Title: Patterns of cannabis use and prospective associations with health issues among young males.

Authors: Baggio S, N'Goran AA, Deline S, Studer J, Dupuis M, Henchoz Y, Mohler-Kuo M, Daeppen JB, Gmel G

Journal: Addiction (Abingdon, England)

Year: 2014 Jun

Volume: 109

Issue: 6

Pages: 937-45

DOI: 10.1111/add.12490

Patterns of cannabis use and prospective associations with health issues among young males

Stéphanie Baggio[1], Alexandra A. N'Goran[1], Stéphane Deline[1], Joseph Studer[1], Marc Dupuis[2], Yves Henchoz[1], Meichun Mohler-Kuo[3], Jean-Bernard Daeppen[1], Gerhard Gmel[1,4,5,6]

[1]Alcohol Treatment Centre, Lausanne University Hospital CHUV, Av. Beaumont 21 bis, Pavillon 2, CH-1011 Lausanne, Switzerland, Stephanie.Baggio@chuv.ch, Joseph.Studer@chuv.ch, Stephane.Deline@chuv.ch, Adjua-Alexandra.NGoran@chuv.ch, Yves.Henchoz@chuv.ch, Jean-Bernard.Daeppen@chuv.ch, Gerhard.Gmel@chuv.ch.

[2]Institute of Psychology, University of Lausanne, Geopolis building, CH-1015 Lausanne, Switzerland, marc.dupuis@unil.ch

[3]Institute of Social- and Preventive Medicine, University of Zurich, Hirschengraben 84, CH-8001 Zurich, Switzerland, meichun.mohler-kuo@uzh.ch

[4]Addiction Switzerland, Case postale 870, CH-1001 Lausanne, Switzerland

[5]Centre for Addiction and Mental Health, 250 College St, Toronto, Ontario, M5T 1R8, Canada

[6]University of the West of England, Frenchay Campus, Coldharbour Lane, Bristol BS16 1QY, United Kingdom

Corresponding author and guarantor: S. Baggio; Alcohol Treatment Centre, Lausanne University Hospital CHUV, Av. Beaumont 21 bis, Pavillon 2, CH-1011 Lausanne, Switzerland, Stephanie.Baggio@chuv.ch; Tel.:+41 21 3143951; Fax: +41 21 3140562

Running head: Cannabis use and health issues

Word count: 3,193

Declaration of interest: None

Abstract

Background and Aims. To test prospective associations between cannabis disorder symptoms/frequency of cannabis use and health issues and to investigate stability *vs* transience in cannabis use trajectories.

Design. Two waves of data collection from the longitudinal Cohort Study on Substance Use Risk Factors (C-SURF).

Setting. A representative sample of young Swiss men in their early twenties from the general population.

Participants. A total of 5,084 young men (mean age 19.98 ± 1.19 years at Time 1).

Measurements. Cannabis use (lifetime use, frequency of use, cannabis disorder symptoms) and self-reported measures of health issues (depression, mental/physical health, health consequences) were assessed. Significant changes in cannabis use were tested using t-test/Wilcoxon rank test for paired data. Cross-lagged panel models provided evidence regarding longitudinal associations between cannabis use and health issues.

Findings. Most of the participants (84.45%) remained in the same use category and cannabis use kept to similar levels at Times 1 and 2 ($p=.114$ and $p=.755$). Cross-lagged panel models showed that cannabis disorder symptoms predicted later health issues (e.g. depression, $\beta=.087$, $p<.001$; health consequences, $\beta= .045$, $p<.05$). The reverse paths from health issues to cannabis disorder symptoms and the cross-lagged panel model between frequency of cannabis use and health issues were non-significant.

Conclusions. Patterns of cannabis use showed substantial continuity among young people in their early twenties. The clinically important measure of cannabis use was the number of symptoms of cannabis use disorder rather than the frequency of cannabis use.

Key words. Cannabis disorder symptoms; Frequency of cannabis use; Health issues; Prospective associations; Trajectory.

Introduction

Cannabis is the most widely used illicit drug worldwide, and young adulthood is a period of active cannabis use (1, 2). Numerous studies have underlined the detrimental effects of cannabis use on health, including neuropsychological and cognitive impairment (3-6), and mental health problems (7-11). However, although neuropsychological impairment has been studied through causal pathways (3, 12), debate continues about the causal association of cannabis use and mental health problems, and the incidence of psychiatric disorders and schizophrenia that result from repeated cannabis use in teenage years and young adulthood (11, 13-18).

