**High-Potency Cannabis, Mental Health and Substance Use in Adolescence: Results from a UK General Population Sample**

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Question

Does use of high-potency cannabis (compared to use of low potency cannabis) increase risks for cannabis problems, common mental disorders and psychotic experiences when early-life mental health symptoms and frequency of use are controlled for?

Findings

In this cohort study, after adjusting for frequency of cannabis use and early adolescent mental health use of high-potency cannabis was associated with a significant increase in frequency of cannabis use, likelihood of cannabis problems, and likelihood of anxiety disorder. Those using high-potency cannabis had a small increase in likelihood of psychotic experiences; however, this attenuated after adjustment for frequency of cannabis use.

Meaning

Risks for cannabis use problems and anxiety disorders are higher amongst those reporting use of high-potency cannabis, and provision of public health messaging regarding the importance of reducing both frequency of cannabis use and the potency of the drug, and limiting the availability of high-potency cannabis, may be effective for reducing these harms.

Abstract (350/350 words)

Importance

Cannabis use is consistently linked to poorer mental health outcomes, and there is evidence use of higher potency cannabis increases these risks. To date, no studies have described the relationship between cannabis potency and concurrent mental health in a general population sample, or addressed confounding using longitudinal data.

Objective

Explore the relationship between cannabis potency and substance use/mental health outcomes, accounting for preceding mental health and frequency of use.

Design

Data from the Avon Longitudinal Study of Parents and Children (ALSPAC), a birth cohort of Participants born between 1 April 1991 and 31 December 1992. Present data on outcomes and exposures were collected at age 24.

Setting

UK population.

Participants

Participants who reported recent cannabis use.

Exposure

Self-reported type of cannabis most commonly used in the past year, coded to a binary exposure of use of high potency cannabis or lower potency cannabis.

Main outcomes and measures

Outcomes were reported frequency of cannabis use, reported cannabis use problems, recent use of other illicit drugs, tobacco dependence, alcohol use disorder, depression, generalised anxiety disorder, and psychotic-like experiences. The study uses secondary data, and consequently the hypotheses were formulated after data collection.

Results

Past-year cannabis use was reported by 1087 participants. Of these, 13% reported use of high potency cannabis. Most of this sample were female (53%). Use of high-potency cannabis was associated with increased frequency of cannabis use (AOR 4.38, 95% CI 2.89-6.63), cannabis problems (AOR 4.08, 95% CI 1.41-11.81), increased likelihood of anxiety disorder (AOR 1.92, 95%CI 1.11 – 3.32), and small increase in likelihood of psychotic experiences which attenuated after adjustment for frequency of use (AOR 1.29, 95% CI 0.67 – 2.50). There was little evidence of a relationship between use of high-potency cannabis and alcohol use disorder, illicit drug use, tobacco dependence or depression.

Conclusions and relevance

This study provides the first general population evidence that use of high potency cannabis is associated with mental health and addiction. Limiting the availability of high-potency cannabis may reduce the number of individuals who develop cannabis use disorders, prevent cannabis use escalating to a regular behaviour, and reduce impacts on mental health.

**Introduction**

Globally, cannabis is the most commonly used internationally regulated drug,1 and policy is liberalising worldwide2. The primary psychoactive component of cannabis is delta-9-tetrahydrocannabinol (THC). The potency (concentration of THC) may be an important predictor of cannabis’s impact on health. Experimental studies indicate effects of THC intoxication are dose-dependent, with higher doses causing greater memory impairment and transient psychotic-like symptoms.3 Policy liberalisation has been accompanied by proliferation of high-potency cannabis in legal markets,4,5 and THC concentrations have increased in markets where cannabis remains illegal.6

Cannabis use is consistently linked to poorer mental health outcomes,7,8 and there is evidence higher potency cannabis is associated with higher risks. A case-control study of first episode psychosis in England found those who self-reported using higher-potency cannabis were twice as likely to have a psychotic disorder, compared to participants who did not use cannabis.9 When the study was replicated in a multinational case-control study of first-episode psychosis across 11 sites in Europe and Brazil, incidence of psychosis across sites was positively correlated with the prevalence of high potency cannabis use in the site-specific control samples.10 In a self-selecting sample of people who use drugs, use of high-potency strains of cannabis was associated with self-report of lifetime depression11 and cannabis dependence.12 These findings indicate availability of high-potency cannabis may increase risks of poorer mental health, addiction and need for treatment amongst those who are using the drug.

