TITLE PAGE:

TITLE: Psychotic-like experiences with cannabis use predict cannabis cessation and desire to quit- A cannabis discontinuation hypothesis

Running Title: Cannabis induced PLEs predict cessation and desire to quit

Authors: Musa Sami[1,2] MRCPsych; Caitlin Notley[3] PhD; Christos Kouimtsidis[4,5] PhD; Michael Lynskey[6] PhD; Sagnik Bhattacharyya[1,2*] PhD

Affiliation:

1 Institute of Psychiatry, Psychology & Neuroscience, King's College London, United Kingdom.

2 South London and Maudsley NHS Foundation Trust, United Kingdom

3 Norwich Medical School, University of East Anglia , Norwich, United Kingdom

4 Surrey and Borders Partnership NHS Foundation Trust, United Kingdom

5 Department of Medicine, Division of Brain Sciences, Imperial College London, United Kingdom

6 National Addiction Centre, Addiction Sciences Building, King's College London, United Kingdom.

***Corresponding author:** Department of Psychosis Studies, Institute of Psychiatry, Psychology & Neuroscience, King's College London, De Crespigny Park, London SE5 8AF, UK, Email: sagnik.2.bhattacharyya@kcl.ac.uk

Word Count: Abstract: 216; Main text: 4416

ABSTRACT

Background: Evidence suggests cannabis-induced psychotic-like experiences may be a marker of psychosis proneness. The effect of such experiences on cannabis use has not systematically been examined.

Methods: We undertook a mixed-methods online survey of 1231 cannabis users (including 926 continued users) using the Cannabis Experiences Questionnaire. We examined the effect of psychotic-like and pleasurable experiences on cessation of cannabis and intention to quit. Socio-demographic variables, cannabis use parameters, and substance misuse history were included as covariates. Free-text data explored subjective reasons for changes in use.

Results: Cessation of cannabis use was associated with greater psychotic-like experiences ($p<0.001$, Exp(B) 1.262, 95%CI: 1.179-1.351) whilst continued cannabis users were more likely to report pleasurable experiences ($p<0.001$, Exp(B) 0.717, 95%CI 0.662-0.776). Intention to quit cannabis in continued users was associated with greater psychotic-like experiences ($p<0.003$, Exp(B) 1.131, 95%CI: 1.044-1.225) whilst intention to not quit was significantly associated with increased pleasurable experiences ($p<0.015$, Exp(B) 0.892, 95%CI 0.814-0.978). Whereas former users clearly ascribed cessation to negative experiences; continued users who expressed intention to quit less readily ascribed the intention to negative experiences.

Conclusions: Elucidation of psychotic-like experiences may form the basis of a therapeutic intervention for those who wish to quit. Cessation in those with cannabis-induced psychotomimetic experiences may offset the risk for development of psychotic disorder, in this higher risk group.

MANUSCRIPT

Introduction:

Cannabis use is widespread with an estimated 125-203 million users worldwide(Degenhardt & Hall 2012). Initiation of cannabis use has been associated with increased risk of onset of psychotic symptoms whilst continued use is associated with persistence of such symptoms(Kuepper *et al.* 2011) and onset of psychotic disorder(Moore *et al.* 2007; Marconi *et al.* 2016). This is consistent with meta-analytic and independent evidence that continued cannabis use is associated with greater risk of relapse in those with pre-existing psychotic disorder(Schoeler *et al.* 2016a, 2016b) and that this association is more likely than not to reflect a causal effect of continued cannabis use on outcome(Schoeler *et al.* 2016c). This convergence of evidence suggests that persistence of use is a key determinant of the effect of cannabis use on outcome both in healthy and unwell cannabis users. Therefore, understanding what factors influence persistence of use or indeed trigger cessation or a desire to quit is critical to developing effective interventions that may help limit harm from cannabis use.

Work to date has focused on established social constructs as predictors of cessation and has demonstrated that increasing age and maturity are associated with cessation (the “maturing out” hypothesis)(Kandel & Logan 1984) whilst social context, poor health and prior illicit drug use are associated with ongoing use(Kandel & Raveis 1989). Other work has also pointed toward peer involvement and school problems(van den Bree *et al.* 2005) as well as

psychological dependence and drug myths(Little *et al.* 2013) as associated with persistence of cannabis use in young people.

Experiences during the transient intoxication state immediately following cannabis use, which can constitute both pleasurable and undesirable experiences have also been examined to determine their effect on subsequent use. Both early and persisting pleasurable experiences have been shown to be associated with heavier use and dependence(Le Strat *et al.* 2009; Scherrer *et al.* 2009). However evidence is equivocal about the effect of undesirable experiences on subsequent cannabis use patterns, with studies showing both association with decreased(Lyons *et al.* 1997; Zeiger *et al.* 2010) as well as heavier or problematic use(Grant *et al.* 2005; Scherrer *et al.* 2009). This may reflect the fact that existing literature examining the association between undesirable experiences during cannabis use and subsequent pattern of use have focused on a wide array of undesirable effects, including drowsiness, confusion and nausea rather than on effects such as ‘psychotic-like experiences’, which arguably are perhaps the most distressing and frightening experiences in someone expecting to enjoy a relaxing effect. Unlike the relatively rare occurrence of psychotic disorder associated with cannabis use(Moore *et al.* 2007; Marconi *et al.* 2016) psychotic-like experiences, such as paranoia, hallucinations or dysphoria, are not uncommon, reported by up to 15% of cannabis users in a community sample(Thomas 1996). Whether the occurrence of undesirable experiences such as psychotic-like experiences in particular whilst using cannabis has an influence on subsequent cannabis use behaviour is therefore an important question to examine. However, to our knowledge this has not been systematically examined to date.

Employing a well-validated(Barkus *et al.* 2006; Bianconi *et al.* 2016; Quinn *et al.* 2016) self-report questionnaire that has been used to record subjective experiences associated with cannabis use, previous and more recent exploratory factor analyses have shown that the immediate transient experiences associated with cannabis use cluster into 'paranoid-dysphoric experiences' and 'pleasurable experiences'(Barkus *et al.* 2006; Quinn *et al.* 2016). Hence, in the present study we sought to investigate whether experiences during cannabis use (both psychotomimetic and pleasurable) are associated with cessation of use or a future intention to quit in a non-clinical sample. We hypothesised that (i) psychotic-like experiences would be associated with cessation of cannabis use and a desire to quit, whereas (ii) pleasurable experiences would conversely be associated with continuation of cannabis use and a desire to continue. Furthermore, we triangulated analysis using a mixed-methods approach to qualitatively explore subjective reasons reported by users as being linked to continued use. We inductively coded qualitative data independently of the quantitative analysis in order to allow participants' own views relating to changes in their patterns of use (continuation, escalation, more 'measured' use or complete cessation) to their reported cannabis experiences, to emerge.

Methods:

Ethical approval was obtained from the King's College, London Research Ethics Committee (REMAS). We have followed the STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) guidelines for reporting of cross-sectional studies(von Elm *et al.* 2007).

A web-based modified version of the Cannabis Experiences Questionnaire (CEQ) was administered to an internet sample.

Sample selection:

Participants were recruited through advertising on the study recruitment pages at King's College London, the London Cannabis Club, cannabis advocacy sites such as CLEARUK and social media including Facebook, Twitter and Tumblr. An internet domain name for the survey was registered and advertised (www.thecannabissurvey.com). Adults aged 18 years and above who had previously used cannabis were invited to complete the survey. A small-scale raffle (£10-£50 Amazon voucher for three participants on completion) was offered as an incentive. The survey ran over a 10-month period from December 2015 until September 2016. We aimed for a sample size of 1000 as this would be the largest population-derived sample assessed with the CEQ to date(Barkus *et al.* 2006; Bianconi *et al.* 2016; Quinn *et al.* 2016),

Measures:

The CEQ was developed to investigate participants' self-reports of experiences with cannabis(Barkus *et al.* 2006). It has demonstrated validity and reliability having been administered in student, online, non-clinical and clinical cohorts(Barkus *et al.* 2006; Barkus & Lewis 2008; Bianconi *et al.* 2016; Quinn *et al.* 2016). We have used the modified version previously in a clinical sample via face to face and telephone interview with demonstrable acceptability in collecting cannabis use data. We used a modified version previously administered in our centre (Di Forti *et al.* 2009, 2012, Schoeler *et*

al. 2016b, 2016c). For brevity, and in order to facilitate data collection, the survey restricted itself to nine intoxication experiences and did not collect data on the after effects of cannabis use. Prior to this we had not tested the modified version online, although other groups have administered alternative versions of the CEQ to electronic and online sample and reported acceptable psychometric properties(Barkus & Lewis 2008; Quinn *et al.* 2016).

Predictor variables:

The administered survey included six items focusing on psychotic-like experiences (fearfulness, feeling of going crazy, feeling nervy, suspiciousness, seeing visions and hearing voices) and three items on pleasurable effects (being full of plans, feeling happy, being able to understand the world better). These were scored on a Likert scale assessing the frequency of ever having experienced the specified effect using established anchor points (1 rarely or never, 2 from time to time, 3 sometimes, 4 more often than not, 5 almost always).