Moreover, there is also a debate about which measure of cannabis use should be taken into account: does cannabis dependence alone lead to mental health problems, or are frequent cannabis users (i.e. not necessarily dependent cannabis users) also affected by an increase in detrimental health issues? Frequency of use refers to cannabis use, which may be used in a non-problematic way, without any negative consequences. Cannabis dependence is a substance-use disorder, which implies frequent (daily) use and negative effects on users' live. Some studies have reported that both frequency of cannabis use and cannabis dependence are linked to mental health problems (11, 18-21), but others have pointed out that frequent cannabis use is not associated with increased internalising disorders such as depression (19, 22, 23). This study aimed to fill in these gaps, by testing causal pathways from frequency of cannabis use and cannabis dependence to mental health issues (mental health problems, depression). Additional health issues were added to investigate the consequences of cannabis use in young adulthood more precisely (e.g. physical health problems and health consequences).

Investigating trajectories of cannabis use in early adulthood was an additional aim. Several studies have shown that cannabis use is stable during late adolescence and early adulthood (24-28). About 80% of young adults remain in the same category of use (cannabis use/non-use). For example, Schulenberg et al (24), Arrial et al. (26) and Brook et al. (27) reported 80%, 87.2% and 81.4% of continuity in cannabis use/non-use, respectively. However, the focus of these studies was rarely to investigate trajectories themselves because the initiation of cannabis use has often already occurred by the late teenage years or early twenties (29, 30). They focused rather on identifying protective factors or risk factors surrounding increased cannabis use and the detrimental consequences of that use. Indeed, this interesting result of cannabis use stability across late adolescence and early adulthood has not yet been highlighted.

Thus, this study's aims were twofold: 1) to investigate cannabis use trajectories and find out whether the patterns of cannabis use among young adults were stable or transient; 2) to test prospective pathways between symptoms of cannabis use disorder/frequency of cannabis use and health issues (mental health issues and more general health issues).

Method

Participants and procedures

The data presented here were collected in the Cohort Study on Substance Use Risk Factors (C-SURF), a longitudinal study designed to assess substance use patterns and their related consequences in young Swiss men. Participants were enrolled in three of Switzerland's six army recruitment centres. These three centres cover 21 of the country's 26 cantons (including all French-speaking ones) and are located in Lausanne (French-speaking), Windisch and Mels

(German-speaking). There is no pre-selection for this conscription, and all young men around 20 years-old are evaluated to determine their eligibility for military, civil or no service because army recruitment is obligatory in Switzerland. Thus, all young Swiss men around 20 years-old were eligible for study inclusion. The recruitment centers were only used to enroll participants. Assessment of baseline and follow-up data was carried out outside the army environment and independently of eligibility for military service. Participants who gave a written consent to participate in recruitment centers were invited two weeks later by mail or email to fill in a paper and pen or an online questionnaire, according to the favorite way they indicated in the written consent. For follow-up, all the participants were similarly invited to fill in the questionnaire, by mail or email.

Baseline data (Time 1) were collected between September 2010 and March 2012, and follow-up data (Time 2) were collected between January 2012 and April 2013, with an average of 15 ± 2.8 months between the two assessments. A total of 5,990 participants filled in the baseline questionnaire, and 5,223 (87.2%) filled in the follow-up questionnaire. Missing values were listwise deleted, and the final sample consisted of 5,084 participants (95.6% of the follow-up sample). A previous study about sampling and non-response bias can be found in Studer et al. (31). As this study reported that non-response bias was small in the sample and because missing values were less than 5%, listwise deletion was preferred to multiple-imputation which can introduce bias in statistical inference. The study protocol (Protocol No. 15/07) was approved by Lausanne University Medical School's Clinical Research Ethics Committee.

Measures

Prevalence of cannabis use. Participants were asked if they had used cannabis (hashish, marijuana or grass) during the past 12 months. This question allowed the identification of changes in cannabis use: *non-users* (participants who had not used cannabis in the 12 months

prior to Times 1 and 2), *continuing users* (participants who had used cannabis in the 12 months prior to both Times 1 and 2), *late onset users* (participants whose first cannabis use occurred in the 12 months prior to Time 2, and were *non-users* at Time 1), and *matured out users* (participants who used cannabis in the 12 months prior to Time 1, but not in the 12 months prior to Time 2). Age of first cannabis use was also assessed at Time 1. For *late onset users*, first use was settled to actual age at Time 2. Table 1 gave an overview of the subgroups of cannabis users.