The strength of association between use cannabis and mental health outcomes is increased when cannabis use is frequent; consequently, increased frequency of use may confound the relationship between cannabis potency and mental health outcomes.12 Understanding the extent to which harms of high-potency cannabis are due to the THC content of the drug, and the extent to which they may be accounted for by increased frequency of use, is important for informing policy decisions around taxation and limits on drug potency.

To date, no studies of the relationship between cannabis potency and mental health have been conducted in a general population sample. General population studies can provide a valid estimate of the impact of cannabis potency at the population level, which may be crucial for informing policy makers and clinical service providers. We use data from the Avon Longitudinal Study of Parents and Children (ALSPAC); a large general population birth cohort where contemporaneous data were collected when participants were aged 24 on cannabis potency, cannabis use frequency, and validated measures of mental health outcomes, and prospective measures of adolescent mental health up to age 24.

Aims

1. Describe the use of different potencies of cannabis amongst a population of UK adolescents.
2. Explore the association between cannabis potency and problems resulting from cannabis use, use and disordered use of other substances, common mental disorders, and psychotic experiences by comparing those who use high-potency cannabis with those who use lower potency cannabis.
3. Determine the extent to which such associations are explained by adolescent mental health at age 12/13, age of cannabis use onset, and current frequency of cannabis use.

**Methods**

Study population

ALSPAC is a UK population-based birth cohort, the methods of which have previously been outlined.13,14 See Supplementary Materials for full details.

The sample for the present analyses was the 1087 participants who reported on their past-year cannabis use whilst attending the ALSPAC clinic between June 2015 and October 2017 at mean age 24 (standard deviation 0.83) (see figure 1). Data on the 2085 individuals who participated in the age-24 assessment but were excluded based on reporting no recent cannabis use are available in Appendix 1.

Measures

See supplementary materials for further details on all measures described below.

Exposure

Those who reported past-year cannabis use were asked “What type of cannabis have you most commonly used or taken in the last 12 months?” and were able to select from the following options: “herbal cannabis/marijuana”, “skunk/other stronger types of herbal cannabis”, “hashish/resin/solid”, “other”, or “don’t know”. Consistent with previous research which has validated self-reported data on three cannabis types against quantified concentrations of THC and CBD among young UK cannabis users,15 we categorised cannabis as either high potency (typically ≥10% THC; “skunk/other stronger types of herbal cannabis”) or low potency (typically <10% THC; “herbal cannabis/marijuana” or “hashish/resin/solid” or “other”).10

Outcomes

*Cannabis use frequency at age 24*

Participants were asked “in the last 12 months, how often have you used cannabis?”. This variable was dichotomised to “Monthly use or less” or “weekly/daily use”.

*Problematic cannabis use at age 24*

Those who self-reported two or more of the Cannabis Abuse Screening Test (CAST)16 items within the past year were classified as having recently experienced problems as a result of their cannabis use.

*Other substance use and dependencies at age 24*

Participant self-report of any illicit drugs in the past 12 months was categorised as recent other illicit drug use. The reference group was comprised of those who reported no recent use of these other illicit drugs (including those who had never used these drugs). Participants were categorised as nicotine dependent if they self-reported daily nicotine use and endorsed 3 or more of the Fagerström Test for Nicotine Dependence17 criteria, indicating low/medium/high/very high nicotine dependence. The reference group was comprised of those who met criteria for very low dependence, and those who were not using nicotine every day or had never smoked. DSM-5 criteria for alcohol use disorder (AUD)18 were used to identify participants experiencing alcohol use problems. Participants were categorised as experiencing moderate/severe AUD if they self-reported four or more of the AUD criteria. The reference group was comprised of those who endorsed less than four of the AUD criteria (including those who had never drunk alcohol).

*Mental health at age 24*

Participants completed a self-administered computerised CIS-R,19 a tool for lay interviewers to assess psychiatric disorders in the community. Participants who met criteria for moderate or severe DSM-IV20 Major Depressive Disorder (MDD) at time of interview were categorised as experiencing depression. Participants who met DSM-IV criteria for Generalised Anxiety Disorder20 (GAD) were categorised as experiencing anxiety. Participants were rated on psychotic experiences (PE) using the PLIKS semi-structured interview administered by trained researchers.21,22 Those were rated as having suspected or definite hallucinations, delusions or thought interference in the past 12 months, which were either frequent (at least monthly) or caused them distress (reported as quite or very distressing), were classified as having had a recent PE. For the purposes of these analyses, PEs were excluded if they only happened when the participant was either falling asleep or waking up, ill with a high temperature, or within 2 hours of drinking alcohol or taking drugs.