Outcome variables:

Outcome variables were collected as dichotomous 'yes/no' answers (i) for all those who had ever used cannabis whether they continued to use; and (ii) in a further question restricted to those who continued to use cannabis, whether they intended to quit in the future.

Covariate variables:

Socio-demographic variables collected were: age, sex (male, female) and occupational status. Additional parameters of cannabis, alcohol and other drug use collected included: Age of first cannabis use, Frequency of cannabis

use (every day, a few times a week, a few times each month, a few times each year, only once or twice), other substance misuse history for tobacco, alcohol, cocaine, ecstasy and non-prescribed medication (used regularly, used frequently, used less than 5 times, never used). History of lifetime contact with mental health services or requiring treatment was collected as a dichotomous (yes/no) variable.

Qualitative data:

Free-text fields were used for the collection of qualitative data with specific questions on: reasons for initiation, continuation and/or cessation of cannabis use, thoughts about future cessation or continuation of use, subjective reasons given for changes in patterns of use.

Statistical Analysis

CEQ scores for psychotic-like experiences and pleasurable experiences were calculated by simple summation of Likert scales as followed previously.(Barkus *et al.* 2006) The range of total possible scores for psychotic like experiences was 6-30, whereas pleasurable experiences score ranged from 3-15. Since psychotic and pleasurable experiences represent underlying continua, summed scores were treated as a continuous variable.

Descriptive statistics for the predictor, covariate and outcome variables were estimated as means and standard deviations (SD) for continuous variables (psychotic-like experiences score, pleasurable experiences score, age, age of first use of cannabis), and as frequencies and percentages for all other variables (sex, occupation, frequency of cannabis use, any prior mental health

contact, history of use of: alcohol, tobacco, non-prescription medications, cocaine and ecstasy).

First exploratory analyses, including t-tests for continuous variables and chi-square test for categorical variables were undertaken to compare the cessation versus continuation user groups and further within continued users to compare those with future intention to quit versus those with no intention to quit. Multivariable binary logistic regression analyses were undertaken to examine the association between psychotic-like experiences and pleasurable experiences as predictors with cessation/continuation and future intention to quit/no intention to quit as outcomes. In order to account for potential confounders, the following measures were included in these models as covariates: age, sex, occupation, age of first use of cannabis, frequency of cannabis use, past drug history and contact with mental health services. All predictor and covariate variables were entered into the regression model simultaneously. Checking Variation Inflation Factor confirmed there was no multicollinearity amongst predictor and covariate variables at a conservative threshold (VIF<2.5 in all instances).

Missing data: Fisher's 2x2 exact test was undertaken to see if there was a significant effect of missing data between groups (continued vs. discontinued and future intention to quit vs. no intention to quit) for all covariates (age, sex, occupation, mental health contact, age of first use, frequency of first use, alcohol, tobacco, non prescribed medication, cocaine and ecstasy history) (see Table 1). There were no significant differences in rates of missing data between groups for continued users who had intention to quit vs. no intention to quit. There were furthermore no significant differences for rates of missing

data for continued vs discontinued users for all covariates except for occupation (4.6% vs 1.0%, p=0.03) and frequency of use (3.0% vs 7.2%, p<0.01), however even in these two instances the overall differences in proportions of missing data between groups was ajudged to be small and not evidence systematic bias in missing data. Consequently we undertook a complete case analysis, (where there were no missing data for all covariates specified above) to account for missing data (see supplementary material) in preference to imputation methods.

Sensitivity analyses: we re-ran the statistical analyses with the complete case data excluding participants with a history of psychotic or manic illness. Furthermore to ensure that those who reported discontinuation would be objectively considered to have ceased use we re-ran the analysis with discontinued users restricted to the group who had reported last use of cannabis to be at least six months previously. To ensure any relationships were not accounted for by infrequent or experimental users we checked whether the relationship between experiences and discontinuation / future discontinuation survived across differing levels of use by running the logistic regression with data split by frequency of use. In this case frequency of use was removed as a covariate from logistic regression models.

Statistical Analysis was undertaken in SPSS version 20.

Qualitative Analysis

Open-ended questionnaire responses to questions on reasons stated for discontinued cannabis use (experiences), descriptions of negative experiences, and stated reasons for changes in patterns of use over time

were transcribed, collated and inductively coded by an independent researcher who had not been involved in the design of the quantitative survey (CN). Following a thematic approach(Braun & Clarke 2006), no *a priori* coding structure was applied, but themes were allowed to 'emerge' naturally from the data, and were grouped in meaningful ways to assist with interpretation of the data. Analysis was discussed and verified at regular team meetings. This analysis was undertaken independently but in parallel with the quantitative analysis.

Results:

Demographics:

In total, 1425 participants responded to the survey. Five participants were excluded due to being under 18. Of the remaining data was available for 1231 participants who had ever used cannabis (see Fig 1). Complete case data was available for 940 participants. Summary demographic and predictor, outcome and covariate data are reported in Table 1. 845/1231 (68.6%) were male, whereas 375/1231 (30.5%) were female. Age ranged from 18-77 years (mean 29.5, median 26, standard deviation 10.3). 469 (38.1%) of the respondents reported previous mental health contact. While this was not quantified based on free-text information this appeared to be mostly related to anxiety, depression or stressful experiences and involved treatment within the primary care setting or by counseling. 25/1231 (2.0%) participants included in the analysis referred to a diagnosis of psychotic or manic illness.

Although we did not routinely ask for country, 494/531 (93.0%) of those who agreed to a follow-up study gave their place of residence in the United

Kingdom, with 23/531 (4.3%) responding from Sweden, although there were also a few responses from the USA, Brazil, Mauritius, Greece and Zimbabwe.

Cannabis Use:

926/1231 (75.2%) continued to use the substance. 167/907 (18.4%) of continued users agreed that they would like to stop in the future. In all users pleasurable experiences were more frequently reported than psychotic experiences. Age of first cannabis use ranged from 7-55 years (mean 16.7, median 16, SD 3.7).

Cannabis experiences:

Pleasurable experiences exceeded psychotic-like experiences. 915/1123 (81.4%) of respondents in this sample reported that they experienced happiness either most or all of the times they used cannabis, whilst 66/1119 (5.9%) of respondents endorsed ‘feeling nervy’, the most common dysphoric experience. A considerable proportion of cannabis users had ever experienced psychotic or dysphoric experiences when using cannabis: feeling suspicious: 524/1117 (46.9%); feeling nervy: 491/1119 (43.9%); feeling fearful: 302/1123 (27.1%); seeing visions: 187/1118 (16.7%); feeling like going crazy or mad: 145/1121 (12.9%); and hearing voices: 100/1117 (9.0%).

Cannabis Experiences cessation vs. continuation

Psychotic-like experiences and pleasurable experiences scores by ceased and continued users are shown in Table 2a. Those who had ceased reported greater frequency of experiencing psychotic-like experiences ($t=7.05$, $p<0.001$) whereas continued cannabis users were significantly more likely to report pleasurable experiences than those who had ceased ($t=-16.67$,

p<0.001). These findings remained when the complete data-set was analysed and further when those with a history of psychotic or manic illness were excluded(see supplementary data).

Results from a logistic regression analysis are summarized in Table 3a. Cessation of cannabis use was significantly associated with psychotic-like experiences (higher score predicts cessation), pleasurable experiences (lower score predicted cessation), age (older age predicted cessation), sex (being female predicted cessation) and frequency of cannabis use (less frequent use predicted cessation). Tobacco use was also borderline significant (p=0.51), indicating more frequent tobacco use predicted continuation.

Cannabis Experiences in continued users: No intention to quit vs. Future intention to quit.

Within continued cannabis users, future intention to quit was significantly associated with greater psychotic-like experiences (t=3.95, p<0.001) and lower pleasurable experiences (t=-2.37, p=0.017) (see Table 2b). These findings were replicated when the complete data-set was analysed (see supplementary data). Logistic regression (Table 3b) analyses suggested that future intention to quit was significantly associated with psychotic-like experiences (higher score predicted future intention to quit) pleasurable experiences (lower score predicted future intention to quit), age (lower age predicted future intention to quit), sex (being females predicted future intention to quit) and history of tobacco use (more frequent use predicted future intention to quit). History of non-prescribed medication use was also borderline significant (p=0.49, less frequent use predicted future to quit).

Sensitivity analyses:

On sensitivity analyses, when the complete data-set was analysed (i) with those with psychosis or manic illness excluded and (ii) restricted to discontinued users who reported last use of cannabis more than six months previously, psychotic-like experiences and pleasurable experiences significantly predicted cessation in the same direction. The same relationship between psychotic like experiences and pleasurable experiences remained statistically significant when restricted to daily users (see supplementary data).

