk of new-onset diabetes by around 30% in women without diabetes.⁵⁰ In women with established T2DM, HT has been

shown to reduce fasting plasma glucose levels and significantly improve insulin sensitivity, with reductions in HOMA-IR of up to 30–35%, probably mediated through enhanced insulin signalling and reduced systemic inflammation.^{50,52}

Progesterone has a complex, tissue-specific effect on glucose homeostasis. The metabolic effects of progestogens are type- and dose-dependent, with some synthetic progestins promoting hepatic glycogen storage, inducing hyperinsulinemia, and impairing insulin action in muscle and adipose tissue.^{53,54} These effects generally oppose those of estrogen and contribute to increased insulin resistance. Increased insulin resistance has been reported with progestins exhibiting glucocorticoid activity, such as MPA and levonorgestrel. Metabolically neutral progestogens, including micronized progesterone, dydrogesterone, and standard MHT doses of norethisterone acetate (NETA), appear to have minimal adverse effects on insulin sensitivity.^{1,54}

In diabetic women, HT may slightly alter insulin resistance and affect glycaemic control at the initiation of treatment, depending on the type of progestin used. With minor adjustments to doses of oral antidiabetics or insulin, these changes are manageable. The HT route should ideally be guided by the 10-year risk of Atherosclerotic Cardiovascular Disease (ASCVD). If the risk is less than 5%, any route can be prescribed; if the risk is moderate (5–10%), only the transdermal route is advised to avoid the risk of venous thromboembolism.⁵⁵ All types of HT are considered Category 1 for oral antidiabetics and insulin.² There is currently no strong evidence of clinically significant pharmacokinetic interactions between oral hypoglycaemics/insulin and standard HT, but benefits and risks should be individualised.^{2,56}

Obesity

Increasing body mass index (BMI) is associated with a higher burden of adverse health outcomes in midlife and postmenopausal women. Higher BMI is linked to more frequent and severe vasomotor symptoms,⁵⁷ likely due to impaired thermoregulation, chronic low-grade inflammation, and altered estrogen metabolism in adipose tissue.⁵⁸ Obesity is also a well-established risk factor for venous thromboembolism (VTE), with excess adiposity promoting a prothrombotic state through inflammation, endothelial dysfunction, and coagulation activation.^{1,59} These risks may be further amplified in the presence of oral MHT; transdermal estrogens alone or combined with progesterone might be safe with respect to thrombotic risk.⁶⁰

Increasing BMI also confers a higher risk of hormone-dependent cancers, particularly postmenopausal breast and endometrial cancer, due to increased peripheral aromatisation of androgens to estrogens and prolonged estrogen exposure without progesterone opposition.^{61,62} Obesity is a central driver of metabolic syndrome and insulin resistance and is strongly associated with the development of type 2 diabetes mellitus, mediated by adipose tissue dysfunction, ectopic fat deposition, and chronic inflammation.⁶³ These metabolic disturbances contribute substantially to the elevated risk of cardiovascular disease observed in women with higher BMI. Obesity is independently associated with hypertension, dyslipidemia, atherosclerosis, and adverse cardiovascular outcomes across the life course.⁶⁴

Cardiovascular and thrombotic risks associated with MHT in obese women vary by route of administration. A meta-analysis of 22 studies showed that oral HT increases the risk of first VTE, while non-oral HT does not significantly increase VTE risk.⁶⁵ In women with increased BMI, oral estrogen markedly increases VTE risk, whereas transdermal estrogen does not add risk beyond that associated with BMI alone (ESTHER study).⁶⁶ Progesterone preparations with a neutral metabolic profile, like micronised progesterone, dydrogesterone and transdermal norethisterone are usually preferred.⁵⁴

Incretin therapies are a class of medications used primarily to treat type 2 diabetes (and increasingly obesity). They work by enhancing the action of incretin hormones glucose-dependent insulintropic polypeptide (GIP) and glucagon-like peptide-1 (GLP-1), which are gut-derived hormones released after meals that help regulate blood glucose.⁶⁷ GLP-1 receptor agonist Semaglutide, and dual agonist for GLP-1 and GIP receptors Tirzepatide, are administered once weekly. They are the most effective drugs approved for obesity and insufficiently controlled type 2 diabetes mellitus, leading to significant weight loss. They also improve cardio-metabolic health outcomes and survival in obesity and advanced cardiac disease.^{68,69} As obesity and diabetes increase the risk of VTE, transdermal estrogen is preferred as it does not increase the risk of VTE, unlike oral estrogen.⁶⁵ Absorption of transdermal estrogen is not affected by oral medications. If treatment with incretin-based therapies for diabetes or obesity is proposed in a woman using oral HT for menopausal symptoms, a change to the transdermal HT is advisable.⁶⁹ Both semaglutide and tirzepatide result in delayed gastric emptying and gastrointestinal side effects are common. In women using combined

HT along with Semaglutide or Tirzepatide, the potential concern is reduced absorption of oral progestogens due to delayed gastric emptying.⁶⁹

Women with obesity have an increased risk of endometrial hyperplasia and cancer, therefore, to ensure proper endometrial protection while on semaglutide/ tirzepatide, progesterone dosing may need adjusting with different HT preparations, based on limited available evidence.⁶⁹ If HT is in the form of a combined estrogen-progestogen patch, no change in progestogen dosing is required. With the 52-mg levonorgestrel intrauterine device (LNG-IUS) (within 5 years of insertion), no change is required as endometrial protection is maintained. If oral progestogen or oral micronised progesterone was being used, consider switching to a 52-mg LNG-IUS device, or increasing the progestogen/progesterone dose at initiation of semaglutide or tirzepatide for four weeks, and maintaining the higher dose for four weeks after each incretin dose increase. Vaginal progesterone, which is currently an off-licence use for HT, does not require any change in dosing.⁶⁹ The 52 mg LNG-IUS provides reliable contraception and endometrial protection during combined HT, unaffected by incretin therapies, and is perhaps the best option for women at higher risk of endometrial pathology.⁶⁹

Dyslipidemia

ET has a dose dependent beneficial effect on lipid profile. It reduces total cholesterol (TC) and LDL-cholesterol and increases HDL-C.⁷⁰ The effect on triglycerides varies according to the route of administration: oral ET may increase levels, while transdermal ET has little to no effect or may slightly reduce it.⁷⁰ Both CEE and E2 improve lipid parameters by reducing TC and LDL-C, but their hepatic effects differ.⁷⁰⁻⁷² Oral CEE produces a greater increase in HDL-cholesterol than E2, and also significantly raises triglyceride levels (TGs) due to hepatic first-pass effects,⁷² whereas E2, particularly when administered transdermally, has minimal effects on TGs and a more metabolically neutral lipid profile.⁷¹ In women with preexisting hypertriglyceridemia along with risk factors for CVD, the transdermal route is preferred.

A recent meta-analysis concluded that 17 β -estradiol plus NETA improves atherogenic lipid parameters ($\downarrow$ TC, $\downarrow$ LDL-C, $\downarrow$ TG) but is associated with a modest, duration-dependent reduction in HDL-C, the clinical significance of which remains uncertain.⁷³

Tibolone significantly reduces TC, HDL-C, and TGs. Reduction of LDL-C is modest and observed only with short-term use (≤ 26 weeks), with greater reductions in TC and TGs seen in women with BMI ≥ 25 kg/m².^{72,74} It is considered Category 1-2.

Progestogens have minimal effect on estrogen-induced reductions in LDL- and TC, but attenuate estrogen-related increases in HDL and TGs in a progestogen-specific manner, with opposing effects increasing in the following order: dydrogesterone, micronized progesterone, cyproterone acetate, medroxyprogesterone acetate, transdermal norethindrone acetate, norgestrel, and oral norethindrone acetate.⁷² In general, transdermal ET and EPT modify lipid profile less than oral MHT. For statins, oral ET and EPT and transdermal ET and EPT are all considered Category 1-2. Vaginal HT is category 1.² No significant interactions have been documented between MHT and statins; combined use is generally safe with standard monitoring.²

Thyroid Disorders

Menopause and thyroid dysfunction share symptoms, including menstrual irregularities, mood changes, increased sweating, sleep disturbances, and hair loss. Clinicians should be aware of this overlap to facilitate early detection of coexisting thyroid disease.⁷⁵ MHT is a safe and effective option for managing menopausal symptoms in women with thyroid disorders. Untreated or overtreated thyroid disease during menopause can adversely affect cardiovascular health and bone density, whereas MHT helps prevent hip fractures. Additionally, combined levothyroxine (LT4) supplementation and MHT may improve non-alcoholic fatty liver disease (NAFLD).⁷⁵

Oral ET increases thyroxine-binding globulin (TBG) through hepatic first-pass metabolism, leading to reduced free thyroxine levels and a higher LT4 requirement in women with hypothyroidism.^{76,77} In contrast, transdermal estrogen does not significantly increase TBG and usually does not necessitate adjustment of LT4 dose.^{76,77} Progestogens have no clinically relevant effect on thyroid hormone levels. Thyroid function (TSH $\pm$ free T4) should be reassessed 6–8 weeks after initiating or changing oral MHT, with LT4 dose adjustment as required. Thyroid hormones are considered Category 1-2 for oral ET, oral EPT and Tibolone, and Category for 1 for transdermal ET, EPT and vaginal HT.²

Venous Thromboembolism (VTE)

In a 12-week randomized study (N=202), low-dose HT (1 mg E2 + 0.5 mg NETA), standard-dose HT (2 mg E2 + 1 mg NETA), and tibolone (2.5 mg) showed distinct coagulation effects. Standard-dose HT caused the greatest reductions in coagulation factors and inhibitors, while tibolone produced greater reductions in factor VII with smaller or opposite effects on anticoagulant proteins.⁷⁸

The effects of HT on VTE risk varies with the route, dose, type and combination with progesterone. Oral ET is associated with a greater risk for VTE, especially when combined with Progestins (MPA >NETA). In a Swedish case-control study, current HT use increased VTE risk (OR 1.72). The risk was highest with systemic EPT (OR 2.85) and lower with ET alone (OR 1.31).⁸⁰ Oral EPT increased VTE risk, with slightly higher odds for MPA than NETA, whereas transdermal EPT was not associated with increased VTE risk.⁷⁹ Neither transdermal estrogen alone nor local (vaginal) estrogen increased VTE risk.⁷⁹

In women with a history of VTE in the past, details of whether it was provoked or due to thrombophilia should be elicited. If her menopausal symptoms require HT, a shared decision should be taken before prescribing HT, and the transdermal route is preferred.⁸⁰

Warfarin (Vitamin K antagonist) inhibits the synthesis of vitamin K-dependent clotting factors. MHT particularly oral estrogen, induces a procoagulant state and increases VTE risk.^{60,81} Although no consistent pharmacokinetic interaction with warfarin has been demonstrated, the overall clinical thrombotic risk is increased.⁸² When co-prescribing oral MHT, caution should be exercised, and in some women, it may be necessary to adjust the dose of warfarin (anticoagulant), especially at the beginning, or change the route of HT administration.² (Category 1-2) Transdermal routes may be preferred in such cases (Category 1).² Starting tibolone often causes a sudden increase in anticoagulation, so the anticoagulant dose needs to be adjusted to bring the INR back to the target range.⁸³ (Category 2)

Autoimmune Diseases

Autoimmune diseases like rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), Sjogren's disease and multiple sclerosis (MS) are often seen in midlife women and can pose a problem in management. They have been assumed to have a close relationship with the menopausal status.⁸⁴ Hormonal fluctuations during menopause transition can trigger autoimmunity and modify disease trajectories, emphasizing their immunomodulatory significance.⁸⁵ In menopausal women, MHT may reduce the risk of developing Anti-Citrullinated Protein Antibodies (ACPA)-positive RA, while it does not affect the risk of ACPA-negative RA.⁸⁵ In patients with established RA, MHT does not appear to increase the risk of disease flares.⁸⁵ Overall, MHT does not significantly alter RA risk in postmenopausal women, but short-term use (≤ 3 years), especially with estrogen/progestogen or tibolone, may increase the risk.⁸⁶ HT has been found to be associated with better physical QOL in postmenopausal women with MS,⁸⁷ possibly due to its immunomodulatory and neuroprotective effects.⁸⁸ HT is linked to a modestly increased risk of systemic autoimmune diseases, particularly SLE and systemic sclerosis, suggesting a role of exogenous estrogens in disease pathogenesis independent of socio-economic factors.⁸⁹

Corticosteroids remain a cornerstone of therapy for many systemic autoimmune and inflammatory diseases, particularly for inducing remission and managing disease flares.⁹⁰ The concomitant use of estrogens could reduce the metabolism of the corticosteroid therapy, and it may be necessary to reduce its dose if it is long-term.^{91,92} Estrogens may decrease hepatic metabolism of corticosteroids, resulting in increased effects of corticosteroids.⁹³ Corticosteroids are considered Category 2 for both oral and transdermal ET, EPT and Tibolone and Category 1 for vaginal HT.² In antiphospholipid antibody syndrome with thrombocytopenia, HT is avoided as no safety data is available.

Epilepsy

The relationship between menopause and epilepsy is complex, but evidence-based guidelines for managing epilepsy during this transition are lacking. Estrogen can be a potent proconvulsant, whereas progesterone is an anticonvulsant, and it is well established that women with epilepsy can have changes in seizure tendency related to their menstrual cycle (catamenial epilepsy).⁹⁴ Fluctuations in estrogen and progesterone during MT and menopause can influence neuronal excitability and alter antiseizure medication clearance, thereby affecting seizure frequency and severity.⁹⁵ Women with epilepsy are at increased risk of early menopause and osteoporosis, making consideration of MHT clinically relevant. Evidence on the impact of MHT on seizure control is limited and conflicting.⁹⁵

Estrogens and progestogens are metabolized by cytochrome P450 3A4. Antiseizure medications (ASMs) that are potent hepatic enzyme inducers, including phenobarbital, primidone, phenytoin, carbamazepine, oxcarbazepine, and cenobamate, and weaker CYP3A4 inducers such as topiramate, perampanel, and clobazam, accelerate the metabolism of sex steroids, resulting in reduced circulating hormone concentrations.⁹⁴ In addition, some ASMs, such as carbamazepine and oxcarbazepine, increase sex hormone-binding globulin (SHBG), further lowering bioavailable estrogen. Therefore, MHT in women receiving these ASMs may require careful clinical monitoring and, in some cases, dose adjustment to maintain therapeutic efficacy.⁹⁶

Conversely, oral HT could interfere with the metabolism of ASMs, potentially diminishing their efficacy.² A very small RCT reported that CEE/MPA is associated with a dose-related increase in seizure frequency in postmenopausal women with epilepsy.⁹⁶ ASMs are considered Category 4 for oral ET, EPT and Tibolone and Category 3-4 for transdermal ET and EPT.⁹⁵ Vaginal ET is category 1.²

Gall Bladder Disease

Oral estrogen is associated with an increased risk of cholecystitis and cholelithiasis, possibly due to the first-pass hepatic metabolism. With a history of gall bladder disease, the oral route is best avoided. Transdermal estrogen is devoid of any action on the gall bladder.⁹⁷

Meningiomas And Hepatic Haemangiomas

Estrogen use has been associated with increased size of brain meningiomas and hepatic hemangiomas. A meta-analysis reported that longer exposure to effect of female sex hormones may increase the risk of meningioma in women, yet additional studies are warranted.⁹⁸ Hepatic hemangiomas have been shown to enlarge more frequently in women exposed to exogenous female sex hormones compared with controls, although significant enlargement occurs only in a minority of patients.⁹⁹ Routine liver ultrasound monitoring in women with hepatic hemangiomas is therefore advisable for women on HT.

Aromatase Inhibitors (AIs)

Systemic MHT is contraindicated in breast cancer survivors. Low-dose vaginal estrogen is generally not recommended in women taking AIs, as even small amounts can be absorbed systemically, raising estrogen levels within the postmenopausal range and potentially stimulating occult breast cancer cells.¹⁰⁰ However, ultralow-dose 0.005% estradiol gel does not significantly affect systemic estrogen, FSH, or LH levels in women on AIs and has been shown in randomised trials to improve signs of vulvovaginal atrophy compared with placebo.^{101,102} Long-term safety and effects on recurrence remain unknown, so treatment should be individualized. If considered, treatment should only be prescribed after thorough discussion between the patient, her gynaecologist, and the oncologist treating her.¹⁰³

Multivitamins

No significant clinically relevant interactions were observed with MHT.

Calcium

No significant clinically relevant interactions were observed with MHT.

Minoxidil

Minoxidil is safe and effective for women on MHT, and may even offer additive benefits for hair regrowth during menopause.¹⁰⁴ No documented clinically significant drug-drug interactions exist between minoxidil (topical or low-dose oral) and MHT.

SYNOPSIS

- Women using MHT frequently have coexisting chronic medical conditions. Disease-specific pharmacotherapy may interact with MHT through pharmacokinetic and pharmacodynamic mechanisms, while menopausal hormonal changes themselves can modify drug efficacy, safety, and tolerability.
- Commonly prescribed medications in midlife women are antihypertensives, antidiabetics, lipid-lowering agents, anti-obesity drugs, thyroid medications, anticoagulants, antiseizure drugs, and supplements. The menopause practitioner should be aware of the adverse effects, contraindications, and clinically relevant interactions with different MHT formulations, routes and doses, which can influence the cardiovascular, metabolic, thrombotic, and endocrine outcomes.

- Pharmacological interaction categories of drug and hormone can be categorised into four types – Category 1: safe or preferred combination, Category 2: Allowed with minor adjustments or monitoring, Category 3: Use only if benefits outweigh risks and Category 4: Avoid unless strong justification.
- Transdermal estrogen consistently demonstrates a more favourable safety profile in women with cardiometabolic risk factors, obesity, diabetes, hypertension, and increased VTE risk, due to avoidance of hepatic first-pass metabolism. Metabolically neutral progestogens such as micronized progesterone and dydrogesterone are generally preferred. Vaginal estrogen remains the safest option for local symptoms, with minimal systemic effects in most settings.
- Special clinical situations, including thyroid disease, obesity treated with incretin therapies, epilepsy, autoimmune disorders, prior VTE, gallbladder disease, and hormone-sensitive conditions, require tailored decision-making using evidence-based eligibility categories to guide co-prescription. While most chronic disease medications can be safely combined with appropriately selected MHT, certain combinations require caution.
- Understanding disease-specific effects and drug-hormone interactions is key to optimizing outcomes and improving quality of life in midlife and older women. Optimal menopausal care requires an integrated, individualized approach that balances symptom control, accounts for comorbidities and concurrent medications, emphasizes shared decision-making and ongoing monitoring with long-term safety.

RESEARCH AGENDA

MHT is underutilised in women with co-morbidities. High-quality studies are required to investigate the safety and efficacy of MHT in women taking other drugs.

REFERENCES

1. Kapoor E, Kling JM, Lobo AS, Faubion SS. Menopausal hormone therapy in women with medical conditions. *Best Pract Res Clin Endocrinol Metab.* 2021 Dec;35(6):101578. doi: 10.1016/j.beem.2021.101578.
2. Fasero M, Quereda F, Andraca L, Coronado PJ, HT Eligibility Criteria Group. Pharmacological interactions and menopausal hormone therapy: a review. *Menopause.* 2023 Aug 1;30(8):873–80. doi: 10.1097/GME.0000000000002219.
3. Igbo Pemu P, Ofili E. Hypertension in Women: Part I. *J Clin Hypertens.* 2008 May;10(5):406–10. doi: 10.1111/j.1751-7176.2008.06552.x.
4. Khalil H, Zeltser R. Antihypertensive Medications. In: *StatPearls.* Treasure Island (FL): StatPearls Publishing; 2025.
5. McKeever RG, Patel P, Hamilton RJ. Calcium Channel Blockers. In: *StatPearls.* Treasure Island (FL): StatPearls Publishing; 2025.
6. Rydberg DM, Mejyr S, Loikas D, Schenck-Gustafsson K, von Euler M, Malmstrom RE. Sex differences in spontaneous reports on adverse drug events for common antihypertensive drugs. *Eur J Clin Pharmacol.* 2018 Sept;74(9):1165–73. doi: 10.1007/s00228-018-2480-y.
7. Hage FG, Mansur SJ, Xing D, Oparil S. Hypertension in women. *Kidney Int Suppl.* 2013 Dec;3(4):352–6. doi: 10.1038/kisup.2013.76.
8. Maher RL, Hanlon J, Hajjar ER. Clinical consequences of polypharmacy in elderly. *Expert Opin Drug Saf.* 2014 Jan;13(1):57–65. doi: 10.1517/14740338.2013.827660.
9. Hendriksen LC, Omes-Smit G, Koch BCP, Ikram MA, Stricker BH, Visser LE. Sex-Based Difference in the Effect of Metoprolol on Heart Rate and Bradycardia in a Population-Based Setting. *J Pers Med.* 2022 May 25;12(6):870. doi: 10.3390/jpm12060870.
10. Ganesan K, Rana MBM, Sultan S. Oral Hypoglycemic Medications. In: *StatPearls.* Treasure Island (FL): StatPearls Publishing; 2025.
11. Chaudhury A, Duvoor C, Reddy Dendi VS, Kraleti S, Chada A, Ravilla R, et al. Clinical Review of Antidiabetic Drugs: Implications for Type 2 Diabetes Mellitus Management. *Front Endocrinol.* 2017;8:6. doi: 10.3389/fendo.2017.00006.
12. Milner Z, Akhondi H. Repaglinide. In: *StatPearls.* Treasure Island (FL): StatPearls Publishing; 2025.
13. Hernandez AV, Usmani A, Rajamanickam A, Moheet A. Thiazolidinediones and risk of heart failure in patients with or at high risk of type 2 diabetes mellitus: a meta-analysis and meta-regression analysis of placebo-controlled randomized clinical trials. *Am J Cardiovasc Drugs Drugs Devices Interv.* 2011;11(2):115–28. doi: 10.2165/11587580-000000000-00000.
14. van Dalem J, Brouwers MCGJ, Stehouwer CDA, Krings A, Leufkens HGM, Driessen JHM, et al. Risk of hypoglycaemia in users of sulphonylureas compared with metformin in relation to renal function and sulphonylurea metabolite group: population based cohort study. *BMJ.* 2016 July 13;354:i3625. doi: 10.1136/bmj.i3625.
15. Slopian R, Wender-Ozegowska E, Rogowicz-Frontczak A, Meczkaliski B, Zozulinska-Ziolkiewicz D, Jaremek JD, et al. Menopause and diabetes: EMAS clinical guide. *Maturitas.* 2018 Nov;117:6–10. doi: 10.1016/j.maturitas.2018.08.009.
16. Paschou SA, Anagnostis P, Pavlou DI, Vryonidou A, Goulis DG, Lambrinoudaki I. Diabetes in Menopause: Risks and Management. *Curr Vasc Pharmacol.* 2019;17(6):556–63. doi: 10.2174/1570161116666180625124405.
17. Zhou W, Tao J, Zhou X, Chen H. Insulin Degludec, a Novel Ultra-Long-Acting Basal Insulin versus Insulin Glargine for the Management of Type 2 Diabetes: A Systematic Review and Meta-Analysis. *Diabetes Ther Res Treat Educ Diabetes Relat Disord.* 2019 June;10(3):835–52. doi: 10.1007/s13300-019-0624-4.
18. Donnor T, Sarkar S. Insulin- Pharmacology, Therapeutic Regimens and Principles of Intensive Insulin Therapy. In: Feingold KR, Adler RA, Ahmed SF, Anawalt B, Blackman MR, Chrousos G, et al., editors. *Endotext* [Internet]. South Dartmouth (MA): MDText.com, Inc.; 2000 [cited 2026 Feb 5]. Available from: <http://www.ncbi.nlm.nih.gov/books/NBK278938/>

19. Alqahtani MS, Alzibali KF, Mahdi AMM, Alharbi OMA, Harbi RHA, Alkhalidi HSM, et al. Lipid-Lowering Medications for Managing Dyslipidemia: A Narrative Review. *Cureus*. 2024 July;16(7):e65202. doi: 10.7759/cureus.65202.
20. Taher ZA, Taher AA, Radi S. An Update on Dyslipidemia Management and Medications: A Review. *Cureus*. 2024 Mar;16(3):e56255. doi: 10.7759/cureus.56255.
21. Lilja JJ, Kivist KT, Neuvonen PJ. Grapefruit juice-simvastatin interaction: effect on serum concentrations of simvastatin, simvastatin acid, and HMG-CoA reductase inhibitors. *Clin Pharmacol Ther*. 1998 Nov;64(5):477–83. doi: 10.1016/S0009-9236(98)90130-8.
22. Chakhtoura M, Haber R, Ghezzawi M, Rhayem C, Tcheroyan R, Mantzoros CS. Pharmacotherapy of obesity: an update on the available medications and drugs under investigation. *EClinicalMedicine*. 2023 Apr;58:101882. doi: 10.1016/j.eclinm.2023.101882.
23. Tchang BG, Aras M, Kumar RB, Aronne LJ. Pharmacologic Treatment of Overweight and Obesity in Adults. In: Feingold KR, Adler RA, Ahmed SF, Anawalt B, Blackman MR, Chrousos G, et al., editors. *Endotext*. South Dartmouth (MA): MDText.com, Inc.; 2000.
24. Patil N, Rehman A, Anastasopoulou C, Jialal I. Hypothyroidism. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2025.
25. Eghtedari B, Correa R. Levothyroxine. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2025.
26. Awosika AO, Singh G, Correa R. Methimazole. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2025.
27. Amisha F, Rehman A. Propylthiouracil (PTU). In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2025.
28. Alquwaizani M, Buckley L, Adams C, Fanikos J. Anticoagulants: A Review of the Pharmacology, Dosing, and Complications. *Curr Emerg Hosp Med Rep*. 2013 June;1(2):83–97. doi: 10.1007/s40138-013-0014-6.
29. Stanger L, Yamaguchi A, Holinstat M. Antiplatelet strategies: past, present, and future. *J Thromb Haemost JTH*. 2023 Dec;21(12):3317–28. doi: 10.1016/j.jtha.2023.09.013.
30. Subbarao BS, Silverman A, Eapen BC. Seizure Medications. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2025.
31. Javaid M, Kadhim K, Bawamia B, Cartledge T, Farag M, Alkhalil M. Bleeding Risk in Patients Receiving Omega-3 Polyunsaturated Fatty Acids: A Systematic Review and Meta-Analysis of Randomized Clinical Trials. *J Am Heart Assoc*. 2024 May 21;13(10):e032390. doi: 10.1161/JAHA.123.032390.
32. Akintoye E, Sethi P, Harris WS, Thompson PA, Marchioli R, Tavazzi L, et al. Fish Oil and Perioperative Bleeding. *Circ Cardiovasc Qual Outcomes*. 2018 Nov;11(11):e004584. doi: 10.1161/CIRCOUTCOMES.118.004584.
33. Milart P, Woźniakowska E, Wrona W. Selected vitamins and quality of life in menopausal women. *Przegląd Menopauzalny Menopause Rev*. 2018 Dec;17(4):175–9. doi: 10.5114/pm.2018.81742.
34. Aggarwal S, Nityanand null. Calcium and vitamin D in post menopausal women. *Indian J Endocrinol Metab*. 2013 Dec;17(Suppl 3):S618-620. doi: 10.4103/2230-8210.123549.
35. Wobser RW, Takov V. Black Cohosh. In: StatPearls. Treasure Island (FL): StatPearls Publishing; 2025.
36. Booth NL, Overk CR, Yao P, Burdette JE, Nikolic D, Chen SN, et al. The chemical and biologic profile of a red clover (*Trifolium pratense* L.) phase II clinical extract. *J Altern Complement Med*. 2006 Mar;12(2):133–9. doi: 10.1089/acm.2006.12.133.
37. Heck AM, DeWitt BA, Lukes AL. Potential interactions between alternative therapies and warfarin. *Am J Health-Syst Pharm AJHP Off J Am Soc Health-Syst Pharm*. 2000 July 1;57(13):1221–7; quiz 1228–30.
38. Paik DJ, Lee CH. Review of cases of patient risk associated with ginseng abuse and misuse. *J Ginseng Res*. 2015 Apr;39(2):89–93. doi: 10.1016/j.jgr.2014.11.005.
39. Ginseng. In: *Drugs and Lactation Database (LactMed®)*. Bethesda (MD): National Institute of Child Health and Human Development; 2006.
40. “The 2022 Hormone Therapy Position Statement of The North American Menopause Society” Advisory Panel. The 2022 hormone therapy position statement of The North American Menopause Society. *Menopause*. 2022 July 1;29(7):767–94. doi: 10.1097/GME.0000000000002028.
41. Shimbo D, Wang L, Lamonte MJ, Allison M, Wellenius GA, Bavry AA, et al. The effect of hormone therapy on mean blood pressure and visit-to-visit blood pressure variability in postmenopausal women: results from the Women’s Health Initiative randomized controlled trials. *J Hypertens*. 2014 Oct;32(10):2071–81; discussion 2081. doi: 10.1097/HJH.0000000000000287.
42. Ferreira Campos L, de Andrade Costa G, Domingues Feitosa M, Ferreira Felix I, Gabrielli L, C Almeida M da C, et al. Effect of hormone therapy on blood pressure and hypertension in postmenopausal women: a systematic review and meta-analysis. *Menopause*. 2024 June 1;31(6):556–62. doi:10.1097/GME.0000000000002359.
43. Fardoun M, Dehaini H, Shaito A, Mesmar J, El-Yazbi A, Badran A, et al. The hypertensive potential of estrogen: An untold story. *Vascul Pharmacol*. 2020 Jan;124:106600. doi: 10.1016/j.vph.2019.106600.
44. Yuan Q, Santos HO, Alshahrani MS, Baradwan S, Ju H. Does tibolone treatment have favorable effects on obesity, blood pressure, and inflammation? A meta-analysis of randomized controlled trials. *Steroids*. 2022 Feb;178:108966. doi: 10.1016/j.steroids.2022.108966.
45. J S, D W, L W, Q X, J W, C M, et al. Serum Progesterone is Negatively Associated with Hypertension and Blood Pressure Indicators Among Men and Postmenopausal Women. *Horm Metab Res Horm Stoffwechselforschung Horm Metab*. 2023 Apr;55(4). doi: 10.1055/a-2024-0708.
46. Stevenson JC, Rozenberg S, Maffei S, Egarter C, Stute P, Romer T. Progestogens as a component of menopausal hormone therapy: the right molecule makes the difference. *Drugs Context*. 2020;9:2020-10-1. doi: 10.7573/dic.2020-10-1.
47. Đogo A, Dožić B, Vujović S, Srebro D, Dožić I. Effects of continuous-combined oral drospirenone- estradiol on blood pressure, body weight & lipid profile in early menopausal women. *Indian J Med Res*. 2021 June;154(6):857–65. doi: 10.4103/ijmr.IJMR_478_20.
48. Preston RA, Norris PM, Alonso AB, Ni P, Hanes V, Karara AH. Randomized, placebo-controlled trial of the effects of drospirenone-estradiol on blood pressure and potassium balance in hypertensive postmenopausal women receiving hydrochlorothiazide. *Menopause*. 2007;14(3 Pt 1):408–14. doi: 10.1097/01.gme.0000243572.63322.f7.
49. de Lauzon-Guillain B, Fournier A, Fabre A, Simon N, Mesrine S, Boutron-Ruault MC, et al. Menopausal hormone therapy and new-onset diabetes in the French Etude Epidemiologique de Femmes de la Mutuelle Generale de l’Education Nationale (E3N) cohort. *Diabetologia*. 2009 Oct;52(10):2092–100. doi: 10.1007/s00125-009-1456-y.
50. Salpeter SR, Walsh JME, Ormiston TM, Greyber E, Buckley NS, Salpeter EE. Meta-analysis: effect of hormone-replacement therapy on components of the metabolic syndrome in postmenopausal women. *Diabetes Obes Metab*. 2006 Sept;8(5):538–54. doi: 10.1111/j.1463-1326.2005.00545.x.

