Comparing the effects of cannabis and tobacco use on physical health using a co-twin control design

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**Conflict of Interest Declaration**

None.

**Abstract**

**Aims.** Prior research on the influence of cannabis use on anthropometrics, cardiovascular and pulmonary functioning, and other indicators of physical health has reported mixed results. Therefore, we examined whether cannabis use (indexed by frequency of use) is associated with physical health outcomes phenotypically and after controlling for shared genetic and environmental factors via a longitudinal co-twin control design.

**Design.** We tested the phenotypic associations of adolescent, young adult, and adult cannabis frequency with adult physical health outcomes while controlling for tobacco frequency, sex, and SES. Next, multilevel models were used to test these associations between- and within-twin pairs.

**Setting.** United States.

**Participants.** Participants include approximately 677 twins (308 twin pairs) born between 1979-1990 across three assessment waves during adolescence, young adulthood, and adulthood.

**Measurements.** Cannabis and tobacco frequency were quantified by number of days used in the past month. Physical health was quantified by objective and subjective measures while SES was quantified by a measure of financial distress.

**Findings.** At the phenotypic level, adult cannabis use was associated with lower resting heart rate (HR; β=-0.221 (-0.320, -0.121), *p*=.000). Young adult cannabis frequency was associated with a lower adult BMI, only among MZ twins (-0.112 (-0.183, -0.041), adjusted *p*=.050). Several associations between adult cannabis use and physical health at the within-twin level were significant, including lower BMI (β=-0.154 (-0.248, -0.061), adjusted *p*=.023), smaller waist circumference (β=-0.403 (-0.633, -0.173), adjusted *p*=.023), lower resting HR (β=-0.345 (-0.553, -0.136), adjusted *p*=.023), and lower FEV1/FVC (β=-0.149 (-0.244, -0.054), adjusted *p*=.050). In contrast, tobacco frequency was consistently associated with poorer physical health outcomes (e.g., higher resting HR (phenotypic: β=0.186 (0.096, 0.276), adjusted *p*=.024; within-twin: β=0.147 (0.058, 0.235), adjusted *p*=.020).

**Conclusions.** Contrary to tobacco frequency, we found little support for cannabis use causing poorer physical health outcomes.

**INTRODUCTION**

 Unlike tobacco, there are disparate findings about whether cannabis negatively affects physical health. Tobacco use has numerous negative impacts on health, including a strong link with lung cancer and chronic obstructive pulmonary diseases (COPDs)(1). The consequences of cannabis use on physical health are not well understood, specifically, if and how cannabis use influences body mass index (BMI), cardiovascular function, pulmonary/respiratory function, and other indicators of physical health. Although cannabis and tobacco smoke have some similarities regarding chemical compositions, like carcinogens(2), there are differences in the main psychoactive compounds and how each substance is smoked(3); thus, it is unknown whether cannabis affects physical health in similar ways as tobacco.

 There is inconsistent evidence regarding the long-term effects of cannabis on BMI. Some studies have reported no association between cannabis use and BMI(4-7), while other cross-sectional studies have found a positive association between cannabis use and BMI(8, 9), abdominal fat(10), and metabolic syndrome(11). However, the most consistent evidence has been a negative association between cannabis use and BMI when comparing users and non-users(12-14) and when examining a dose-dependent association(15-18). Cannabis use is also associated with other factors that are commonly associated with lower BMI including lower rates and risk factors of diabetes(14, 19, 20) and cardiometabolic syndrome diagnoses(17, 21).

 The long-term effects of cannabis use on cardiovascular health are unclear. One experimental study reported associations between higher saliva THC levels and increased heart rate (HR)(22). Case reports have also been published on rare cardiovascular deaths among young adults who recently used(23)(24). One study found that HR variability significantly increased among those who tested positive for THC compared to controls(25). Research on the impact of cannabis use on blood pressure (BP), another indicator of cardiovascular health, is currently inconclusive. One study of over 12,000 adults, found that recently active cannabis users had higher systolic BP compared to non-users and a dose-dependent association between past 30-day use and systolic BP(26). Contrary to the previous study, two studies reported that greater cannabis use is associated with decreases in systolic/diastolic BP(16, 17).

Pulmonary/respiratory function is another area of physical health with conflicting results regarding the association with cannabis use. A systematic review of experimental studies on short-term cannabis exposure reported an increase in forced expiratory volume in 1 second (FEV1; total amount of air exhaled in 1-second) by 0.15-0.25 L(27). Other studies have found a positive dose-dependent association with cannabis

joint-years and elevated forced vital capacity (FVC; total amount of air exhaled forcefully)(16, 28). Other studies have reported that cannabis use is associated with reduction in FEV1 and FEV1/FVC ratio; however, the association was negligible after controlling for tobacco use(29-31). A recent review found that cannabis smoking is not associated with measures of pulmonary function(2). Although long-term cannabis use is associated with increased cough, phlegm, and wheezing(27), there is inconsistent evidence whether long-term use is associated with changes in FEV1, FVC, or FEV1/FVC.

 The literature on associations between cannabis use and physical health is inconsistent. To clarify the role of cannabis use on physical health, we used a co-twin control design, which controls for genetic and environmental factors shared by members of a family, allowing us to conduct a controlled natural experiment. Monozygotic (MZ) twins share 100% of their genetic makeup and shared environmental factors (e.g., grew up in the same household) and dizygotic (DZ) twins share 50% of their genetic makeup and 100% of shared environmental factors. By comparing twins who are discordant for their cannabis use, we can make stronger inferences about the effect of cannabis use on physical health.

If within-twin pair effects are significant across MZ and DZ pairs and are not attenuated relative to the phenotypic effect, then the observed effect is not due to familial confounds (i.e., supports a causal association). If the DZ within-twin pair effect is about ½ the magnitude of the phenotypic effect and is negligible among MZ twins, this suggests complete confounding by familial factors (i.e., does not support a causal association). If the DZ within-twin pair effect is about ¾the magnitude of the phenotypic effect and is about ¼ the magnitude among MZ twins, this suggests some confounding by familial factors (i.e., partial support for a causal association). Effects only present within MZ twin pairs suggests that the genetic and environmental correlations, from bivariate biometric twin models, may be in the opposite direction, which would yield non-significant within- and DZ twin pair effects. Analyses were not pre-registered, and results should be considered exploratory.

**METHODS**

**Participants**

Participants are part of an ongoing study, the Colorado Adoption/Twin Study of Lifespan behavioral development and cognitive aging (CATSLife)(32) which includes twins from the foundational Longitudinal Twin Study (LTS), examining cognitive, emotional, and behavioral development(33). The original LTS sample consists of same-sex twins assessed from infancy to adulthood, totaling 439 twin pairs (N=878). The CATSlife study collected data from 677 individual LTS twins (N=308 twin pairs, 164 MZ twin pairs, 144 DZ twin pairs) with data from the adult assessment and the sample size ranges for each analysis depending on whether data is also present from the adolescent and/or young adult assessment. Missing data for outcome variables ranged from 0%-7%. Consistent with the race/ethnic distribution at the time of recruitment, the sample is 53.9% females and 91.6% Caucasian (including 9.7% Hispanic/Latinx), 1.3% American Indian/Alaska Native, 0.3% Native Hawaiian/Pacific Islander, 5.6% multiracial, and 1.2% unknown/not reported(32, 33). During adolescence, young adulthood, and adulthood approximately 12, 47, and 62 participants, respectively, endorse near daily cannabis use. Around 60% of the sample continues to reside in Colorado. Assessments for the project occurred between 2015-2019 after recreational cannabis was legalized in Colorado. Due to recreational cannabis legalization, past month prevalence rates of cannabis, alcohol, and tobacco use are higher than the national average(34), but consistent with Colorado state averages(34). A more detailed description of the participant characteristics and total N for each measure are included in Tables 1 and 2.