Qualitative Analysis

In total 1107 unique participants provided qualitative feedback. 312 unique 'open' codes were inductively derived from the data. Qualitative coding broadly identified the dominant themes of significant negative experiences as impacting on continued cannabis use (see supplementary data on coding 'Why did you stop/Negative psychological symptoms'). Within coding of responses to the question 'why have patterns of use changed?', 121 codes were broadly categorised into individual, interpersonal, community, organisational and policy level themes. Additional themes related specifically to constituents of cannabis, the micro-context of use and the concept of 'maturation'. Drawing on subjective participant perspectives, negative experiences were linked to the type of cannabis used, particularly strong types of cannabis (skunk) and synthetic cannabis. Participants made clear links between their negative experiences, their cannabis use, and their future intentions, such that negative experiences were considered to be somewhat protective of future cannabis use (see supplementary data on coding 'Why have patterns of use changed/negative effects'). Indeed, our coding clusters

particularly around individual level factors, suggesting that experience at the individual level of perception and interpretation is critical in informing continued patterns of cannabis use. Those who did not report severe negative experiences also discussed future intention to discontinue cannabis use, but intentions in these cases were framed around 'growing older', moving away from cannabis use, and discontinued use to match life events (notably getting married, starting a family, starting full time employment) (see supplementary data on coding 'would you like to stop using cannabis one day/maturing out).

Discussion:

We investigated the impact of desirable and undesirable transient subjective experiences such as 'pleasurable' and 'psychotic-like experiences' respectively on subsequent cannabis use behaviour as indexed by cessation or continuation of cannabis use as well as future intention to quit in those who continue to use cannabis in a large internet-based participant survey. Our results from a combination of quantitative and qualitative analyses converge to demonstrate that psychotic-like experiences are strongly associated with both cannabis cessation and future intention to quit. These results survived controlling for potential confounding factors that may also be associated with these outcomes and is particularly evident in those who use cannabis most frequently.

Qualitative data further support these relationships such that those who have discontinued cannabis are more ready to clearly ascribe this to negative experiences. However, those who intend to stop using cannabis in the future

do not necessarily ascribe intention to stop to anticipated negative experiences. Together, the significant association between negative subjective experiences and cessation may suggest that the elucidation of such experiences may form the basis of a therapeutic intervention for those who express a desire to quit.

Conversely, this study clearly demonstrates that pleasurable experiences are associated with continued use and lack of intention to quit. This is in line with previous studies in this area(Grant *et al.* 2005; Scherrer *et al.* 2009). Cannabis is thus evidently experienced as a pleasurable drug and this would appear to account for its ongoing and continued use.

To date there is no consensus in the literature as to whether adverse experiences are associated with reduced or heavier use(Lyons *et al.* 1997; Grant *et al.* 2005; Scherrer *et al.* 2009; Zeiger *et al.* 2010). To our knowledge no prior studies have systematically looked to examine specifically the effect of cannabis induced psychotic-like experiences on cannabis cessation. Two studies have however reported on incidental findings which support the direction of our findings. Whilst validating the Cannabis Experiences Questionnaire Stirling et al noted continued cannabis users to report more positive and less negative experiences than past users(n=185)(Stirling *et al.* 2008). Whilst testing whether psychotic-like experiences are a marker of psychosis proneness, Mason and colleagues noted that a greater acute psychotomimetic state effect was associated with less frequent cannabis use (n=140)(Mason *et al.* 2009). Our data extends previous work by clearly indicating that psychotic-like experiences are associated with cessation and are attributed as one of the main drivers underlying cessation by those who

have successfully stopped. Furthermore, by demonstrating an association between psychotic-like experiences and a future intention to cease, which is not consciously recognised as such by continued users, these results also suggest a potential intervention target. Given that our data show psychotic-like experiences in both continued and discontinued users, this may indicate that as pleasurable experiences are predominant they may override occasional negative experiences, even if the experience is severe. However the results of this study may have implications beyond this.

A central argument against the relationship between cannabis use and psychosis risk has been that whereas cannabis prevalence and potency has increased over the last four decades there has been not been a corresponding increase in population level incidence of psychotic disorders(Frisher *et al.* 2009) as would be expected were cannabis use to be causally linked to psychosis risk. This has been argued to critically weaken the case for the association between cannabis and psychosis and remains an ongoing area of controversy(Hill 2015; Gage *et al.* 2016).

There is now a growing body of evidence to suggest that psychotic-like experiences with cannabis use, such as have been measured in this study, may act as a tractable marker for identifying those at putative psychotic risk. In an independent study patients with psychotic illness have been shown to experience more profound cannabis effects compared to Healthy Controls (HCs)(Bianconi *et al.* 2016). Administration of Delta-9-tetrahydrocannabinol (THC), the major psychotomimetic constituent of cannabis, has been demonstrated to elicit an increased psychotomimetic response in individuals with a psychotic illness as compared to HCs(D'Souza *et al.* 2005).

Furthermore increased schizotypy, a marker of psychosis-proneness, predicts increased psychotic-like experiences in cannabis users(Barkus *et al.* 2006). A large patient-sibling and sibling-control design study has demonstrated increased sensitivity of sub-threshold psychotic experiences to cannabis use amongst sibling-pairs of patients with psychosis as compared to controls(Kahn *et al.* 2011). Controlled experimental studies have demonstrated that variations in genes implicated in psychosis such as COMT, AKT1 and DAT1 may moderate greater sensitivity to the psychotomimetic effects of cannabis and its neurophysiological underpinnings in non-clinical populations(Henquet *et al.* 2006; Bhattacharyya *et al.* 2012). Taken together, increased sensitivity to cannabis-induced psychotomimetic experiences have been found in (i) patients with psychosis (ii) those with psychosis proneness and (iii) those with family history and genetic liability to psychosis, as compared to the general population. Thus the CEQ psychotic-like experiences score, as measured in this study, may give an indication of psychosis risk, although prospectively designed studies would be required to absolutely quantify this.

If individuals with cannabis-induced psychotic-like experiences (who are at a putatively higher risk of developing disorder) were to discontinue use, as our results suggest, this may off-set the greater risk of developing psychotic disorder associated with cannabis use. We suggest that this might in turn explain the relative stability of rates of psychotic disorder over time despite the growing use of more potent forms of cannabis. Hence, we posit a discontinuation hypothesis leading to those at the highest risk of cannabis-induced psychosis self-selecting themselves out of continued use and hence

protecting themselves from the risk of developing enduring psychotic disorders.

Such an explanation is consistent with evidence that those at clinically high-risk of psychosis discontinue cannabis use once breakthrough psychotic symptoms appear(Valmaggia *et al.* 2014) and independent evidence in the general population that subthreshold psychotic experiences, measured using the Community Assessment of Psychic Experience (CAPE) questionnaire (as distinct from cannabis induced psychotic-like experiences) predict cessation of cannabis use over six months to five years(van Gastel *et al.* 2014).

These results are to be considered in light of certain limitations: the outcome measure reported self-reported continued use (yes/no) may vary or wane over time. However our findings remained in the same direction when we restricted the discontinued group to those who reported last use at least six months previously. Further the cross-sectional nature of our study precludes conclusions regarding the precise nature of these relationships. Nevertheless, the associations reported survived adjustment for multiple potential demographic and substance misuse confounders and were consistent across two different outcome measures. Arguably, the pragmatic design that we have employed using a convenience sample, rather than a probability sample also limits the generalizability of these results. While this would have been expected to result in under-reporting of psychotic-like symptoms associated with cannabis use as our sample was drawn from advertisements on social media and cannabis campaigning platforms, this did not occur, with around 40% of the sample acknowledging they have either felt suspicious or nervy at some point from cannabis use. Arguably, the online data acquisition design

accorded anonymity allowing for more honest engagement with the survey as evident from the abundant qualitative data. Of note, a higher proportion of our sample (38.1%) reported a lifetime history of mental health contact than would be expected in the general population. Although we adjusted for mental health contact in our data, this did not include substance misuse treatment, which maybe seen as a limitation. Further we cannot completely exclude response bias or recall bias: those who have discontinued are likely to have used cannabis in the more distant past than those who continue use, and those who discontinue may be more likely to highly rate negative experiences. However, these biases are unlikely to have systematically affected the results as negative experiences are also rated similarly in those who continue to use but intend to quit in future.

Finally, one must also consider the items used and the construct validity of the Cannabis Experiences Questionnaire for the experiences used and the sample studied. Principal Component Analysis of 55 different experiences (43 immediate, 12 after-effects) in a previous British non-clinical cohort using an electronic survey has demonstrated the nine experiences we administered to load significantly with factor loading >0.5 onto their respective subscales (psychotic-like experiences and pleasurable effects)(Barkus & Lewis 2008). A further analysis of all the original experiences showed the nine experiences we administered to load similarly onto distinct subscales with factor >0.5 in the same manner, except for visual hallucinations which were not part of the solution(Stirling *et al.* 2008). A two-factor model for immediate experiences has recently been confirmed in independent non-clinical populations although notably auditory and visual hallucinations were not part of the final 13 item solution(Quinn *et al.* 2016). However, this latent structure has not been

universally validated in clinical populations: in a recent US sample in a first episode clinical population (n=194), Exploratory Factor Analysis using the original experiences identified four subscales amongst patients: distortions of reality and self-perception; euphoria effects; slowing and amotivational effects; and anxiety and paranoia effects(Birnbaum *et al.* 2017). This is similar, although not identical to another study involving both first episode patients and controls (patients n=252; controls n=207) where a four factor model was derived from 14 experiences namely: anxiety-paranoid experiences; cognitive experiences; enjoyable experiences and psychotic experiences(Bianconi *et al.* 2016). One explanation for this could be that cannabis experiences maybe differentially experienced in clinical and non-clinical populations as suggested by the authors of both studies(Bianconi *et al.* 2016; Birnbaum *et al.* 2017), hence our results in a non-clinical sample cannot be generalized to patient groups which would need to be studied separately.