Insert Table 1 about here

Frequency of cannabis use. Frequency of cannabis use was assessed at Times 1 and 2 by asking participants how many times they had used cannabis during the past 12 months. Answers were collected on a 5-point scale coded 1 for 'monthly or less', 2 for '2–4 times a month', 3 for '2–3 times a week', 4 for '4–5 times a week', and 5 for 'every day or almost every day'.

Cannabis disorder symptoms. At Times 1 and 2, participants were asked about symptoms of cannabis use disorder during the past 12 months using the Cannabis Use Disorder Identification Test, CUDIT (32). This is a ten-item assessment tool for evaluating cannabis misuse (abuse and dependence); it is scored 0 (no misuse) to 40 (misuse). A continuous score was used to better capture variability among cannabis users.

Depression. The Major Depressive Inventory (ICD-10)–WHO-MDI was used at Times 1 and 2 to assess levels of depression (33, 34). This is a ten-item questionnaire that screens answers on a six-point scale from 0 (never) to 5 (all the time). A continuous scale (ranging from 0 to 50) was used instead of a cut-off, to better capture variability across the range of symptoms for

depression and the severity of depression states. The total scale score of MDI has been previously described as a sufficient statistic (33).

Mental and physical health. Physical and mental health were assessed at Times 1 and 2 using the Short Form Health Survey (SF-12) (35), with two subscales: the mental component summary (dealing with mental and social health), and physical component summary (dealing with physical health). These subscales were calculated according to their standard scoring, giving 2 composite scores ranging from 0 (health problem) to 100 (no health problem). The mental component summary primarily covered sadness, nervousness and depression.

Health consequences. At Times 1 and 2, seven health consequences were selected from standard instruments (36-39). These were not explicitly substance related as the use of substance-attributed consequences introduces bias (40). They included accident/injury, admittance to an emergency department, attempted suicide, need for medical treatment, overnight stay in hospital, outpatient surgery, and treatment of an accident/injury in an emergency department. Each consequence was coded 0 if it had not occurred in the past 12 months and 1 if it had occurred at least once during the past 12 months. A mean score was then calculated.

Statistical analyses

Two series of analyses investigated the two aims of the study: investigating cannabis use trajectories and testing the causal pathways between cannabis use and health issues.

1) *Cannabis use trajectories*

First, descriptive statistics for the whole sample (N=5,084) were calculated to investigate patterns of cannabis use at Times 1 and 2. Associations of cannabis use (cannabis disorder

symptoms, frequency of cannabis use) with health-related outcomes were tested with Spearman correlations.

Then, significant changes in cannabis use across time were tested using the t-test for paired samples for number of cannabis disorder symptoms and the related-samples Wilcoxon signed rank test for frequency of cannabis use. These analyses involved cannabis users and not non-cannabis users (N=1,939) including participants who used cannabis at Time 1 and/or Time 2, with measurements on cannabis use were settled at zero (cannabis disorder symptoms and frequency of cannabis use) for those who had not used cannabis in the 12 months prior to Times 1 or 2.

2) *Longitudinal pathways between cannabis use and health issues*

To provide evidence regarding the direction of the relationship between cannabis use and health issues, cross-lagged panel models were used. These models indicate predominant causal influences and allow an examination of whether one variable predict subsequent changes in the other variable, and of the reserve lagged associations. The 'causal winner' (41) is the variable that predicts the other without being predicted itself in return.

Two models were tested: one for the cannabis disorder symptoms, and the other for frequency of cannabis use. Models included a) autoregression (i.e. the regression between the same variable at Time 1 and Time 2), b) synchronous correlations (i.e. correlations between different variables at the same time point), c) causal paths with cross-lagged paths from cannabis use to health issues, and d) reverse-causal paths with cross-lagged paths from health issues to cannabis use. Figure 1 presents the model for the cannabis disorder symptoms. The same model was tested for frequency of cannabis use, with the difference that frequency of cannabis use was an ordinal

variable, so 5 dichotomous variables were used for Time 1 (independent variable), with frequency of cannabis use equal zero as the reference group. Maximum likelihood estimation was used for the cannabis disorder symptoms model and robust weighted least squares estimator (WLSMV) for the frequency of cannabis use model. Linear regressions were computed for continuous outcomes and probit regressions with theta parameterization for ordinal outcomes.

