

# Hormone therapy for breast cancer linked with lower dementia risk

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Hormone modulating therapy (HMT) used for the treatment of breast cancer was associated with a 7% lower risk of developing Alzheimer's disease and related dementias later in life, according to a new study

published in [JAMA Network Open](#).

The study, which is one of the largest of its kind, found that although HMT was linked with protection against the development of dementia overall, the association decreased with age and varied by race.

"Our findings emphasize the importance of being cognizant of individual patient factors when we prescribe medications or develop treatment plans for breast cancer," said senior author Francesmary Modugno, Ph.D. M.P.H., professor of obstetrics, gynecology and reproductive sciences at the University of Pittsburgh and member of Magee-Womens Research Institute and UPMC Hillman Cancer Center.

"It's not one-size-fits-all. We need to think about each individual patient to optimize outcomes and minimize risks."

About two-thirds of [breast cancer patients](#) have tumors that are hormone receptor positive, meaning that they grow in response to estrogen or progesterone. For these patients, HMT can impede tumor growth by blocking hormones from attaching to these receptors.

While use of HMT is linked with increased survival, there is conflicting evidence about whether it increases or decreases the risk of developing Alzheimer's disease and related dementias (ADRD), debilitating conditions that are characterized by [memory loss](#), changes in mood or behavior, and difficulties with thinking, problem-solving and reasoning.

To improve understanding about the risk of ADRD following HMT in breast cancer patients, Modugno, teamed up with lead author Chao Cai, Ph.D., assistant professor at the University of South Carolina College of Pharmacy. They used a [federal database](#) of people aged 65 and older to identify women who were diagnosed with breast cancer between 2007 and 2009 and who did not have a previous ADRD diagnosis or history of

using HMT before their breast cancer diagnosis.

Of 18,808 patients who fit the criteria, 66% had received HMT within three years of their diagnosis and 34% had not. During an average of 12 years of follow-up, 24% of HMT users and 28% of non-HMT users developed ADRD.

To calculate the risk of developing ADRD, the researchers accounted for the risk of death associated with increased age and duration of exposure to HMT.

They found that while HMT use was associated with an overall decrease in the relative risk of developing ADRD, the protective effect of HMT was most pronounced in patients aged 65 through 69 and diminished with age. Notably, when patients aged over 80, there was an increased risk of ADRD in HMT users.

"Our study suggests that younger women may benefit more from HMT in terms of reduced risk of developing Alzheimer's disease and other types of dementia," said Cai. "The benefits of HMT decreased for women aged 75 and older, particularly in those who identified as white. This suggests that the timing of HMT initiation is crucial and treatment plans should be tailored to a patient's age."

Black women aged 65 through 74 who used HMT had a 24% reduction in relative risk of developing ADRD, which dropped to 19% after age 75. White women aged 65 through 74 had an 11% reduction in risk of ADRD with HMT use, but this beneficial association disappeared after age 75.

"Black women have higher rates of breast [cancer](#) and tend to have higher lifetime stress due to structural racism and other societal factors, which are associated with worse outcomes," said Modugno. "We don't know

the mechanisms behind the racial disparities we saw with HMT and risk of ADRD, but it's possible that these factors could contribute. It deserves further investigation."

There are three main types of HMT: selective estrogen receptor modulators, aromatase inhibitors and selective estrogen receptor degraders. The analysis found that risk of developing ADRD varied by HMT type.

According to Cai, estrogen has neuroprotective effects, so these therapies could influence ADRD risk by mimicking estrogen, influencing estrogen production or modulating estrogen receptor levels. HMT might also affect clearance of a protein called beta-amyloid, stability of tau protein and vascular health, all of which are closely linked to brain health and ADRD risk.

"The relationship between HMT for [breast cancer](#) and dementia risk is complex and influenced by multiple factors," explained Cai. "Ongoing research is needed to further understand the mechanisms behind this association and provide clearer guidance on the use of HMT."

A limitation of the study was that it only included patients over 65. In the future, Cai and Modugno will include [younger women](#) who haven't reached menopause yet to further understand the link between HMT and dementia risk.

Other authors on the study were Kaowao Strickland, M.P.H., Sophia Knudsen, Sarah Beth Tucker, and Chandana Sai Chidrala, M.S., all of the University of South Carolina.

**More information:** Alzheimer disease and related dementia following hormone-modulating therapy in patients with breast cancer, *JAMA Network Open* (2024). [DOI: 10.1001/jamanetworkopen.2024.22493](https://doi.org/10.1001/jamanetworkopen.2024.22493)

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