

Over-Active Bladder therapy

Common treatments for an Over-Active Bladder include anticholinergics and β 3-adrenergic receptor agonists. However, many of these can lead to side effects such as dry mouth, constipation and cognitive impairment, which makes the search for safer alternatives desirable. Vibegron, a new β 3-adrenergic receptor agonist, offers a promising solution and has been approved for use in a number of countries.

The efficacy and safety of vibegron has been evaluated through clinical trials using a once-daily 75 mg dose and assessing micturition frequency, urge urinary incontinence, urgency episodes, and volumes voided over a 12-week period ([Frankel et al Therap Clin Risk Manage 2022;18:171-82.](#)) It was found to improve symptoms and positively impact on daily living and well-being. Given that it is safe, well-tolerated, and does not affect blood pressure or heart rate, it is a potentially valuable treatment option for better managing OAB symptoms.

A randomised clinical trial has explored the efficacy of a **multicomponent** intervention, including cognitive concepts, in improving health-related quality of life for women with moderate to severe overactive bladder symptoms ([Funada et al JAMA Netw Open 2024;7:e241784.](#))

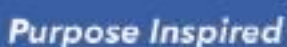
Conducted in Japan, the trial involved 80 women who were assigned to either the intervention group, receiving four 30-minute weekly sessions, or a control group on a waiting list. Both groups continued their baseline treatments during the study period.

Results showed a significant improvement in quality-of-life scores in the active involvement group compared to the controls. Additionally, the intervention group showed superiority in reducing the frequency of micturition and urgency, so the study authors concluded that the multicomponent intervention effectively improved the clinical situation for women with moderate to severe OAB, supporting its use as a treatment option that incorporates cognitive behavioural therapy.

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Recurrent UTIs

Antibiotic and alternate forms of treatment are used in attempts to prevent repeated urinary tract infections and one such strategy involves taking D-mannose, a monosaccharide, which is thought to work by inhibiting bacterial adherence to uroepithelial cells. To test its efficacy, a trial was conducted involving 600 women assigned to receive either 2 grams of D-mannose or placebo for 6 months. The primary outcome was the incidence of clinically recurrent UTIs ([Hayward et al JAMA Intern Med 2024 doi 10.1001/jamainternmed.2024.0264](#)). The mannose therapy was no better than the placebo with the researchers concluding that D-mannose should not be recommended for preventing future episodes of UTIs in primary care settings.

A more promising, but not as widely utilised form of treatment is the use of whole-cell inactivated bacteria ([Lorenzo-Gómez et al NEJM Evid 2022 doi 10.1056/EVIDoa2100018](#)). This vaccine-like approach over a 9-month period, showed a significant reduction in UTI recurrence without clinically-limiting adverse effects. Larger trials are anticipated but announcements by the manufacturers have been enthusiastic ([Baudon Medscape 2024](#) & [Scott Medscape 2024](#)).

Novel treatment for G-US of Menopause

Although topical estrogens are the medication most recommended for the treatment of the Genito-Urinary Syndrome of Menopause, there may be those who would prefer an oral preparation for aesthetic or other reasons. Full Menopausal Hormonal Therapy does improve vaginal symptoms in peri- and postmenopausal women but lasofoxifene is a nonsteroidal selective estrogen receptor modulator that has been researched as an alternative medication.

Two trials of nearly 1,000 participants with a mean age of 60 years specifically studied lasofoxifene for the relief of bothersome symptoms and looked at objective changes to vaginal pH and local cell morphology over 12 weeks in placebo-controlled research ([Kagan et al Menopause 2024;31:494-504](#)). The women who took lasofoxifene showed notable improvements compared to those on the placebo. They experienced less severe symptoms, had better vaginal pH levels, and healthier vaginal cell patterns. Some benefits were noticeable as soon as two weeks into the treatment.

While some women reported mild to moderate side effects, such as hot flashes, these were generally manageable and there were very few serious side effects. Overall, lasofoxifene significantly helped with vaginal symptoms and was generally safe to use.

