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International Menopause Society (IMS) recommendations and key messages on women's midlife health and menopause

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REVIEW ARTICLE

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International Menopause Society (IMS) recommendations and key messages on women's midlife health and menopause

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ABSTRACT

Following a rigorous systematic review of the literature, the International Menopause Society (IMS) has produced detailed new recommendations and key messages on women's midlife health, menopause and menopause hormone therapy (MHT) to help guide healthcare professionals to optimize their support and guidance to women at this critical stage of life. The term MHT has been used to cover therapies including estrogens, progestogens, gonadomimetics and combined regimens. This guidance provides a summary of the recommendations and key messages generated from the systematic review process. The longer version, including the detailed text, key meta-analyses, references, figures and supplementary materials, will be published simultaneously online and can be accessed via the IMS website (https://www.imsociety.org/statements/ims-recommendations/). The quality of evidence and the strength of recommendations used in this guideline are based on the Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) and the Appraisal of Guidelines for Research & Evaluation II (AGREE II) approaches. The new recommendations now include levels of evidence, grades of recommendations, good practice points and key messages.

The recommendations were developed by a body of 38 authors and 27 support team members derived from the IMS and other organizations. Global stakeholder surveys, targeted at both healthcare providers and consumers, were initially conducted to identify the key questions. A Publication Steering Committee (PSC) provided oversight of the process through regular meetings and ensured consistency of methodology. By the end of the process, 30 completed sections were submitted by the authors to individual lead reviewers selected from the PSC to provide peer review and finally endorsed by the PSC, IMS board and stakeholders. Overall, 342 recommendations (285 supported by research data and 57 good practice points) and 40 key messages have been formulated. These span a diverse range of health topics, including lifestyle, midlife body changes, vasomotor symptoms, genitourinary syndrome of menopause, osteoporosis, cardiometabolic health, dementia, premature ovarian insufficiency and various malignancies. A new section addresses the often-overlooked topic of sarcopenia which requires urgent attention. Current controversial topics, such as the influence of the media, the role of the pharmaceutical industry and publication ethics, are also explored. The overall aim of these recommendations and guidelines is to provide the blueprint for support and guidance to women on midlife health and menopause, given the latest available evidence. In preparing these international recommendations, experts have endeavored to consider geographical variations in medical care, prevalence of diseases/conditions, symptom severity, availability and licensing of MHT and alternatives, and country-specific attitudes of the public, medical community and health authorities towards menopause management.

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Introduction

We are now living in an era where information about women's midlife health and menopause is much more easily accessible by healthcare professionals (HCPs) and the public. However, the quality of this information is variable and can often be polarized, misleading and disempowering [1,2]. Attitudes from social media toward the management of menopause have significantly influenced how women manage their individual menopause experience. With this background, it was imperative that the International Menopause Society (IMS) provided updated information which was derived from rigorous systematic reviews of the best research available to facilitate evidence-based management by HCPs. A recent publication that formally appraised menopause guidance emphasized the importance of only extracting and comparing the recommendations from the most robust national and international documents [3]. It is hoped that the robust methodology applied in producing this latest IMS guidance will optimize the provision of high-quality, locally relevant information, thus empowering women to personalize their menopause management choices.

The IMS is grateful to the large expert writing group for their enormous efforts to provide these new evidence-based recommendations and key messages on women's midlife health and menopause. In the time that has passed since publication of our last recommendations [4], new research into the health of midlife women and re-evaluation of existing data have allowed clinicians worldwide to gain more clarity into the role of MHT and alternatives, not only in the alleviation of troublesome menopausal symptoms but also in the prevention of diseases of aging.

The format of these new recommendations has evolved considerably since the last publication. The scope of the project was to provide guidance on the overall management of midlife health and menopause. The rigorous methodology required commencement with initial stakeholder surveys to define the key Population, Intervention, Comparison, and Outcome (PICO) questions, with topic-specific systematic reviews by two independent reviewers, where appropriate. This resulted in either an update or a complete rewrite of the previous text. The expert authors were asked to produce lists of recommendations, including the strength of the recommendations and levels of evidence, good practice points (GPPs) and key messages. These have been published in this article as a summary of high-quality evidence where available, and as quick reference points for HCPs requiring an overview of good practice in our specialty. A more detailed version, containing the full text and references, is available online.

It is hoped that this guidance will provide an overview that serves as a common platform on issues related to the various aspects of menopause, which can be easily adapted and modified according to local needs. Throughout the document, the term menopause hormone therapy (MHT) has been used to cover therapies including estrogens, progestogens and combined therapies. In view of national and regional variations in MHT availability, issues regarding specific MHT regimens and dosages are covered in more detail in the full text online document, including a table of some treatment options (https://www.imsociety.org/statements/ims-recommendations/). In line with research on the topic, terminology and discussion, the guideline is focused on women, but the IMS recognizes that there are individuals who are transgender or who do not identify with the terms used in the literature. Although the term 'women' is used, it is not intended to isolate, exclude or diminish any individual's experience nor to discriminate against any group.

Methodology: searches/levels/evidence grades

This guideline was developed by a body of experts derived primarily but not exclusively from the IMS. The Ovid MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science and ClinicalTrials.gov databases were searched for relevant publications using the MeSH (Medical Subject Headings) and keyword search specific to each specialist area within menopause physiology and medicine. Information was also sourced from international guidance documents (consensus statement/position statement/clinical practice guideline) published by organizations such as the IMS, the European Menopause and Andropause Society (EMAS), The Menopause Society (TMS), the Endocrine Society, International Osteoporosis Foundation (IOF) and European Society for Clinical and Economic Aspects of Osteoporosis (ESCEO). Particular attention was paid by the authors to new publications from 2016 onwards, the last time the IMS Recommendations were updated. Covidence, an online systematic review management tool, was used by the majority of authors for uploading and selecting relevant articles. The topics to be included were informed by an international survey of consumers and HCPs.

The quality of evidence and the strength of recommendations used in this 2025 guideline are based on the Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) [5] and the Appraisal of Guidelines for Research & Evaluation II (AGREE II) [6] approaches. Article selection was based on predefined relevance criteria, including alignment with the clinical questions, population characteristics, study design and reported outcomes. Following selection, the quality of original research was evaluated using the GRADE framework, which considers five key domains: risk of bias, inconsistency, indirectness, imprecision and publication bias. In principle, recommendations should be derived from all available clinical practice guidelines. However, a full AGREE II assessment of each guideline is a resource-intensive process. Therefore, we predominantly relied on the most recent systematic reviews and on critical appraisals of menopause guidelines that had applied the AGREE II tool to ensure methodological rigor and evidence-based recommendations [3,7]. Compared to the 2016 IMS Recommendations, this update applies a more structured and transparent methodology by systematically incorporating these formal assessment tools – reflecting a notable shift toward greater methodological rigor.

Table 1 presents the definitions for levels of evidence (⊕⊕⊕⊕ [HIGH] to ⊕◯◯◯ [VERY LOW]) and grades of recommendations (A, B, C or D) used when assessing the quality of data and strength of recommendations in each section. Each recommendation is based on both the level of evidence

Table 1. Quality of evidence and letter grades of recommendations.

Quality of evidence	*Description*	*Examples*	*Grades of recommendation*	*Criteria*
⊕⊕⊕⊕ HIGH	Further research is very unlikely to change our confidence in the estimate of effect	High-quality systematic reviews and meta-analyses of randomized controlled trials or observational studies Randomized clinical trials without serious limitations Well-performed observational studies with very large effects (or other qualifying factors)	A	At least one systematic review and meta-analysis of randomized controlled trials, or randomized controlled trials or observational studies rated as ⊕⊕⊕⊕, and directly applicable to the target population and demonstrating overall consistency of results
⊕⊕⊕◯ MODERATE	Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate	Well-conducted systematic reviews and meta-analyses of randomized controlled trials or observational studies Randomized clinical trials with serious limitations Well-performed observational studies yielding large effects	B	A body of evidence including studies rated as ⊕⊕⊕◯ directly applicable to the target population and demonstrating overall consistency of results
⊕⊕◯◯ LOW	Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate	Systematic reviews and meta-analyses of randomized controlled trials or observational studies with serious limitations Randomized clinical trials with very serious limitations Observational studies without special strengths or important limitations	C	A body of evidence including studies rated as ⊕⊕◯◯ directly applicable to the target population and demonstrating overall consistency of results
⊕◯◯◯ VERY LOW	Any estimate of effect is very uncertain	Randomized clinical trials with very serious limitations and inconsistent results Observational studies with serious limitations Unsystematic clinical observations (e.g. case series or case reports)	D	A body of evidence including studies rated as ⊕◯◯◯ directly NOT applicable to the target population and demonstrating overall inconsistency of results
Good practice point/ expert opinion	Recommended best practice based on the clinical experience of the guideline development group	Based on expert consensus where formal evidence is lacking		Context-specific advice based on clinical expertise

Note: the authors have strived for a consistent style of assessment and reporting by providing clear guidelines to the section authors at the beginning of the guideline process. However, due to the multi-author nature of this document, some variation in the consistency of data reporting and interpretation is inevitable.

and other factors such as feasibility, values, preferences, and the balance of benefits and harms.

Areas where advice has been provided in the absence of good evidence, but based on extensive experience, are annotated as GPPs.

Areas where evidence-based information has been provided as a statement, but not as a recommendation for management per se, are referred to as 'Key Messages'. A Key Message (KM) may (or may not) have a level of evidence assigned but not a strength of recommendation.

Key explanatory notes

Topics 27-29 were included due to interest ascertained in the healthcare professional and public stakeholder surveys, but it should be noted that the recommendations and key messages were derived from expert opinion as these topics were not amenable to formal systematic reviews of the scientific literature.

The ⊕ symbols (e.g. ⊕⊕⊕⊕) indicate the quality of the underlying evidence – how confident we are that the effect estimate is accurate.

The letter grades (A–D), on the other hand, represent the strength of the recommendation – that is, how strongly the evidence is rated or an intervention recommended. These grades are based not only on the quality of evidence, but also on factors such as feasibility, values, preferences, and the balance of benefits and harms (where consideration is being given to the recommendation being implemented).

For example, if the level of evidence is high (⊕⊕⊕⊕), but the recommendation would be difficult to implement – for example, due to feasibility/resource restraints – then a lower strength of recommendation (B) can be given (e.g. ⊕⊕⊕⊕ B).

Conversely, if the level of evidence is moderate (⊕⊕⊕◯), but there is concern that failure to implement the recommendation would have a deleterious effect on health/quality of life, then a strong recommendation (A) can be given (e.g. ⊕⊕⊕◯ A).

A Publication Steering Committee (PSC) was set up consisting of the chair/lead author, representatives from the IMS secretariat, key authors, a librarian, a methodologist and a statistician to provide oversight of the process through regular meetings and issuing of guidance. Draft sections were submitted by the author(s) to lead reviewers selected from the PSC to provide peer review. The sections were then returned to the authors, who answered any queries and returned the documents to the reviewers for final approval and inclusion in the overall recommendation manuscript. The final draft of the manuscript was reviewed by the PSC and the IMS Executive Committee and Board. Healthcare provider (HCP) and public opinions were then sought regarding the final draft before publication.

Results (recommendations and key messages)

The following sections summarize the recommendations and key messages within each topic/key question.