51. Margolis KL, Bonds DE, Rodabough RJ, Tinker L, Phillips LS, Allen C, et al. Effect of oestrogen plus progestin on the incidence of diabetes in postmenopausal women: results from the Women's Health Initiative Hormone Trial. *Diabetologia*. 2004 July;47(7):1175–87. doi: 10.1007/s00125-004-1448-x.
52. Kanaya AM, Herrington D, Vittinghoff E, Lin F, Grady D, Bittner V, et al. Glycemic effects of postmenopausal hormone therapy: the Heart and Estrogen/progestin Replacement Study. A randomized, double-blind, placebo-controlled trial. *Ann Intern Med*. 2003 Jan 7;138(1):1–9. doi: 10.7326/0003-4819-138-1-200301070-00005.
53. Spencer CP, Godsland IF, Cooper AJ, Ross D, Whitehead MI, Stevenson JC. Effects of oral and transdermal 17beta-estradiol with cyclical oral norethindrone acetate on insulin sensitivity, secretion, and elimination in postmenopausal women. *Metabolism*. 2000 June;49(6):742–7. doi: 10.1053/meta.2000.6238.
54. Fz S, Jp H, S W, Dr M. Progestogens used in postmenopausal hormone therapy: differences in their pharmacological properties, intracellular actions, and clinical effects. *Endocr Rev* [Internet]. 2013 Apr [cited 2026 Feb 6];34(2). doi: 10.1210/er.2012-1008. Available from: <https://pubmed.ncbi.nlm.nih.gov/23238854/>
55. Stuenkel CA, Davis SR, Gompel A, Lumsden MA, Murad MH, Pinkerton JV, et al. Treatment of Symptoms of the Menopause: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab*. 2015 Nov;100(11):3975–4011. doi: 10.1210/jc.2015-2236.
56. Mauvais-Jarvis F, Manson JE, Stevenson JC, Fonseca VA. Menopausal Hormone Therapy and Type 2 Diabetes Prevention: Evidence, Mechanisms, and Clinical Implications. *Endocr Rev*. 2017 June 1;38(3):173–88. doi: 10.1210/er.2016-1146.
57. Anderson DJ, Chung HF, Seib CA, Dobson AJ, Kuh D, Brunner EJ, et al. Obesity, smoking, and risk of vasomotor menopausal symptoms: a pooled analysis of eight cohort studies. *Am J Obstet Gynecol*. 2020 May;222(5):478.e1-478.e17. doi: 10.1016/j.ajog.2019.10.103.
58. Kapoor E, Collazo-Clavell ML, Faubion SS. Weight Gain in Women at Midlife: A Concise Review of the Pathophysiology and Strategies for Management. *Mayo Clin Proc*. 2017 Oct;92(10):1552–8. doi: 10.1016/j.mayocp.2017.08.004.
59. Holst AG, Jensen G, Prescott E. Risk factors for venous thromboembolism: results from the Copenhagen City Heart Study. *Circulation*. 2010 May 4;121(17):1896–903. doi: 10.1161/IRCULATIONAHA.109.921460.
60. Canonico M, Fournier A, Carcaillon L, Olie V, Plu-Bureau G, Oger E, et al. Postmenopausal hormone therapy and risk of idiopathic venous thromboembolism: results from the E3N cohort study. *Arterioscler Thromb Vasc Biol*. 2010 Feb;30(2):340–5. doi: 10.1161/ATVBAHA.109.196022.
61. Reeves GK, Pirie K, Beral V, Green J, Spencer E, Bull D, et al. Cancer incidence and mortality in relation to body mass index in the Million Women Study: cohort study. *BMJ*. 2007 Dec 1;335(7630):1134. doi: 10.1136/bmj.39367.495995.AE.
62. Lauby-Secretan B, Scoccianti C, Loomis D, Grosse Y, Bianchini F, Straif K, et al. Body Fatness and Cancer--Viewpoint of the IARC Working Group. *N Engl J Med*. 2016 Aug 25;375(8):794–8. doi: 10.1056/NEJMs1606602.
63. Kahn SE, Cooper ME, Del Prato S. Pathophysiology and treatment of type 2 diabetes: perspectives on the past, present, and future. *Lancet*. 2014 Mar 22;383(9922):1068–83. doi: 10.1016/S0140-6736(13)62154-6.
64. Powell-Wiley TM, Poirier P, Burke LE, Despes JP, Gordon-Larsen P, Lavie CJ, et al. Obesity and Cardiovascular Disease: A Scientific Statement From the American Heart Association. *Circulation*. 2021 May 25;143(21):e984–1010. doi: 10.1161/CIR.0000000000000973.
65. Rovinski D, Ramos RB, Figuera TM, Casanova GK, Spritzer PM. Risk of venous thromboembolism events in postmenopausal women using oral versus non-oral hormone therapy: A systematic review and meta-analysis. *Thromb Res*. 2018 Aug;168:83–95. doi: 10.1016/j.thromres.2018.06.014.
66. Canonico M, Oger E, Conard J, Meyer G, Levesque H, Trillot N, et al. Obesity and risk of venous thromboembolism among postmenopausal women: differential impact of hormone therapy by route of estrogen administration. The ESTHER Study. *J Thromb Haemost JTH*. 2006 June;4(6):1259–65. doi: 10.1111/j.1538-7836.2006.01933.x.
67. Nauck MA, Quast DR, Wefers J, Pfeiffer AFH. The evolving story of incretins (GIP and GLP-1) in metabolic and cardiovascular disease: A pathophysiological update. *Diabetes Obes Metab*. 2021 Sept;23 Suppl 3:5–29. doi: 10.1111/dom.14496.
68. Al-Sharafi BA, Odhaib SA. Optimizing hormone replacement therapy for postmenopausal women with type 2 diabetes: a review. *Explor Endocr Metab Dis*. 2025;2:101430.
69. Mukherjee A, Ghaem-Maghamsi S, Syed AA. Use of incretin-based therapies in women using hormone replacement therapy (HRT). *Post Reprod Health*. 2025 Jun;31(2):127–131. doi: 10.1177/20533691251343069. Epub 2025 May 16. PMID: 40378270.
70. Anagnostis P, Bitzer J, Cano A, Ceausu I, Chedraui P, Durmusoglu F, et al. Menopause symptom management in women with dyslipidemias: An EMAS clinical guide. *Maturitas*. 2020 May;135:82–8. doi: 10.1016/j.maturitas.2020.03.007.
71. Effects of estrogen or estrogen/progestin regimens on heart disease risk factors in postmenopausal women. The Postmenopausal Estrogen/Progestin Interventions (PEPI) Trial. The Writing Group for the PEPI Trial. *JAMA*. 1995 Jan 18;273(3):199–208.
72. Godsland IF. Effects of postmenopausal hormone replacement therapy on lipid, lipoprotein, and apolipoprotein (a) concentrations: analysis of studies published from 1974-2000. *Fertil Steril*. 2001 May;75(5):898–915. doi: 10.1016/s0015-0282(01)01699-5.
73. A AZ, Ma G, P J, Bl IO, P J, S B, et al. The effect of 17β-estradiol plus norethisterone acetate treatment on the lipid profile in women: a dose-response meta-analysis of randomized controlled trials. *Exp Gerontol* [Internet]. 2022 Aug [cited 2026 Feb 6];165. doi: 10.1016/j.exger.2022.111855. Available from: <https://pubmed.ncbi.nlm.nih.gov/35640782/>
74. Lv C, Zhang W, Tan X, Shang X, Găman MA, Salem H, et al. The effect of tibolone treatment on lipid profile in women: A systematic review and dose-response meta-analysis of randomized controlled trials. *Pharmacol Res*. 2021 July;169:105612. doi: 10.1016/j.phrs.2021.105612.
75. Mintziori G, Veneti S, Poppe K, Goulis DG, Armeni E, Erel CT, et al. EMAS position statement: Thyroid disease and menopause. *Maturitas*. 2024 July;185:107991. doi: 10.1016/j.maturitas.2024.107991.
76. Mazer NA. Interaction of estrogen therapy and thyroid hormone replacement in postmenopausal women. *Thyroid Off J Am Thyroid Assoc*. 2004;14 Suppl 1:S27-34. doi: 10.1089/105072504323024561.
77. Arafah BM. Increased need for thyroxine in women with hypothyroidism during estrogen therapy. *N Engl J Med*. 2001 June 7;344(23):1743–9. doi: 10.1056/NEJM200106073442302.
78. Eilertsen AL, Sandvik L, Mowinckel MC, Andersen TO, Qvigstad E, Sandset PM. Differential effects of conventional and low dose oral hormone therapy (HT), tibolone, and raloxifene on coagulation and fibrinolysis. *Thromb Res*. 2007;120(3):371–9. doi: 10.1016/j.thromres.2006.10.013.

79. Bergendal A, Kieler H, Sundström A, Hirschberg AL, Kocoska-Maras L. Risk of venous thromboembolism associated with local and systemic use of hormone therapy in peri- and postmenopausal women and in relation to type and route of administration. *Menopause*. 2016 June;23(6):593–9. doi:10.1097/GME.0000000000000611.
80. Tremollieres F, Brincat M, Erel CT, Gambacciani M, Lambrinoudaki I, Moen MH, et al. EMAS position statement: Managing menopausal women with a personal or family history of VTE. *Maturitas*. 2011 June;69(2):195–8. doi: 10.1016/j.maturitas.2011.03.011.
81. Canonico M, Plu-Bureau G, Lowe GDO, Scarabin PY. Hormone replacement therapy and risk of venous thromboembolism in postmenopausal women: systematic review and meta-analysis. *BMJ*. 2008 May 31;336(7655):1227–31. doi: 10.1136/bmj.39555.441944.BE.
82. Baglin TP, Keeling DM, Watson HG, British Committee for Standards in Haematology. Guidelines on oral anticoagulation (warfarin): third edition--2005 update. *Br J Haematol*. 2006 Feb;132(3):277–85. doi: 10.1111/j.1365-2141.2005.05856.x.
83. McLintock LA, Dykes A, Tait RC, Walker ID. Interaction between hormone replacement therapy preparations and oral anticoagulant therapy. *BJOG Int J Obstet Gynaecol*. 2003 Aug;110(8):777–9.
84. Farage MA, Miller KW, Maibach HI. Effects of menopause on autoimmune diseases. *Expert Rev Obstet Gynecol*. 2012 Nov;7(6):557–71. doi: 10.1586/eog.12.63.
85. Motta F, Di Simone N, Selmi C. The Impact of Menopause on Autoimmune and Rheumatic Diseases. *Clin Rev Allergy Immunol*. 2025 Mar 21;68(1):32. doi: 10.1007/s12016-025-09031-8.
86. Yuk JS, Seo YS, Im YH, Kim JH. Menopausal hormone therapy and risk of seropositive rheumatoid arthritis: A nationwide cohort study in Korea. *Semin Arthritis Rheum*. 2023 Dec;63:152280. doi: 10.1016/j.semarthrit.2023.152280.
87. Bove R, White CC, Fitzgerald KC, Chitnis T, Chibnik L, Ascherio A, et al. Hormone therapy use and physical quality of life in postmenopausal women with multiple sclerosis. *Neurology*. 2016 Oct 4;87(14):1457–63. doi: 10.1212/WNL.0000000000003176.
88. Voskuhl R, Kuhle J, Siddarth P, Itoh N, Patel K, MacKenzie-Graham A. Decreased neurofilament light chain levels in estriol-treated multiple sclerosis. *Ann Clin Transl Neurol*. 2022 Aug;9(8):1316–20. doi: 10.1002/acn3.51622.
89. Patasova K, Dehara M, Mantel N, Bixo M, Arkema EV, Holmqvist M. Menopausal hormone therapy and the risk of systemic lupus erythematosus and systemic sclerosis: a population-based nested case-control study. *Rheumatology*. 2025 June 1;64(6):3563–70. doi: 10.1093/rheumatology/keaf004.
90. Coutinho AE, Chapman KE. The anti-inflammatory and immunosuppressive effects of glucocorticoids, recent developments and mechanistic insights. *Mol Cell Endocrinol*. 2011 Mar 15;335(1):2–13. doi: 10.1016/j.mce.2010.04.005.
91. Drug Interactions between Estradiol and Prednisone. *Drugs.com*; <https://www.drugs.com/Interactions>
92. Bm F, Hj S, Fj F. Pharmacokinetic interaction of contraceptive steroids with prednisone and prednisolone. *Eur J Clin Pharmacol* [Internet]. 1984 [cited 2026 Feb 6];26(4). doi: 10.1007/BF00542149. Available from: <https://pubmed.ncbi.nlm.nih.gov/6734709/>
93. RAYOS (prednisone) delayed-release tablets: Highlights of prescribing information [Internet]. U.S. Food and Drug Administration (Center for Drug Evaluation and Research, CDER);
94. Sveinsson O, Tomson T. Epilepsy and menopause: potential implications for pharmacotherapy. *Drugs Aging*. 2014 Sept;31(9):671–5. doi: 10.1007/s40266-014-0201-5.
95. Voinsecu P, Smith K, Pegg E, Bromley R, Latt T, Norton A. The Intersection of Menopause and Epilepsy: A Review of Current Knowledge and Gaps. *Eur J Med*. 2025;102–13.
96. Harden CL, Herzog AG, Nikolov BG, Koppel BS, Christos PJ, Fowler K, et al. Hormone replacement therapy in women with epilepsy: a randomized, double-blind, placebo-controlled study. *Epilepsia*. 2006 Sept;47(9):1447–51. doi: 10.1111/j.1528-1167.2006.00507.x.
97. Manson JE, Chlebowski RT, Stefanick ML, Aragaki AK, Rossouw JE, Prentice RL, et al. Menopausal hormone therapy and health outcomes during the intervention and extended poststopping phases of the Women's Health Initiative randomized trials. *JAMA*. 2013 Oct 2;310(13):1353–68. doi: 10.1001/jama.2013.278040.
98. Qi ZY, Shao C, Huang YL, Hui GZ, Zhou YX, Wang Z. Reproductive and exogenous hormone factors in relation to risk of meningioma in women: a meta-analysis. *PloS One*. 2013;8(12):e83261. doi: 10.1371/journal.pone.0083261.
99. Glinkova V, Shevah O, Boaz M, Levine A, Shirin H. Hepatic haemangiomas: possible association with female sex hormones. *Gut*. 2004 Sept;53(9):1352–5. doi: 10.1136/gut.2003.038646.
100. Lubian Lopez DM. Management of genitourinary syndrome of menopause in breast cancer survivors: An update. *World J Clin Oncol*. 2022 Feb 24;13(2):71–100. doi: 10.5306/wjco.v13.i2.71.
101. Hirschberg AL, Sánchez-Rovira P, Presa-Lorite J, Campos-Delgado M, Gil-Gil M, Lidbrink E, et al. Efficacy and safety of ultra-low dose 0.005% estriol vaginal gel for the treatment of vulvovaginal atrophy in postmenopausal women with early breast cancer treated with nonsteroidal aromatase inhibitors: a phase II, randomized, double-blind, placebo-controlled trial. *Menopause*. 2020 May;27(5):526–34. doi: 10.1097/GME.0000000000001497.
102. Sanchez-Rovira P, Hirschberg AL, Gil-Gil M, Bermejo-De Las Heras B, Nieto-Magro C. A Phase II Prospective, Randomized, Double-Blind, Placebo-Controlled and Multicenter Clinical Trial to Assess the Safety of 0.005% Estriol Vaginal Gel in Hormone Receptor-Positive Postmenopausal Women with Early Stage Breast Cancer in Treatment with Aromatase Inhibitor in the Adjuvant Setting. *The Oncologist*. 2020 Dec;25(12):e1846-1854. doi: 10.1634/theoncologist.2020-0417.
103. The benefits and risks of HRT before and after a breast cancer diagnosis. 2025 Sept 8;1–14.
104. Choe SJ, Lee S, Choi J, Lee WS. Therapeutic Efficacy of a Combination Therapy of Topical 17 α -Estradiol and Topical Minoxidil on Female Pattern Hair Loss: A Noncomparative, Retrospective Evaluation. *Ann Dermatol*. 2017 June;29(3):276–82. doi: 10.5021/ad.2017.29.3.276.

ARTIFICIAL INTELLIGENCE, APPS, & SOCIAL MEDIA



Keywords: Artificial intelligence, menopause care, healthcare disparities, ethics, digital apps, social media

INTRODUCTION

Menopause represents a critical transition in women's health, affecting approximately 1.3 billion women globally by 2030.¹ This natural biological process, characterised by the cessation of menstruation and declining estrogen levels, brings a complex constellation of physical, psychological, and metabolic changes that significantly impact quality of life.²⁻⁵ Women experience diverse symptoms ranging from vasomotor disturbances to mood alterations, sleep disruptions, cognitive changes, and increased risks of cardiovascular disease, osteoporosis, and metabolic syndrome.^{2,4,5}

Despite its universality, menopause care faces persistent challenges: limited specialist access, inadequate awareness among both patients and healthcare providers, significant individual variability in symptom presentation and severity, and insufficient personalisation of treatment approaches.^{2,6} Traditional clinical approaches often struggle to capture the multidimensional nature of menopausal health, requiring detailed history-taking, increased manpower, increased consultation time, and challenges in individualised decision-making.⁷

Artificial intelligence (AI) is increasingly influencing many aspects of modern life, and its role is expected to expand further in the coming years. In healthcare, AI has already made substantial contributions, a fact underscored by the 2024 Nobel Prize in Chemistry. The award recognised David Baker (University of Washington) for pioneering AI-enabled approaches to protein design and structure prediction, and Demis Hassabis and John Jumper (DeepMind) for developing AlphaFold, an AI system capable of accurately predicting the three-dimensional structures of proteins from their amino acid sequences. This milestone underscores the transformative potential of AI-driven tools to advance biomedical research and clinical innovation. Artificial intelligence has emerged as a transformative technology with the potential to address these challenges. Machine learning algorithms can analyse complex, high-dimensional datasets, including electronic health records, wearable sensor data, patient-reported outcomes, and genomic information, to identify patterns invisible to traditional statistical methods.^{2,8,9}

Over the past decade, menopause care has undergone a rapid digital transformation, driven by advances in artificial intelligence, mobile health (mHealth) applications, wearable technologies, telemedicine platforms, and social media networks.¹⁰⁻¹² These innovations have enabled the development of AI-based predictive models, digital symptom-monitoring tools, personalised interventions, and clinical decision-support systems in menopause care.^{4,13,14} This technological revolution offers the potential to address longstanding gaps in menopause care through multiple mechanisms: continuous symptom monitoring via smartphone applications; AI-powered predictive analytics for personalised risk assessment; peer-to-peer support through online communities; evidence-based educational content accessible on demand; and the integration of patient-generated data into clinical decision-making.^{4,15-17}

This chapter provides a comprehensive examination of how technology is reimagining the menopause experience, synthesising evidence from recent studies spanning AI applications, mobile health interventions, social media platforms, and online communities.

COMPLEXITY OF MENOPAUSE

The menopausal transition encompasses three distinct phases: menopause transition, menopause, and postmenopause.^{2,7} This transition is characterised by fluctuating hormone levels, particularly declining estrogen and progesterone, which trigger cascading physiological changes across multiple organ systems.^{4,5} The symptom profile varies dramatically among individuals, influenced by genetic factors, ethnicity, socioeconomic status, lifestyle, and environmental exposures.⁵ Beyond immediate symptoms, menopause marks a critical window for long-term health risks. Postmenopausal women face elevated risks of cardiovascular disease, osteoporosis and fractures, metabolic syndrome, cognitive decline, and certain cancers.^{4,5} Early menopause before age 45 is associated with shorter life

expectancy, increased all-cause mortality, and accelerated ageing. Regional and ethnic variations exist; for example, Indian women experience menopause at younger ages compared to Western populations, necessitating earlier preventive interventions.⁵

Traditional menopause care has been characterised by episodic clinical encounters, typically occurring only when symptoms become severe enough to prompt medical consultation.^{18,19} This reactive model has several limitations. First, the significant shortage of menopause specialists means that most women receive care from primary care providers who may lack specialised training in menopause management.¹⁸ Second, the episodic nature of clinical visits provides only snapshots of symptom patterns, missing the dynamic fluctuations that characterise the menopausal transition.^{16,20}

AI AS A PARADIGM SHIFT IN HEALTHCARE

Artificial intelligence encompasses a broad range of computational techniques that enable machines to perform tasks typically requiring human intelligence, such as pattern recognition, prediction, classification, and decision-making.^{12,13} In healthcare, AI offers several transformative capabilities: analysing vast, heterogeneous datasets to identify subtle patterns; generating personalised predictions and recommendations; continuously learning and improving from new data; and scaling expertise to underserved populations.^{4,13}

Machine learning (ML), a subset of AI, uses algorithms that learn from data without explicit programming. Supervised learning methods, such as classification and regression, train on labelled datasets to predict outcomes; unsupervised learning (clustering) discovers hidden patterns in unlabeled data.^{2,5} Deep learning, utilising multi-layered neural networks, excels at processing complex, high-dimensional data such as medical images, time-series physiological signals, and natural language.^{19,21} The “black box” problem in menopause describes the limited ability to clearly link hormonal changes with symptom severity, disease risk, and treatment response. This uncertainty arises from complex neuroendocrine mechanisms, marked individual variability, and the lack of reliable biomarkers, resulting in largely symptom-based, trial-and-error management approaches.

Recent advances in explainable AI (XAI) address the “black box” problem by making model predictions interpretable and transparent, a critical requirement for clinical adoption.^{2,22-24} Large language models (LLMs) represent another frontier, capable of answering patient queries, synthesising medical literature, and supporting clinical education.^{24,25}

AI METHODS AND CLINICAL APPLICATIONS IN MENOPAUSE AND RESEARCH

Depression And Mental Health Prediction

Depression represents a prevalent concern during menopause, yet limited specialist access and knowledge gaps hinder effective intervention.^{2,6} Ali et al. developed a supervised machine learning system that achieved 99.04% accuracy in predicting depression among menopausal women, using Random Forest and XGBoost with 14 significant features.³ The system evaluated multiple performance metrics, including sensitivity, specificity, precision, recall, F-measure, ROC, PRC, and AUC, demonstrating robust diagnostic support capability. Britto et al. achieved 97% accuracy using Random Forest to predict depression severity in menopausal women, positioning their model as a promising AI-powered tool for this domain.⁶ These high accuracy rates suggest AI can effectively screen for depression, potentially enabling earlier intervention and improved mental health outcomes.

Vasomotor Symptom Prediction And Management

Vasomotor symptoms affect 60-80% of menopausal women and significantly impair quality of life. Machine learning identifies key determinants and predicts symptom severity. Ryu et al. applied five machine learning methods to predict vasomotor symptoms using general hospital data from 3,298 Korean women aged 40-80. Random Forest achieved the best performance (mean squared error 0.93), far superior to linear regression (12.49) and ANNs (1.52-1.58). Variable importance analysis identified the most critical determinants: age, menopause age, thyroid-stimulating hormone, monocyte count, triglyceride, gamma-glutamyl transferase, blood urea nitrogen, cancer antigen 19-9, C-reactive protein, and low-density lipoprotein cholesterol. This provides an invaluable decision support system and suggests preventive measures targeting thyroid function, lipid profile, liver function, and inflammation markers.⁸

Personalised Nutrition And Lifestyle Recommendations

AI enables tailored dietary and lifestyle interventions based on individual symptom profiles and health data: Logapriya et al. developed a comprehensive recommendation system for personalised Shatavari nutrition

recommendations for menopausal women, achieving 96% accuracy with LightGBM. The system integrated data from medical records, structured surveys, and health monitoring apps to track symptom severity, heart rate, temperature, sleep, and dietary intake. By combining collaborative and content-based filtering, the system provided accurate, individualised health and lifestyle recommendations to enhance quality of life during menopausal transition.²⁶ In a related study, Logapriya et al. constructed a menopause-focused recommendation system for dietary guidance, achieving maximum accuracies of 0.92 for linear regression and 0.95 for logistic regression. The system applied collaborative and content-based filtering to ensure highly accurate, information-based suggestions.²⁷

Symptom Identification And Monitoring

Explainable AI models enable accurate, transparent symptom detection: Mall et al. developed explainable AI models leveraging machine learning and large datasets (self-reported symptoms, clinical records) to identify perimenopause symptoms with high accuracy and reliability. Practical applications include symptom tracking, personalised applications, remote monitoring, predictive analytics, and treatment efficacy assessment, improving clinical decision-making and patient outcomes.²² Sarkar tested multiple models (SVM, random forest, deep learning, logistic regression) for diagnosing perimenopausal symptoms. The proposed enhanced hybrid deep learning strategy, utilising deep neural networks and attention processes, outperformed traditional models in recall, accuracy, and precision. The study emphasised ethical considerations, including data protection, privacy legislation, and preventing prejudice.²¹ Sar et al. explored advanced machine learning algorithms and NLP techniques for modelling perimenopausal health and proposed personalised digital interventions to improve healthcare delivery.²

Health Risk Prediction And Stratification

AI models predict long-term health risks associated with menopause. Panjwani et al. examined AI applications in postmenopausal health, including risk prediction, symptom monitoring, and personalised care. The paper highlighted unsupervised machine learning clustering for detecting cardiovascular diseases, deep learning for detecting vertebral fractures and osteoporosis, and AI algorithms for predicting osteoporotic fractures. AI-enabled diagnosis for ovarian endometriomas using PSO-enhanced random forest was also discussed.⁴ Singh et al. explored machine learning approaches to predict health risks (osteoporosis, cardiovascular disease, cognitive loss) during perimenopause and menopause, aiming to improve women's quality of life through personalised healthcare solutions.⁷ A study by Huang et al from Taiwan used machine learning models to screen high-risk women for osteoporosis.²⁸ Fang et al.'s knowledge graph-based approach addressed the critical need for early intervention in chronic conditions like osteoporosis, cardiovascular disease, and metabolic syndrome during menopause. Their model demonstrated superior efficacy in forecasting menopausal diseases by integrating co-occurrence relationships among medical concepts with numerical EHR data.²⁹

Clinical Diagnosis And Decision Support

AI assists clinicians in diagnosis and management decisions. A Canadian study developed and validated a machine learning algorithm for identifying "problematic menopause" in primary care electronic medical records. The algorithm (two occurrences of ICD-9-CM code 627 within 24 months OR one occurrence of ATC code G03CA) achieved 81.5% sensitivity, 93.5% specificity, 73.8% positive predictive value, and 95.7% negative predictive value. This case definition enables epidemiological study and will inform future research on menopause management in primary care settings.³⁰ Chao et al. designed an intelligent nursing diagnosis system for menopausal women's healthcare, combining a cross-layer CNN-SVM for behavioural classification with a home care bed monitoring system that detects posture, heart rate, blood oxygen, and other physiological indicators. The system provides remote diagnostic functionality, enhancing automation and safety and enriching nursing bed functions.¹⁹

Patient Education And Information Access

Large language models offer new avenues for patient and clinician education, though with important caveats. Deva et al. evaluated LLM-based chatbots for menopause-related queries using a mixed-methods approach. Their findings highlighted both the promise and limitations of traditional evaluation metrics for sensitive health topics, underscoring the need for customised, ethically grounded evaluation frameworks to advance safe and effective use of LLMs in healthcare.²⁴ Karam et al. assessed the accuracy, completeness, and readability of four LLMs (ChatGPT 3.5, Gemini, ChatGPT 4.0, OpenEvidence) in answering questions about menopause and hormone therapy. This research provides insight into the quality of AI-generated health information but stops short of recommending clinical deployment without further validation.²⁵

IMPLICATIONS OF AI IN MENOPAUSE HEALTHCARE

Access To Specialised Care In Resource-Limited Settings

AI-powered tools can extend expertise on menopause to underserved populations. Vivian et al. proposed an ANN-based model designed to enhance menopause care for women in Nigeria's rural areas, where access to specialists is severely limited. By enabling real-time symptom monitoring and assessment through trained stand-alone systems, AI can bridge geographic and economic barriers to quality care.¹⁴

The scarcity of menopause specialists globally makes AI-driven decision support particularly valuable.^{3,6} Automated screening tools for depression, symptom severity assessment, and risk stratification can help primary care providers deliver more effective, evidence-based care without requiring specialised training.^{3,6,30}

Enabling Precision And Individualised Treatment

The heterogeneity of menopausal experiences demands personalised approaches. AI excels at integrating multiple data sources, including clinical history, laboratory values, genetic markers, lifestyle factors, and patient-reported outcomes, to generate individualised predictions and recommendations.^{4,7,26,27} Panjwani et al. emphasised AI's role in holistic, personalised postmenopausal care, moving beyond one-size fits-all approaches to tailored interventions based on individual risk profiles.⁴ Personalised nutrition recommendations, as demonstrated by Logapriya et al., exemplify how AI can optimise lifestyle interventions for individual symptom patterns and health goals.^{26,27} Machine learning models can identify subgroups of women with similar symptom trajectories or risk profiles, enabling targeted interventions.^{4,8} This precision approach has the potential to improve treatment efficacy while minimising unnecessary interventions and side effects.

Continuous Monitoring And Early Intervention

AI-powered wearable devices and mobile applications enable continuous, passive monitoring of physiological signals and symptoms.^{4,14,19,22} This real-time data collection facilitates early detection of symptom exacerbations or emerging health risks, allowing timely intervention before conditions worsen.^{19,22} Chao et al.'s intelligent monitoring system integrates AI into home care infrastructure, automatically detecting physiological indicators and enabling remote diagnosis.¹² Such systems can provide reassurance, reduce healthcare utilisation for routine monitoring, and alert providers to concerning changes requiring attention.

Enhancing Clinical Decision-Making

AI serves as a powerful clinical decision support tool, synthesising complex information to assist, rather than replace, clinician judgment.^{8,29,30} Ryu et al.'s vasomotor symptom prediction model provides clinicians with evidence-based insights into key determinants of vasomotor symptoms, informing preventive strategies.⁸ The Canadian case definition algorithm helps primary care providers systematically identify women requiring specialised menopause care.³⁰ Knowledge graph approaches, as demonstrated by Fang et al., can integrate diverse medical concepts and relationships to support comprehensive disease prediction and management planning.²⁹ This holistic view helps clinicians consider interconnected health factors rather than isolated symptoms.

ADDRESSING HEALTHCARE DISPARITIES

Regional, ethnic, and socioeconomic factors significantly influence the onset of menopause and associated health risks. AI models trained on diverse, representative datasets can help identify and address these disparities. Malik et al.'s narrative review examined how racial/ethnic and socioeconomic factors influencing menopause onset may be linked to cardiovascular disease risk, endometrial cancer risk, stroke, and other health problems.⁵ However, this potential benefit depends critically on ensuring training datasets include diverse populations. Models trained predominantly on Western populations may not generalise to other ethnic groups, potentially exacerbating rather than reducing disparities.⁵

GAPS AND LIMITATIONS

Limited Clinical Validation And Outcome Data

A pervasive limitation across the literature is the lack of prospective clinical validation and real-world outcome data. Most studies report algorithmic performance metrics (accuracy, sensitivity, specificity) on retrospective datasets but do not demonstrate an impact on actual patient outcomes, clinical workflows, or healthcare costs.^{3,4,7,13-16} For

example, while Ali et al. achieved 99.04% accuracy in depression prediction³ and Britto et al. reported 97% accuracy⁶. Neither study evaluated whether implementing these models in clinical practice improves depression detection rates, treatment initiation, or patient well-being. Similarly, high-performing nutrition recommendation systems^{26,27} lack evidence of adherence, behavioural change, or symptom improvement when deployed in real-world settings. This gap between algorithmic performance and clinical utility represents a critical barrier to implementation. Rigorous prospective trials are needed to demonstrate that AI tools improve patient-centred outcomes, not just prediction accuracy.

ETHICAL CONSIDERATIONS

Ethical issues receive inadequate attention in most menopause AI research. The key concerns are:

- *Data privacy and security:* Menopause-related data is highly sensitive, encompassing reproductive health, mental health, sexual function, and genetic information. Few studies explicitly address data protection measures, consent processes, or compliance with privacy regulations.^{11,15}
- *Algorithmic bias and fairness:* AI models can perpetuate or amplify existing healthcare disparities if training data underrepresents certain populations or reflects biased clinical practices. Sarkar emphasised the need to prevent prejudice in AI model development¹¹ but most studies do not assess fairness across demographic subgroups or discuss bias mitigation strategies.
- *Informed consent and autonomy:* As AI systems make increasingly consequential predictions and recommendations, ensuring patients understand how their data is used and retain autonomy over healthcare decisions becomes critical. This issue is largely absent from current literature.
- *Accountability and liability:* When AI-assisted decisions lead to adverse outcomes, questions of responsibility arise. The literature does not adequately address liability frameworks or accountability mechanisms.
- *Lack of patient-centred usability studies:* Most studies focus on algorithmic development, with minimal attention to patient acceptability, usability, or experience.^{4,22,31,32}

Deva et al. proposed the need for customised, ethically grounded evaluation frameworks for LLMs in healthcare.¹⁸, and Mishra emphasised ethical responsibility in handling sensitive health data, but these remain exceptions rather than the norm.¹⁵

CRITICAL QUESTIONS REMAIN UNANSWERED

Do Women Trust AI-Generated Recommendations For Menopause Management?

- Are AI-powered interfaces intuitive and accessible for diverse users, including older women with varying digital literacy?
- How do women prefer to receive AI-assisted care—through mobile apps, web portals, or integrated into clinical encounters?
- What concerns do women have about AI in this intimate health domain?
- Without patient-centred design and evaluation, even technically sophisticated AI tools may fail to achieve adoption or may inadvertently create new barriers to care.

