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## **The genetic contribution of cannabis use in opioid addiction: An investigation into sex differences**

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In Canada, trends in cannabis use rates have increased in the general population from 14.0% to 16.7% from 2018 to 2019. Individuals living with Opioid Use Disorder (OUD) have increased rates of cannabis use in comparison to the general population. Research on the short- and long-term impacts of cannabis use in OUD patients, including its use as a harm reduction strategy, has been inconclusive. Further, a genetic component may contribute to cannabis dependence; however, replication of findings has been inconsistent. To investigate the genetics variants associated with cannabis use in the OUD population, associations between pre-selected *ANKFN1*, *CADM2*, and *CNR1* single nucleotide polymorphisms (SNPs) and regular cannabis use (yes/no) (n=1221) and heaviness of cannabis (product of number of days used within a 30-day period and typical amount in grams) (n=1046) were tested. Within the whole population the G allele of rs1448602 [Beta=5.15, 95% confidence interval (CI): 1.44, 8.85, p=0.006] was significantly associated with heaviness of cannabis use and in males the A allele of rs1431318 [odds ratio (OR)=1.35, CI: 1.08, 1.70, p=0.009] and the A allele of rs1019238 [OR=0.77, CI: 0.62, 0.95, p=0.020] were significantly associated with regular cannabis use. Thus, significant associations on chromosome 3 on the *CADM2* gene and chromosome 17 on the *ANKFN1* gene were observed for heaviness of cannabis use and regular cannabis use, respectively. While replication is required, this study provides an important first step in understanding the genetic association between cannabis use in individuals living with OUD.