Covariates

*Prospective Measures from Early Childhood and Adolescence*

Childhood socioeconomic position was assessed through measures from maternal questionnaires completed during pregnancy; variables were maternal educational attainment, and parents’ occupation class. Child’s ethnic background was derived from parent’s reported ethnicity (coded as white or Black and Minority Ethnic Group).

To account for mental health symptoms preceding cannabis use onset (mean age of cannabis onset in sample 16.7, 95% CI 16.5 - 16.9) continuous score measure of depression symptoms at age 13 was included in analyses of MDD and GAD. These were assessed through the self-completed Mood and Feelings Questionnaire (MFQ) at age 13,23 a tool for measuring depression in children and young people. The number of PE (assessed by PLIKS21, a semi-structured interview administered by trained researchers) reported at age 12 was included in the analysis of the outcome of PE at age 24.

Age of cannabis use onset was self-reported in ALSPAC at ages 14, 15, 16, 18, 20, 22 and 24. Participants who reported lifetime use of cannabis at any of these time points were asked at what age they first used cannabis. Participants’ earliest report of age at first cannabis use was used to derive a variable of age of onset of cannabis use.

Ethics

Ethical approval for the study was obtained from the ALSPAC Ethics and Law Committee and the Local Research Ethics Committees. Informed consent for the use of data collected via questionnaires and clinics was obtained from participants following the recommendations of the ALSPAC Ethics and Law Committee at the time.

Analysis

All analyses were conducted in Stata version 15.1. The relationship between use of high-potency cannabis and substance use/mental health at age 24 was analysed using univariable and multivariable logistic regression, with cannabis potency as the independent variable. Three separate multivariable models were run for each outcome; 1) adjusting for gender and childhood socioeconomic position, 2) additional adjustment for age of a) age of cannabis use onset for models of substance use outcomes, b) depression symptom score at age 13 for models of MDD/GAD outcomes, and PEs at age 12 for the model with PE as outcome (time points selected to ensure mental health symptoms precede cannabis use onset), and 3) adjusted as in model 2, with inclusion of a categorical measure of cannabis use frequency. This allowed estimation of the extent to which pre-existing symptoms of mental health disorders, and the frequency of cannabis use, explained any relationship between use of high-potency cannabis and substance use/mental health outcomes. Results are presented as Odds Ratios (OR) with 95% Confidence Intervals (95% CI). Propensity score models were applied to complete case data as a sensitivity test; see Supplementary Materials 2.

Missing data and imputation

As outcomes and exposures were collected at the same time point, the majority of missing data were in the covariates assessed at earlier ages (see Appendix Table A1). Missing data in all analysis variables (exposures, outcomes, covariates) were addressed through multiple imputation using chained equations, which uses a series of univariate regression models to impute each incomplete variable sequentially. Each model included all other analysis variables as predictors, along with the following auxiliary variables: ethnicity, experiencing bullying between ages 0-16, parental separation ages 0-16, parent mental health problems age 0-16, parent substance use age 0-16, MFQ score at age 16 and 18, number of self-reported psychotic-like experiences at age 14, and conduct disorder symptoms to age 13. Estimates were obtained by pooling results across 40 imputed datasets using Rubin’s rules, and assessment of Monte Carlo variability confirmed this as a suitable number of imputations.24.

**Results**

Of the 1087 participants reporting past-year cannabis use at age 24, 12.8% reported use of high-potency cannabis. Use of lower potency forms of cannabis was reported by 87.2% of those who used cannabis in the past year (see Appendix Table A1 for data on this and all analysis variables; all N’s estimated from imputed proportions).

High-potency use was more common in those who were male and those who reported regular cannabis use, recent cannabis problems, recent other illicit drug use, tobacco dependence, AUD, depression, GAD, and PE. See Table 1 for data.

Cannabis use outcomes

There was a strong association between use of high-potency cannabis use and frequency of cannabis use at age 24. This was attenuated by adjustment for sociodemographic factors and by the age of onset of cannabis use, but those reporting use of high-potency cannabis remained more than four times as likely to report using cannabis at least weekly compared to those reporting use of lower potency forms of cannabis (Adjusted Odds Ratio (AOR) 4.38, 95% Confidence Intervals (CI) 2.89-6.63). There was also a very strong unadjusted association between use of high-potency cannabis and reporting recent cannabis problems. This was greatly attenuated by adjustment for age of cannabis onset and frequency of cannabis use, but people reporting use of high-potency cannabis were still more than four times as likely to report having recently experienced problems as a result of their cannabis use (AOR 4.08, 95% CI 1.41-11.81). See Table 2 and Figure 2 for results.

