

Do Hormone Treatments for Menopause Increase Dementia Risk?

A new study suggests a link, but experts caution that there's more to the story.



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A large new study in Denmark suggested that hormone therapy — which women use to manage menopausal symptoms — was associated with an increased risk of developing Alzheimer's disease and other types of dementia. The study found that the heightened risk was even present in women who started the therapy at 55 or younger and in short term users.

The authors of the study warned that it was unable to distinguish between the effects of the hormones and the menopausal symptoms that drove women to seek treatment, which themselves are associated with an increased risk of dementia. And in the same journal where the Danish study was published, researchers from the Mayo Clinic and Harvard Medical School issued an editorial, titled "A Causal Link Remains Unlikely," noting that the study didn't provide evidence that hormone therapy causes Alzheimer's or other dementias.

Using Denmark's national registry, the study examined the medical records of more than 5,500 women who were diagnosed with dementia and Alzheimer's between 2000 and 2018 and compared them with over 55,800 women who had not been diagnosed with the conditions. The study found that women who used hormones had a 24 percent higher rate of dementia (including Alzheimer's) than the women who didn't use hormones.

The findings echo previous studies that have identified some associations between taking hormones for menopause symptoms and dementia, some of which had limitations that were similar to the current study. In 2003, the Women's Health Initiative in the U.S. found that women aged 65 and over on hormone therapy had a greater risk of developing dementia than those who took a placebo.

“As with any pharmaceutical treatment, hormone therapy also has side effects,” said Dr. Nelsan Pourhadi, a researcher at the Danish Dementia Research Centre at Copenhagen University Hospital Rigshospitalet and the lead author of the recent study. “These should be weighed up against the benefits.”

Dr. Pourhadi noted that this study and others like it shouldn't alarm women so much that they abandon their hormone therapy treatments. Last week, the North American Menopause Society sent out a notice to its members, who are made up of certified practitioners, that the study “shouldn't change practice,” said Dr. Stephanie Faubion, medical director for N.A.M.S. and a director of the Mayo Clinic Center for Women's Health.

The study, she added, is a source of uncertainty and fear but doesn't provide much helpful information.

Confounding Factors

The biggest limitation of the study is that it was observational, Dr. Faubion said, and was therefore unable to establish causation.

Some experts suggest that the true connection may be between the symptoms of menopause and dementia. “If you have symptoms of menopause — hot flashes, insomnia, depression, brain fog — you're more likely to ask for hormones,” said Dr. Lisa Mosconi, director of the Alzheimer's Prevention Program at Weill Cornell Medicine. Studies have shown that those symptoms do have a link with the development of Alzheimer's and other dementias.

For example, hot flashes have been linked with the amount of white matter hyperintensities, which are small lesions in the part of the brain that contains the fibers connecting the neuron cells, Dr. Mosconi said. A study published last year showed that higher rates of hot flashes were linked to an increase in the amount of white matter hyperintensities. The lesions are “considered a risk factor for dementia,” Dr. Mosconi said. (It's not clear whether hot flashes cause damage to the brain or if the hot flashes and the white matter damage share an underlying cause.)

Insomnia in midlife — which can be driven by night sweats — is considered a risk factor for developing neurodegenerative diseases later in life. “Certain proteins, which are the precursors of Alzheimer’s disease, build up over the day in the brain. And when we sleep, there’s actually a mechanical wave, like a wave in the ocean, that pushes those out of the brain,” said Dr. Pauline Maki, director of the Women’s Mental Health Research Program at the University of Illinois Chicago. “We know that many women go with their hot flashes untreated for years and years and have disturbed sleep night after night after night — so that’s an important consideration as well.” Studies have yet to show that insomnia specifically caused by night sweats is a risk factor for dementia, but it’s an ongoing area of research, Dr. Maki said.

Depression in midlife — another common symptom of menopause — is also considered a risk factor for developing dementia later in life.

The Danish study doesn’t clarify whether these underlying issues drove women to seek out hormone therapies in the first place, nor did it consider genetic predisposition for developing Alzheimer’s, both of which Dr. Pourhadi acknowledged could be viable explanations for its results.

Contradictory Evidence

Just as there are previous studies that show a link between hormone therapy and neurodegenerative diseases, there are a number of studies that show the opposite: that hormone therapy is associated with a reduced risk of developing dementia and Alzheimer’s, Dr. Mosconi said. One observational study, published in 2021, looked at the medical records of nearly 380,000 women and found that the long-term use of hormone therapy had a seemingly “protective effect” against neurodegenerative diseases overall.

And, Dr. Mosconi added, three separate studies that randomly gave women hormone therapy or a placebo — which is considered the gold standard for determining the effects of drugs — found that hormone use had no negative effects on cognition. These studies, including one published in 2013 that looked again at the Women’s Health Initiative data in the U.S., concluded that starting hormone therapy at 55 or younger was a major factor in mitigating negative effects on cognition.

The experts also noted that the Danish study only looked at the effects of a particular formulation of hormones — estrogen with synthetic progestins — whereas other formulations, like bio-identical progesterone or, for women who have had a hysterectomy, estrogen alone, can have vastly different outcomes, Dr. Faubion said. “We lump hormone therapy into a single group and we really shouldn’t,” she said. “These are all very different chemical compounds and they don’t affect the body in the same way, and so we should stop referring to them as a single entity.”

Alisha Haridasani Gupta is a reporter on the Well desk, focused on women’s health, health inequities and trends in functional medicine and wellness. Previously, she wrote the In Her Words newsletter, covering politics, business, technology, health and culture through the gender lens. More about Alisha Haridasani Gupta