1. Midlife body changes – metabolic and governing principles

- Weight gain and body composition changes are common among midlife women. ⊕⊕⊕⊕ KM
- Midlife weight gain in women is mostly a result of chronological aging, and not menopause. ⊕⊕⊕◯ KM
- The aging-related decrease in total energy expenditure is the most important cause of midlife weight gain. ⊕⊕⊕⊕ KM
- Menopause-related decline in estrogen is the major cause of an increase in abdominal adiposity among midlife women. ⊕⊕⊕⊕ KM
- Increased abdominal obesity, even in the presence of a normal body mass index (BMI), confers a significant cardiometabolic risk in postmenopausal women. ⊕⊕⊕⊕ KM
- MHT effectively manages menopause symptoms but does not have a direct impact on body weight. ⊕⊕⊕⊕ KM
- Midlife women should be screened for weight gain, and appropriate counseling and management options should be offered. Behavioral modification, calorie restriction and regular physical activity are the most important interventions for preventing and managing midlife weight gain. ⊕⊕⊕⊕ A
- Menopause symptoms, particularly vasomotor symptoms (VMS), sleep disturbances and mood disorders, should be diligently managed to help improve adherence to healthy lifestyle measures for weight management. ⊕⊕⊕◯ B
- In the absence of a contraindication, MHT should be considered for the management of menopause symptoms in postmenopausal women, but MHT should not be used for weight management or for improving body composition. ⊕⊕⊕⊕ A
- Estrogen-based MHT can attenuate the body fat distribution changes of menopause and lower insulin resistance in a dose and formulation-dependent manner, but MHT use is not indicated for this reason. ⊕⊕⊕⊕ A
- Anti-obesity medications can be an important adjunct to lifestyle interventions for weight loss in midlife women who meet the BMI criteria for their use. However, these therapies can be expensive and typically require long-term use. ⊕⊕⊕⊕ A

2. Diagnosis of menopause including Stages of Reproductive Aging Workshop+10 (STRAW+10)

- Staging of reproductive aging should generally follow the STRAW+10 guidelines. GPP
- The diagnosis of menopause is a clinical diagnosis not dependent on special investigations. Supportive criteria described in STRAW+10 should be used for staging women who cannot be staged based on menstrual cycle characteristics. GPP
- Presently, the gold standard STRAW+10 criteria for determining menopause stage are based on menstrual cycle characteristics, including regularity and skipping of menstrual cycles, with blood tests for estradiol, follicle stimulating hormone (FSH) and/or anti-Müllerian hormone (AMH) conducted only as supportive criteria or as primary criteria for women who cannot otherwise be staged. ⊕⊕⊕⊕ A
- While the STRAW+10 guidelines, which rely on menstrual cycle irregularity, provide a useful clinical framework for identifying menopausal stages, the onset of menopausal symptoms is frequently earlier than suggested by STRAW+10, and VMS together with changed menstrual flow may signal the onset of the menopause transition. KM
- In women >40 years of age, the onset of moderately-to-severely bothersome VMS, regardless of menstrual cycle changes, should prompt a clinical evaluation of reproductive staging. ⊕⊕⊕◯ A
- The diagnosis of POI should be suspected in women younger than age 40 years with amenorrhea or irregular menstrual cycles for more than 4 months and with confirmed FSH values >25 IU/L. GPP
- Menopause between ages 40 and <45 years is termed early menopause. GPP

3. Lifestyle, diet, exercise

- Obesity may exacerbate menopausal symptoms, particularly VMS, while diets rich in fruits and vegetables may help alleviate these symptoms; however, their effect is debatable. ⊕⊕⊕◯ B
- HCPs should be aware that weight loss of 5–10% is sufficient to improve many of the abnormalities associated with insulin resistance. ⊕⊕⊕⊕ B
- Key food groups such as vegetables, fruits, legumes, nuts, whole grains, olive oil and fish are fundamental components of a health-promoting dietary pattern, offering protective effects on metabolic pathways and supporting long-term weight regulation. ⊕⊕⊕◯ B
- The Mediterranean diet appears to attenuate age-related increases in BMI and waist circumference, with more pronounced effects observed when combined with a hypocaloric diet and regular physical activity. ⊕⊕⊕⊕ B
- Adherence to a Mediterranean diet, as defined by the traditional food pyramid, has been associated with a reduced risk of cardiovascular disease ⊕⊕⊕⊕ A; improvements in intermediate cardiovascular outcomes, such as blood pressure, lipid profile, metabolic syndrome and type 2 diabetes prevention ⊕⊕⊕◯ B; as well as benefits in cognitive function, mood regulation, the incidence of certain cancer types and overall mortality reduction. ⊕⊕◯◯ C
- The Dietary Approaches to Stop Hypertension (DASH) diet has been shown to improve lipid profiles and reduce blood pressure, although evidence supporting its long-term effects on clinical outcomes remains limited. ⊕⊕◯◯ C
- Regular exercise in midlife and older women is recommended to improve bone and muscle health,

reduce cardiovascular and all-cause mortality, and decrease the risk of falls and fractures. ⊕⊕⊕⊕ B
- At least 150 min of moderate-intensity exercise per week is recommended as optimal; with two additional weekly sessions of resistance exercise providing further benefit. ⊕⊕⊕⊕ B
- The fitness of the older adult should be considered when recommending the intensity of aerobic activity. GPP
- Smoking should be stopped or avoided. ⊕⊕⊕⊕ A
- HCPs should inform women that a healthy lifestyle includes socializing and being physically and mentally active. GPP

4a. Vasomotor symptoms/menopause hormone therapy

- HCPs should inform women that VMS, such as hot flushes and night sweats, are hallmark features of the menopause transition and menopause, and can markedly impair quality of life. ⊕⊕⊕⊕ A
- MHT is the most effective treatment for VMS. Where available, it should therefore be offered to women with bothersome VMS who do not have significant contraindications or are not MHT averse. ⊕⊕⊕⊕ A
- When used for the treatment of VMS, MHT is typically recommended to women younger than 60 years old or within 10 years of menopause after a full evaluation of benefits and risks. ⊕⊕⊕⊕ A
- HCPs should be aware that both transdermal and oral estrogen routes are effective in treating VMS, with low to moderate doses of MHT alleviating symptoms in more than 80% of postmenopausal women. ⊕⊕⊕⊕ A
- Where symptom control is inadequate with low to moderate doses, a stepwise approach involving appropriate investigation, dose escalation, a change in preparation or the route of administration may be considered to optimize individual therapeutic response, whilst reducing potential risks. GPP
- Estrogen-only therapy (ET) is recommended for women without an intact uterus, while an estrogen–progestogen combination is recommended for women with an intact uterus. ⊕⊕⊕⊕ A
- Tibolone, a selective tissue estrogenic activity regulator (STEAR) has been shown to significantly reduce VMS compared to placebo in postmenopausal women (odds ratio 0.33, 95% confidence interval 0.27–0.41). ⊕⊕⊕⊕ A
- Estetrol (E4) (a native estrogen in the fetal liver thought to have selective tissue actions), in an oral dose of 15 mg daily has been shown to reduce both the frequency and severity of moderate to severe hot flushes in postmenopausal women. At the time of writing, this had not yet received marketing approval. ⊕⊕⊕⊕ A
- HCPs should be informed that routine measurement of serum estradiol levels to determine the appropriate dose of MHT is generally not recommended. However, serum estradiol level measurement may be helpful in women who report inadequate symptom relief, persistent adverse effects and women with POI or early menopause. GPP
- Women should be counseled that there is no definitive, evidence-based guideline on the optimal method for discontinuing MHT, and VMS may recur in up to 87% of cases following the discontinuation of MHT. ⊕⊕◯◯ C

4b. Vasomotor symptoms: non-hormonal pharmacological

- MHT remains the gold standard treatment for menopausal hot flashes for healthy symptomatic menopausal women when initiated close to menopause. However, for women with health conditions considered strong contraindications to hormone therapy (HT) or those who cannot or choose not to take MHT, non-hormonal pharmacologic therapies are needed. KM
- A new class of neurokinin-targeted therapies, which are non-hormonal treatments, offers an evidence-based approach for effective treatment. Neurokinin receptor antagonists reduce the frequency and severity of VMS in postmenopausal women by modulating kisspeptin, neurokinin B and dynorphin neurons (KNDy) in the hypothalamus, with effectiveness appearing slightly lower than that of MHT. KM
- Neurokinin-targeted therapies should be considered as a preferred evidence-based, effective non-hormonal option because of the high quality of the randomized controlled trial (RCT) data supporting their efficacy. KM
  - Fezolinetant is an NK3 receptor antagonist, shown to be effective in phase 3 clinical trials with key government approvals for VMS. ⊕⊕⊕⊕ A
  - Elinzanetant is a dual NK1 and NK3 receptor antagonist, shown to be effective in phase 3 clinical trials, with multiple key government approvals for VMS and shown to be effective for endocrine therapy-associated VMS in women with breast cancer. ⊕⊕⊕⊕ A
- RCTs of non-hormonal pharmacologic agents shown to be effective in reducing VMS due to menopause, but without government approval for VMS (except for paroxetine salt 7.5 mg in the USA), include selective serotonin and norepinephrine receptor inhibitors, gabapentinoids, oxybutynin and clonidine. KM
  - Gabapentin is effective with drowsiness as a major side effect compared to selective serotonin reuptake inhibitors (SSRIs)/serotonin–norepinephrine reuptake inhibitors (SNRIs). ⊕⊕⊕◯ B
  - Oxybutynin, approved to treat overactive bladder, has shown effectiveness in reducing VMS. ⊕⊕⊕◯ B
  - Paroxetine should be avoided in women receiving tamoxifen due to its effect on CYP2D6. ⊕⊕⊕◯ B
  - Stellate ganglion blockade has been shown to be effective in small trials, but skilled operators are required to perform it. ⊕⊕⊕◯ B
  - Clonidine is no longer recommended as a first-line treatment due to low potency and side effects. ⊕⊕◯◯ C
- The duration of treatment of VMS with non-hormonal agents should be reviewed periodically, as with hormonal interventions. GPP

5. Genitourinary syndrome of menopause and sexuality

Genitourinary syndrome of menopause

- HCPs should be aware that vulvovaginal atrophy (VVA) and genitourinary syndrome of menopause (GSM) are not identical. GSM includes a wider range of signs and symptoms that may have different causes. GPP
- HCPs should be aware that GSM is very common, clinical presentation may be variable and GSM may have a big impact on quality of life. ⊕⊕⊕⊕ A
- HCPs should be proactive in screening and diagnosing GSM because the impact of the condition is underestimated and inadequately treated. ⊕⊕◯◯ C
- HCPs should offer individualized treatment considering evidence-based data, preferences and needs of women, and access to different options. GPP
- HCPs should treat symptomatic GSM with the aim of improving quality of life and intimate relationships. ⊕⊕⊕⊕ A
- HCPs should be aware and inform women that GSM is a chronic condition that does not resolve without treatment and may return upon discontinuation of therapy. ⊕⊕⊕◯ B
- Long-term treatment is often required as symptoms can recur on cessation of therapy. ⊕⊕◯◯ C
- Systemic risks have not been identified with vaginal low-potency/low-dose estrogens. ⊕⊕⊕◯ B
- HCPs should consider treating asymptomatic women with signs of GSM because symptoms may develop over time and women may benefit from early treatment. GPP
- HCPs should offer vaginal estrogen therapy to improve genitourinary and sexual symptoms associated with the menopause. ⊕⊕⊕⊕ A
- HCPs should consider adding vaginal estrogen therapy if GSM symptoms persist when using MHT. ⊕⊕◯◯ C
- HCPs should be aware that intravaginal dehydroepiandrosterone (DHEA) and ospemifene are alternative options to vaginal estrogen therapy. ⊕⊕⊕◯ B
- HCPs should be aware that there is a lack of data comparing the effectiveness of vaginal estrogen therapy, DHEA and ospemifene for vaginal dryness and dyspareunia. ⊕⊕◯◯ C
- HCPs should offer treatment with vaginal lubricants and moisturizers to women with symptoms of vaginal dryness and dyspareunia. Vaginal lubricants and moisturizers can be used alone or combined with other treatments. ⊕⊕⊕⊕ A
- HCPs should be aware that there is a lack of data regarding the use of systemic or vaginal testosterone for the treatment of GSM. GPP
- HCPs should review women with GSM annually or when it is clinically needed. GPP
- HCPs can consider offering different products with long-term use because response to treatment or availability of products may vary. GPP
- HCPs should be aware that long-term safety varies among different treatments depending on their characteristics. ⊕⊕⊕◯ B
- HCPs should inform women that there is insufficient evidence to recommend the use of laser therapy. ⊕⊕◯◯ C
- HCPs should inform women that there is insufficient evidence to recommend the use of complementary medicines/therapies. GPP
- HCPs should consider referring women to a physiotherapist when pelvic floor abnormalities are associated with GSM. ⊕⊕◯◯ C
- HCPs should consider referring women to a psychotherapist/sex therapist when psychosexual factors are associated with GSM. ⊕⊕◯◯ C