 The Institutional Review Board at the University of Colorado Boulder approved all study protocols and procedures. During adolescence, participant assent and parental consent were obtained. Once participants turned 18 years old, participant consent was obtained.

**Measures**

*Socioeconomic Status (SES).*

 SES was determined by the Incharge Financial Distress/Financial Well-Being Scale which consists of 8 items about levels of stress and worry over their current financial situation. Response options range from 1 (e.g., overwhelming stress about finances) to 10 (e.g., no stress about finances) which were reverse coded. The mean of all the questions was used in analyses(35, 36).

*Substance use*.

 Participants were asked the number of days that cannabis and tobacco were used in the past six months during adolescent and young adult assessments(37) and in the past month during the adult assessment(38). Participants who denied using tobacco or cannabis were given a zero. To ease the interpretation of results, we divided the cannabis and tobacco variables from adolescence and young adulthood by 6. A one-unit increase corresponds to an increase of one day/month of use.

*Physical health.*

*Objective measures of physical health***.** Research staff administered physical health functioning measures following PhenX Toolkit standard protocols(38) and only collected health data at the adult measurement wave via the CATSLife assessment (M=29.30 years). Additional details about objective measures of physical health are included in the supplemental materials.

 *Anthropometrics.* Staff measured height/weight using a balance beam scale with a height rod (ABCO Health-o-meter) and waist/hip circumference using a tape measure in centimeters.

 *Cardiovascular function*. BP and HR were measured three times at one-minute intervals using a digital BP monitor (Omron IntelliSense machine HEM-907XL). The median was used as the outcome.

 *Pulmonary function*. Pulmonary function was assessed using a spirometer (NDD EasyOne Plus Frontline Spirometer) via three trials at one-minute intervals. Median score (in liters) was used for forced vital capacity (FVC), forced expiratory volume in 1-second (FEV1), and FEV1/FVC ratio. Forced vital capacity (FVC) is the total air exhaled, while forced expiratory volume in 1-second (FEV1) is the total air exhaled in the first second. FEV1/FVC ratio represents the proportion of vital capacity exhaled in the first second.

 *Grip Strength*. A hand-held digital dynamometer (Jamar Smart Hand Dynamometer) measured hand grip strength via three trials completed in 20-second intervals. The highest number achieved across the trials is the outcome variable in pounds.

*Self-reported measures of physical health.* Participants completed questions regarding frequency of chronic pain, gum disease, nausea, weight problems (i.e., large changes in weight), difficulty breathing, skin problems, rapid HR, headaches, and injuries. Response options are 0=never to 5=daily. All self-reported measures were previously developed for the Colorado Adoption Project(39, 40) except for the question about frequency of gum disease which was adapted from the AddHealth study(41). One question developed for the CATSLife study asked if participants exercised in the past 24 hours, and if so, for how long (minutes)(32). Participants were given a zero if they denied exercising in the past 24 hours.

 *Diet/nutrition.* Three questions each were added together to create two separate variables for healthy and unhealthy diet. These questions asked about frequency of consuming healthy (i.e. fruit/vegetables/leafy greens) and unhealthy food (i.e. french fries, doughnuts/muffins/sweet rolls, and cookies/cake/pie/brownies) in the past 30 days. Response options ranged from 0=never to 9=5 times/day. Although all questions were not included in the assessment, these questions were taken from the Nutrition and Dietary Supplement of the PhenX Toolkit(38), which used the National Cancer Institute’s Five-Factor Screener(42). There was one question about frequency of fast food consumption in the past seven days (response options range from 0=0 to 7=>20) which was taken from the AddHealth study(41).

**Analytic Procedures**

 We estimated regression and multilevel models using Mplus 8(43). Adolescent, young adult, and adult cannabis frequency were separately run as predictors with each adult physical health variable as the outcome. For each analysis, we estimated the associations with and without controlling for the parallel measure of tobacco frequency. Results controlling for tobacco frequency were included in the main paper because some significant associations between cannabis use and physical health became negligible after controlling for tobacco frequency; results without controlling for tobacco frequency are included in the supplemental material. Sex was controlled for in all models (grand-mean centered). Phenotypic models controlled for financial distress (grand-mean centered). We only report unstandardized coefficients because standardized coefficients are not recommended for multilevel models(44). To correct for multiple testing, we used the p.adjust function from the stats package in R which applies the Hochberg’s correction (i.e., provides adjusted p-values)(45). Multiple testing correction was applied as a family-wise correction to each drug category and at each wave. Only effects that are significant after correcting for multiple testing are reported. Visual inspection of scatterplots consisting of cannabis frequency and continuous outcomes suggest that these associations are linear. This is the first study (in the searchable literature) to examine phenotypic and between- and within-twin pair associations between cannabis use and physical health. Thus, our aims being exploratory guided our decision to examine all potential associations between cannabis use and physical health across all analyses. to confirm co-twin control results

*Model 1: Phenotypic Associations.*Phenotypic associations were estimated between cannabis exposure during adolescence, young adulthood, and adulthood and measures of adult physical health. The “type=complex” option was used for phenotypic analyses because it accounts for the non-independence of twin pairs by using a sandwich estimator, providing the same estimates as a standard regression but corrects the standard errors for non-independence.

*Model 2: Within-Family Exposure.*We estimated multilevel regression models between cannabis frequency and physical health between- (first-level) and within-families (second-level) while controlling for the within-family effects of tobacco frequency. Linear and logistic multilevel models were conducted for continuous and categorical outcomes, respectively. Cannabis frequency was averaged in twin pairs, which was used to estimate between-family effects. Each twin’s deviation from the twin pair average of cannabis and tobacco frequency were used to estimate twin-specific risk (i.e., within-family effect). This within-family index assesses the effect of differential exposure in each family, which takes into account the unmeasured shared environmental and genetic factors that make twins alike(46). Random between-family intercepts were included for health outcomes while fixed effects were estimated for each substance use variable. Lastly, we included an interaction term for the within-family effect by zygosity. We calculated MZ within-family effects, DZ within-family effects, and the average within-family effect for both MZ and DZ twins(47). We grand-mean centered all independent variables, except for individual within-family effects which were centered within each twin pair. More details about model 2 is included in the supplemental material.

**RESULTS**

**Model 1: Phenotypic Associations**

 Table 3 displays the associations between cannabis frequency and measures of physical health while controlling for sex, SES, and tobacco frequency. Adolescent and young adult cannabis frequency was not associated with adult physical health outcomes. Increases in adult cannabis frequency were associated with decreases in HR (β=-0.221, adjusted *p*<.001).

 Adolescent and young adult tobacco frequency were not associated with adult physical health outcomes. Adult tobacco frequency were associated with a higher resting HR, more frequent chronic pain, and eating fewer fruits/vegetables.

