Genitourinary Syndrome of Menopause: AUA/SUFU/AUGS Guideline (2025)

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SUMMARY

Purpose

Genitourinary syndrome of menopause (GSM) describes the spectrum of symptoms and physical changes resulting from declining estrogen and androgen concentrations in the genitourinary tract during the menopausal transition.[1] There has not been a consensus reached about the number or type of symptoms (vulvovaginal, urinary, or sexual) needed to diagnose GSM, nor a requirement for identifying concurrent physical signs.[2, 3] Furthermore, the urinary symptoms associated with GSM are also linked with other common urologic conditions in older patients, such as overactive bladder, making identification, evaluation, and treatment complex.[4] This guideline provides information to clinicians regarding identification, diagnosis, counseling, and treatment for patients with GSM to optimize symptom control and quality of life while minimizing adverse events. The strategies defined in this document were derived from evidence-based and consensus-based processes; however, shared decision-making is the optimal strategy to individualize level of impact and ultimate interventions. Outreach to the marginalized and underserved GSM population is essential; this guideline will give clinicians across a multitude of disciplines the tools to evaluate, manage, and treat GSM patients.

Methodology

The systematic review utilized in the creation of this guideline is based on research conducted by the Minnesota Evidence-based Practice Center (EPC) under contract to the Agency for Healthcare Research and Quality (AHRQ) and funded by the Patient Centered Outcomes Research Institute (PCORI).[5] Low and moderate risk of bias studies were synthesized and provided Grading of Recommendations Assessment, Development and Evaluation (GRADE) certainty of evidence (COE) ratings for 8 patient-centered outcomes identified by the Core Outcomes in Menopause (COMMA) review[1] as most important to patients and clinicians, including: (1) pain with sex, (2) vulvovaginal dryness, (3) vulvovaginal discomfort/irritation, (4) dysuria, (5) change in Most Bothersome Symptom (MBS), (6) distress, bother, or interference of genitourinary symptoms, (7) satisfaction with treatment, and (8) treatment side effects.

After assessing 107 publications for risk of bias (RoB), the EPC extracted and synthesized effectiveness and/or harms outcomes from 68 publications that were rated low, some concerns, or moderate RoB (24 estrogen publications, 35 non-estrogen, 11 energy-based, and 4 moisturizers). Of 39 high, serious, or critical RoB publications, the EPC extracted long-term harms from only 15 uncontrolled studies of energy-based interventions (all serious or critical RoB due to confounding). An additional 66 publications evaluating 46 non-hormonal interventions, including natural products, mind/body practices, and educational interventions, were described in an evidence map. When sufficient evidence existed, the body of evidence for a particular treatment was assigned a strength rating of A (high), B (moderate) or C (low) for support of Strong, Moderate, or Conditional Recommendations. In the absence of sufficient evidence, additional information is provided as Clinical Principles and Expert Opinions.

GUIDELINE STATEMENTS

Shared Decision Making

1. Clinicians and patients should engage in shared decision-making, taking into consideration the best available evidence and the patient's expressed values, preferences, and goals of GSM care. *(Clinical Principle)*

Screening & Diagnosis

2. Clinicians should screen patients at risk for, or presenting with signs of, GSM for genital, sexual, and/or urinary symptoms using a focused medical, sexual, and psychosocial history. *(Clinical Principle)*
3. Patients with symptoms of GSM should undergo a genitourinary examination. *(Clinical Principle)*
4. Clinicians should educate patients with GSM about genitourinary signs and symptoms that result from decreased sex steroid hormones. *(Clinical Principle)*
5. During evaluation of patients with GSM, clinicians should assess for coexisting genitourinary conditions, utilizing additional testing or referral when appropriate. *(Clinical Principle)*
6. In patients with GSM and psychosocial and/or sexual health concerns, clinicians may refer to a credentialed therapist. *(Expert Opinion)*
7. In patients with GSM and pelvic floor dysfunction, clinicians may refer to a physical therapist specializing in pelvic floor conditions. *(Expert Opinion)*

Hormonal Interventions

8. Clinicians should offer the option of local low-dose vaginal estrogen to patients with GSM to improve vulvovaginal discomfort/irritation, dryness, and/or dyspareunia. *(Strong Recommendation; Evidence Level: Grade C)*
9. Clinicians should offer the option of vaginal dehydroepiandrosterone (DHEA) to patients with GSM to improve vulvovaginal dryness and/or dyspareunia. *(Moderate Recommendation; Evidence Level: Grade C)*
10. Clinicians may offer the option of ospemifene to patients with GSM to improve vulvovaginal dryness and/or dyspareunia. *(Conditional Recommendation; Evidence Level: Grade C)*
11. In patients with GSM who are on systemic estrogen therapy, clinicians should offer the option of local low-dose vaginal estrogen or vaginal dehydroepiandrosterone (DHEA). *(Expert Opinion)*
12. In patients with GSM and comorbid genitourinary conditions (e.g., overactive bladder), clinicians may offer the option of local low-dose vaginal estrogen to improve genitourinary symptoms. *(Expert Opinion)*
13. In patients with GSM and recurrent urinary tract infections, clinicians should recommend local low-dose vaginal estrogen to reduce the risk for future urinary tract infections. *(Moderate Recommendation; Evidence Level: Grade B)*

Non-Hormonal Interventions

14. Clinicians should recommend the use of vaginal moisturizers and/or lubricants, either alone or in combination with other therapies, to improve vaginal

dryness and/or dyspareunia in patients with GSM. *(Moderate Recommendation; Evidence Level: Grade C)*

15. Clinicians should counsel patients that the evidence does not support the use of alternative supplements in the treatment of GSM. *(Expert Opinion)*
16. Clinicians should counsel patients to avoid vulvovaginal irritants and/or cleansers which may exacerbate the signs and symptoms of GSM. *(Expert Opinion)*

Energy-Based Interventions

17. Clinicians should counsel patients that the evidence does not support the use of CO_2 laser, ER:YAG laser, or radiofrequency in the treatment of GSM-related vulvovaginal dryness, vulvovaginal discomfort/irritation, dysuria, quality of life, change in bothersome symptoms, satisfaction with treatment, or dyspareunia. *(Moderate Recommendation, Evidence Level: Grade C)*
18. In the context of shared decision-making, and with the disclosure that these therapies are considered experimental outside of clinical trials, clinicians may consider CO_2 laser treatment in patients who are not candidates for, or prefer alternatives to, FDA-approved treatments for GSM-related vulvovaginal dryness, vulvovaginal discomfort/irritation, dysuria, and/or dyspareunia. *(Expert Opinion)*

Breast and Endometrial Cancer

19. Clinicians should inform patients of the absence of evidence linking local low-dose vaginal estrogen to the development of breast cancer. *(Expert Opinion)*
20. For patients with GSM who have a personal history of breast cancer, clinicians may recommend local low-dose vaginal estrogen in the context of multi-disciplinary shared decision-making. *(Expert Opinion)*
21. Clinicians should counsel patients with GSM that neither vaginal dehydroepiandrosterone (DHEA) nor ospemifene increase the risk for breast cancer. *(Expert Opinion)*
22. Clinicians should counsel patients with GSM that local low-dose vaginal estrogen, does not increase the risk for endometrial hyperplasia with atypia or endometrial cancer. *(Moderate Recommendation; Evidence Level: Grade C)*
23. Clinicians should counsel patients with GSM that neither vaginal dehydroepiandrosterone (DHEA) nor ospemifene increase the risk for endometrial hyperplasia with atypia or endometrial cancer. *(Moderate Recommendation; Evidence Level: Grade C)*

Endometrial Surveillance

24. Clinicians should not perform endometrial surveillance in patients with GSM solely due to their use of local low-dose vaginal estrogen, vaginal dehydroepiandrosterone (DHEA), or ospemifene. *(Expert Opinion)*

Follow-Up

25. After initiation of treatment, clinicians should reassess patients with GSM to monitor response. *(Clinical Principle)*
26. Clinicians should counsel patients receiving therapy for GSM that long-term treatment and follow-up may be required to manage signs and symptoms. *(Clinical Principle)*

INTRODUCTION

The source of the Introduction and Methodology text below, as well as some text summarizing evidence results, is drawn from the evidence report used to create this Guideline, "Genitourinary Syndrome of Menopause: A Systematic Review," by the Minnesota Evidence-based Practice Center Program at the Agency for Healthcare Research and Quality (AHRQ) and funded by the Patient-Centered Outcomes Research Institute (PCORI®)[5] The use of this report to derive clinical practice guidelines does not imply endorsement by PCORI®, AHRQ, or U.S. Department of Health and Human Services.

Genitourinary syndrome of menopause (GSM) describes the spectrum of symptoms and physical changes resulting from declining estrogen and androgen concentrations in the genitourinary tract during perimenopause and after menopause.[1] Menopause, which is defined as the phase that begins 12 months after the last menstrual period, is characterized by the natural decline in ovarian function and associated physiological changes that occur in most women in their early 50s.[6] For some individuals, menopause is associated with vasomotor symptoms (i.e., hot flashes/flushes and/or night sweats) and/or genitourinary symptoms, with wide variability in prevalence, duration, and severity.[7]

Since introduction of the term GSM in 2014,[1] no consensus has been reached about the number or type of symptoms (vulvovaginal, urinary, or sexual) needed to diagnose GSM, nor a requirement for identifying concurrent physical signs.[2, 3] Vulvovaginal symptoms associated with menopause include dryness, burning, and irritation.[8] Urinary symptoms include urgency, frequency, dysuria, and recurrent urinary tract infections (UTI).[9] The vulvovaginal and urinary effects of menopause are often considered the cause of sexual symptoms of GSM, including dyspareunia and bleeding during intercourse, as well as broader impacts on sexual function, such as reduced libido, arousal, and orgasm.[9-11] Physical changes associated with GSM include labial atrophy, reduced moisture, introital stenosis, and clitoral atrophy.[1] The vaginal surface may be friable and hypopigmented, with petechiae, ulcerations, and tears; urethral findings may include caruncles, prolapse, or polyps.[4] However, presence and severity of physical exam findings do not directly correlate with self-reported GSM symptoms.[4, 12, 13]

Clinicians generally diagnose GSM based on symptoms, with or without related physical findings, and after ruling out other etiologies or co-occurring pathologies (e.g., infectious vaginitis, vulvar lichen sclerosus, dermatitis, lichen planus, or an active UTI).[9, 14, 15] Objective measures of postmenopausal vaginal changes include the Vaginal Maturation Index (VMI)[16] and vaginal pH.[17] The VMI demonstrates a shift from superficial cells to parabasal cells as the vaginal epithelium thins, and vaginal pH then rises as fewer

superficial epithelial cells exfoliate and break down to release glycogen and glucose, which would typically be broken down into lactic acid by *Lactobacilli* in an estrogenized vagina.[8] Trials have sometimes limited inclusion to patients with moderate to severe GSM symptoms, 5% or fewer superficial cells on VMI, and vaginal pH greater than 5, however these measures are neither required nor commonly used for clinical diagnosis and treatment of GSM.[18]

GSM prevalence estimates in postmenopausal patients vary widely from 13 to 87 percent.[19] This inconsistency stems from many factors including variation in the symptoms and/or signs assessed and evaluated, the symptom assessment tools used, and the demographics and settings of study populations.[19] Unlike vasomotor symptoms of menopause (i.e., hot flashes and/or night sweats), the prevalence and intensity of some genitourinary symptoms, such as vulvovaginal dryness, increase with advancing age.[20, 21] GSM may be associated with reduced quality of life (QoL) and sexual functioning, and a higher likelihood of urinary complaints, all of which may interfere with interpersonal relationships.[22-27] Despite the potentially disruptive nature of GSM, only about half of individuals with GSM symptoms report discussing their symptoms with their clinicians, and of those who did, most said the clinician did not initiate the conversation.[28, 29]

Several organizations recommend identifying GSM through a case-finding approach, by screening patients for symptoms with routine questions.[30-32] However, few tools have been validated for GSM assessment and existing tools are limited to vulvovaginal symptoms.[10, 33] The urinary symptoms associated with GSM are also linked with other common urologic conditions in older patients, such as overactive bladder (OAB), making identification, evaluation, and treatment of these symptoms complex.[4] A causal relationship between reduced hormone levels and urinary symptoms remains controversial.[34-36] Some have even questioned whether GSM meets the definition of a disease syndrome.[37] These questions create uncertainty around the optimal approach to screening, identification, evaluation, and management of GSM.

