

# Do recent data on use of menopausal HT and subsequent risk of dementia indicate an association?

**No. In general, use of hormone therapy (HT) is not associated with risk of dementia,** according to a large observational study that included 16,291 cases of women diagnosed with dementia and 68,726 controls who used menopausal HT. Data were obtained from 2 large primary care databases in the United Kingdom.

*Vinogradova Y, Denning T, Hippisley-Cox J, et al. Use of menopausal hormone therapy and risk of dementia: nested case-control studies using QResearch and CPRD databases. BMJ. 2021;374:n2182. doi: 10.1136/bmj.n2182.*

## EXPERT COMMENTARY

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Much interest has surrounded whether the use of menopausal HT impacts future risk of cognitive decline. Recently, Vinogradova and colleagues conducted an observational study using data from 2 large primary care databases, QResearch and the Clinical Practice Research Datalink (CPRD), in the United Kingdom.<sup>1</sup> The investigators conducted case-control studies that included women aged 55 and older diagnosed with dementia and up to 5 controls without dementia. Only cases and controls with at least 10 years of medical records prior to the index date (that

is, the time of dementia diagnosis in cases) were included. Since early symptoms of dementia prior to diagnosis may cause sleep problems and dysphoria (which also may be symptoms of menopause), HT prescriptions during the 3 years prior to the index date were excluded.

## Details of the study

Among 16,291 cases and 68,726 controls, the women's mean age was approximately 83 years. Cases were identified by using codes for dementia from patients' clinical records or records of prescriptions for drugs used to treat dementia.

More than half the women were being treated for hypertension, and 14% of women in both groups had used HT. Women were considered users of estrogen-only therapy if they had no prescriptions containing a progestogen after their first prescription for systemic estrogen as the start of exposure to HT. Those with any subsequent prescription containing a progestogen were classified as combined HT users.

**Results.** In an analysis adjusted for all available potential confounders—including lifestyle factors, ethnicity, family history of dementia, early menopause, oophorectomy/hysterectomy, comorbidities, and use of other relevant drugs—the use of HT was not associated with risk of dementia.

## FAST TRACK

*In an analysis of data from 2 large primary care databases adjusted for all potential confounders, the use of HT was not associated with risk of dementia*

*Dr. Kaunitz reports serving as a consultant to Mithra and Pfizer and that the University of Florida receives grant or research support from Mithra.*

doi: 10.12788/obgm.0161

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## WHAT THIS EVIDENCE MEANS FOR PRACTICE

The authors of this British large observational study took pains to minimize potential bias. The finding that long-term use of estrogen-only HT may be neuroprotective is consistent with results of recent studies in the United States and Finland,<sup>2-4</sup> as well as with the Women's Health Initiative randomized trial, which found that with 18 years of follow-up, treatment with conjugated estrogen alone was associated with a 26% reduced risk of death from Alzheimer disease.<sup>5</sup> Overall, however, the main message we should glean from this important study by Vinogradova and colleagues is that women with bothersome vasomotor symptoms considering use of menopausal HT can be reassured that such therapy has little if any impact on future risk of cognitive decline.

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A reduced risk of dementia was noted among women who had been taking

estrogen-only HT for 10 years or more (odds ratio [OR], 0.85; 95% confidence interval [CI], 0.76-0.94). An elevated risk of Alzheimer disease was noted among women who had used estrogen-progestin HT for 5 to 9 years (OR, 1.19; CI, 1.06-1.33).<sup>1</sup>

### Study strengths and limitations

The authors pointed out that this study's main strengths were that it had a very large sample size representative of the general population and that its design permitted capture of all known cases as well as precision recording for prescribed drugs. On the other hand, the study is limited by the possible lack of data for some older women before the index date; that is, menopause in this latter group started before their registration or before these data were gathered electronically by their practice. ●

### References

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