**Model 2: Within-Family Exposure**

 Table 4 presents the between-family and within-twin results for the associations between cannabis frequency and physical health outcomes while controlling for sex and tobacco frequency. There were no significant effects between adolescent and young adult cannabis frequency with adult physical health outcomes. There was one exception, young adult cannabis frequency was associated with BMI among MZ twins only; a one-day/month increase in cannabis use, relative to a participant’s co-twin, was associated with a lower BMI score by 0.112 (adjusted *p*=.050).

 Consistent with the findings from young adult cannabis frequency, an increase of one-day/month of adult cannabis use was associated with a 0.154 lower BMI (adjusted *p*=.023), 0.403cm smaller waist circumference (adjusted *p*=.023), and 0.345 beats/minute lower resting HR (adjusted *p*=.023). These results were only present among the MZ twins. A one-day/month increase of adult cannabis use was associated with a decrease in 0.149 percentage points in FEV1/FVC (adjusted *p*=.050) at the total within-twin level.

 Across all time points, an increase in tobacco use was associated with a greater frequency of rapid HR. At various time points, greater tobacco frequency was associated with a higher resting HR, eating fewer fruits/vegetables, and greater frequency of chronic pain, problems breathing, loss of appetite, weight problems, gum disease, and consuming fast food.

To examine whether associations between cannabis use with BMI, waist circumference, resting HR, and FEV1/FVC are specific to a particular age or from persistent use, examined whether these outcomes were also associated with lifetime cannabis and tobacco frequency using a co-twin control design. We created average cannabis and tobacco frequency variables across all time points (i.e. lifetime cannabis and tobacco frequency) (see (48)). We found that an increase of one-day/month of lifetime cannabis use was associated with a 0.164 decrease in BMI at the total within-twin level (95% confidence interval: -0.278--0.050, *p*=.005) and a 0.197 decrease in BMI among MZ twins (-0.328--0.066, *p*=.003). This effect was not present for DZ twins (*β*=-0.119 (-0.303-0.066), *p*=.209) and it was not significant at the total within-twin level for tobacco (*β*=-0.027 (-0.219-0.165), *p*=.782). Only among MZ twins, an increase of one-day/month in lifetime cannabis frequency was associated with a 0.539cm smaller waist circumference (-0.874--0.203, *p*=.002) and 0.351 beats/minute lower resting HR (-0.698--0.003, *p*=.048). These associations were not significant at the within-twin level (waist: *β*=-0.226 (-0.568-0.036), *p*=.084, HR: *β*=-0.233 (-0.489-0.022) *p*=.073), among DZ twins (waist: *β*=0.009 (-0.491-0.509), *p*=.972, HR: β=-0.105 (-0.476-0.266), *p*=.579), or at within-twin level of lifetime tobacco frequency (waist: *β*=0.136 (-0.069-0.340), *p*=.195, HR: *β*=0.180 (-0.002-0.363), *p*=.053). Lastly, the association between cannabis frequency and FEV1/FVC was not significant at the within-twin level (*β*=-0.120 (-0.303, 0.063), *p*=.198), among MZ twins (*β*=-0.088 (-0.237-0.061), *p*=.245), among DZ twins (*β*=-0.205 (-0.541-0.132), *p*=.234), and for lifetime tobacco frequency (*β*=-0.081 (-0.249-0.086), *p*=.339).

**DISCUSSION**

 This study estimated the effect of cannabis frequency across adolescence to adulthood on adult physical health outcomes among a sample who primarily use cannabis casually using a co-twin control design. Adolescent cannabis use was not associated with adult physical health at any level of analyses. At the within-twin level, young adult cannabis use was associated with a lower BMI, but only among MZ twins. Adult cannabis exposure was associated with a lower HR and more frequent loss of appetite at the phenotypic level. There were no significant between-family effects for adult cannabis exposure. Only among MZ twins, adult cannabis frequency was associated with a lower BMI, a smaller waist circumference, and lower HR. Further, these effects were more pronounced when aggregating cannabis frequency across ages. At the total within-twin level, greater adult cannabis use was associated with a lower FEV1/FVC ratio. Thus, within-family comparisons provided some support for cannabis use being associated with physical health, after accounting for familial confounds. Contrary to cannabis, tobacco use was associated with poorer physical health outcomes, consistent with prior research about the health effects of tobacco use(49, 50). Although these effects suggest associations between tobacco use and poorer physical health, the physical health outcomes may be within the range that is considered normal.

There was an unexpected pattern of findings for BMI and hip/waist circumference, wherein there were positive genetic correlations and negative non-shared environmental correlations with adult cannabis frequency. These findings suggest that genetic factors related to cannabis use may be associated with increased BMI and waist circumference, but some environmental factors related to cannabis use may be associated with decreased BMI and waist circumference. It is possible that some genetic factors may drive drug use and other consummatory behaviors (e.g., via self-regulation), but some environmental factors driving cannabis use may be associated with healthy behaviors. A more interesting possibility is that while genetic factors may predispose to both cannabis use and higher BMI and hip/waist circumference, cannabis use itself results in lower values. It is also possible that individuals with a lower BMI may be more likely to use cannabis. These contrary directions of influence could result in our observations of a within pair association of cannabis use with lower BMI and waist circumference values for MZ pairs, but no significant association at the total within-twin level or within DZ pairs.

Most of the extant literature suggests that cannabis use is associated with a lower BMI(12-17). Our results are consistent with the literature, and in addition, cannabis use was associated with a smaller waist circumference. Results from this study did not provide any clues to why those who use cannabis have a lower BMI. Specifically, there were no within-twin pair associations between cannabis exposure with healthy or unhealthy diet, exercise, nausea, or loss of appetite. Acute intoxication from cannabis use is known to stimulate appetite, also known as the “munchies”(51). Prior studies have reported increased caloric intake acutely(52) and self-reported poorer diets among users compared to non-users but without resulting in a higher BMI(53). These results suggest that adults may develop tolerance, through continued cannabis use, to the effects of cannabis use on appetite, known as the “munchies”.

 Our findings that cannabis use in adulthood was associated with lower HR, but not BP, reveal new information about associations between cannabis and cardiovascular function. Our results are inconsistent with previous research reporting increases in HR acutely(22) and long-term(25). Other factors, like a lower BMI, may contribute to the association observed between cannabis and lower HR (e.g., (54)). We also found that greater tobacco frequency was associated with a higher HR, consistent with a recent meta-analysis(55). We did not find associations between cannabis or tobacco frequency with BP. Previous research has reported higher systolic BP among those who use cannabis compared to non-using controls(26) while negative associations have been found when examining dose-dependent associations(16, 17). A recent meta-analysis did not observe associations between tobacco and BP(50).

 Higher adult cannabis frequency was associated with lower FEV1/FVC. This is consistent with some of the literature suggesting that FEV1/FVC is reduced among those who use cannabis, however, these studies also found that after controlling for tobacco use, the association between cannabis use and FEV1/FVC were no longer significant(29-31). Although not statistically significant, we did see an increase in FVC, which may contribute to the lower FEV1/FVC ratio. Surprisingly, tobacco use was not associated with lower FEV1/FVC, however, this may be related to the few people using tobacco products (N=119 endorsed past month tobacco use at the adult assessment wave) or our participants may be too young to show any noticeable effects of tobacco on pulmonary function (e.g., (56)).