Absence Of Cost-Effectiveness Analysis

Economic evaluation is conspicuously absent from the menopause AI literature.^{4,22,31,32} Implementing AI systems requires substantial investment in infrastructure, data management, algorithm development, validation, maintenance, and training. Whether these costs are justified by improved outcomes, reduced healthcare utilisation, or enhanced efficiency remains unknown. Cost-effectiveness analysis is essential for healthcare decision-makers considering AI adoption. Without economic evidence, even clinically effective AI tools may not be implemented due to resource constraints.

GAPS IN SPECIFIC CLINICAL DOMAINS

Certain Menopause-Related Domains Receive Limited Ai Attention

- *Cognitive Changes:* Despite concerns about menopause-related cognitive changes and dementia risk, few studies

focus on AI for cognitive assessment or prediction.^{5,7,33}

- *Sexual Health:* Sexual dysfunction is common during menopause but rarely addressed in AI research.
- *Bone Health:* While osteoporosis risk is mentioned^{4,5,7} Few studies have developed AI tools specifically for bone health assessment or fracture prediction in menopausal populations.
- *Hormone Therapy Decision Support:* Given the complexity and controversy surrounding hormone therapy, AI could assist in personalised risk-benefit assessment, yet this application is underdeveloped.²⁵

Gaps In Integration With Clinical Workflows

Most AI tools are developed in isolation without consideration of how they would integrate into existing clinical workflows, electronic health record systems, or care pathways.^{12,30} Successful implementation requires seamless integration that enhances, rather than disrupts, clinicians' efficiency. Chao et al.'s nursing diagnosis system demonstrates one integration approach.¹⁹, but most studies do not address practical implementation challenges, such as data interoperability, user interface design, alert fatigue, workflow disruption, or training requirements.

MOBILE HEALTH APPLICATIONS FOR MENOPAUSE MANAGEMENT

The mobile application ecosystem for menopause has expanded dramatically, with dozens of apps now available offering diverse features and intervention approaches.^{11,15} A comprehensive assessment of 18 menopause smartphone apps revealed variable quality and functionality, ranging from simple symptom trackers to platforms that integrate tracking, data visualisation, community features, audio guides, and personalised content.^{11,15} Common features include symptom logging (hot flushes, night sweats, mood changes, sleep disturbances), menstrual period tracking, trigger identification, educational content, lifestyle recommendations, and progress visualisation.^{15,16,34}

More sophisticated apps incorporate evidence-based therapeutic interventions. Cognitive behavioural therapy (CBT) modules address the psychological and behavioural aspects of symptom management, teaching techniques for managing hot flushes, improving sleep, and reducing anxiety.^{34,35} Exercise coaching features provide personalised physical activity programs tailored to the needs and capabilities of menopausal women.¹⁷ Nutrition guidance offers dietary recommendations based on individual health profiles and preferences.^{26,27} Some apps include mindfulness and relaxation exercises, hypnotherapy audio sessions, and stress management tools.^{36,37}

The Health & Her app is a comprehensive commercial platform that enables users to monitor symptoms, triggers, and menstrual periods while engaging in various digital activities that promote health and well-being.¹⁶ The Peppy Health menopause application provides specialist-led education and personalised support specifically designed for working women.³⁸ The Emmii app, developed with input from menopause-certified primary care clinicians, offers symptom tracking, personalised treatment recommendations based on clinical protocols, and a discussion guide to facilitate patient-clinician communication.¹⁸ The Menopause Assistant Manager (MAMA) app combines personalised information provision, exercise coaching, and appointment and medication management.¹⁷

Specialised interventions targeting specific symptoms have shown particularly promising results. The Evia app, delivering audio-recorded hypnotherapy for menopausal hot flushes, achieved a 53.7% average reduction in daily hot flushes, with 69.9% of women experiencing clinically significant ($\geq 50\%$) reductions.³⁶ Hot flash severity also decreased significantly for 60.8% of users. This app-delivered hypnosis intervention demonstrates the potential for nonhormonal, accessible treatments that can be scaled to reach large populations.³⁶ A mobile-based combined exercise intervention application (Rebone) for menopausal symptom management demonstrated statistically significant improvements after eight weeks in menopausal symptoms ($p=0.002$), quality of life ($p=0.002$), depression ($p=0.001$), stress ($p=0.027$), and insomnia ($p=0.000$) compared to control groups.³⁸ The treatment group exercised more frequently and performed more appropriate workouts, with qualitative feedback indicating that mobile-based interventions are effective for menopausal women.³⁸

A multimodal, technology-assisted intervention for menopause after cancer, incorporating digital CBT for insomnia (dCBT-I) using Sleepio and self-management strategies for vasomotor symptoms via the myPatientSpace mobile application, improved global quality of life scores from 62.2 to 70.4 at six months ($P<0.001$). At least 50% reductions were observed in vasomotor symptom frequency and bother, while insomnia prevalence decreased from 93.1% to 45.2% ($p<0.001$).³⁷

COMPREHENSIVE DIGITAL HEALTH PLATFORMS

The “Menopausando” platform, a predominantly Portuguese-language digital health education platform, enables information exchange, promotes autonomy, and supports informed decision-making through community forums and peer interaction. While it aims to support women during menopausal transition and postmenopause, the platform currently lacks rigorous outcome metrics for effectiveness.³⁹

SOCIAL MEDIA & ONLINE COMMUNITIES: PEER SUPPORT & INFORMATION EXCHANGE

Social media platforms and online communities have emerged as critical spaces for women navigating menopause, providing peer support, information exchange, and validation of experiences that have historically been silenced or stigmatised.^{10,39,40} The PatientsLikeMe online support group exemplifies the value of these communities for menopause support. A retrospective analysis of women’s experiences with vasomotor symptoms on this platform revealed that VMS significantly impacted multiple life domains: physical health (43%), mental well-being (36%), social activities (21%), and productivity (14%). Hot flushes and night sweats were the most commonly reported symptoms. Women shared diverse management strategies, including temperature regulation (43%), lifestyle changes (36%), over-the-counter supplements like Estroven (29%), hormone therapy (21%), and contraceptives (21%).⁴⁰

Social media has become an increasingly relevant tool for health education, enabling rapid dissemination of information and facilitating dialogue between patients, healthcare providers, and researchers.³⁹ However, the quality and accuracy of menopause information on social media platforms vary considerably, raising concerns about misinformation and its potential impact on health decisions.^{24,25} Despite these concerns, social media platforms offer unique opportunities for health education at scale. The “Menopausando” digital health education platform leverages social media principles to support women during menopausal transition and postmenopause, enabling information exchange and promoting informed decision-making. Such platforms can bridge the gap between clinical expertise and community knowledge when designed with appropriate quality controls and professional input.³⁹ Retrospective text and qualitative analyses of patient experiences on platforms like Patients Like Me provide rich, naturalistic data on symptom management strategies, treatment effectiveness, and quality of life impacts. These analyses reveal the diversity of women’s experiences and the gap between clinical recommendations and real-world practices.⁴⁰

INTEGRATED ECOSYSTEMS: THE FUTURE OF DIGITAL MENOPAUSE CARE

The ultimate vision for digital menopause care is a fully integrated ecosystem that seamlessly combines mobile apps, wearable sensors, AI analytics, telemedicine platforms, electronic health records, and online communities.^{4,12} In such systems, data flows bidirectionally: patient-generated data from apps and wearables informs clinical decision-making, while clinical insights and treatment plans are delivered back to patients through digital platforms.^{18,41}

FUTURE DIRECTIONS AND RECOMMENDATIONS

Malik et al.’s narrative review of over 100 medical and AI articles identified substantial gaps in the literature. Specifically, 40 of 100 suitable articles highlighted the need for research on how regional, racial/ethnic, and socioeconomic factors influencing menopause onset are linked to health risks. This underscores the need for more diverse, globally representative research.⁵

PRIORITISE PROSPECTIVE CLINICAL TRIALS

The field must transition from retrospective algorithm development to prospective clinical validation. Randomised controlled trials comparing AI-assisted care to standard care are essential to demonstrate impact on patient-centred outcomes: symptom severity, quality of life, treatment adherence, healthcare utilisation, and costs. Implementation science approaches should evaluate real-world effectiveness, barriers to adoption, and sustainability.

- Data privacy and security standards
- Informed consent processes for AI-assisted care
- Algorithmic fairness assessment and bias mitigation strategies
- Transparency and explainability requirements
- Accountability and liability frameworks
- Patient autonomy and shared decision-making

SYNOPSIS

- The convergence of artificial intelligence, mobile health applications, social media platforms, and online communities offers unprecedented opportunities to address longstanding gaps in menopause care, such as limited specialist access, inadequate personalisation, episodic rather than continuous support, and societal stigma that discourages open discussion.
- Artificial intelligence represents a transformative opportunity for menopause healthcare, offering unprecedented capabilities for personalised prediction, diagnosis, symptom management, and risk stratification.
- The digital transformation of menopause care is still in its early stages, with tremendous potential yet to be realised. By learning from early successes and failures, addressing current limitations, and maintaining focus on women's needs and preferences, the field can develop digital ecosystems that truly reimagine menopause, making it a well-supported, openly discussed, and empowering life transition for all women, regardless of geography, socioeconomic status, or cultural background.
- Technology alone cannot solve all challenges in menopause care, but when thoughtfully designed, rigorously evaluated, and equitably implemented, it can be a powerful tool for improving the health, well-being, and quality of life of the 1.3 billion women who will experience menopause by 2030.

RESEARCH AGENDA

Artificial Intelligence-driven sentiment and information analysis of menopause related discussions on Indian social media platforms.

REFERENCES

1. Hill K. The demography of menopause. *Maturitas* [Internet]. 1996 [cited 2026 Feb 12];23(2):113–27. Available from: <https://www.sciencedirect.com/science/article/pii/037851229500968X>
2. Sar A, Choudhury T, Sille R. Advanced Techniques in Machine Learning for Perimenopause: Navigating Hormonal Transitions-Harnessing Cutting-Edge Machine Learning for Perimenopausal Insights. In: *Utilizing AI Techniques for the Perimenopause to Menopause Transition* [Internet]. IGI Global; 2024 [cited 2026 Feb 12]. p. 282–306. Available from: <https://www.igi-global.com/chapter/advanced-techniques-in-machine-learning-for-perimenopause/354582>
3. Ali MM, Algashamy HAA, Alzidi E, Ahmed K, Bui FM, Patel SK, et al. Development and performance analysis of machine learning methods for predicting depression among menopausal women. *Healthc Anal* [Internet]. 2023 [cited 2026 Feb 12];3:100202. Available from: <https://www.sciencedirect.com/science/article/pii/S2772442523000692>
4. Panjwani GAR, Maddukuri S, Ansari RA, Jain S, Chavan M, Gogula NSAR, et al. Artificial Intelligence in Postmenopausal Health: From Risk Prediction to Holistic Care. *J Clin Med* [Internet]. 2025 Oct 28 [cited 2026 Feb 12];14(21):7651. doi: 10.3390/jcm14217651. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC12608235/>
5. Malik M, Garg P, Malik C. Artificial intelligence-based prediction of health risks among women during menopause. *Artif Intell Mach Learn Women's Health Issues* [Internet]. 2024 [cited 2026 Feb 12];137–50. Available from: <https://www.sciencedirect.com/science/article/pii/B9780443218897000105>
6. Britto KA, Varnikaa DT, Sathishkumar R, Dolorosa EA. ML Model For Detection of Depression in Menopause Women. In: *2024 3rd International Conference on Artificial Intelligence For Internet of Things (AIIoT)* [Internet]. IEEE; 2024 [cited 2026 Feb 12]. p. 1–6. Available from: <https://ieeexplore.ieee.org/abstract/document/10574652/>
7. Singh B, Kaunert C. Changeover From Perimenopause to Menopause and Tailored Healthcare: Predict Health Risks Among Women via Machine Learning. In: *Utilizing AI Techniques for the Perimenopause to Menopause Transition* [Internet]. IGI Global; 2024 [cited 2026 Feb 12]. p. 124–47. Available from: <https://www.igi-global.com/chapter/changeover-from-perimenopause-to-menopause-and-tailoredhealthcare/354576>
8. Ryu KJ, Yi KW, Kim YJ, Shin JH, Hur JY, Kim T, et al. Machine learning approaches to the determinants of women's vasomotor symptoms using general hospital data. 2020 [cited 2026 Feb 12]; Available from: <https://scholar.archive.org/work/rnw2lsnpvhlbgfklkl3v3vsm/access/wayback/https://arxiv.org/abs/2007.14144v1>
9. Fang Y, Liu F, Zhang X, Chen L, Liu Y, Yang L, et al. Mapping global prevalence of menopausal symptoms among middle-aged women: a systematic review and meta-analysis. *BMC Public Health* [Internet]. 2024 July 2 [cited 2026 Jan 20];24(1):1767. doi: 10.1186/s12889-024-19280-5. Available from: <https://bmcpublichealth.biomedcentral.com/articles/10.1186/s12889-024-19280-5>
10. Duffecy J, Rehman A, Gorman S, Huang YL, Klumpp H. Evaluating a Mobile Digital Therapeutic for Vasomotor and Behavioral Health Symptoms Among Women i Midlife: Randomized Controlled Trial. *JMIR MHealth UHealth* [Internet]. 2025 June 17 [cited 2026 Feb 12];13:e58204. doi: 10.2196/58204. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC12187029/>
11. Greffin K, Muehlmann M, Pauleikhoff A, Stelling B, Muehlan H, Stach M, et al. Embracing change: Navigating menopause with the help of mobile health apps in Germany. *Compr Psychoneuroendocrinology* [Internet]. 2025 Sept 25 [cited 2026 Feb 12];24:100320. doi: 10.1016/j.cpnec.2025.100320. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC12519169/>
12. Ang SB, Hillard T. Preparing for the future: artificial intelligence in menopausal health care. *Climacteric* [Internet]. 2025 Mar 4 [cited 2026 Feb 12];28(2):95–7. doi: 10.1080/13697137.2025.2469476. Available from: <https://www.tandfonline.com/doi/full/10.1080/13697137.2025.2469476>

13. Garg R, Munshi A. Revolutionizing Menopause Management: Harnessing the Potential of Artificial Intelligence. *J -Life Health* [Internet]. 2024 [cited 2026 Feb 12];15(2):53–4. doi: 10.4103/jmh.jmh_104_24. Available from: <https://pmc.ncbi.nlm.nih.gov/articles/PMC11321517/>
14. Onyinyechi Vivian A, IfiokeEffiong U. Improved Model for Menopause Management using Artificial Neural Network (ANN. *International Journal of Advances in Engineering and Management (IJAEM)*; 2025. doi: 10.35629/5252-0708768774.
15. Sillence E, Hardy C, Kemp E. "This App Just Gets Me": Assessing the Quality, Features and User Reviews of Menopause Smartphone Apps. *J Consum Health Internet* [Internet]. 2023 Apr 3 [cited 2026 Feb 12];27(2):156–72. doi: 10.1080/15398285.2023.2204287. Available from: <https://www.tandfonline.com/doi/full/10.1080/15398285.2023.2204287>
16. Andrews R, Lancaster D, Bache K, Lacey AS. Does Health & Her app use improve menopausal symptoms? A longitudinal cohort study. *BMJ Open* [Internet]. 2023 [cited 2026 Feb 12];13(12):e077185. Available from: <https://bmjopen.bmj.com/content/13/12/e077185.abstract>
17. Kim NY, Han DH, Hong JS, Shim Y, Yoon YJ, Kim HJ, et al. Validation of the efficacy of a personalized information-provision and exercise-coaching app on the quality of life of menopausal women. *Maturitas* [Internet]. 2024 [cited 2026 Feb 12];189:108113. Available from: <https://www.sciencedirect.com/science/article/pii/S0378512224002081>
18. Karam J, Paul MM, Shufelt C, Ravikumar P, Fratianni AM, Oloyede S, et al. Evaluating the Efficacy of a Mobile Phone App in Enhancing Menopause Knowledge and Shared Decision-Making: Protocol for a Randomized Controlled Trial. *JMIR Res Protoc* [Internet]. 2025 [cited 2026 Feb 12];14(1):e76536. Available from: <https://www.researchprotocols.org/2025/1/e76536/>
19. Chao Q, Ma W, Xu R, Wu L, Zhang Y, He M, et al. Menopausal Women's Health Care Method Based on Computer Nursing Diagnosis Intelligent System. Singh DrD, editor. *J Healthc Eng* [Internet]. 2021 July 24 [cited 2026 Feb 12];2021:1–12. doi: 10.1155/2021/4963361. Available from: <https://www.hindawi.com/journals/jhe/2021/4963361/>
20. De P, Haque SM. Recent Trends and Techniques in Monitoring Menopausal Transition. In: *Utilizing AI Techniques for the Perimenopause to Menopause Transition* [Internet]. IGI Global; 2024 [cited 2026 Feb 12]. p. 93–123. Available from: <https://www.igi-global.com/chapter/recent-trends-and-techniques-in-monitoring-menopausal-transition/354575>
21. Sarkar P. Developing Explainable AI Models to Identify Perimenopause Symptoms. In: *Utilizing AI Techniques for the Perimenopause to Menopause Transition* [Internet]. IGI Global; 2024 [cited 2026 Feb 12]. p. 215–41. Available from: <https://www.igi-global.com/chapter/developing-explainable-ai-models-to-identify-perimenopause-symptoms/354580>
22. Mall P, Raina D. Developing Explainable AI Models to Identify Perimenopause Symptoms: Identification of Symptoms for Perimenopause. In: *Utilizing AI Techniques for the Perimenopause to Menopause Transition* [Internet]. IGI Global; 2024 [cited 2026 Feb 12]. p. 201–14. Available from: <https://www.igi-global.com/chapter/developing-explainable-ai-models-to-identify-perimenopause-symptoms/354579>
23. Negmatova G, Baxronova C, Iskandarova F. GLOBAL PERSPECTIVES ON PRECISION MANAGEMENT OF MENOPAUSAL SYNDROME. *Probl Solut Sci Innov Res* [Internet]. 2025 [cited 2026 Feb 12];2(6):102–7. Available from: <https://universalconference.us/universalconference/index.php/pssir/article/view/4693>
24. Deva R, S M, Zhou J, Chahine EB, Davenport-Nicholson A, Kaonga NN, et al. A Mixed- Methods Evaluation of LLM-Based Chatbots for Menopause [Internet]. *arXiv*; 2025 [cited 2026 Feb 12]. doi: 10.48550/arXiv.2502.03579. Available from: <http://arxiv.org/abs/2502.03579>
25. Karam J, Shufelt C, Safwan N, Kapoor E, Christmas MM, Faubion SS. Evaluation of the accuracy and readability of large language model responses on menopause and hormone therapy. *Menopause* [Internet]. 2024 [cited 2026 Feb 12];10–1097. Available from: https://journals.lww.com/menopausejournal/fulltext/9900/evaluation_of_the_accuracy_and_readability_of.566.aspx
26. Logapriya E, Surendran R, Soniya M, Kumar PS. Personalized Shatavari Nutrition Recommendations for Menopausal Women using Machine Learning Algorithms. In: *2024 5th International Conference on Smart Electronics and Communication (ICOSEC)* [Internet]. IEEE; 2024 [cited 2026 Feb 12]. p. 1342–9. Available from: <https://ieeexplore.ieee.org/abstract/document/10722322/>
27. Logapriya E, Surendran R, Appathurai K. Optimizing Health Through Nutrition: Machine Learning Insights for Menopausal Women. In: *2024 International Conference on Innovation and Intelligence for Informatics, Computing, and Technologies (3ICT)* [Internet]. IEEE; 2024 [cited 2026 Feb 12]. p. 94–101. Available from: <https://ieeexplore.ieee.org/abstract/document/10824417/>
28. Huang WC, Chen IS, Yu HC, Chen CS, Wu FZ, Hsu CL, et al. A simple and user-friendly machine learning model to detect osteoporosis in health examination populations in Southern Taiwan. *Bone Rep* [Internet]. 2025 [cited 2026 Feb 12];24:101826. Available from: <https://www.sciencedirect.com/science/article/pii/S2352187225000038>
29. Fang Y, Xu Y, Ding H, Zhao J, Wang Y, Jin H. A method and practice for menopausal disease prediction based on knowledge graph. In: *2023 IEEE International Conference on Medical Artificial Intelligence (MedAI)* [Internet]. IEEE; 2023 [cited 2026 Feb 12]. p. 10–8. Available from: <https://ieeexplore.ieee.org/abstract/document/10403192/>
30. Pham ANQ, Cummings M, Yuksel N, Sydora B, Williamson T, Garies S, et al. Development and validation of a case definition for problematic menopause in primary care electronic medical records. *BMC Med Inform Decis Mak* [Internet]. 2023 Oct 5 [cited 2026 Feb 12];23(1):202. doi: 10.1186/s12911-023-02298-x. Available from: <https://bmcmmedinformdecismak.biomedcentral.com/articles/10.1186/s12911-023-02298-x>
31. Mishra P. Optimizing Perimenopausal Care: A Deep Dive Into Explainable AI. In: *Utilizing AI Techniques for the Perimenopause to Menopause Transition* [Internet]. IGI Global; 2024 [cited 2026 Feb 12]. p. 242–81. Available from: <https://www.igi-global.com/chapter/optimizing-perimenopausal-care/354581>
32. Vargas-Hernandez VM. Artificial Intelligence in Menopause Management. *Mathews J Gynecol Obstet* [Internet]. 2025 [cited 2026 Feb 12];9(1):1–4. Available from: <https://www.mathewsopenaccess.com/full-text/artificial-intelligence-in-menopausemanagement>
33. Shaklai S, Serebro M, Greenman Y, Yom-Tov E. Hot flashes linked to linguistic markers of cognitive impairment: observational study of social media posts. *Menopause* [Internet]. 2024 [cited 2026 Feb 12];10–1097. Available from: https://journals.lww.com/menopausejournal/fulltext/9900/hot_flashes_linked_to_linguistic_markers_of.579.aspx
34. Branquinho M, Monteiro F, Fonseca A. Development of a CBT-Based e-Health Intervention for Menopausal Symptoms ("Cuidar-ME"): Perspectives from Mental Health Professionals and (Peri)menopausal Women. *Int J Cogn Behav Ther* [Internet]. 2025 Sept 9 [cited 2026 Feb 12]; doi: 10.1007/s41811-025-00266-z. Available from: <https://link.springer.com/10.1007/s41811-025-00266-z>
35. Pourshahrokhi N, Hunter MS, Bazrafshan F, Ahmadian L. A randomized controlled trial comparing mobile-app-based cognitive behavioral therapy with and without therapist support versus face-to-face therapy: study protocol. *Eur J Obstet Gynecol Reprod Biol* [Internet]. 2025 [cited 2026 Feb 12];114662. Available from: <https://www.sciencedirect.com/science/article/pii/S0301211525009388>
36. Scheffrahn K, Hall C, Mu z V, Elkins G. User Outcomes for an App-Delivered Hypnosis Intervention for Menopausal Hot Flashes: Retrospective Analysis. *JMIR Form Res* [Internet]. 2025 [cited 2026 Feb 12];9:e63948. Available from: <https://formative.jmir.org/2025/1/e63948>

37. Donohoe F, O'Meara Y, Roberts A, Comerford L, Valcheva I, Kearns U, et al. Multimodal, Technology-Assisted Intervention for the Management of Menopause after Cancer Improves Cancer-Related Quality of Life—Results from the Menopause after Cancer (Mac) Study. *Cancers* [Internet]. 2024 [cited 2026 Feb 12];16(6):1127. Available from: <https://www.mdpi.com/2072-6694/16/6/1127>
38. Schei TS, Abernethy K. The impact of a specialist-led digital health application on menopause symptoms in the workplace: A single-arm, longitudinal evaluation. *Maturitas* [Internet]. 2024 [cited 2026 Feb 12];187:108005. Available from: <https://www.sciencedirect.com/science/article/pii/S0378512224001002>
39. Ignacio MDO, Martins MG, Portella CFS, Santiago AE, Zangirolami-Raimundo J, Baracat EC, et al. 'Menopausando': a digital health education platform for women in the transition to menopause and postmenopause. *Climacteric* [Internet]. 2025 Sept 9 [cited 2026 Feb 12];1–7. doi: 10.1080/13697137.2025.2548798. Available from: <https://www.tandfonline.com/doi/full/10.1080/13697137.2025.2548798>
40. Shepherd JA, Shiozawa A, Schild AL, Singh D, Mancuso SA. Retrospective text and qualitative analyses of patient experience and management of vasomotor symptoms due to menopause: voices from the PatientsLikeMe community. *Menopause* [Internet]. 2024 [cited 2026 Feb 12];31(9):789–95. Available from: https://journals.lww.com/menopausejournal/fulltext/2024/09000/retrospective_text_and_qualitative_analyses_of.9.aspx
41. De P, Haque SM. Recent Trends and Techniques in Monitoring Menopausal Transition. In: *Utilizing AI Techniques for the Perimenopause to Menopause Transition* [Internet]. IGI Global; 2024 [cited 2026 Feb 12]. p. 93–123. Available from: <https://www.igiglobal.com/chapter/recent-trends-and-techniques-in-monitoring-menopausal-transition/354575>

Section 13

CLINICAL AIDS

- 57. Setting up a Menopause Clinic
- 58. Menopause Proforma
- 59. Management tools
- 60. Pathways
- 61. Prescription writing for Menopausal symptoms

SETTING UP A MENOPAUSE CLINIC

Keywords: Levels of care, requirements

57

AIM

To offer comprehensive, friendly services under one roof for the care of climacteric and geriatric women. These specialised menopause clinics are meant to be dedicated to meeting the unique and changing medical needs of women from perimenopause through the golden years.

LEVELS OF CARE

Level I-Primary Care Unit- Primary Physician Led – First-contact care, screening, lifestyle counselling, basic management, and referral when indicated.

Level II- Secondary Care Unit Gynaecologist Led – Comprehensive gynaecological evaluation, initiation of hormonal and nonhormonal therapies, and management of gynaecological comorbidities

Level III-Tertiary Care Unit- Menopause specialist and multidisciplinary unit – Advanced, risk-stratified care by menopause specialists in collaboration with multidisciplinary teams, including cross-speciality referrals

REQUIREMENTS

Level I--- Primary Care Unit

Premises: Waiting area and consultation room.

Personnel: Core Team---Primary Physician and a Paramedic.

Instruments and equipment: Weight machine, stadiometer, sphygmomanometer, measuring tape, thermometer, speculum of various sizes, acetic acid, Lugol's Iodine, pH sticks, examination table with provision for lithotomy position, Pap's smear kits, ultrasound(optional)

Stationary: Menopause porforma, Risk assessment tools(BMI Chart, Risk assessment charts - OSTA, Globorisk-India, SARC-F Questionnaire), prescription pads, investigation requisition forms, educational charts and leaflets, computer(optional).

Level II - Secondary Care Unit

Premises: Reception, waiting area and consultation rooms, counselling room, well-equipped laboratory, and minor operation theatre.

Personnel: Gyneacologist, nutritionist, physiotherapist, counsellor and paramedical personnel.

Ancillary Team: Visiting consultants to be invited on predetermined days as needed; may include: Endocrinologist, Physician, Cardiologist. Orthopaedic Surgeon, Neurologist, Psychiatrist, Ophthalmologist, Urologist, Physiotherapist, Nutritionist, Dentist, Psychologist/Counsellor.

Instruments and equipment: Weight machine, stadiometer, sphygmomanometer, measuring tape, thermometer, speculum of various sizes, acetic acid, Lugol's Iodine, pH sticks, examination table with provision for lithotomy position, Pap's smear kits, ultrasound machine, colposcope, hysteroscope.

Stationary: Menopause forms, prescription pads, Risk assessment tools(BMI Chart, Risk assessment charts - OSTA, Globorisk-India, SARC-F Questionnaire), investigation requisition forms, educational charts and leaflets, and a computer.

Level III - Tertiary Care Unit

Premises: Reception, waiting area and consultation rooms, counselling room, well-equipped laboratory, and minor operation theatre.

Personnel: Menopause Specialist, nutritionist, physiotherapist, counsellor, paramedical personnel and allied speciality consultants.

Instruments and equipment: Weight machine, stadiometer, sphygmomanometer, measuring tape, thermometer, speculum of various sizes, acetic acid, Lugol's Iodine, pH sticks, examination table with provision for lithotomy position, Pap's smear kits, ultrasound, DXA colposcope, hysteroscope, mammography.

Stationary: Menopause porforma, prescription pads, investigation requisition forms, educational charts and leaflets, computer. Risk assessment tools (BMI Chart, Risk assessment charts - OSTA, Globorisk-India, SARC-F Questionnaire).

Essential For Both Levels Of Care

Documentation, record-keeping, and a client recall system are essential to maintaining continuity of comprehensive health care.

Use of Internet: A clinic website and email services may save a lot of time. We can also set up a helpline via this medium or by phone.

Optional:- Affiliated non-medical services for aesthetic care, hobbies, and occupational therapy. Seminars, workshops, helpline training program for professionals, educational and group activities for women

CONCLUSION

Every clinician who wants to set up a menopausal clinic must ensure that patient visits are kept to a minimum and that the maximum benefit is achieved through a single primary visit each year. A comprehensive, friendly approach would go a long way in popularising such a venture

REFERENCES

1. Malik S. (2010). FOGSI FOCUS: The Menopause. [online] Available from issuu.com/fogsi/docs/menopause_booklet. [Accessed July, 2016].
2. Jha UP. Menopause and the role of HRT in Indian women-A Second National Revised Consensus and Policy Development Document. 2002.
3. Unni J. Updated recommendation of postmenopausal hormone therapy. International Menopause Society. J Indian Menopause Society Suppl. 2007. pp. 17-19.

MENOPAUSE PROFORMA

IMS - INDIAN MID-LIFE REGISTRY LEVEL3

Name: _____ Date: _____
 Age: _____ Reg. No.: _____
 Marital status: _____ Tel. No.: _____
 Occupation: _____ Address: _____
 Community: _____ Socioeconomic status: _____
 Age at menopause: _____ Urban/Rural: _____ Educational Status: _____
 Type of menopause: _____ Natural/Surgical/Premature: _____
 If surgical date: _____ Indications: TAH/TAH with USOP/TAH with BSOP
 Complaints: _____

MENOPAUSE SYMPTOMS (Form in Medical History)

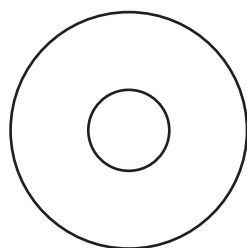
0 None; 1 Mild; 2 Moderate; 3 Severe; 4 Very severe

Visit	1	2	3	4	5	6	7	8	9	10
1. Hot flushes, sweating										
2. Heart discomfort										
3. Sleep problems										
4. Depressive mood										
5. Irritability										
6. Anxiety										
7. Physical and mental exhaustion										
8. Sexual problems										
9. Bladder problems**										
10 .Dryness of the vagina*										
11. Joint and muscular discomfort										
12. Overall assessment										

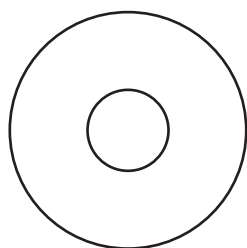
Others: Dry skin/Crawling under the skin/New facial hair/Change in weight
 First symptom of menopause:
 Gynecological history: Menstrual cycle: Regular/Irregular
 Flow pattern before menopause: No change/Stopped abruptly/Scanty
 Irregular: Short cycle/Long cycle/Mixed duration:
 History of PMS/Dysmenorrhea/Mastalgia/Mood change/Menstrual headache/PCOD/Fibroid/
 Endometriosis
 Any other:
 Obstetric history: PLA LCB
 Lactation: Complete/Incomplete duration-Postpartum depression:
 Contraception:
 Surgical history:
 Family history: DM/HTN/IHD/Stroke/Cancer/Early menopause/Osteoporosis/Alzheimer's /Psychotic
 illness Personal history: DM/HTN/IHD/Dyslipidemia/Asthma/Gallstones/Rheumatoid
 arthritis/Psychotic illness/Thy-roid
 Addiction: Caffeine/Alcohol/Tobacco
 Allergies:
 Medication:
 Diet: Veg/Non-veg/Adequate in calcium
 Milk/Milk Products - Y/N - Cup- : legumes-Y/N: millets-Y/N: vegetables-Y/N: til/sesame-Y/N: nuts-Y/N
 Routine physical activity: Sedentary/Household/Heavy work
 Exposure to sunlight: Duration- : Time of the day-
 Exercise: Walking/Yoga/Aerobic/Resistance (hours/week)
 Mental attitude: Positive/Negative
 Spiritual attitude: Yes/No
 Hobbies:
 Recent stressful events:
 Physical examination: Height: Weight: BMI: Hip/Waist ratio
 BP: PR: Heart: Lung: Thyroid:
 Teeth: Eye: Ears: Spine:
 Varicosities: Lymph nodes: Edema:
 Skin: Hair: frontal balding/Hirsutism
 Muscle mass and strength: Getting up from chair-Easily/With difficulty

Date	Breast -R/L	BP	HT	WT	WC

Breast: Dense/Granular/Nodular/Lump



Right



Left

Abdomen:

Local:

Vulva:

P/V:

Urethra:

Vestibule:

Vagina:

Cervix:

P/R:

Investigations and Follow-up:

Date								
CBP, ESR								
Urine analysis								
Urine C/S								
Vaginal pH								
RBS								
FBS								
HbA1c								
25OH Vitamin D								
STSH								
Cholesterol								
Triglyceride								
HDL								
LDL								
VLDL								
Blood urea								
Serum creatinine								
LFT								

Stool for occult blood								
Serum FSH								
Serum estradiol								

Date								
Pap smear								
Colposcopy								
Ultrasound								
Endometrial biopsy								
Mamography Right/Left								
Ultrasound Breast Right/Left								

DXA	Date							
Hip	BMD							
	T							
	Z							
	Impression							
Spine	BMD							
	T							
	Z							
	Impression							
Radius	BMD							
	T							
	Z							
	Impression							

Comprehensive chart for grading the health status based on tools for invasive breast cancer, CVD and Skeletomuscular health

Tools	5/10 Yr Risk Score	Lifetime Risk Score	Status
Invasive Breast Cancer Gail			
GloboRisk-India			
OSTA/SCORE/FRAX			
SARC-F			

Group 1. Healthy, no VMS/Healthy with risk factors for disease, no VMS/Healthy with latent risk factors for disease, no VMS/Healthy with comorbidities no VMS

Group 2. Healthy, with VMS/Healthy with risk factors for disease, with VMS / Healthy with latent risk factors for disease, with VMS/Healthy with comorbidities with VMS

Consent

I certify that I have explained the nature, purpose, benefits, risks and alternatives to the proposed treatment procedure. I have also offered to answer any questions and have fully answered all such questions. I believe that the patient/relative/guardian has fully understood what I have explained and answered.