Nonetheless, the range of GSM treatments has increased substantially in recent years.[32, 38] Traditional therapies, such as vaginal estrogen, moisturizers, and lubricants restore, alleviate symptoms, or avoid friction, respectively. Estrogen binds to receptors in the vagina, vulva, urethra, bladder, and pelvic floor, shifts the vaginal cytology toward superficial cells, away from parabasal cells, and reduces the vaginal pH. Vaginal moisturizers increase the fluid content in the endothelium and reduce the vaginal pH. Personal lubricants can be water, silicone, or oil-based and are primarily used to provide short-term lubrication during sexual activity; lubricants are often used as a placebo or control treatment in clinical trials. Newer hormonal approaches include vaginal dehydroepiandrosterone (DHEA), vaginal oxytocin, selective estrogen receptor modulators (SERMs), and testosterone. DHEA is a precursor to both androgens and estrogens that is transformed into estradiol and testosterone within vaginal cells. Oxytocin is a pituitary hormone primarily implicated in uterine labor contractions and lactation, but vaginal oxytocin gel has also been shown to reduce vaginal pH and increase the proportion of superficial cells in small studies. SERMs have varied estrogen agonist/antagonist effects throughout the body; among SERMs, ospemifene has unique

estrogen receptor agonist activity in vaginal tissue. Complementary therapies, including oral and vaginal natural products (e.g., herbal supplements, phytoestrogens, vitamins, probiotics), mind-body practices, pelvic floor physical therapy (PFPT), and educational interventions, offer various mechanisms of action while appealing to individuals who wish to avoid hormonal treatments. Finally, energy-based treatments such as laser and radiofrequency devices claim to stimulate collagen formation, angiogenesis, and epithelial thickening by causing microtrauma or heating superficial tissue layers.

Some of these treatments aim to improve a broad range of GSM symptoms, while others target a specific bothersome symptom. Randomized controlled trials (RCTs) are typically short term, and lack long-term intervention efficacy, adherence, or harms data. Study populations are often not comparable and confounding variables can impact the validity of the findings. Consequently, guidance for longer-term follow-up and surveillance as well as treatment in special populations, such as patients with a history of hormonally sensitive breast cancer, has relied on expert consensus in the absence of robust evidence.[30, 32, 39]

This guideline endeavors to provide information to clinicians regarding identification, diagnosis, counseling and treatment for patients with GSM to optimize symptom control and improve QoL while minimizing adverse effects (AE). The strategies defined in this document were derived from evidence-based and consensus-based processes. However, shared decision-making (SDM) is the optimal strategy to individualize level of impact and ultimate interventions. As outreach to this marginalized and underserved population is essential, the Panel trusts this document will guide all types of clinicians who evaluate, manage and treat patients with GSM across a multitude of disciplines.

Methodology

The systematic review utilized in the creation of this guideline is based on research conducted by the Minnesota Evidence-based Practice Center (EPC) under contract to the Agency for Healthcare Research and Quality (AHRQ) and funded by the Patient Centered Outcomes Research Institute (PCORI). Searches covered publication dates from database inception through December 11, 2023. To improve applicability of findings to U.S. patients and clinicians, the EPC included only U.S.-available interventions. Where evidence was sufficient without an unacceptable amount of clinical heterogeneity, the EPC conducted pairwise meta-analyses. For studies that evaluated non-hormonal interventions (other than vaginal moisturizers), an evidence map describing study characteristics was created. For hormonal and energy-based interventions, and vaginal moisturizers, low and moderate risk of bias studies were synthesized and the EPC provided Grading of Recommendations Assessment, Development and Evaluation (GRADE) certainty of evidence (COE) ratings for 8 patient-centered outcomes identified by the Core Outcomes in Menopause (COMMA) review[1] as most important to patients and clinicians, including: (1) pain with sex, (2) vulvovaginal dryness, (3) vulvovaginal discomfort/irritation, (4) dysuria, (5) change in Most Bothersome Symptom (MBS), (6) distress, bother, or interference of genitourinary symptoms, (7) satisfaction with treatment, and (8) treatment side effects. The EPC derived COE from statistical rather than clinical significance or

effect magnitude, in part because validated measures of clinically meaningful differences do not exist for most outcomes.

RESULTS

After assessing 107 publications for risk of bias (RoB), the EPC extracted effectiveness and/or harms outcomes from 68 publications describing trials or prospective, controlled observational studies that were rated low, some concerns, or moderate RoB (24 estrogen publications, 35 non-estrogen, 11 energy-based, and 4 moisturizers). Of 39 high, serious, or critical RoB publications, the EPC only extracted long-term harms from 15 uncontrolled studies of energy-based interventions (all serious or critical RoB due to confounding). Among 19 high RoB randomized controlled trials (RCT), the most common source of bias was missing outcome data. An additional 66 publications evaluating 46 non-hormonal interventions are described in an evidence map. Most non-hormonal interventions in the evidence map were focused on natural products (i.e., herbal or botanical supplements, vitamins) and were small in sample size. Five trials[1-3, 6, 7] (9 publications) compared active interventions from more than one category with placebo and are counted more than once in the description above. The relevant arms of each trial are described in their respective sections.

KEY QUESTIONS (APPENDIX A)

No studies evaluated Key Questions (KQ) related to GSM screening (KQ1) or directly addressed appropriate follow-up intervals (KQ4) or the effectiveness and harms of endometrial surveillance (KQ5).

For efficacy/effectiveness (KQ2) and harms (KQ3), the certainty of evidence for most intervention-comparison-outcome combinations was low or very low; COE was moderate or high for only a few comparisons. Overall, for KQ2 the EPC concluded that vaginal estrogen, vaginal DHEA, vaginal moisturizers, and oral ospemifene, may all improve at least some GSM symptoms, primarily vulvovaginal dryness and, to a lesser extent, dyspareunia. No treatment significantly improved vaginal discomfort/irritation or dysuria. Placebo effect was high, particularly in studies using a lubricating vaginal gel or cream placebo. Evidence does not demonstrate the efficacy of energy-based therapies (carbon dioxide [CO_2] or Erbium-doped yttrium aluminum garnet [Er:YAG] laser), vaginal or systemic testosterone, vaginal oxytocin, oral raloxifene, or bazedoxifene for any GSM symptoms.

Compared with placebo, vaginal estrogen may improve vulvovaginal dryness, MBS, and treatment satisfaction (low COE), but probably results in little to no difference in QoL (moderate COE) and may result in little to no difference in dyspareunia or dysuria (low COE). Compared with no treatment, vaginal estrogen may improve vulvovaginal dryness and dyspareunia and may result in little to no difference in vulvovaginal discomfort/irritation or dysuria (low COE).

Among non-estrogen hormonal interventions, vaginal DHEA compared with placebo may improve vulvovaginal dryness, dyspareunia, and QoL (low COE), but may result in more

AEs (low COE). Oxytocin compared with placebo probably results in little to no difference in MBS (moderate COE) and may result in little to no difference in serious AEs (low COE). Ospemifene compared with placebo may improve vulvovaginal dryness and dyspareunia (low COE) and results in higher treatment satisfaction (high COE), but results in little to no difference in vulvovaginal discomfort/irritation (high COE) and may result in little to no difference in AEs (low COE). Raloxifene added to vaginal estrogen or moisturizer compared with vaginal estrogen or moisturizer plus placebo may result in little to no difference in vulvovaginal dryness, discomfort/irritation, dysuria, and dyspareunia (low COE). Bazedoxifene may improve QoL less than placebo (low COE). Oral bazedoxifene or raloxifene compared with placebo may result in higher treatment satisfaction (low COE).

Systemic estrogen plus systemic testosterone compared with systemic estrogen alone may result in little to no difference in vulvovaginal dryness and dyspareunia (low COE). Vaginal moisturizers compared with placebo may improve vulvovaginal dryness (low COE) but may result in little to no difference in MBS (low COE). Vaginal moisturizers compared with placebo probably result in little to no difference in AEs (moderate COE). Among energy-based interventions, CO_2 laser (compared with sham laser) may result in little to no difference in MBS, dysuria, QoL, or serious AEs (low COE). Compared with vaginal estrogen cream, CO_2 laser may result in little to no difference in vulvovaginal dryness, dyspareunia, discomfort/irritation, dysuria, QoL, or serious AEs (low COE). Er:YAG laser compared with sham laser may result in little to no difference in QoL (low COE).

For the eight COMMA outcomes defined above, the evidence was very uncertain (very low COE) for all other studied intervention-comparator-outcome combinations. The full report contains results for additional effectiveness outcomes, including recurrent urinary infections, sexual function, urinary incontinence, physical signs of vulvovaginal atrophy, common AEs, and warnings reported by the U.S. Food and Drug Administration (FDA).

Harms reporting (KQ3) was limited, in part, by studies not being sufficiently powered to evaluate infrequent but serious harms, though most studies did not find evidence of frequent serious harms. Infrequent AEs varied by treatment. For example, vaginal estrogen was associated with vaginal bleeding, discharge, and breast tenderness; vaginal DHEA was associated with increased facial hair, voice changes, and headaches; oral ospemifene was associated with hot flushes and vaginal candidiasis; and CO_2 laser was associated with vaginal bleeding, pain, and discharge. For KQ4, limited evidence within studies of effective treatments, suggests that symptoms begin improving within 1-2 months and continue to improve through 12 weeks (average length of study follow-up). For endometrial outcomes (KQ5), among hormonal interventions, ospemifene was associated with thickened endometrial lining, proliferative endometrial histology, and one case of endometrial hyperplasia. In 6 of 10 studies that evaluated endometrial stimulation up to 36 weeks, vaginal estrogen was associated with cases of vaginal bleeding, a nominal increase in endometrial thickness, proliferative endometrium, and one case of endometrial hyperplasia in a polyp. Limited evidence suggests that vaginal DHEA, vaginal oxytocin, oral bazedoxifene and raloxifene, and vaginal testosterone are not associated

with clinically relevant endometrial stimulation as measured by transvaginal ultrasound or endometrial biopsy in primarily short-term studies and 3 year-long studies.