Bladder and pelvic floor

- There is a wide variation in symptoms and signs of urogenital aging. ⊕⊕⊕⊕ A
- HCPs should be aware that lower urinary tract symptoms such as urinary frequency, nocturia and urgency are extremely common in postmenopausal women and the prevalence of incontinence in women increases with age. ⊕⊕⊕⊕ A
- HCPs should be aware that the co-existence of bladder symptoms and the menopause does not necessarily mean that menopause is the prime causative factor. ⊕⊕⊕◯ B
- Lifestyle changes and bladder retraining are recommended as first-line therapy for overactive bladder symptoms. ⊕⊕⊕⊕ A
- All women complaining of stress urinary incontinence will benefit from pelvic floor muscle training in the first instance. ⊕⊕⊕◯ B
- Vaginal estrogen therapy should be considered in postmenopausal women with lower urinary tract symptoms. ⊕⊕⊕⊕ A
- Vaginal estrogen therapy is recommended for the prevention of recurrent urinary tract infections (RUTIs). ⊕⊕⊕⊕ A
- HCPs should be aware that the optimal preparation and duration of vaginal estrogen therapy is not known. GPP
- Antimuscarinic drugs, combined with vaginal estrogen therapy, constitute first-line medical treatment in postmenopausal women with symptoms suggestive of an overactive bladder. ⊕⊕⊕⊕ A
- The use of systemic MHT does not seem to prevent urinary incontinence and is not recommended in the management of urinary incontinence or recurrent lower urinary tract infections. ⊕⊕◯◯ C
- There is currently insufficient evidence to recommend non-estrogen based therapies such as DHEA, ospemifene and vaginal laser for the management of urinary symptoms in postmenopausal women. ⊕◯◯◯ D

Sexual function

- HCPs should be aware that menopause can have a significant impact on sexual well-being and function. ⊕⊕⊕⊕ A
- HCPs should introduce the topic of sexuality routinely and sensitively during menopause consultation. GPP
- HCPs should follow a standard process of care for assessment and management of the most common changes in sexual function, that is, hypoactive sexual desire disorder (HSDD). GPP
- HCPs should recognize and effectively treat GSM as part of the management of changes in sexual function even though there is insufficient evidence of improvement in overall sexual function. GPP
- HCPs should be aware that a personalized management using the biopsychosocial model is needed to improve the quality of sexual life. GPP
- HCPs should consider the general and sexual health of the partner, as well as intimacy and relationship issues, to address sexual symptoms in partnered women. GPP
- HCPs should be aware that MHT prescribed for other indications may improve sexual function, although the benefit is generally small. ⊕⊕⊕⊕ A
- HCPs should consider the use of transdermal testosterone, in doses that approximate physiological premenopausal testosterone, to treat changes in sexual function in menopausal women with a diagnosis of HSDD. ⊕⊕⊕⊕ A
- HCPs should be aware that evidence to use other pharmacological strategies e.g, bremelanotide to treat menopausal sexual symptoms is limited. Very recently, flibanserin has been FDA approved for use in menopausal women. GPP
- HCPs should counsel on the insufficient evidence of complementary medicines/therapies in enhancing specific domains (desire, arousal, orgasm) of the sexual response. ⊕◯◯◯ D
- HCPs should be aware that the use of psycho-education is proven to have valuable benefits in postmenopausal women. ⊕⊕◯◯ B
- HCPs should consider individual and interpersonal psychosocial interventions to improve menopausal changes in sexual function. ⊕⊕◯◯ B

Special populations

Premature ovarian insufficiency

- HCPs should offer vaginal estrogen therapy to improve genitourinary and sexual symptoms. ⊕⊕⊕⊕ A
- Women with POI may be offered vaginal estrogen therapy if genitourinary symptoms are not fully relieved by using systemic HT. ⊕⊕⊕◯ B
- Vaginal lubricants and moisturizers can be used for the treatment of vaginal discomfort and dyspareunia in women with POI and can be combined with other treatments. ⊕⊕⊕⊕ A
- There is currently insufficient evidence to recommend vaginal laser or thermal energy for the management of genitourinary symptoms in women with POI. GPP

Breast cancer and other gynecological cancers

- HCPs should be aware that GSM is frequent and can be severe in breast cancer survivors. ⊕⊕⊕◯ B
- HCPs should offer vaginal lubricants and moisturizers for treatment of vaginal dryness and dyspareunia in women with GSM as first-line treatment. ⊕⊕⊕⊕ A
- HCPs should be aware that when limited evidence is present, the most conservative strategy to treat GSM should be applied. GPP
- Vaginal estrogen therapy, DHEA or ospemifene should not be used as the first line in breast cancer survivors. GPP
- HCPs may consider vaginal estrogen therapy, DHEA or ospemifene in individual breast cancer survivors taking into account evidence-based data, tumor characteristics, the preferences and needs of women, and access to different treatment options. GPP
- HCPs should be aware that for the majority of gynecological cancers, vaginal estrogen therapy, prasterone or ospemifene can be used but attention should be paid to the tumor characteristics. ⊕⊕◯◯ C
- HCPs should inform women that there is currently insufficient evidence to recommend vaginal laser or thermal energy for the management of GSM. ⊕⊕◯◯C

6. Osteoporosis

- Women with osteoporosis should be advised that osteoporosis is a life-long disease and cannot be cured. Planning of the sequencing of drugs and possible drug-free periods should be addressed at the initiation of therapy. GPP
- The duration of therapy and the sequence of drugs and drug-free periods are drug-specific. KM
- Anabolic and anti-resorptive therapy should not be routinely combined. KM
- In sequential therapy, anabolic therapy should preferably be given before antiresorptive drugs. ⊕⊕⊕⊕ A
- Postmenopausal osteoporosis and fractures are avoidable, serious conditions that are underdiagnosed and undertreated. ⊕⊕⊕⊕ B
- Menopause is associated with significant bone loss that is preventable with a variety of drugs. ⊕⊕⊕⊕ A
- Although osteoporosis is defined by low bone mineral density (BMD), this is only one risk factor for fracture. Estimates as to the probability of future fracture, as well as intervention thresholds, should take into account all risk factors. This can best be done using a risk calculator such as the Fracture Risk Assessment Tool (FRAX), Garvan or other population-specific risk

calculators. ⊕⊕⊕⊕ A https://www.fraxplus.org/calculation-tool?country%E2%80%89=%E2%80%899

- Intervention thresholds should be based on FRAX probabilities for major osteoporotic fracture (MOF) or hip fracture over the next 10 years. A country-specific age-adjusted intervention threshold should be calculated as a risk equivalent to that associated with a prior fracture in a woman of the same age with average BMI. The best example of such a model is that developed by the National Osteoporosis Guidelines Group (NOGG) UK. If not available, set threshold values should be used (US model). GPP
- Stratification of the risk of fracture into low, high or very high is helpful in decision-making for the need and type of therapy. GPP
- All perimenopausal and early menopausal women should be screened by FRAX (without dual-energy X-ray absorptiometry [DXA]) or locally developed screening tools and with DXA if risk is established. All women should be screened by DXA at age 65 years if not screened before. GPP
- All postmenopausal women should be educated on a bone-friendly lifestyle, including physical activity (resistance/weight-bearing exercise and falls prevention) and diet containing the recommended calcium intake and vitamin D. This is also an essential adjuvant to any pharmacological intervention. ⊕⊕⊕⊕ A
- MHT is first-line therapy for the prevention of menopause-related bone loss. Benefits are most likely to outweigh any risks when initiated within 10 years after menopause or before age 60 years. Cessation of therapy leads to rapid bone loss. MHT significantly reduces the risk of osteoporosis-related fractures. ⊕⊕⊕◯ A
- Bisphosphonates (BPs) are potent inhibitors of bone resorption with proven efficacy in the prevention of all osteoporosis-related fractures. It is indicated in women at high and very high risk of fracture. A drug-free period should be considered after 3 years of intravenous therapy and after 5 years of oral therapy. Restarting treatment should be based on FRAX values or markers of bone turnover (MBT) as determined after 18 months off risedronate and ibandronate, 2 years off alendronate and 3 years off zoledronate. Osteonecrosis of the jaw and atypical femoral fracture are rare complications. ⊕⊕⊕⊕ A
- The selective estrogen receptor modulator (SERM) raloxifene is indicated in asymptomatic women at risk of vertebral fracture and/or breast cancer. Additionally, bazedoxifene is also protective of hip fracture in women at high risk of hip fracture. ⊕⊕⊕◯ B
- Denosumab reduces the incidence of all osteoporosis-related fractures and is indicated in women at high and very high risk of fracture. There is no limit on the duration of therapy, but cessation is followed by accelerated bone loss and increased risk of fracture that mandates the use of an anti-resorptive drug, such as a BP. ⊕⊕⊕⊕ A
- Teriparatide is a bone anabolic agent that reduces the risk of all osteoporosis-related fractures. It is first-line therapy for women at very high risk of fracture. Duration of therapy is limited to 2 years, after which it should be followed by an anti-resorptive drug such as a BP or denosumab. ⊕⊕⊕⊕ A
- Abaloparatide is a bone anabolic agent that reduces the risk of vertebral and non-vertebral fractures. It is first-line therapy in women at very high risk of fracture. The duration of treatment is limited to 18 months, after which it should be followed by anti-resorptive therapy such as a BP or denosumab. ⊕⊕⊕◯ B
- Romosozumab has a dual action, stimulating bone formation and inhibiting bone resorption. It reduces all osteoporosis-related fractures, and is first-line therapy in women at very high risk of fracture. The duration of treatment is limited to 12 months, after which it should be followed by anti-resorptive therapy such as a BP or denosumab. ⊕⊕⊕⊕ A
- In women at very high risk of fracture, teriparatide, abaloparatide or romosozumab should precede anti-resorptive therapy. ⊕⊕⊕⊕ A