Doctor

Patient

Signature:

Name:

Management:

Table 1: Menopause Rating Scale

Which of the following symptoms apply to you at this time?					
(X ONE Box For EACH Symptom) For Symptoms That Do Not Apply, Please Mark “None”).					
Symptoms:	None	mild	moderate	Severe	extremely severe
Score	0	1	2	3	4
1. Hot flashes, sweating (episoded of sweating)					
2. Heart discomfort (unusual awareness of heart beat, heart skipping, heart racing, tightness)					
3. Sleep problems (difficulty in falling asleep, difficulty in sleeping through the night, waking up early)					
4. Depressive mood (feeling down, sad, on the verge of tears, lack of drive, mood swings)					
5. Irritability (feeling nervous, inner tension, feeling aggressive)					
6. Anxiety (inner restlessness, feeling panicky)					
7. Physical and mental exhaustion (general decrease in performance, impaired memory, decrease in concentration, forgetfulness)					
8. Sexual problems (change in sexual desire, in sexual activity and satisfaction)					
9. Bladder problems (difficulty in urinating, increased need to urinate, bladder incontinence)					
10. Dryness of vagina (sensation of dryness or burning in the vagina, difficulty with sexual intercourse)					
11. Joint and muscular discomfort (pain in the joints, rheumatoid complaints)					

The degree of symptoms at each visit is documented to assess the severity of symptoms and to follow up on the effectiveness of treatment.

Table 2: Sleep: Insomnia Severity Index, 7-item questionnaire

Description	1	2	3	4	5
1. Difficulty falling asleep					
2. Difficulty staying asleep					
3. Problems waking up too early					
4. Satisfaction with current sleep					
5. Interference with daily functioning					
6. Noticeability of sleep problems by others					
7. Worry/distress about sleep problem					

Total Score: 28 cut-offs: 0-7: No clinically significant insomnia, 8-14: Subthreshold insomnia, 15-21: Moderate insomnia, > 22: Severe insomnia

Table 3: Psychological Health, Patient Health Questionnaire-4, past 2 weeks

Description	0	1	2	3
Little interest or pleasure in doing things				
Feeling down, depressed, or hopeless				
Feeling nervous, anxious, or on edge				
Not being able to stop or control worrying				

Each item scored 0-3; Total Score: 0-12 > 6 suggests clinically relevant psychological distress insomnia

Table 4 Sexual Health: Female Sexual Function Index (FSFI-6): 6-item short form:

	Description (Range)	1	2	3	4	5
1. Desire	Very low → Very high					
2. Arousal	No arousal → Very high arousal					
3. Lubrication	None → Adequate					
4. Orgasm	Never → Almost always					
5. Satisfaction	Very dissatisfied → Very satisfied					
6. Pain	Always pain → No pain					

Total score: / 30

A score ≤19 suggests dysfunction

Table 5 Dietary calcium intake calculator

Source	Calcium (mg)	Number of Total serving	Total calcium (mg)
Dairy	300-525/1 glass milk		
Non-dairy(Default from a balanced diet)	300/1 Katori curds		
Total intake of calcium in mg	200-300		

RISK ASSESSMENT TOOLS

Breast Cancer

The Breast Cancer Risk Assessment Tool, Gail Model, allows health professionals to estimate a woman's risk of developing invasive breast cancer over the next 5 years and up to age 90 (life-time risk).

The tool uses a woman's personal medical and reproductive history and the history of breast cancer among her first-degree relatives (mother, sisters, daughters) to estimate absolute breast cancer risk, her chance or probability of developing invasive breast cancer in a defined age interval.

It needs to be validated in India. This simple tool may be used in the absence of a country-specific validated tool. (Available at <https://www.cancer.gov/bcrisktool>) and classify the women into three groups.

Table 6. Classify breast cancer risk

Method	Low	Moderate	High
Gail Model	<1.67	1.6-5	> 5

Breast Self-Examination (BSE)

BSE is performed by the woman herself and involves examination of the breast, skin and axillae based on palpations by her hands. BSE is recommended so that women understand their breasts for detecting any suspicious changes over time.

BSE should be done immediately after periods or on any fixed day of the month if they are not menstruating. The nodular and lumpy feel of the breast, along with increased pain and tenderness, are physiological findings prior to menstruation and need to be explained to the patient.

Women can be taught to examine their breasts in any of the following ways in both supine and standing positions

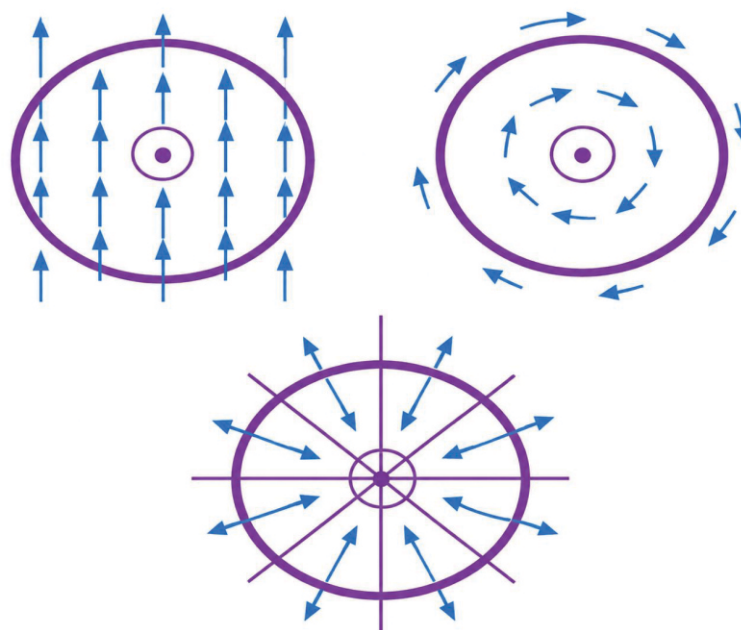


Figure 1 Self breast examination

Screen for Cardiovascular Disease: Refer to Chapter 12. Recommend using Globorisk-India (laboratory or non-laboratory version). use the web calculator at www.globorisk.org or the validated desk/pocket chart)

GLOBALRISK CARDIOVASCULAR RISK PREDICTION CHART

Global Risk Charts estimate the 10-year risk of fatal and non-fatal cardiovascular disease (myocardial infarction and stroke) using country-specific data.

They are simple to use by the paramedics and the clinician, simplified, evidence-based tools suitable for population-level risk estimation and useful tools for guiding management and treatment decisions The charts can help prevent heart attacks and strokes, particularly when used by health workers in primary care.

WHEN ARE THE CHARTS USEFUL FOR STRATIFYING RISK?

Charts are useful for stratifying risk for people with blood pressure <160/100 mm Hg, blood cholesterol <8 mmol/l, or uncomplicated diabetes.

An individual is classified as a high, medium, or low risk over 10 years.

THE FOLLOWING COME UNDER HIGH RISK CATEGORY, NO RISK ASSESSMENT, THEY NEED TO BE TREATED

Persistent raised blood pressure >160/100 mm Hg or blood cholesterol >8 mmol/l or established ischemic heart disease, or diabetes with renal disease.

NOTE THAT CVD RISK MAY BE HIGHER THAN INDICATED BY THE CHARTS IN THE PRESENCE OF THE FOLLOWING :

Already on antihypertensive therapy, premature menopause, obesity (including central obesity);

Already on antihypertensive therapy, premature menopause, obesity (including central obesity); sedentary lifestyle, family history of premature coronary heart disease (CHD) or stroke in first-degree relative (male < 55 years, female < 65 years); raised levels of C-reactive protein, microalbuminuria (indicates increased cardiovascular risk.)

There are two sets of charts.

1. One set can be used in settings where blood cholesterol cannot be measured.

2. The second set is for settings in which blood cholesterol can be measured.

How do you use the charts to assess cardiovascular risk?

- First, make sure that you select the appropriate chart
- If blood cholesterol cannot be measured due to resource limitations, use the charts that do not have total cholesterol
- Before applying the chart to estimate the 10-year cardiovascular risk of an individual, the following information is necessary

Presence or absence of diabetes • Gender • Smoker or non-smoker • Age • Systolic blood pressure • Total blood cholesterol (if in mg/dl divide by 38 to convert to mmol/l)

Once the above information is available, proceed to estimate the 10-year cardiovascular risk as follows.

Step 1: Select the appropriate chart depending on the presence or absence of diabetes

Step 2 Female tables

Step 3: Select smoker or non-smoker boxes

Step 4: Select age group box (if age is 50-59 years, select 50, if 60-69 years, select 60)

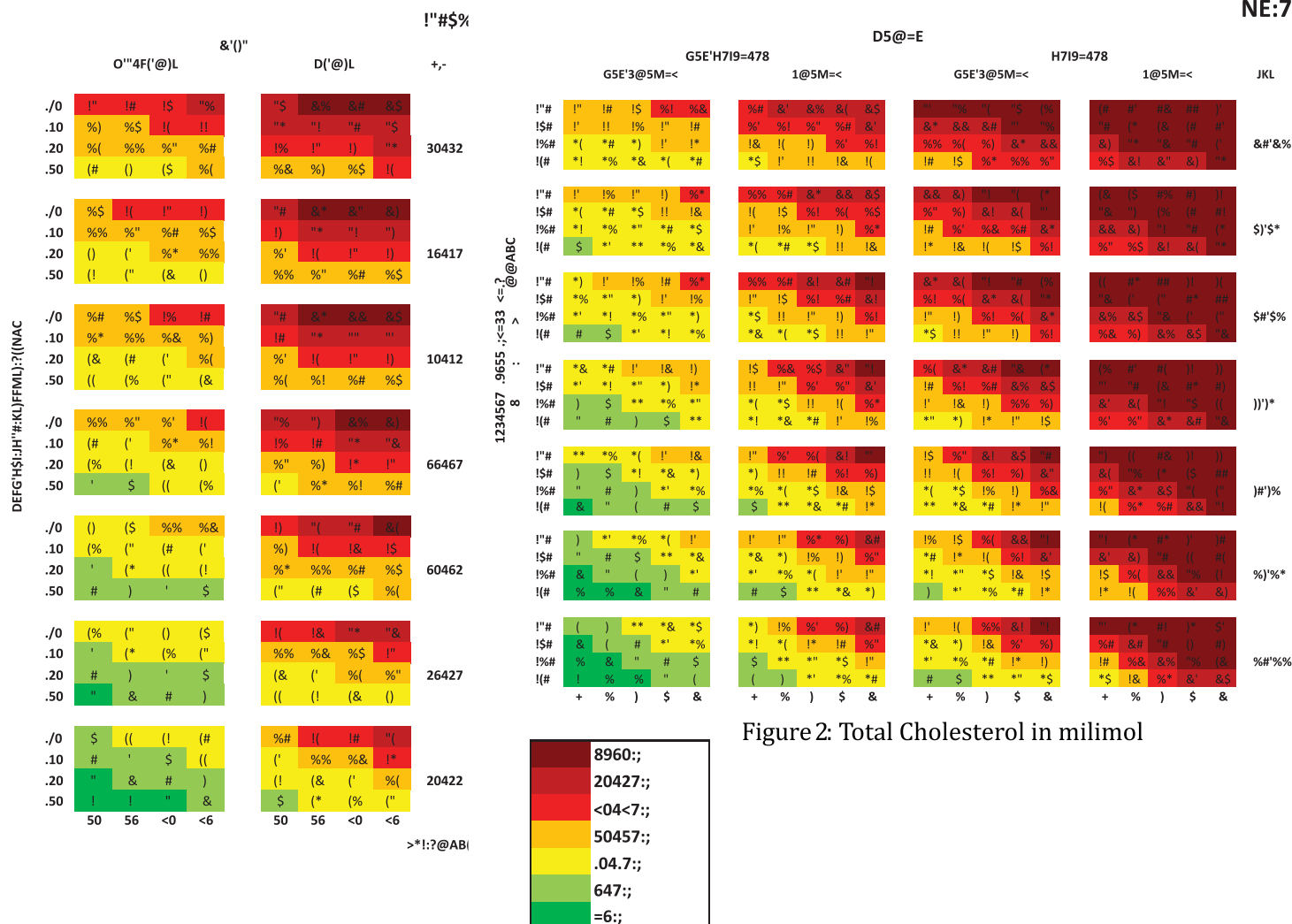
Step 5 Within this box, find the nearest cell where the individual's systolic blood pressure (mm Hg) and total blood cholesterol level (mmol/l) cross.

The colour of this cell determines the 10-year cardiovascular risk. An individual is classified as high risk (maroon and red), medium risk (orange and yellow), or low risk (green) over 10 years.

Globorisk risk prediction charts for India

10 yr risk prediction chart for. CVD event by gender, age, systolic blood pressure, smoking status, cholesterol (with and without) and presence or absence of diabetes mellitus

Refer to Figure 2



Screen for Diabetes: developed by the Indian Diabetes Risk Score (IDRS) to detect undiagnosed Type 2 diabetes. This is a non-invasive and inexpensive way to screen for type 2 Diabetes.
<https://pmc.ncbi.nlm.nih.gov/articles/PMC3659903>

Table 7: Screen for Diabetes with lab results

Test	Prediabetic screen	Diabetes diagnosis
Fasting plasma glucose	100-125mg/d Impaired fasting glucos	≥126mg/dl
2-hr,75g oral glucose tolerance test(GTT)	140-199 mg/dl (impaired glucose tolerance)	≥ 200mg/dl
HbA1c (Glycosylated Hb)	5.7%-6.4%	≥ 6.5%

Screen for Osteoporosis: Refer to Chapter 17 for FRAX, OSTA

Screen for Sarcopaenia: Refer to Chapter 18

Table 8. Screen for Pelvic muscle strength

Grading scale for Pelvic muscle strength (Modified Oxford score).	
0	Lack of muscle response
1	Flicker or nonsustained contraction
2	Presence of low-intensity, but sustained, contraction
3	Moderate contraction feels like an increase in intravaginal pressure that compresses the fingers of the examiner, with small cranial elevation of the vaginal wall
4	Satisfactory contraction, compressing the fingers of the examiner with elevation of the vaginal wall toward the pubic symphysis.
5	Strong contraction, firm compression of the examiner's fingers with positive movement toward the pubic symphysis.

Menopause management: The Indian Mantra. Refer to Figure 3



Figure 3. The Indian Mantra

A sample consent form for prescribing hormone therapy

It is important to understand that, like all medicines, MHT has benefits and possible side effects.

Purpose of MHT: I understand that Menopausal Hormone Therapy is prescribed to manage menopausal symptoms and prevent bone loss in selected women within 10 yrs of natural menopause and during menopause transition. It is strongly recommended for women with premature menopause unless contraindicated.

Benefits Explained: Reduction of increased hot flashes, night sweats, improvement in mood, improved sleep and sexual health, Improvement in vaginal dryness, itching and burning. It prevents postmenopausal bone loss and fractures.

Risks Discussed: all are rare incidents, a small increase in blood clots with oral estrogen in susceptible women, and lower with the nonoral route.

Breast Cancer: Estrogen alone does not increase the risk of breast cancer and has been shown to have 0.7 fewer cases per 1000 women per year in women who have undergone hysterectomy. Estrogen with micronised progesterone or dydrogesterone has minimal breast cancer risk for up to 5 years. Conjugated equine estrogen (CEE) combined with medroxyprogesterone acetate (MPA) was associated with approximately 0.8 additional breast cancer cases per 1000 women per year compared with placebo.

Lifestyle factors such as obesity, physical inactivity and alcohol use contribute more substantially to overall postmenopausal breast cancer risk than MHT.

Side effects discussed: breast tenderness, vaginal bleeding, headaches, bloating.

Patient Responsibilities: Report new symptoms, attend follow-up, and inform if I wish to stop therapy.

Patient Consent

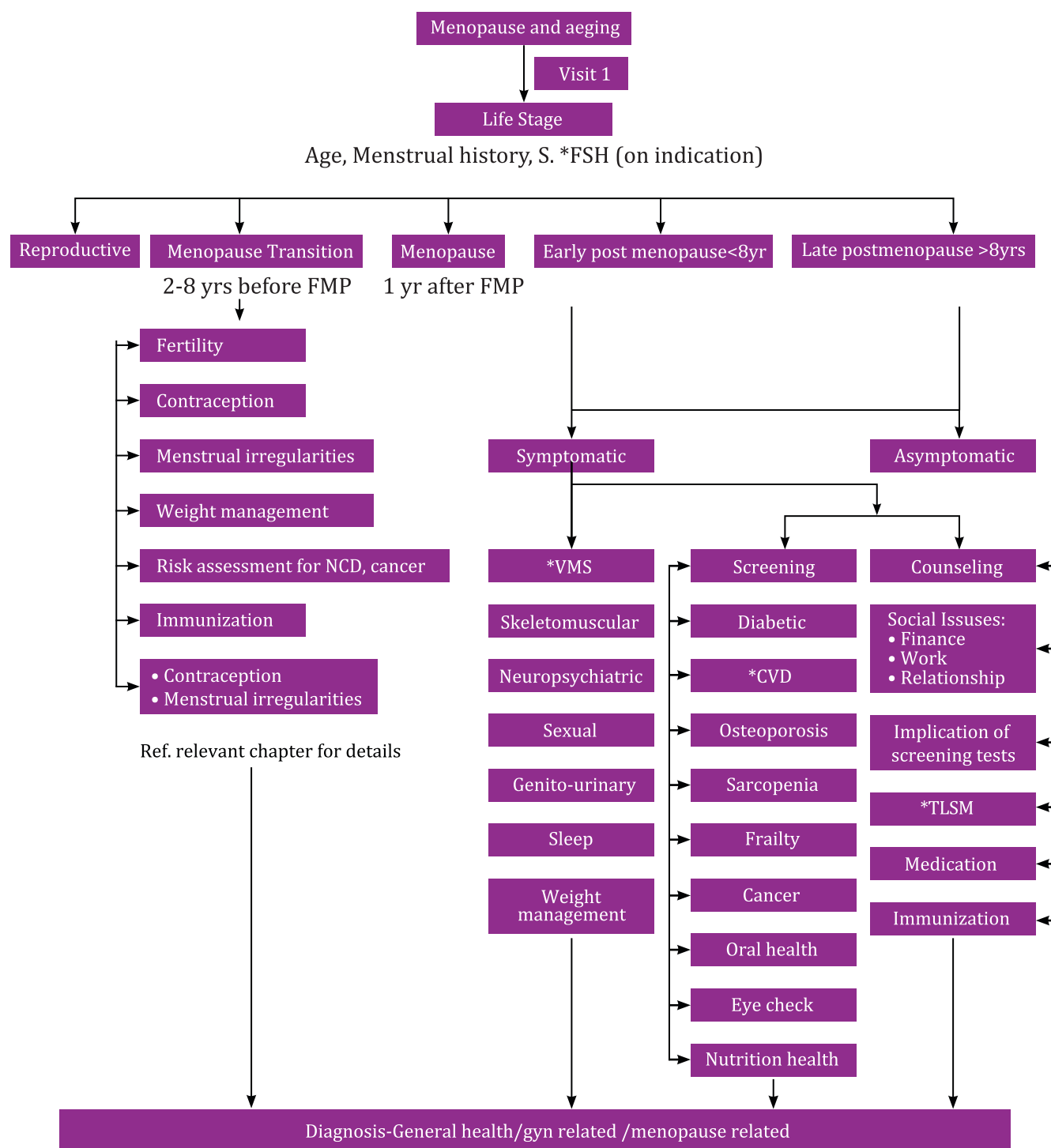
I voluntarily consent to begin/continue MHT.

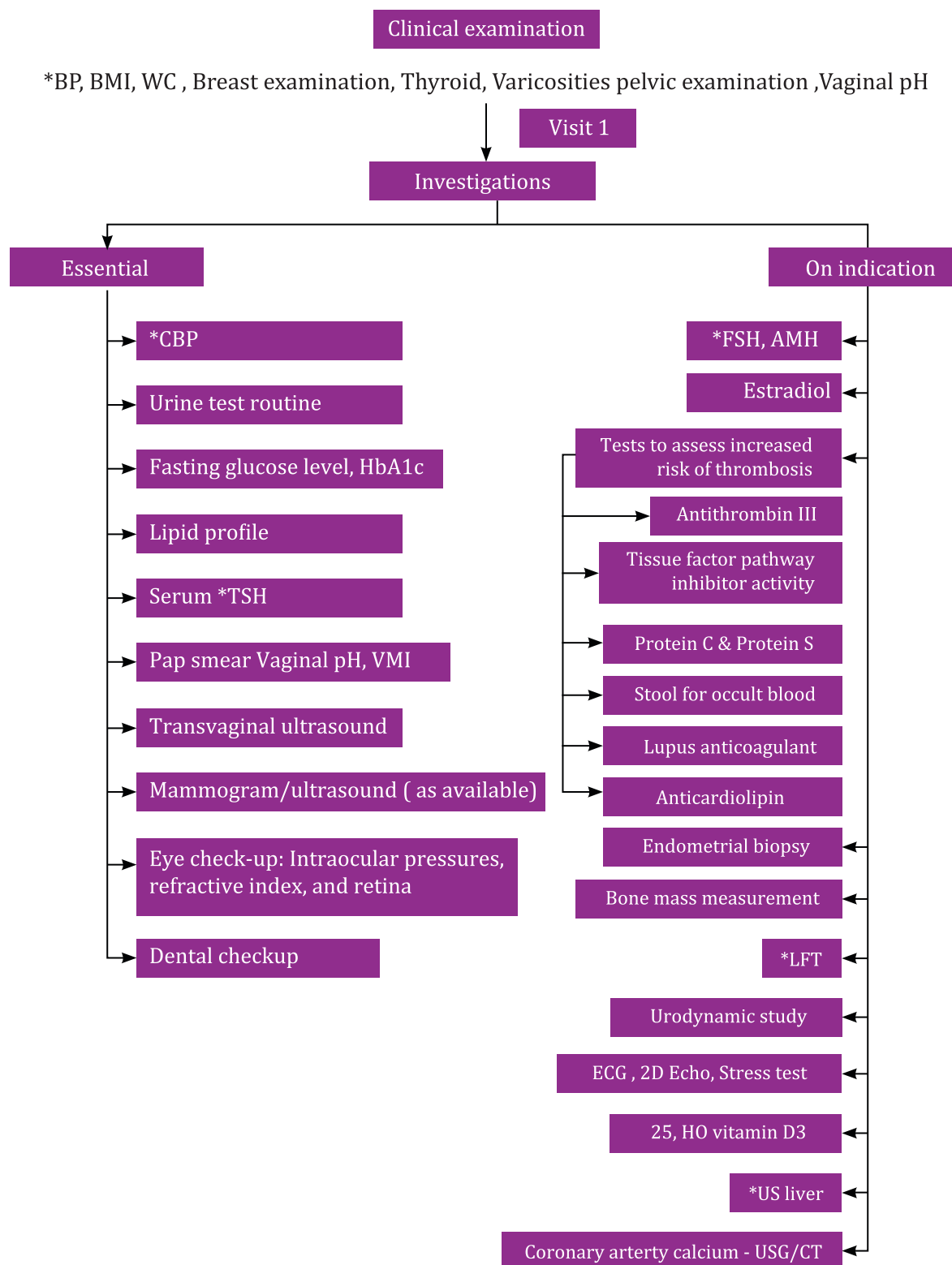
Signature of Patient: _____ Date: _____ Doctor Declaration

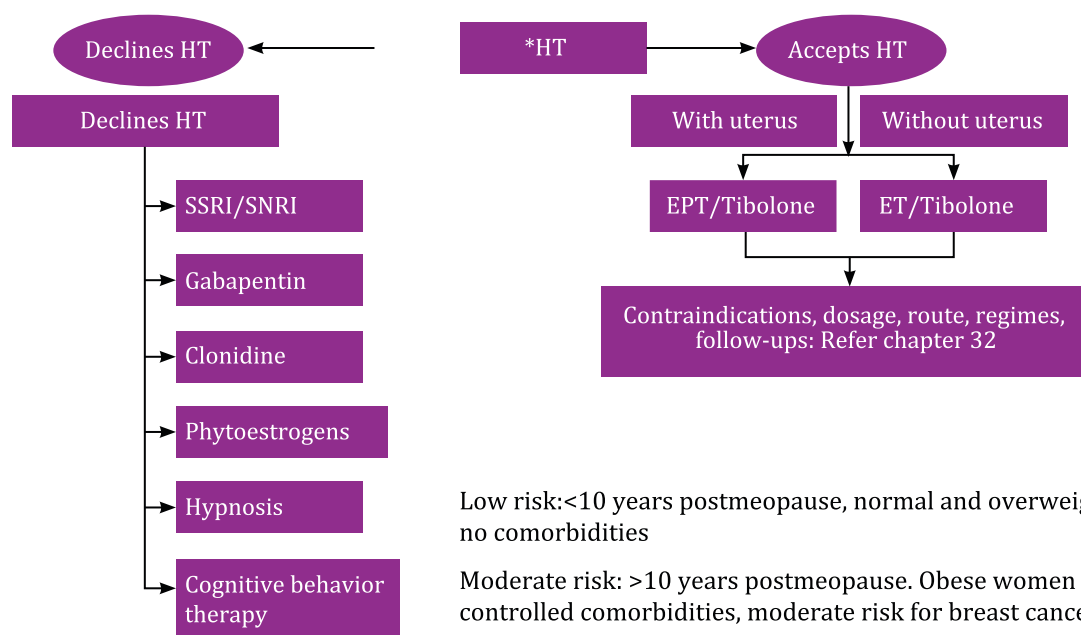
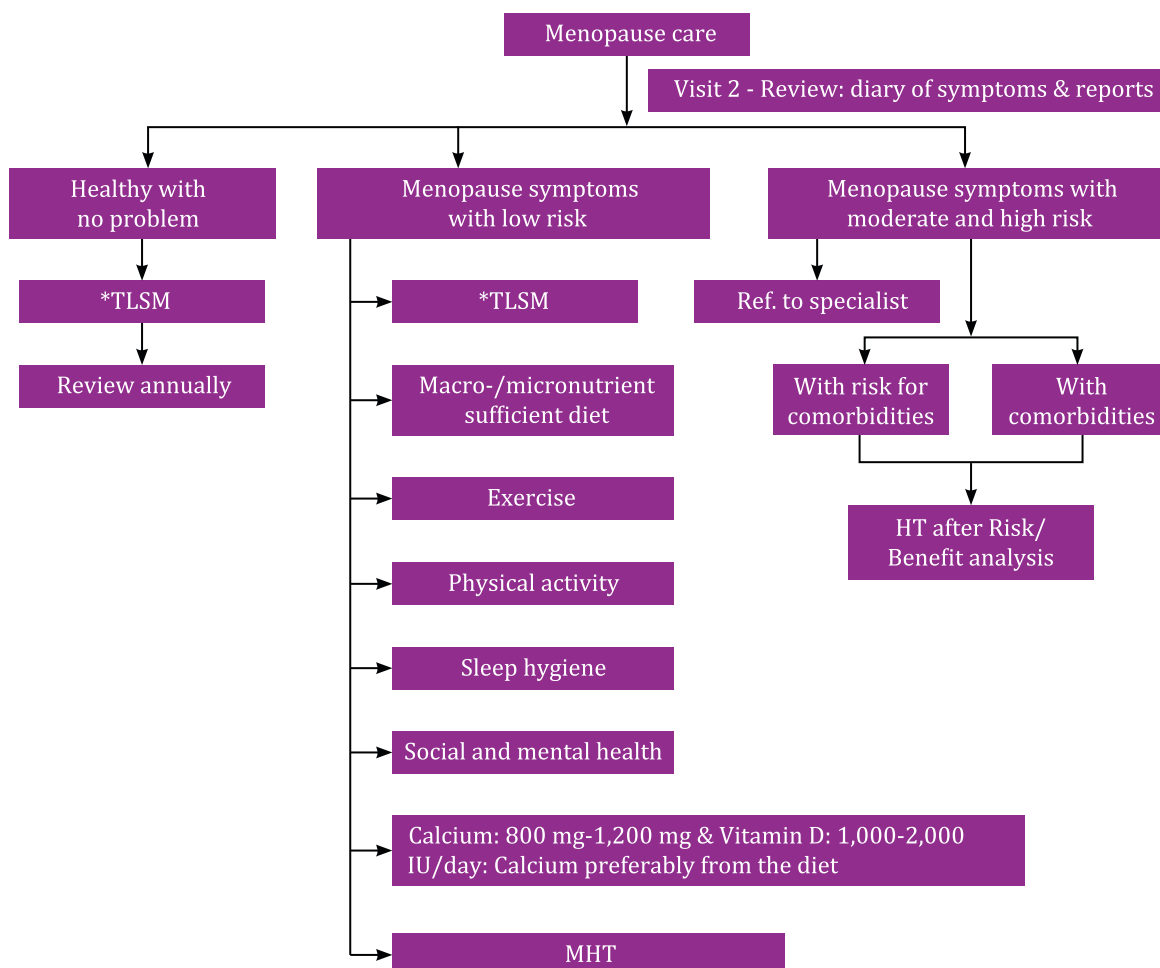
Name of Doctor: _____ Signature: _____

PATHWAYS

Pathways are meant to be a quick reference for the thought process to plan management for the patients. They do not replace the pleasure of leisurely reading the detailed text