Substance use outcomes

Those who reported use of high-potency cannabis were more than twice as likely to report recent use of other illicit drugs within the past 12 months and more than three times as likely to report tobacco dependence. These relationships were largely attenuated by adjustment for sociodemographic factors, age of cannabis onset, and frequency of cannabis use (respectively AOR 1.29, 95% CI 0.77-2.17, and AOR 1.42, 95% CI 0.89-2.27). There was little evidence of an elevation in likelihood of AUD amongst participants who reported use of high-potency cannabis after adjustment for sociodemographic variables, age of cannabis onset and cannabis use frequency (AOR 0.90, 95% CI 0.49-1.64). See Table 2 and Figure 2 for results.

Mental health outcomes

Depression was slightly more common in the high-potency cannabis group, but there was little statistical evidence high potency was associated with depression (AOR 1.28, 95% CI 0.68-2.34).

There was evidence use of high-potency cannabis was associated with moderate elevation in likelihood of GAD. The strength of this association was increased slightly after adjustment for sociodemographic variables, depression symptoms at age 14 and frequency of cannabis use (AOR 1.92, 95% CI 1.11-3.32).

Participants reporting use of high-potency cannabis were almost twice as likely to report frequent or distressing PEs (not occurring directly after drug use), but evidence of association was substantially weakened after adjustment for frequency of cannabis use (AOR 1.29, 95% CI 0.67-2.50). See Table 2 and Figure 2 for results.

**Discussion**

The present study restricts analyses to those who have used different forms of cannabis in order to inform understanding of the implications of the proliferation of high-potency cannabis in legal markets.4,5 In a general population sample of young people in the UK, individuals who use high-potency cannabis (compared to those using lower-potency forms of cannabis) are more likely to be using cannabis regularly, more likely to report having recently experienced problems as a result of their cannabis use, and more likely to concurrently be experiencing use of other illicit drugs, tobacco dependence, alcohol use disorder, anxiety disorder and psychotic experiences. After adjusting for age of onset of cannabis use or early adolescent measures of psychopathology, and frequency of cannabis use, high potency cannabis is associated with large increases in likelihood of frequent cannabis use, of having recently experienced problems as a result of their cannabis use, and a moderate increase in likelihood of experiencing anxiety disorder. The results provide a profile of individuals who use high-potency cannabis, indicating this behaviour is more common amongst individuals who are male, grow up in low SES families, experience early PE’s, and report early-onset cannabis use.

It is important to note the outcomes regarding substance use/mental health may reflect shared predisposing risk factors that could also lead people to select the most potent drug available.25 As the sample excluded those who had not used cannabis, increases in risk for mental health outcomes associated with use of high-potency cannabis are unlikely to be conflated by a shared liability to drug use and mental health disorder. However, evidence shows shared risk factors underlie both exposure to cannabis, and progression to development of dependence26. The profile of substance use outcomes and early-life experiences amongst those who use high-potency cannabis in the present study indicates there may be overlapping risk factors between development of substance use/mental health disorders and the selection of higher-potency forms of cannabis. We have sought to adjust for these factors, but further consideration of the role of cannabis potency in the causal path to mental health disorder is warranted.

The estimate in the present study for likelihood of depression amongst those using high-potency cannabis is similar to estimates observed in a self-selecting sample of drug-using participants (OR 1.18, 95% CI 1.11 – 1.25).11 However, the present estimate demonstrating an increase in likelihood of anxiety disorder amongst those using high-potency cannabis is in contrast to the negligible increase in likelihood of lifetime anxiety disorder (OR 1.05, 95% CI 0.98 – 1.12) observed previously.11 This discrepancy may be due to the previous study relying on self-reported lifetime diagnosis,11 whereas the present study used DSM-IV validated measures of depression and anxiety disorder at the time of assessment. A recent systematic review has indicated cannabis use in adolescence is associated with an increased likelihood of lifetime depression and anxiety,8 although few studies had considered the impact of potency or frequency of cannabis use.