Although this study has notable strengths, there are several limitations worth considering. Since the sample was primarily Caucasian, results may not generalize to ethnically/racially diverse individuals. However, similar results have been demonstrated among more ethnic and racially diverse individuals (e.g., (18)). Prevalence of obesity in this sample (21%) closely resembles the state of Colorado prevalence of obesity (22%)(34) while the national prevalence rates are around 40% among this age range. Although this sample may be healthier than the national average, similar results have been demonstrated between cannabis use and BMI in studies conducted in other states(12-20). In addition, 2%, 7%, and 9% of adolescent, young adult, and adult participants, respectively, endorsed daily cannabis use, thus results may not apply to individuals who use cannabis daily. The study did not collect detailed information on potency of cannabis products used or methods of cannabis ingestion. Thus, we were not able to examine whether different potency or methods of cannabis consumption affect health differentially. The participant age range is 28-35; therefore, most participants have not developed more serious complications from tobacco or cannabis use like COPD. Although numerous studies have documented negative effects of tobacco and cannabis use on health in early adulthood(16, 31, 57). However, this may be the reason for the small effects observed in the associations between cannabis/tobacco use with physical health. Lastly, frequency patterns of cannabis and tobacco use differ which is one possible reason that we did not observe associations between cannabis use and poorer physical health. Adults who use tobacco report using more frequently compared to adults who use cannabis(58).

This study found no evidence of an association between adolescent cannabis frequency and adult physical health among a normative sample of individuals who use cannabis. We found associations between young adult cannabis frequency with a lower BMI and adult cannabis frequency with a lower BMI, smaller waist circumference, lower HR, and lower FEV1/FVC ratio. We cannot determine whether these associations are causal, and the associations had small effect sizes. Results contrast markedly with those for tobacco use which was consistently associated with worse physical health. In a normative twin sample, we found little evidence of associations between frequency of cannabis use, either as adolescents or adults, and poor adult physical health. In general, these results do not support an association between using cannabis once a week (the mean cannabis frequency of the sample in adulthood) and detrimental physical health effects of individuals aged 20-35.

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| Table 1. Descriptive statistics of substance use  |
| Variable  | Adolescence | Young Adulthood | Adulthood |
|  | N |  M (SD) | N | M (SD) | N | M (SD) |
| Age (years) | 641 | 17.24 (0.63) | 640 | 22.79 (1.27) | 677 | 29.30 (1.24) |
| Cannabis  |  |  |  |  |  |  |
|  Frequency past month (days) | 640 | 1.15 (4.51)  | 639 | 3.15 (8.06) | 671 | 3.94 (8.82) |
|  Endorsed use in past six months (%, past month for adulthood) | 640 | 23.44 | 639 | 31.77 | 671 | 28.17 |
| Tobacco |  |  |  |  |  |  |
|  Frequency past month (days) | 624 | 3.38 (8.85) | 639 | 5.96 (11.09) | 672 | 3.97 (9.63) |
|  Endorsed use in past six months (%, past month for adulthood) | 624 | 25.80 | 639 | 38.18 | 672 | 17.71 |
| Alcohol  |  |  |  |  |  |  |
|  Frequency past month (days) | 637 | 0.97 (2.16) | 640 | 5.06 (6.26) | 672 | 7.79 (7.73) |
|  Endorsed use in past six months (%, past month for adulthood) | 637 | 54.95 | 640 | 91.72 | 672 | 81.15 |
| Other drugs |   |  |   |  |  |  |
|  Frequency past month (days) | 639 | 0.30 (2.18) | 637 | 0.79 (3.96) | 671 | 0.36 (2.37) |
|  Endorsed use in past six months (%, past month for adulthood) | 639 | 10.64 | 637 | 19.47 | 671 | 6.71 |
| Note: M = mean and SD=standard deviation.  |

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| Table 2. Descriptive Statistics of adult physical health outcomes |
| Variable | N | Mean/Percent | SD | Range |
| Age | 677 | 29.30 yrs | 1.24 | 28.05-34.55 yrs |
| BMI  | 649 | 26.34 kg/m2 | 5.96 | 16.31-54.93 kg/m2 |
| Waist circumference | 649 | 90.50 cm | 15.99 | 27.00-163.00 cm |
| Hips circumference | 649 | 104.43 cm | 11.85 | 37.00-159.50 cm |
| Systolic BP | 651 | 112.60 mmHG | 12.32 | 78.00-148.00 mmHG |
| Diastolic BP | 651 | 68.74 mmHG | 8.81 | 43.00-101.00 mmHG |
| Resting HR | 651 | 70.34 beats/min | 11.43 | 39.00-108.00 beats/min |
| FVC | 625 | 4.56 L | 0.99 | 0.40-7.40 L |
| FEV1 | 625 | 3.63 L | 0.77 | 0.30-6.40 L |
| FCV/FEV (%) | 625 | 80.09% | 7.42 | 35.48-97.44% |
| Left hand grip | 646 | 78.80 | 24.75 | 20.90-154.50 |
| Right hand grip  | 648 | 87.49 | 26.94 | 32.70-187.70 |
| Chronic pain (%) | 670 | 62.54% | - | - |
| Gum disease (%) | 670 | 17.46% | - | - |
| Loss of appetite (%) | 670 | 29.56% | - | - |
| Nausea (%) | 670 | 57.01% | - | - |
| Weight problems (%) | 670 | 21.64% | - | - |
| Problems breathing (%) | 670 | 30.00% | - | - |
| Skin problems (%) | 670 | 28.81% | - | - |
| Rapid HR (%) | 670 | 37.31% | - | - |
| Headaches (%) | 670 | 75.22% | - | - |
| Injuries (%) | 670 | 58.21% | - | - |
| Unhealthy diet | 664 | 3.77 | 1.93 | 0.00-16.00 |
| Healthy diet | 661 | 9.69 | 4.54 | 0.00-24.00 |
| Fast food | 667 | 1.21 | 1.20 | 0.00-7.00 |
| Exercise engagement in past 24 hours (mins.) | 649 | 21.47 mins. | 46.83 | 0.00-480.00 mins. |
| Note: SD = standard deviation, BMI = Body mass index, BP = blood pressure, HR = heart rate, FVC = forced vital capacity, and FEV1= forced expiratory volume in one second. Chronic pain, gum disease, loss of appetite, nausea, weight problems, problems breathing, skin problems, rapid HR, headaches, and injuries are calculated as the percent who reported >1 (i.e. less than once a year, about once year, about once a month, once a week, or daily). |