Notwithstanding these limitations, using a well-validated measure which has now been used across multiple non-clinical populations(Barkus *et al.* 2006; Barkus & Lewis 2008; Stirling *et al.* 2008; Quinn *et al.* 2016) and a mixed-methods approach, we report converging evidence from quantitative analysis controlling for potential confounders and independent qualitative analysis that psychotic-like experiences may predict cannabis cessation whereas pleasurable experiences may predict continued use as well as quantitative evidence that such experiences may also predict future intention to quit or continue cannabis use.

Together, these findings may suggest that psychotic-like experiences associated with cannabis use may have a protective effect on the risk of subsequent psychotic disorder by influencing future and continued cannabis use behaviour, and may go some way to explaining relative stability of rates of psychotic disorder over time. Prospective longitudinal studies are needed to definitively confirm or refute this possibility.

Declaration of Interest

The authors declare no conflict of interest

Source of funding

SB has been funded by the National Institute for Health Research (NIHR), UK through a Clinician Scientist award (NIHR-CS-11-001) and also supported by the NIHR Biomedical Research Centre for Mental Health BRC Nucleus at the South London and Maudsley NHS Foundation Trust and Institute of Psychiatry, Psychology and Neuroscience, King's College London. MS is funded through a Medical Research Council (UK) Clinical Research Training Fellowship. CN is funded through a Post-Doctoral Fellowship from the UK Society for the Study of Addiction.

Role of the funding source

The views expressed are those of the authors and not necessarily those of the NHS, the NIHR, the MRC, the SSA or the Department of Health. The funders had no role in the preparation, review, or approval of the manuscript; and decision to submit the manuscript for publication. All authors have approved the final version of the paper.

Ethical declaration

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant national and institutional committees on

human experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

Table 1: Demographic data

		All *(n=1231)*	**Ceased** *(n=305)*	**Continued** *(n=926)*	Sig.*	Sig (msng)†	**Intention to Quit** *(n=166)*	**No Intention to Quit** *(n=741)*	Sig.*	Sig (msng)†
Age		x̄=29.5, sem=0.31	x̄=29.5, sem=0.57	x̄=29.5, sem=0.36	0.97		x̄=25.1, sem=0.61	x̄=30.4, sem=0.41	**<0.01**	
	Missing	102 (8.3)	27 (8.9)	75 (8.1)		0.72	15 (9.0)	58 (7.8)		0.64
Sex	Male	845 (68.6)	122 (40.0)	723 (78.1)	**<0.01**		117 (70.5)	592 (79.9)	**<0.01**	
	Female	375 (30.5)	182 (59.7)	193 (20.8)			48 (28.9)	140 (18.9)		
	Missing	11 (0.9)	1 (0.3)	10 (1.1)		0.31	1 (0.6)	9 (1.2)		0.70
Occupation	Full time	600 (48.9)	137 (44.9)	463 (50)	**<0.01**		71 (42.8)	384 (51.8)	**<0.01**	
	Part time	109 (8.9)	25 (8.2)	84 (9.1)			14 (8.4)	69 (9.3)		
	Unemployed	107 (8.9)	12 (3.9)	95 (10.3)			12 (7.2)	82 (11.1)		
	Student	369 (30.0)	128 (42.0)	241 (26.0)			66 (39.8)	168 (22.7)		
	Missing	46 (3.8)	3 (1.0)	43 (4.6)		**0.03**	3 (1.8)	38 (5.1)		0.06
Mental Health contact	Yes	469 (38.1)	133 (43.6)	336 (36.3)	0.39		55 (33.1)	273 (36.8)	0.37	
	No	762 (61.9)	172 (56.4)	590 (63.7)			111 (66.9)	468 (63.1)		
Age at first cbs use		x̄=16.7, sem=0.11	x̄=17.5, sem=0.18	x̄=16.4, sem=0.13	**<0.01**		x̄=16.2, sem=0.24	x̄=16.5, sem=0.14	0.50	
	Missing	4 (0.3)	1 (0.3)	3 (0.3)		1.00	1 (0.6)	2 (0.3)		0.46
Cbs frequency of use	Every day	547 (44.4)	43 (14.1)	504 (54.4)	**<0.01**		87 (52.4)	417 (56.2)	0.49	
	> once week	271 (22.0)	36 (11.8)	235 (25.4)			40 (24.1)	195 (26.3)		
	Few times monthly	162 (13.2)	55 (18.0)	107 (11.6)			24 (14.5)	83 (11.2)		
	Few times yearly	132 (10.7)	84 (27.5)	48 (5.2)			10 (6.0)	38 (5.1)		
	Once or twice	69 (5.6)	65 (21.3)	4 (0.4)			2 (1.2)	2 (0.3)		
	Missing	50 (4.1)	22 (7.2)	28 (3.0)		**<0.01**	3 (1.8)	6 (0.8)		0.22
Alcohol history	Regular use	717 (58.2)	214 (70.2)	503 (54.3)	**<0.01**		92 (55.4)	411 (55.5)	0.34	
	Infrequent use	323 (26.2)	46 (15.1)	277 (29.9)			52 (31.3)	225 (30.4)		
	Use <5 times	31 (2.5)	2 (0.7)	29 (3.1)			3 (1.8)	26 (3.5)		
	Never use	23 (1.9)	3 (1.0)	20 (2.2)			2 (1.2)	18 (2.4)		
	Missing	137 (11.1)	40 (13.1)	97 (10.5)		0.21	17 (10.2)	61 (8.2)		0.44
Tobacco history	Regular use	633 (51.4)	113 (37.1)	520 (56.2)	**<0.01**		102 (61.5)	418 (56.4)	**<0.01**	
	Infrequent use	256 (20.8)	78 (25.6)	178 (19.2)			33 (19.9)	145 (19.6)		
	Use <5 times	125 (10.1)	42 (13.8)	83 (9.0)			11 (6.6)	72 (9.7)		
	Never use	80 (6.5)	32 (10.5)	48 (5.1)			3 (1.8)	45 (6.1)		
	Missing	137 (11.1)	40 (13.1)	97 (10.5)		0.21	17 (10.2)	61 (8.2)		0.44
Non-prescribed med history	Regular use	53 (4.3)	8 (2.6)	45 (4.9)	0.28		9 (5.4)	36 (4.9)	0.76	
	Infrequent use	163 (13.2)	35 (11.5)	128 (13.8)			19 (11.5)	109 (14.7)		
	Use <5 times	224 (18.2)	54 (17.7)	170 (18.4)			30 (18.1)	140 (18.9)		
	Never use	654 (53.1)	168 (55.1)	486 (52.5)			91 (54.8)	395 (53.3)		
	Missing	137 (11.1)	40 (13.1)	97 (10.5)		0.21	17 (10.2)	61 (8.2)		0.44
Cocaine history	Regular use	75 (6.1)	11 (3.6)	64 (6.9)	**<0.01**		12 (7.2)	52 (7.0)	0.99	
	Infrequent use	252 (20.5)	40 (13.1)	212 (22.9)			37 (22.3)	175 (23.6)		
	Use <5 times	302 (24.5)	67 (22.0)	235 (25.4)			42 (25.3)	193 (26.0)		
	Never use	465 (37.8)	147 (48.2)	318 (34.3)			58 (34.9)	260 (35.1)		
	Missing	137 (11.1)	40 (13.1)	97 (10.5)		0.21	17 (10.2)	61 (8.2)		0.44
Ecstasy history	Regular use	136 (11.1)	26 (8.5)	110 (11.9)	**<0.01**		18 (10.8)	92 (12.4)	0.53	
	Infrequent use	300 (24.4)	55 (18.0)	245 (26.5)			50 (30.1)	195 (26.3)		
	Use <5 times	252 (20.5)	51 (16.7)	201 (21.7)			38 (22.9)	163 (22.0)		
	Never use	406 (33.0)	133 (43.6)	273 (29.5)			43 (25.9)	230 (31.0)		
	Missing	137 (11.1)	40 (13.1)	97 (10.5)		0.21	17 (10.2)	61 (8.2)		0.44

Legend: All data count (%ge) unless specified otherwise; x̄: mean; sem: standard error of the mean; cbs: cannabis; *Significance using t-tests for continuous variables, χ^2 tests for proportions (infrequent categories combined if count<5) †Significance for missing data - Fisher's exact test 2x2 contingency test

Table 2a: Cannabis Experiences mean scores by group: Discontinuation vs Continuation

	Ceased Users			Continued Users			t-statistic and p-value[†]
	Male	Female	All	Male	Female	All	
Psychotic-like Experiences	9.93 (0.44) n=102	10.04 (0.36) n=157	10.02 (0.28) n=260	7.90 (0.09) n=657	8.24 (0.23) n=172	7.98 (0.08) n=839	t=7.05 **p<0.001**
Pleasurable Experiences	8.97 (0.32) n=103	7.42 (0.27) n=162	8.02 (0.21) n=266	11.91 (0.08) n=663	11.28 (0.20) n=174	11.78 (0.08) n=847	t=-16.67 **p<0.001**

Legend: Psychotic-like Experiences: CEQ Score Psychotic-like Experiences; Pleasurable Experiences: CEQ Score Pleasurable/Pleasurable Experiences *In boxes:* Mean score (SEM) number in group

[†] Independent samples t-test for cessation vs continuation. Positive t-statistic in direction of cessation.

