

Hormonal Contraceptive Use And Brain Health Outcomes In Polycystic Ovary Syndrome: An Analysis Of The All Of Us Research Program

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Key takeaway: Systemic hormonal contraceptive use was not significantly associated with a composite cognitive health outcome of dementia, stroke, and late-life depression among people with PCOS within the All of Us cohort.

INTRODUCTION	METHODS	RESULTS	CONCLUSIONS	REFERENCES
Polycystic ovary syndrome (PCOS) is a prevalent endocrine condition associated with metabolic dysfunction, psychiatric comorbidity, and altered exposure to sex hormones – factors relevant to brain health across the life course. Hormonal contraceptives (HC) are commonly used for long-term management of PCOS, yet their impact on lifespan brain health remains poorly understood. As sex steroid hormones are hypothesized to affect neurocognitive vulnerability, we aimed to examine HC use in PCOS and its association with a composite outcome of depression, dementia, or stroke representing participant’s brain health profiles.	Using secondary data from the All of Us Research Program, a longitudinal cohort study of Americans, we identified individuals with PCOS stratified by HC use. HC exposure was defined as ever use, and among users, cumulative duration. Sequential logistic regression models adjusting for covariates known as risk factors for cognitive decline (age, low education, type 2 diabetes, hypertension, hyperlipidemia, smoking, and alcohol use) examined associations between HC use and a composite outcome of late-life depression, dementia, or stroke.	Among 4,175 individuals with PCOS (mean age 46.5 years, range 19-94 years), 1,721 (41%) were ever HC users. Of these users, 58 (3.4%) experienced late-life depression, dementia, or stroke. HC users were more likely to have a diagnosis of PCOS in their EHR, and tended to be younger, more educated, and have lower rates of type 2 diabetes, hypertension and hyperlipidemia. HC use, whether defined as ever/never use or categorical or continuous duration, was not significantly associated with the composite outcome in any logistic regression model. In the fully adjusted model, ever HC use was not associated with the outcome (OR 1.37, 95% CI 0.95-1.95, p=0.0886). Similarly, no category of the cumulative duration group was significantly associated with the outcome (OR 1.22 [>10 years] to OR 1.62 [<1 year] or when modelled continuously (OR 0.95, 95% CI 0.89-1.01, p=0.117).	In this analysis of individuals with PCOS, HC use was not significantly associated with a composite outcome of depression, dementia or stroke across adjusted models and definitions of HC exposure. Further research using more granular cognitive outcomes is warranted to corroborate these findings.	Huddleston HG, Jaswa EG, Casaletto KB, et al. Associations of Polycystic Ovary Syndrome With Indicators of Brain Health at Midlife in the CARDIA Cohort. <i>Neurology</i>. 2024;102(4):e208104. doi:10.1212/WNL.0000000000208104 Lee JK, Frank RD, Christenson LR, Fields JA, Rocca WA, Mielke MM. Associations of reproductive factors and exogenous estrogens with global and domain-specific cognition in later life. <i>Alzheimers Dement</i>. 2023;20(1):63-73. doi:10.1002/alz.13394 Clocchiatti-Tuozzo S, Rivier CA, Renedo D, et al. Life’s Essential 8 and Poor Brain Health Outcomes in Middle-Aged Adults. <i>Neurology</i>. 2024;103(10):e209990. doi:10.1212/WNL.0000000000209990
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