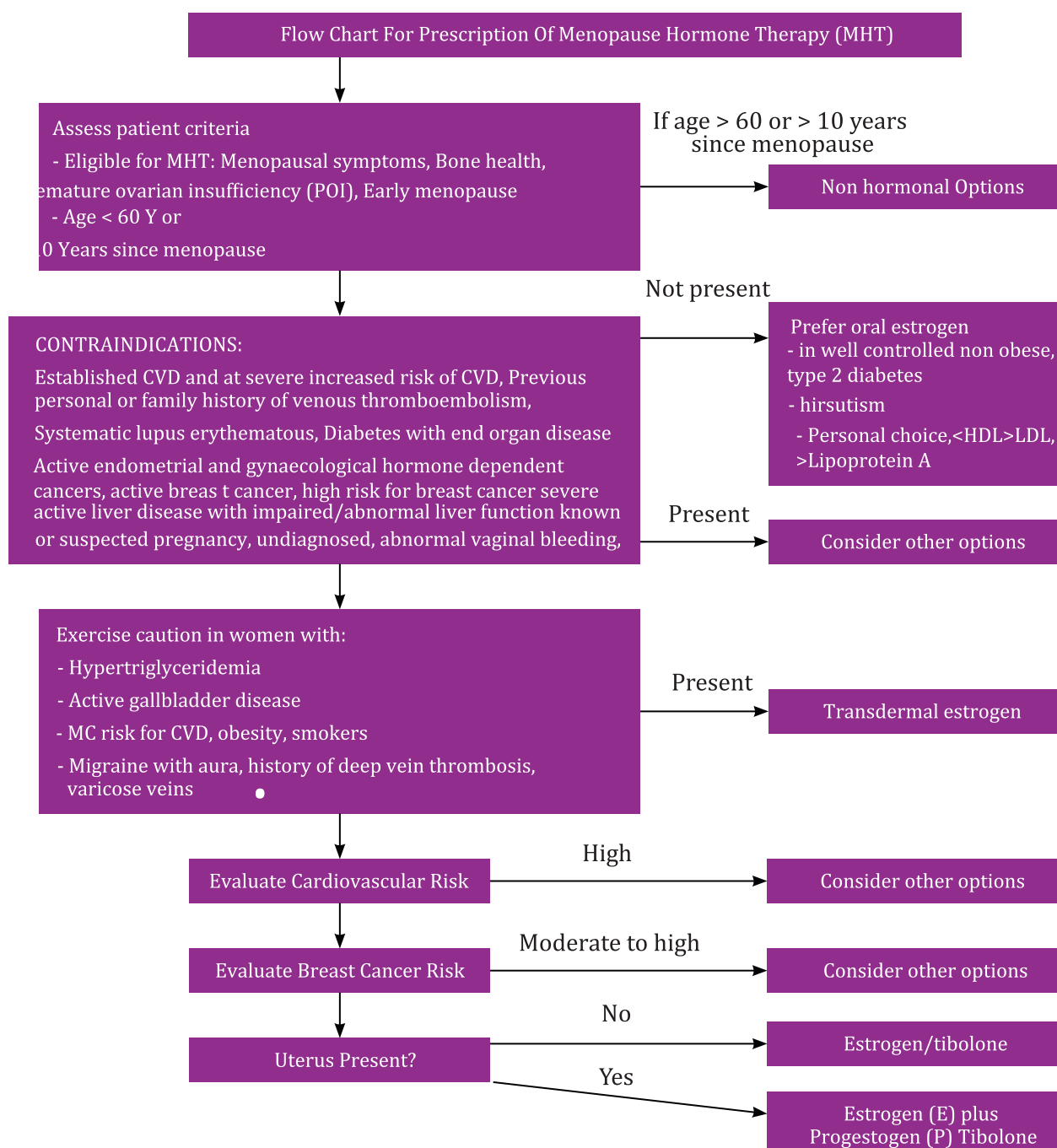


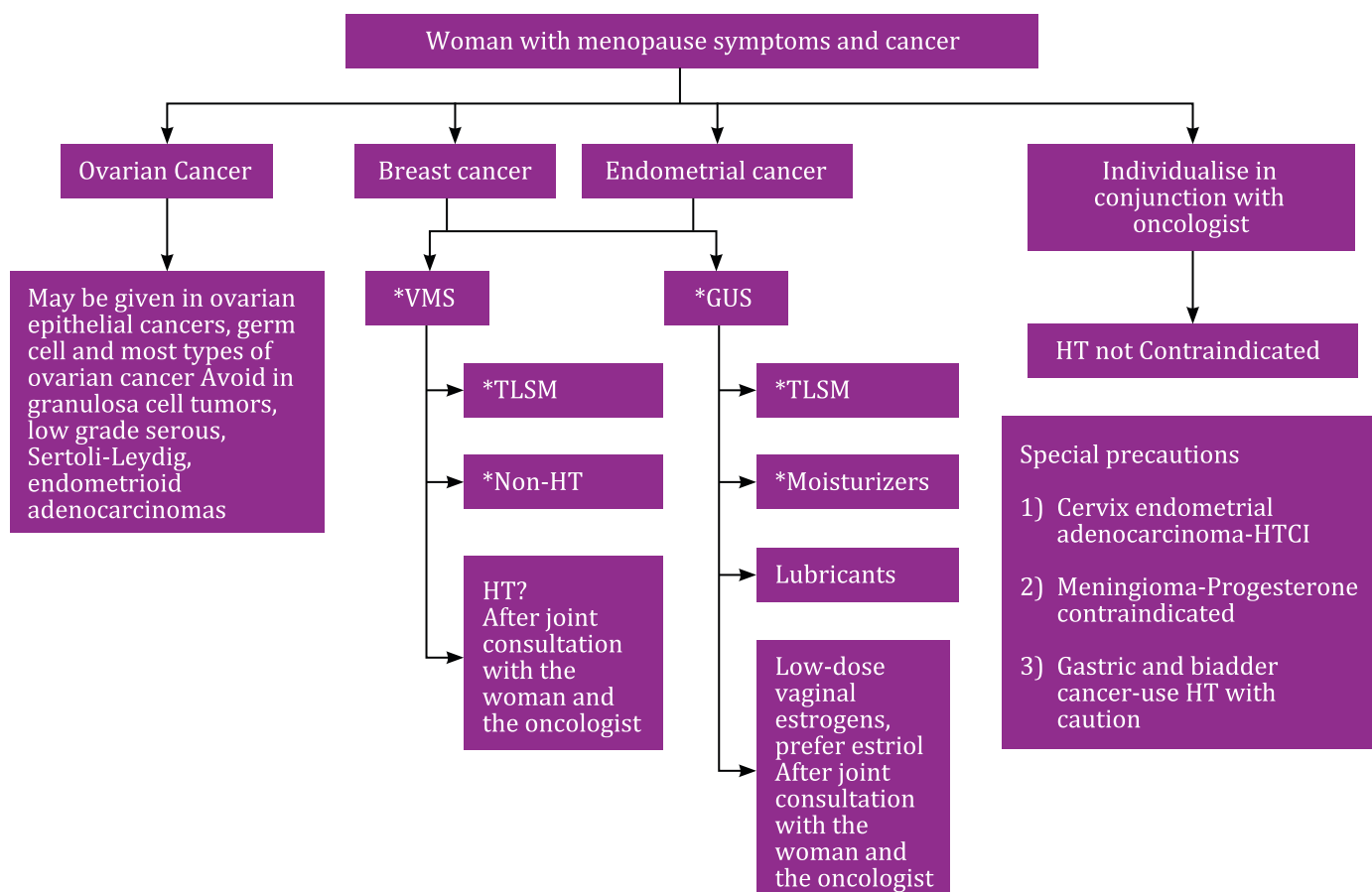


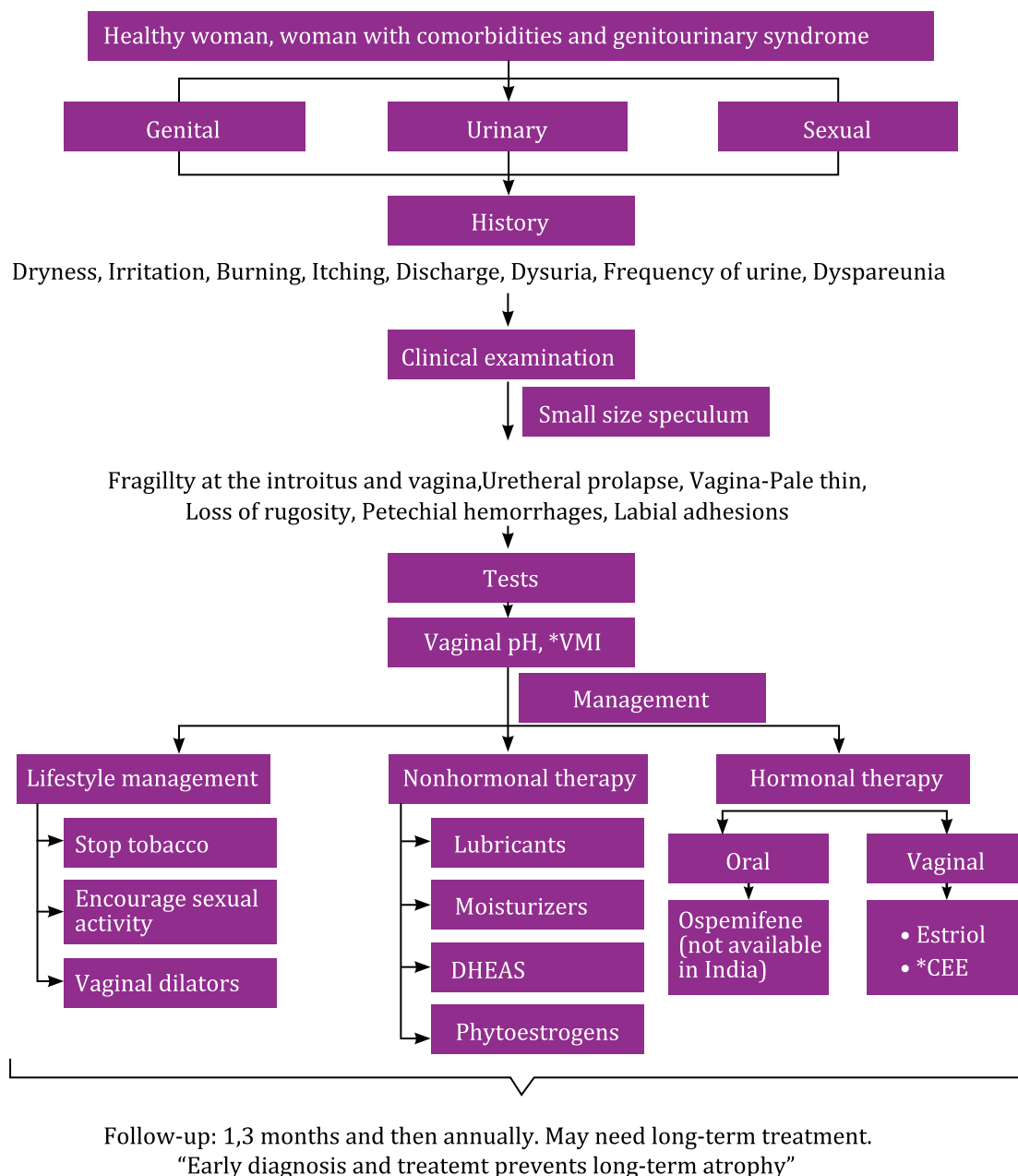
Low risk: <10 years postmenopause, normal and overweight low risk for NCD/ no comorbidities

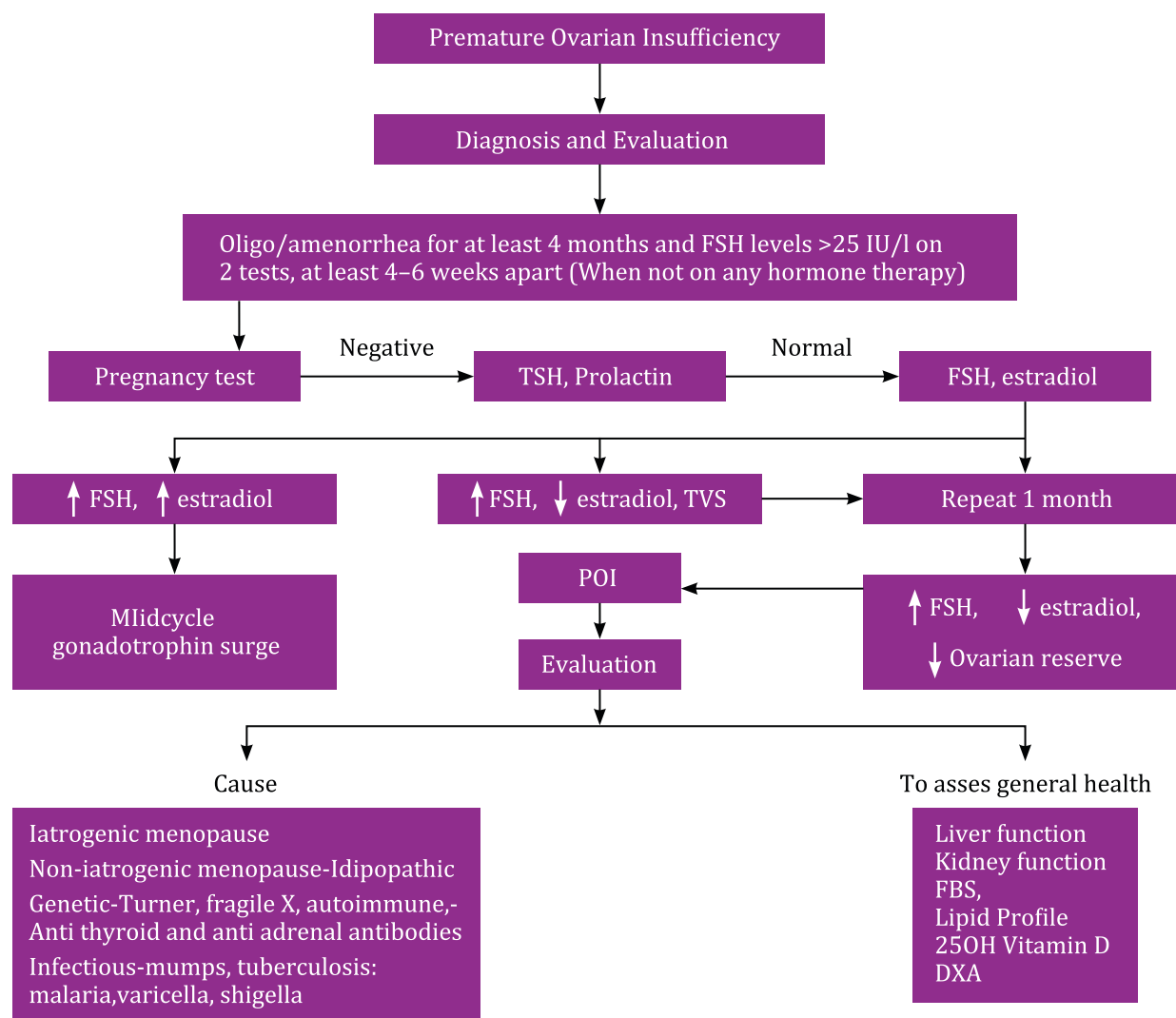
Moderate risk: >10 years postmenopause. Obese women at moderate risk for NCD well controlled comorbidities, moderate risk for breast cancer

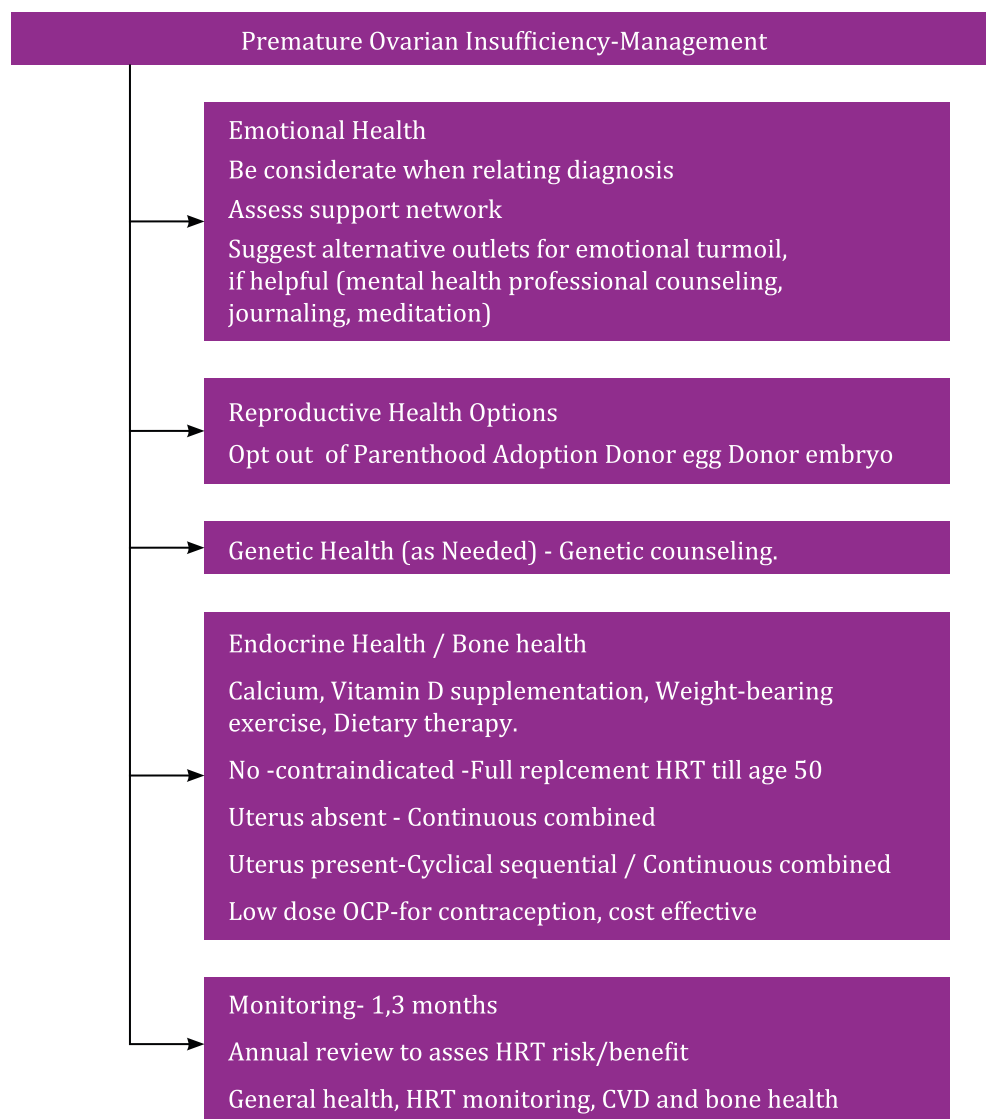
High risk: >20 years postmenopause, Congenital heart disease/Established CVD/VTE/Stroke Transient ischemic attack/myocardial infarction/High risk for breast cancer/ breast ca survivor uncontrolled comorbidities

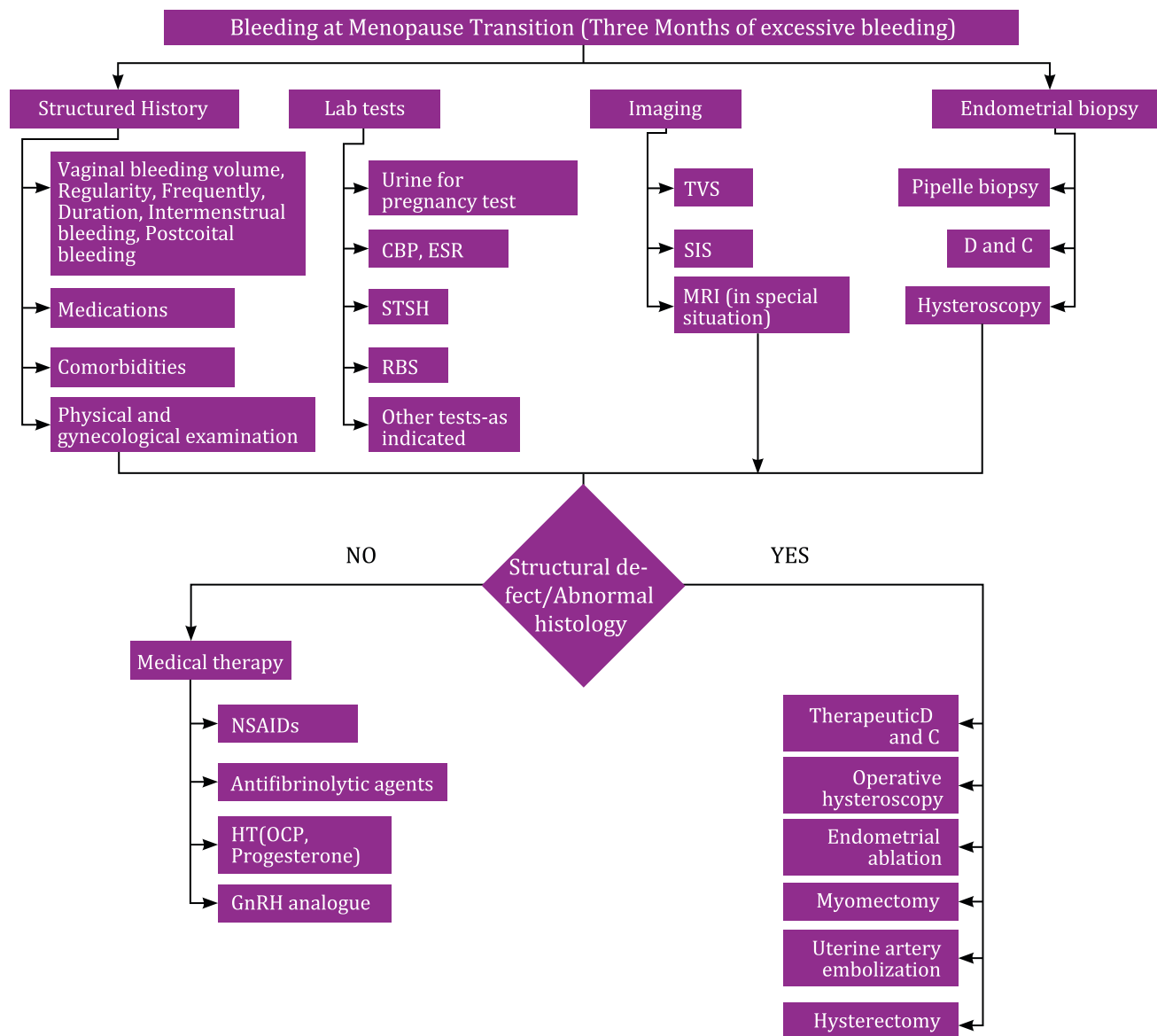


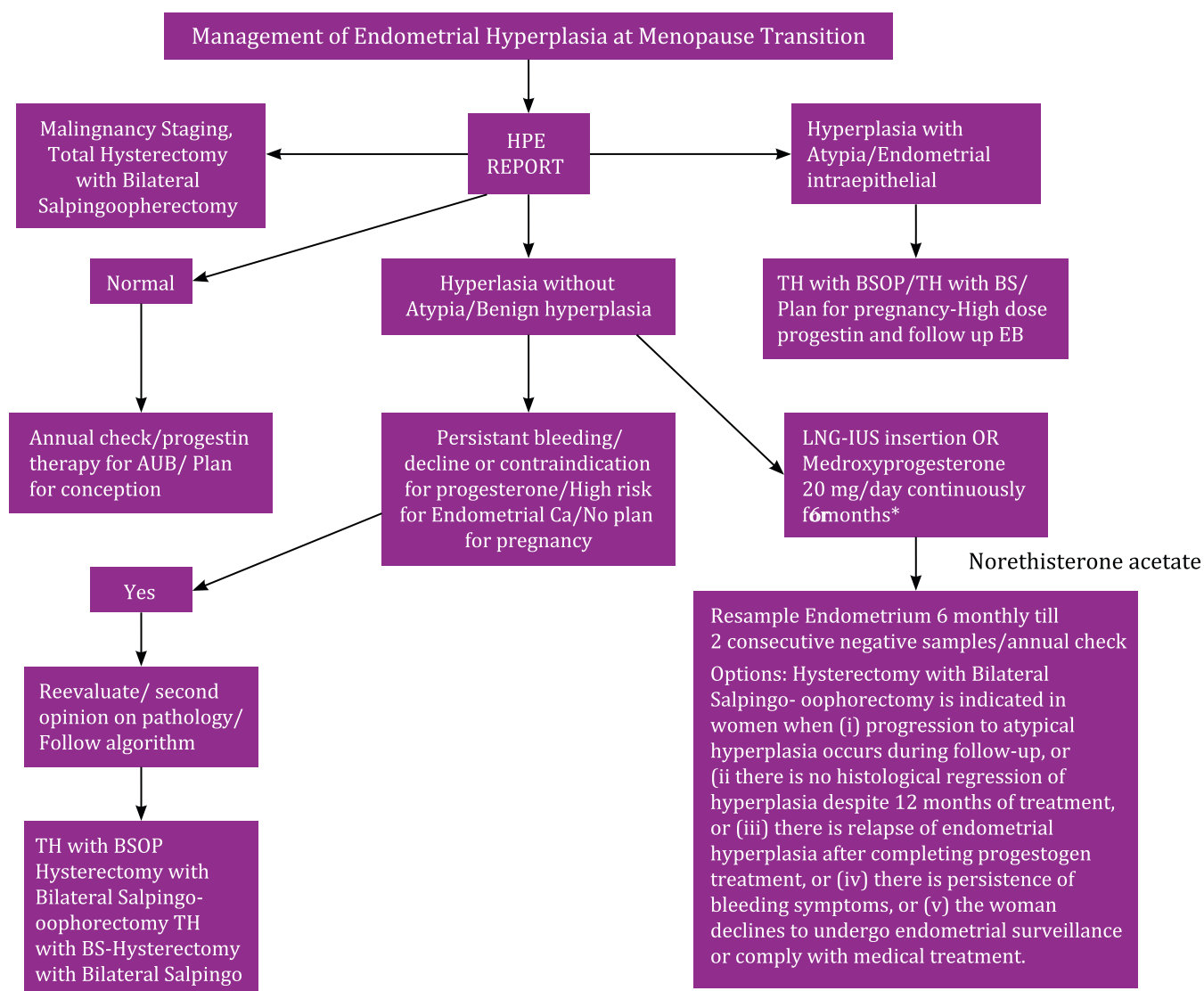


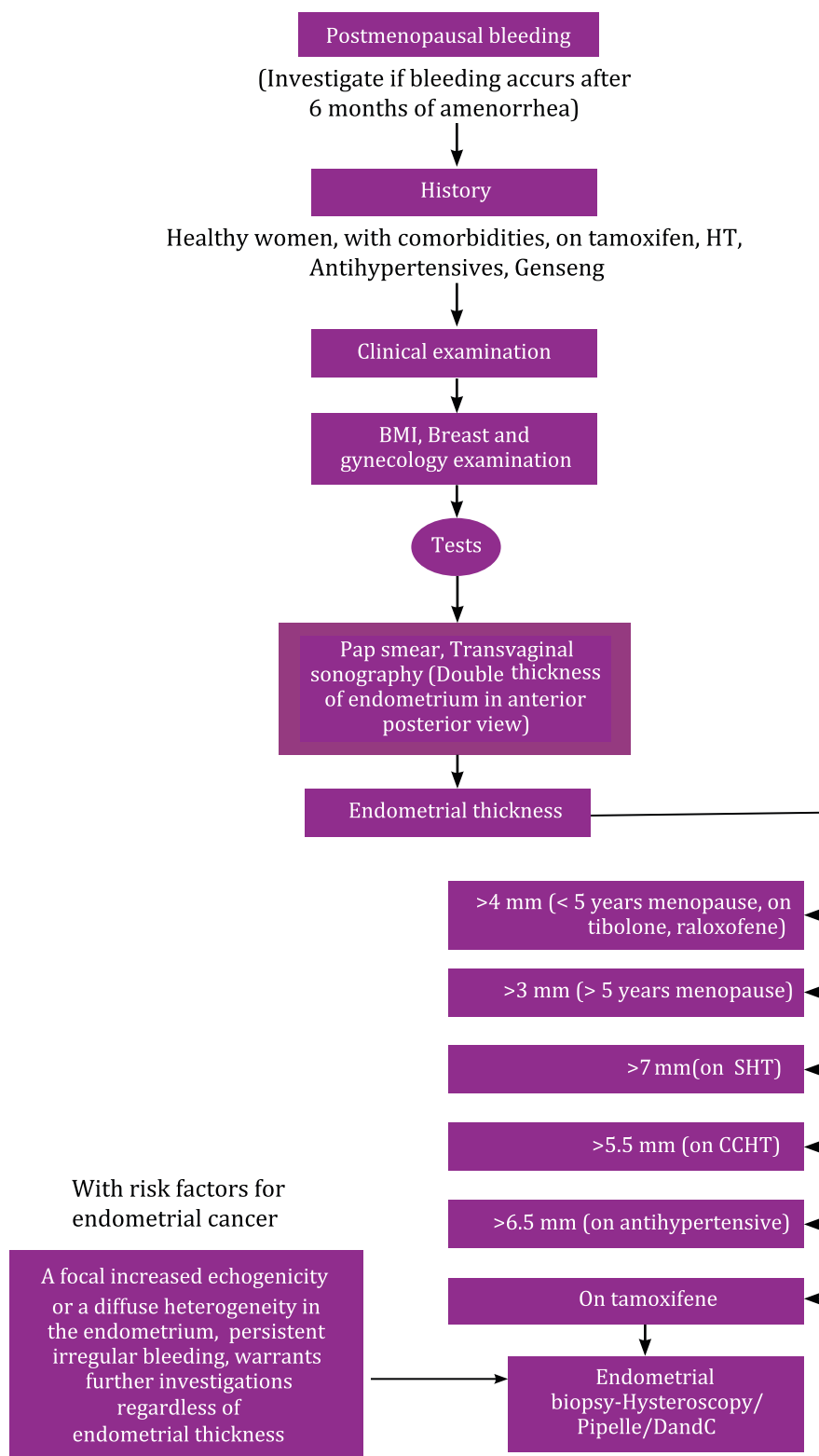


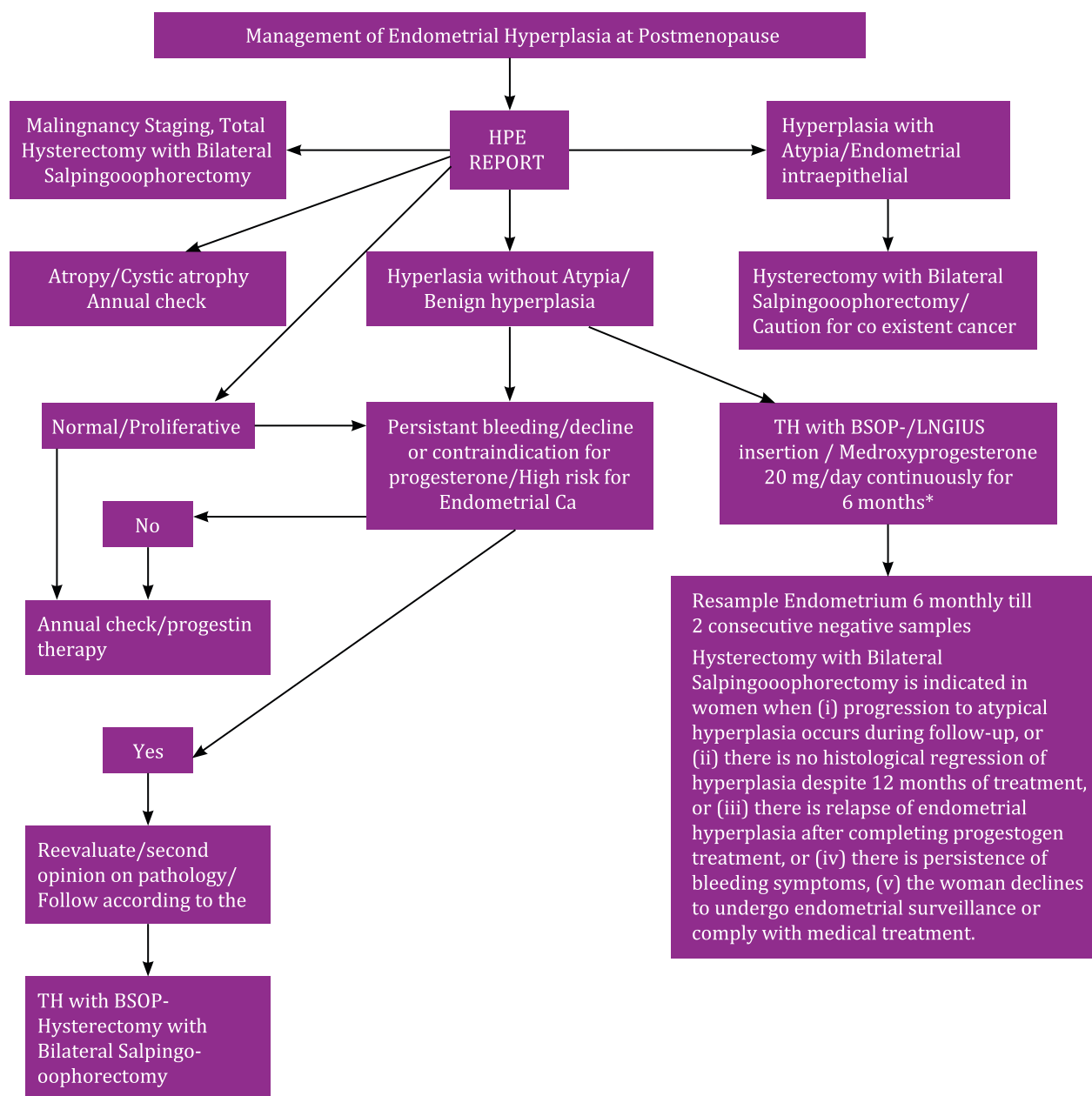


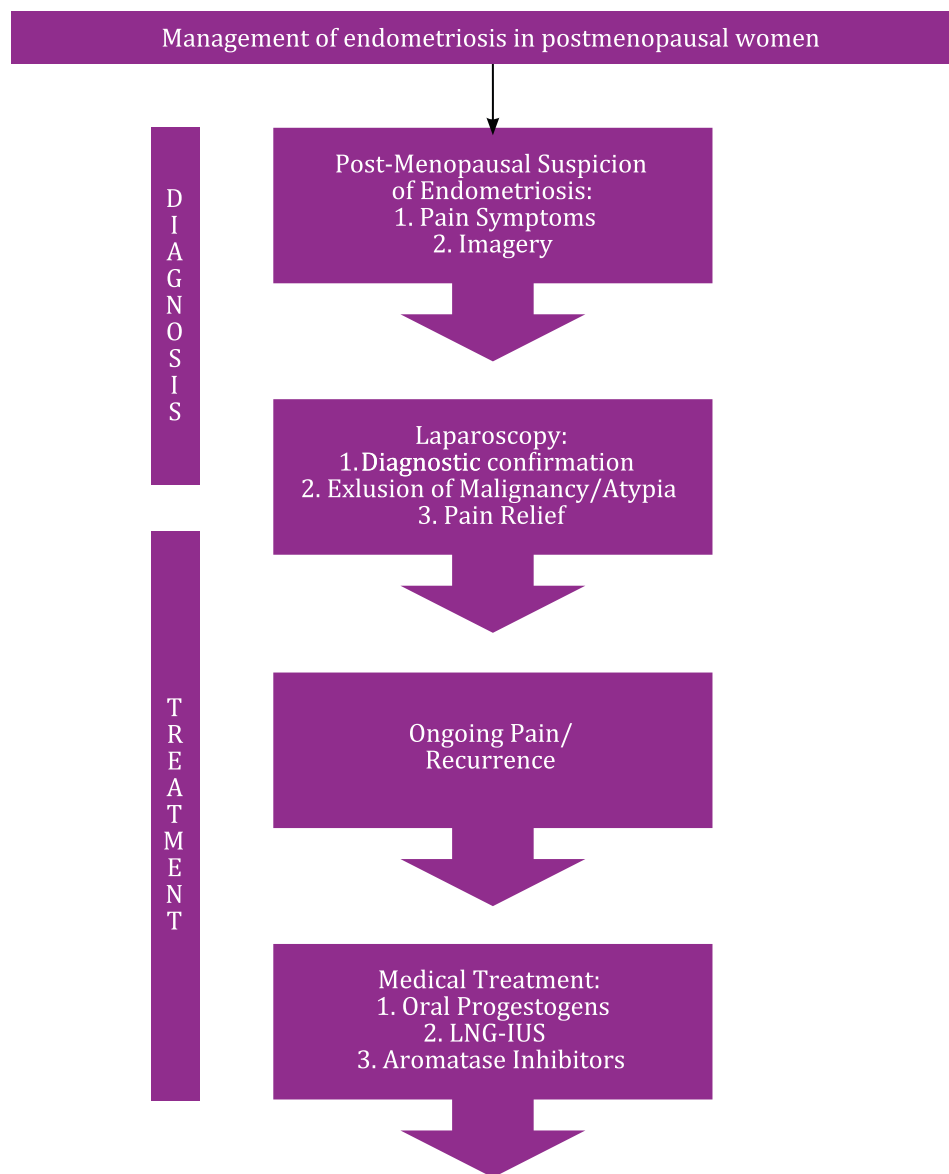












Streuli, H. Gaitzsch, J-M. Wenger & P. Petignat. Endometriosis after menopause: physiopathology and management of an uncommon condition, Climacteric, 2017, 20:2, 138-143,