Table 2b: Cannabis Experiences mean scores by group in Continued Users: Future intention to quit vs No future intention to quit

	Future intention to quit			No intention to quit			t-statistic and p-value[†]
	Male	Female	All	Male	Female	All	
Psychotic-like Experiences	8.74 (0.30) n=102	9.27 (0.54) n=45	8.88 (0.27) n=148	7.75 (0.09) n=555	7.88 (0.25) n=127	7.78 (0.08) n=691	t=3.95 **p<0.001**
Pleasurable Experiences	11.40 (0.22) n=104	11.30 (0.39) n=46	11.38 (0.19) n=151	12.01 (0.09) n=559	11.27 (0.24) n=128	11.86 (0.08) n=696	t=-2.37 **p=0.018**

Legend: Psychotic-like Experiences: CEQ Score Psychotic-like Experiences; Pleasurable Experiences: CEQ Score Pleasurable/Pleasurable Experiences *In boxes:* Mean score (SEM) number in group

[†] Independent samples t-test for Future intention to quit vs. No future intention to quit. Positive t-statistic in direction of future intention to quit.

Table 3a: Logistic Regression for Cannabis Discontinuation/Continuation by co-variate

	B	S.E.	Sig.	Exp(B)	95% C.I.for EXP(B)	
					Lower	Upper
Psychotic-like Experiences	0.233	0.035	**<0.001**	1.262	1.179	1.351
Pleasurable Experiences	-0.333	0.041	**<0.001**	0.717	0.662	0.776
Age	0.049	0.012	**<0.001**	1.050	1.026	1.075
Sex	0.593	0.233	**0.011**	1.809	1.146	2.856
Occupation	-0.003	0.086	0.974	0.997	0.842	1.181
Mental Health Contact	-0.347	0.229	0.130	0.707	0.451	1.108
Age of first cannabis use	-0.015	0.034	0.651	0.985	0.922	1.052
Frequency of cannabis use	0.824	0.104	**<0.001**	2.279	1.859	2.795
Alcohol history	-0.225	0.207	0.276	0.798	0.532	1.197
Tobacco history	0.235	0.121	0.051	1.265	0.999	1.603
Non prescribed medications history	0.055	0.137	0.686	1.057	0.808	1.382
Cocaine history	0.276	0.165	0.094	1.318	0.954	1.820
Ecstasy history	0.006	0.137	0.962	1.006	0.769	1.317
Constant	-4.371	1.202	<0.001	0.013		

Legend: Psychotic-like Experiences: CEQ Score Psychotic-like Experiences; Pleasurable Experiences: CEQ Score Pleasurable/Pleasurable Experiences. Positive Bs in direction of cessation.

Table 3b: Logistic Regression for Future intention to quit / No intention to quit by co-variate

	B	S.E.	Sig.	Exp(B)	95% C.I.for EXP(B)	
					Lower	Upper
Psychotic-like Experiences	0.123	0.040	**0.003**	1.131	1.044	1.225
Pleasurable Experiences	-0.114	00.047	**0.015**	0.892	0.814	0.978
Age	-0.075	0.016	**<0.001**	0.927	0.898	0.958
Sex	0.737	0.248	**0.003**	2.090	1.282	3.408
Occupation	-0.059	0.080	0.492	0.943	0.797	1.115
Mental Health Contact	0.204	0.233	0.388	1.226	0.772	1.945
Age of first cannabis use	0.054	0.037	0.150	1.056	0.981	1.136
Frequency of cannabis use	-0.006	0.118	0.957	0.994	0.789	1.252
Alcohol history	0.178	0.172	0.308	1.195	0.848	1.682
Tobacco history	-0.453	0.143	**0.002**	0.635	0.479	0.842
Non prescribed medications history	0.274	0.137	**0.049**	1.316	1.001	1.730
Cocaine history	-0.079	0.146	0.592	0.924	0.692	1.233
Ecstasy history	-0.002	0.130	0.988	0.998	0.771	1.293
Constant	-1.399	1.261	0.269	0.247		

Legend: Psychotic-like Experiences: CEQ Score Psychotic-like Experiences; Pleasurable Experiences: CEQ Score Pleasurable/Pleasurable Experiences. Positive Bs in direction of future intention to quit.

References:

Barkus E, Lewis S (2008). Schizotypy and psychosis-like experiences from recreational cannabis in a non-clinical sample. *Psychological medicine* **38**, 1267–1276.

Barkus EJ, Stirling J, Hopkins RS, Lewis S (2006). Cannabis-induced psychosis-like experiences are associated with high schizotypy. *Psychopathology* **39**, 175–178.

Bhattacharyya S, Atakan Z, Martin-Santos R, Crippa J a, Kambeitz J, Prata D, Williams S, Brammer M, Collier D a, McGuire PK (2012). Preliminary report of biological basis of sensitivity to the effects of cannabis on psychosis: AKT1 and DAT1 genotype modulates the effects of δ-9-tetrahydrocannabinol on midbrain and striatal function. *Molecular psychiatry* **17**, 1152–5.

Bianconi F, Bonomo M, Marconi A, Kolliakou A, Stilo SA, Iyegbe C, Gurillo Muñoz P, Homayoun S, Mondelli V, Luzi S, Dazzan P, Prata D, La Cascia C, O'Connor J, David A, Morgan C, Murray RM, Lynskey M, Di Forti M (2016). Differences in cannabis-related experiences between patients with a first episode of psychosis and controls. *Psychological Medicine*, 995–1003.

Birnbaum ML, Cleary SD, Ramsay Wan C, Pauselli L, Compton MT (2017). Factor structure of the Cannabis Experiences Questionnaire in a first-episode psychosis sample. *Early Intervention in Psychiatry*, 1–7.

Braun V, Clarke V (2006). Using thematic analysis in psychology. *Qualitative Research in Psychology* **3**, 77–101.

van den Bree MBM, Pickworth WB et al. (2005). Risk Factors Predicting Changes in Marijuana Involvement in Teenagers. *Archives of General Psychiatry* **62**, 311.

D'Souza DC, Abi-Saab WM, Madonick S, Forselius-Bielen K, Doersch A, Braley G, Gueorguieva R, Cooper TB, Krystal JH (2005). Delta-9-tetrahydrocannabinol effects in schizophrenia: Implications for cognition, psychosis, and addiction. *Biological Psychiatry* **57**, 594–608.

Degenhardt L, Hall W (2012). *Extent of illicit drug use and dependence, and their contribution to the global burden of disease*. *The Lancet* **379**, 55–70.

von Elm E, Altman DG, Egger M, Pocock SJ, Gøtzsche PC, Vandenbroucke JP (2007). The Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement: guidelines for reporting observational studies. *Lancet* **370**, 1453–1457.

Di Forti M, Iyegbe C, Sallis H, Kolliakou A, Falcone MA, Paparelli A, Sirianni M, La Cascia C, Stilo SA, Marques TR, Handley R, Mondelli V, Dazzan P, Pariante C, David AS, Morgan C, Powell J, Murray RM (2012). Confirmation that the AKT1 (rs2494732) genotype influences the risk of psychosis in cannabis users. *Biological Psychiatry* **72**, 811–816.

Di Forti M, Morgan C, Dazzan P, Pariante C, Mondelli V, Marques TR, Handley R, Luzi S, Russo M, Paparelli A, Butt A, Stilo SA, Wiffen B, Powell J, Murray RM (2009). High-potency cannabis and the risk of psychosis. *British Journal of Psychiatry* **195**, 488–491.

Frisher M, Crome I, Martino O, Croft P (2009). Assessing the impact of cannabis use on trends in diagnosed schizophrenia in the United Kingdom from 1996 to 2005. *Schizophrenia Research* **113**, 123–128.

