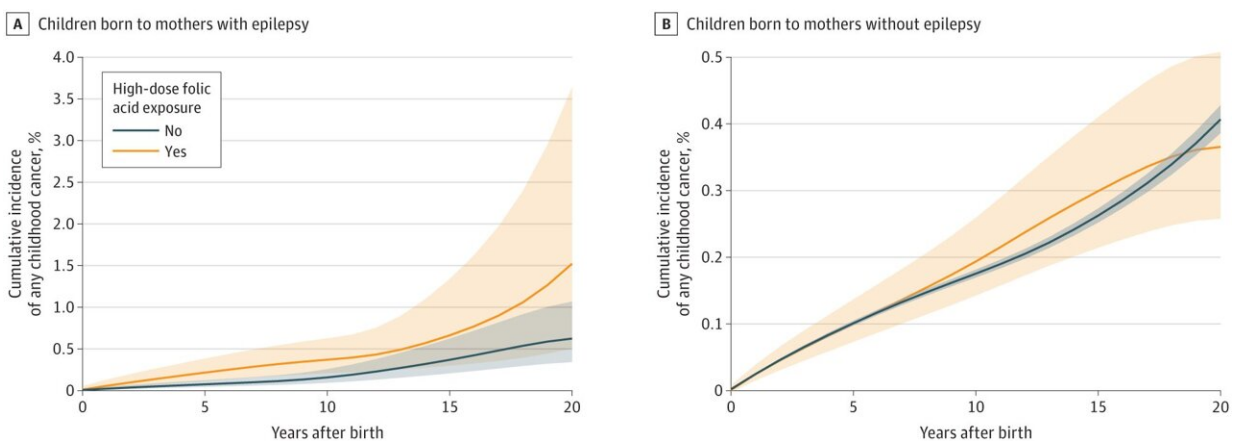


Increased risk of cancer in children born to mothers with epilepsy using high-dose folic acid during pregnancy

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Cumulative incidence of first onset of childhood cancer recorded from birth until 20 years of age with or without maternal prescription fill for high-dose folic acid for mothers with or without a diagnosis of epilepsy. The graph lines were smoothed owing to the Danish Data Protection Act to prevent identification of individuals. Credit: *JAMA Neurology* (2022). DOI: 10.1001/jamaneurol.2022.2977

High-dose folic acid is protective against congenital malformations if the mother is at particular risk of having a child with congenital malformations. Treatment with antiseizure medication in pregnancy is associated with risk of congenital malformations in the children, and women with epilepsy are therefore often recommended a supplementary

high dose of folic acid (4–5 mg daily) before and during pregnancy. However, some studies have raised concern that folic acid can increase the risk of cancer not only in the mother, but in the child when exposed during pregnancy.

This Scandinavian register-based cohort study is a part of the SCAN-AED project which is a large study containing information from several nationwide health registers across the Nordic countries: Denmark, Finland, Iceland, Norway, and Sweden. The researchers examined women who redeemed prescriptions for high-dose [folic acid](#) three months before pregnancy and until birth, and then followed each of their children from birth. In total, this study included 3,379,171 children in which 27,784 were born to mothers with epilepsy including 5,933 mothers with epilepsy who filled a prescription for high dose folic acid.

"We found an increased risk of childhood cancer if the [child](#) was born to a mother with epilepsy who filled for high dose folic acid before or during pregnancy, compared to children born to mothers with epilepsy without such prescription fills. The increased risk of cancer did not change after considering other factors that could explain the risk, such as concomitant fill for antiseizure medication. We did not find an increased [cancer risk](#) among children of mothers without epilepsy who used high-dose folic acid," says lead investigator Håkon Magne Vegrim, MD and Ph.D. student at the University of Bergen.

The findings could not be explained by maternal epilepsy or other comorbidities such as maternal tuberous sclerosis, [diabetes mellitus](#), previous cancer diagnosis or specific antiseizure medications such as valproate or carbamazepine. Although these are unique and concerning results that have potential to change clinical practice worldwide, it should be interpreted with caution:

"The benefit of folic acid supplements for child neurodevelopment in

[pregnant women](#) using antiseizure drugs has been shown in several studies," says senior author, Marte Helene Bjørk, professor of neurology, University of Bergen. "Folate is important for normal growth and brain development of the unborn child. Whereas the current study raise concern about the safety of [high-dose](#) folic acid supplementation, no risk of cancer has been found in children after maternal low dose folic acid (0.4 mg) in pregnancy. Antiseizure medications can interact with the function, uptake, and break down of the vitamin and cause increased need of folate in women using these medications. We need to understand potential mechanisms behind the link we found to cancer in the child, and it is prudent to identify the optimal dose to balance the risks and benefits. "

The study is titled "Cancer Risk in Children of Mothers With Epilepsy and High-Dose Folic Acid Use During Pregnancy" and was published in *JAMA Neurology* September 26, 2022.

More information: Håkon Magne Vegrim et al, Cancer Risk in Children of Mothers With Epilepsy and High-Dose Folic Acid Use During Pregnancy, *JAMA Neurology* (2022). [DOI: 10.1001/jamaneurol.2022.2977](#)

Provided by University of Bergen

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