These two models were tested for all cannabis users, and then only for the subgroup of continuing cannabis users. As the results were very similar (the only difference was that the path coefficients were a little higher for continuing cannabis users), only the models including all cannabis users are presented. Cross-lagged panel models were tested controlling for age of first cannabis use and language (French- and German-speaking); the model for cannabis disorder symptoms was tested controlling for frequency of cannabis use. Cross-lagged panel models were carried out using Mplus 6 (42); other analyses used SPSS 21.

Insert Figure 1 about here

Results

Cannabis use trajectories

At Time 1, participants were 19.98 ± 1.19 years old. Descriptive statistics are shown in Table 2. Most of the participants (84.5%) remained in the same use category and only 15.5% changed their cannabis use between Times 1 and Time 2.

Insert Table 2 about here

Associations between cannabis use and health issues are shown in Table 3 for all cannabis users and continuing cannabis users. Significant but low correlations ($|r| < .30$) are displayed for most outcomes. Both synchronous and longitudinal associations seemed higher for cannabis disorder symptoms rather than frequency of cannabis use. No clear longitudinal pathway between cannabis use and health issues appeared.

Insert Table 3 about here

The subsequent analyses focused on cannabis users only, and on the specific subgroup of continuing users who had values for both Time 1 and Time 2. Table 4 shows cannabis use among these subgroups of users. Both cannabis disorder symptoms and frequency of cannabis use exhibited similar levels at Times 1 and 2 for all cannabis users and continuing cannabis users. Thus, cannabis disorder symptoms and frequency of cannabis use did not differ across time among cannabis users.

Insert Table 4 about here

Longitudinal pathways between cannabis use and health issues

Figure 2 presents the cross-lagged model examining the associations between cannabis disorder symptoms and health issues. Each variable at Time 1 significantly predicted the level of the same variable at Time 2. Moreover, number of cannabis disorder symptoms at Time 1 predicted depression, mental health, physical health and health consequences at Time 2. The reverse-causal

paths from health issues at Time 1 to cannabis disorder symptoms at Time 2 were non-significant.

Insert Figure 2 about here

Figure 3 presents the cross-lagged model examining the association between frequency of cannabis use and health issues. Each variable at Time 1 also significantly predicted the level of the same variable at Time 2. Causal paths from frequency of cannabis use at Time 1 to health issues at Time 2 were all non-significant and reverse-causal paths from health issues at Time 1 to frequency of cannabis use at Time 2 were also non-significant.

Insert Figure 3 about here

Discussion

We have described patterns of cannabis use among young Swiss males, and investigated prospective associations between cannabis use and health issues. Patterns of cannabis use showed that cannabis use was a stable phenomenon among young Swiss males in their early twenties. Indeed, 84.5% of participants remained in the same category (use/non-use) between Time 1 and Time 2, i.e. 15 months later in average. This result was consistent with previous studies which reported about 80% of continuity in cannabis use/non-use at young ages (24, 26-28). Most of the participants who remained in the same category were non-users (61.9%). Only 15.5% of participants changed category and showed transient patterns of cannabis use, with 8.3% being *late onset users* and 7.2% being *matured out users*.

The stability of patterns of cannabis use was investigated among all cannabis users and continuing cannabis users (i.e. participants who used cannabis 12 months prior to both Times 1 and 2). The results showed that these users had stable patterns of cannabis use, as their number of cannabis disorder symptoms and frequency of cannabis use were similar across time. Previous studies showed that cannabis use was stable among young adults because initiation had occurred earlier (29, 30), and the present study highlighted that patterns of cannabis use were also stable across time in the studied sample. It seemed that patterns of cannabis use had already been established at this age in this population. This result may be useful for preventive purposes, as it reveals that interventions aimed against an initiation to cannabis and against cannabis use patterns should occur during teenage years, at least among young males in their early twenties.

