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Oral or Transdermal Hormone Therapy? The Mental Health Risks Are Not the Same

New study suggests that, while both routes of administration are beneficial, transdermal hormone therapy may be preferred for patients with existing mental health concerns

CLEVELAND, Ohio (Oct 21, 2025)—Hormone therapy—oral and transdermal—remains the most effective treatment for such bothersome menopause symptoms as hot flashes and is generally considered safe for most patients. A new study shows that risk profiles are different based on how the hormones are administered. Results of the study will be presented at the 2025 Annual Meeting of The Menopause Society in Orlando October 21-25.

When it comes to hormone therapy, there is not a consistently preferred route of administration. The best option depends on individual health factors and goals. Oral hormone therapy is metabolized differently because it passes through the liver, impacting lipid profiles. Transdermal hormone therapy bypasses the liver to exert a different risk profile. These physiological differences may translate into variable risks for cardiometabolic, neuropsychiatric, and neurodegenerative conditions in postmenopausal women.

A new study involving more than 3,800 postmenopausal women sought to compare the incidence of obesity, cardiovascular disease, anxiety, depression, and Alzheimer's disease among postmenopausal women receiving oral versus transdermal hormone therapy.

What the researchers found was that transdermal hormone therapy was associated with a lower incidence of anxiety and depression when compared to oral hormone therapy. No significant differences were observed between the two routes of administration in the risk of obesity, cardiovascular disease, or Alzheimer's disease.

More detailed results will be discussed at the 2025 Annual Meeting of The Menopause Society as part of the poster presentation titled "Oral vs Transdermal Hormone Therapy in Postmenopausal Women: A Comparison of Obesity, Cardiovascular, Mental Health, and Alzheimer's Disease Risks."

"It was exciting to find statistically significant results in our study, as these findings may help shape more individualized approaches to patient care in the future," says Liying Wei, lead author from Drexel University College of Medicine.

"As we designed this study, we specifically excluded women with established cardiovascular disease (CVD) risk factors such as diabetes, obesity, hyperlipidemia, hypertension, tobacco use, family history of heart disease, and premature menopause to create a CVD risk—free population at baseline. This approach allowed us to more clearly examine the differences between oral and transdermal hormone therapy in relation to CVD outcomes. While our findings suggest that transdermal estrogen may offer potential mental health advantages compared with oral formulations, these results should not be generalized to the broader postmenopausal population. Hormone therapy is not a one-size-fits-all treatment, and the choice

of route of administration should be individualized and made through shared decision-making, particularly for women with a history of depression," says Dr. Xuezhi (Daniel) Jiang, Professor of Obstetrics and Gynecology at Drexel University College of Medicine and Reading Hospital at Tower Health.

While further studies are needed to confirm these associations, the findings suggest potential mental health advantages of transdermal hormone therapy and underscore the importance of considering the route of administration when prescribing menopausal hormone therapy, especially for women with existing or potential mental health concerns.

"It's important to recognize the need for individualized approaches when it comes to treating menopause symptoms, says Dr. Stephanie Faubion, medical director for The Menopause Society. "Fortunately, we have many choices for women when it comes to route of administration, dose, and formulation of hormone therapy, which makes it easier to personalize treatment."

Liying Wei, Drs. Jiang and Faubion are available for interviews prior to the Annual Meeting.

For more information about menopause and healthy aging, visit menopause.org.

The Menopause Society is dedicated to empowering healthcare professionals and providing them with the tools and resources to improve the health of women during the menopause transition and beyond. As the leading authority on menopause since 1989, the nonprofit, multidisciplinary organization serves as the independent, evidence-based resource for healthcare professionals, researchers, the media, and the public and leads the conversation about improving women's health and healthcare experiences. To learn more, visit menopause.org.