7. Sarcopenia

- HCPs should be aware that sarcopenia, a muscle disease characterized by loss of strength, mass, or physical function, is more prevalent in postmenopausal women due to estrogen deficiency. ⊕⊕⊕◯ B
- HCPs should be aware that the diagnosis of sarcopenia is based on various criteria according to different scientific societies, with the most widespread being that of the European Working Group on Sarcopenia in Older People (EWGSOP2): low muscle strength, low muscle mass and low physical performance. ⊕⊕⊕◯ A
- Assessment for sarcopenia should be combined with the identification of osteoporosis to enable appropriate diagnostic and intervention strategies. ⊕⊕⊕◯ B
- MHT is not recommended for treating sarcopenia in postmenopausal women, as current evidence does not demonstrate significant improvements in muscle mass or strength. ⊕⊕◯◯ C
- Non-pharmacological treatment with regular physical exercise (aerobic and resistance) is recommended as the most effective intervention for sarcopenia. ⊕⊕⊕◯ A
- Consider protein (whey and leucine), creatine or L-citrulline supplementation in addition to physical exercise for the management of sarcopenia, although long-term data are lacking. ⊕⊕◯◯ B/C.
- The role of other types of protein supplementation or magnesium is not well established and, therefore, is not recommended. KM
- HCPs should be aware that the effect of vitamin D supplementation on sarcopenia is inconsistent, although benefits are observed regarding falls reduction and bone health. ⊕⊕⊕◯ A/B
- HCPs should be aware that the Mediterranean diet is associated with greater muscle mass and improved bone quality in postmenopausal women, whereas

pro-inflammatory diets are linked to a higher risk of sarcopenia. ⊕⊕◯◯ A/B
- When implementing caloric restriction for weight loss, a protein-rich diet combined with regular physical activity is recommended to maintain muscle mass and avoid muscle loss. ⊕⊕⊕◯ A

8. Skin, cartilage, connective tissues

- Estrogen receptors are widely expressed across all connective tissues. ⊕⊕⊕⊕ KM
- Estrogen deficiency is associated with adverse changes in skin, hair and tendon composition and quality. ⊕⊕⊕◯ KM
- Estrogen deficiency is associated with increased joint pain and thinning of articular cartilage. ⊕⊕◯◯ KM
- Ovarian hormones may have a role in the presentation, severity and progression of auto-immune diseases such as systemic lupus erythematosus (SLE) and rheumatoid arthritis. ⊕◯◯◯ KM
- The quality of the studies published to date examining the impact of sex hormones on connective tissues and autoimmune dysfunction is low and recommendations for treatment cannot be drawn from the currently available data. GPP

9. Cardiometabolic

- Certain cardiovascular risk factors are unique to or disproportionately affect women, especially diabetes mellitus. Unique risk factors include early menopause or POI, hypertensive disorders of pregnancy, gestational diabetes, preterm delivery, polycystic ovary syndrome and autoimmune diseases. Assessment of these sex-specific factors is essential for accurate cardiovascular risk stratification. ⊕⊕⊕◯ A
- In women aged under 60 years who are recently postmenopausal and without cardiovascular disease, estrogen therapy reduces coronary heart disease (CHD) and all-cause mortality. Multiple analyses, including the Cochrane review, meta-analyses and the Women's Health Initiative (WHI) 18-year follow-up, show consistent mortality benefits when HT is initiated before age 60 years or within 10 years of menopause. ⊕⊕⊕⊕ A
- The daily continuous combined oral conjugated equine estrogens (CEE) + medroxyprogesterone acetate (MPA) data are less comprehensive, but other combined therapy regimens appear to be cardioprotective, as shown in the Danish and Finnish studies. ⊕⊕⊕◯ A
- We recommend that HCPs consider the potential benefits of estrogen/MHT for the reduction of all-cause mortality and prevention of CHD in their decision making when initiating MHT in healthy postmenopausal women below age 60 years or within 10 years of menopause onset. Use of MHT solely for primary prevention of CHD is "off label". GPP
- MHT reduces the incidence of new-onset diabetes and this advantage should be considered alongside other preventive effects of MHT, such as reduction of osteoporosis, bone fracture, colon cancer, CVD and all-cause mortality in women aged <60 years of age with no evidence of CVD. ⊕⊕⊕◯ A
- MHT should not be used for secondary prevention but does not appear to increase the risk of CVD events. ⊕⊕⊕◯ B
- Transdermal estrogen, due to a lower risk of thrombosis and inflammation, may be a reasonable option for symptom relief in women with uncontrolled cardiovascular risk factors. ⊕⊕◯◯ B
- The recent removal of "black box" warnings for "HRT" by the US Food & Drug Agency (FDA) accentuates the benefits versus risks ratio to which the cardiometabolic benefits are a major contributor. KM

10. Coagulation: venous thromboembolism

- Individuals at increased risk for venous thromboembolism (VTE) include those with obesity, inherited thrombophilia or a previous history of VTE. KM
- Individuals requiring MHT should be risk assessed and counseled about their risk of VTE. GPP
- Oral estrogen therapy increases the risk of VTE and is not recommended in women at increased risk for VTE. ⊕⊕⊕⊕ A
- Unlike oral estrogen therapy, transdermal estrogen therapy does not increase the risk of VTE, even in the presence of additional risk factors such as obesity, inherited thrombophilia and previous history of VTE. ⊕⊕⊕◯ B
- Transdermal estrogen is recommended for use in high-risk women requiring MHT, in combination with a suitable progestogen in women with an intact uterus. ⊕⊕⊕◯ B
- For combination therapy, the choice of progestogen is important; the use of suitable progestogens is recommended, such as micronized progesterone, dydrogesterone or a levonorgestrel-releasing intrauterine system. ⊕⊕⊕◯ B
- There is no indication for thrombophilia testing before commencing MHT. GPP
- There is no indication for routine anticoagulation as prophylaxis in women starting MHT. GPP
- In women who develop VTE while taking oral MHT, immediate discontinuation of MHT is not required while the individual is on anticoagulation. ⊕⊕⊕◯ B

11. Central nervous system (including dementia)

Alzheimer's disease

- CEE + MPA increases the risk of all-cause dementia in women who initiate MHT at the age of 65 years or

later, with the most common type of dementia being Alzheimer's disease (AD). ⊕⊕⊕◯ B
- ET is associated with lower risk of dementia in premenopausal women who undergo oophorectomy, supporting the use of ET to prevent dementia in women with premature ovarian insufficiency and early menopause.
- The current data do not recommend initiation of MHT for the primary prevention of AD in naturally menopausal women. ⊕⊕⊕◯ B

Parkinson's disease

- Estrogen therapy should not be used for the prevention or treatment of Parkinson's disease (PD) in the majority of women who underwent menopause within the usual age range (45 years onwards). ⊕⊕◯◯ C
- For women who underwent premature (age <40 years) or early menopause (age 40 to <45 years), either spontaneous or iatrogenic, estrogen therapy should be considered for the prevention of PD. ⊕⊕◯◯ C

Stroke

- The effect of MHT on stroke risk depends on the timing of initiation. ⊕⊕⊕⊕ A
- Women who initiate MHT <10 years after menopause onset or at ages <60 years are at similar risk of stroke compared to women who do not take MHT. ⊕⊕⊕⊕ A
- When initiated >10 years after menopause onset or among women >60 years of age, oral estrogen-containing MHT is associated with increased risk of stroke. ⊕⊕⊕⊕ A
- Stroke risk may vary by MHT administration route, dosage or formulation. ⊕⊕◯◯ C
- Transdermal administration routes and lower doses of MHT may be associated with a lower risk compared to oral and higher doses, respectively. ⊕⊕◯◯ C

Migraine

- For perimenopausal and postmenopausal women with migraine with aura, estrogen-containing oral contraceptives are associated with an increased risk for stroke and there may be an increased risk but of lesser magnitude with oral estrogen-containing HT. ⊕⊕⊕◯ B
- In perimenopausal women with migraine without aura, combined oral contraceptives (COCs) given continuously may be helpful in suppressing ovulation and preventing the triggering of menstrual migraines associated with estrogen withdrawal. Formulations containing estradiol or E4 are considered safer due to more favorable thromboembolic profiles. However, COCs should be avoided in perimenopausal women with other vascular risk factors and should be stopped in women who develop migraine after initiation. ⊕◯◯◯ D
- In postmenopausal women with migraine, transdermal formulations of MHT are preferable to oral formulations, due to lower variability in estrogen levels. ⊕⊕◯◯ C
- For migraine, transdermal MHT formulations are preferable to oral formulations due to their more favorable thromboembolic profiles. ⊕⊕⊕◯ B
- In women with migraine with aura, non-hormonal interventions are effective alternative treatments for menopause-related VMS. ⊕⊕◯◯ C

12. Breast cancer

- In considering breast cancer risk when prescribing MHT it is important to assess the baseline risk. GPP
- Breast cancer risk with MHT varies according to the regimen and the individual's baseline risk. Scores are available to help evaluate the baseline risk. The Gail (https://bcrisktool.cancer.gov/), IBIS (https://ibis.ikonopedia.com/) and CanRisk (https://www.canrisk.org/) tools are all freely available. A recommendation cannot be made to use a specific score. ⊕⊕⊕◯ B
- Breast cancer risk observed with MHT may be partially decreased by selecting women with a lower baseline risk, including low breast density, and by providing education about preventive lifestyle measures (reducing body weight, alcohol intake and increasing physical activity). ⊕⊕⊕◯ A
- Increased breast density is associated with a higher risk of breast cancer and MHT should be prescribed with caution. ⊕⊕⊕◯ B
- Careful radiological surveillance should be considered in cases of high breast density in women using MHT. Combined (estrogen–progestogen) MHT can increase breast density, which may require additional radiological surveillance. ⊕⊕⊕◯ B
- The risk of breast cancer attributable to MHT is small and is similar to, or lower than, the increased risks associated with common lifestyle factors such as reduced physical activity, obesity and alcohol consumption. ⊕⊕⊕⊕ A
- Combined MHT is associated with an increased risk of breast cancer that increases with duration and decreases progressively after treatment. ⊕⊕⊕⊕ A
- Sequential combined regimens may pose lower risk than continuous combined regimens. ⊕⊕⊕◯ B
- Estrogen-alone MHT is associated with a lower risk of breast cancer than that with combined MHT regimens. ⊕⊕⊕◯ B
- There is no difference in risk between oral or transdermal estradiol. There is no robust evidence linking risk with dose. ⊕⊕◯◯ C
- The increased risk of breast cancer is primarily associated with the addition of a synthetic progestogen to estrogen therapy (e.g. CEE + MPA continuous combined therapy) and related to the duration of use. ⊕⊕⊕⊕ A
- The risk appears lower with micronized progesterone, or with dydrogesterone than with another synthetic progestogen, and this may be associated with a

better risk profile for breast cancer than with other synthetic progestogens. ⊕⊕⊕◯ B
- There are not enough data to fully evaluate possible differences in the incidence of breast cancer using different types, doses and routes of progestogens and androgen administration. ⊕⊕◯◯ C
- Data do not suggest any increased breast cancer risk from vaginal delivery of hormones in women with no history of breast cancer. ⊕⊕◯◯ B
- The levonorgestrel intrauterine device is not recommended in women at high baseline risk of breast cancer. ⊕⊕⊕◯ B
- MHT, including tibolone, is not recommended for women with breast cancer or for those at high risk of breast cancer. ⊕⊕⊕⊕ A
- No increase in the rates of breast cancer or in breast density has been observed with testosterone therapy in postmenopausal women. There are insufficient data from RCTs to assess long-term risk. ⊕⊕◯◯ C
- If mastalgia develops on MHT, it may be a sign of poor breast tolerance and necessitate the adaptation of dose/type of treatment. ⊕⊕◯◯ C
- Proactive management of menopausal symptoms in breast cancer survivors improves quality of life and medication adherence. ⊕⊕⊕◯ A
- Individuals affected by breast cancer should be offered routine proactive enquiry about menopausal symptoms and these should be addressed. GPP
- There is no evidence that non-hormonal therapies used for the treatment of VMS after breast cancer affect breast cancer recurrence rates or mortality, and these can be offered as first-line treatment. ⊕⊕⊕⊕ A
- Trials show no evidence that non-hormonal treatments for GSM affect breast cancer recurrence rates or mortality. ⊕⊕⊕◯ A
- Vaginal estrogen therapy is effective for GSM in breast cancer survivors and appears safe in women on tamoxifen. ⊕⊕⊕◯ B
- In women on aromatase inhibitors who have not responded to non-hormonal treatments, individualized treatment options should be discussed with a breast cancer specialist. ⊕⊕◯◯ C
- There is a lack of safety data supporting the use of MHT (estrogen therapy or estrogen–progestogen therapy) in breast cancer survivors. ⊕⊕⊕◯ B

