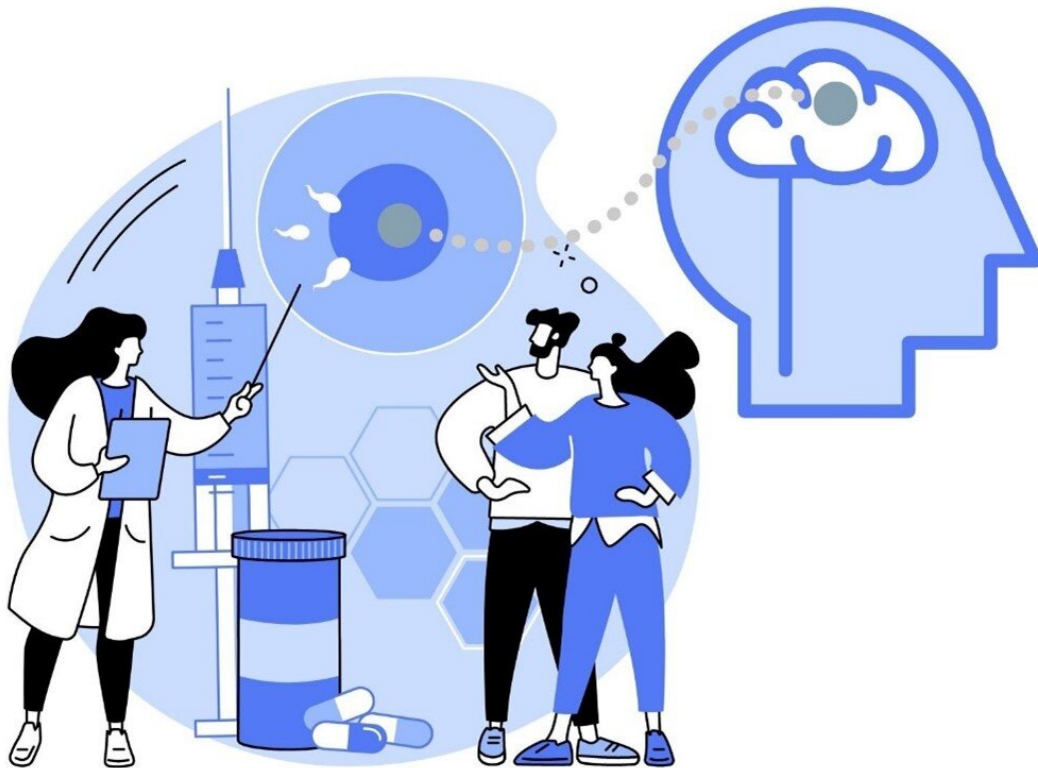


Female hormones could provide clues to higher risk of dementia in women

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Reproductive factors and the risk of dementia. Credit: Jessica Gong (CC-BY 4.0, creativecommons.org/licenses/by/4.0/)

Life events that influence levels of the female hormone estrogen may be linked to a woman's risk of developing dementia in later life, according

to new research.

The analysis found that some reproductive events—like an early or late start to menstruation, early menopause and hysterectomy—were linked to higher risk of dementia while ever having been pregnant or having had an abortion and later menopause were linked to lower risk.

But childbearing was not one of them, with a similar relationship observed between the number of children and dementia risk in men and women.

Lead author Jessica Gong from The George Institute for Global Health said that although it appeared reproductive events related to changes in hormone levels in women may be involved in dementia risk, the exact relationship was still unknown.

"While the risk of developing dementia increases with age, we don't yet know whether the higher rates seen in women are simply because they live longer," explained Ms Gong. "But it's possible that female-specific reproductive factors may be able to explain some of the sex differences."

Dementia is fast becoming a global epidemic, currently affecting an estimated 50 million people worldwide. This is projected to triple by 2050—mainly driven by aging populations. Rates of dementia and associated deaths are both known to be higher in women than men.

Estradiol is the most predominant form of estrogen during reproductive life (from the start of menstruation to menopause) and estriol is the primary estrogen during pregnancy. Use of hormones that originate from outside the body, such as oral contraceptives during reproductive years, and hormone replacement therapy (HRT) in later life can also influence estrogen levels.

To examine these relationships in more detail, George Institute researchers analyzed data on a total of 273,240 women without dementia who were registered with the UK Biobank, a large-scale biomedical database. After adjusting for other factors that could have influenced the results, they found the following were associated with an increased risk of dementia:

- Early and late first occurrence of menstruation, younger age at first birth, and hysterectomy—specifically hysterectomy without surgical removal of one or both ovaries, or if the hysterectomy took place after ovary removal.

Conversely, the factors associated with a decreased risk were ever having been pregnant, ever having had an abortion, longer reproductive lifespan and later menopause.

"With regard to external hormones, the use oral contraceptive pills was associated with a lower risk of dementia, but our study findings did not support an association between HRT and dementia risk," Ms Gong said.

The authors proposed that risk variation in women may not be associated with childbearing because a similar pattern was observed between number of children fathered and dementia risk among a similar number men in the same study.

"We found that the higher dementia risk linked to early (natural and artificial) menopause was more pronounced in women of lower socioeconomic status," she added.

"Social deprivation is likely to be an important determinant of dementia risk as well as other aspects of women's health."

With dementia on the rise and in the absence of significant treatment

breakthroughs, the focus has been on reducing the risk of developing the disease.

"More research is needed to understand whether these differences are associated with life-long exposure to the body's own estrogen, and whether external hormone use could influence the risk of developing dementia," added Ms Gong.

"Our findings may be helpful for identifying high-risk women to participate in future clinical trials to assess potential preventive measures and treatments."

More information: Gong J, Harris K, Peters SAE, Woodward M (2022) Reproductive factors and the risk of incident dementia: A cohort study of UK Biobank participants. *PLoS Med* 19(4): e1003955. doi.org/10.1371/journal.pmed.1003955

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