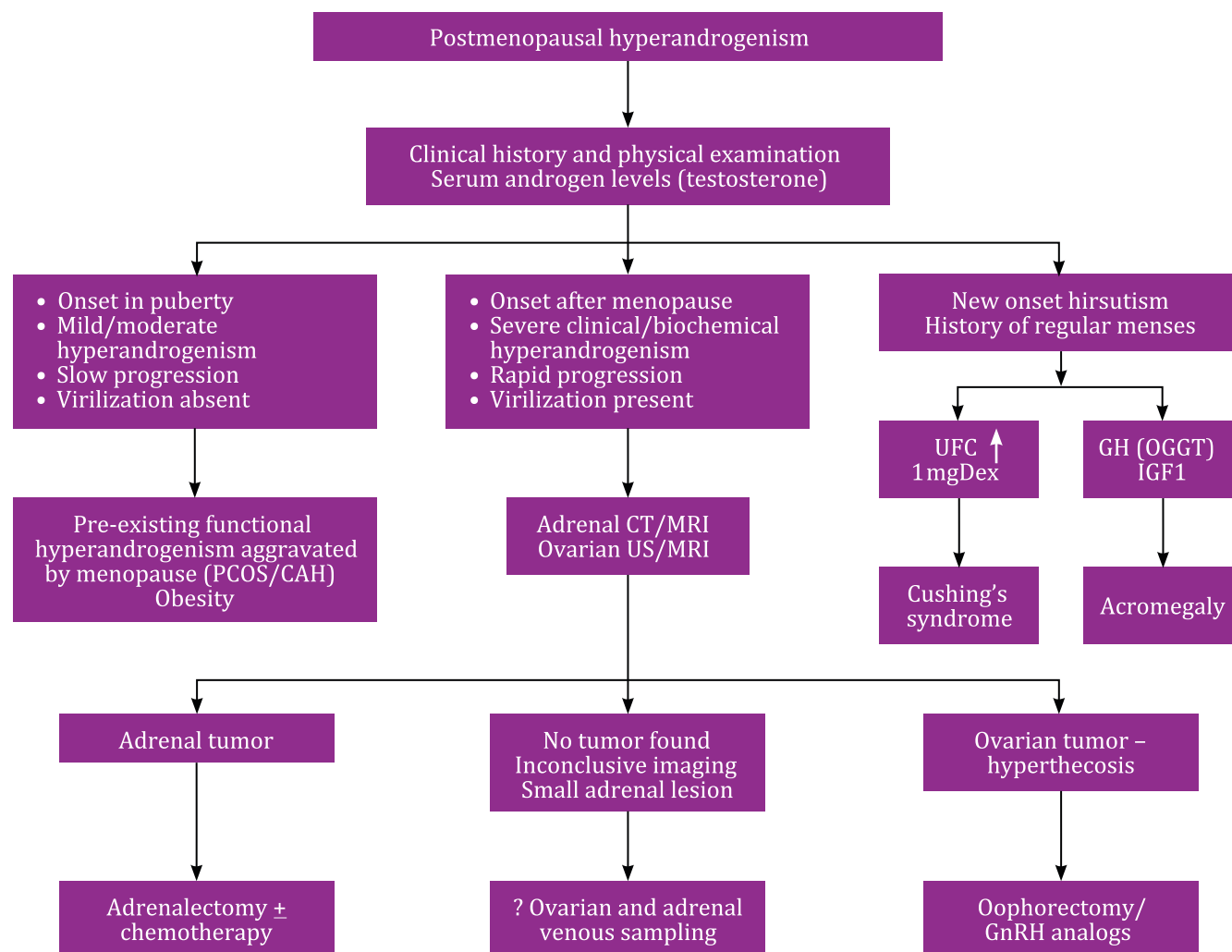
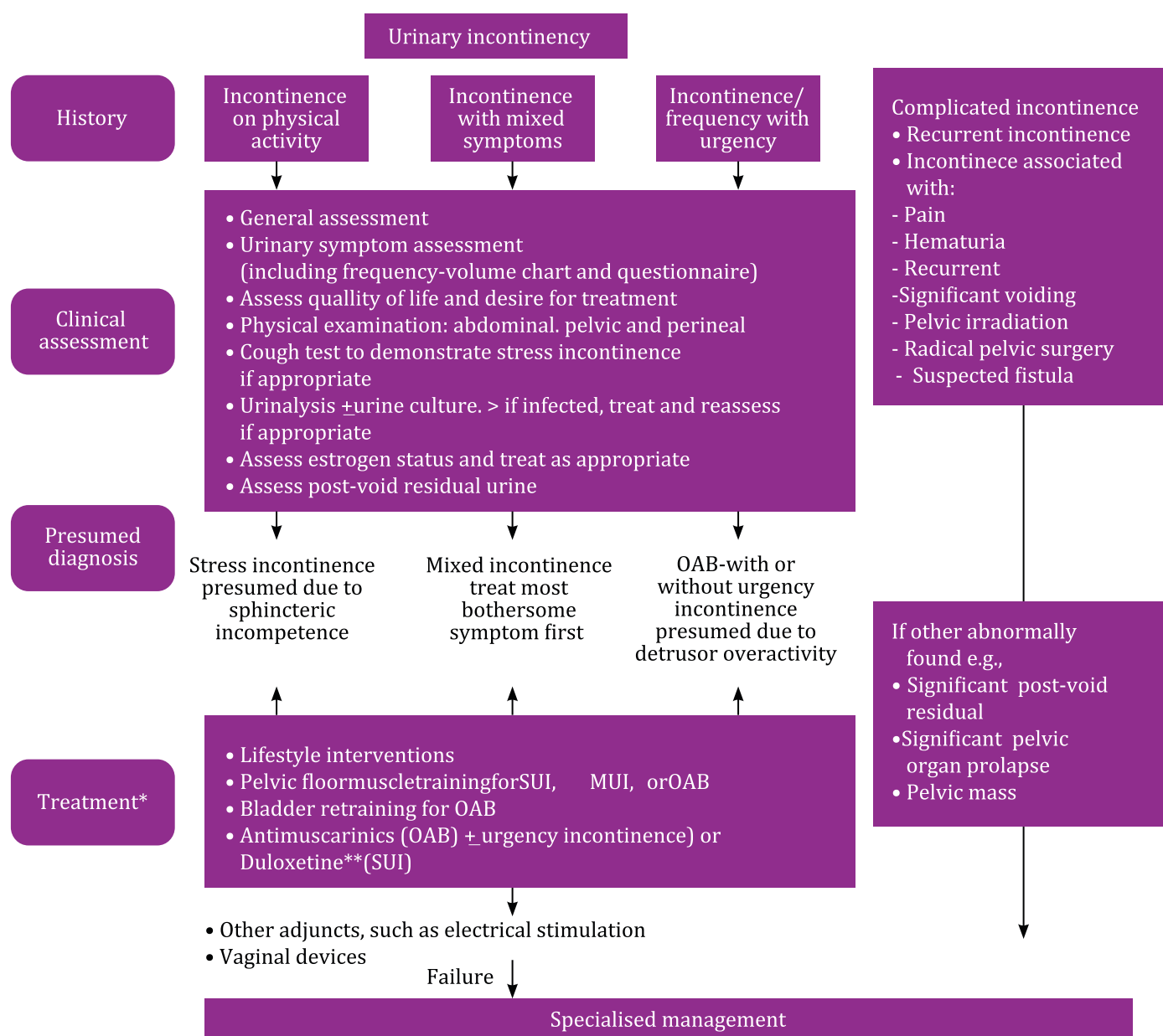


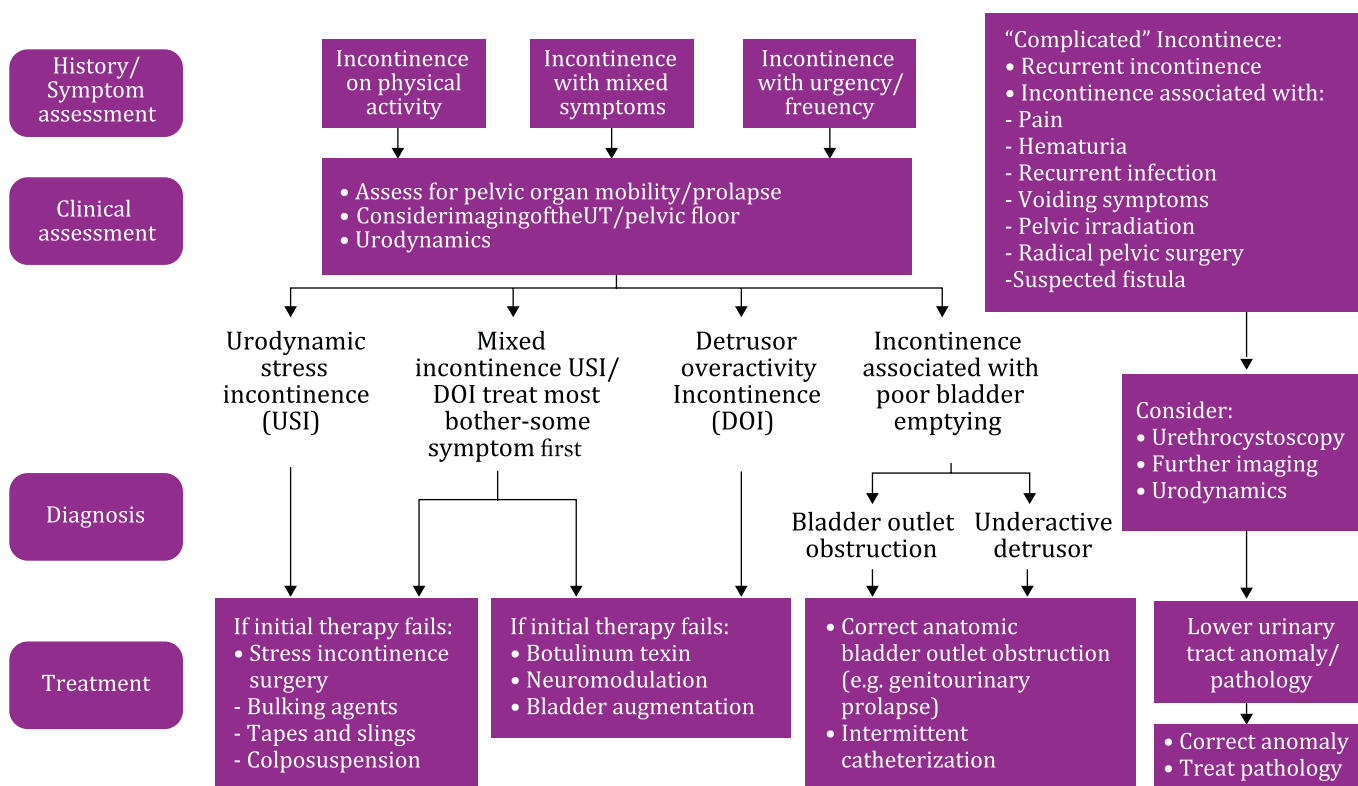
Figure 2

PCOS, polycystic ovary syndrome; CAH, congenital adrenal hyperplasia; UFC, urinary free cortisol; Dex, dexamethasone; GH, growth hormone; OGTT, oral glucose tolerance test; IGF1, insulin-like growth factor 1. Adopted with modification from references 'Rothman MS & Wierman ME. How should

postmenopausal androgen excess be evaluated? Clinical Endocrinology 2011 75: 160–164' and 'Alpanes M, Gonzalez-Casbas JM, Sanchez J, Pian H & Escobar-Morreale HF. Management of postmenopausal virilization. Journal of Clinical Endocrinology and Metabolism 2012; 97: 2584–2588'.

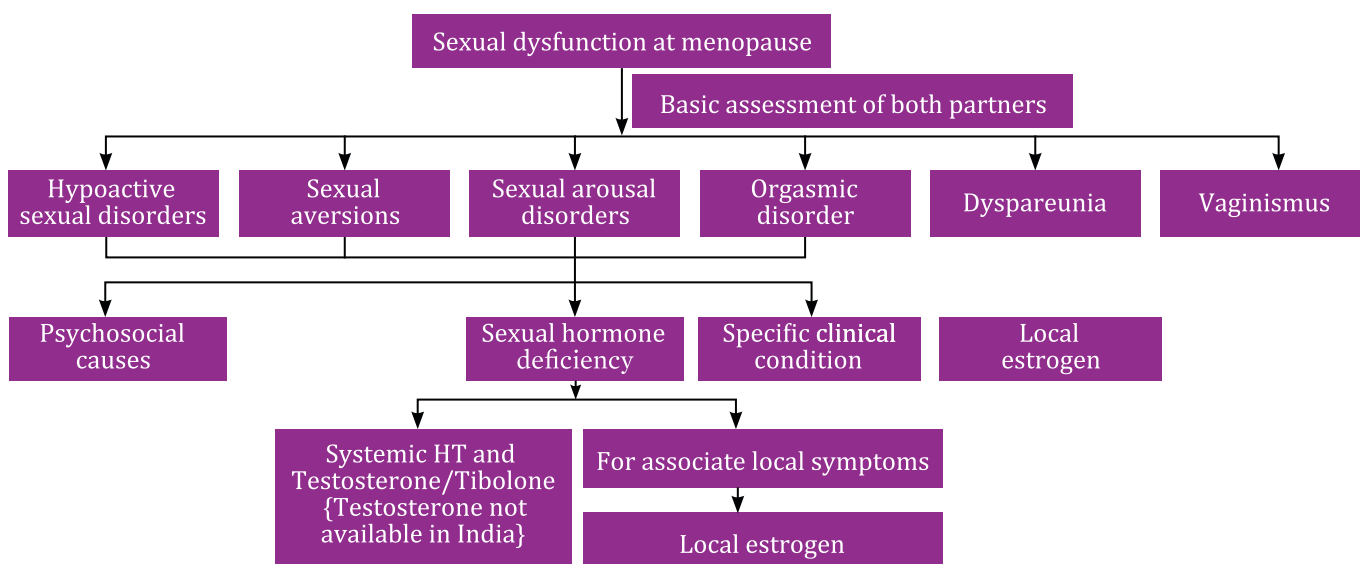


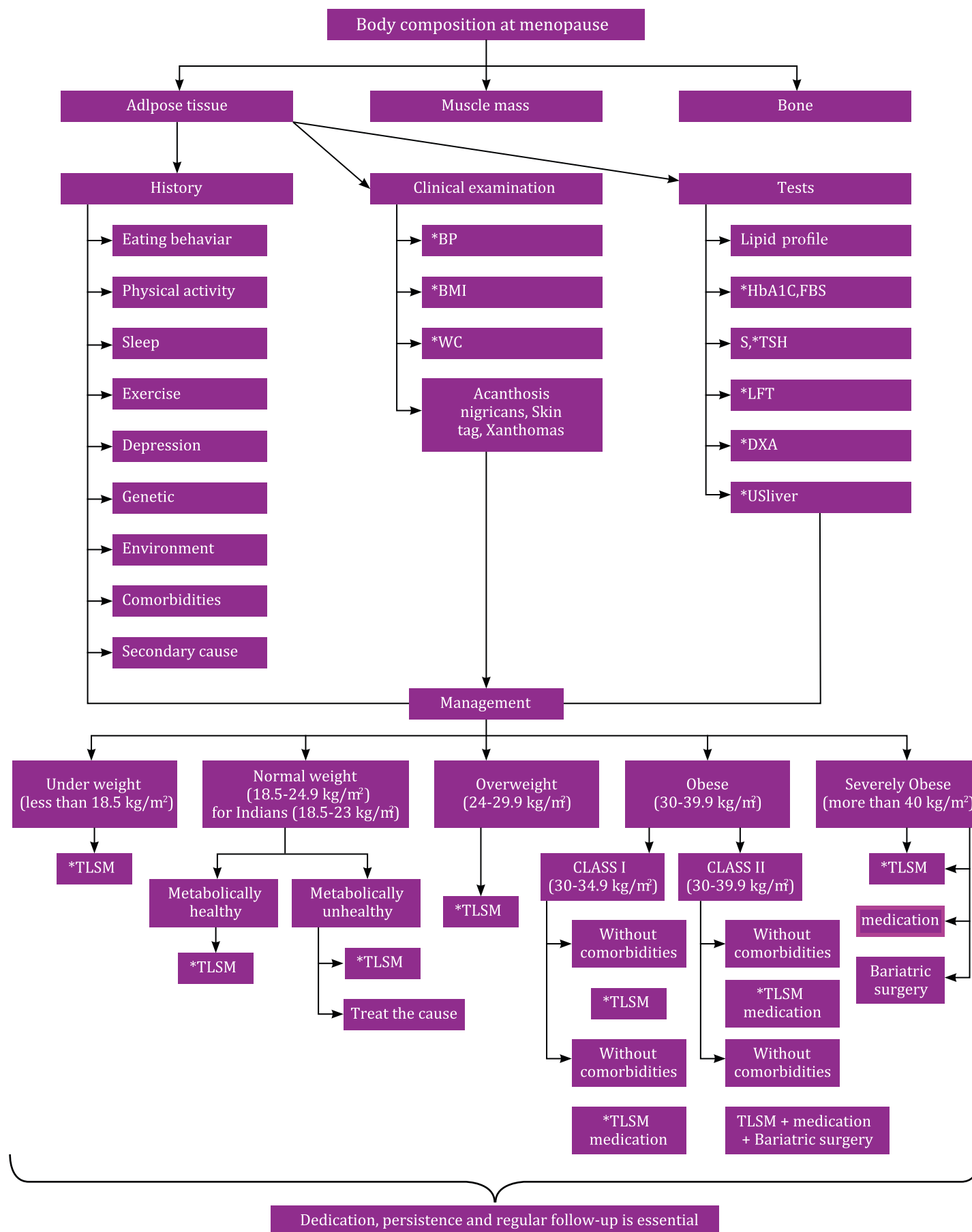
Initial management of urinary incontinence in women
(OAB: Overactive bladder; SUI: Stress urinary incontinence; mixed urinary incontinence).
Adapted from Giarenis I, Cardozo L. Managing urinary incontinence: what works? Climacteric.
2014;17(Suppl 2):26-33

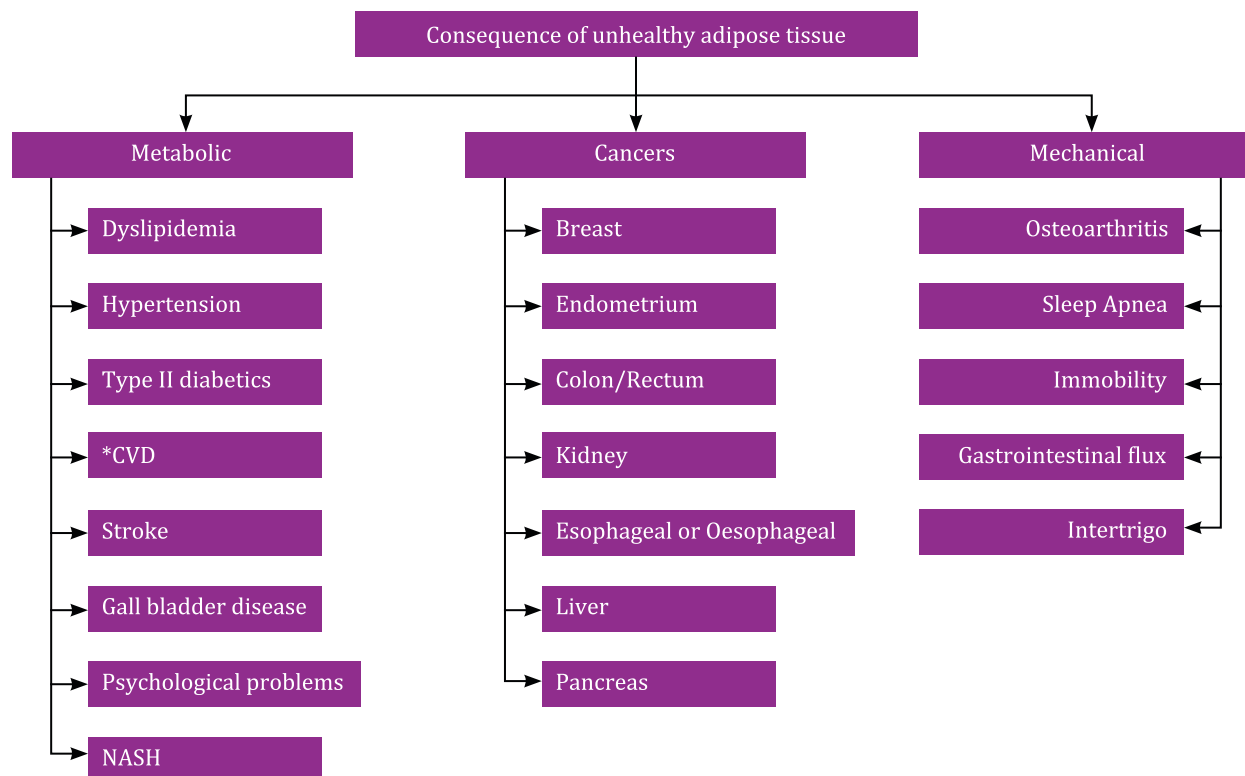


Specialized management of urinary incontinence in women (UT, urinary tract).

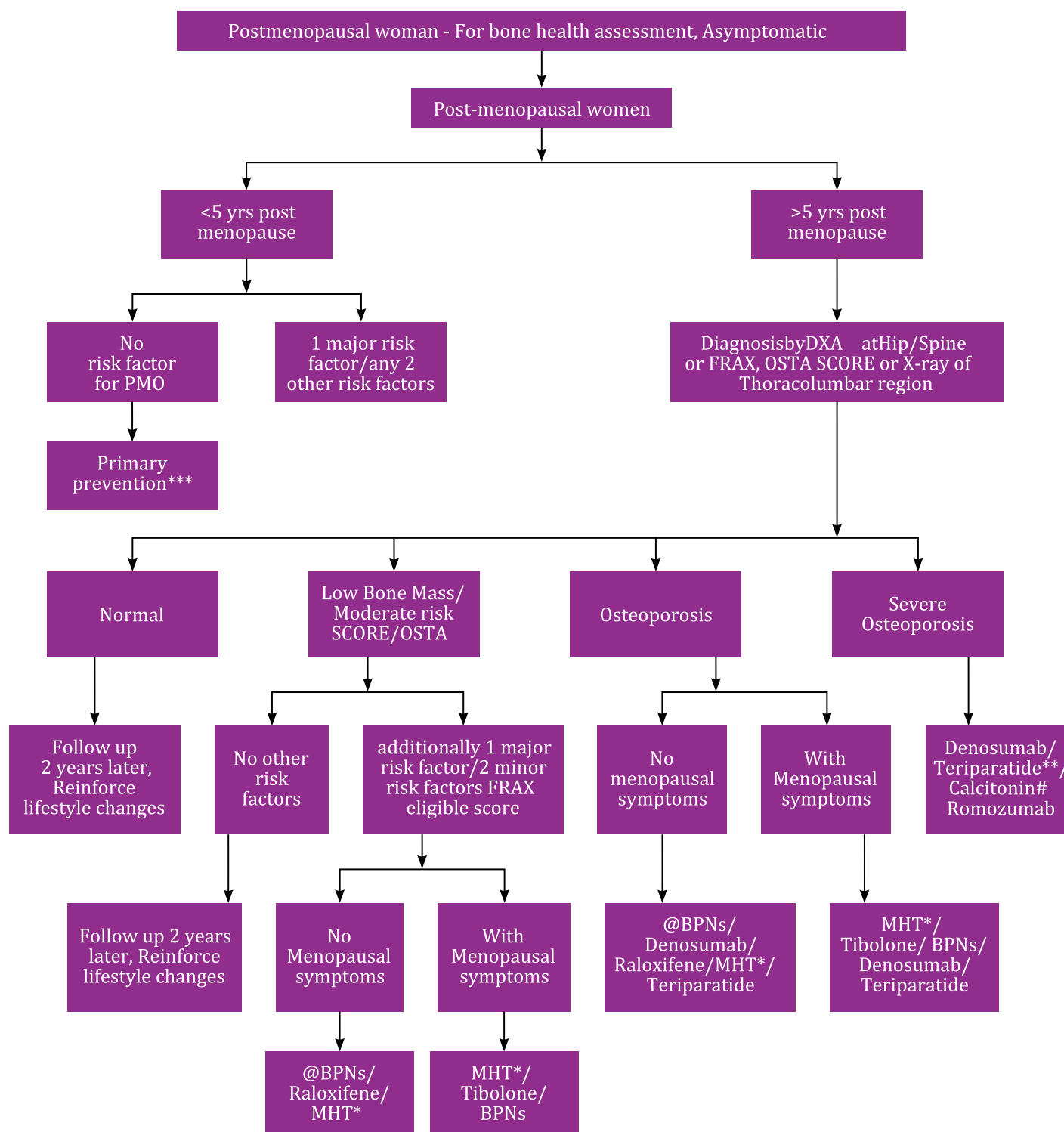
Adapted from Giarenis I, Cardozo L. Managing urinary incontinence: what works? Climacteric. 2014;17(suppl 2):26-33.







Life expectancy reduces by 2–4 years for obese individual
and 8–10 years for severely obese.