13. Endometrial safety and bleeding

- Optimization of modifiable factors such as BMI and diabetes can reduce episodes of unscheduled bleeding on MHT and endometrial cancer risk. ⊕⊕⊕◯ A
- Ensure compliance with the prescribed medication with particular attention to the timing of pill/gel/patch/spray application and the timing/duration of progestogen. GPP
- A monthly progestogen (sequential or continuous), in a dose proportionate to the estrogen dose, is recommended in women with a uterus. ⊕⊕⊕⊕ A
- Women using sequential MHT should have a minimum of 10 days norethisterone (NET) or MPA, or 12 days of dydrogesterone or micronized progesterone per 28-day cycle. ⊕⊕⊕⊕ A
- Women taking cyclical progestogen for less than the recommended time/month should be advised that they have an increased risk of endometrial hyperplasia and cancer which increases with dose and duration of treatment. ⊕⊕⊕◯ B
- Women taking appropriately dosed sequential micronized progesterone should be advised that this does not appear to increase endometrial cancer risk but there is limited evidence for its use beyond 5 years. ⊕⊕⊕◯ B
- Amenorrhoeic postmenopausal women taking a continuous combined MHT preparation (standard dose) should be aware that they have a lower endometrial cancer risk than non-MHT users. ⊕⊕⊕⊕ A
- Women taking a sequential MHT over the age of 45 years should be offered a change to continuous combined MHT after 5 years or by age 54 years, whichever comes first. ⊕⊕⊕◯ B
- Women taking high-dose estrogens should be informed that there are limited data relating to the optimal progestogen dose needed to provide endometrial protection. Higher doses of progestogen in proportion to the dose of estrogen are recommended. ⊕⊕◯◯ B
- The 52-mg levonorgestrel intrauterine device (LNG IUD) offers endometrial protection against ultra-low to high-dose estrogen for up to 5 years of use in both perimenopausal and postmenopausal women. ⊕⊕⊕⊕ A
- Women with a malpositioned 52-mg LNG IUD should be aware that it is uncertain whether this provides adequate endometrial protection when used as part of MHT. If the IUD is >2 cm from the fundus, within the cervical canal (fully or partially) or there are relevant symptoms (e.g. pain or bleeding), then it is suggested that the IUD is removed and replaced. ⊕◯◯◯ C
- Women presenting with unscheduled bleeding on MHT should be assessed for their individual risk factors for endometrial cancer, their bleeding pattern and the type and dose of MHT preparation they are taking. GPP
- Pelvic and abdominal examinations should be performed where applicable and initial investigations should be considered, including cervical cytological screening, a lower genital tract infection screen and a pelvic ultrasound. GPP
- In the absence of risk factors for endometrial cancer, the overall risk of endometrial cancer is likely to be lower than those of a similar age not on MHT, so adjustments in the progestogen dose or type may be considered before further investigation. ⊕⊕◯◯ A

- If unscheduled bleeding continues after 6 months of MHT usage, investigation and further adjustments/change to the progestogen regimen are needed. ⊕⊕⊕◯ A
- If there is one major or two minor risk factors for endometrial cancer, then further investigations should be performed immediately. ⊕⊕⊕⊕ A
- The initial investigation should be a transvaginal ultrasound. The priority for these investigations will include multiple factors, including the presence of risk factors for endometrial cancer, the type of MHT preparation, the type of bleeding and local resources. ⊕⊕⊕◯ A
- On continuous combined MHT, an endometrial thickness >4 mm is considered abnormal ⊕⊕⊕⊕ A
- On sequential combined MHT, the endometrial thickness can vary throughout the cycle. Ideally, the ultrasound should be timed just after the withdrawal bleed and any measurement >7mm should warrant further investigation. An increased endometrial thickness outside this time frame should prompt a re-scan at the appropriate time. ⊕⊕◯◯ B
- Women with an endometrial thickness within normal parameters should be reassured and offered adjustments to their MHT. If bleeding persists beyond 6 months despite a normal result, then endometrial assessment is recommended. ⊕⊕◯◯ A
- When the endometrial thickness is abnormal, or if the endometrial thickness cannot be adequately visualized, further endometrial assessment is recommended. ⊕⊕⊕◯ A
- In the absence of significant risk factors for endometrial cancer, there is no need to stop the MHT before investigation and suitable adjustments to the progestogen can be made during this time. ⊕⊕◯◯ B
- Endometrial assessment can either be performed by a blind outpatient endometrial biopsy or hysteroscopy with endometrial sampling, if acceptable to the woman and within clinic resources. ⊕⊕◯◯ B
- If unscheduled bleeding persists 3 months after a negative blind biopsy, then hysteroscopic assessment is advised. ⊕⊕◯◯ B
- In the presence of an insufficient sample on blind biopsy, hysteroscopy should be considered. ⊕◯◯◯ B
- If proliferative endometrium is reported on blind biopsy in women on continuous combined MHT and there are risk factors for endometrial cancer, then hysteroscopy is advised. ⊕⊕◯◯ B
- If hyperplasia with atypia or endometrial cancer is reported, advise weaning off MHT, discuss non-hormonal alternatives and refer urgently to a relevant specialist for further management. ⊕⊕⊕◯ A
- If unscheduled bleeding persists for more than 6 months after a previous negative hysteroscopy, consider repeat investigations. ⊕◯◯◯ B
- Consider switching women with ongoing unscheduled bleeding on continuous combined MHT back to sequential MHT, particularly if they are still in perimenopausal age. ⊕◯◯◯ B
- Consider lowering the estrogen dose, as lower doses are associated with higher rates of amenorrhea. ⊕◯◯◯ B
- Consider increasing the dose and duration (with sequential therapy) of the progestogen. ⊕◯◯◯ B
- Consider switching from micronized progesterone to oral Norethisterone Acetate (NETA) or MPA as these have higher rates of amenorrhea than micronized progesterone. ⊕⊕◯◯ B
- If it is clinically safe to do so, consider switching to an oral preparation as oral MHT may achieve greater cumulative rates of amenorrhea than transdermal MHT. ⊕◯◯◯ B
- Consider the 52-mg LNG IUD as an option (if available), particularly in women who have endometrial cancer risk factors. ⊕⊕◯◯ B
- Alternative options include CEE with bazedoxifene or tibolone where available. If the woman is aged under 50 years and has no risk factors for thrombosis, an estradiol-containing COC preparation can be considered. KM
- If bleeding is persistent, consider reducing or stopping the MHT and offer non-hormonal alternatives. GPP

14. Ovarian cancer

- In individuals with ovaries, there is a very slight increase in ovarian cancer risk with combined MHT. ⊕⊕⊕⊕ A
- In individuals with ovaries, there is a very slight increase in ovarian cancer risk with estrogen-only MHT taken for 5 years or more. ⊕⊕⊕⊕ A
- Pre-diagnosis use of MHT does not appear to have a detrimental impact on ovarian cancer outcomes. ⊕⊕⊕◯ B
- MHT is not usually contraindicated following treatment for epithelial ovarian cancer, and potential risks and benefits should be discussed with women. ⊕⊕⊕◯ A
- Although the majority of high-grade serous and endometrioid ovarian cancers express the estrogen receptor, the limited RCT data do not suggest an increased risk of disease recurrence with systemic MHT. It may be appropriate to offer non-hormonal options in the first instance, particularly for women who do not have the health impacts of a premature or early menopause. ⊕⊕⊕◯ B

15. Lung cancer

- Although estrogen receptors are present in healthy and cancerous lung tissue, recent studies do not confirm a firm link between natural and surgical menopause status and risk of lung cancer. KM
- Data on MHT and lung cancer are inconsistent, with no clear effect of MHT on lung cancer incidence or mortality. KM
- HCPs should be advised that the role of menopause and MHT on lung cancer incidence and mortality remains inconclusive. ⊕⊕⊕◯ B

- Whilst HCPs should consider the risk of lung cancer when advising women about MHT, it should not be a reason to avoid prescribing if there are no other risks or contraindications. ⊕⊕⊕◯ A
- When counseling women about risk factors for lung cancer, it is important to emphasize the key modifiable risks such as smoking. GPP
- HCPs should be informed that it remains unclear what the optimal MHT regimen and duration is to minimize lung cancer risks, and more research is required to confirm this. ⊕⊕◯◯ B
- Women diagnosed with lung cancer who are deriving benefit from their MHT may not need to discontinue it, as there does not appear to be an adverse effect on survival times, and there may even be a beneficial effect. ⊕⊕⊕◯ B

16. Colorectal cancer

- Given its high global prevalence as the third most commonly diagnosed malignancy, colorectal cancer (CRC) requires the implementation of effective risk mitigation strategies. GPP
- Consistent findings from epidemiological studies indicate a lower incidence of CRC in women relative to men. ⊕⊕⊕◯ B
- The lower incidence of CRC in women relative to men may reflect a protective effect of estrogen. KM
- While several studies have reported an inverse association between endogenous estrogen levels and CRC risk, the evidence remains inconclusive. ⊕⊕⊕◯ B
- A protective role of MHT has been supported by findings from the combined estrogen–progestin arm of the WHI trial and corroborated by a comprehensive umbrella review; however, the observed protective effect attenuated over time, and no significant reduction in CRC-specific mortality was observed. ⊕⊕⊕◯ B
- Inter-individual variability in genetic determinants of estrogen signaling may account for differential responsiveness to estrogen-mediated protection, potentially influencing observed heterogeneity in CRC outcomes. ⊕⊕◯◯ C
- Despite suggestive evidence, HT is not currently endorsed as a viable strategy for CRC risk reduction. ⊕⊕⊕◯ B
- Current public health guidelines advocate for the adoption of a healthy lifestyle, emphasizing a diet rich in fruits, vegetables and whole grains, and routine CRC screening, primarily via colonoscopy or fecal occult blood testing, as the most effective evidence-based interventions to reduce CRC incidence and mortality. GPP

17. Cervical cancer

- MHT may be considered for symptomatic women with human papillomavirus (HPV)-independent cervical cancer, particularly those experiencing premature or early menopause due to treatment. However, due to limited data on safety in this subgroup, careful individualized assessment is recommended, and non-hormonal options may be preferred where risk is uncertain. ⊕⊕⊕◯ C
- MHT is unlikely to be protective against the development of cervical cancer, and more research is required to assess any link between MHT and HPV-independent cervical cancer. GPP

18. Upper gastrointestinal cancer

- Postmenopausal women should be managed similarly to men. ⊕⊕⊕◯ C
- MHT might be of some benefit to prevent and slow down the progression of (early) hepatocellular carcinoma, thereby improving the outcome. ⊕⊕⊕◯ C
- For most women, lifestyle modification will have a larger benefit on liver-related outcomes compared to MHT. ⊕⊕⊕⊕ B
- Observational studies suggest that MHT may be associated with a reduced risk of gastric cancer in postmenopausal women. ⊕⊕◯◯ C
- Reproductive factors associated with prolonged estrogen exposure, such as later menopause and higher parity, are also linked to a lower risk of gastric cancer. ⊕⊕◯◯ C
- For esophageal cancer, the evidence for a protective effect of MHT is less clear with some indication of a possible protective association for adenocarcinoma. ⊕⊕◯◯ C
- Mechanistic studies provide biologic plausibility for a protective role of estrogen in liver and gastric cancer, and highlight the need for further research in this area. GPP