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Editorial comment. The Genito-urinary Syndrome of Menopause is probably the most under-rated symptom complex of the peri- post-menopause. It is sometimes "tolerated as part of the transition" and its role in dyspareunia, together with reduced libido may make it a relegated or avoided topic for discussion. Given the distress it may cause and the range of effective responses available - it should be on the list of direct enquiries in a routine consultation.

Topical estrogen therapy safety

The Genito-urinary Syndrome of Menopause (GSM) treatment with topical estrogens has been the topic of publications in two circumstances in recent months.

Breast cancer survivors

The question of its use in breast cancer survivors is important as anti-estrogen oncology therapy may exacerbate symptoms to the point of precluding satisfactory sexual relations. Research into this specific topic comes from France where a large group of participants provided the following data: ([Brooks Medscape 2024](#))

- Patients included in the study had a median age of 54 years; 85% were HR-positive, and 15% were HR-negative. The researchers conducted subgroup analyses based on HR status and endocrine therapy regimen.
- More than 1700 started vaginal estrogen therapy – 56%, promestriene; 34%, estriol; and 10% used both.
- Initiation of vaginal estrogen therapy led to a modest decrease in disease-free survival in patients with HR-positive tumors (–2.1 percentage points at 5 years), particularly in those concurrently treated with an aromatase inhibitor (–3.0 percentage points).
- No decrease in disease-free survival was observed in patients with HR-negative tumors or in those treated with tamoxifen.
- In aromatase inhibitor users, starting estriol led to a "more severe and premature" decrease in disease-free survival (–4.2 percentage point after 3 years) compared with initiating promestriene (1.0 percentage point difference at 3 years).

United States FDA warnings

The FDA has insisted that the "Black Box" warnings that appear on products containing low-dose estrogens, should remain in place. This includes topical



estrogens and is not consistent with rulings from other country's legislative bodies where over-the-counter purchases are actively being pursued.

Evidence from distinguished sources will hopefully persuade a change of heart so that users are not intimidated by package inserts as required at present ([Manson et al JAMA 2024;331:1748-60](#)).

MHT and blood pressure

The effect of Menopausal Hormonal Therapy on blood pressure and the incidence of hypertension in postmenopausal women has been evaluated in a systematic review and meta-analysis ([Ferreira Campos et al Menopause 2024;31:556-62](#)). The review included randomised clinical trials and prospective observational studies, focusing on systolic blood pressure (SBP), diastolic blood pressure (DBP), and hypertension incidence. It encompassed 80,000 women, of whom 30,000 used MHT. They found that oral conjugated equine estrogens plus progestogen increased SBP, however, no significant effects on SBP were observed with the use of oral or transdermal estradiol plus progestogen, estradiol alone, or tibolone. Additionally, no significant effect on DBP was noted for any MHT formulation. The analysis also revealed that women using oral estrogen plus progestogen had a higher risk of developing hypertension compared to those who never used MHT.

The study concluded that the impact of MHT on blood pressure is formulation-dependent, with combined conjugated equine estrogens plus progestogen increasing SBP and hypertension risk. In contrast, estradiol-based therapies and tibolone did not show significant effects on blood pressure or hypertension risk. This highlights the importance of considering the specific type of estrogen in MHT formulations when assessing cardiovascular risk in postmenopausal women.

Editorial comment. One wonders if blood pressure and other cardiovascular effects of MHT might look different if the WHI trial data were excluded. For scientific integrity the findings have to be included, but oral conjugated equine estrogens plus progestogens are obsolete therapy and late post-menopausal initiation of any MHT, is not accepted practice.

Detailed results from the data collected above suggest a lowering of SBP when the WHI results are left out, so one hopes that future analyses will reflect real-world MHT use. The final word in the association of MHT and cardiovascular health is a long way from being decided.



Menopause symptoms and race

Two articles have appeared in *Menopause* recently concerning the impact of race, ethnicity, and socioeconomic status on menopause symptom severity.