DETERMINING THE EVIDENCE STRENGTH

The GRADE[40] system was used to determine the aggregate evidence quality for each outcome, or group of related outcomes, informing Key Questions. GRADE defines a body of evidence in relation to how confident guideline developers can be that the estimate of effects as reported by that body of evidence is correct. Evidence is categorized as high, moderate, low and very low, and assessment is based on the aggregate risk of bias for the evidence base, plus limitations introduced as a consequence of inconsistency, indirectness, imprecision and publication bias across the studies.[41] Upgrading of evidence is possible if the body of evidence indicates a large effect or if confounding would suggest either spurious effects or would reduce the demonstrated effect.

The American Urological Association (AUA) employs a 3-tiered strength of evidence system to underpin evidence-based guideline statements. Table 1 summarizes the GRADE categories, definitions and how these categories translate to the AUA strength of evidence categories. In short, high certainty by GRADE translates to AUA A-category strength of evidence, moderate to B, and both low and very low to C.

Table 1: Strength of Evidence Definition

AUA Strength of Evidence Category	GRADE Certainty Rating	Definition
A	High	• Very confident that the true effect lies close to that of the estimate of the effect
B	Moderate	• Moderately confident in the effect estimate • The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different
C	Low	• Confidence in the effect estimate is limited • The true effect may be substantially different from the estimate of the effect
	Very Low	• Very little confidence in the effect estimate • The true effect is likely to be substantially different from the estimate of effect

AUA NOMENCLATURE: LINKING STATEMENT TYPE TO EVIDENCE STRENGTH

The AUA nomenclature system explicitly links statement type to body of evidence strength, level of certainty, magnitude of benefit or risk/burdens, and the Panel's judgment regarding the balance between benefits and risks/burdens **(Table 2)**. ***Strong Recommendations*** are directive statements that an action should (benefits outweigh risks/burdens) or should not (risks/burdens outweigh benefits) be undertaken because net benefit or net harm is substantial. ***Moderate Recommendations*** are directive statements that an action should (benefits outweigh risks/burdens) or should not (risks/burdens outweigh benefits) be undertaken because net benefit or net harm is moderate. ***Conditional Recommendations*** are non-directive statements used when the evidence indicates there is no apparent net benefit or harm or when the balance between benefits and risks/burden is unclear. All three statement types may be supported by any body of evidence strength grade. Body of evidence strength Grade A in support of a Strong or Moderate Recommendation indicates the statement can be applied to most patients in most circumstances and that future research is *unlikely to change confidence*. Body of evidence strength Grade B in support of a Strong or Moderate Recommendation indicates the statement can be applied to most patients in most circumstances, but better evidence *could change confidence*. Body of evidence strength Grade C in support of a Strong or Moderate Recommendation indicates the statement can be applied to most patients in most circumstances, but better evidence is *likely to change confidence*. Body of evidence strength Grade C is only rarely used in support of a Strong Recommendation. Conditional Recommendations can also be supported by any evidence strength. When body of evidence strength is Grade A, the statement indicates benefits and risks/burdens appear balanced, the best action depends on patient circumstances, and future research is *unlikely to change confidence*. When body of evidence strength Grade B is used, benefits and risks/burdens appear balanced, the best action also depends on individual patient circumstances, and better evidence *could change confidence*. When body of evidence strength Grade C is used, there is uncertainty regarding the balance between benefits and risks/burdens, alternative strategies may be equally reasonable, and better evidence is *likely to change confidence*.

Where gaps in the evidence existed, ***Clinical Principles*** or ***Expert Opinions*** are provided via consensus of the Panel. A ***Clinical Principle*** is a statement about a component of clinical care widely agreed upon by urologists or other clinicians for which there may or may not be evidence in the medical literature. ***Expert Opinion*** refers to a statement based on members' clinical training, experience, knowledge, and judgment for which there may or may not be evidence in the medical literature.

Table 2: AUA Nomenclature Linking Statement Type to Level of Certainty, Magnitude of Benefit or Risk/Burden, and Body of Evidence Strength

Evidence Grade	Evidence Strength A (High Certainty)	Evidence Strength B (Moderate Certainty)	Evidence Strength C (Low Certainty)
Strong Recommendation (Net benefit or harm substantial)	• Benefits > Risks/ Burdens (or vice versa) • Net benefit (or net harm) is substantial • Applies to most patients in most circumstances and future research is unlikely to change confidence	• Benefits > Risks/ Burdens (or vice versa) • Net benefit (or net harm) is substantial • Applies to most patients in most circumstances but better evidence could change confidence	• Benefits > Risks/ Burdens (or vice versa) • Net benefit (or net harm) appears substantial • Applies to most patients in most circumstances but better evidence is likely to change confidence (rarely used to support a Strong Recommendation)
Moderate Recommendation (Net benefit or harm moderate)	• Benefits > Risks/ Burdens (or vice versa) • Net benefit (or net harm) is moderate • Applies to most patients in most circumstances and future research is unlikely to change confidence	• Benefits > Risks/ Burdens (or vice versa) • Net benefit (or net harm) is moderate • Applies to most patients in most circumstances but better evidence could change confidence	• Benefits > Risks/Burdens (or vice versa) • Net benefit (or net harm) appears moderate • Applies to most patients in most circumstances but better evidence is likely to change confidence
Conditional Recommendation (Net benefit or harm comparable to other options)	• Benefits=Risks/Burdens • Best action depends on individual patient circumstances • Future research is unlikely to change confidence	• Benefits=Risks/ Burdens • Best action appears to depend on individual patient circumstances • Better evidence could change confidence	• Balance between Benefits & Risks/Burdens unclear • Net benefit (or net harm) comparable to other options • Alternative strategies may be equally reasonable • Better evidence likely to change confidence
Clinical Principle	A statement about a component of clinical care that is widely agreed upon by urologists or other clinicians for which there may or may not be evidence in the medical literature		
Expert Opinion	A statement achieved by consensus of the Panel that is based on members' clinical training, experience, knowledge, and judgment for which there may or may not be evidence in the medical literature		

PANEL FORMATION

The GSM Guideline Panel was created in 2022 by the American Urological Association Education and Research, Inc and in in collaboration with the Society of Urodynamics,

Female Pelvic Medicine & Urogenital Reconstruction (SUFU) and the American Urogynecologic Society (AUGS). The Practice Guidelines Committee (PGC) of the AUA selected the Panel Chairs who in turn appointed the additional panel members based on an open nomination process. SUFU and AUGS each appointed two panelists. Additionally, the Panel included patient representation. Funding of the Guideline was provided by the AUA; panel members received no remuneration for their work. Funding for the AHRQ systematic review was provided by the PCORI.

PEER REVIEW

An integral part of the guideline development process at the AUA is external peer review. The AUA conducted a thorough peer review process to ensure that the document was reviewed by experts in the diagnosis and treatment of Genitourinary Syndrome of Menopause. In addition to reviewers from the AUA PGC, Science and Quality Council (SQC), and Board of Directors (BOD), the document was reviewed by representatives from SUFU and AUGS and external content experts. A call for reviewers was placed on the AUA website from September 27 – October 11, 2024, to allow any additional interested parties to request a copy of the document for review. The guideline was also sent to the Urology Care Foundation and the AUA Public Policy & Advocacy team to open the document further to the patient perspective. The draft guideline document was distributed to 45 nominated peer reviewers, including 8 external reviewers (i.e., peer reviewers who responded to the call for comments), and 5 reviewers nominated by AUGS and SUFU; 40 AUA Committee members (PGC, SQC, BOD) and 16 AUA staff. All peer review comments were blinded and sent to the Panel for review. In total, 43 reviewers provided comments, including 6 external reviewers. At the end of the peer review process, a total of 594 comments were received. Following comment discussion, the Panel revised the draft as needed. Once finalized, the guideline was submitted for approval to the AUA PGC, SQC, and BOD, the SUFU Executive Committee; and the AUGS Board of Directors for final approval.

GUIDELINE STATEMENTS

Shared Decision-Making

GUIDELINE STATEMENT 1

Clinicians and patients should engage in shared decision-making, taking into consideration the best available evidence and the patient's expressed values, preferences, and goals of GSM care. *(Clinical Principle)*

Discussion

Screening & Diagnosis

GUIDELINE STATEMENT 2

Clinicians should screen patients at risk for, or presenting with signs of, GSM for genital, sexual, and/or urinary symptoms using a focused medical, sexual, and psychosocial history. *(Clinical Principle)*

GUIDELINE STATEMENT 3

Patients with symptoms of GSM should undergo a genitourinary examination. *(Clinical Principle)*

Discussion

GUIDELINE STATEMENT 4

Clinicians should educate patients with GSM about genitourinary signs and symptoms that result from decreased sex steroid hormones. *(Clinical Principle)*

Discussion

GUIDELINE STATEMENT 5

During evaluation of patients with GSM, clinicians should assess for coexisting genitourinary conditions, utilizing additional testing or referral when appropriate. *(Clinical Principle)*

Discussion

GUIDELINE STATEMENT 6

In patients with GSM and psychosocial and/or sexual health concerns, clinicians may refer to a credentialed therapist. *(Expert Opinion)*

Discussion

GUIDELINE STATEMENT 7

In patients with GSM and pelvic floor dysfunction, clinicians may refer to a physical therapist specializing in pelvic floor conditions. *(Expert Opinion)*

Discussion

Hormonal Interventions

While there is a large body of evidence that is supportive of both vaginal and systemic hormonal approaches to the management of GSM, there is insufficient evidence to compare the efficacy of these hormonal interventions against one another. Thus, this guideline is not meant to support a stepwise progression through different hormonal approaches, but instead to provide evidence to support a process of SDM between the clinician and patient in choosing an appropriate therapy. While there is insufficient information to recommend one hormonal therapy over another, the greatest amount of evidence and experience exists for vaginal estrogen supplementation. The consensus of the Panel is that the choice of agent should be considered not only using evidence of efficacy and AEs, but also of patient preference, accessibility, and ability to use consistently (i.e., patient dexterity, anatomy, social support).

There was insufficient evidence to support clinical recommendations for vaginal and systemic testosterone and oxytocin. The existing evidence and its limitations are detailed below.