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| Table 3. Unstandardized coefficients for the phenotypic analyses of the association between cannabis frequency with physical health |
|  | **Cannabis effect****(95% CI)** | ***p*-value** | **Tobacco effect****(95% CI)** | ***p*-value** |
| **Adolescent substance Use** |  |  |
|  BMI | -0.117 | .036 | 0.087 | .039 |
|  Waist circumference | -0.109 | .419 | 0.221 | .034 |
|  Hip circumference | -0.206 | .045 | 0.105 | .207 |
|  Systolic BP  | 0.025 | .792 | 0.037 | .542 |
|  Diastolic BP | -0.008 | .916 | 0.080 | .081 |
|  Resting HR | -0.085 | .547 | 0.163 | .012 |
|  FVC | 0.005 | .712 | -0.001 | .880 |
|  FEV1 | 0.004 | .681 | 0.001 | .651 |
|  FEV1/FVC (%) | 0.078 | .450 | 0.046 | .238 |
|  Left hand grip | -0.023 | .891 | 0.141 | .161 |
|  Right hand grip  | 0.072 | .704 | 0.065 | .590 |
|  Chronic pain  | -0.006 | .633 | 0.004 | .460 |
|  Gum disease  | -0.017 | .312 | 0.014 | .040 |
|  Loss of appetite  | 0.003 | .712 | 0.004 | .444 |
|  Nausea  | -0.055 | .313 | 0.034 | .511 |
|  Weight problems | 0.000 | .984 | 0.014 | .024 |
|  Problems breathing | 0.000 | .993 | 0.007 | .296 |
|  Skin problems | 0.010 | .459 | 0.001 | .919 |
|  Rapid HR | 0.004 | .720 | 0.013 | .043 |
|  Headaches | -0.001 | .959 | -0.001 | .919 |
|  Injuries | -0.005 | .729 | -0.003 | .609 |
|  Unhealthy diet | 0.008 | .614 | -0.006 | .511 |
|  Healthy diet | 0.038 | .310 | 0.005 | .859 |
|  Fast food | -0.005 | .656 | 0.004 | .496 |
|  Exercise engagement  | -0.715 | .019 | -0.073 | .816 |
| **Young adult substance use** |  |  |
|  BMI | -0.047 | .132 | 0.056 | .036 |
|  Waist circumference | -0.016 | .727 | 0.114 | .013 |
|  Hip circumference | -0.060 | .299 | 0.066 | .188 |
|  Systolic BP  | 0.063 | .277 | -0.009 | .831 |
|  Diastolic BP | -0.034 | .490 | 0.072 | .038 |
|  Resting HR | -0.058 | .182 | 0.129 | .003 |
|  FVC | 0.008 | .057 | -0.001 | .702 |
|  FEV1 | 0.004 | .289 | -0.002 | .484 |
|  FEV1/FVC (%) | -0.032 | .466 | -0.016 | .564 |
|  Left hand grip | 0.138 | .150 | 0.079 | .296 |
|  Right hand grip  | 0.059 | .554 | 0.094 | .299 |
|  Chronic pain  | 0.003 | .587 | 0.009 | .039 |
|  Gum disease  | 0.000 | .998 | 0.008 | .135 |
|  Loss of appetite  | -0.010 | .158 | 0.015 | .006 |
|  Nausea  | -0.006 | .305 | 0.008 | .063 |
|  Weight problems | -0.002 | .812 | 0.014 | .007 |
|  Problems breathing | 0.000 | .980 | 0.013 | .010 |
|  Skin problems | 0.010 | .183 | -0.013 | .033 |
|  Rapid HR | 0.004 | .646 | 0.007 | .154 |
|  Headaches | -0.009 | .162 | 0.005 | .225 |
|  Injuries | 0.002 | .689 | 0.008 | .049 |
|  Unhealthy diet | 0.007 | .503 | -0.005 | .535 |
|  Healthy diet | 0.018 | .419 | -0.050 | .004 |
|  Fast food | -0.009 | .081 | 0.012 | .010 |
|  Exercise engagement  | -0.371 | .090 | 0.004 | .984 |
| **Adult substance use** |  |  |
|  BMI | -0.011 | .702 | -0.001 | .962 |
|  Waist circumference | -0.014 | .856 | 0.063 | .368 |
|  Hip circumference | -0.027 | .626 | -0.038 | .474 |
|  Systolic BP  | -0.011 | .836 | 0.012 | .804 |
|  Diastolic BP | -0.056 | .228 | 0.059 | .120 |
|  Resting HR | **-0.241** | **.000\*\*\*** | **0.163** | **.001\*** |
|  FVC | 0.008 | .039 | -0.001 | .852 |
|  FEV1 | 0.002 | .581 | -0.001 | .800 |
|  FEV1/FVC (%) | -0.079 | .057 | 0.003 | .925 |
|  Left hand grip | 0.146 | .081 | 0.030 | .727 |
|  Right hand grip  | 0.090 | .312 | 0.071 | .458 |
|  Chronic pain  | 0.003 | .613 | **0.015** | **.002\*** |
|  Gum disease  | -0.010 | .842 | 0.130 | .009 |
|  Loss of appetite  | 0.009 | .078 | 0.008 | .098 |
|  Nausea  | 0.004 | .439 | 0.011 | .021 |
|  Weight problems | 0.004 | .535 | 0.007 | .168 |
|  Problems breathing | 0.002 | .737 | 0.017 | .004 |
|  Skin problems | 0.004 | .514 | -0.008 | .175 |
|  Rapid HR | 0.005 | .381 | 0.012 | .031 |
|  Headaches | -0.010 | .068 | 0.009 | .068 |
|  Injuries | 0.003 | .594 | 0.006 | .274 |
|  Unhealthy diet | 0.006 | .653 | 0.000 | .989 |
|  Healthy diet | 0.017 | .408 | **-0.062** | **.000\*\*\*** |
|  Fast food | -0.002 | .703 | 0.010 | .036 |
|  Exercise engagement  | -0.172 | .420 | 0.102 | .711 |
| Note: Analyses controlled for sex and SES. BMI = Body mass index, BP = blood pressure, HR = heart rate, FVC = forced vital capacity, FEV1= forced expiratory volume in one second, exercise engagement = length of exercise in minutes over the past 24 hours. Asterisks indicate significance after correction for multiple testing. \* = adjusted *p* <.05, \*\* = adjusted *p* <.01, and \*\*\* = adjusted *p* <.001. Bold indicates significance remained after correction for multiple testing.  |