***Primary Prevention for all -Nutrition, Lifestyle Modification, Adequate Vitamin D and Calcium, Exercise, Avoid bone depleting agents,

@Bisphosphonates- Drug holiday after 3 years for IV Zoledronate, 5 years for oral, Consider continuation after drug holiday

Denosumab - Effective on vertebral, hip and non-vertebral fractures, long term management without drug holiday, even for those with Cr Cl <30 ml/min

Raloxifene Effective on vertebral fractures at high risk of breast cancer

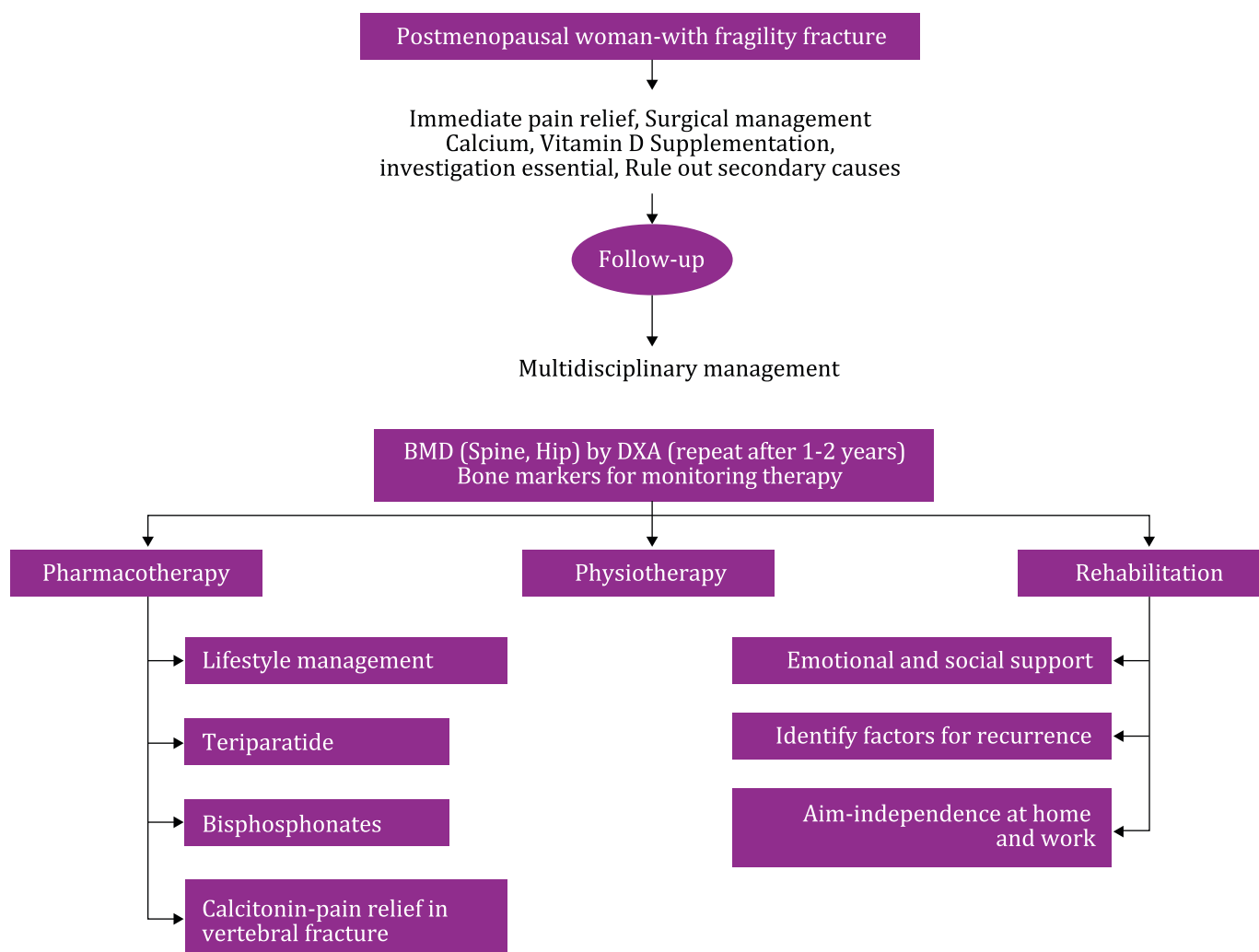
**Teriparatide - Can be used upto 2 years, effective on vertebral fractures

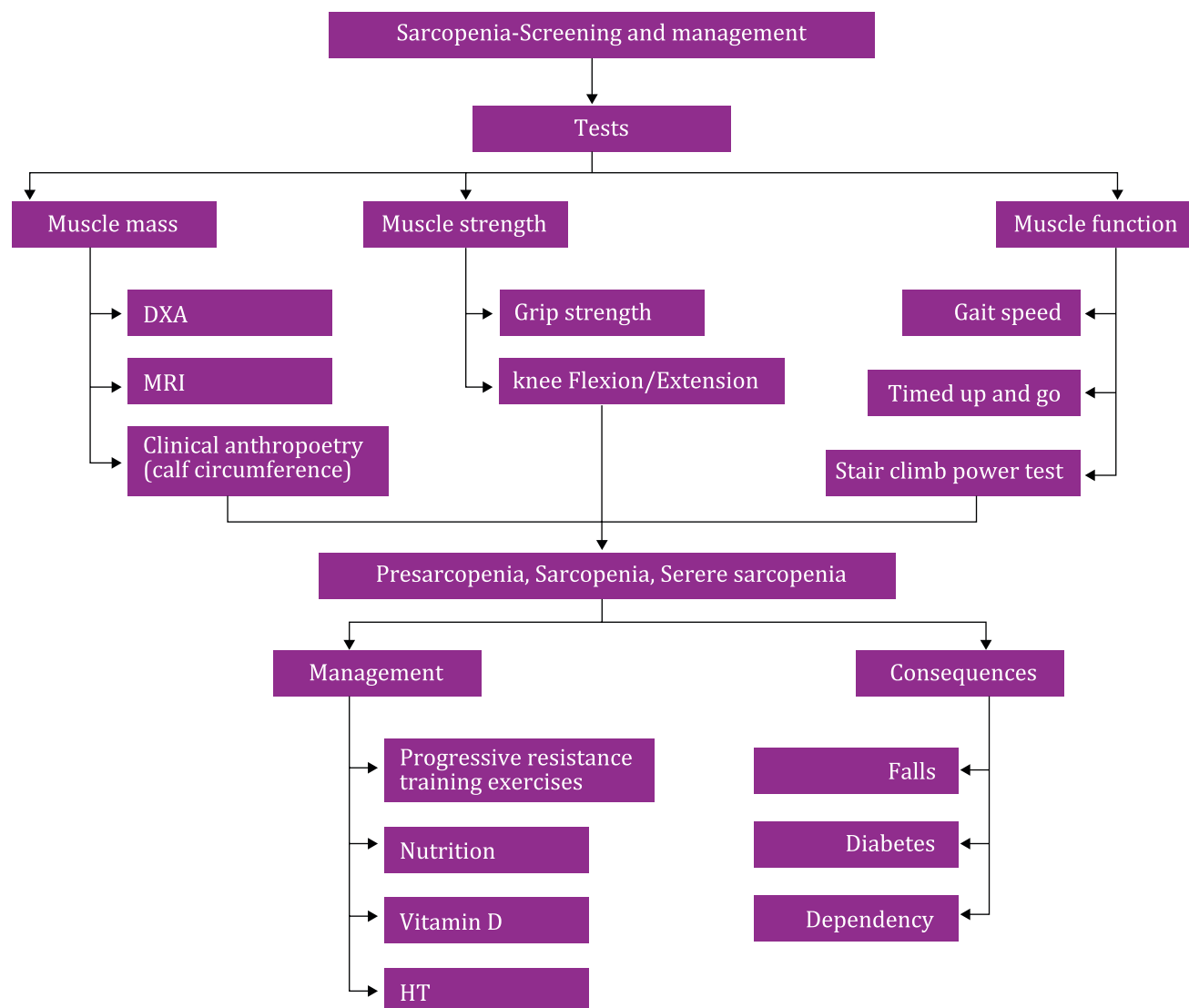
*MHT - Menopausal hormone therapy to be used within 10 yrs of menopause, pre-initiation workup, review annually, individualize therapy

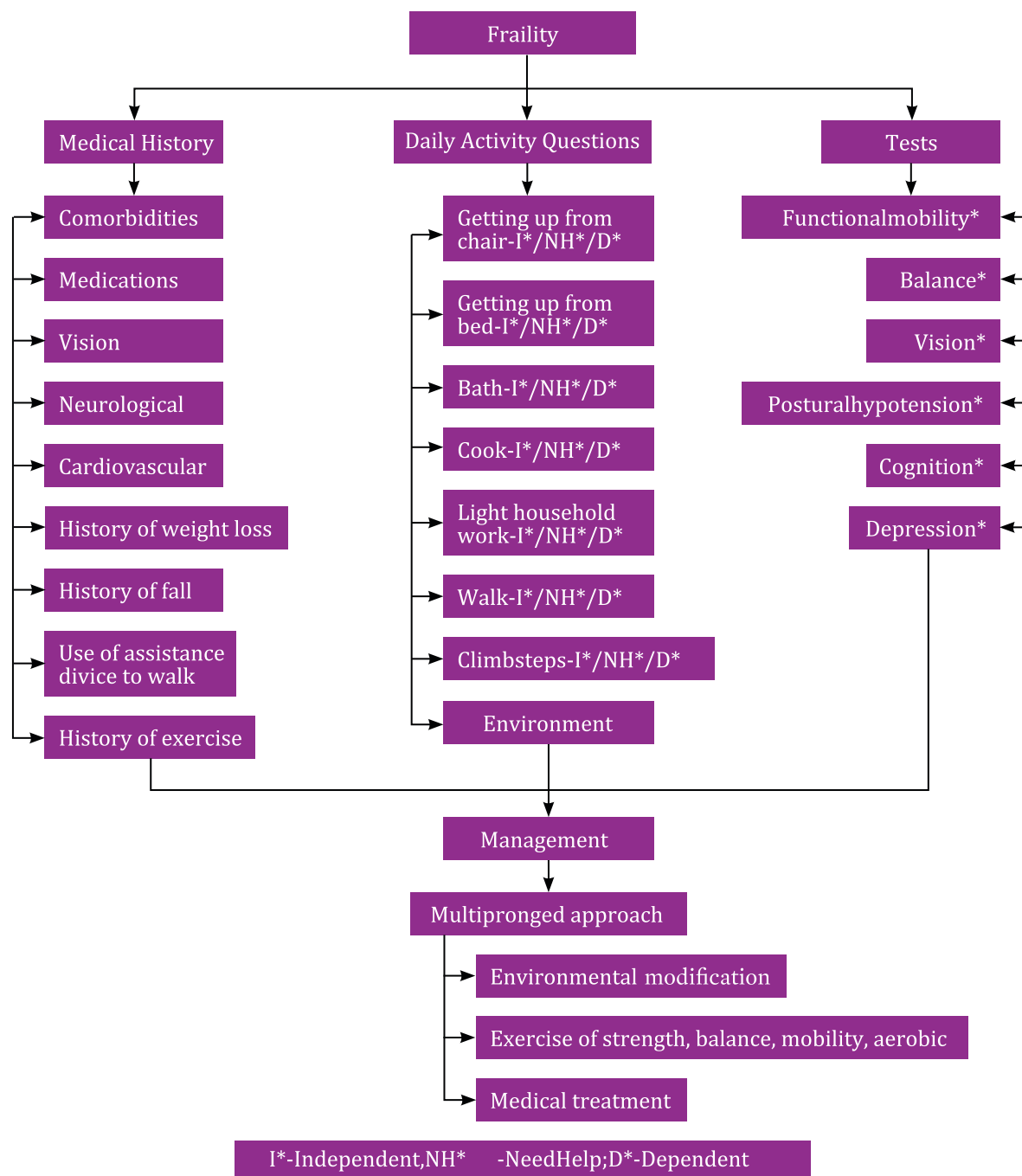
Calcitonin - Analgesic, short term for three months in vertebral fractures, 5 yrs post-menopause

FRAX: WHO fracture risk algorithm, SCORE: Simple calculated osteoporosis risk estimation, OSTA: Osteoporosis self assessment tool for Asians,

DXA: Dual-energy X-ray absorptiometry, PMO: Post-menopausal osteoporosis.







TESTS

1) Functional Mobility

Timed up and go: To stand up from a chair and walk 10 feet as fast as possible, turn, walk back, and sit down. The risk of falling is high if the time taken is more than 12 seconds.

2) Vision: Snellen chart

3) Postural hypotension: Fall in systolic blood pressure by 20 mm Hg or more from lying to sitting or standing position.

4) Balance: Single leg stand-should be more than or equal to 10 seconds for each leg.

5) Cognition: Mini mental state examination

6) Depression: Modifier Geriatric Depression Scale

OSTEOARTHRITIS

BASIC PRINCIPLE AND CORE SET

Combination of treatment modalities, including non-pharmacological and pharmacological therapies is strongly recommended

Core set:

- Information/Education
- Weight loss if over weight
- Exercise program (i.e. aerobic, strengthening, or resistance exercises)

STEP 1: Background treatment

If still symptomatic

Chronic SYSDOA: prescription
glucosamine sulfate and/or chondroitin
sulfate $\pm$ as needed paracetamol

If still symptomatic ADD

Topical NSAIDs

Referral to physical therapist for: If needed
(To control Malalignment)

- Knee braces
- Insoles

If symptomatic ADDITION at anytime

- Walking Aids (Stick, walker)
- Thermal Agents (Heat and Cold)
- Mechanotherapy or Manual Therapy
(Flexibility, stretching)
- Bandage therapy
- Hydro therapy
- Tai chi

STEP 2: Advanced pharmacological management in the persistent symptomatic patient

If still or severely symptomatic

Intermittent or long cycles of oral NSAIDs

Normal GI RISK

- Non selective NSAIDs with PPI
- COX-2 selective NSAID
(preferred with concomitant PPI)

INCREASED GI RISK*

- Prefer COX-2 selective
NSAIDs (celecoxib) with PPI
- Be mindful of complication
with any NSAID

INCREASED CV RISK

- Limit use of any NSAIDs
- Treatment duration
<30 days for celecoxib, and
<7 days for nonselective NSAIDs

INCREASED RENAL RISK

- Avoid NSAIDs [†]

* Including use of low-dose aspirin † With glomerular filtration rate <30 cc/min; caution in other cases

If still symptomatic

- Intraarticular hyaluronate
- Intraarticular corticosteroids

Step 3: Last pharmacological attempts

- Short-term weak opioids
- Duloxetine

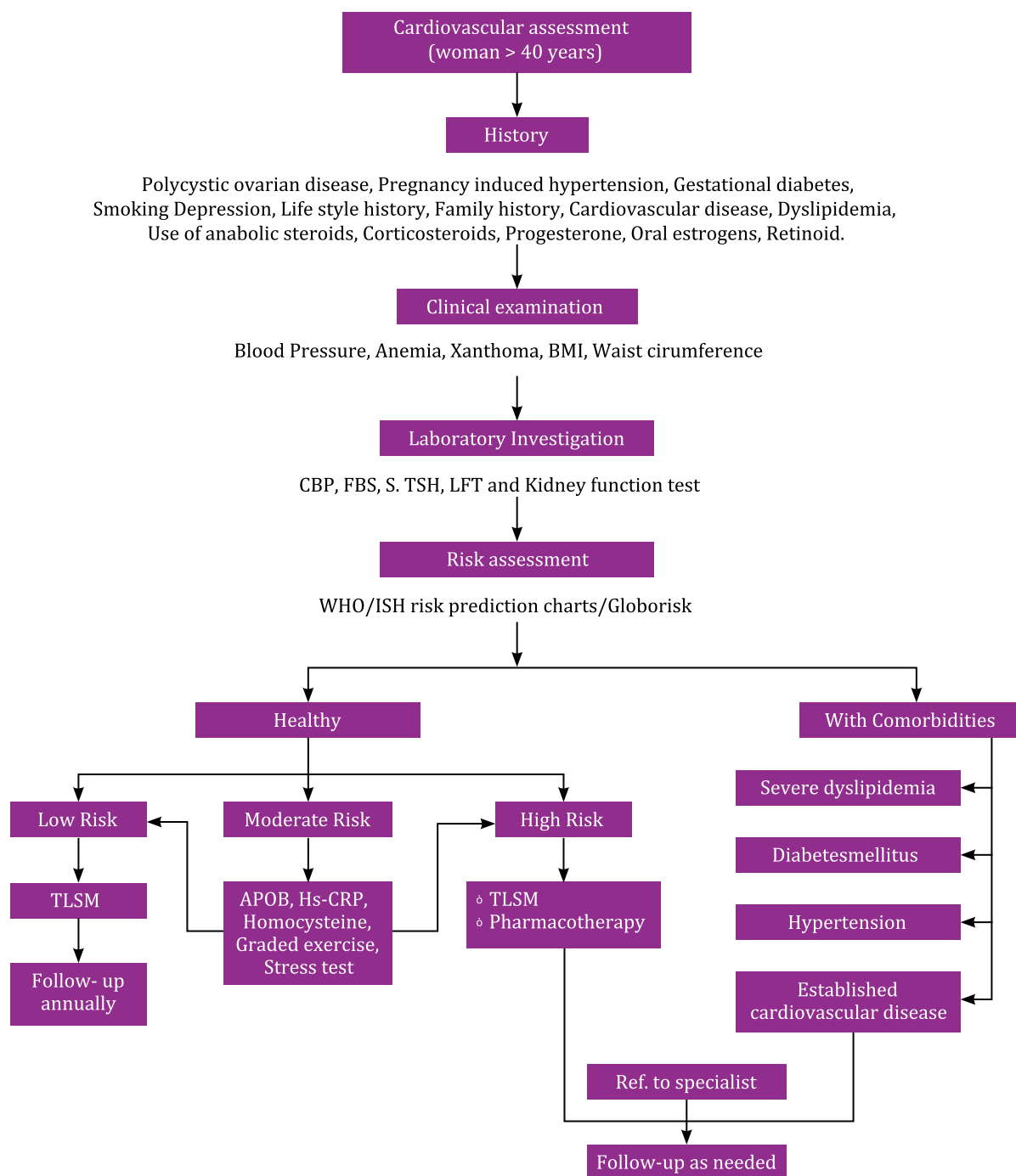
Step 4: End stage disease management and surgery

If severely symptomatic and poor quality of life

- Total joints replacement
- (Unicompartmental knee replacement)

If contraindicated

- Opioid analgesics



ABBREVIATIONS

CBP, ESR	Complete blood picture, erythrocyte sedimentation rate
S. TSH	Serum thyroid stimulating hormones
HbA1c	Glycosylated hemoglobin
RBS	Random blood sugar
LFT	Liver function test
S. FSH	Serum follicle stimulating hormone
AMH	Anti-Mullerian hormone
HsCRP	Hisk risk C-reactive protein
APOB	Apolipoprotein B
US Liver	Ultrasound liver
VMI	Vaginal maturation index
BMI	Body mass index
MRI	Magnetic resonance imaging
WC	Waist circumference
BP	Blood pressure
VMS	Vasomotor symptoms
GUS	Genitourinary syndrome
FMP	Final menstrual period
USG	Ultrasonography

CVD	Cardiovascular disease
NICD	Noncommunicable diseases
NAFLD	Nonalcoholic fatty liver disease
HT	Hormone therapy
ET	Estrogen therapy
SHT	Sequential hormone therapy
CCHT	Continuous combined hormone therapy
CEE	Conjugated equine estrogen
DHEA	Dehydroepiandrosterone sulfate
TLSM	Therapeutic lifestyle management
NSAIDS	Nonsteroidal anti-inflammatory draug
AFA	Antifibrinolytic agents
OCP	Oral contraceptive pills
GnRH	Gonadotropin releasing hormone
TVS	Transvaginal sonography
D&C	Dilatation and curettage
DXA	Dual-energy X-rayabsorptiometry
SIS	Saline infusion sonography
CT	Computed tomography

PRESCRIPTION WRITING FOR MENOPAUSAL SYMPTOMS

61

Keywords: Lifestyle Modifications, Co-prescription, hormone therapy

GENERAL ADVICE

1. Therapeutic Lifestyle Modifications Diet

- Total fat 25–35% of total calories
- Carbohydrate 50–60% of total calories
- Protein 15% of total calories, fiber 20–30 g/day
- Limit saturated fats less than 7% of calories
- Cholesterol to less than 200 mg/day.
- Per day requirement is two level tablespoon of oil, one teaspoon of salt, 100 grams of fruit and 300 grams of vegetables, avoid visible sugar, not more than 6 teaspoon, include high fiber (25–40 g/day) diet, 8–10 glasses of water. Handful of nuts more than five times per week
- **Recommendations for Physical activity and Exercise**
- Exercise should include aerobic, muscle strengthening, breathing and balance. 30 minutes of moderate intensity physical activity mostly 5 days a week. Muscle strengthening activities should be included at least 2 days/week.
- 30 minutes/day: For fitness and reduced risk of chronic disease
- 60 minutes/day: For prevention of weight gain
- 60–90 minutes/day: To avoid regain of weight loss

Sleep:

- Proper sleep scheduling: Keep regular bedtime and waking time, avoid spending excessive time in bed
- Avoid use of sleep disrupting products: Avoid caffeine, alcohol, nicotine before bedtime
- Avoid stimulating activities close to bedtime: Avoid exercise 2 hours before bedtime
- Avoid use of bed for activities other than sleep: Avoid watching television or using gadgets, reading, snacking. Be thankful for what you have and avoid disturbing thoughts. Pray, meditate or concentrate on positive thoughts.
- Get out of bed if unable to fall asleep
- Restrict naps to 30 minutes in the early afternoon
- Exercise regularly
- Limit liquids in the evening
- Bedroom environment: Dim light, no television or cellphone or computer. Encourage social interaction, engage in activities that stimulate the mind

CO-PRESCRIPTION

Calcium 1,000 mg from the diet or supplement with Vitamin D 1,000–2,000 IU daily or 60,000 IU/ month or exposure of arms/legs/face to sunlight daily for 20 minutes between 11AM -2 PM is an important part of every prescription.

MENOPAUSAL HORMONE THERAPY

STAGE OF MENOPAUSE AND SYSTEMIC REGIME

Systemic Regime Depending on The Stage of Menopause
In a women with uterus Menopause Transition and Menopause <1YR 1. Sequential combined regime - Continuous estrogen and cyclical progesterone 12-14 days/month, (Not a contraceptive) 2. Low dose contraceptive pill if not contraindicated
Postmenopause 1. Continuous combined-Continuous estrogen and continuous progesterone 2. Tibolone
Premature ovarian insufficiency 1. Standard/High dose estrogen and cyclical or continuous progesterone (Not a contraceptive) 2. Oral contraceptive pill if not contraindicated 3. Tibolone

Systemic Regime Depending on The Stage of Menopause	Regime For Local Therapy In GSM
In a women without uterus. 1. Continuous estrogen alone 2. Tibolone 3. Progesterone is added along with estrogens in hysterectomised woman in cases of endometriosis, endometrial ablation, supracervical hysterectomy, grad1, Stage 1 endometrial carcinoma	For correction of deficiency Estriol cream - 0.5mg/day of vaginal application or Tab Estriol 1-8mg/day single dose before a meal OR Conjugated equine estrogen- 0.3 mg-1.25mg/day of vaginal application for 15 days For Maintenance Therapy Tab estriol 1mg/daily or Estriol Cream 0.5mg or Conjugated equine estrogen- 0.3 mg- twice weekly for two months to one year.

Terminology - Dosage and types of Systemic Estrogen used in MHT

Estrogens	Ultra low	Low	Standard	High
Conjugated equine estrogens (mg,CEE)-oral	0.15	0.3, 0.45	0.625	1.25
17 β -estradiol (mg) oral	0.5	1	2	4
17 β -estradiol (mg) Transdermal patch	0.014	0.025	0.05	0.1
17 β -estradiol (mg) Transdermal gel	0.375	0.75	1.5	3
Estradiol valerate (mg)-oral		1	2	4

Types of progesterone used in MHT

Progestogens		
Progesterone	Oral-200/Vaginal 100	Oral-300/Vaginal 300
Dydrogesterone	5	10
Levonorgestrel	0.02	

Sexual Dysfunction:

For Low Libido

Tibolone 2.5 mg OD $\times$ 6 weeks–3 months. OR

Start low-dose transdermal estradiol and increase as needed.

Vaginal estriol succinate cream 0.5 mg or tab estriol 1 mg,

2 mg/vaginal conjugated equine estrogen if urogenital atrophy is present.

MHT Formulations Available In India

Systemic Therapy

Estrogen:

Oral-CEE 0.3 mg/0.625 mg (Premarin), 17 β -estradiol

1 mg/2 mg (Estrabet), Estradiol valerate 1 mg/2 mg

Transdermal estrogen gel - 0.75mg per 1.25gm of gel and 1.5mg per 2.5 gm of gel (Estrabet gel, Oestrogel gel).

Progesterone

Dydrogesterone 10mg, Micronized Progesterone

-100,200,300,400mg, Levonorgestrel Intrauterine Device

-52mg-release 20 mcg/day

Combination of Estrogen and Progesterone

Continuous sequential-17- β estradiol 1 mg and 10 mg of dydrogesterone (Femostan 1/10)

Continuous combined-17 beta-estradiol and dydrogesterone 5 mg daily (Femostan 1/5)

Tibolone -2.5mg/day

Estrogen Therapy For Genitourinary Syndrome

Estriol cream -0.5mg/ 0.5gm of cream(Evalon cream);

Oral Estriol(Evalon)-1/2 mg

Conjugated equine estrogen-0.625mg/1gm of cream (Premarin cream)

Non Hormonal Treatments for Relief of Menopausal Symptoms

Do not prescribe paroxetine, fluoxetine to women taking tamoxifen

Choice of medication depends on the symptom

Selection of medication depending on the predominant symptom.

Isoflavones: 70 mg–100 mg daily × 6 weeks–3 months

(equol producer patients have to be identified)

Lycopene: 18–24 mg daily:

Genitourinary Syndrome

Soya Isoflavones gel- Iseren gel One tube of 7gms

containing 5gms of the isoflavone ,single vaginal use twice weekly

Non-Hormonal management of symptoms

	Gabapentin or pregabalin	SSRI or SNRI	CBT or hypnosis
VMS*	++	++	
Sleep`	+++	+/-	
Mood		+++	

Medication	Dosage
SSRIs and SNRIs	
Paroxetine	10-20 mg/day
Venlafaxine	37.5-150 mg/day
Desvenlafaxine	25-150 mg/day
Fluoxetine	10-20 mg/day

Anticonvulsant	
Gabapentin	100 mg at night, increase to 300 mg three times per day
Pregabalin	35 mg at night, increase to 15 mg twice times daily

BIBLIOGRAPHY

1. Archer DF, for the EstroGel Study Group. Percutaneous 17β-estradiol gel for the treatment of vasomotor symptoms in postmenopausal women. Menopause. 2003;10:516–521.
2. Evalon Prescribing information
3. Premarin vaginal cream prescribing information, CDS 20 Wyeth Limited, 2008
4. Scott RT, Ross B, Anderson C, Archer DF. Pharmacokinetics of percutaneous estradiol: a crossover study using a gel and a transdermal system in comparison with oral micronized estradiol. Obstet Gynecol. 1991;77:758–764.

Section 14

CLINICAL AIDS

- 62. Journey of visionaries
- 63. A unified mission for Menopause care
Indian Mid-Life Registry: From Evidence Gaps to Evidence Generation
- 64. Women's reflections on menopause

JOURNEY OF VISIONARIES

62

Keywords: Menopause, biology, perception, lived experience, perimenopause

Indian Menopause Society in 2026 and beyond through a Kaleidoscope

ऊर्ध्वमूलमधःशाखमश्वत्थं प्राहुरव्ययम् । छन्दांसि यस्य पर्णानि यस्तं वेद स वेदवित् ॥

Gita shloka 15.1

The Indian Menopause Society (IMS) has progressed today, in its breadth, depth, and height, encompassing its growth from North to South and East to West of India, with 53 Societies and 6450 Members. This growth reminds me of a picture of Urdhva Mulaha [Figure 1]. There is always a temptation to compare the ever-progressive growth of an organization with that of a Banyan Tree. But I think founders were inspired to see that individuals with intuitive qualities are drawn to help make the multidisciplinary society a progressive one that can continue to grow through cross-breeding ideas and collective efforts to improve multidimensional and multidisciplinary Menopause Health Care.

As I consider the genesis of the remarkably progressive society, the IMS, my thoughts go back to 1995. In a small room adjacent to the Radiology and Imaging Department of a Multispecialty Modern Medical Hospital, Hinduja National Hospital and Medical Research Center, a multidisciplinary group of physicians, including internists, surgeons, oncologists, and gynecologists, had gathered to brainstorm an idea that could shape a model healthcare module to address the needs of Indian women transiting through the menopausal period and associated health issues. The unfolding of the history of IMS, from its inception in 1995 to 2018, has been sensitively, beautifully, and esthetically woven into a decorative coffee-table book by the then president of our society. One can sense the enthusiasm, dedication, and newness of each subsequent president and their team as they contribute to the field of Menopause Health Science and Care in those pages since 1995. The society's journal, namely, Journal of Midlife Health, has also been highlighted with pride as an indexed journal in many research databases, including PubMed.

Since the society's inception, the annual conferences have become an important platform for updating, sharing, and learning about emerging developments in the field from national and international experts. The difficult period of imposed isolation during the COVID-19 pandemic was effectively handled by holding the National Conference online.

The Speciality Menopause Healthcare Training module IMS's flagship, was shaped a decade and a half ago under the chairmanship of the then IMS president. She herself had taken the speciality training and been credentialed as a Menopause Practitioner. The credentialed IMS menopause practitioner (CIMP) competency examination is now regularly conducted after the eligible has completed training in accordance with the syllabus officially prepared and undated by the special cell under the President. Graduated practitioners receive certificates at the National Annual Conferences.

Periodic exchanges of emerging national data on diverse topics were strengthened through collaboration and, subsequently, by becoming members and/or occupying office-bearer positions in many International Societies. A vast canvas of yet unattended and emerging areas has begun to unfold over the last few years. IMS members have also served as leaders in several international societies around the world. The IMS has shaped and periodically updated Clinical Practice Guidelines (CPG), which have been very popular not only at home but also used, praised, and considered trustworthy by many International Menopause Societies. The humongous and intimidating task of writing, collating, and editing, while incorporating advancing fields rapidly, while sustaining its relevance for the Indian perspective, remains.



Another noteworthy aspect is the originality of the “35+ club.” The concept captures the evolving endocrine environment and feedback mechanisms around age 35, offering a key chance for prevention and early disease detection, thereby emphasizing the program significance. Its broad acceptance and adoption by multiple chapters earlier, and now by individual societies, have fostered a celebratory atmosphere while raising awareness of menopause and related health changes well before the typical age of menopause.

A thought always comes to my mind that self-confidence and praise should be tempered by sober introspection, including what we have not yet done, and it's glaring in front of our eyes. Opportunities knocking at the door are ignored when we are hyperfocused on the already-travelled path. There is an urgent need to expand the associate membership of IMS for groups working in similar areas, including basic scientists, allied fields such as social scientists, anthropologists, and other government-recognized systems of medicine, for trans-system dialogs and debates.

Highly qualified medical professionals from the Indian diaspora have returned home as part of a reverse brain drain, and many are attracting them to join in various capacities. Some have also chosen to provide clinical care to women living in rural and tribal areas of India, helping to expand society's horizons.

In the end, I am proud of the unstoppable progress IMS has made. I am grateful to Meeta for asking me to visit IMS today and to see its picturesque progress through a kaleidoscope.

Rama Ashok Vaidya^{1,2}

¹Founder President, IMS,

²Division of Endocrine and Metabolic Disorders, Kasturba Integrative Health Sciences - Medical Research Foundation, Mumbai, Maharashtra, India

Menopause Medicine Comes of Age: A Founder's Message

The woman's health milestone of menopause has finally come of age both socially and medically. Yet, with recognition has come a flood of misinformation, unproven therapies, and misplaced claims of expertise. The Indian Menopause Society (IMS) is to be commended for these state-of-the-science updated Clinical Practice Guidelines (CPG) on Menopause 2026, summarising all we currently know and need to know.

My recognition of the “menopause void” was triggered in 1964, when, as a young resident in Johannesburg, I was assigned to review a paper titled “*The Fate of the Non-Treated Postmenopausal Woman a Plea for Adequate Estrogen from the Cradle to the Grave.*”^[1] At that time, menopause in textbook was defined in a single line : “physiological amenorrhea.” My search for scientific evidence for estrogen's broader health claims found none, but it sparked a lifelong pursuit.

In 1967, with the support of an open-minded mentor, I established the world's first *Menopause Research Clinic* at Groote Schuur Hospital, Cape Town.^[2] My early studies culminated in the first randomized controlled trial of estrogen therapy (1970), marking the beginning of menopause as a legitimate field of clinical and scientific inquiry^[3]

Serendipity came to the fore in April 1973, when I received a letter from one Pieter van Keep, MD, PhD, Director-General of The International Health Foundation (IHF) based in Geneva, Switzerland expressing interest in my early medical publications, telling me of his early social studies on menopause, and inviting my research collaboration. The germinal ideas for much of organized menopause-related medicine had its origin on 1 day in May 1973, over 50 years ago when I met Pieter van Keep.

Over a single day of intense discussion, and more than one glass of wine we conceived the idea of a menopause club, later to become the International Menopause Society (IMS), scientific meetings that became the International Menopause Congresses, and a newsletter, later evolving into *Maturitas*, the first dedicated menopause journal. Our shared conviction was that menopause (my basic and clinical science research approach melded well with Pieter's psychosocial interests) should be addressed through multidisciplinary collaboration linking biology, psychology, and social science. That belief remains central to the success of IMS, *North American Menopause Society* (NAMS), and the global menopause movement.

By the mid-1970s, we had convened the first *International Menopause Congress*, and I introduced a standard set of definitions on menopause terminology and worked with the World Health Organization and IMS to further develop this process.^[4,5] The STRAW staging system was based on my published modification of the original staging table of van Keep and Kellerhals from the 1970's.^[6] Later, the founding of the NAMS in 1988 furthered our mission of scientific rigor and professional education, leading to the launch of *Menopause* (journal of NAMS), and the *Certified Menopause Menopause Practitioner* program.

For me at least, after almost 60 years of studying the menopause, the wheel has indeed turned full circle. I published in 1969 on the state of the art of postmenopausal hormone therapy at that time.” My conclusion *“The possible major disadvantages of long-term therapy on the one hand are a fear of carcinogenesis and thrombogenesis. These risks, if valid, are extremely rare. On the other hand, the possible advantages of long-term therapy are also as yet unproven. Exogenous oestrogens are of undoubted value in the relief of symptoms such as hot the associated bouts of perspiration, and atrophic vaginitis.*

Their use in the prevention of coronary arterial disease and the problems of osteoporosis hold promise but the results of long-term prospective studies must be awaited before their routine use for the prevention of these disorders can be advocated... an important contribution of the gynecologist would be a more conservative approach to the removal of normal ovaries from the premenopausal female,”¹ remains largely true today.

The 2002 termination of the Women’s Health Initiative (WHI) estrogen-progestin arm was a pivotal moment. Amid public confusion, I convened experts through NAMS to publish the first evidence-based position statements on menopausal hormone therapy. These emphasized transparency, conflict-interest disclosure, and independence from industry influence - principles that remain vital today. Persistent impediments include misinterpretation of the WHI findings, limited funding for fundamental research, the erosion of public trust, algorithmic rather than individualized care, and pseudoscientific noise from media voices lacking accountability. Above all, medicine must measure value not merely by risk-benefit ratios but by improvements in *women’s quality of life*.

The IMS CPG 2026 exemplifies these ideals, scientifically grounded, culturally contextual, and ethically transparent. May it empower clinicians to deliver informed, compassionate, and personalized menopause care. For, as Edward Gibbon said, “I have but one lamp by which my feet are guided, and that is the lamp of experience.” That lamp continues to light the path forward toward informed, compassionate, and individualized care for every woman at midlife and beyond.

Wulf Utian^{1,2}

¹Department of Reproductive Endocrinology, Case Western Reserve University,

²Cleveland Clinic, Cleveland, OH, USA

REFERENCES

1. Wilson RA, Wilson TA. The fate of the non-treated postmenopausal woman – A plea for adequate estrogen from the cradle to the grave. J Am Geriatr Soc 1963;11:347.
2. Utian WH. Menopause clinics: Purpose, function and international comparisons. In: van Keep PA, Utian WH, Vermuelen A, editors. The Controversial Climacteric. Lancaster: MTP Press, Lancs; 1982. p. 14761.
3. Utian WH, Feminine forever? Current concepts on the menopause. S Afr J Obstet Gynaecol 1968;-61:07.
4. Utian WH, Serr D. The climacteric syndrome. In: van Keep PA, Greenblatt RB, Albeaux Fernet M, editors. Consensus on Menopause Research. Lancaster: MTP Press; 1976. p. 1-4.
5. Utian WH. Menopause - A proposed new functional definition. Maturitas 1991; 14:1-2
6. Utian WH. Menopause in Modern Perspective. New York: Appleton Century Crofts; 1980.
7. Utian WH. The pros and cons of longterm oestrogen administration to the postmenopausal female. Med Proceed 1969;15:30713.