19. Quality of life – psychosocial/psychological/cognitive health

- In women experiencing bothersome menopause symptoms, MHT improves menopause-related quality of life. ⊕⊕⊕◯ B
- In women experiencing bothersome menopause symptoms, MHT does not improve global or general health-related quality of life. ⊕⊕◯◯ C
- HCPs should be aware that the menopause transition may represent a window of vulnerability for the development of anxiety symptoms in non-anxious women. Anxiety symptoms may remain elevated across the menopause transition in women with high anxiety, but menopause stage is unrelated to anxiety symptoms. VMS appear more strongly related to anxiety symptoms than menopause stage. ⊕⊕◯◯ C
- HCPs should be aware that anxiety symptoms often co-occur with menopause symptoms, including moderate to severe VMS and poor sleep. ⊕⊕◯◯ C

- The effects of MHT on anxiety disorders is unknown. ⊕⊕◯◯ C
- There is insufficient evidence to recommend the use of MHT use for the treatment of anxiety symptoms in perimenopausal and postmenopausal women. ⊕⊕◯◯ C
- Except in premature ovarian insufficiency or early menopause, MHT is not recommended to prevent or treat cognitive decline at any age. ⊕⊕⊕⊕ A
- In women older than 65 years, CEE+MPA may be harmful to cognition. ⊕⊕⊕◯ B
- MHT has neutral effects on cognition in the natural early postmenopause. ⊕⊕⊕⊕ A
- MHT may confer benefits to cognition when initiated immediately after hysterectomy with bilateral oophorectomy. ⊕⊕⊕◯ B
- The effects of MHT on cognition among women with moderate-to-severe VMS and in perimenopausal women are unknown. KM
- There is some evidence that ET improves anhedonia in perimenopausal women without depressive disorders. It is yet unknown whether ET improves depressive symptoms more generally in perimenopausal women. ⊕⊕◯◯ C
- ET may improve depressive symptoms in perimenopausal women with depressive disorders in both the presence and absence of VMS. Efficacy of ET in this population appears similar to that of antidepressants. ⊕⊕◯◯ C
- ET may be effective in lowering depressive symptoms in postmenopausal women without depressive disorders. ⊕⊕◯◯ C
- ET is not efficacious for the improvement of depressive symptoms in postmenopausal women with depression. ⊕⊕◯◯ C
- MHT may prevent the emergence of clinically significant depressive symptoms in euthymic women across the menopause transition, but more evidence is needed before recommending MHT for this use. ⊕⊕◯◯ C
- In midlife women with depressive disorders, improvements in mood were associated with improvements in sleep but not VMS. ⊕⊕◯◯ C
- ET might augment clinical response to antidepressants in perimenopausal women with VMS. ⊕⊕◯◯ C
- HCPs should be aware that sleep disturbance is a common menopause symptom, particularly wakefulness after sleep onset. ⊕⊕⊕⊕ A
- HCPs should be aware that night-time VMS are strongly associated with awakenings. ⊕⊕⊕⊕ A
- HCPs should be aware that poor sleep across the menopause transition is related to numerous health outcomes, including changes in mood and cognition, as well as AD, hypertension, cardiovascular disease, diabetes and all-cause mortality. ⊕⊕⊕◯ B
- MHT improves sleep in women with VMS but does not appear to affect sleep in midlife women more generally. ⊕⊕⊕◯ B
- Transdermal estrogen may improve sleep quality in perimenopausal women, beyond its effects on VMS and other symptoms. ⊕⊕◯◯ C
- Micronized progesterone taken before bedtime improves various sleep outcomes in postmenopausal women. ⊕⊕◯◯ C
- Cognitive behavioral therapy for insomnia (CBT-I) is recommended as first-line treatment of sleep disturbance in women across the menopause transition. ⊕⊕⊕⊕ A

20. Androgen therapy

- Studies to date have shown that testosterone blood concentration declines across the reproductive years, does not change acutely with natural menopause and increases from the seventh decade of life, while DHEA blood levels decline progressively with age. ⊕⊕⊕◯ B
- Most available immunoassays lack precision for measurement of testosterone within the female range and reference ranges differ between assays; there is no blood level below which a woman can be designated as being testosterone deficient. ⊕⊕⊕⊕ A
- Postmenopausal HSDD is an evidence-based indication for a therapeutic trial of a physiological dose of testosterone therapy. ⊕⊕⊕⊕ A
- All women presenting with sexual concerns should have a comprehensive biopsychosocial assessment and modifiable factors addressed before testosterone is prescribed. ⊕⊕⊕⊕ A
- Available data do not support the prescription of testosterone for women for any symptom or condition (other than postmenopausal HSDD) or for disease prevention. Evidence quality ranges from ⊕⊕⊕◯ B to ⊕⊕⊕⊕ A
- The available data do not support the use of systemic DHEA therapy for the treatment of female changes in sexual function or any other clinical symptoms or condition. ⊕⊕⊕◯ B
- Intravaginal DHEA (prasterone) is an effective option for the treatment of dyspareunia secondary to VVA. ⊕⊕⊕⊕ A

21. Perimenopausal contraception

- Considering contraceptive choices is important for perimenopausal women. Contraception counseling should be tailored to the individual, considering comorbidities, risk factors and personal preference. ⊕⊕◯◯ C
- A change in bleeding pattern is common in perimenopausal women. Any 52-mg LNG IUD, some progestogen-only pills (POP) and combined hormonal contraception (CHC) decrease bleeding and are

associated with an improvement in quality of life, but long-term use of CHC increases the risk of prediabetes and type 2 diabetes mellitus in women with metabolic risk factors. ⊕⊕⊕◯ B

- A COC containing nomegestrol acetate (NOMAC) with 17β-estradiol (E2) is not associated with an increase in VTE risk compared to levonorgestrel containing COCs and can be considered for perimenopausal women. ⊕⊕⊕⊕ A
- The benefits and risks of different progestogen-only contraceptive methods need to be considered when prescribing, such as benefits associated with a reduction in bleeding and risks to bone health with depot medroxyprogesterone acetate (DMPA). ⊕⊕⊕⊕ A
- There is a modest reversible reduction in BMD with DMPA, which is not exacerbated by menopause. This has not been observed with any other contraceptive methods including relugolix, a gonadotropin-releasing hormone antagonist, in combination with estradiol and NETA. ⊕⊕◯◯ C
- Relugolix in combination with estradiol and NETA is a treatment for uterine fibroids and endometriosis, which provides contraception, reduces bleeding and pain influencing quality of life, and maintains bone density. ⊕⊕⊕◯ B
- A small increase in the risk of developing breast cancer with both CHC and progestogen-only contraceptive methods has been reported. These data are not specific to perimenopausal women and risk declines with cessation, with no breast cancer related risk after 10 years. ⊕⊕⊕⊕ A
- Use of a 52-mg LNG IUD with low-dose estrogen in perimenopausal women appears to be the most effective option to alleviate perimenopausal symptoms and to provide long-term health benefits such as endometrial protection and bleeding control. For women not eligible for a 52-mg LNG IUD or who decline this option, COCs or progestogen-only contraceptive choices are an option but may have fewer additional benefits for perimenopausal women. ⊕⊕⊕◯ B

22. Premature ovarian insufficiency/early menopause

- POI is both an endocrine and a gonadal condition defined as loss of ovarian activity in women younger than age 40 years. Early menopause (menopause between ages 40 and 45 years) also has similar ramifications. KM
- The diagnosis of POI is based on 4 months or more of menstrual disturbance/amenorrhea and one FSH level >25 IU/l, as per the European Society of Human Reproduction and Embryology (ESHRE) 2024 POI guideline (www.eshre.eu/Guidelines-and-Legal/Guidelines/Premature-ovarian-insufficiency). GPP
- FSH assessment should be repeated after 4–6 weeks if there is diagnostic uncertainty. FSH testing for the diagnosis of POI does not have to be timed to a specific day of the menstrual cycle. GPP
- HCPs should be aware that POI is not a rare condition and occurs in up to 3.5–3.7% of the global population. ⊕⊕⊕⊕ A
- HCPs should be aware that the clinical presentation of POI is variable, including oligo-amenorrhea, symptoms of estrogen deficiency, infertility or underlying cause of POI. Symptoms may be minimal, intermittent and/or vary in severity. ⊕⊕◯◯ B
- HCPs should be aware that POI is a heterogeneous disorder with multiple etiologies, the most common being idiopathic. With the advent of more precise genetic assessments, more genetic causes are being found. ⊕⊕◯◯ A
- HCPs should inform women that POI is associated with menopausal symptoms, infertility, decreased quality of life, poorer psychological and sexual well-being, and increased risk of cardiovascular disease, osteoporosis, impaired muscle parameters, cognitive decline, dementia and Parkinsonism. Untreated POI is associated with decreased life expectancy. ⊕⊕◯◯ A
- Investigation for causes of POI should include hormone analysis, screening for autoimmune causes and pelvic ultrasound. Where available, karyotyping, fragile X premutation testing and additional genetic testing, such as next-generation gene sequencing, are suggested after appropriate counseling. ⊕⊕◯◯ B
- It is important to inform the woman of the diagnosis of POI with empathy in a sensitive and caring manner. Women should be provided with evidence-based information and counseling (www.eshre.eu/Guidelines-and-Legal/Guidelines/Premature-ovarian-insufficiency). GPP
- Comprehensive evaluation after diagnosis is recommended to personalize treatment and optimize quality of life and to maintain long-term health. GPP
- Women with POI should be advised about lifestyle, diet and exercise to optimize cardiometabolic and bone health, although POI-specific data are lacking. ⊕⊕◯◯ C
- HCPs should be aware that the main treatment of POI is HT (Hormone Replacement Therapy (HRT) or COC) which should be initiated promptly and continued at least until the usual age of menopause. ⊕⊕⊕◯ A
- HT should be offered whether there are symptoms or not, for primary prevention to reduce the risks of morbidity and mortality. ⊕⊕◯◯ A
- HCPs should be aware that HRT should not be regarded as being contraceptive unless combined with an intrauterine progestogen-releasing device. ⊕⊕⊕◯ A
- HCPs should be aware that women with POI may require higher doses of HT than those at the usual age of menopause to achieve adequate symptom control and bone protection. ⊕⊕◯◯ B
- A progestogen should be used in combination with estrogen in all women with POI with an intact uterus for endometrial protection, and the dose of progestogen should be increased when higher doses of estrogen are used. ⊕⊕◯◯ A

- Women with POI can be informed that there is no evidence that the risk of breast cancer with HT is higher than in women of the same age group with normal ovarian function. ⊕⊕◯◯ C
- A biopsychosocial approach should be used by HCPs for diagnosing and managing HSDD in women with POI, and consideration should be given to prescribing testosterone therapy where appropriate. ⊕⊕◯◯ C
- Non-hormonal pharmacologic and non-pharmacologic therapies can be considered where HT is contraindicated but women should be informed that evidence specific to POI is lacking. ⊕◯◯◯ C
- HCPs should be aware that there is insufficient evidence for efficacy and safety to recommend routine use of complementary therapies in women with POI. ⊕⊕◯◯ B
- Women with POI should be informed that, currently, there are no interventions which can reliably increase ovarian activity and natural conception rates. ⊕⊕⊕◯ A
- Women with POI who do not achieve a pregnancy naturally should be informed that, currently, the best fertility options are oocyte/embryo donation with assisted reproduction technology (ART) or adoption. ⊕⊕⊕◯ A
- Regular review and multidisciplinary care are suggested for the optimal management of women with POI. GPP

