

Genetic Liability to Cannabis Use Disorder and COVID-19 Hospitalization

Supplemental Information

Supplemental Table S1. COVID-19 Genetic Correlations When Accounting for Potential Confounding Variables in Primary Analysis but excluding the Townsend Deprivation Index.

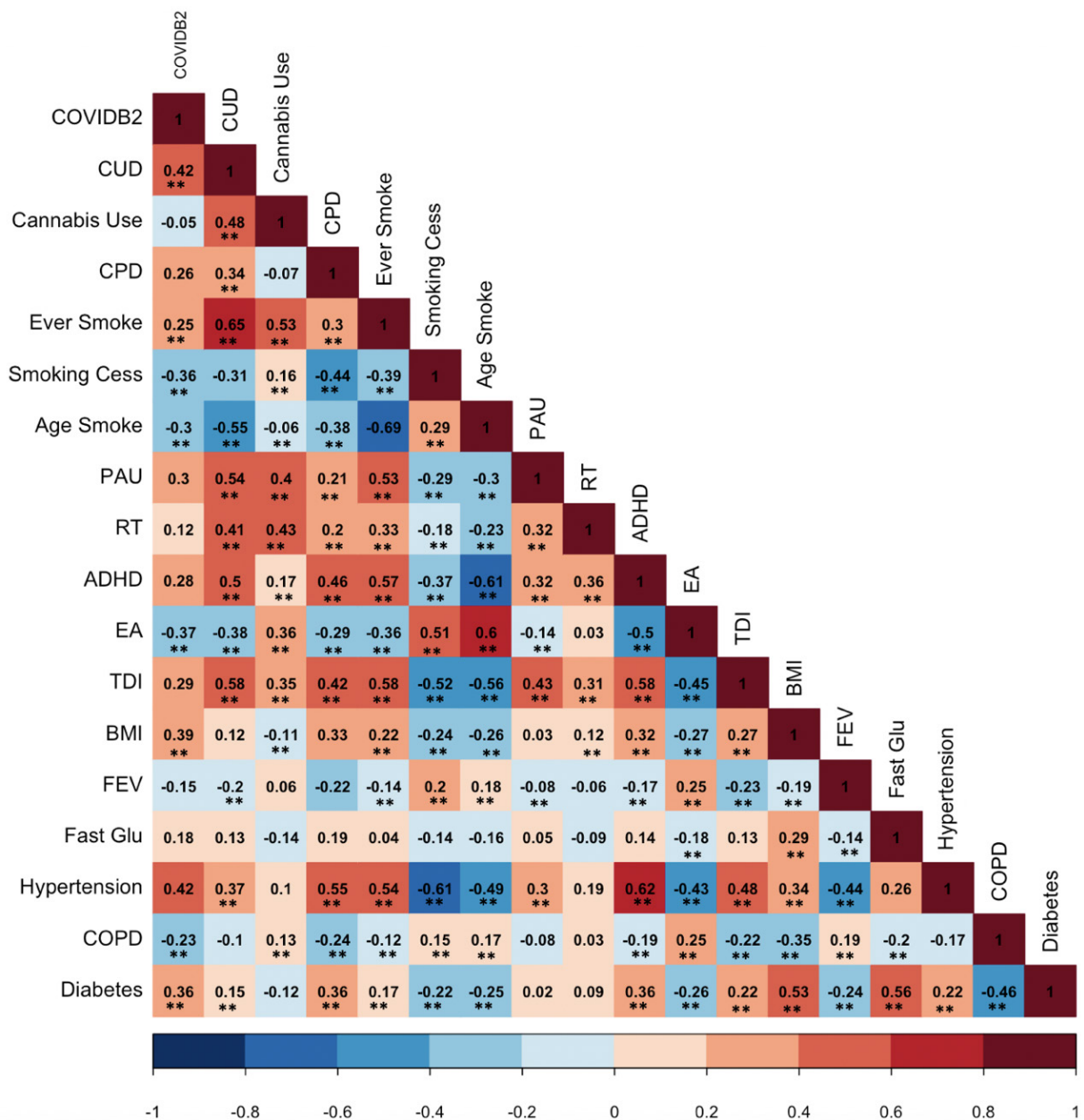
Substance Use Phenotype	CUD	β Substance Use Phenotype ^a	EA	BMI	FEV	Fast Gluc	β Risk	β ADHD
Cannabis Use	0.541*	-0.272	-0.010	0.322*	0.020	-0.021	-0.006	-0.046
CPD	0.364*	0.036	-0.186*	0.324*	0.014	0.007	-0.029	-0.106
Age Smoke	0.387*	0.072	-0.211*	0.333*	0.011	0.010	-0.027	-0.074
Smoking Cessation	0.363*	-0.171	-0.112	0.321*	0.019	-0.002	-0.055	-0.103
Ever Smoke	0.434*	-0.128	-0.188*	0.343*	0.012	-0.004	-0.030	-0.057
Problematic Alcohol Use	0.295	0.148	-0.198*	0.338*	0.009	0.009	-0.039	-0.110