Longitudinal pathways between cannabis use and health issues were then tested. The results showed that cannabis disorder symptoms should be considered as a predictor of health issues, but that frequency of cannabis use should not, in line with the conclusions of studies reporting that frequency of cannabis use was not related to health issues (19, 22, 23). Indeed, cross-lagged panel models showed a causal path between cannabis disorder symptoms and health issues (depression, mental health, physical health, health consequences), but not reversed causal paths between health issues and cannabis disorder symptoms. It is interesting to see that the cannabis disorder symptoms lead to health issues despite its substantial continuity across time. Even a stable (i.e. not increasing) number of cannabis disorder symptoms may lead to poorer health outcomes. On the other hand, frequency of cannabis use did not predict health issues and so did not appear as a cause of deteriorated health. One can suspect that users reporting many cannabis disorder symptoms are also heavy cannabis users, but the frequency of cannabis use was controlled for in the cross-lagged model for cannabis disorder symptoms. Thereby, the number

of cannabis disorder symptoms seems not only to reflect the magnitude of use, but also something different in the style or type of use.

This study had some limitations. The main one was that it did not include women. More studies are needed to see whether these patterns and causal pathways also fit women's substance use behaviour. Another shortcoming was that the frequency of cannabis use was assessed using an ordinal scale. Further investigations with continuous scales are needed to more accurately capture the variability between cannabis users and patterns of use. A third limitation was the use of the number of cannabis disorder symptoms, which is not strictly speaking an assessment of cannabis dependence, even if it does give an overview of both cannabis abuse and dependence. Moreover, even if cross-lagged models allow the assessment of possible causal associations, they cannot prove causality (43). Evaluating causal relationships is especially hard when substance use is at focus, as individuals vulnerable to psychiatric disease may use more psychoactive substances than normal. Finally, data used in this study were self-reported. Although self-reported data on risky behaviors and substance use are generally considered valid (44), it could introduce various forms of bias including recall bias, pressure to give desirable answers and non-response bias. Self-rating for health issues, especially for depression and mental health assessment also did not allow knowing the factual clinical state of the participants. More investigations with external diagnosis are needed. However, SF12 and MDI are documented as reliable and validated measures of mental health status, with high responsiveness, sensitivity, empirical validity and associations with presence and seriousness of mental condition (33, 35).

For all these reasons, the results of this study should be interpreted cautiously and conclusions about causal pathways between health issues and cannabis use need more investigations, including external diagnosis for health-related outcomes and cannabis use.

In conclusion, the substantive contributions of this study are twofold. First, cannabis use patterns (prevalence rates and changes in use, number of cannabis disorder symptoms and frequency of cannabis use) showed substantial continuity among young Swiss males in their early twenties. Although results for prevalence rates had been shown in previous studies, to our knowledge, none of them had underlined this phenomenon. This study also highlighted that not only were prevalence rates of cannabis use stable across time, but so were the ways in which continuing users used cannabis—at least for males at this young age of around 20 years old. Therefore, interventions dealing with cannabis use and heavy cannabis use should already target teenagers, as by their early twenties users have shown that they have settled patterns of use. Second, the clinically important measure of cannabis use was the number of symptoms of cannabis use disorder rather than the frequency of cannabis use, with cannabis disorder symptoms but not frequency of cannabis use predicting health issues. Prevention programmes should focus more on cannabis disorder symptoms than on the frequency of cannabis use, whilst not neglecting users who do not show higher number of cannabis disorder symptoms across time.

Funding

Swiss National Science Foundation FN 33CS30_139467.

References

1. SAMHSA. Results from the 2010 National Survey on Drug Use and Health: Summary of national findings, Rockville, MD: Office of Applied Studies; 2011.
2. EMCDDA. The state of the drugs problem in Europe, Lisbon: European Monitoring Center for Drugs and Drug Addiction; 2011.
3. MEIER M. H., CASPI A., AMBLER A., HARRINGTON H., HOUTS R., KEEFE R. S. E. et al. Persistent cannabis users show neuropsychological decline from childhood to midlife, PNAS 2012.
4. SOLOWIJ N., BATTISTI R. The continuing effects of cannabis on memory in humans: a review, Curr Drug Abuse Rev 2008: 1: 81-98.
5. SOLOWIJ N., STEPHENS R. S., ROFFMAN R. A., BABOR T., KADDEN R., MILLER M. et al. Cognitive functioning of long-term heavy cannabis users seeking treatment, JAMA 2002: 287: 1123-1131.
6. RAVER S. M., HAUGHWOUT S. P., KELLER A. Adolescent Cannabinoid Exposure Permanently Suppresses Cortical Oscillations in Adult Mice, Neuropsychopharmacology 2013.
7. ARSENEAULT L. Cannabis use in adolescence and risk for adult psychosis: longitudinal prospective study, BMJ 2002: 325: 1212-1213.
8. HAYATBAKHSH M. R., NAJMAN J. M., JAMROZIK K., MAMUN A. A., ALATI R., BOR W. Cannabis and anxiety and depression in young adults: a large prospective study, J Am Acad Child Adolesc Psychiatry 2007: 46: 408-417.
9. PATTON G. C. Cannabis use and mental health in young people: cohort study, BMJ 2002: 325: 1195-1198.