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| Table 4. Within- and between-family unstandardized regression coefficients for the association between cannabis frequency with physical health while controlling for tobacco frequency |
|  | **Cannabis Effect** | **Tobacco Effect** |
|  | **Total****(95% CI)** | **p-value** | **MZ****(95% CI)** | **p-value** | **DZ****(95% CI)** | **p-value** | **Between****(95% CI)** | **p-value** | **Total****(95% CI)** | **p-value** |
| **Adolescent Substance Use** |
|  BMI | -0.130 (-0.279 – 0.020) | .089 | -0.022 (-0.149 – 0.104) | .730 | -0.237 (-0.517 – 0.043) | .097 | -0.038 (-0.211 – 0.135) | .668 | 0.062 (-0.015 – 0.139) | .116 |
|  Waist circumference | -0.147 (-0.505 – 0.211)  | .421 | 0.029 (-0.387 – 0.444) | .892 | -0.322 (-0.907 – 0.262)  | .280 | 0.012 (-0.408 – 0.433)  | .954 | 0.208 (0.010 – 0.407) | .040 |
|  Hip circumference | -0.179 (-0.486 – 0.128)  | .253 | 0.003 (-0.327 – 0.333)  | .985 | -0.360 (-0.882 – 0.162)  | .176 | -0.134 (-0.451 – 0.184) | .408 | 0.086 (-0.085 – 0.256)  | .325 |
|  Systolic BP  | -0.148 (-0.362 – 0.065) | .173† | -0.362 (-0.676 – -0.048) | .024 | 0.066 (-0.225 – 0.356) | .657 | 0.115 (-0.144 – 0.375)  | .384 | 0.040 (-0.073 – 0.152)  | .489 |
|  Diastolic BP | 0.023 (-0.114 – 0.159)  | .746 | -0.104 (-0.239 – 0.031) | .133 | 0.149 (-0.086 – 0.384)  | .215 | -0.055 (-0.251 – 0.141) | .582 | 0.103 (0.018 – 0.188)  | .018 |
|  Resting HR | -0.014 (-0.305 – 0.278)  | .927 | 0.010 (-0.425 – 0.444) | .965 | -0.037 (-0.419 – 0.345)  | .849 | -0.125 (-0.552 – 0.302)  | .566 | 0.175 (0.048 – 0.303)  | .007 |
|  FVC | -0.001 (-0.015 – 0.013)  | .884 | 0.003 (-0.016 – 0.023)  | .731 | -0.006 (-0.025 – 0.014)  | .578 | 0.024 (0.000 – 0.048) | .046 | 0.000 (-0.006 – 0.006)  | .916 |
|  FEV1 | 0.002 (-0.011 – 0.014) | .802 | 0.003 (-0.014 – 0.020)  | .746 | 0.000 (-0.017 – 0.017)  | .977 | 0.014 (-0.008 – 0.035)  | .217 | 0.002 (-0.003 – 0.007) | .380 |
|  FEV1/FVC (%) | 0.049 (-0.061 – 0.159)  | .380 | -0.002 (-0.160 – 0.157)  | .984 | 0.101 (-0.044 – 0.246)  | .174 | -0.125 (-0.263 – 0.013)  | .076 | 0.049 (-0.003 – 0.100)  | .063 |
|  Left Hand Grip | 0.018 (-0.375 – 0.411)  | .929 | 0.053 (-0.455 – 0.562)  | .837 | -0.018 (-0.619 – 0.583)  | .954 | 0.025 (-0.370 – 0.419)  | .902 | 0.066 (-0.109 – 0.241)  | .457 |
|  Right Hand Grip  | 0.112 (-0.298 – 0.522)  | .592 | 0.231 (-0.250 – 0.712)  | .347 | -0.008 (-0.668 – 0.652)  | .981 | 0.151 (-0.298 – 0.600)  | .510 | -0.002 (-0.203 – 0.198) | .982 |
|  Chronic pain  | 0.006 (-0.033 – 0.045)  | .752† | 0.059 (-0.001 – 0.120)  | .055 | -0.048 (-0.097 – 0.002)  | .059 | -0.015 (-0.065 – 0.036)  | .570 | 0.018 (-0.001 – 0.036)  | .058 |
|  Gum disease  | -0.060 (-0.128 – 0.009)  | .086 | -0.092 (-0.119 – 0.057)  | .046 | -0.026 (-0.124 – 0.072)  | .599 | -0.031 (-0.119 – 0.057)  | .495 | 0.038 (0.000 – 0.076)  | .049 |
|  Loss of appetite  | 0.011 (-0.045 – 0.067) | .695 | 0.002 (-0.079 – 0.082)  | .969 | 0.021 (-0.053 – 0.095)  | .583 | -0.012 (-0.081 – 0.056)  | .730 | 0.026 (-0.003 – 0.055)  | .077 |
|  Nausea  | -0.028 (-0.064 – 0.009)  | .135 | -0.028 (-0.068 – 0.013)  | .179 | -0.028 (-0.087 – 0.032)  | .361 | -0.026 (-0.082 – 0.030)  | .366 | 0.018 (-0.002 – 0.038)  | .084 |
|  Weight problems | 0.032 (-0.050 – 0.113)  | .451 | 0.042 (-0.096 – 0.180) | .552 | 0.021 (-0.060 – 0.102)  | .612 | -0.027 (-0.085 – 0.031)  | .355 | **0.048 (0.022 – 0.075)**  | **.000\*\*\*** |
|  Problems breathing | -0.019 (-0.067 – 0.029)  | .446 | 0.014 (-0.048 – 0.076)  | .656 | -0.052 (-0.125 – 0.021)  | .162 | 0.009 (-0.061 – 0.080)  | .799 | 0.034 (0.008 – 0.060)  | .012 |
|  Skin problems | 0.017 (-0.031 – 0.066)  | .486 | 0.013 (-0.034 – 0.061) | .577 | 0.021 (-0.061 – 0.103)  | .610 | 0.013 (-0.072 – 0.098)  | .762 | 0.012 (-0.016 – 0.041) | .396 |
|  Rapid HR | -0.022 (-0.059 – 0.015)  | .240 | 0.012 (-0.028 – 0.052) | .555 | -0.056 (-0.117 – 0.005)  | .072 | 0.019 (-0.061 – 0.099)  | .638 | **0.037 (0.013 – 0.061)**  | **.002\*** |
|  Headaches | 0.038 (-0.011 – 0.086)  | .127 | 0.071 (-0.009 – 0.150)  | .081 | 0.004 (-0.050 – 0.059)  | .878 | -0.027 (-0.099 – 0.045)  | .455 | 0.016 (-0.010 – 0.041)  | .235 |
|  Injuries | -0.012 (-0.060 – 0.035)  | .612 | 0.012 (-0.073 – 0.097)  | .786 | -0.037 (-0.079 – 0.006)  | .088 | -0.002 (-0.053 – 0.049)  | .938 | 0.001 (-0.019 – 0.021)  | .928 |
|  Unhealthy diet | -0.034 (-0.102 – 0035)  | .332 | -0.007 (-0.104 – 0.091)  | .893 | -0.061 (-0.160 – 0.038)  | .226 | 0.039 (-0.017 – 0.094)  | .172 | -0.008 (-0.029 – 0.013)  | .461 |
|  Healthy diet | 0.046 (-0.042 – 0.135)  | .304 | 0.092 (-0.045 – 0.229)  | .187 | 0.000 (-0.119 – 0.120)  | .997 | 0.054 (-0.041 – 0.148)  | .265 | -0.027 (-0.075 – 0.021)  | .276 |
|  Fast food | 0.003 (-0.072 – 0.077)  | .942 | -0.011 (-0.105 – 0.083)  | .822 | 0.016 (-0.094 – 0.126)  | .769 | -0.041 (-0.102 – 0.020)  | .184 | 0.030 (0.006 – 0.053)  | .015 |
|  Exercise engagement  | -0.239 (-0.942 – 0.464)  | .506 | 0.138 (-0.363 – 0.638) | .590 | -0.613 (-1.958 – 0.732)  | .372 | -1.163 (-2.251 – -0.076)  | .036 | 0.052 (-0.606 – 0.711)  | .876 |
