BACKGROUND

• Cannabis is the most frequently used and abused illicit drug.
• 22.5% lifetime prevalence in Europeans aged 15-64.
• A risk factor for developing substance dependence.

AIMS & METHODS

• Estimate trait heritability based on genetic relatedness (Yang et al., 2010)
• Identify common and population specific SNPs associated with the trait by using gee (Carey, 2012) accessed from Plink (Purcell et al., 2007).
• Hunt for genes conferring susceptibility to initiate cannabis use by employing the extended Simes test (Li et al. 2011).
• Sample: 6744 individuals (mean age=39.09, SD=17.45; 61% females) from the Netherlands Twin Register.
• GoNL (Boomsma et al., 2014) reference panel used to impute unobserved genotypes.

RESULTS

• Heritability on the observed scale estimated at 25% (SE=0.08, p = 0.0016).
• rs35917943 on chromosome 19 showed the strongest association signal (p=1.62E-7, Fig. 1)
• Top genes in the gene-based analysis (Fig. 2):
  * ZNF181 (p=3.7E-6)
  * MIR643 (p=3.03E-5, start position 52785049)

CONCLUSIONS

A significant proportion of variance in liability to initiate cannabis use is explained collectively by the SNPs.

Several interesting candidate genes were suggested by gene-based analyses.

Investigating these genes in replication samples and considering them jointly in pathway analyses shall provide additional insights into the etiology of the early stage of cannabis use.