Gage SH, Hickman M, Zammit S (2016). *Association between cannabis and psychosis: Epidemiologic evidence*. *Biological Psychiatry* **79**, 549–556.
van Gastel WA, Vreeker A, Schubart CD, MacCabe JH, Kahn RS, Boks MPM (2014). Change in cannabis use in the general population: A longitudinal study on the impact on psychotic experiences. *Schizophrenia Research* **157**
Grant JD, Scherrer JF, Lyons MJ, Tsuang M, True WR, Bucholz KK (2005). Subjective reactions to cocaine and marijuana are associated with abuse and dependence. *Addictive Behaviors* **30**, 1574–1586.
Henquet C, Rosa A, Krabbendam L, Papiol S, Fananás L, Drukker M, Ramaekers JG, van Os J (2006). An experimental study of catechol-o-methyltransferase Val158Met moderation of delta-9-tetrahydrocannabinol-induced effects on psychosis and cognition. *Neuropsychopharmacology : official publication of the American College of Neuropsychopharmacology* **31**, 2748–2757.
Hill M (2015). Perspective: Be clear about the real risks. *Nature* **525**, S14–S14.
Kandel DB, Logan JA (1984). Patterns of Drug-Use from Adolescence to Young Adulthood .1. Periods of Risk for Initiation, Continued Use, and Discontinuation. *American Journal of Public Health* **74**, 660–666.
Kandel DB, Raveis VH (1989). Cessation of illicit drug use in young adulthood. *Archives of general psychiatry* **46**, 109–116.
Kuepper R, van Os J, Lieb R, Wittchen H-U, Höfler M, Henquet C (2011). Continued cannabis use and risk of incidence and persistence of psychotic symptoms: 10 year follow-up cohort study. *BMJ (Clinical research ed.)* **342**, d738.
Little MA, Spruijt-Metz D, Pokhrel P, Sun P, Ann Rohrbach L, Sussman S (2013). Predicting self-initiated marijuana use cessation among youth at continuation high schools. *Frontiers in Psychiatry* **4**
Lyons MJ, Toomey R, Meyer JM, Green AI, Eisen SA, Goldberg J, True WR, Tsuang MT (1997). How do genes influence marijuana use? The role of subjective effects. *Addiction* **92**, 409–417.
Marconi A, Di Forti M, Lewis CM, Murray RM, Vassos E (2016). Meta-analysis of the Association Between the Level of Cannabis Use and Risk of Psychosis. *Schizophrenia bulletin* **42**, 1262–1269.
Mason O, Morgan CJA, Dhiman SK, Patel A, Parti N, Curran H V (2009). Acute cannabis use causes increased psychotomimetic experiences in individuals prone to psychosis. *Psychological Medicine* **39**, 951–6.
Moore THM, Zammit S, Lingford-Hughes A, Barnes TRE, Jones PB, Burke M, Lewis G (2007). Cannabis use and risk of psychotic or affective mental health outcomes: A systematic review. *The Lancet* **370**, 319–328.
Pairs S (2011). Evidence that familial liability for psychosis is expressed as differential sensitivity to cannabis: an analysis of patient-sibling and sibling-control pairs. *Archives of general psychiatry* **68**, 138–147.
Quinn CA, Wilson H, Cockshaw W, Barkus E, Hides L (2016). Development and validation of the cannabis experiences questionnaire - Intoxication effects checklist (CEQ-I) short form. *Schizophrenia Research*
Scherrer JF, Grant JD, Duncan AE, Sartor CE, Haber JR, Jacob T, Bucholz KK (2009). Subjective effects to cannabis are associated with use, abuse and dependence after adjusting for genetic and environmental influences. *Drug and Alcohol Dependence* **105**, 76–82.
Schoeler T, Monk A, Sami MB, Klamerus E, Foglia E, Brown R, Camuri G, Altamura AC, Murray R, Bhattacharyya S (2016a). Continued versus discontinued cannabis use in patients with psychosis: A systematic review

and meta-analysis. *The Lancet Psychiatry* **3**, 215–225.
Schoeler T, Petros N, Di Forti M, Klamerus E, Foglia E, Ajnakina O, Gayer-Anderson C, Colizzi M, Quattrone D, Behlke I, Shetty S, McGuire PK, David A, Murray RM, Bhattacharyya S (2016b). Effects of continuation, frequency and type of cannabis use on relapse in the first two years following onset of psychosis - an observational study. . The Author(s). Published by Elsevier Ltd. This is an Open Access article under the CC BY license *Lancet Psychiatry* **366**, 1–7.
Schoeler T, Petros N, Di Forti M, Pingault J-B, Klamerus E, Foglia E, Small A, Murray R, Bhattacharyya S (2016c). Association Between Continued Cannabis Use and Risk of Relapse in First-Episode Psychosis. *JAMA Psychiatry* **35**, 557–574.
Stirling J, Barkus EJ, Nabosi L, Irshad S, Roemer G, Schreudergoidheijt B, Lewis S (2008). Cannabis-induced psychotic-like experiences are predicted by high schizotypy: Confirmation of preliminary results in a large cohort. *Psychopathology* **41**, 371–378.
Le Strat Y, Ramoz N, Horwood J, Falissard B, Hassler C, Romo L, Choquet M, Fergusson D, Gorwood P (2009). First positive reactions to cannabis constitute a priority risk factor for cannabis dependence. *Addiction* **104**, 1710–1717.
Thomas H (1996). A community survey of adverse effects of cannabis use. *Drug Alcohol Depend* **42**, 201–207.
Valmaggia LR, Day FL, Jones C, Bissoli S, Pugh C, Hall D, Bhattacharyya S, Howes O, Stone J, Fusar-Poli P, Byrne M, McGuire PK (2014). Cannabis use and transition to psychosis in people at ultra-high risk. *Psychological medicine* **44**, 2503–12.
Zeiger JS, Haberstick BC, Corley RP, Ehringer MA, Crowley TJ, Hewitt JK, Hopfer CJ, Stallings MC, Young SE, Rhee SH (2010). Subjective effects to marijuana associated with marijuana use in community and clinical subjects. *Drug and Alcohol Dependence* **109**, 161–166.

Supplemental Data

Complete Case Data

This comprised 940 cases where complete data was available.

Table 1a: Cannabis Experiences mean scores by group: Discontinued vs Continued Use

	Ceased Users			Continued Users			t-statistic and p-value[†]
	Male	Female	All	Male	Female	All	
Psychotic-like Experiences	9.83 (0.43) n=95	10.14 (0.39) n=137	10.01 (0.29) n=232	7.85 (0.09) n=554	8.40 (0.25) n=154	7.97 (0.09) n=708	t=6.72 **p<0.001**
Pleasurable Experiences	9.02 (0.33) n=95	7.37 (0.29) n=137	8.04 (0.22) n=232	11.94 (0.09) n=554	11.29 (0.22) n=154	11.80 (0.09) n=708	t=-15.62 **p<0.001**

Legend: Psychotic-like Experiences: CEQ Score Psychotic-like Experiences; Pleasurable Experiences: CEQ Score Pleasurable/Pleasurable Experiences *In boxes:* Mean score (SEM) number in group
[†] Independent samples t-test for discontinuation vs continuation. Positive t-statistic in direction of discontinuation.

Table 1b: Cannabis Experiences mean scores by group in Continued Users: Future intention to quit vs No future intention to quit

	No intention to quit			Future intention to quit			t-statistic and p-value[†]
	Male	Female	All	Male	Female	All	
Psychotic-like Experiences	7.72 (0.09) n=467	8.05 (0.28) n=110	7.78 (0.09) n=577	8.57 (0.32) n=87	9.30 (0.55) n=44	8.82 (0.28) n=131	t=3.47 **p=0.001**
Pleasurable Experiences	12.03 (0.09) n=467	11.26 (0.26) n=110	11.89 (0.09) n=577	11.40 (0.24) n=87	11.36 (0.40) n=44	11.38 (0.21) n=131	t=-2.26 **p=0.024**

Legend: Psychotic-like Experiences: CEQ Score Psychotic-like Experiences; Pleasurable Experiences: CEQ Score Pleasurable/Pleasurable Experiences *In boxes:* Mean score (SEM) number in group
[†] Independent samples t-test for Future intention to quit vs. No future intention to quit. Positive t-statistic in direction of future intention to quit.

Complete Case Data with those with history of psychosis or manic illness removed

This comprised 915 cases.

Table 2a: Cannabis Experiences mean scores by group: Discontinued vs Continued Use

	Ceased Users			Continued Users			t-statistic and p-value[†]
	Male	Female	All	Male	Female	All	
Psychotic-like Experiences	9.79 (0.43) n=92	10.05 (0.39) n=131	10.01 (0.29) n=223	7.84 (0.09) n=544	8.41 (0.26) n=148	7.96 (0.09) n=692	t=6.48 **p<0.001**
Pleasurable Experiences	9.04 (0.34) n=92	7.44 (0.30) n=131	8.04 (0.22) n=223	11.91 (0.09) n=544	11.26 (0.23) n=148	11.77 (0.09) n=692	t=-14.94 **p<0.001**

Legend: Psychotic-like Experiences: CEQ Score Psychotic-like Experiences; Pleasurable Experiences: CEQ Score Pleasurable/Pleasurable Experiences *In boxes:* Mean score (SEM) number in group
[†] Independent samples t-test for discontinuation vs continuation. Positive t-statistic in direction of discontinuation.

_____

Table 2b: Cannabis Experiences mean scores by group in Continued Users: Future intention to quit vs No future intention to quit

	No intention to quit			Future intention to quit			t-statistic and p-value[†]
	Male	Female	All	Male	Female	All	
Psychotic-like Experiences	7.70 (0.09) n=458	8.08 (0.29) n=106	7.77 (0.09) n=564	8.58 (0.33) n=86	9.30 (0.57) n=42	8.80 (0.29) n=128	t=3.42 **p=0.001**
Pleasurable Experiences	12.02 (0.10) n=458	11.22 (0.27) n=106	11.87 (0.10) n=564	11.36 (0.24) n=86	11.36 (0.42) n=42	11.36 (0.21) n=128	t=-2.27 **p=0.024**

Legend: Psychotic-like Experiences: CEQ Score Psychotic-like Experiences; Pleasurable Experiences: CEQ Score Pleasurable/Pleasurable Experiences *In boxes:* Mean score (SEM) number in group
[†] Independent samples t-test for Future intention to quit vs. No future intention to quit. Positive t-statistic in direction of future intention to quit.