| **Young Adult Substance Use** |
|  BMI | -0.086 (-0.153 - -0.018)  | .013 | **-0.112 (-0.183 – -0.041)**  | **.002\*** | -0.059 (-0.172 – 0.055)  | .312 | -0.005 (-0.089 – 0.079)  | .908 | 0.040 (-0.010 – 0.089)  | .118 |
|  Waist circumference | -0.145 (-0.367 – 0.078)  | .202 | -0.284 (-0.510 – -0.059)  | .014 | -0.004 (-0.384 – 0.377)  | .985 | 0.086 (-0.153 – 0.324)  | .481 | 0.143 (0.026 – 0.260) | .017 |
|  Hip circumference | -0.103 (-0.244 – 0.152) | .150 | -0.164 (-0.307 – -0.020) | .025 | -0.042 (-0.282 – 0.198)  | .732 | 0.002 (-0.148 – 0.152)  | .979 | 0.049 (-0.043 – 0.142) | .297 |
|  Systolic BP  | 0.154 (0.013 – 0.295)  | .033 | 0.070 (-0.117 – 0.257)  | .465 | 0.239 (0.026 – 0.453)  | .028 | 0.026 (-0.117 – 0.169)  | .720 | 0.007 (-0.075 – 0.088)  | .874 |
|  Diastolic BP | 0.054 (-0.070 – 0.179)  | .394 | -0.008 (-0.134 – 0.119)  | .905 | 0.117 (-0.097 – 0.330)  | .284 | -0.051 (-0.172 – 0.069)  | .404 | 0.080 (0.015 – 0.144)  | .015 |
|  Resting HR | -0.089 (-0.276 – 0.098) | .350 | -0.097 (-0.378 – 0.185)  | .501 | -0.081 (-0.329 – 0.166)  | .519 | -0.053 (-0.220 – 0.113) | .529 | 0.020 (0.007 – 0.033)  | .003 |
|  FVC | 0.000 (-0.006 – 0.007) | .915 | 0.003 (-0.005 – 0.010) | .498 | -0.002 (-0.013 – 0.009)  | .719 | 0.014 (0.005 – 0.024) | .004 | -0.001 (-0.005 – 0.004)  | .807 |
|  FEV1 | -0.002 (-0.010 – 0.006) | .606 | 0.003 (-0.004 – 0.010)  | .374 | -0.007 (-0.021 – 0.006)  | .301 | 0.008 (-0.002 – 0.018)  | .123 | -0.002 (-0.006 – 0.002)  | .404 |
|  FEV1/FVC (%) | -0.040 (-0.155 – 0.075)  | .493 | 0.014 (-0.083 – 0.110)  | .777 | -0.096 (-0.185 – 0.047)  | .372 | -0.069 (-0.185 – 0.047) | .243 | -0.032 (-0.079 – 0.015)  | .186 |
|  Left hand grip | 0.247 (0.026 – 0.468)  | .028 | 0.106 (-0.096 – 0.307)  | .303 | 0.391 (-0.010 – 0.792)  | .056 | 0.100 (-0.146 – 0.347)  | .425 | 0.053 (-0.089 – 0.195) | .467 |
|  Right hand grip  | 0.144 (-0.071 – 0.358)  | .189 | 0.094 (-0.181 – 0.369) | .503 | 0.193 (-0.140 – 0.526) | .256 | 0.045 (-0.218 – 0.308)  | .737 | 0.054 (-0.113 – 0.222) | .524 |
|  Chronic pain  | 0.024 (-0.017 – 0.065)  | .254 | 0.030 (-0.011 – 0.070)  | .154 | 0.018 (-0.054 – 0.091)  | .622 | 0.002 (-0.026 – 0.030)  | .896 | **0.024 (0.009 – 0.039)**  | **.002\*** |
|  Gum disease  | 0.038 (-0.010 – 0.086)  | .121 | 0.037 (-0.027 – 0.101)  | .257 | 0.039 (-0.030 – 0.108)  | .270 | -0.008 (-0.053 – 0.037)  | .716 | 0.030 (0.004 – 0.057)  | .025 |
|  Loss of appetite  | -0.019 (-0.059 – 0.021)  | .358 | -0.028 (-0.079 – 0.023) | .275 | -0.009 (-0.071 – 0.053)  | .770 | -0.017 (-0.051 – 0.017)  | .319 | **0.041 (0.021 – 0.062)**  | **.000\*\*\*** |
|  Nausea  | -0.012 (-0.043 – 0.018) | .431 | -0.008 (-0.044 – 0.027)  | .644 | -0.016 (-0.067 – 0.034)  | .520 | -0.010 (-0.038 – 0.018) | .474 | 0.022 (0.005 – 0.038)  | .010 |
|  Weight problems | -0.015 (-0.064 – 0.034) | .543 | -0.026 (-0.097 – 0.046) | .484 | -0.004 (-0.070 – 0.061)  | .894 | 0.008 (-0.031 – 0.046) | .686 | **0.038 (0.016 – 0.060)** | **.001\*** |
|  Problems breathing | 0.058 (0.020 – 0.096)  | .003† | 0.020 (-0.019 – 0.058)  | .316 | 0.099 (0.002 – 0.155)  | .004 | -0.020 (-0.057 – 0.017)  | .294 | **0.044 (0.025 – 0.064)**  | **.000\*\*\*** |
|  Skin problems | 0.018 (-0.030 – 0.065) | .469† | 0.078 (0.011 – 0.145)  | .023 | -0.045 (-0.114 – 0.024)  | .201 | 0.015 (-0.025 – 0.054)  | .473 | -0.023 (-0.047 – 0.001)  | .063 |
|  Rapid HR | 0.024 (-0.010 – 0.059)  | .169 | 0.026 (-0.020 – 0.072)  | .264 | 0.023 (-0.029 – 0.075)  | .393 | 0.005 (-0.029 – 0.038)  | .777 | **0.025 (0.009 – 0.042)**  | **.002\*** |
|  Headaches | -0.009 (-0.042 – 0.024)  | .583 | -0.003 (-0.044 – 0.039)  | .904 | -0.016 (-0.067 – 0.035)  | .538 | -0.016 (-0.047 – 0.014)  | .296 | 0.016 (-0.001 – 0.033)  | .065 |
|  Injuries | 0.008 (-0.026 – 0.042) | .652 | 0.030 (-0.012 – 0.071)  | .160 | -0.015 (-0.068 – 0.038)  | .575 | 0.006 (-0.023 – 0.035)  | .694 | 0.022 (0.004 – 0.039)  | .017 |
|  Unhealthy diet | 0.002 (-0.024 – 0.028)  | .894 | -0.006 (-0.038 – 0.027)  | .736 | 0.009 (-0.032 – 0.051)  | .661 | 0.010 (-0.016 – 0.036)  | .453 | 0.000 (-0.017 – 0.016)  | .954 |
|  Healthy diet | -0.018 (-0.092 – 0.055)  | .622 | 0.004 (-0.094 – 0.102) | .935 | -0.042 (-0.151 – 0.068)  | .453 | 0.025 (-0.026 – 0.076)  | .333 | **-0.060 (-0.094 – -0.026)** | **.001\*** |
|  Fast food | 0.002 (-0.037 – 0.040)  | .938 | 0.017 (-0.040 – 0.074)  | .558 | -0.015 (-0.068 – 0.039)  | .595 | -0.024 (-0.054 – 0.006)  | .122 | **0.031 (0.014 – 0.048)** | **.000\*\*\*** |
|  Exercise engagement | 0.079 (-0.652 – 0.809) | .832 | 0.624 (-0.339 – 1.586)  | .204 | -0.470 (-1.552 – 0.612)  | .395 | -0.651 (-1.135 – -0.166) | .009 | 0.033 (-0.397 – 0.464)  | .880 |
| **Adult Substance use** |
|  BMI | -0.064 (-0.128 – 0.001)  | .054† | **-0.154 (-0.248 – -0.061)**  | **.001\*** | 0.028 (-0.061 – 0.117)  | .538 | 0.062 (-0.012 – 0.137)  | .101 | -0.014 (-0.068 – 0.039)  | .599 |