GUIDELINE STATEMENT 8

Clinicians should offer the option of local low-dose vaginal estrogen to patients with GSM to improve vulvovaginal discomfort/irritation, dryness, and/or dyspareunia. *(Strong Recommendation; Evidence Level: Grade C)*

Discussion

GUIDELINE STATEMENT 9

Clinicians should offer the option of vaginal dehydroepiandrosterone (DHEA) to patients with GSM to improve vulvovaginal dryness and/or dyspareunia. *(Moderate Recommendation; Evidence Level: Grade C)*

Discussion

GUIDELINE STATEMENT 10

Clinicians may offer the option of ospemifene to patients with GSM to improve vulvovaginal dryness and/or dyspareunia. *(Conditional Recommendation; Evidence Level: Grade C)*

Discussion

GUIDELINE STATEMENT 11

In patients with GSM who are on systemic estrogen therapy, clinicians should offer the option of local low-dose vaginal estrogen or vaginal dehydroepiandrosterone (DHEA). *(Expert Opinion)*

Discussion

GUIDELINE STATEMENT 12

In patients with GSM and comorbid genitourinary conditions (e.g., overactive bladder), clinicians may offer local low-dose vaginal estrogen to improve genitourinary symptoms. *(Expert Opinion)*

Discussion

GUIDELINE STATEMENT 13

In patients with GSM and recurrent urinary tract infections, clinicians should recommend local low-dose vaginal estrogen to reduce the risk for future urinary tract infections. *(Moderate Recommendation; Evidence Level: Grade B)*

Discussion

Non-Hormonal Interventions

GUIDELINE STATEMENT 14

Clinicians should recommend the use of vaginal moisturizers and/or lubricants, either alone or in combination with other therapies, to improve vaginal dryness and/or dyspareunia in patients with GSM. (*Moderate Recommendation; Evidence Level: Grade C)*

Discussion

GUIDELINE STATEMENT 15

Clinicians should counsel patients that the evidence does not support the use of alternative supplements in the treatment of GSM. *(Expert Opinion)*

Discussion

GUIDELINE STATEMENT 16

Clinicians should counsel patients to avoid vulvovaginal irritants and/or cleansers which may exacerbate the signs and symptoms of GSM. *(Expert Opinion)*

Discussion

Energy-Based Interventions

GUIDELINE STATEMENT 17

Clinicians should counsel patients that the evidence does not support the use of CO_2 laser, ER:YAG laser, or radiofrequency in the treatment of GSM-related vulvovaginal dryness, vulvovaginal discomfort/irritation, dysuria, quality of life, change in bothersome symptoms, satisfaction with treatment, or dyspareunia. *(Moderate Recommendation, Evidence Level: Grade C)*

GUIDELINE STATEMENT 18

In the context of shared decision-making, and with the disclosure that these therapies are considered experimental outside of clinical trials, clinicians may consider CO_2 laser treatment in patients who are not candidates for, or prefer alternatives to, FDA-approved treatments for GSM-related vulvovaginal dryness, vulvovaginal discomfort/irritation, dysuria, and/or dyspareunia. *(Expert Opinion)*

Discussion

Breast and Endometrial Cancer

GUIDELINE STATEMENT 19

Clinicians should inform patients of the absence of evidence linking local low-dose vaginal estrogen to the development of breast cancer. *(Expert Opinion)*

Discussion

GUIDELINE STATEMENT 20

For patients with GSM who have a personal history of breast cancer, clinicians may recommend local low-dose vaginal estrogen in the context of multi-disciplinary shared decision-making. *(Expert Opinion)*

Discussion

GUIDELINE STATEMENT 21

Clinicians should counsel patients with GSM that neither vaginal dehydroepiandrosterone (DHEA) nor ospemifene increase the risk for breast cancer. *(Expert Opinion)*

Discussion

GUIDELINE STATEMENT 22

Clinicians should counsel patients with GSM that local low-dose vaginal estrogen does not increase the risk for endometrial hyperplasia with atypia or endometrial cancer. *(Moderate Recommendation; Evidence Strength: Level C)*

Discussion

GUIDELINE STATEMENT 23

Clinicians should counsel patients with GSM that neither vaginal dehydroepiandrosterone (DHEA) nor ospemifene increase the risk for endometrial hyperplasia with atypia or endometrial cancer. *(Moderate Recommendation; Evidence Level: Grade C)*

Discussion

Endometrial Surveillance

GUIDELINE STATEMENT 24

Clinicians should not perform endometrial surveillance in patients with GSM solely due to their use of local low-dose vaginal estrogen, vaginal dehydroepiandrosterone (DHEA), or ospemifene. *(Expert Opinion)*

Discussion

Follow-Up

GUIDELINE STATEMENT 25

After initiation of treatment, clinicians should reassess patients with GSM to monitor response. *(Clinical Principle)*

Discussion

GUIDELINE STATEMENT 26

Clinicians should counsel patients receiving therapy for GSM that long-term treatment and follow-up may be required to manage signs and symptoms. *(Clinical Principle)*

Discussion

FUTURE DIRECTIONS

Comparable to other functional urologic conditions, GSM is a symptom and sign-based diagnosis made after careful clinical evaluation and at the exclusion of other causes. The hormonal imbalances that drive development of GSM manifest differently in each patient so tailoring individualized management strategies is fundamental for establishing goals of care. Thus, there is no single intervention for GSM which is universally effective or acceptable. Indeed, additional urologic and gynecologic conditions, such as OAB or sexual dysfunction, may co-exist with GSM and may need additional diagnosis-specific targeted treatment to meet the patient's goals.

Understanding the concept of trauma-informed care for the GSM patient and utilizing language that supports patient choice and safety is important for clinicians during history-taking, performing physical exams, and providing treatment. Defining mechanisms for standardizing clinical training regarding counseling and logistics of examinations to preserve a patient's dignity and avoiding negative triggers will empower both clinicians and patients. Given the intimate and impactful nature of GSM, patients should be cared for in a wholistic manner where diagnostic and treatment strategies are implemented in a compassionate and patient-centered manner.

In addition to the aforementioned need for standardized diagnostic criteria and outcomes, further exposure across disciplines to the terminology of GSM would assist to demystify the condition and further expand opportunities for access to care, as well as development of future interventions. Mandated within the framework of definitions would be standardized reporting for AE associated with treatments, or lack thereof, for patients with GSM.

Qualitative studies of the patient perspective on GSM[183] have identified themes including: the need for education on medications including usage instructions, discussion on potential side effects, interest in alternative therapies, and needing support for and validation of GSM and GSM symptoms from health care clinicians. Understanding and overcoming patient-centered barriers to common treatments is critical for driving both compliance and policy.[184] This guideline serves to begin the conversation to increase awareness and establish evidence-based best practices for clinicians. Future studies should continue to explore and include patient's knowledge, attitudes, and beliefs, so that the medical community can better meet GSM patients' needs.

With a standard language for GSM, it is important to collaborate and codify across disciplines to be able to accurately express symptoms such that they may be objectively measured. Broadly, phenotyping our patients to describe the manifestations of GSM on vaginal, urinary, and general pelvic health domains is critical to provide clinically meaningful and standardized research outcomes. A future direction may involve differentiation of the symptoms associated with GSM to best define what is implied by a syndrome.

With regards to expanding the relevance of research outcomes, intentional, community-engaged efforts to recruit clinically relevant and racialized, minoritized, and systematically excluded patient populations who have been historically left out of clinical trials and research studies must be implemented to increase the relevance and robustness of research outcomes. Including a broader, more inclusive population to reflect the real-world experience of patients and clinicians is key to increase the generalizability of research findings. Contemporary outreach efforts engaging local organizations and implementing telehealth strategies may facilitate inclusive engagement. Additionally, defining best practices with regards to time of follow up, including more long-term evaluation, is critically important for a condition that typically worsens or is subject to influence of comorbid conditions over time. The panel expressed the need for evaluation of otherwise marginalized populations outside of the traditional postmenopausal patient for inclusion in research to explore and establish best practices. This includes transgender patients, patients on systemic estrogen, young women using oral contraceptives, breast- or chest-feeding patients, individuals with hypothalamic amenorrhea, patient on gonadotropin regulating hormone for endometriosis or uterine fibroids, post-oophorectomy patients, and further analysis of the impact of interventions on cancer survivors. Further understanding of the wide manifestation of sex steroid deficiencies, including low and elevated follicle stimulating hormone impacts[19, 30] should expand inclusion and drive recruitment in future clinical trials to serve patients with GSM.

Even with commonly accepted treatment strategies that have been outlined in these guidelines, there remain significant gaps in the comparative effectiveness of interventions. As the treatment decisions are individualized, these types of safety and efficacy parameters become a critical aspect of patient counseling. As outlined in earlier sections, the panel appreciates the impact of current boxed warning of estrogen products and advocates for national efforts to update these labels to reflect contemporary literature, particularly regarding low-dose vaginal estrogen. Development of studies defining and standardizing dosing and scheduling of interventions are important to reduce variation and comparison of therapies. Patient engagement and advocacy will help drive research on issues and research questions that matter most to patients with GSM. Comparative effectiveness studies and studies utilizing patient-centered outcome measures are essential to provide patients with information they need to make informed decisions about their health.

A singular limitation of the data interrogated in this guideline is the lack of high-level data detailing GSM treatment on commonly coexistent bladder symptoms and signs including OAB and recurrent UTIs. Future research in this arena is essential to determine best practices for prevention of conditions that negatively affect the QoL of an aging population. Additionally, future research efforts should be directed to understand the influence of local low-dose vaginal estrogen in patients being concurrently treated with systemic estrogen therapies as this represents a substantial population of high-impact.

And with regards to cost and access, this guideline does not address financial impact of either GSM or the treatments thereof. However, the panel acknowledges the potential

financial burden for patients and expresses to the need to explore the issues of cost and access in future research.[182]

In conclusion, the GSM is a common and undertreated condition affecting patients across the lifespan. Safe and effective treatments exist that alleviate bothersome symptoms and improve QoL. Increased education and awareness is critical to reach those affected by GSM. While there are evidence-based best practices in the area of GSM, future research is needed to deepen our understanding of this condition.