A better understanding of the relationship between potency and frequency is required to get a clearer understanding of the independent effects of potency on mental health. We found similar effect sizes for the relationship between use of high-potency cannabis and report of frequent/distressing psychotic experiences (not attributable to drug use) to those observed in case-control studies of first episode psychosis.9,10 However, in our study we observed a substantial attenuation in effect size, by approximately 66%, after adjustment for frequency of cannabis use. The present findings related to cannabis problems and frequency of use are consistent with previous evidence for a positive association between days of use of high potency cannabis and dependence severity.12 In this previous study there was a linear relationship between number of days of high-potency cannabis use per month and severity of dependence score (beta 0.15, 95% CI 0.02 – 0.28). Increased frequency of cannabis use could plausibly causes individuals to use higher-potency cannabis through the development of tolerance to the effects of cannabis; if so, then it is appropriate to consider cannabis use frequency as a confounding factor in the relationship to mental health. However, if use of higher-potency cannabis leads to increased frequency of use, plausibly though high-potency cannabis delivering THC more efficiently than lower potency cannabis, it would be more appropriate to explore the mediating effect of cannabis frequency.

Strength and Limitations

This study is the first to describe the relationship between cannabis potency and concurrent mental health and substance abuse in a general population sample, and the first to use longitudinal data to address confounding by early mental health symptoms and age of onset of cannabis use in this relationship. However, there are several limitations to consider.

First, given the data are collected in the context of an illegal cannabis market, we cannot be certain participants are accurately informed about the potency of the cannabis they are using. It is plausible the ability to identify type of cannabis is higher amongst those frequently using the drug, although evidence suggests frequency of use does not moderate the relationship between self-reported identification of cannabis type and actual THC concentration in young UK cannabis users.15

Second, the exposures and outcomes we examined were cross-sectional. As questions on type of cannabis used were only asked at age 24 it is plausible the presence of anxiety disorder or psychotic experiences have led to the use of high-potency cannabis at age 24. Adjusting for measures of psychopathology in adolescence had little effect on our estimates.

Third, recent use of high-potency cannabis was reported by only 12.8% of participants, which may result in some of the analyses being underpowered (see Appendix Table A1). Fourth, as a result of attrition within ALSPAC those who took part in the age-24 wave of the study were more likely to be white, female and more affluent than the population from which the participants were originally drawn from.14 Additionally, as there is a dearth of nationally representative data on the demographics of those who use cannabis, we cannot be certain the present sample is representative of the cannabis use population in the UK, or globally. The analyses would benefit from replication in larger, representative samples, but to our knowledge ALSPAC is the only longitudinal general population sample to include measures of cannabis potency at present. Characteristics of those who did not report cannabis use at age 24 are in Appendix Table A2.

Implications

Use of high-potency cannabis may occur as part of a profile of other illicit drug use and substance dependency, likely driven by shared risk factors underlying these behaviours and the selection of high-potency strains. The present study suggests risks for cannabis use problems and anxiety disorders are further increased amongst those reporting use of high-potency cannabis, even after accounting for sociodemographic factors, adolescent mental health and frequency of cannabis use. Providing public health messaging regarding the importance of reducing both frequency of cannabis use and the potency of the drug, and limiting the availability of high-potency cannabis, may be effective for reducing the harms associated with cannabis use.

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LH and JH had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Funders played no role in design and conduct of the study; collection, management, analysis, and interpretation of the data; preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication.

Author contributions

JH, MH, SZ, MC, MM and JM oversaw the data collection. LH, JH, MH and SZ developed the concept and scope of the paper. LH and JH produced the analysis plan. LH conducted all analyses and drafted the manuscript. All authors made substantial contributions to the interpretation of the data and contributed to revising the manuscript critically. All authors approved the final version of the study to be published and are accountable for all aspects of the work.

# Declaration of interests

MH reports personal fees from Gilead, Abbvie, and MSD. All other authors declare no competing interests. LH reports grants from The Wellcome Trust during the conduct of the study.

