

# I treat menopause and its symptoms, and hormone replacement therapy can help – here's the science behind the FDA's decision to remove warnings

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Published: November 18, 2025 8:14am EDT



Reanalyses of earlier research have shown that hormone therapy is safe and effective for many women going through menopause.

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For more than 20 years, hormone therapy for menopause has carried a warning label from the Food and Drug Administration describing the medication's risk of serious harms – namely, cancer, cardiovascular disease and possibly dementia.

On Nov. 10, 2025, the FDA announced that drugmakers should remove these “black box” safety warnings.

The Conversation U.S. asked Genevieve Hofmann, a women's health nurse practitioner at the University of Colorado Anschutz Medical Campus, to explain how the decision will affect health care for people going through menopause or postmenopause.

## **How did the FDA's decision come about?**

When people think of hormone therapy for menopause, they generally think of systemic estrogen and progestogens – for example, pills or patches that deliver hormones throughout the body.

Health care providers prescribed hormone therapy to manage symptoms of menopause such as hot flashes, night sweats and brain fog much more widely in the 1980s and 1990s than they do today. That's because in the early 2000s, researchers analyzed data from a study called the Women's Health Initiative and reported that hormone therapy increased the risk of breast cancer, heart disease, blood clots and stroke, as well as cognitive decline after menopause.

After this research was first published in 2002, the use of hormone therapy fell by 46% within six months – both because clinicians were reluctant to prescribe it and patients were fearful of taking it. In 2003, the FDA added black box warnings – the most serious warnings, indicating a risk of serious harm or death – to all estrogen-containing hormone products for menopause.

But researchers soon pointed out methodological flaws in the analysis. And over the past two decades, careful reanalyses of data from that study, as well as newer studies, have shown that systemic hormone therapy is very safe for most women, though there are nuances surrounding its use.

Meanwhile, women's health experts have been increasingly vocal in the past five years in calling to remove the black box warnings from a form of hormone menopause therapy that's applied locally, not systemically. Topical localized estrogen is applied directly to the vagina and surrounding areas, usually in the form of a cream or vaginal insert. It's used to treat the genitourinary syndrome of menopause, which manifests as genital and urinary symptoms.

Even though topical estrogen products are extremely safe and were not evaluated in the Women's Health Initiative study, the FDA warnings were added to them, too.

In July 2025, the FDA held an expert panel to discuss what's currently known about the risks and benefits of hormone therapy for menopause. At the meeting, most experts urged the agency to remove the warning labels on topical vaginal estrogen products.

The Nov. 10 announcement was the outcome of that discussion, and it included both systemic and topical hormone therapy.

## **Why is systemic estrogen no longer considered unsafe?**

Researchers are now finding that the balance of risks and benefits of systemic hormone therapy for menopause seems to depend strongly on when someone starts hormones, as well as the type, dose and length of use.

For women under 60 or within 10 years of their final period, the therapy is much safer than it is for older women. A 2017 follow-up of Women's Health Initiative participants showed that overall deaths from any causes actually decreased in this younger cohort of menopausal women taking hormones.

For women who are more than 10 years from their final menstrual period, starting hormone therapy may increase their risk of cardiovascular disease. Researchers now refer to this as the timing hypothesis. Newer studies also support this idea.

Also, some ways of delivering hormones to the body turned out to be safer than others. Taking estrogen orally, as pills or tablets, carries a higher risk of blood clots. Those risks go away when it's delivered through the skin using a patch, gel or spray. Many more options for hormone therapy exist today than in the early 2000s.

Additionally, it's well established that hormone therapy improves bone health by preventing bone loss. Some studies suggest that in younger menopausal women, it may actually protect against cardiovascular disease, though this link is not yet proven and needs more study.

Unfortunately, many people missed out on the timing window. In my practice, I see patients who went through menopause 10 or 15 years ago and either didn't get hormone therapy at the time or stopped taking it when the initial Women's Health Initiative results came out. Now, they are hearing about the benefits, and many want to try it. But their higher cardiovascular risk may overshadow the benefit.

## **What about topical estrogen?**

Genitourinary syndrome of menopause is ubiquitous – it affects every person with ovaries who goes through menopause, and the symptoms tend to worsen with age.

They include vaginal dryness, painful sex and urinary issues such as an increase in urgency or frequency, along with incontinence. Urinary tract infections often tend to get more frequent with menopause, particularly in older women. Treating them can require multiple courses of antibiotics.

Tissues in the genitourinary area are loaded with estrogen receptors – proteins in cells that bind the hormone. So adding some estrogen back to these areas can help restore the quality and thickness of these tissues, and possibly even promote the growth of healthy bacteria around the vagina and the urinary tract. The treatment can greatly improve quality of life and promote better health and longevity.

Despite topical estrogen's safety and effectiveness, the FDA did not distinguish between it and systemic estrogen when adding the black box warnings in 2003. For this reason, many providers whose patients have symptoms relating to the genitourinary syndrome of menopause have been reluctant to prescribe it. Often, providers simply don't know that it has a different safety profile than systemic estrogen.

## **How will removing the black box warnings affect patients?**

Overall, I see this as a big win for women and their ability to manage the symptoms of menopause. I think this will make clinicians and patients far less anxious about prescribing and taking this medication.

Clinicians like me who specialize in women's health and menopause – and who have been following the research – have been safely prescribing hormone therapy all along. But many general practitioners who often lacked either menopause-specific training or the time and resources to stay on top of the latest findings have been more reluctant to do so.

Safety concerns that led to the black box warnings, especially in regard to local vaginal estrogen, have turned out to be overblown. While clinicians still need to consider who is a good candidate for systemic hormone use, the evidence shows that for most people, it is a safe option.

Even more important, patients who were previously convinced that hormone therapy was unsafe may feel more comfortable discussing it with their provider and considering it. And if they do receive a prescription for hormone therapy, I hope that the likelihood of them starting this effective treatment is no longer hindered by reading a scary package insert that was based on outdated evidence.

While this medication is not a silver bullet that reverses aging, starting hormones at the right time can safely improve symptoms that diminish people's quality of life. So if you're having symptoms that are bothersome, consider asking your provider about menopause hormone therapy to help manage them.

Genevieve Hofmann has participated in advisory boards with Astellis Pharma and Mayne Pharma. She is President-elect of the Board of Directors of National Association of Nurse Practitioner's in Women Health Board.

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