REFERENCES

1. Portman, D. J., Gass, M. L., Vulvovaginal Atrophy Terminology Consensus Conference, P.: Genitourinary syndrome of menopause: new terminology for vulvovaginal atrophy from the International Society for the Study of Women's Sexual Health and the North American Menopause Society. J Sex Med, **11:** 2865, 2014
2. Castelo-Branco, C., Peralta, S., Ferrer, J. et al.: The dilemma of menopause and hormone replacement--a challenge for women and health-care providers: knowledge of menopause and hormone therapy in Spanish menopausal women. Climacteric, **9:** 380, 2006
3. Cucinella, L., Martini, E., Tiranini, L. et al.: Genitourinary syndrome of menopause: Should we treat symptoms or signs? Current Opinion in Endocrine and Metabolic Research, **26:** 100386, 2022
4. Mitchell, C. M., Waetjen, L. E.: Genitourinary Changes with Aging. Obstet Gynecol Clin North Am, **45:** 737, 2018
5. Danan, E., Diem, S., Sowerby, C. et al.: Genitourinary Syndrome of Menopause. Comparative Effectiveness Review No. 272. (Prepared by the Minnesota Evidence-based Practice Center under Contract No. 75Q80120D00008.) AHRQ Publication No. 24-EHC022. PCORI® Publication No. 2024-SR-02 Rockville, MD: Agency for Healthcare Research and Quality. July 2024. DOI: https://doi.org/10.23970/AHRQEPCCER272. Posted final reports are located on the Effective Health Care Program search page.
6. Greendale, G. A., Lee, N. P., Arriola, E. R.: The menopause. Lancet, **353:** 571, 1999
7. Hickey, M., Hunter, M. S., Santoro, N. et al.: Normalising menopause. BMJ, **377:** e069369, 2022
8. Mayo Clinic Proceedings: Vulvovaginal atrophy. 2010
9. Gandhi, J., Chen, A., Dagur, G. et al.: Genitourinary syndrome of menopause: an overview of clinical manifestations, pathophysiology, etiology, evaluation, and management. Am J Obstet Gynecol, **215:** 704, 2016
10. Gabes, M., Knuttel, H., Stute, P. et al.: Measurement properties of patient-reported outcome measures (PROMs) for women with genitourinary syndrome of menopause: a systematic review. Menopause, **26:** 1342, 2019
11. Kingsberg, S., Kellogg, S., Krychman, M.: Treating dyspareunia caused by vaginal atrophy: a review of treatment options using vaginal estrogen therapy. Int J Womens Health, **1:** 105, 2010

12. Greendale, G. A., Zibecchi, L., Petersen, L. et al.: Development and validation of a physical examination scale to assess vaginal atrophy and inflammation. Climacteric, **2:** 197, 1999
13. Phillips, N. A., Bachmann, G. A.: The genitourinary syndrome of menopause. Menopause, **28:** 579, 2021
14. Faubion, S. S., Sood, R., Kapoor, E.: Genitourinary Syndrome of Menopause: Management Strategies for the Clinician. Mayo Clin Proc, **92:** 1842, 2017
15. Lewis, F. M.: Vulval symptoms after the menopause - Not all atrophy! Post Reprod Health, **21:** 146, 2015
16. McEndree, B.: Clinical application of the vaginal maturation index. Nurse Pract, **24:** 48, 1999
17. Roy, S., Caillouette, J. C., Roy, T. et al.: Vaginal pH is similar to follicle-stimulating hormone for menopause diagnosis. Am J Obstet Gynecol, **190:** 1272, 2004
18. Weber, M. A., Limpens, J., Roovers, J. P.: Assessment of vaginal atrophy: a review. Int Urogynecol J, **26:** 15, 2015
19. Mili, N., Paschou, S. A., Armeni, A. et al.: Genitourinary syndrome of menopause: a systematic review on prevalence and treatment. Menopause, **28:** 706, 2021
20. Cagnacci, A., Xholli, A., Sclauzero, M. et al.: Vaginal atrophy across the menopausal age: results from the ANGEL study. Climacteric, **22:** 85, 2019
21. Kingsberg, S. A., Wysocki, S., Magnus, L. et al.: Vulvar and vaginal atrophy in postmenopausal women: findings from the REVIVE (REal Women's VIews of Treatment Options for Menopausal Vaginal ChangEs) survey. J Sex Med, **10:** 1790, 2013
22. Moral, E., Delgado, J. L., Carmona, F. et al.: The impact of genitourinary syndrome of menopause on well-being, functioning, and quality of life in postmenopausal women. Menopause, **25:** 1418, 2018
23. Nappi, R. E., Kingsberg, S., Maamari, R. et al.: The CLOSER (CLarifying Vaginal Atrophy's Impact On SEx and Relationships) survey: implications of vaginal discomfort in postmenopausal women and in male partners. J Sex Med, **10:** 2232, 2013
24. Nappi, R. E., Kokot-Kierepa, M.: Women's voices in the menopause: results from an international survey on vaginal atrophy. Maturitas, **67:** 233, 2010
25. Nappi, R. E., Palacios, S.: Impact of vulvovaginal atrophy on sexual health and quality of life at postmenopause. Climacteric, **17:** 3, 2014
26. Parish, S. J., Nappi, R. E., Krychman, M. L. et al.: Impact of vulvovaginal health on postmenopausal women: a review of surveys on symptoms of vulvovaginal atrophy. Int J Womens Health, **5:** 437, 2013
27. Pinkerton, J. V., Bushmakin, A. G., Komm, B. S. et al.: Relationship between changes in vulvar-vaginal atrophy and changes in sexual functioning. Maturitas, **100:** 57, 2017
28. Kingsberg, S. A., Krychman, M., Graham, S. et al.: The Women's EMPOWER Survey: Identifying Women's Perceptions on Vulvar and Vaginal Atrophy and Its Treatment. J Sex Med, **14:** 413, 2017

29. Simon, J. A., Kokot-Kierepa, M., Goldstein, J. et al.: Vaginal health in the United States: results from the Vaginal Health: Insights, Views & Attitudes survey. Menopause, **20:** 1043, 2013
30. Faubion, S. S., Larkin, L. C., Stuenkel, C. A. et al.: Management of genitourinary syndrome of menopause in women with or at high risk for breast cancer: consensus recommendations from The North American Menopause Society and The International Society for the Study of Women's Sexual Health. Menopause, **25:** 596, 2018
31. Stuenkel, C. A., Davis, S. R., Gompel, A. et al.: Treatment of Symptoms of the Menopause: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab, **100:** 3975, 2015
32. Panel., T. N. G. P. S. E.: The 2020 genitourinary syndrome of menopause position statement of The North American Menopause Society. Menopause, **27:** 976, 2020
33. Huang, A. J., Gregorich, S. E., Kuppermann, M. et al.: Day-to-Day Impact of Vaginal Aging questionnaire: a multidimensional measure of the impact of vaginal symptoms on functioning and well-being in postmenopausal women. Menopause, **22:** 144, 2015
34. Augoulea, A., Moros, M., Kokras, N. et al.: Association of menopausal symptoms with sociodemographic factors and personality traits. Prz Menopauzalny, **18:** 191, 2019
35. Christmas, M. M., Iyer, S., Daisy, C. et al.: Menopause hormone therapy and urinary symptoms: a systematic review. Menopause, **30:** 672, 2023
36. Hamer, M. A., Kallen, K., Lidfeldt, J. et al.: Serum estradiol does not differentiate stress, mixed and urge incontinent women around menopause. A report from the Women's Health in the Lund Area (WHILA) study. Eur J Obstet Gynecol Reprod Biol, **159:** 209, 2011
37. Vieira-Baptista, P., Marchitelli, C., Haefner, H. K. et al.: Deconstructing the genitourinary syndrome of menopause. Int Urogynecol J, **28:** 675, 2017
38. Kagan, R., Kellogg-Spadt, S., Parish, S. J.: Practical Treatment Considerations in the Management of Genitourinary Syndrome of Menopause. Drugs Aging, **36:** 897, 2019
39. Gelfand, M. M.: It might be wise to consider adding androgen to the estrogen or estrogen-progestin regimens in the appropriate patients. Menopause, **11:** 505, 2004
40. Guyatt, G., Oxman, A. D., Akl, E. A. et al.: GRADE guidelines: 1. Introduction-GRADE evidence profiles and summary of findings tables. J Clin Epidemiol, **64:** 383, 2011
41. Balshem, H., Helfand, M., Schünemann, H. J. et al.: GRADE guidelines: 3. Rating the quality of evidence. J Clin Epidemiol, **64:** 401, 2011
42. National Quality Partners™ Shared Decision Making Action Team: National Quality Partners Playbook™: Shared Decision Making in Healthcare. 2018
43. Makarov, D., Fagerlin, A., Finkelstein, J. et al.: Implementation of Shared Decision Making into Urological Practice. 2022

44. Elwyn, G., Frosch, D., Rollnick, S.: Dual equipoise shared decision making: definitions for decision and behaviour support interventions. Implement Sci, **4:** 75, 2009
45. Legare, F., Stacey, D., Pouliot, S. et al.: Interprofessionalism and shared decision-making in primary care: a stepwise approach towards a new model. J Interprof Care, **25:** 18, 2011
46. https://decisionaid.ohri.ca/ip-sdm.html: https://decisionaid.ohri.ca/docs/develop/IP-SDM-Model.pdf
47. The SHARE Approach. Content last reviewed October 2024. Agency for Healthcare Research and Quality, Rockville, MD. https://www.ahrq.gov/sdm/share-approach/index.html
48. Parish, S. J., Hahn, S. R.: Hypoactive Sexual Desire Disorder: A Review of Epidemiology, Biopsychology, Diagnosis, and Treatment. Sex Med Rev, **4:** 103, 2016
49. Felitti, V. J., Anda, R. F., Nordenberg, D. et al.: REPRINT OF: Relationship of Childhood Abuse and Household Dysfunction to Many of the Leading Causes of Death in Adults: The Adverse Childhood Experiences (ACE) Study. Am J Prev Med, **56:** 774, 2019
50. Rouch, I., Strippoli, M. F., Dorey, J. M. et al.: Early-life adversity predicting the incidence of multisite chronic pain in the general population. Eur Psychiatry, **67:** e67, 2024
51. Travis, K. J., Huang, A. J., Maguen, S. et al.: Military Sexual Trauma and Menopause Symptoms Among Midlife Women Veterans. J Gen Intern Med, **39:** 411, 2024
52. Gibson, C. J., Huang, A. J., McCaw, B. et al.: Associations of Intimate Partner Violence, Sexual Assault, and Posttraumatic Stress Disorder With Menopause Symptoms Among Midlife and Older Women. JAMA Intern Med, **179:** 80, 2019
53. Baquedano, L., Rejas-Gutierrez, J., Coronado, P. J.: Development and psychometric properties of a measurement to ascertain the impact of genitourinary symptoms on health-related quality of life in menopausal women: the Cervantes-GSM questionnaire. Menopause, **30:** 512, 2023
54. Erekson, E. A., Yip, S. O., Wedderburn, T. S. et al.: The Vulvovaginal Symptoms Questionnaire: a questionnaire for measuring vulvovaginal symptoms in postmenopausal women. Menopause, **20:** 973, 2013
55. Streicher, L. F.: Diagnosis, causes, and treatment of dyspareunia in postmenopausal women. Menopause, **30:** 635, 2023
56. Harlow, S. D., Gass, M., Hall, J. E. et al.: Executive summary of the Stages of Reproductive Aging Workshop + 10: addressing the unfinished agenda of staging reproductive aging. J Clin Endocrinol Metab, **97:** 1159, 2012
57. Levine, K. B., Williams, R. E., Hartmann, K. E.: Vulvovaginal atrophy is strongly associated with female sexual dysfunction among sexually active postmenopausal women. Menopause, **15:** 661, 2008
58. https://www.aasect.org/referral-directory.
59. Dumoulin, C., Hay-Smith, J., Habee-Seguin, G. M. et al.: Pelvic floor muscle training versus no treatment, or inactive control treatments, for urinary incontinence