Table 3a: Logistic Regression for Cannabis Discontinuation/Continuation by co-variate for Complete Case Data with those with history of psychosis or manic illness removed

	B	S.E.	Sig.	Exp(B)	95% C.I.for EXP(B)	
					Lower	Upper
Psychotic-like Experiences	0.235	0.035	**<0.001**	1.265	1.180	1.356
Pleasurable Experiences	-0.318	0.041	**<0.001**	0.727	0.671	0.789
Age	0.049	0.012	**<0.001**	1.050	1.025	1.076
Sex	0.587	0.236	**0.013**	1.799	1.133	2.857
Occupation	-0.013	0.088	0.879	0.987	0.831	1.172
Mental Health Contact	-0.317	0.232	0.173	0.728	0.462	1.149
Age of first cannabis use	-0.012	0.034	0.731	0.988	0.925	1.056
Frequency of cannabis use	0.857	0.107	**<0.001**	2.356	1.909	2.908
Alcohol history	-0.247	0.211	0.241	0.781	0.516	1.181
Tobacco history	0.199	0.122	0.104	1.220	0.960	1.550
Non prescribed medications history	0.048	0.139	0.730	1.049	0.798	1.379
Cocaine history	0.287	0.168	0.087	1.333	0.960	1.851
Ecstasy history	0.011	0.139	0.938	1.011	0.770	1.326
Constant	-4.636	1.229	**<0.001**	0.010	-	-

Legend: Psychotic-like Experiences: CEQ Score Psychotic-like Experiences; Pleasurable Experiences: CEQ Score Pleasurable/Pleasurable Experiences. Positive Bs in direction of discontinuation.

Table 3b: Logistic Regression for Future intention to quit / No intention to quit by co-variate for Complete Case Data with those with history of psychosis or manic illness removed

	B	S.E.	Sig.	Exp(B)	95% C.I.for EXP(B)	
					Lower	Upper
Psychotic-like Experiences	0.128	0.041	**0.002**	1.136	1.233	1.048
Pleasurable Experiences	-0.118	0.047	**0.012**	0.888	0.975	0.810
Age	-0.073	0.017	**<0.001**	0.929	0.961	0.899
Sex	0.729	0.255	**0.004**	2.075	3.425	1.258
Occupation	-0.059	0.087	0.497	0.943	1.119	0.794
Mental Health Contact	0.204	0.239	0.394	1.225	1.961	0.767
Age of first cannabis use	0.060	0.037	0.106	1.063	1.143	0.987
Frequency of cannabis use	-0.019	0.121	0.875	0.981	1.242	0.775
Alcohol history	0.153	0.177	0.386	1.166	1.647	0.824
Tobacco history	-0.461	0.144	**0.001**	0.631	0.837	0.475
Non prescribed medications history	0.318	0.144	**0.027**	1.374	1.821	1.036
Cocaine history	-0.041	0.149	0.785	0.960	1.285	0.717
Ecstasy history	-0.013	0.133	0.923	0.987	1.282	0.760
Constant	-1.706	1.284	0.184	0.182	-	-

Legend: Psychotic-like Experiences: CEQ Score Psychotic-like Experiences; Pleasurable Experiences: CEQ Score Pleasurable/Pleasurable Experiences. Positive Bs in direction of future intention to quit.

Complete Case Data with discontinued groups restricted to those who have discontinued for 6 months or more

This comprised 785 cases.

Table 4: Cannabis Experiences mean scores by group: Discontinued (specified more than 6 months) vs Continued Use

	Ceased Users			Continued Users			t-statistic and p-value[†]
	Male	Female	All	Male	Female	All	
Psychotic-like Experiences	11.08 (0.81) n=37	10.73 (0.78) n=40	10.01 (0.29) n=223	7.85 (0.09) n=554	8.40 (0.25) n=154	7.97 (0.09) n=708	t=5.15 **p<0.001**
Pleasurable Experiences	9.84 (0.51) n=37	8.20 (0.55) n=40	8.04 (0.22) n=223	11.94 (0.09) n=554	11.29 (0.22) n=154	11.80 (0.09) n=708	t=-7.09 **p<0.001**

Legend: Psychotic-like Experiences: CEQ Score Psychotic-like Experiences; Pleasurable Experiences: CEQ Score Pleasurable/Pleasurable Experiences *In boxes:* Mean score (SEM) number in group
[†] Independent samples t-test for discontinuation vs continuation. Positive t-statistic in direction of discontinuation.

Table 5: Logistic Regression for Cannabis Discontinuation/Continuation by co-variate for Complete Case Data with discontinued users restricted to those who specified last use more than 6 months prior

	B	S.E.	Sig.	Exp(B)	95% C.I.for EXP(B)	
					Lower	Upper
Psychotic-like Experiences	0.249	0.044	**<0.001**	1.282	1.175	1.399
Pleasurable Experiences	-0.271	0.056	**<0.001**	0.762	0.683	0.851
Age	0.033	0.016	**0.039**	1.034	1.002	1.067
Sex	0.357	0.330	0.279	1.429	0.749	2.727
Occupation	0.002	0.119	0.989	1.002	0.793	1.264
Mental Health Contact	-0.456	0.329	0.165	0.634	0.333	1.207
Age of first cannabis use	-0.022	0.051	0.664	0.978	0.884	1.081
Frequency of cannabis use	0.713	0.141	**<0.001**	2.041	1.549	2.688
Alcohol history	-0.307	0.309	0.320	0.736	0.402	1.347
Tobacco history	0.126	0.167	0.448	1.135	0.819	1.573
Non prescribed medications history	0.241	0.206	0.241	1.273	0.850	1.905
Cocaine history	0.202	0.227	0.374	1.224	0.784	1.912
Ecstasy history	0.267	0.192	0.163	1.307	0.897	1.903
Constant	-5.682	1.791	**0.002**	0.003	-	-

Legend: Psychotic-like Experiences: CEQ Score Psychotic-like Experiences; Pleasurable Experiences: CEQ Score Pleasurable/Pleasurable Experiences. Positive Bs in direction of discontinuation.

Table 6: Logistic Regression for Cannabis Discontinuation/Continuation and Future intention to quit / No intention to quit for Complete Case Data by frequency of use

	Discontinuation vs continuation					Future Intention to quit vs no intention				
	n	Psychotic Like Experiences	p-value	Pleasurable experiences	p-value	n	Psychotic Like Experiences	p-value	Pleasurable experiences	p-value
Daily Use	427	1.328	**<0.001**	0.731	**<0.001**	393	1.156	**0.016**	0.82	**0.004**
More than once weekly	224	1.571	**<0.001**	0.532	**<0.001**	190	1.043	0.643	0.922	0.464
A few times each month	129	1.225	**0.02**	0.805	**0.026**	82	1.091	0.558	0.906	0.447
A few times each year	104	1.177	0.059	0.699	**<0.001**	39	Not calculated as numbers too small			
Only once or twice	56	0.965	0.923	0.368	0.528	4	Not calculated as numbers too small			

Legend: Psychotic-like Experiences: CEQ Score Psychotic-like Experiences; Pleasurable Experiences: CEQ Score Pleasurable/Pleasurable Experiences. Numbers in columns are Exp(B) (adjusted Odds Ratios) from Logistic Regression. Exp(B)>1 in direction of discontinuation/future intention to quit.

Qualitative data:[*]

<'Why did you stop?'>
Coding Report for dominant code – 'Negative psychological symptoms'

Reference 1

Started feeling negative symptoms such as paranoia and loss of control over thoughts.

Reference 2

Using cannabis increased my feelings of depression and anxiety for a period of time after ingestion. I decided to stop using cannabis when the feelings of depression and anxiety that its use stimulated outweighed the enjoyment I experienced from cannabis use.

Reference 3

Panic attacks and other anxiety symptoms. Relative with mental illness relating to drug use

Reference 4

negative effects on mood and productivity

Reference 5

I didn't like it. Because I knew it was illegal, it made me feel a heightened sense of paranoia almost every time. It wasn't worth it after a while.

Reference 6

I tended to binge and realised this was unhelpful in terms of my mood and mental stability.

Reference 7

I did not like the experience whenever I used it

Reference 8

made me paranoid and unhappy

Reference 9

Just haven't used it in a while, but might use it again, when there is a chance. My last experiences with it seemed make me rather anxious for a while, and then relaxed me.

Reference 10

It is an awful drug, it completely effected my entire perceptions such that I felt the effect for more than two weeks.

Reference 11

paranoia

[*] Using participants' original spelling and grammar

Reference 12

I didn't enjoy the feeling of having less control

Reference 13

My reactions grew worse and worse, at times vomiting, anxiety, etc. Although in the end I smoked very rarely and very little and could enjoy it, my previous experiences scarred me.