|  Waist circumference | -0.129 (-0.303 – 0.044)  | .144† | **-0.403 (-0.633 – -0.173)**  | **.001\*** | 0.147 (-0.115 – 0.409)  | .270 | 0.172 (-0.028 – 0.372)  | .093 | 0.031 (-0.089 – 0.151) | .609 |
|  Hip circumference | -0.070 (-0.212 – 0.072)  | .331† | -0.262 (-0.460 – -0.064)  | .009 | 0.124 (-0.079 – 0.326)  | .231 | 0.073 (-0.064 – 0.210)  | .294 | -0.055 (-0.147 – 0.037)  | .238 |
|  Systolic BP  | 0.112 (0.009 – 0.215)  | .034 | 0.045 (-0.090 – 0.180)  | .512 | 0.179 (0.023 – 0.335)  | .024 | -0.025 (-0.159 – 0.110)  | .720 | 0.004 (-0.087 – 0.095)  | .933 |
|  Diastolic BP | 0.050 (-0.061 – 0.160)  | .377† | -0.090 (-0.236 – 0.056)  | .229 | 0.191 (0.028 – 0.353)  | .021 | -0.044 (-0.149 – 0.061)  | .409 | 0.066 (-0.007 – 0.139)  | .075 |
|  Resting HR | -0.210 (-0.359 – -0.060)  | .006 | **-0.345 (-0.553 – -0.136)**  | **.001\*** | -0.073 (-0.286 – 0.140)  | .502 | -0.209 (-0.347 - -0.071)  | .003 | **0.147 (0.058 – 0.235)**  | **.001\*** |
|  FVC | 0.005 (-0.002 – 0.012)  | .153 | 0.007 (-0.001 – 0.016)  | .096 | 0.003 (-0.008 – 0.014)  | .602 | 0.007 (-0.001 – 0.016) | .085 | 0.002 (-0.003 – 0.007)  | .496 |
|  FEV1 | -0.004 (-0.010 – 0.003)  | .297 | 0.001 (-0.006 – 0.008)  | .842 | -0.008 (-0.019 – 0.003)  | .169 | 0.001 (-0.007 – 0.009)  | .763 | 0.002 (-0.002 – 0.006)  | .345 |
|  FEV1/FVC (%) | **-0.149 (-0.244 – -0.054)**  | **.002\*** | -0.103 (-0.179 – -0.027)  | .008 | -0.196 (-0.371 – -0.022)  | .027 | -0.093 (-0.191 – 0.006)  | .065 | -0.001 (-0.059 – 0.056)  | .960 |
|  Left hand grip | 0.163 (-0.023 – 0.348)  | .086 | 0.114 (-0.071 – 0.298)  | .227 | 0.212 (-0.111 – 0.535) | .198 | 0.146 (-0.066 – 0.359) | .177 | -0.006 (-0.161 – 0.150)  | .944 |
|  Right hand grip  | 0.240 (0.061 – 0.419)  | .008 | 0.251 (0.065 – 0.437)  | .008 | 0.229 (-0.071 – 0.530)  | .135 | 0.047 (-0.175 – 0.269)  | .678 | 0.011 (-0.157 – 0.179)  | .900 |
|  Chronic pain  | 0.002 (-0.037 – 0.041)  | .927 | -0.010 (-0.052 – 0.101) | .682 | 0.014 (-0.045 – 0.073) | .635 | 0.020 (-0.009 – 0.048) | .181 | **0.037 (0.022 – 0.052)**  | **.000\*\*\*** |
|  Gum disease  | 0.016 (-0.029 – 0.060)  | .492 | -0.001 (-0.065 – 0.064) | .988 | 0.032 (-0.027 – 0.091)  | .286 | 0.002 (-0.036 – 0.039)  | .929 | **0.042 (0.016 – 0.068)**  | **.001\*** |
|  Loss of appetite  | 0.014 (-0.018 – 0.045)  | .399 | 0.008 (-0.035 – 0.052)  | .717 | 0.019 (-0.025 – 0.064)  | .399 | 0.032 (0.005 – 0.060)  | .022 | 0.027 (0.004 – 0.049)  | .020 |
|  Nausea  | -0.006 (-0.038 – 0.027)  | .723 | 0.005 (-0.030 – 0.039)  | .793 | -0.017 (-0.072 – 0.039)  | .555 | 0.017 (-0.012 – 0.045)  | .243 | 0.028 (0.010 – 0.046) | .003 |
|  Weight problems | -0.006 (-0.048 – 0.036)  | .776 | -0.020 (-0.085 – 0.046) | .554 | 0.008 (-0.044 – 0.060)  | .764 | 0.030 (-0.004 – 0.064)  | .082 | 0.026 (0.002 – 0.049)  | .033 |
|  Problems breathing | 0.013 (-0.024 – 0.050) | .494 | 0.003 (-0.039 – 0.046)  | .882 | 0.023 (-0.038 – 0.084)  | .462 | 0.020 (-0.011 – 0.051)  | .210 | **0.047 (0.026 – 0.067)**  | **.000\*\*\*** |
|  Skin problems | -0.008 (-0.053 – 0.037)  | .724 | 0.002 (-0.051 – 0.053)  | .934 | -0.019 (-0.092 – 0.054) | .614 | 0.021 (-0.011 – 0.053)  | .204 | -0.010 (-0.034 – 0.014) | .411 |
|  Rapid HR | 0.010 (-0.022 – 0.042)  | .537 | 0.021 (-0.028 – 0.069)  | .403 | -0.001 (-0.042 – 0.040)  | .968 | 0.020 (-0.009 – 0.049) | .172 | **0.033 (0.014 – 0.052)** | **.001\*** |
|  Headaches | -0.026 (-0.065 – 0.012)  | .179 | -0.023 (-0.078 – 0.032)  | .405 | -0.029 (-0.083 – 0.024)  | .279 | -0.005 (-0.033 – 0.023)  | .710 | 0.025 (0.007 -0.043) | .008 |
|  Injuries | 0.003 (-0.035 – 0.041)  | .875 | 0.016 (-0.036 – 0.069) | .542 | -0.011 (-0.065 – 0.044)  | .703 | 0.011 (-0.020 – 0.042)  | .499 | 0.018 (0.001 – 0.036)  | .041 |
|  Unhealthy diet | 0.022 (-0.017 – 0.060)  | .274 | 0.020 (-0.019 – 0.060)  | .318 | 0.023 (-0.043 – 0.089)  | .498 | 0.004 (-0.023 – 0.030) | .786 | 0.004 (-0.012 – 0.020) | .665 |
|  Healthy diet | -0.008 (-0.077 – 0.061)  | .821 | 0.043 (-0.046 – 0.133)  | .340 | -0.061 (-0.166 – 0.045) | .258 | 0.006 (-0.045 – 0.057)  | .817 | **-0.071 (-0.106 - -0.036)**  | **.000\*\*\*** |
|  Fast food | 0.001 (-0.037 – 0.039)  | .966 | -0.001 (-0.050 – 0.048)  | .968 | 0.003 (-0.056 – 0.062)  | .929 | 0.012 (-0.014 – 0.038)  | .382 | 0.025 (0.006 – 0.043) | .008 |
|  Exercise engagement | 0.783 (0.158 – 1.409)  | .014 | 1.022 (0.119 – 1.925)  | .027 | 0.555 (-0.283 – 1.393)  | .194 | -0.557 (-0.993 - -0.120)  | .012 | 0.139 (-0.426 – 0.703) | .630 |
| Note: Analyses controlled for sex. MZ=monozygotic twins, DZ=dizygotic twins, BMI=Body mass index, BP=blood pressure, HR=heart rate, FVC=forced vital capacity, FEV1=forced expiratory volume in one second, and exercise engagement = length of exercise in minutes over the past 24 hours. † indicates MZ and DZ twins significantly different. Asterisks indicate significance after correction for multiple testing. \* = adjusted *p* <.05, \*\* = adjusted *p* <.01, and \*\*\* = adjusted *p* <.001. Bold indicates significance remained after correction for multiple testing (adjusted *p*<.05)  |