in women: a short version Cochrane systematic review with meta-analysis. Neurourol Urodyn, **34:** 300, 2015
60. Mercier, J., Morin, M., Zaki, D. et al.: Pelvic floor muscle training as a treatment for genitourinary syndrome of menopause: A single-arm feasibility study. Maturitas, **125:** 57, 2019
61. Mercier, J., Morin, M., Tang, A. et al.: Pelvic floor muscle training: mechanisms of action for the improvement of genitourinary syndrome of menopause. Climacteric, **23:** 468, 2020
62. Mitchell, C. M., Larson, J. C., Crandall, C. J. et al.: Association of Vaginal Estradiol Tablet With Serum Estrogen Levels in Women Who Are Postmenopausal: Secondary Analysis of a Randomized Clinical Trial. JAMA Netw Open, **5:** e2241743, 2022
63. Constantine, G. D., Graham, S., Lapane, K. et al.: Endometrial safety of low-dose vaginal estrogens in menopausal women: a systematic evidence review. Menopause, **26:** 800, 2019
64. Constantine, G. D., Simon, J. A., Pickar, J. H. et al.: The REJOICE trial: a phase 3 randomized, controlled trial evaluating the safety and efficacy of a novel vaginal estradiol soft-gel capsule for symptomatic vulvar and vaginal atrophy. Menopause, **24:** 409, 2017
65. Agrawal, P., Singh, S. M., Able, C. et al.: Safety of Vaginal Estrogen Therapy for Genitourinary Syndrome of Menopause in Women With a History of Breast Cancer. Obstet Gynecol, **142:** 660, 2023
66. McVicker, L., Labeit, A. M., Coupland, C. A. C. et al.: Vaginal Estrogen Therapy Use and Survival in Females With Breast Cancer. JAMA Oncol, **10:** 103, 2024
67. Meaidi, A., Pourhadi, N., Lokkegaard, E. C. et al.: Association of vaginal oestradiol and the rate of breast cancer in Denmark: registry based, case-control study, nested in a nationwide cohort. BMJ Med, **3:** e000753, 2024
68. Bhupathiraju, S. N., Grodstein, F., Stampfer, M. J. et al.: Vaginal estrogen use and chronic disease risk in the Nurses' Health Study. Menopause, **26:** 603, 2018
69. Archer, D. F., Kimble, T. D., Lin, F. D. Y. et al.: A Randomized, Multicenter, Double-Blind, Study to Evaluate the Safety and Efficacy of Estradiol Vaginal Cream 0.003% in Postmenopausal Women with Vaginal Dryness as the Most Bothersome Symptom. J Womens Health (Larchmt), **27:** 231, 2018
70. Bachmann, G., Bouchard, C., Hoppe, D. et al.: Efficacy and safety of low-dose regimens of conjugated estrogens cream administered vaginally. Menopause, **16:** 719, 2009
71. Fernandes, T., Costa-Paiva, L. H., Pinto-Neto, A. M.: Efficacy of vaginally applied estrogen, testosterone, or polyacrylic acid on sexual function in postmenopausal women: a randomized controlled trial. J Sex Med, **11:** 1262, 2014
72. Freedman, M., Kaunitz, A. M., Reape, K. Z. et al.: Twice-weekly synthetic conjugated estrogens vaginal cream for the treatment of vaginal atrophy. Menopause, **16:** 735, 2009
73. Lima, S. M., Yamada, S. S., Reis, B. F. et al.: Effective treatment of vaginal atrophy with isoflavone vaginal gel. Maturitas, **74:** 252, 2013

74. Mitchell, C. M., Reed, S. D., Diem, S. et al.: Efficacy of Vaginal Estradiol or Vaginal Moisturizer vs Placebo for Treating Postmenopausal Vulvovaginal Symptoms: A Randomized Clinical Trial. JAMA Intern Med, **178:** 681, 2018
75. Eriksen, B.: A randomized, open, parallel-group study on the preventive effect of an estradiol-releasing vaginal ring (Estring) on recurrent urinary tract infections in postmenopausal women. Am J Obstet Gynecol, **180:** 1072, 1999
76. Ayton, R. A., Darling, G. M., Murkies, A. L. et al.: A comparative study of safety and efficacy of continuous low dose oestradiol released from a vaginal ring compared with conjugated equine oestrogen vaginal cream in the treatment of postmenopausal urogenital atrophy. Br J Obstet Gynaecol, **103:** 351, 1996
77. Nachtigall, L. E.: Clinical trial of the estradiol vaginal ring in the U.S. Maturitas, **22 Suppl:** S43, 1995
78. Kingsberg, S. A., Derogatis, L., Simon, J. A. et al.: TX-004HR Improves Sexual Function as Measured by the Female Sexual Function Index in Postmenopausal Women With Vulvar and Vaginal Atrophy: The REJOICE Trial. J Sex Med, **13:** 1930, 2016
79. Chaikittisilpa, S., Soimongkol, K., Jaisamrarn, U.: Efficacy of oral estrogen plus testosterone gel to improve sexual function in postmenopausal women. Climacteric, **22:** 460, 2019
80. Davis, S. R., Robinson, P. J., Jane, F. et al.: Intravaginal Testosterone Improves Sexual Satisfaction and Vaginal Symptoms Associated With Aromatase Inhibitors. J Clin Endocrinol Metab, **103:** 4146, 2018
81. Penteado, S. R., Fonseca, A. M., Bagnoli, V. R. et al.: Effects of the addition of methyltestosterone to combined hormone therapy with estrogens and progestogens on sexual energy and on orgasm in postmenopausal women. Climacteric, **11:** 17, 2008
82. Raghunandan, C., Agrawal, S., Dubey, P. et al.: A comparative study of the effects of local estrogen with or without local testosterone on vulvovaginal and sexual dysfunction in postmenopausal women. J Sex Med, **7:** 1284, 2010
83. Tungmunsakulchai, R., Chaikittisilpa, S., Snabboon, T. et al.: Effectiveness of a low dose testosterone undecanoate to improve sexual function in postmenopausal women. BMC Womens Health, **15:** 113, 2015
84. Melisko, M. E., Goldman, M. E., Hwang, J. et al.: Vaginal Testosterone Cream vs Estradiol Vaginal Ring for Vaginal Dryness or Decreased Libido in Women Receiving Aromatase Inhibitors for Early-Stage Breast Cancer: A Randomized Clinical Trial. JAMA Oncol, **3:** 313, 2017
85. McHorney, C. A., Rust, J., Golombok, S. et al.: Profile of Female Sexual Function: a patient-based, international, psychometric instrument for the assessment of hypoactive sexual desire in oophorectomized women. Menopause, **11:** 474, 2004
86. Fianu Jonasson, A., Bixo, M., Sundstrom Poromaa, I. et al.: Safety and Efficacy of an Oxytocin Gel and an Equivalent Gel but Without Hormonal Ingredients (Vagivital((R)) Gel) in Postmenopausal Women with Symptoms of Vulvovaginal Atrophy: A Randomized, Double-Blind Controlled Study. Med Devices (Auckl), **13:** 339, 2020

87. Zohrabi, I., Abedi, P., Ansari, S. et al.: The effect of oxytocin vaginal gel on vaginal atrophy in postmenopausal women: a randomized controlled trial. BMC Womens Health, **20:** 108, 2020
88. Abedi, P., Zohrabi, I., Ansari, S. et al.: The Impact of Oxytocin Vaginal Gel on Sexual Function in Postmenopausal Women: A Randomized Controlled Trial. J Sex Marital Ther, **46:** 377, 2020
89. Archer, D. F., Labrie, F., Bouchard, C. et al.: Treatment of pain at sexual activity (dyspareunia) with intravaginal dehydroepiandrosterone (prasterone). Menopause, **22:** 950, 2015
90. Barton, D. L., Sloan, J. A., Shuster, L. T. et al.: Evaluating the efficacy of vaginal dehydroepiandosterone for vaginal symptoms in postmenopausal cancer survivors: NCCTG N10C1 (Alliance). Support Care Cancer, **26:** 643, 2018
91. Labrie, F., Archer, D., Bouchard, C. et al.: Intravaginal dehydroepiandrosterone (Prasterone), a physiological and highly efficient treatment of vaginal atrophy. Menopause, **16:** 907, 2009
92. Labrie, F., Archer, D. F., Koltun, W. et al.: Efficacy of intravaginal dehydroepiandrosterone (DHEA) on moderate to severe dyspareunia and vaginal dryness, symptoms of vulvovaginal atrophy, and of the genitourinary syndrome of menopause. Menopause, **25:** 1339, 2018
93. Panjari, M., Bell, R. J., Jane, F. et al.: A randomized trial of oral DHEA treatment for sexual function, well-being, and menopausal symptoms in postmenopausal women with low libido. J Sex Med, **6:** 2579, 2009
94. Scheffers, C. S., Armstrong, S., Cantineau, A. E. et al.: Dehydroepiandrosterone for women in the peri- or postmenopausal phase. Cochrane Database Syst Rev, **1:** CD011066, 2015
95. Archer, D. F., Goldstein, S. R., Simon, J. A. et al.: Efficacy and safety of ospemifene in postmenopausal women with moderate-to-severe vaginal dryness: a phase 3, randomized, double-blind, placebo-controlled, multicenter trial. Menopause, **26:** 611, 2019
96. Bachmann, G. A., Komi, J. O., Ospemifene Study, G.: Ospemifene effectively treats vulvovaginal atrophy in postmenopausal women: results from a pivotal phase 3 study. Menopause, **17:** 480, 2010
97. Portman, D., Palacios, S., Nappi, R. E. et al.: Ospemifene, a non-oestrogen selective oestrogen receptor modulator for the treatment of vaginal dryness associated with postmenopausal vulvar and vaginal atrophy: a randomised, placebo-controlled, phase III trial. Maturitas, **78:** 91, 2014
98. Constantine, G., Graham, S., Portman, D. J. et al.: Female sexual function improved with ospemifene in postmenopausal women with vulvar and vaginal atrophy: results of a randomized, placebo-controlled trial. Climacteric, **18:** 226, 2015
99. Portman, D. J., Bachmann, G. A., Simon, J. A. et al.: Ospemifene, a novel selective estrogen receptor modulator for treating dyspareunia associated with postmenopausal vulvar and vaginal atrophy. Menopause, **20:** 623, 2013
100. Goldstein, S. R., Bachmann, G. A., Koninckx, P. R. et al.: Ospemifene 12-month safety and efficacy in postmenopausal women with vulvar and vaginal atrophy. Climacteric, **17:** 173, 2014

