**Alzheimer’s and HRT:**

**Study suggests sweet spot to avoid dementia**

By Sandee LaMotte, CNN  7 minute read  Updated 9:45 AM EDT, Wed April 5, 2023

**Nearly 40% of dementia cases can be prevented with one small health change**

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Alzheimer’s disease strikes women harder than men — over two-thirds of those who descend into dementia’s devastating twilight are female at birth. That’s likely due to biological reasons that remain poorly understood, according to the [Alzheimer’s Association](https://www.alz.org/blog/alz/february_2016/why_does_alzheimer_s_disease_affect_more_women_tha).

**[Gene discovery may explain why more women get Alzheimer's disease](https://www.cnn.com/2022/06/30/health/female-alzheimer-gene-discovered-wellness-scn/index.html)**

One key piece of the enigma: Women lose sexual hormones such as estrogen when they undergo menopause, either naturally through the body’s decreased productionor by removal of the ovaries via surgery. However, just how the loss of those hormones and the impact of hormone replacement therapy, or HRT, affects dementia risk is also unclear.

A new study may have uncovered a piece or two of the puzzle. Women who underwent [early (age 40 to 45) or premature (before age 40)](https://www.womenshealth.gov/menopause/early-or-premature-menopause) menopause or women who began hormone replacement therapy more than five years after menopause had higher levels of tau in their brains, according to the study [published Monday](https://jamanetwork.com/journals/jamaneurology/fullarticle/2802791?guestAccessKey=6a999ea8-47db-4e1c-ad0c-d7984fecbe55&utm_source=For_The_Media&utm_medium=referral&utm_campaign=ftm_links&utm_content=tfl&utm_term=040323) in the journal JAMA Neurology.

Tau tangles, along with plaques made up of beta-amyloid proteins, are hallmark signs of Alzheimer’s disease.

“This is the first study showing a delayed use of hormone therapy seems to be associated with increased levels of Alzheimer’s disease markers in the brain,” said lead author Gillian Coughlan, a research fellow in neurology at Massachusetts General Hospital in Boston.

However, these changes only occurred in women who already had higher levels of beta-amyloid in their brain tissue, Coughlan told CNN.

“Most of the associations we saw between menopause and tau protein occurred in the context of high amyloid,” Coughlan said. “Now a large portion of the older population do accumulate amyloid as they get older — it’s not that uncommon.”

**Taking hormone replacement therapy did not affect dementia risk unless it was started late, a new study said.**

Tau deposits, however, are more uncommon, she said, adding that it takes both tau tangles and beta-amyloid to develop Alzheimer’s disease. “Usually if you’ve a combination of beta-amyloid and tau, then you would typically develop cognitive decline within a few years,” Coughlan said.

“What we found is women who have early menopause or have a very late use of hormone therapy might be at higher risk, but only if they were already on the Alzheimer’s disease continuum, with elevated levels of amyloid,” she said. “Women with very low levels of amyloid and early menopause did not have such an association.”

The study also found that women who began hormone therapy “at the right time, proximal to menopause age, didn’t have higher or lower tau proteins in the brain,” Coughlan said. “This is good as it means we may still be able to use hormone therapy to treat severe menopausal symptoms.”

Dr. Richard Isaacson, an Alzheimer’s preventive neurologist at the Institute for Neurodegenerative Diseases, considered the scientific paper important. Enter your email to subscribe to the CNN Five Things Newsletter.

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“While it’s not the first time a study has shown that early treatment with hormone replacement therapy may be more protective for a women’s brain, it did suggest for the first time that greater amounts of tau protein may be associated with later initiation of hormone treatment,” said Isaacson, who was not involved in the study.

**[21 ways to reduce your Alzheimer's risk, backed by research](https://www.cnn.com/2020/07/20/health/alzheimers-disease-prevention-wellness/index.html)**

“This study doesn’t show that hormone therapy causes Alzheimer’s. The researchers didn’t look at whether the participants went on to develop symptoms of dementia and we can’t be sure of cause and effect in this kind of research,” said Sara Imarisio, head of strategic initiatives at Alzheimer’s Research UK, in a statement.

“Hormone therapy provides important benefits to many women, helping to combat the symptoms that menopause can bring,” said Imarisio, who was not involved in the study. “Women who take, or are thinking of taking, hormone therapy should not be put off by these results, and anyone concerned about the effects of this treatment should speak to their doctor.”

**Hormone replacement therapy**

The average age of menopause onset — defined as when a woman hasn’t had a period for 12 months in a row — is 51, although women can naturally go into menopause between the ages of 40 and 58, according to the [North American Menopause Society](https://www.menopause.org/for-women/menopauseflashes/menopause-symptoms-and-treatments/menopause-101-a-primer-for-the-perimenopausal). Symptoms such as hot flashes and night sweats can occur years in advance, in what is called perimenopause.