10. VAN LAAR M., VAN DORSSELAER S., MONSHOUWER K., DE GRAAF R. Does cannabis use predict the first incidence of mood and anxiety disorders in the adult population?, Addiction 2007: 102: 1251-1260.

11. CHEUNG J. T. W., MANN R. E., IALOMITEANU A., STODUTO G., CHAN V., ALA-LEPPILAMPI K. et al. Anxiety and mood disorders and cannabis use, Am J Drug Alcohol Abuse 2010: 36: 118-122.

12. SCHNEIDER M. Puberty as a highly vulnerable developmental period for the consequences of cannabis exposure, Addict Biol 2008: 13: 253-263.

13. DEGENHARDT L., COFFEY C., ROMANIUK H., SWIFT W., CARLIN J. B., HALL W. D. et al. The persistence of the association between adolescent cannabis use and common mental disorders into young adulthood, Addiction 2013: 108: 124-133.

14. HUIZINK A. C. Commentary on Degenhardt et al. (2013): Specific effect of adolescent cannabis use on anxiety – tentative explanations, Addiction 2013: 108: 134-135.

15. MANRIQUE-GARCIA E., ZAMMIT S., DALMAN C., HEMMINGSSON T., ANDREASSON S., ALLEBECK P. Cannabis, schizophrenia and other non-affective psychoses: 35 years of follow-up of a population-based cohort, Psychol Med 2012: 42: 1321-1328.

16. DE GRAAF R., RADOVANOVIC M., VAN LAAR M., FAIRMAN B., DEGENHARDT L., AGUILAR-GAXIOLA S. et al. Early cannabis use and estimated risk of later onset of depression spells: Epidemiologic evidence from the population-based World Health Organization World Mental Health Survey Initiative, Am J Epidemiol 2010: 172: 149-159.

17. FERGUSSON D. M., BODEN J. M. Cannabis use and later life outcomes, Addiction 2008: 103: 969-976; discussion 977-978.

18. MATHEWS R. R. S., HALL W. D., GARTNER C. E. Depression and psychological distress in tobacco smokers and people with cannabis dependence in the National Survey of Mental Health and Wellbeing, Med J Aust 2011: 195.

19. VAN DER POL P., LIEBREGTS N., DE GRAAF R., TEN HAVE M., KORF D. J., VAN DEN BRINK W. et al. Mental health differences between frequent cannabis users with and without dependence and the general population, Addiction 2013: 108: 1459-1469.

20. DEGENHARDT L., HALL W., LYNSKEY M. Exploring the association between cannabis use and depression, Addiction 2003: 98: 1493-1504.

21. LEV-RAN S., ROERECKE M., LE FOLL B., GEORGE T. P., MCKENZIE K., REHM J. The association between cannabis use and depression: a systematic review and meta-analysis of longitudinal studies, Psychol Med 2013: 1-14.

22. ZVOLENSKY M. J., BERNSTEIN A., SACHS-ERICSSON N., SCHMIDT N. B., BUCKNER J. D., BONN-MILLER M. O. Lifetime associations between cannabis, use, abuse, and dependence and panic attacks in a representative sample, J Psychiatr Res 2006: 40: 477-486.

23. MOORE T. H. M., ZAMMIT S., LINGFORD-HUGHES A., BARNES T. R. E., JONES P. B., BURKE M. et al. Cannabis use and risk of psychotic or affective mental health outcomes: a systematic review, Lancet 2007: 370: 319-328.