Note. Standardized beta estimates for Cannabis Use Disorder (CUD) and substance use phenotypes were taken from a multiple regression parameterized in gSEM. ^aSubstance use phenotypes were entered and tested separately to avoid multicollinearity amongst them. Each row represents genetic correlations with COVID-19 hospitalization from one model. The multiple rows indicate the separate models run substituting each substance use phenotype (listed in the first column). The model was COVID hospitalization = CUD + substance use phenotype + BMI + Educational Attainment + Forced Expiration + Fasting Glucose + ADHD + Risk-taking + error. The original GWAS accounted for standard GWAS covariates (age, sex, genetic principal components, etc). **Bold*** represents $p < .05$. CUD = Cannabis Use Disorder, Cannabis Use = any lifetime cannabis use, CPD = Cigarettes per day, Age Smoke = Age of smoking initiation, Ever Smoke = Ever smoking tobacco, EA = educational attainment, , BMI = body mass index, FEV = 1 second forced expiration volume, Fast Gluc = fasting glucose, ADHD = attention deficit hyperactivity disorder, Risk = Risk-taking.

Supplemental Table S2. COVID-19 Genetic Correlations When Accounting for Potential Confounding Variables that are diagnostic indices of chronic conditions. We estimated the genetic correlation between CUD and COVID-19 hospitalization, while accounting for the same substance use phenotypes, educational attainment (EDU), BMI, Townsend Deprivation Index (TDI) and impulsivity (risk-taking and ADHD) GWAS but instead of FEV (1-second Forced Expiratory Volume), we included COPD as a covariate and instead of Fasting Glucose, we included GWAS summary data for Type 2 Diabetes and Hypertension.

Substance Use Phenotype	β CUD	β Substance Use Phenotype [#]	β EDU	β COPD	β Hypertension	β BMI	β T2D	β TDI	β Risk	β ADHD
Cannabis Use	<i>0.502</i>	-0.266	0.028	0.003	0.311	<i>0.186</i>	0.180	0.011	0.015	-0.244
CPD	0.378*	-0.094	<i>-0.154</i>	0.010	0.342	0.204*	0.222	-0.067	-0.004	-0.263
Age Smoke	0.390*	0.096	<i>-0.189</i>	0.004	0.313	0.200*	<i>0.206</i>	0.032	-0.066	-0.246
Smoking Cessation	0.377*	-0.064	-0.136	0.010*	0.271	<i>0.204</i>	0.196	-0.099	-0.016	-0.245
Ever Smoke	0.456*	-0.207	-0.150	0.005	0.354	0.205*	0.198	-0.043	-0.005	-0.239
Problematic Alcohol Use	<i>0.308</i>	0.147	<i>-0.177</i>	0.004	0.288	0.210*	<i>0.217</i>	-0.107	-0.017	-0.268

Note. Standardized beta estimates for Cannabis Use Disorder (CUD) and substance use phenotypes were taken from a multiple regression parameterized in gSEM. [#]Substance use phenotypes were entered and tested separately to avoid multicollinearity amongst them. Each row represents genetic correlations with COVID-19 hospitalization from one model. The multiple rows indicate the separate models run substituting each substance use phenotype (listed in the first column). The model was COVID hospitalization = CUD + substance use phenotype + BMI + Educational Attainment + COPD + Hypertension + BMI + Diabetes + ADHD + Risk-taking + error. The original GWAS accounted for standard GWAS covariates (age, sex, genetic principal components, etc). **Bold*** represents $p < .05$. *Italics* represents marginal significance at .10. CUD = Cannabis Use Disorder, Cannabis Use = any lifetime cannabis use, CPD = Cigarettes per day, Age Smoke = Age of smoking initiation, Ever Smoke = Ever smoking tobacco, EDU = educational attainment, TDI = Townsend deprivation index, BMI = body mass index, ADHD = attention deficit hyperactivity disorder, Risk = Risk-taking, COPD= Chronic Obstructive Pulmonary Disease; T2D=Type 2 Diabetes.



Supplemental Figure S1. Expanded correlation matrix of traits, including disease and dimensional traits, visualized as a heat map. COVID-19 Hosp = COVID-19 hospitalization (Variable COVIDB2 from the COVID Host Genomics initiative (4)). TDI = Townsend Deprivation Index, EA = Education attainment, BMI = Body Mass Index. FEV = Forced Expiration Volume for 1 second, Fast Gluc = Fasting Glucose, Age Smoke = Age of smoking initiation. RT=Risk-taking. COPD = Chronic Obstructive Pulmonary Disease **=Bonferroni significant for all test run.