23. Non-pharmacological interventions

- Cognitive behavioral therapy (CBT) is recommended as an effective non-hormonal therapy for alleviation of bothersome VMS in both menopausal women and breast cancer survivors. ⊕⊕⊕⊕ A
- HCPs should be aware that CBT is also effective in improving mood, sleep and quality of life. ⊕⊕⊕⊕ A
- CBT is effective in different intervention modalities, offering a range of less costly interventions to help lower medical costs, and is useful for those women unable to attend therapy in person. ⊕⊕⊕◯ B
- HCPs should be aware that clinical hypnosis enhances mind and body interaction. ⊕⊕⊕⊕ A
- Clinical hypnosis is recommended as an effective therapy to reduce the frequency and severity of menopausal VMS. ⊕⊕⊕◯ B
- HCPs should be aware that studies have shown an association between weight gain, central adiposity and vasomotor symptom prevalence. ⊕⊕⊕◯ B
- HCPs should be aware that attainment of normal weight is a desirable public health outcome, and limited evidence suggests that weight loss may be recommended to alleviate VMS in some women. ⊕⊕◯◯ D
- A healthy diet is important for good health outcomes and disease prevention. ⊕⊕⊕⊕ A
- Data from clinical trials do not confirm the benefit of dietary modifications to alleviate VMS. ⊕⊕◯◯ D
- Due to a lack of evidence, paced respiration is not recommended for the alleviation of VMS. ⊕⊕◯◯ D

24. Complementary therapies

- HCPs should enquire about concurrent use of complementary therapies and conventional approaches, and about patient preferences with regard to management of the menopause. GPP
- Women should be informed that regulation of complementary therapies varies, misinformation is common and credible scientific information that is free of commercial interest should always be sought. GPP
- HCPs should engage in respectful, patient-centered shared decision-making, considering individual values and preferences, when it comes to discussing complementary therapies. GPP
- We suggest that complementary therapies, if chosen, are used as an adjunct to conventional options in the first instance. GPP
- HCPs should be informed that the use of traditional medicines may be an important and well-accepted part of an individual's cultural background and should consider this when discussing the use of complementary therapies. GPP
- Women and HCPs could consider electro-acupuncture for VMS but there is insufficient evidence to recommend manual acupuncture. ⊕⊕◯◯ C
- There is insufficient evidence to recommend the use of acupuncture for menopausal symptoms, anxiety and depression, quality of life and sleep; however, some studies demonstrate efficacy for menopausal symptoms and psychological symptoms, and acupuncture is likely to be safe. ⊕⊕◯◯ C
- There is insufficient evidence to recommend acupuncture + Chinese herbal medicine (CHM) for sleep quality in general; however, HCPs and women may consider the combination in women with perimenopausal insomnia. ⊕⊕⊕◯ C
- CHM could be considered for improving menopausal symptoms, sleep quality and blood pressure. ⊕⊕⊕◯ C
- HCPs and women should be informed that short-term use of CHM (up to 1 year) appears to be safe. ⊕⊕⊕◯ A
- HCPs and women could consider black cohosh for managing vasomotor and menopausal symptoms; however, black cohosh should not be considered for managing psychological symptoms. ⊕⊕⊕◯ C
- HCPs should inform women that short-term use (3–6 months) of isopropanolic black cohosh extract appears to be safe. ⊕⊕◯◯ A
- HCPs and women could consider supplementation with 1200 mg calcium and 800 IU vitamin D daily to reduce fracture risk in postmenopausal osteoporosis. However, routine calcium and vitamin D supplementation is not recommended for fracture prevention in women without osteoporosis or deficiency states. HCPs should discuss the potential for increase in cardiovascular risk, which has been reported in some long-term studies, when recommending calcium and vitamin D for other indications. ⊕⊕⊕◯ A
- HCPs and women could consider using soy-derived isoflavones to manage hot flushes and for

menopausal symptoms; however, there is insufficient evidence to recommend red clover for reducing hot flush frequency. ⊕⊕◯◯ C

- While dietary intake of soy foods is unlikely to be harmful, HCPs and women should exercise caution with soy isoflavone supplementation if there is a family history of breast cancer or past history of estrogen receptor-negative breast cancer. ⊕⊕◯◯ B
- Probiotics could be considered for improving lumbar BMD in menopausal women. A greater effect may be seen in women with osteopenia rather than osteoporosis, and with >12 months duration. ⊕⊕◯◯ C
- HCPs and women could consider traditional Chinese exercises such as Tai Chi and Qi Gong for improving BMD in postmenopausal osteoporosis. The evidence is stronger for Tai Chi; however, Tai Chi is not superior to other forms of moderate exercise such as walking or the skipping rope, or as an adjunct to calcium and vitamin D, and differences in BMD for Tai Chi may be small. Tai Chi should be practiced for 6 months or more for a greater impact on bone health. ⊕⊕◯◯ C
- HCPs and women could consider traditional Chinese exercises, particularly Tai Chi and Baduanjin, for management of depressive symptoms in the perimenopause and postmenopause. ⊕⊕◯◯ C
- Yoga can be offered to women for management of menopausal symptoms and could be considered for other benefits including sleep and mood symptoms, and for improving some but not all aspects of cardiometabolic health (including BMI, diastolic blood pressure and some lipid parameters). ⊕⊕◯◯ C
- HCPs and women could consider mindfulness-based interventions (MBIs) for management of stress, anxiety, depression and sleep disturbances during the menopausal transition and postmenopause. ⊕⊕◯◯ C
- Women and HCPs could consider massage and touch therapies for the management of VMS, menopausal symptoms, quality of life, and improving sleep quality and mood symptoms. ⊕⊕◯◯ C
- Evidence ratings for other interventions, including a large number of herbs and nutrients, are very low. Overall, evidence is insufficient to recommend the use of these interventions. GPP

25. Compounded 'bioidentical' or 'natural' hormones

- Prescribing of compounded bioidentical hormone therapy (cBHT) is not recommended due to safety and efficacy concerns, including lack of quality control and rigorous regulatory oversight, and absence of scientific evidence of safety, purity and efficacy. ⊕⊕⊕◯ A
- The use of blood serum assays or salivary hormone levels to prescribe the appropriate dose of cBHT is not recommended by major menopause societies. ⊕⊕⊕⊕ A
- Women should be informed that cBHT is not standardized and does not undergo the same strict regulatory processes as is the case for MHT. ⊕⊕⊕◯ A
- Women should be informed that, unlike cBHT, MHT is strictly regulated and distributed with relevant package inserts and safety warnings. ⊕⊕⊕⊕ A
- Women requesting cBHT should be informed about safety issues, and encouraged to use or switch to MHT which is stringently tested for strength, purity and quality. ⊕⊕⊕◯ A
- Women should be informed that MHT is available in a wide range of doses and delivery methods, which facilitates individualization of therapy, allowing HCPs to tailor MHT regimens for individuals. ⊕⊕⊕⊕ A

26. Emerging insights, therapies and technologies in menopause

- Digital health solutions have the potential to improve access to care for women with menopausal symptoms. ⊕⊕◯◯ C
- Machine learning and artificial intelligence (AI) have increased the speed of discovery of genetic and metabolic pathways that cause POI, with potential development of diagnostic and prognostic kits as well as possible interventions. ⊕⊕⊕◯ B
- Changes in the microbiome may mediate reductions in menopausal symptoms associated with lifestyle diet and activity changes. ⊕⊕◯◯ C
- Newer interventions for menopausal symptoms in the pipeline include medical therapies such as Estetrol as well as novel device-based cooling. ⊕◯◯◯ D
- Development of newer scales for menopause which are population appropriate, accompanied with the segmentation of menopausal symptom subtypes, allows for individualization of care for better outcomes. ⊕⊕◯◯ C

27. Influence of the media

- There is a clear need for a broader understanding among women and media practitioners of how science works and how guidelines are formulated. However, recommendations about using the media are not easy to make, nor clearly supported by unequivocal evidence. Unlike the way in which guidelines are developed, a thorough literature search will not reveal a catalog of data from which recommendations might be systematically derived. In the case of the media, the best evidence has come from experience, both from the way in which menopause has been represented historically in the media and from our own place within it. Such recommendations thus defy grading for level of evidence, but they are based on how the media works and how menopause has, in the past and the present, claimed its place within it. KM
- It is also clear that science reporting is not easy, with roadblocks on the road to a clear story noted

as medical terminology, data-loaded research, uncooperative sources, conflicts of interest and elusive human interest in a research paper. These problems are compounded by fewer trained journalists than ever before, with many today assigned to stories in which they have no special interest and who have varying levels of scientific literacy, like their audiences. But they too must translate a scientific text into a narrative understood by their readers. So, it is the responsibility of everyone, not the media alone, to ensure that the voice of authority – in a clinical paper, in guidelines, in official announcements – is expressed in clear language amenable to the public. This is already starting to happen, evident in patient summaries in some journals and guidelines and in press releases – for example in the recently updated ESHRE guidelines on POI (www.eshre.eu/Guidelines-and-Legal/Guidelines/Premature-ovarian-insufficiency). KM

- *The Lancet*'s recent series on menopause made a plea for 'impartial information', which puts demands not just on the source of that information but also on its recipient. Biases may be commercial or ideological, but it will be useful if readers can identify the source of the information and make a value judgment on its worth and independence. KM
- To this extent, expert individuals and organizations should be encouraged to embrace social media to express a message which is clear and consistent. However, whether written or presented, the message should have a voice of authority and confidence, thereby offering a reassuring reference point for readers. KM
- Press releases continue to be the main source of medical news, and organizations with developments of public health interest in menopause should be encouraged to make greater use of them. Distribution need no longer be difficult; EurekAlert, for example, a web portal run by the American Academy for the Advancement of Science, is today's universal repository for embargoed news from the journals and universities. This offers a direct line to accredited science journalists throughout the world for a clear and accurate message. KM

28. Role of the pharmaceutical industry

- The need for new pharmaceutical agents for the management of menopause is critical. KM
- The pharmaceutical industry is responsible for the development, manufacturing and distribution of those agents. KM
- The pharmaceutical industry invests a significant amount in biomedical research conducted by industry, academic researchers and others. KM
- The pharmaceutical industry plays a significant role in the education related to those agents. KM
- Any involvement with the pharmaceutical industry in any educational activity should be transparent and declared by all those involved. KM

29. Publication ethics

- Publication ethics are of concern to everyone involved in the preparation, publication and reading of the scientific literature. KM
- The use of AI in scientific research and manuscript preparation is a developing area. However, its use must be disclosed in manuscripts and manuscript cover letters, and human authors must take responsibility for the accuracy of the information imparted. KM
- Care must be taken to avoid plagiarism and generally also duplicate publication. KM
- Research integrity is critical to the scientific process. Disclosure and transparency are an important part of research integrity. KM

Discussion

In this United Nations Decade of Healthy Aging, it is estimated that more than a billion women will soon be in a menopausal age group globally. There is currently a concerning 'women's health gap'; women live 25% more of their lives in poor health when compared to men [8]. This is partly due to the increasing incidence of non-communicable diseases such as osteoporosis, cardiovascular disease and dementia, which become increasingly prevalent after menopause. The increasing prevalence of POI, where greater risk of chronic disease is associated with younger age of menopause, is of additional concern.