Hormone replacement therapy has been a loaded topic for many women since early, misguided results were[published in 2002](https://jamanetwork.com/journals/jama/fullarticle/196628) from a study called the [Women’s Health Initiative clinical trial](https://clinicaltrials.gov/ct2/show/NCT00000611). That preliminary analysis found an estrogen and progestin combo — the type of HRT prescribed at the time — increased the risk of heart disease as well as stroke, blood clots, dementia and breast cancer. The study was halted early due to the dangers.

**[Hot flashes connected to heart attacks and cognitive decline, studies say](https://www.cnn.com/2019/09/24/health/hot-flashes-link-to-heart-attack-stroke-wellness/index.html)**

Fallout was dramatic. By the end of the year, hormone therapy use [dropped 30%](https://www.ncbi.nlm.nih.gov/pubmed/22207318/)when analyzed by insurance claims. By 2009, hormone therapy claims had dropped more than 70%.

Ten years later, the Women’s Health Initiative findings[were debunked.](https://academic.oup.com/jcem/article/98/5/1771/2536695)Because the original analysis looked at women age 65 and older, who were already at greater risk for heart attacks, blood clots and stroke, the initial 2002 results were flawed because they failed to consider a woman’s age at the start of replacement therapy.

But the damage was done. Even today, many doctors are uncomfortable prescribing the use of hormone therapy, leaving many women to suffer through devastating symptoms without recourse.

Current [medical guidelines](https://www.guidelinecentral.com/guideline/1971153/) suggest the benefits of hormone therapy for hot flashes, night sweats, vaginal pain and dryness, urinary issues, and bone loss outweigh the risks for women younger than 60 who are within 10 years of the onset of menopause — and who have no known or suspected history of breast cancer, blood clots, stroke or other [contraindications](https://www.ncbi.nlm.nih.gov/books/NBK493191/#:~:text=Contraindications%20for%20oral%20or%20transdermal,are%20still%20candidates%20for%20HRT).

It’s a different story for women who are older than 60 or who start hormone therapy more than 10 years after the onset of menopause. “The benefit-risk ratio appears less favorable because of the greater absolute risks of coronary heart disease, stroke, venous thromboembolism, and dementia,” according to the [2022 hormone therapy position statement](https://pubmed.ncbi.nlm.nih.gov/35797481/) of The North American Menopause Society.

**What brain scans show**

In the new JAMA Neurology study, a team of researchers from Boston-based Massachusetts General Hospital and Brigham and Women’s Hospital analyzed brain scans of 193 women and 99 men with normal cognitive function for beta-amyloid and tau pathology.

That may sound like a small study, but it isn’t, Coughlan said: “When using brain scans to actually look at disease in the brain, this is considered a large sample size.”

**[Hormone replacement therapy not linked to an increased risk of developing dementia, study finds.](https://www.cnn.com/2021/09/30/health/hormone-replacement-therapy-menopause-hrt-dementia-wellness/index.html)**

The study found women had more tau buildup in several parts of the brain than men of a similar age, said Tara Spires-Jones, professor of neurodegeneration and deputy director of the Centre for Discovery Brain Sciences at the University of Edinburgh in Scotland. She wasn’t involved in the study.

“Further, females had higher tau burden than males when they also have amyloid pathology in the brain,” Spires-Jones said in a statement.

Women in the new study all used the type of hormone therapy — the estrogen and progestin mix — that was used by the women in the Women’s Health Initiative clinical trial that caused so much controversy, Coughlan said.

“If (our study) is replicated, we may have found a potential biological basis for the results of the Women’s Health Initiative clinical trial, which found women 65 and above were more likely to develop dementia later in life if they took that one type of hormone therapy,” she said.

However, today women have many other options for hormone replacement, depending on their individual needs.

The study had some limitations — most participants were White and the study did not say who then went on to develop dementia, experts said. In addition, there were not enough people in the study with a genetic risk for Alzheimer’s, said Dr. Liz Coulthard, an associate professor in dementia neurology at the University of Bristol in the United Kingdom, who was not involved in the study.

**[Hormone replacement therapy tied to Alzheimer's risk, study says, but experts urge caution](https://www.cnn.com/2019/03/06/health/alzheimers-hormone-replacement-therapy-study/index.html)**

“Recently we found out that HRT might have different effects in people at high genetic risk (apoE4 gene positive), but this is not featured here,” Coulthard said in a statement.

“The results here are scientifically interesting,” she added. “But research into the relationship between HRT, menopause and Alzheimer’s is beset by multiple small studies, all confounded by the different reasons people are prescribed HRT and accuracy of memory for menopause age and HRT use.

“As a result, women are receiving conflicting or poorly justified advice as to whether HRT use may be helpful or not for future brain health,” Coulthard said. “A balanced, well-powered trial of HRT over many years is the only way we will really understand whether HRT is harmful to brain health.”