101. Simon, J. A., Lin, V. H., Radovich, C. et al.: One-year long-term safety extension study of ospemifene for the treatment of vulvar and vaginal atrophy in postmenopausal women with a uterus. Menopause, **20:** 418, 2013
102. Cameron, A. P., Chung, D. E., Dielubanza, E. J. et al.: The AUA/SUFU Guideline on the Diagnosis and Treatment of Idiopathic Overactive Bladder. J Urol, **212:** 11, 2024
103. Nelken, R. S., Ozel, B. Z., Leegant, A. R. et al.: Randomized trial of estradiol vaginal ring versus oral oxybutynin for the treatment of overactive bladder. Menopause, **18:** 962, 2011
104. Tseng, L. H., Wang, A. C., Chang, Y. L. et al.: Randomized comparison of tolterodine with vaginal estrogen cream versus tolterodine alone for the treatment of postmenopausal women with overactive bladder syndrome. Neurourol Urodyn, **28:** 47, 2009
105. Anger, J., Lee, U., Ackerman, A. L. et al.: Recurrent Uncomplicated Urinary Tract Infections in Women: AUA/CUA/SUFU Guideline. J Urol, **202:** 282, 2019
106. Lethaby, A., Ayeleke, R. O., Roberts, H.: Local oestrogen for vaginal atrophy in postmenopausal women. Cochrane Database Syst Rev, **2016:** CD001500, 2016
107. Nappi, R. E., Davis, S. R.: The use of hormone therapy for the maintenance of urogynecological and sexual health post WHI. Climacteric, **15:** 267, 2012
108. Rahn, D. D., Carberry, C., Sanses, T. V. et al.: Vaginal estrogen for genitourinary syndrome of menopause: a systematic review. Obstet Gynecol, **124:** 1147, 2014
109. The 2022 Hormone Therapy Position Statement of The North American Menopause Society Advisory Panel: The 2022 hormone therapy position statement of The North American Menopause Society. Menopause, **29:** 767, 2022
110. Raz, R., Stamm, W. E.: A controlled trial of intravaginal estriol in postmenopausal women with recurrent urinary tract infections. N Engl J Med, **329:** 753, 1993
111. Ferrante, K. L., Wasenda, E. J., Jung, C. E. et al.: Vaginal Estrogen for the Prevention of Recurrent Urinary Tract Infection in Postmenopausal Women: A Randomized Clinical Trial. Female Pelvic Med Reconstr Surg, **27:** 112, 2021
112. Tan-Kim, J., Shah, N. M., Do, D. et al.: Efficacy of vaginal estrogen for recurrent urinary tract infection prevention in hypoestrogenic women. Am J Obstet Gynecol, **229:** 143 e1, 2023
113. Organization, W. H.: WHO/United Nations Population Fund (UNFPA) specifications for plain lubricants. . WHO Drug Information, **33:** 562, 2019
114. Lee, Y. K., Chung, H. H., Kim, J. W. et al.: Vaginal pH-balanced gel for the control of atrophic vaginitis among breast cancer survivors: a randomized controlled trial. Obstet Gynecol, **117:** 922, 2011
115. Nappi, R. E., Kotek, M., Brestansky, A. et al.: Treatment of vulvo-vaginal atrophy with hyaluronate-based gel: a randomized controlled study. Minerva Obstet Gynecol, **74:** 480, 2022
116. Piersen, C. E.: Phytoestrogens in botanical dietary supplements: implications for cancer. Integr Cancer Ther, **2:** 120, 2003
117. Carmignani, L. O., Pedro, A. O., Montemor, E. B. et al.: Effects of a soy-based dietary supplement compared with low-dose hormone therapy on the urogenital

system: a randomized, double-blind, controlled clinical trial. Menopause, **22:** 741, 2015
118. Kim, H. I., Kim, M. K., Lee, I. et al.: Efficacy and Safety of a Standardized Soy and Hop Extract on Menopausal Symptoms: A 12-Week, Multicenter, Randomized, Double-Blind, Placebo-Controlled Clinical Trial. J Altern Complement Med, **27:** 959, 2021
119. Lima, S. M., Bernardo, B. F., Yamada, S. S. et al.: Effects of Glycine max (L.) Merr. soy isoflavone vaginal gel on epithelium morphology and estrogen receptor expression in postmenopausal women: a 12-week, randomized, double-blind, placebo-controlled trial. Maturitas, **78:** 205, 2014
120. Ribeiro, A. E., Monteiro, N. E. S., Moraes, A. V. G. et al.: Can the use of probiotics in association with isoflavone improve the symptoms of genitourinary syndrome of menopause? Results from a randomized controlled trial. Menopause, **26:** 643, 2018
121. Azari, N., Mehrabi, E., Javadzadeh, Y. et al.: Comparison of the effect of vaginal vitamin E cream with conjugated estrogen vaginal cream on vulvovaginal atrophy and overactive bladder syndrome: a randomized controlled trial. African Journal of Urology, **29:** 35, 2023
122. Golmakani, N., Parnan Emamverdikhan, A., Zarifian, A. et al.: Vitamin E as alternative local treatment in genitourinary syndrome of menopause: a randomized controlled trial. Int Urogynecol J, **30:** 831, 2019
123. Keshavarzi, Z., Janghorban, R., Alipour, S. et al.: The effect of vitamin D and E vaginal suppositories on tamoxifen-induced vaginal atrophy in women with breast cancer. Support Care Cancer, **27:** 1325, 2019
124. Radnia, N., Hosseini, S. T., Vafaei, S. Y. et al.: The effect of conjugated estrogens vaginal cream and a combined vaginal cream of vitamins D and E in the treatment of genitourinary syndrome. J Family Med Prim Care, **12:** 507, 2023
125. Arjmand, M., Abbasi, H., Behforouz, A.: The effect of vitamin D on urgent urinary incontinence in postmenopausal women. Int Urogynecol J, **34:** 1955, 2023
126. Kamronrithisorn, T., Manonai, J., Vallibhakara, S. A. et al.: Effect of Vitamin D Supplement on Vulvovaginal Atrophy of the Menopause. Nutrients, **12**, 2020
127. Markland, A., Tangpricha, V., Mark Beasley, T. et al.: Comparing Vitamin D Supplementation Versus Placebo for Urgency Urinary Incontinence: A Pilot Study. J Am Geriatr Soc, **67:** 570, 2019
128. Mazalzadeh, F., Hekmat, K., Namjouyan, F. et al.: Effect of Trigonella foenum (fenugreek) vaginal cream on vaginal atrophy in postmenopausal women. J Family Med Prim Care, **9:** 2714, 2020
129. Safary, M., Hakimi, S., Mobaraki-Asl, N. et al.: Comparison of the Effects of Fenugreek Vaginal Cream and Ultra Low- Dose Estrogen on Atrophic Vaginitis. Curr Drug Deliv, **17:** 815, 2020
130. Hidalgo, L. A., Chedraui, P. A., Morocho, N. et al.: The effect of red clover isoflavones on menopausal symptoms, lipids and vaginal cytology in menopausal women: A randomized, double-blind, placebo-controlled study. Gynecological Endocrinology, **21:** 257, 2005
131. Khayatan, J., Iravani, M., Moghimipour, E. et al.: The effect of red clover vaginal cream on sexual function in postmenopausal women: a randomized,

controlled clinical trial. Iranian Journal of Obstetrics, Gynecology and Infertility, **22:** Pe26, 2019
132. Ahmadizad, P., Shohani, M., Direkvand Moghadam, A. et al.: Comparison of the effect of licorice vaginal cream and estrogen vaginal cream on sexual function of postmenopausal women: An RCT. Int J Reprod Biomed, **20:** 963, 2022
133. Sadeghi, M., Namjouyan, F., Cheraghian, B. et al.: Impact of Glycyrrhiza glabra (licorice) vaginal cream on vaginal signs and symptoms of vaginal atrophy in postmenopausal women: A randomized double blind controlled trial. J Tradit Complement Med, **10:** 110, 2020
134. Vahedpoorfard, Z., Ferdosi, S., Rahimi, H. et al.: Effect of Humulus lupulus L. (Hop) on Postmenopausal Sexual Dysfunction: A Randomized Clinical Trial. Int J Clin Pract, **2023:** 9528335, 2023
135. Suwanvesh, N., Manonai, J., Sophonsritsuk, A. et al.: Comparison of Pueraria mirifica gel and conjugated equine estrogen cream effects on vaginal health in postmenopausal women. Menopause, **24:** 210, 2017
136. Abedi, P., Najafian, M., Yaralizadeh, M. et al.: Effect of fennel vaginal cream on sexual function in postmenopausal women: A double blind randomized controlled trial. J Med Life, **11:** 24, 2018
137. Bosak, Z., Iravani, M., Moghimipour, E. et al.: Effect of Chamomile Vaginal Gel on the Sexual Function in Postmenopausal Women: A Double-Blind Randomized Controlled Trial. J Sex Med, **19:** 983, 2022
138. Bosak, Z., Iravani, M., Moghimipour, E. et al.: Evaluation of the influence of chamomile vaginal gel on dyspareunia and sexual satisfaction in postmenopausal women: A randomized, double-blind, controlled clinical trial. Avicenna J Phytomed, **10:** 481, 2020
139. Karimi, F., Babazadeh, R., Zojaji, A. et al.: Squill oil for decreasing dyspareunia and increasing sexual satisfaction in menopausal women: A triple-blind randomized controlled trial. Avicenna J Phytomed, **11:** 464, 2021
140. Karimi, F. Z., Nazari, N., Rakhshandeh, H. et al.: The effect of nettle vaginal cream on subjective symptoms of vaginal atrophy in postmenopausal women. Eur J Obstet Gynecol Reprod Biol, **285:** 41, 2023
141. Larmo, P. S., Yang, B., Hyssala, J. et al.: Effects of sea buckthorn oil intake on vaginal atrophy in postmenopausal women: a randomized, double-blind, placebo-controlled study. Maturitas, **79:** 316, 2014
142. Le Donne, M., Caruso, C., Mancuso, A. et al.: The effect of vaginally administered genistein in comparison with hyaluronic acid on atrophic epithelium in postmenopause. Arch Gynecol Obstet, **283:** 1319, 2011
143. Manonai, J., Chittacharoen, A., Theppisai, U. et al.: Effect of Pueraria mirifica on vaginal health. Menopause, **14:** 919, 2007
144. Postigo, S., Lima, S. M., Yamada, S. S. et al.: Assessment of the Effects of Tribulus Terrestris on Sexual Function of Menopausal Women. Rev Bras Ginecol Obstet, **38:** 140, 2016
145. Sritonchai, C., Manonai, J., Sophonsritsuk, A. et al.: Comparison of the effects of Pueraria mirifica gel and of placebo gel on the vaginal microenvironment of postmenopausal women with Genitourinary Syndrome of Menopause (GSM). Maturitas, **140:** 49, 2020