Menopause-associated problems potentially reduce both the life and health spans of women. It has been estimated by the World Economic Forum and McKinsey Institute that dealing with menopause-associated problems in the women's health gap can result in approximate gains of 2.4 million annual disability adjusted life years (DALYs) and US$120 billion in annual gross domestic product globally [8]. With a rapidly growing population of women at midlife, menopause and beyond, it is imperative that research and evidence-based management supported by guidelines continues to optimize women's quality of life and long-term well-being.

The mission of the IMS is to work globally to promote and support access to best-practice healthcare for women through their menopause transition and post-reproductive years, enabling them to achieve this with optimal health and well-being. Through effective communication and evidence-based education about menopause, women can be empowered to make informed personalized choices aligned with their individual goals.

This article provides an easily accessible summary of the recommendations and key messages for the management of midlife health and menopause. The full version of the recommendations is available as a living document on the IMS website; a few of the sections will also be submitted to

Climacteric and other journals as individual papers containing additional data and meta-analyses generated by the systematic review process. The recommendations are based on the best available evidence or, where data of sufficient quality are absent, on GPPs from our expert authors.

The current IMS recommendations represent an update of the 2016 IMS recommendations; the key questions and topics covered in the 2016 version were updated based on the results of a scoping survey of HCPs via their stakeholder organizations and the public. The evidence supporting the recommendations was modified based on data published between 2016 and 2025, and prior to 2016 where required by the PICO questions and new topics. Important new topics added included sections on sarcopenia, perimenopausal contraception and the novel neurokinin-targeted therapies.

These new IMS evidence-based recommendations are intended to form the blueprint to support the optimal care of all women in midlife and menopause globally and followed on from the recent IMS editorial [1] and the 2024 and 2025 White papers for the respective World Menopause Days [9,10]. The theme of the editorial and subsequent papers called for a well-balanced narrative on the menopause momentum and addressed key controversies on menopause, lifestyle, MHT and alternatives.

The last few years have seen a renaissance in interest in menopause in many countries. Although this is generally good as it has led to the dissemination of a considerable amount of information, some of this was misinformation and disinformation, often for the purpose of commercial gain.

The aim of these recommendations was therefore to rigorously interrogate the existing data through a formal systematic review process and to commission experts in their field to interpret these data and produce the best evidence possible for the effective and safe management of the menopause. However, it should be emphasized that adherence to guidance does not guarantee a successful or specific outcome, nor does it establish a standard of care. Also, practice guidelines do not replace the need for application of clinical judgment to each individual clinical presentation, nor variations based on locality, facility type, resources and cultural considerations.

It is also important to note that the evidence supporting these recommendations is derived from research largely performed on women living in Western countries. This may not necessarily be directly applicable to other women in other parts of the world. The IMS is aware of the geographical variations related to different priorities of medical care, different prevalence of diseases, and country-specific attitudes of the public, the medical community and health authorities toward menopause management, different availability and licensing of products, all of which may impact on the use of MHT.

It is important that the adaptation of these recommendations is made relevant to each individual country and region, hence the involvement from the outset of numerous national and regional societies and the public in the development of the key questions and subsequent endorsement of the guidance. There is, of course, a key role for other position statements and guidance that represent clinically important local, regional and international practice [11–17].

Nonetheless, it is hoped that the publication of these recommendations will be followed by an update of the consensus statement in which areas of common interest and relevance worldwide can be further explored and agreed upon [18]. Equally important is continuing to investigate what we do not know, and projects such as the global Menopause Priority Setting Partnership (MAPS) [19] and the Exploration of the Mental and Physical Health impact in Menopausal women (MARIE) [20] collaborative are also important if we are to achieve a greater understanding of the impact of diverse social and cultural influences on health outcomes in menopause, midlife and beyond.

The development, dissemination and implementation of globally relevant recommendations and guidelines therefore mandates collaboration with organizations that have common interests and goals. The recent update of the ESHRE POI guideline [21] was achieved through a partnership of the ESHRE with the American Society for Reproductive Medicine (ASRM), Monash University and the IMS and the involvement of numerous stakeholder organizations. Similarly, it is hoped that through collaboration with our stakeholder organizations and 67 IMS-affiliated menopause societies (https://www.imsociety.org/membership/cams/), the updated IMS recommendations will be adopted as widely as possible. The IMS peer-reviewed journal *Climacteric* will act as a conduit for the information, and development and translation of HCP educational tools such as IMS Professional Activity for Refresher Training (IMPART) (https://www.imsociety.org/education/impart-registration/) and updated clinical toolkits [22] will facilitate this. Information for the public (e.g. infographics, algorithms, videos, etc.) will be equally important in global implementation; this information will be made available through the IMS consumer portal, Menopause Info (https://www.menopauseinfo.org/).

Conclusions

A well-balanced conversation informed by evidence-based recommendations is crucial to the ethical management of women's midlife health and menopause.

Any treatment, hormonal or otherwise, should be underpinned by optimizing lifestyle, diet, exercise, avoiding or stopping smoking and minimizing alcohol consumption.

The principles and practice of lifestyle management of menopause were well covered in the 2025 IMS White Paper [10].

The efficacy and safety of MHT and alternative therapies depend on various factors; before prescribing, consideration should be given to the following principles as per the five Ws in the 2024 White paper and executive summary, which addressed the key controversies [9]:

- Who is MHT for?
- What types and doses of MHT?
- When should it be started and stopped?
- Why is MHT important?
- Where can MHT be accessed?

It is hoped that these new IMS recommendations and Key Messages on women's midlife health and menopause will provide readers with greater clarity regarding the safe and effective management of the menopause, as well as a pathway to further research opportunities. Key action points (outlined in the following section) are essential to ensure continued progress in improving the health of individual women, their families and society as a whole.

Key action points

- Women: improve access to evidence-based, balanced information to increase health literacy, and empower informed decisions and self-management, thereby increasing proactive confidence to maintain menopausal health.
- Government/institutions: encourage evolution of policy toward supporting research and clinical management of women's health, in particular during the menopause transition and beyond.
- HCPs: continue to strive to increase education and training for healthcare professionals to optimize evidence-based menopause management.
- Media: engage positively, highlighting the importance of evidence-based, non-sensationalist information.
- Pharma industry: encourage research and development of therapeutic interventions that minimize adverse effects and maximize benefits and improve the supply of affordable medications globally, especially to low and middle-income countries.
- MHT and alternatives: clarification of differences in action/risk profiles to maximize benefits and minimize adverse effects and provision of the widest possible armamentarium of treatment options to facilitate personalized care.

Full text recommendations

The full recommendations text and supporting documents are available online at https://www.imsociety.org/statements/ims-recommendations/.

Disclosure statement

T. Hillard is a current International Menopause Society (IMS) Board member and Editor-in-Chief of *Climacteric*, and has received honoraria for lecturing and participating in advisory boards from Astellas and Besins. N. Panay is immediate past president of IMS and a current IMS Board Member. He has lectured and acted in an advisory capacity for Abbott, Astellas, Bayer, Besins, Gedeon Richter, Mithra, Novo Nordisk, SeCur, Theramex and Viatris. A. Vincent is a current IMS board member and has received honoraria or participated in advisory boards for Astellas, Besins, IQ Fertility and Theramex. The remaining authors declare no conflicts of interest.

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Key links

Link 1: https://www.imsociety.org/statements/ims-recommendations/
Link 2: https://www.eshre.eu/Guidelines-and-Legal/Guidelines/Premature-ovarian-insufficiency
Link 3: https://www.imsociety.org/membership/cams/
Link 4: https://www.imsociety.org/education/impart-registration/
Link 5: https://www.menopauseinfo.org/

Endorsements (received at time of publication)

Asia Pacific Menopause Federation (APMF)
Australasian Menopause Society (AMS)
British Menopause Society (BMS)
Canadian Menopause Society (CMS)
European Menopause and Andropause Society (EMAS)
Federación Latinoamericana de Sociedades de Climaterio y Menopausia (FLASCYM)
International Menopause Society (IMS) Executive and Board
International Society for Gynecological Endocrinology (ISGE)
Royal College of Obstetricians and Gynaecologists (RCOG)
South African Menopause Society (SAMS)
Thai Menopause Society
The recommendations have also been endorsed by key public women's health stakeholder representatives.

Abbreviations

AD	Alzheimer's disease
AGREE II	Appraisal of Guidelines for Research & Evaluation II
AI	Artificial intelligence
AMH	Anti-Müllerian hormone
AMS	Australasian Menopause Society
APMF	Asia-Pacific Menopause Federation
ART	Assisted reproduction technology
ASRM	American Society for Reproductive Medicine
BMD	Bone mineral density
BMI	Body mass index
BMS	British Menopause Society
BP	Bisphosphonate
cBHT	Compounded bioidentical hormone therapy
CBT	Cognitive behavioral therapy
CBT-I	Cognitive behavioral therapy for insomnia
CEE	Conjugated equine estrogens
CHC	Combined hormonal contraception
CHD	Coronary heart disease
CHM	Chinese herbal medicine
COC	Combined oral contraceptive
CRC	Colorectal cancer
DALYs	Disability adjusted life years
DASH	Dietary Approaches to Stop Hypertension
DHEA	Dehydroepiandrosterone
DMPA	Depot medroxyprogesterone acetate
DXA	Dual-energy X-ray absorptiometry
E2	17β-Estradiol
E4	Estetrol
EMAS	European Menopause and Andropause Society
ESCEO	European Society for Clinical and Economic Aspects of Osteoporosis
ESHRE	European Society of Human Reproduction and Embryology
ET	Estrogen-only therapy
EWGSOP2	European Working Group on Sarcopenia in Older People
FLASCYM	Federación Latinoamericana de Sociedades de Climaterio y Menopausia
FRAX	Fracture Risk Assessment Tool
FSH	Follicle-stimulating hormone
GPP	Good practice point
GRADE	Grades of Recommendation, Assessment, Development, and Evaluation
GSM	Genitourinary syndrome of menopause
HCP	Healthcare professional
HPV	Human papillomavirus
HRT	Hormone replacement therapy
HSDD	Hypoactive sexual desire disorder
HT	Hormone therapy
IMPART	IMS Professional Activity for Refresher Training
IMS	International Menopause Society
IOF	International Osteoporosis Foundation
ISGE	International Society of Gynecological Endocrinology
KNDy	Kisspeptin, neurokinin B and dynorphin neurons
LNG IUD	Levonorgestrel intrauterine device
MAPS	Menopause Priority Setting Partnership
MARIE	Exploration of the Mental and Physical Health impact in Menopausal women
MBI	Mindfulness-based intervention
MBT	Markers of bone turnover
MeSH	Medical Subject Headings
MHT	Menopause hormone therapy
MOF	Major osteoporotic fracture
MPA	Medroxyprogesterone acetate
NET	Norethisterone
NETA	Norethisterone Acetate
NOGG	National Osteoporosis Guidelines Group
NOMAC	Nomegestrol acetate
PD	Parkinson's disease
PICO	Population, Intervention, Comparison, and Outcome
POI	Premature ovarian insufficiency

POP	Progestogen-only pills
PSC	Publication Steering Committee (IMS)
RCOG	Royal College of Obstetricians and Gynaecologists
RCT	Randomized controlled trial
RUTI	Recurrent urinary tract infection
SAMS	South African Menopause Society
SERM	Selective estrogen receptor modulator
SLE	Systemic lupus erythematosus
SNRI	Serotonin–norepinephrine reuptake inhibitor
SSRI	Selective serotonin reuptake inhibitor
STEAR	Selective tissue estrogenic activity regulator
STRAW	Stages of Reproductive Aging Workshop
TMS	The Menopause Society (formerly North American Menopause Society [NAMS])
VMS	Vasomotor symptoms
VTE	Venous thromboembolism
VVA	Vulvovaginal atrophy
WHI	Women's Health Initiative