A UNIFIED MISSION FOR MENOPAUSE CARE

63

MESSAGE FROM THE PRESIDENT ELECT- THE INTERNATIONAL MENOPAUSE SOCIETY 2026

The 2026 Clinical Practice Guidelines on Menopause of the Indian Menopause society provide a holistic guidance for the physicians in the care of midlife women. The comprehensive guidance from diagnosis to management will improve the care for the midlife women and optimise their health for better quality of life in their latter years. Congratulations to the Indian Menopause Society for a very impactful Clinical Practice Guidelines on Menopause!

With best wishes,

Ang Seng Bin

President-Elect of International Menopause Society 2026

Chair of the APMF Consensus

Dear Colleagues,

Warm Greetings! Today, in the era of science and technology, a woman's lifespan has increased. So, a woman passes more than one-third of her life in the menopausal age group. A woman is considered the pivot of the family. So, her health is of utmost importance for the betterment of a family, society, and ultimately the nation. Today, the Indian Menopause Society (IMS) is rocking at the national and international levels. The IMS's main mission is to help a midlife woman lead a healthy, happy life.

Of course, today, everyone is interested in endoscopy and infertility, but at the same time, the proper knowledge of menopause management is also a need of the hour.

I am so lucky that, in 2020, when I was the Secretary General of the IMS, the Clinical Practice Guidelines (CPGs) were updated. This year, as the President of the IMS, we will launch the Updated CPGs 2026.

It gives me great pleasure to share with you the Clinical Practice Guidelines on Menopause (CPG-M 2026), was developed under the aegis of IMS. These guidelines represent a landmark effort to advance evidence-based, context-specific, and holistic care for women during the menopausal transition and postmenopause.

Menopause is no longer viewed merely as a physiological event requiring treatment only when symptoms become troublesome. Contemporary evidence clearly identifies this life stage as a critical window for preventive health interventions, early risk assessment, and long-term well-being. The newly released CPG-M reframes menopause care by integrating global scientific evidence with Indian data and expert consensus, thereby ensuring relevance, feasibility, and scientific rigour for real-world clinical practice in our country.

Recognising the diversity of healthcare delivery models and population characteristics in India, the CPG-M offers country-specific recommendations that cannot be directly extrapolated from Western guidelines. A major strength of this document is its structured, three-tier healthcare approach and its emphasis on multidisciplinary care, involving gynaecologists, physicians, endocrinologists, cardiologists, oncologists, psychologists, nutritionists, physiotherapists, and policymakers.

Key objectives of the guidelines are as follows:

- Systematic assessment, diagnosis, risk stratification, and individualised management of menopausal women
- Supporting primary care physicians with clear referral pathways
- Integrating menopausal health into national noncommunicable disease strategies
- Promoting the establishment of structured menopause clinics across levels of care
- Stimulating research in menopausal medicine, especially in the Indian context.

The document has been developed using a rigorous methodology, including the PICOTS framework, systematic literature searches, expert appraisal, and internal and external peer review.

Recommendations are graded using the GRADE system, ensuring transparency and reliability.

Importantly, the guidelines reflect a balanced and evidence-based approach to menopausal hormone therapy, emphasising individualised risk–benefit assessment, shared decision-making, and ongoing review.

By adopting these guidelines, healthcare professionals can significantly improve the quality of care, facilitate early detection of chronic diseases, strengthen preventive health strategies, and contribute to healthy ageing in women. Despite gaps in Indian research data, the CPG-M lays a strong foundation for future studies and policy initiatives.

I strongly encourage all clinicians and stakeholders involved in women’s health to read, use, and widely disseminate these guidelines, so that together we can move closer to the IMS vision:

“Fit @ Forty, Strong @ Sixty, and Independent @ Eighty,” which I have elaborated.

“Fit @ 40, Fancy @ 50, Strong @ 60, Sexy @ 70, Independent @ 80, Naughty @ 90, and Healthy @ 100.”

With best wishes,
Dr. Anita Shah

डॉ. अभिजात शेट
अध्यक्ष
Dr. Abhijat Sheth
Chairman



MESSAGE

I extend my warm greetings and best wishes to the Indian Menopause Society for its continued academic leadership in women's health. The *IMS Clinical Practice Guidelines on Menopause 2026* and the *Executive Summary Supplement of the Journal of Mid-Life Health* mark an important milestone in promoting evidence-based, holistic, and culturally relevant care. By focusing on the health of women aged 35 years and above, these guidelines will help clinicians identify risks early, promote healthy ageing, and enhance quality of life across midlife and beyond. The National Medical Commission appreciates this significant contribution to strengthening women's health education and clinical standards in India.

Warm regards,


(Dr. Abhijat Sheth)



अखिल भारतीय आयुर्विज्ञान संस्थान
अंसारी नगर, नई दिल्ली -110029 (भारत)
ALL INDIA INSTITUTE OF MEDICAL SCIENCES
ANSARI NAGAR, NEW DELHI - 110029, (INDIA)
Ph. 011-26594805/4800, Email: director@aiims.gov.in
11th August 2025

दिनांक/Dated :

MESSAGE

It gives me immense pleasure to extend my warm congratulations to the Indian Menopause Society on the release of the Clinical Practice Guidelines on Menopause.

Menopause represents a significant phase in a woman's life, bringing with it a spectrum of physiological, psychological, and emotional changes. As healthcare providers, it is imperative that we remain updated and aligned with evidence-based practices to offer optimal care to women navigating this transition. These guidelines are a timely and comprehensive resource, reflecting the latest scientific advances and the unique sociocultural context of Indian women.

I commend the Indian Menopause Society for their dedication and scholarly rigour in bringing together a multidisciplinary perspective in these guidelines. This initiative will undoubtedly serve as an invaluable tool for clinicians, academicians, and policymakers alike.

Let us work together to ensure that every woman in India receives respectful, informed, and compassionate care during her menopausal journey.

With best wishes,

 M. Srinivas

(Prof. M. Srinivas)

Director

Ph. 011-26594805/4800

director@aiims.gov.in

Indian Mid-Life Registry : Generating Real-World Evidence for Menopause Care in India

"Data is the soul of research-they endure; study design and methodology are its heart-they evolve with time."

Meeta¹

Background and Rationale

India has a large and diverse population of women transitioning through menopause and living for several decades thereafter. Yet systematically collected, longitudinal real-world data describing their symptoms, comorbidities, risk factors and changing health needs remain limited. Much of the evidence informing menopause care originates from populations outside India and may not fully reflect the demographic, socioeconomic, cultural and healthcare characteristics of Indian women. Systematically collected Indian real-world data are therefore needed to complement evidence from randomised controlled trials, population-based studies and international cohorts. Recognising this evidence gap, the Indian Menopause Society (IMS) conceived the Indian Mid-Life Registry (IMLR) as a national platform for generating structured clinical data on women at midlife and beyond.

Design and Scope of the Indian Mid-Life Registry

The IMLR is a prospective, longitudinal, multicentric registry designed for 10 years of structured digital data collection and follow-up. Participating clinicians contribute standardised clinical information from women seen in routine practice. The registry has no predetermined population-sampling strategy and therefore represents women accessing participating clinical services rather than a population-based sample. Data are collected across domains relevant to menopause and healthy ageing, including menopausal status and symptoms, menstrual and gynaecological history, medical and surgical history, personal and family history, lifestyle and social factors, anthropometric measurements, general and systemic examination, and relevant health-risk assessment. A particular strength of the registry is its prospective annual follow-up, which allows evaluation of trajectories of menopausal symptoms, risk factors, comorbidities, and health outcomes over time. Its digital structure supports standardised data capture in routine clinical practice. The objectives include generating Indian real-world evidence, promoting structured electronic health records, enabling collaborative research, and using India-specific evidence to refine future clinical practice recommendations.

Chronological Milestones : From Concept to National Initiative

Meeta, the Founder Chair, conceptualised the IMLR in 2020, coinciding with the IMS Silver Jubilee, and briefed the IMS leadership. The IMS funds the project, with an initial support from Pfizer. Development and brainstorming took place in 2021 in collaboration with the IMS and Medeva teams. The team signed a Memorandum of Understanding with Medeva in April 2021, followed by a pre-pilot at Tanvir Hospital, Hyderabad, on April 10, 2021. We published an invitation to participate in the Journal of Mid-life Health in June 2021. After ethics submission and approval, we invited pilot participants in October 2021, and individual training began in November. Hands-on workshops and pilot meetings continued as we developed standardised clinical proformas and data-entry processes. The IMLR was formally inaugurated on 19 January 2022 and has since evolved into an ongoing multicentric IMS initiative. Regular IMLR meetings have also become a peer-learning forum where clinicians discuss menopause care, challenging clinical scenarios, risk-assessment approaches, and data-quality issues. This educational dimension complements the registry's primary role as a platform for real-world evidence generation.

The registry is fully digital, with Medeva serving as the scientific and technology partner and the platform customised to the requirements of the IMS registry. Importantly, the registry also collects follow-up information, enabling it to move beyond a snapshot of menopause health and provide an opportunity to understand changes in symptoms, risk factors, and health outcomes over time.

Current status

The August 2026 IMLR Status Report records 7,097 consultations and 5,392 patients overall. The registry continues to expand through participating IMS clinicians across India.

IMLR contributing clinicians

The Indian Mid-Life Registry acknowledges the valuable contribution of all participating clinicians to this national real-world evidence initiative. Contributors are listed below in descending order of cumulative patient enrolment, based on the August 2026 IMLR Status Report:

Meeta Meeta (3,261), A. B. Chitra (556), Sangeeta Pahwa (428), Asna Ashraf (153), Amrita Sarkari (140), Madhubala Manickavasagam (110), Jyoti Shah (115), Manjit Mohi (73), Geeta Reddy (67), Jyothika A. Desai (63), Kiran Aggarwal (76), Kunwar Shipra (46), Neelam Aggarwal (37), Jyoti Jaiswal (35), Sudha Sharma (33), Bipasa Sen (30), Sheela Mane (30), Pratibha Singh (27), Jignesh R. Shah (25), Jyothi Unni (20), Ami Yogesh Mehta (19), N. Hephzibah Kirubamani (17), Seema Sharma (12), Ritu Jain (11), M. Lakshmi Rathna (8), Choranur Ambuja (6), Naini Tandon (6), Kiran Pandey (5), Maninder Ahuja (4), Tripura Sundari (3), Kiran Chandna (2), Renuka Malik (15), Shobhana Mohandas (2), Aarti Gupta (1), Anita Jayant Shah (1), Archana Dwivedi (1), Binal D. Shah (1), Gowri Meena Selvaraj (1), Jamuna Devi Gudidevuni (1), Manoj Chellani (1), Navneet Takkar (1), Pooja Gupta (1), Pushpa Sethi (1), Ratnabali Chakravorty (1), Reeta Agarwal (1), Rekha Rani (1), Revathy Janakiram (1), and Vandana Narula (1).

From Registry Data to Scientific Evidence

Since its inception, the registry has begun translating routinely collected clinical data into research outputs across several important areas of midlife health. These include studies of

- BMI and waist circumference at midlife and beyond (Oral Presentation, The International Menopause Society World Congress, Sydney)
- Genitourinary syndrome of menopause (Oral Presentation, The International Menopause Society 20th World Congress, Sydney)
- Anaemia and its association with menopausal symptoms (Oral Presentation, The International Menopause Society Rio)
- Vitamin D status and its association with obesity (Oral Presentation, The International Menopause Society Rio),
- Estrogen-deficiency symptoms in late postmenopause (Poster, The International Menopause Society Rio)
- Cardiovascular risk assessment using WHO and Globorisk models across STRAW+10 stages (Poster, The International Menopause Society Rio)
- Abnormal uterine bleeding during the menopausal transition (Poster, The International Menopause Society Rio)
- A key early registry publication was a multicenter study of genitourinary syndrome of menopause (GSM), published in *Climacteric* in 2025. The study used data from the Indian Midlife Registry to provide multicenter evidence on the prevalence and clinical profile of GSM among Indian women, adding to the limited body of Indian real-world evidence in this important area of menopause care.

Relevance to the IMS Clinical Practice Guidelines

A major objective of the IMS Clinical Practice Guidelines is to contextualise international evidence for Indian women. The IMLR provides a mechanism for progressively strengthening this India-specific evidence base. Associations observed in registry analyses should not be interpreted as proof of causality. They provide important India-specific real-world evidence, while randomised trials, systematic reviews and well-designed comparative studies remain essential for evaluating treatment efficacy, safety and causal effects.

Future Directions

The long-term scientific value of the IMLR will depend on expanding geographic representation, improving the completeness and quality of longitudinal follow-up, standardising definitions, validating clinical variables, and using rigorous statistical methods. Longitudinal analyses will be particularly valuable for studying symptom trajectories, cardiovascular and metabolic risk, bone and musculoskeletal health, genitourinary health, and associations between therapeutic interventions and real-world outcomes. Continued peer-reviewed publication of IMLR data will be important for scientific scrutiny and for incorporating valid findings into subsequent guidelines.

Looking Ahead: A Call To Participate

The IMLR's institutional strength lies in its democratic governance. Led by Founder Chair Meeta and Co-Chair Jyoti Shah, the registry uses an impartial requisition queue system. This allows any participating IMS member to submit research proposals and leverage the collective dataset for peer-reviewed publication. The IMLR remains open to IMS members interested in contributing to this national initiative. Participating in the IMLR offers clinicians multiple unique professional benefits

1. **Clinical Practice Modernisation:** Clinicians gain access to a world-class, customised clinical EMR platform that enhances daily patient care.
2. **Training & Implementation Support:** Upon onboarding, participating doctors receive standard protocols, ethics committee approvals valid across India, case record forms, and direct one-on-one digital training.
3. **Academic Recognition:** Contributing members are given active opportunities to lead, co-author, and publish original research papers utilising the national dataset.

How to Register and Join the Initiative

Reach out directly via the following channel: **Email** drmeeta919@gmail.com | midliferegistry@gmail.com

Conclusion

The IMLR should therefore be viewed as a dynamic national evidence-generation platform rather than solely as a repository of clinical information. Its continuing value will lie in generating longitudinal India-specific evidence that identifies unmet needs, informs research priorities, contextualises international evidence and progressively strengthens future editions of the IMS Clinical Practice Guidelines.

References

1. Meeta M, Tandon VR. An Enriching Journey. *J Midlife Health*. 2022 Jan Mar;13(1):1-2. doi: 10.4103/jmh.jmh_78_22. Epub 2022 May 2. PMID: 35707310; PMCID: PMC9190961.
2. Ashraf AB, Meeta M, Chitra AB, Pahwa S, Shah J, Mohi M, et al. Genitourinary syndrome of menopause: a multicenter study from the Indian Midlife Registry. *Climacteric*. 2025;28(3):329-336. doi:10.1080/13697137.2025.2496681.
3. Meeta M, Anuradha M, Ashraf AB, Aggarwal K, Digumarti L, Singh T, et al. Clinical Practice Guidelines for Menopause: an executive summary and recommendations: Indian Menopause Society 2026. *J Midlife Health*. 2026;17(Suppl 1):S12-S116. doi:10.4103/jmh.jmh_302_25.
4. Indian Menopause Society. Indian Mid-Life Registry protocol and registry records. Indian Menopause Society; 2021-2026. Unpublished data.

WOMEN'S REFLECTIONS ON MENOPAUSE

Keywords: Menopause, biology, perception, lived experience, perimenopause

64

BEYOND BIOLOGY: A WOMAN'S REFLECTION

Menopause is often described biologically as the cessation of menstruation; however, for every woman, the lived experience is far more than a hormonal transition. While the biological changes may be relatively consistent, the experience of menopause is deeply shaped by perception. The way a woman understands menopause through her beliefs, culture, upbringing, education, spirituality, and the messages she has received throughout life deeply influences how she experiences it.

Just as Figure 1 depicts three women carrying the same pot in different ways, menopause, too, is a shared biological event carried differently by every woman. Some experience it as loss, others as liberation; some as uncertainty, others as wisdom and renewal. Comparison is neither fair nor meaningful, because each woman carries her responsibilities, emotions, and transitions in her own unique way.

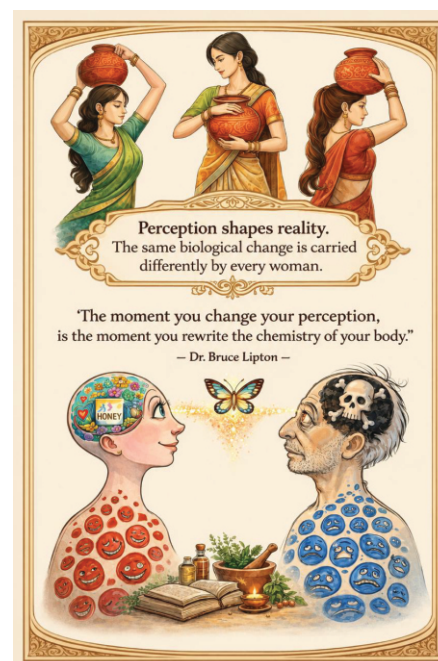


Figure 1 : Perception shapes reality

"The moment you change your perception is the moment you rewrite the chemistry of your body."

Bruce Lipton

Perception has the power to transform experience. Refer to Figure 1. A positive perspective can transform menopause into a phase of strength, freedom, and self-discovery, while fear, stigma, and negative cultural messaging may make the same transition feel burdensome and distressing. Just as a honey bee may be seen either as a source of honey or as a source of fear because of its sting, menopause, too, can be perceived either as a time of decline or as a period of wisdom, renewal, and personal growth. Perspective determines experience.

Across cultures, menopause has often been celebrated as a passage into authority, freedom, and wisdom. In some tribal societies, women enter "wise women's circles." Among Mayan communities, there is said to be no specific word for "hot flash," reflecting a different cultural lens through which menopause is understood. In Indian traditions, menopause has been viewed as *mukti*, freedom from ritual restrictions, and post-menopausal women often become the "family ministers," guiding decisions related to marriages, finances, and household matters. Ancient Ayurveda describes menopause as *rajonivritti*, a stage in which energy once lost monthly is redirected toward *ojas*, the vital essence associated with wisdom, strength, and spiritual growth.

The ancient Indian concept of life stages also reflects this transition. After the years of *Grihastha* family responsibility, a woman enters *Vanaprastha*, the stage of gradual detachment, reflection, and respected social standing, followed by *Sanyasa*, a life of inner freedom and spiritual fulfilment. Ageing, in this perspective, is not decay, but the enrichment of the soul and mind. Menopause, therefore, should not be seen merely as the end of fertility, but as a second birth, a spiritual, emotional, and social transformation. It is not the decline of womanhood, but the beginning of a new identity: stronger, wiser, freer, and deeply reflective, a liberation not only from biological cycles, but also from emotional burdens and limitations.

This chapter moves beyond hormones and hot flashes to honour the real stories of women, their struggles, resilience, healing, and wisdom because menopause is not merely a medical event, but a profound life transition.

REFLECTIONS FROM REAL LIVES

Perimenopause has been a deeply personal journey for me, but it also made me reflect on my mother's experience of menopause decades ago. Over the last six years, I have struggled with severe sleep deprivation, unexplained body aches, gut issues, vaginal dryness, and persistent fatigue. I am grateful that these experiences are now more openly discussed. My friends and I can talk about our symptoms, share resources, and access information that simply did not exist when my mother underwent a hysterectomy and entered surgical menopause at 40.

I still remember people joking about her "suddenly feeling hot and then cold," as though it were amusing rather than a genuine struggle. I remember her frustration with sudden weight gain and her determination to lose it. She would wake at 4 a.m. to run on the treadmill, yet no one advised her about strength training or bone health. Today, at nearly 80, she is severely osteoporotic, has muscle weakness, recurrent UTIs, and still experiences hot flashes.

Looking back, I realise how much women's suffering was normalised and left unspoken. Perhaps the most important change today is not only better medical understanding, but also the permission to speak.

Aarti Vir, Ceramic artist, nuclear family

My hidden battle began after the birth of my second child, postpartum depression, COVID, and perimenopause, all at once. I expected motherhood the second time to feel easier, more familiar, more joyful. Instead, I found myself slipping into persistent sadness, unexplained physical pain, and a stream of negative thoughts I could not control.

At first, I assumed it was normal post-delivery exhaustion. I did not realise I was experiencing postpartum depression. Then I tested positive for COVID, which delayed my recovery and worsened my emotional exhaustion. At the same time, I was unknowingly entering early perimenopause, which intensified everything. The combination left me overwhelmed, disconnected, and unable to function like I once did. Even with support around me, I struggled to explain what I was feeling because I barely understood it myself.

Recovery took nearly three years. It was traumatic, but it taught me the importance of recognising women's silent struggles and seeking help without shame. Many women fight such hidden battles quietly. Sharing these stories is the first step toward healing.

Archana Kavali, Resource manager, Nuclear family

Menopause, for me, was a long and silent journey. I entered perimenopause at 41 without understanding what was happening to my body. Hot flashes, irritability, sleepless nights, and deep physical discomfort became part of daily life. Some nights, I would wake drenched in heat and take cold showers just to cope. What made it harder was the silence around menopause. Nobody talked about it, and much of it was simply endured. I strongly believe menopause education must become a priority. I wish someone had told me earlier about the importance of protein, strength training, and mobility. This year, after one full year without my menstrual cycle, I officially attained menopause at 53. I still have symptoms, but now I face them with awareness and acceptance. Reading, learning, and speaking to other women helped me greatly. If my story helps even one woman feel less alone and more prepared, it is worth sharing.

Mona Budhraj, Educationist, Nuclear family

My menopause transition was complicated by fibroids, adenomyosis, and severe anaemia. It was physically exhausting and emotionally draining, and surgery seemed inevitable. But my wish for conservative management was respected. Four months of progesterone therapy, dietary modifications, and careful follow-up gradually balanced my hormones and made my symptoms manageable and thankfully helped me transit into menopause. Instead of feeling overwhelmed, I felt supported and understood.

Today, I continue with yearly check-ups, a healthy diet, exercise, and gratitude for my well-being. I have even restarted high-altitude Himalayan treks, which demand strength, stamina, and strong bones. The lifestyle changes were difficult at first, but now they are a joyful part of my life. Menopause taught me that healing is not just treatment, it is trust, discipline, and reclaiming strength.

Deepa Reddy, Tech business professional and Happiness and Wellbeing coach, Nuclear family

Menopause was a tumultuous chapter, marked by unrelenting bleeding and crimson stains. My doctor's discerning eye detected polyps; guided by cutting-edge technology, she excised the aberrant growths without anaesthesia. Her

ministrations were a balm to my soul, restoring my joie de vivre. Three years hence, I have emerged triumphant, radiant and rejuvenated. Coconut oil proved a gentle panacea for intimacy's tender challenges. The freedom from the bleeding bequeathed me a life replete with joy and fulfilment.

Suchitrachandrabose, Choreographer, Joint family

Early menopause brought confusion more than anything else. Some people said to avoid HT, others strongly recommended it. The conflicting advice left me uncertain and anxious. I did all the research I could before finally meeting a menopause specialist who explained everything clearly. For the first time, I understood the benefits and considerations of HT. Along with treatment, lifestyle guidance made a huge difference. One of the biggest changes I noticed was in how I handle stress. Situations I once managed easily suddenly felt overwhelming during menopause. HT also made me understand the importance of long-term heart and bone health. Every woman must understand her own body and seek genuine expert advice rather than fear-based opinions. With age comes wisdom; menopause should not interrupt that journey.

Sonali Ohri, Business, Joint Family

About two years ago, I began experiencing significant mental and physical changes, and that was when I learned that I had entered perimenopause. This transition started to disrupt my daily life and had a profound effect on my psychological well-being.

One of the most difficult symptoms was persistent brain fog, which affected my ability to remember things, communicate clearly, and function effectively both at work and at home. Gradually, it began to interfere with my daily routine and confidence. These challenges were accompanied by extreme mood swings, episodes of depression lasting several days, and increased emotional sensitivity. This emotional instability impacted both my work and personal relationships, leading to a loss of confidence and a tendency to withdraw from social interactions.

Physically, I experienced hot flashes, extreme body heat, irregular periods with acute pain, vaginal dryness, and fluctuations in my thyroid levels. These symptoms further intensified my emotional distress and made the transition even more challenging. Understanding that these changes were part of perimenopause helped me make sense of what I was going through. It also made me realise how important awareness, timely medical guidance, and emotional support are for women during this phase of life. Sharing this experience is important to me because many women silently go through these struggles without recognising what is happening. With better awareness and open conversations, this journey can become less confusing and far more manageable.

Sinnu Menon, Professional, Joint Family

Menopause is certainly not the "pause" button on your TV remote. It feels more like the remote control of your body has all its wires mixed up; it does not know whether to pause, mute, restart, or simply shut down. Nearly ten years of life can feel like different seasons of a long and unpredictable series, each phase more intense than the last. Mood swings, depression, irregular periods, weight gain, body aches, urinary infections, and constant fatigue become part of everyday life. You feel emotionally fragile, physically exhausted, and often on the edge of a breakdown. What makes it harder is that life does not slow down. Your partner may be dealing with his own midlife crisis, ageing parents need care, and children are stepping into adulthood. Yet, you are still expected to remain strong for everyone else.

This journey taught me that seeking therapy is not a weakness, being a little selfish is not wrong, and prioritising physical and mental well-being is necessary. I do not know if all the symptoms will ever disappear, but I do know that awareness, support, and self-care make the journey far more manageable.

Anjali Shashidhar, Instructional Designer, Nuclear family

As a cancer survivor at 42, navigating life after treatment was already physically and emotionally challenging. The early onset of menopause added another layer of discomfort, uncertainty, and fear. What made the biggest difference was adopting a holistic approach. Understanding what was happening to my body gave me reassurance and reduced much of the fear that comes with early menopause after cancer treatment.

Along with regular check-ups and necessary investigations, I adopted a healthy diet and consistent lifestyle practices, such as exercise, breathwork, sunlight exposure, and daily affirmations. This helped me regain confidence, emotional balance, and a sense of control. Today, I feel more empowered and more in tune with my body. I have learned that healing is not only about medical treatment, but also about mindset, self-care, and trusting the process. The guidance, support, and encouragement from my doctors helped me move through this phase with strength and positivity.

Inderpreet Kaur, Homemaker/Artist, Joint Family

After my hysterectomy due to Grade 4 endometriosis and ovarian cysts, at the age of 41, my life changed in ways I never expected. I struggled with severe hot flashes, mood swings, weight gain, and irritability that made even simple daily activities feel overwhelming. On top of that, I was diagnosed with hypothyroidism and soon became prediabetic. It felt as though my body was no longer my own, and I was left feeling physically drained and emotionally exhausted.

I tried my best to cope, but nothing seemed to truly help. Gradually, I had almost come to accept that this was going to be my new normal. I met a menopause specialist and felt heard, understood, and reassured. I was explained everything clearly, and, most importantly, it gave me hope at a time when I needed it the most. Within just one month of starting treatment, I experienced nearly 80% relief. My hot flashes reduced drastically, my mood became more stable, and I finally began to feel like myself again. The difference in my energy levels, comfort, and overall well-being has been truly life-changing.

Amina Begum, Homemaker, Joint Family

Menopause is a phase we rarely talk about, yet it quietly transforms us in ways we do not expect. I went through perimenopause and post-menopause, carrying far more than just physical changes. Unless someone experiences it themselves, it is difficult to truly understand what it feels like.

There were days filled with unexplained tears, constant irritation, hot flashes, body aches, fatigue, and a sudden drop in energy that made even ordinary life overwhelming. Irregular and heavy periods, especially while travelling, added both physical discomfort and emotional exhaustion. Weight gain during this phase was another struggle, making it even harder to accept the changes in my body. What made it more difficult was the lack of understanding around me. At times, I felt alone when I needed empathy the most.

I strongly believe there should be greater awareness about menopause, not only for women, but also for their families. Support from spouses and loved ones can make a huge difference. I coped by listening to music, talking to friends, exercising, travelling, and with the help of medication. Looking back, this journey taught me patience, resilience, and the importance of being kinder to myself and to others who may be silently struggling. Sometimes, a little patience, compassion, and understanding can make all the difference.

Bharati Jain, Homemaker, Nuclear family

Perimenopause felt like a quiet storm, one I could hear but no one else. Between the physical heat, emotional shifts, and mental fog, I often feared I was losing the original version of myself. But through HT, self-advocacy, and learning to listen to my body, I discovered a more intentional version of myself instead. At 54, I am less concerned with external expectations and more focused on inner balance. This journey taught me that while I cannot control the changing tides of biology, I can choose how I navigate them. With the support of HT and a strong commitment to movement, I have learned to manage this phase with confidence. Fitness is no longer just about the miles I walk it is about creating a strong foundation for my body, mind, and spirit.

I no longer see menopause as a decline, but as a sharpening of my own resolve. I moved through the fog by picking up the iron and trusting my own strength. For me, muscle is longevity, and weight training became the way back home to myself.

Anita Medasani, Graphic Designer, Nuclear Family

After completing the demanding Dzungri and Pin Bhaba Pass treks, I arrived at a powerful realisation: life does not simply continue after menopause; it can rise to entirely new heights.

A few years earlier, at 47, menopause had brought a cascade of challenges. A diagnosis of rheumatoid arthritis and osteoporosis made even the simplest movements feel daunting. There were days when walking ten feet seemed impossible. But that difficult phase became a turning point. Somewhere along the way, I discovered a new passion for trekking. I needed a dream that felt bigger than my fears, and I chose the mountains. I realised that every mountain I climbed outside was also helping me climb the mountain within me, the mountain of self-doubt, fear, and limitations I once believed defined me. With every step upward, I built resilience, quietened doubt, and rediscovered my own inner strength.

With consistent medical guidance, the right medications, and proper supplements, I began rebuilding slowly but

steadily. My doctor often reminded me, “Medication is only half the solution; lifestyle, diet, exercise, and sleep are the other half.” I took that to heart. I committed myself to a disciplined diet, daily breathing practices, and five days a week at the gym. From struggling to move to standing atop Himalayan passes, this journey taught me that menopause is not an ending, but a powerful beginning. With the right support and unwavering dedication, our dreams do not diminish; they expand.

Embrace the change. Your greatest adventures may still lie ahead.

Rama Regulla, Data, Insights & Analytics Professional / Mom of two boys / Plant lover / Trekker / Slow travel enthusiast, Joint Family

Bridging The Clinical & The Personal Gap: “A Gynaecologist’s Journey Through Genotourinary Syndrome”

Anonymous

As a gynaecologist, I learned that textbooks provide knowledge, but lived experience provides empathy. When I entered menopause at 46, I felt fortunate to escape severe bleeding and hot flashes. But by 49, I developed genitourinary syndrome of menopause (GSM), and everything changed. Post-coital cystitis, bladder cramps, pain, and emotional exhaustion became my reality. Managing estrogen creams, lubricants, and HRT taught me that GSM is not just “dryness”; it quietly erodes intimacy, movement, confidence, and quality of life. I had to skip aerobics classes just so my body could heal. That personal frustration opened my eyes to the silent suffering of countless patients who never shared their distress.

Today, I ask every midlife woman gently about intimacy and discomfort, even if she visits for unrelated complaints. That one simple question has uncovered countless hidden cases of GSM.

I realise we are not merely treating a mucosal lining; we are restoring dignity, relationships, and a woman’s sense of self. My own struggle made me a better physician. It has strengthened my resolve that no woman should walk this path alone. It has taught me that True healing, I have learned, lies not only in treatment protocols, but in listening, understanding, and offering an empathetic hand to guide her.

CONCLUDING REFLECTION

Medicine often views menopause as a hormone deficiency state, but women experience it as far more of a “change of life,” shaped by family, work, identity, ageing parents, partners, and personal transformation. The journey often moves from confusion and loss of control to understanding, confidence, and renewal. It is not simply about symptoms, but about identity, dignity, and adaptation. Some aspects are universal, some are shaped by culture, and some are within our control. What remains constant is the need to listen to women’s lived experiences.

Bell’s three models of menopause care, the biological, psychological, and environmental, teach us that menopause is not merely a condition to be treated, but a life transition to be understood. Hormones may ease symptoms, but empathy restores confidence, knowledge rebuilds strength, and support renews identity. Menopause care is not simply about adding years to life, but about adding life, dignity, and meaning to those years.

“God, grant me the serenity to accept the things I cannot change, the courage to change the things I can, and the wisdom to know the difference.”

Reinhold Niebuhr



Indian
Menopause Society