Reference 14

Only used very infrequently and don't use now because I don't enjoy it and don't want it to negatively affect my mental health.

Reference 15

Cannabis in England seemed stronger than back home and made me feel more anxious. I also used to smoke a lot of hash and I could not find a good hash source in England.

Reference 16

Affected academic performance, caused paranoia, also against religous beliefs.

Reference 17

Started getting anxiety attacks when going through menopause

Reference 18

difficult life experiences led to too much rumination with cannabis, leading to paranoia!

Reference 19

Smoked variety of very strong cannabis over the course of a weekend and felt anxious and mildly paranoid for a day or do afterwards

Reference 20

I didn't like the effect it had on me. Made me quite paranoid and just didn't enjoy the effect on me.

Reference 21

The cannabis I was able to get, was presumably skunk, and it made me extremely anxious and paranoid. In the past I took other varieties that could be quite pleasant. The Paranoid thought patterns are very unpleasent. I was also worried about my family history of schizophrenia, my bipolar disorder and potential drug interactions.

Reference 22

I started to have medical problems as paranoia, anxiety or depression

Reference 23

When I got my first appointment at a psychiatric clinic, I decided to quit. I had always told myself that I would take an eventual psychiatric treatment seriously and not smoking pot during it

seemed like a no brainer...

Reference 24

It stopped giving me new ideas and good vibes. I just got ""stoned"" and then it wasn't any fun.

Reference 25

does not have a good effect on me- feeling of tiredness, difficulty to concentrate, slight feelings of anxiety, irritable

Reference 26

It started to make me feel anxious

Reference 27

I wasn't enjoying it anymore. It had started to have an adverse effect on my mood.

Reference 28

Enjoyed feeling less and less. Became anxious and slightly paranoid and then had a 3 month extreme psychotic episode which stopped after I stopped smoking cannabis.

Reference 29

paranoia and 'busy head' couldn;t sleep

Reference 30

caused paranoia.

Reference 31

It made me very anxious and paranoid. Also interfered with homework and school.

Reference 32

Started making me feel uncomfortable and anxious

Reference 33

was making me feel low, concerns about lung health risks, worked with children

Reference 34

It made me feel anxious in social situations, i got completely list in my own thoughts. Paranoia

Reference 35

hated the smell and the high made me feel paranoid and sluggish

Reference 36

Had the episode of submission and then onwards was advised not to use again

Reference 37

Made me anxious

Reference 38

I smoked it daily when I was a teenager, then as I got older I mostly used it after/during using different drugs. I grew to dislike it more as time went on because it made me anxious, paranoid, difficultly sleeping and led me to over think things a lot.

Reference 39

I only enjoyed it in a certain group of people. Normally when on a comedown from MDMA. Didn't enjoy it too much made me paranoid. Ruined the buzz from the other drug.

Reference 40

It made me feel anxious and paranoid

Reference 41

It became not a fun experience any more, became paranoid both when using it and when not using and started having negative reactions to it too regularly

Reference 42

It was the right thing to do, health wise. I was having mental issues, and one day I decided to stop and haven't ever since.

Reference 43

Paranoia

Reference 44

it made me too forgetful, it interfered with my daily routines. I stopped paying attention to the world around me.

Reference 45

Experienced only adverse effects - could not concentrate

Reference 46

Had a paranoid reaction one time

< If your pattern of use has changed over time why>
Coding report for dominant code 'negative effects'

Reference 1

It stopped feeling good and the effects I had did not seem to affect my friends.

Reference 2

peaked during undergraduate degree, stopped due to negative effects

Reference 3

it was fun at first but then rather than get giggly it made me very paranoid and withdrawn both during smoking and in the weeks after, so I stopped completely.

Reference 4

Hard to wake up in the morning for work after smoking

Reference 5

stopped - paramoia

Reference 6

From 19-23 I smoked daily, after low moods and anxiety/panic attack I completely stopped and have been smoking again 2-3 times a week for the past few months

Reference 7

at first it was a novel thhing, exciting, like having alcohol for the first time in social settings. The people that had it aged 17 seemed cool. However as I grew up and left sixth form I realised I didnt enjoy it that much, I saw the negative effects of it during my gap year and began saying no until my friendship group changed etc. I dont miss it to be honest

Reference 8

After about a year of smoking somewhat regularly I had a very bad reaction which threw me off. Smoked half a joint at a club, started throwing up, felt very dizzy, had to be picked up. The weed came from a person I knew quite well, he did not have these reactions.

Reference 9

After a few years of every week (sometimes every day) usage I realized that I was spending too much time for nothing. Also, I had a few episodes of panic attack and it was correlated with high usage. Additionally, every day usage makes you lazy, weak, unconcentrated etc.

Reference 10

tried it a few times on and off with friends, didn't really get or understand the effects of it other than it made me feel dizzy, so stopped doing it

Reference 11

When I was younger I had easy access to it and it was my preferred drug of choice so I used it a lot (4-5 a week). It was also social consumption where evenings were spent with friends watching movies, smoking cannabis and just generally chilling. I started smoking less cannabis when i started going out more and using other drugs. I then stopped using cannabis when I found that it was getting too strong and only making me anxious.

Reference 12

Because of the panic attacks i am scared to try it again and I have no access to a safe supply. If it was legal I would grow my own and use it as plant medicine.

Reference 13

i did it a few times with friends but i disliked it

Reference 14

experimental use. suffered with nausea/vomiting

Reference 15

has got less- I smoked it when i was 14/15 but had a bad experience and havent smoked since

Reference 16

My intensity of use diminished gradually. For the last few years I was smoking 100mg or less. But a daily use pattern persisted. My job is in substance misuse so the tell tale signs around the eyes became a problem. My life became busier and more responsible and in the end I found the effects were unwanted, less pleasant and too long acting. As a father, the effect on sleep began to count - meaning I would feel tired in the morning even having smoked very small amounts. Also, my partner doesn't like the smell on my breath.

Reference 17

at the age of 18 I used to smoke almost everyday (my friends smoked everyday as well) but around 19 I started to have medical problems as paranoia, around 20 I started to go to the psychiatrist and I stopped smoking cannabis.

Reference 18

I stopped smoking because I moved to Korea. It also held me back generally from achieving what I wanted to do. It slowed me down cognitively and significantly decreased my affective states.

Reference 19

Between the ages of 19 and 24 I smoked it very heavily. Between 24 and 33 I only smoked it sporadically due to pregnancy and breastfeeding. By 34 I had stopped completely because I had children to look after and career ambitions. Cannabis use was just a waste of my time and by that point I experienced extreme anxiety when smoking it.

Reference 20

It was helping my ADHD but killing my motivation, so I don't use it as much anymore

Reference 21

Availability when I was younger like 16-19. And availability now Iam 21. Furthermore I don't do it much nowadays because it dumbs down my thinking and personally I don't like that .

Reference 22

caused severe paranoid episode aged 21 and stopped at this point.

Reference 23

I cannot handle the effects - I don't like feeling so anxious/paranoid

Reference 24

I stopped as I realised I didn't enjoy it, it made me paranoid and was a waste of money

Reference 25

Had unexpected physiological responses (e.g fainting, auditory sensitivity,overeating) When paired with other abusive substances it resulted in negative emotional/psychological affects that were debilitating for me in my daily routine/life

Reference 26

found cannabis bad for mental health

Reference 27

It has increased due to traumatic life events

Reference 28

Don't use it hardly ever anymore cos I have a negative reaction to it so if I do it'll be like 1 or 2 tokes which is usually okay but try not to

<Would you like to stop using cannabis one day>
Coding report for exemplar code – 'maturing out'

Reference 1

I don't see myself using cannabis for the rest of my life. I am currently enjoying it, as a young person, but I do not depend on it and definitely will stop in the next few years.

Reference 2

Well i wouldn't see myself using cannabis when I've had children or when I get a full time job

Reference 3

I don't use it regularly but on occasion, I don't see myself using cannabis as I get older.

Reference 4

When I am older and have a family I will not be a frequent user of cannabis but I would not be opposed to engaging in the activity every so often.

Reference 5

I do not see cannabis as something which will be suited for every stage of my life. There will be a time where it would become irresponsible (e.g. when I have children etc)

Reference 6

Growing older may have to focus on other responsibilities

Reference 7

I don't see myself smoking when I have more work / family responsibility.

Reference 8

I'm believe I will stop some day, when I have matured more. Right now my current living situation and lift style can accommodate smoking cannabis, but someday that may change, like if I have children, get married, or get a more serious job.

Reference 9

Can't get stoned for the rest of my life

Reference 10

i don't intend to do anything forever. everything eventually gets boring, people change, life goes on.

Reference 11

In the future I'm likely to have responsibilities (eg a career/family) that may mean I will not be able to use it

Reference 12

Maybe not stop 100%. But definitely cut down a lot after uni and when/if I have children it won't be smoked around them.

Reference 13

Eventually as I get older and start getting a job, it'll be best to stop and just focus on my career

Reference 14

I've been smoking weed for the last 7 years, and I am still smoking, but I believe that you can't really smoke till the end of you life...don't know why.

Reference 15

It's not a forever sort of thing