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Figure 1: Flow diagram showing the ALSPAC analysis sample

Figure 2: Fully adjusted (including frequency of use – see methods) associations between use of high-potency cannabis and outcomes

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  | **High potency cannabis use**  **N = 141** | | **Lower potency cannabis use**  **N = 946** | | **Chi square P value** |
| **N** | **%** | **N** | **%** |
| Regular cannabis use | 80 | 56.8 | 170 | 17.6 | ≤0.001 |
| Recent cannabis use problems | 14 | 10.1 | 9 | 0.8 | ≤0.001 |
| Recent use of other illicit drugs | 117 | 82.9 | 624 | 66.5 | ≤0.001 |
| Recent tobacco dependence | 52 | 37.0 | 143 | 15.1 | ≤0.001 |
| Recent alcohol use disorder | 21 | 15.1 | 94 | 10.0 | ≤0.001 |
| Major Depression (moderate/severe symptoms) | 17 | 11.7 | 95 | 9.7 | ≤0.001 |
| Generalised Anxiety disorder | 27 | 19.1 | 114 | 11.6 | ≤0.001 |
| Psychotic-like experiences | 17 | 12.4 | 66 | 7.1 | ≤0.001 |
| Male | 100 | 71.6 | 407 | 43.4 | ≤0.001 |
| Low maternal education | 27 | 19.2 | 123 | 13.1 | ≤0.001 |
| Lower parent occupational class | 45 | 32.2 | 274 | 29.2 | ≤0.001 |
| Black or Minority Ethnic Group | 7 | 5.3 | 50 | 5.3 | 0.941 |
|  | **Mean** | **Confidence Intervals** | **Mean** | **Confidence Intervals** |  |
| Age of cannabis use onset | 14.7 | 14.3 – 15.1 | 16.9 | 16.8 – 17.2 |
| MFQ score age 13 | 5.6 | 4.65 – 6.49 | 5.6 | 5.26 – 5.95 |
| Number PE age 12 | 0.33 | 0.18 – 0.48 | 0.20 | 0.16 – 0.24 |

Table 1: Association between type of cannabis and demographic, substance abuse and mental health outcomes in 1087 participants who reported recent cannabis use (all N estimated from imputed proportions

Table 2. Logistic regression analysis (OR, 95% CI) of association between high-potency cannabis (N=141) and substance use and mental health outcomes (all figures from imputed data)

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Outcome variables** | **Univariable**  **OR (95% CI)**  **P values** | **Adjusted for childhood sociodemographic factors**  **AOR (95% CI)**  **P values** | **Adjusted for prospective mental health measures AOR (95% CI)**  **P values** | **Adjusted for frequency of cannabis use**  **AOR (95% CI)**  **P values** |
| Regular cannabis use | **6.21** (4.24-9.11)  ≤0.001 | **5.81** (3.90-8.65)  ≤0.001 | **4.38**1(2.89-6.63)  ≤0.001 | - |
| Recent cannabis use problems | **13.17** (5.41-32.04)  ≤0.001 | **13.52** (5.28-34.60)  ≤0.001 | **8.45**1(3.04-23.50)  ≤0.001 | **4.08** (1.41-11.81)  0.009 |
| Recent use of other illicit drugs | **2.47** (1.53-3.97)  ≤0.001 | **2.19** (1.35-3.56)  0.002 | 1.501 (0.91-2.49)  0.114 | 1.29 (0.77-2.17)  0.339 |
| Tobacco dependence | **3.31** (2.23-4.92)  ≤0.00 | **3.30** (2.18-4.99)  ≤0.001 | **2.05**1 (1.31-3.19)  0.002 | 1.42 (0.89 – 2.27)  0.142 |
| Alcohol Use Disorder | 1.60(0.94-2.73)  0.080 | 1.49 (0.86-2.56)  0.153 | 0.991 (0.56-1.76)  0.973 | 0.90 (0.49-1.64)  0.730 |
| Major Depression (moderate/severe symptoms) | 1.24 (0.70-2.18)  0.461 | 1.61 (0.89-2.93)  0.115 | 1.542 (0.84-2.82)  0.163 | 1.28 (0.68-2.32)  0.440 |
| Generalised Anxiety disorder | **1.77** (1.09-2.86)  0.020 | **2.35** (1.41-3.92)  ≤0.001 | **2.28**2(1.36-3.83)  0.002 | **1.92** (1.11-3.32)  0.019 |
| Psychotic-like experiences | **1.81** (1.01-3.24)  0.047 | **2.03** (1.10-3.73)  0.023 | **1.86**3(1.00-3.46)  0.050 | 1.29 (0.67-2.50)  0.451 |
| Multivariable model adjustment is incremental. Prospective mental health measure adjustment: 1Age of cannabis use onset 2Depression symptom score at age 13 3Number of psychotic experiences at age 12  OR = Odds Ratio 95% CI = 95% Confidence Intervals | | | | |