146. Vale, F. B. C., Boroni, J. D., Geber, G. et al.: Effect of Tribulus Terrestris in the Treatment of Female Sexual Dysfunction and Clitoral Vascularization. Results of a Randomized Study Comparing Two Different Dosage Regimes. J Sex Marital Ther, **47:** 696, 2021
147. Warinsiriruk, P., Tantitham, C., Cherdshewasart, W. et al.: Effects of Pueraria mirifica on vaginal artery vascularization in postmenopausal women with genitourinary syndrome of menopause. Maturitas, **160:** 4, 2022
148. Yaralizadeh, M., Abedi, P., Najar, S. et al.: Effect of Foeniculum vulgare (fennel) vaginal cream on vaginal atrophy in postmenopausal women: A double-blind randomized placebo-controlled trial. Maturitas, **84:** 75, 2016
149. Margesson, L. J.: Contact dermatitis of the vulva. Dermatologic Therapy, **17:** 20, 2004
150. FDA Commissioner Scott Gottlieb, M. D.: Statement from FDA Commissioner Scott Gottlieb, M.D., on efforts to safeguard women's health from deceptive health claims and significant risks related to devices marketed for use in medical procedures for "vaginal rejuvenation", July 30, 2018
151. Eftekhar, T., Forooghifar, T., Khalili, T. et al.: The Effect of the CO(2) Fractional Laser or Premarin Vaginal Cream on Improving Sexual Function in Menopausal Women: A Randomized Controlled Trial. J Lasers Med Sci, **11:** 292, 2020
152. Li, F. G., Maheux-Lacroix, S., Deans, R. et al.: Effect of Fractional Carbon Dioxide Laser vs Sham Treatment on Symptom Severity in Women With Postmenopausal Vaginal Symptoms: A Randomized Clinical Trial. Jama, **326:** 1381, 2021
153. Page, A. S., Verbakel, J. Y., Verhaeghe, J. et al.: Laser versus sham for genitourinary syndrome of menopause: A randomised controlled trial. Bjog, **130:** 312, 2023
154. Paraiso, M. F. R., Ferrando, C. A., Sokol, E. R. et al.: A randomized clinical trial comparing vaginal laser therapy to vaginal estrogen therapy in women with genitourinary syndrome of menopause: The VeLVET Trial. Menopause, **27:** 50, 2020
155. Ruanphoo, P., Bunyavejchevin, S.: Treatment for vaginal atrophy using microablative fractional CO2 laser: a randomized double-blinded sham-controlled trial. Menopause, **27:** 858, 2020
156. Salvatore, S., Pitsouni, E., Grigoriadis, T. et al.: CO(2) laser and the genitourinary syndrome of menopause: a randomized sham-controlled trial. Climacteric, **24:** 187, 2021
157. Alvisi, S., Lami, A., Baldassarre, M. et al.: Short-Term Efficacy and Safety of Non-Ablative Laser Treatment Alone or with Estriol or Moisturizers in Postmenopausal Women with Vulvovaginal Atrophy. J Sex Med, **19:** 761, 2022
158. Eftekhar, T., Ghorbani, L., Ghanbari, Z. et al.: Comparison of the Effect of Radiofrequency and Laser Treatment on Mixed Urinary Incontinence and Vulvovaginal Atrophy in Iranian Menopausal Women: A Randomized Controlled Trial. International Journal of Women's Health and Reproduction Sciences, **9:** 061, 2019

159. Chiengthong, K., Bunyavejchevin, S.: Efficacy of Erbium YAG laser treatment in overactive bladder syndrome: a randomized controlled trial. Menopause, **30:** 414, 2023
160. Stephenson, J.: FDA Orders Estrogen Safety Warnings: Agency Offers Guidance for HRT Use. JAMA, **289:** 537, 2003
161. Crandall, C. J., Hovey, K. M., Andrews, C. A. et al.: Breast cancer, endometrial cancer, and cardiovascular events in participants who used vaginal estrogen in the Women's Health Initiative Observational Study. Menopause, **25:** 11, 2018
162. Cold, S., Cold, F., Jensen, M. B. et al.: Systemic or Vaginal Hormone Therapy After Early Breast Cancer: A Danish Observational Cohort Study. J Natl Cancer Inst, **114:** 1347, 2022
163. Hussain, I., Talaulikar, V. S.: A systematic review of randomised clinical trials - The safety of vaginal hormones and selective estrogen receptor modulators for the treatment of genitourinary menopausal symptoms in breast cancer survivors. Post Reprod Health, **29:** 222, 2023
164. Howlader, N., Noone, A., Krapcho, M. et al.: SEER Cancer Statistics Review, 1975-2017, National Cancer Institute. Bethesda, MD,. https://seer.cancer.gov/csr/1975_2017/ based on November 2019 SEER data submission, posted to the SEER web site, April 2020.
165. Le Ray, I., Dell'Aniello, S., Bonnetain, F. et al.: Local estrogen therapy and risk of breast cancer recurrence among hormone-treated patients: a nested case-control study. Breast Cancer Res Treat, **135:** 603, 2012
166. Crandall, C. J., Diamant, A., Santoro, N.: Safety of vaginal estrogens: a systematic review. Menopause, **27:** 339, 2020
167. Crean-Tate, K. K., Faubion, S. S., Pederson, H. J. et al.: Management of genitourinary syndrome of menopause in female cancer patients: a focus on vaginal hormonal therapy. Am J Obstet Gynecol, **222:** 103, 2020
168. Santen, R. J.: Vaginal administration of estradiol: effects of dose, preparation and timing on plasma estradiol levels. Climacteric, **18:** 121, 2015
169. Gupta, P., Sturdee, D. W., Palin, S. L. et al.: Menopausal symptoms in women treated for breast cancer: the prevalence and severity of symptoms and their perceived effects on quality of life. Climacteric, **9:** 49, 2006
170. Falk, S. J., Bober, S.: Vaginal Health During Breast Cancer Treatment. Curr Oncol Rep, **18:** 32, 2016
171. Robison, K., Kulkarni, A., Dizon, D. S.: Sexual Health in Women Affected by Gynecologic or Breast Cancer. Obstet Gynecol, **143:** 499, 2024
172. Kingsberg, S. A., Larkin, L., Krychman, M. et al.: WISDOM survey: attitudes and behaviors of physicians toward vulvar and vaginal atrophy (VVA) treatment in women including those with breast cancer history. Menopause, **26:** 124, 2019
173. Treatment of Urogenital Symptoms in Individuals With a History of Estrogen-dependent Breast Cancer: Clinical Consensus. Obstet Gynecol, **138:** 950, 2021
174. Beste, M. E., Kaunitz, A. M., McKinney, J. A. et al.: Vaginal estrogen use in breast cancer survivors: a systematic review and meta-analysis of recurrence and mortality risks. Am J Obstet Gynecol, **232:** 262, 2025

175. Simon, J. A., Goldstein, I., Kim, N. N. et al.: The role of androgens in the treatment of genitourinary syndrome of menopause (GSM): International Society for the Study of Women's Sexual Health (ISSWSH) expert consensus panel review. Menopause, **25:** 837, 2018
176. Labrie, F., Derogatis, L., Archer, D. F. et al.: Effect of Intravaginal Prasterone on Sexual Dysfunction in Postmenopausal Women with Vulvovaginal Atrophy. J Sex Med, **12:** 2401, 2015
177. Barton, D. L., Shuster, L. T., Dockter, T. et al.: Systemic and local effects of vaginal dehydroepiandrosterone (DHEA): NCCTG N10C1 (Alliance). Support Care Cancer, **26:** 1335, 2018
178. Tanmahasamut, P., Jirasawas, T., Laiwejpithaya, S. et al.: Effect of estradiol vaginal gel on vaginal atrophy in postmenopausal women: A randomized double-blind controlled trial. J Obstet Gynaecol Res, **46:** 1425, 2020
179. Goetsch, M. F., Garg, B., Lillemon, J. et al.: Treating where it hurts-a randomized comparative trial of vestibule estradiol for postmenopausal dyspareunia. Menopause, **30:** 467, 2023
180. Pinkerton, J. V., Kaunitz, A. M., Manson, J. E.: Vaginal estrogen in the treatment of genitourinary syndrome of menopause and risk of endometrial cancer: an assessment of recent studies provides reassurance. Menopause, **24:** 1329, 2017
181. ACOG Practice Bulletin No. 141: management of menopausal symptoms. Obstet Gynecol, **123:** 202, 2014
182. Stair, S., Chyu, J., Rangwala, S. et al.: PD24-12 BARRIERS TO PERI- AND POST-MENOPAUSAL WOMEN USING VAGINAL ESTROGEN THERAPY INCLUDE COST AND FEAR OF SIDE EFFECTS. Journal of Urology, **211**, 2024
183. Stair, S. L., Palmer, C. J., Lee, U. J.: Wealth of Knowledge and Passion: Patient Perspectives on Vaginal Estrogen as Expressed on Reddit. Urology, **182:** 79, 2023
184. Stair, S. L., Chyu, J., Rangwala, S. et al.: Experiences With Genitourinary Syndrome of Menopause and Barriers to Vaginal Estrogen Usage Reported by a National Sample of 1500 Women. Urology, **196:** 115, 2025

Abbreviations

AEs	Adverse effects
AHRQ	Agency for Healthcare Research and Quality
AI	Aromatase inhibitors
AUA	American Urological Association
AUGS	American Urogynecologic Society
BOD	Board of Directors
CE	Conjugated estrogen
CO_2	Carbon dioxide
COE	Certainty of evidence
COMMA	Core Outcomes in Menopause
DHEA	Dehydroepiandrosterone
DIVA	Day-to-Day Impact of Vaginal Aging
EPC	Evidence-based practice center

Er:YAG	Erbium-doped yttrium aluminum garnet
FDA	U.S. Food and Drug Administration
FSFI	Female sexual function index
GSM	Genitourinary syndrome of menopause
GRADE	The Grading of Recommendations Assessment, Development, and Evaluation
IIQ-7	Incontinence Impact Questionnaire
IP-SDM	Interprofessional shared decision-making
KQ	Key Question
MBS	Most bothersome symptom
OAB	Overactive bladder
PCORI	Patient Centered Outcomes Research Institute
PGC	Practice Guidelines Committee
PFMT	Pelvic floor muscle training
PMB	Post menopausal bleeding
QoL	Quality of life
RCT	Randomized controlled trial
RoB	Risk of bias
rUTI	Recurrent UTI
SERMS	Selective estrogen receptor modulators
SDM	Shared decision making
SQC	Science and Quality Council
SUFU	Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction
UDI-6	Urogenital Distress Inventory
UTI	Urinary tract infection
VAS	Vaginal assessment scale
VMI	Vaginal Maturation Index
VSQ	Vulvovaginal Symptom Questionnaire

APPENDIX A

Key Questions

KQ1. What are the effectiveness and harms of screening strategies to identify genitourinary syndrome of menopause (GSM) in postmenopausal women? Does screening impact patient reported symptoms or improve quality of life (QoL)?

KQ2. What are the effectiveness and comparative effectiveness of hormonal, non-hormonal, and energy-based interventions when used alone or in combination for treatment of GSM symptoms? Which treatments show improvement for which symptoms?

KQ3. What are the harms (and comparative harms) of hormonal, non- hormonal, and energy-based interventions for GSM symptoms?

KQ4. What is the appropriate follow-up interval to assess improvement, sustained improvement, or regression of symptoms of GSM in women treated with hormonal, non-hormonal, and energy-based interventions?

KQ5. What are the effectiveness, comparative effectiveness, and harms of endometrial surveillance among women who have a uterus and are using hormonal therapy for GSM?