

## **Influence of cannabis on the risk of transition in young people at ultra-high risk of psychosis (ICAAR study): a longitudinal study**

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**Objectives:** There is evidence of an association between exposure to cannabis and the emergence of schizophrenia. However, little is known about longitudinal effects of cannabis exposure and the influence of genetic factors and neurodevelopment on the transition to psychosis. We designed a study on the Influence of Cannabis in Adolescents and Adults at Risk mental state (ICAAR) in order to fulfill these gaps.

**Methods:** 312 individuals characterized as Ultra-High Risk (UHR, n=170), First Episode Psychosis (FEP, n=54) and non-at-risk Help-Seeking Controls (HSC, n=88) were included in ICAAR using the Comprehensive Assessment of At Risk Mental States (CAARMS). Participants responded to questionnaires of cannabis consumption, neurodevelopment at baseline and after 6- and 12-months follow-ups, and a blood sample was collected for genetic assessment. We compared the three groups at baseline and UHR versus HSC according to whether they had converted to psychosis or not at follow-up. We examined the influence of cannabis, neurodevelopment and genetic factors in the conversion to psychosis using univariate comparisons.

**Results:** The three groups did not present sociodemographic or non-psychotic clinical characteristics differences. We found no association between conversion and neurodevelopment or polygenic risk scores of schizophrenia. At baseline, FEP consumed significantly more cannabis compared to UHR and HSC. After 12 months, we observed that 37 out of 100 UHR and 5 out of 31 HSC converted to psychosis and conversion rates were positively correlated with persistent or increased consumption of cannabis, regardless of mental state risk.

**Conclusion:** This prospective study is the first to consider the influence of cannabis in the progression of psychotic illness, associated with neurodevelopment and genetic measures. It shows that, while there is no major impact of cannabis exposure at baseline, continuing cannabis appears to be associated with exacerbated conversion to psychosis. These results strongly support the emphasis to actively limit cannabis consumption in UHR.

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