24. SCHULENBERG J. E., MERLINE A. C., JOHNSTON L. D., O'MALLEY P. M., BACHMAN J. G., LAETZ V. B. Trajectories of marijuana use during the transition to adulthood: The big picture based on national panel data, J Drug Issues 2005: 35: 255-279.

25. PERKONIGG A., LIEB R., HÖFLER M., SCHUSTER P., SONNTAG H., WITTCHEN H. U. Patterns of cannabis use, abuse and dependence over time: incidence, progression and stability in a sample of 1228 adolescents, Addiction 1999: 94: 1663-1678.

26. ARRIA A. M., GARNIER-DYKSTRA L. M., CALDEIRA K. M., VINCENT K. B., WINICK E. R., O'GRADY K. E. Drug use patterns and continuous enrollment in college: results from a longitudinal study, J Stud Alcohol Drugs 2013: 74: 71-83.

27. BROOK J. S., LEE J. Y., BROWN E. N., FINCH S. J., BROOK D. W. Developmental trajectories of marijuana use from adolescence to adulthood: personality and social role outcomes, Psychol Rep 2011: 108: 339-357.

28. SILINS E. A. Patterns and correlates of cannabis use in young adulthood, Sydney: University of New South Wales; 2011.

29. KANDEL D. B., CHEN K., WARNER L. A., KESSLER R. C., GRANT B. Prevalence and demographic correlates of symptoms of last year dependence on alcohol, nicotine, marijuana and cocaine in the U.S. population, Drug Alcohol Depend 1997: 44: 11-29.

30. KANDEL D. B., LOGAN J. A. Patterns of drug use from adolescence to young adulthood: I. Periods of risk for initiation, continued use, and discontinuation, Am J Public Health 1984: 74: 660-666.

31. STUDER J., BAGGIO S., MOHLER-KUO M., DERMOTA P., GAUME J., BERTHOLET N. et al. Examining non-response bias in substance use research—Are late respondents proxies for non-respondents?, Drug Alcohol Depend 2013: 132: 316-323.

32. ADAMSON S. J., SELLMAN J. D. A prototype screening instrument for cannabis use disorder: the Cannabis Use Disorders Identification Test (CUDIT) in an alcohol-dependent clinical sample, Drug Alcohol Rev 2003: 22: 309-315.

33. BECH P., RASMUSSEN N. A., OLSEN L. R., NOERHOLM V., ABILDGAARD W. The sensitivity and specificity of the Major Depression Inventory, using the Present State Examination as the index of diagnostic validity, J Affect Disord 2001: 66: 159-164.

34. OLSEN L. R., JENSEN D. V., NOERHOLM V., MARTINY K., BECH P. The internal and external validity of the Major Depression Inventory in measuring severity of depressive states, Psychol Med 2003: 33: 351-356.

35. WARE J., JR., KOSINSKI M., KELLER S. D. A 12-Item Short-Form Health Survey: Construction of scales and preliminary tests of reliability and validity, Med Care 1996: 34: 220-233.

36. HIBELL B., GUTTERMSSON U., AHLSTRÖM S., BALAKIREVA O., BJANASON T., KOKKEVI A. et al. The 2011 ESPAD report - Substance use among students in 36 European countries, Stockholm: ESPAD; 2012.

37. BUCHOLZ K. K., CADORET R., CLONINGER C. R., DINWIDDIE S. H., HESSELBROCK V. M., NURNBERGER J. I., JR. et al. A new, semi-structured psychiatric interview for use in genetic linkage studies: A report on the reliability of the SSAGA, J Stud Alcohol 1994: 55: 149-158.

38. HESSELBROCK M., EASTON C., BUCHOLZ K. K., SCHUCKIT M., HESSELBROCK V. A validity study of the SSAGA--a comparison with the SCAN, Addiction 1999: 94: 1361-1370.

39. WECHSLER H., DAVENPORT A., DOWDALL G., MOEYKENS B., CASTILLO S. Health and behavioral consequences of binge drinking in college. A national survey of students at 140 campuses, JAMA 1994: 272: 1672-1677.

40. GMEL G., LABHART F., FALLU J.-S., KUNTSCHE E. The association between drinking motives and alcohol-related consequences - room for biases and measurement issues?, Addiction 2012: 107: 1580-1589.