The first study used an online telehealth platform to collect data that included a modified Menopause Rating Scale and demographic information ([Kochersberger et al Menopause 2024;31:478-83](#)). The researchers employed a model to evaluate symptom severity, adjusting for factors such as age, body mass index, smoking, bilateral oophorectomy status, and socio-economic status (SES).

The study comprised nearly 70,000 participants and found that women identifying as Black, Hispanic, Indigenous/First Nations, Middle Eastern, and those with two or more races/ethnicities reported higher levels of symptom severity compared to their White counterparts. Specifically, Black women had higher odds of experiencing hot flashes, Hispanic women reported more skin/hair changes, Indigenous women had increased painful sex, and Middle Eastern women experienced more weight changes. Asian and South Asian participants reported lower symptom severity.

Even after accounting for SES, the racial and ethnic disparities in symptom severity persisted, indicating that these differences are not solely due to socioeconomic factors. The findings highlight the independent role of race and ethnicity in menopause symptom severity and underscore the importance of addressing social, cultural, and economic factors to reduce disparities.

The second study is entitled “Does everyday discrimination account for the increased risk of vasomotor symptoms in Black women?” and draws its information from the *Study of Women's Health Across the Nation (SWAN)* data base. See information below.

The researchers explored the link between discrimination and vasomotor symptoms (VMS) in a cohort of more than 2,000 women from diverse racial and ethnic backgrounds. The analysis examined both concurrent and chronic associations between discrimination and VMS, adjusting for known risk factors. Results indicated that higher levels of discrimination were significantly associated with any VMS, and frequent VMS. Specifically, discrimination increased the odds of reporting any VMS and of having a continuously high VMS trajectory over time. However, after adjusting for discrimination, Black women still had a higher likelihood of reporting VMS compared to White women, suggesting that discrimination contributes to, but does not fully explain the elevated VMS risk in Black women.



The study concludes that discrimination is a significant factor in the experience of VMS, particularly in Black women. Addressing discrimination and its health impacts is crucial for reducing disparities in menopause symptoms and improving the quality of life in women experiencing the menopause transition.

These outcomes support the information coming from the 2023 meeting of the *Menopause Society* where a series of papers described racial disparities in MHT prescribing ([Haelle Medscape 2023](#)).

SWAN: Study of Women's Health Across the Nation

The Study of Women's Health Across the Nation (SWAN) is an American initiative begun in 1994 and is a pioneering longitudinal, multi-site study into the menopause transition and women's health.

It has followed more than 3,000 midlife women since its conception and has accumulated a wealth of findings about the development of medical interventions, plus educational programmes for women in their midlife and older, including information about cardiovascular disease, menopausal symptoms, mental health and cognitive function.

The [NIA Biobank](#), is the biologic specimen bank for SWAN and contains blood and urine specimens collected at each study participant's annual visit. As such it will continue to be a source of data far into the future.

Ovarian cancer screening

The *UK Collaborative Trial of Ovarian Cancer Screening* published some years ago, looked at the use of Cancer Antigen 125 and transvaginal ultrasound in the detection of ovarian cancer ([Menon et al Lancet 2021;397:2182-93](#)). This method did not result in an increase in stage 1 and 2 detections and may have been responsible for an increase in invasive investigations, so its use for routine population screening was not recommended.

The advent of cell-free DNA fragments in blood specimens (liquid biopsies) has raised expectations to revitalise malignancy detection in a range of tissues. A presentation at the American Association for Cancer Research meeting contained encouraging data about screening for early ovarian cancer ([Medina et al AACR Conf 2024](#)). Using machine learning, the researchers combined cfDNA results with 2 known protein biomarkers (CA125) and Human Epididymis protein (HE4) to create an algorithm for detecting ovarian cancer with a specificity of 99% plus sensitivities of



70%, 75%, 85% and 100% for stages I to IV respectively. This technique is known as combining “fragmentomic and proteomic features” and although it has only been tested on select groups, the claim is that it will potentially provide “a new paradigm for population-wide ovarian cancer screening and clinical diagnostic utility.”

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