41. ROGOSSA D. A critique of cross lagged correlation, Psychol Bull 1980: 88.

42. MUTHÉN L. K., MUTHÉN B. O. Mplus user's guide. Sixth edition Los Angeles, CA: Muthén & Muthén; 2010.

43. BURKHOLDER G. J., HARLOW L. L. An illustration of a longitudinal cross-lagged design for larger structural equation models, Struct Equ Modeling 2003: 10: 465-486.

44. FORD T. Practitioner review: How can epidemiology help us plan and deliver effective child and adolescent mental health services, J Child Psychol Psychiatry 2008: 49: 900-914.

Table 1. Subgroups of cannabis users

	Cannabis use	
	Time 1	Time 2
Non-users	no	no
Continuing users	yes	yes
Matured out users	yes	no
Late onset users	no	yes

Table 2. Descriptive statistics for cannabis use and health issues

	Overall	Non-users	Continuing users	Late onset users	Matured out users
N (%)	5,084	3,145 (61.9)	1,149 (22.6)	423 (8.3)	367 (7.2)
Health issues (Time 1)					
Depression (0-50)	7.00	6.30	8.39	7.39	8.29
Mental health (0-100)	47.35	48.30	45.47	46.53	46.04
Physical health (0-100)	53.16	53.17	53.03	53.50	53.01
Health consequences (0-7)	1.36	1.28	1.50	1.39	1.52
Health issues (Time 2)					
Depression (0-50)	7.87	7.15	9.22	9.33	8.10
Mental health (0-100)	45.32	46.16	43.59	43.94	45.15
Physical health (0-100)	53.5	53.44	53.67	53.80	53.20
Health consequences (0-7)	1.49	1.42	1.64	1.59	1.51

Non-users: no cannabis use 12 months prior to Times 1 and 2; continuing users, cannabis use 12 months prior to both Times 1 and 2; late onset users, cannabis use 12 months prior to Time 2, but not Time 1; matured out users, cannabis use 12 months prior to Time 1, but not Time 2.

Table 3. Associations between cannabis use and health-related issues

			Cannabis disorder symptoms		Frequency of cannabis use	
			Time 1	Time 2	Time 1	Time 2
All cannabis users (N=1,939)	Time 1	Depression	.178***	.124***	.138***	.102***
		Mental health	-.142***	-.105***	-.105***	-.081***
		Physical health	-.042*	-.021	-.038	-.023
		Health consequences	.067***	.037	.051*	.057**
	Time 2	Depression	.137***	.154***	.098***	.130***
		Mental health	-.108***	-.128***	-.070**	-.104***
		Physical health	-.025	-0.02	-.030	-.022
		Health consequences	.066***	.068***	0.45*	.057**
Continuing cannabis users (N=1,149)	Time 1	Depression	.238***	.201***	.102**	.097**
		Mental health	-.150***	-.148***	-.052	-.051
		Physical health	-.131***	-.080**	-.083**	-.067*
		Health consequences	.112***	.080**	.070*	.069*
	Time 2	Depression	.198***	.202***	.061*	.087**
		Mental health	-.139***	-.162***	-.033	-.054
		Physical health	-.121***	-.117***	-.097**	-.123***
		Health consequences	.097***	.110***	.039	.084**

* p < .05; ** < .01; *** p < .001.

Table 4. Cannabis use among cannabis users

	Time 1	Time 2	p-val.
All cannabis users (N = 1,939)			
Age of first cannabis use	16.32 (2.44)	-	-
Cannabis disorder symptoms[1]	4.89 (6.43)	4.70 (6.10)	.114
Frequency of cannabis use[2]	-	-	.755
No cannabis use	21.8	18.9	-
Monthly or less	44.0	46.0	-
2-3 times a month	11.5	14.7	-
2-3 times a week	7.8	7.4	-
4-5 times a week	4.7	3.8	-
Every day or almost every day	10.2	9.2	-
Continuing cannabis users (N = 1,149)			
Age of first cannabis use	15.57 (1.96)	-	-
Cannabis disorder symptoms[1]	7.09 (6.90)	6.81 (6.64)	.066
Frequency of cannabis use[2]	-	-	.203
No cannabis use	-	-	-
Monthly or less	48.7	47.3	-
2-3 times a month	16.5	20.8	-
2-3 times a week	11.7	11.0	-
4-5 times a week	7.3	5.8	-
Every day or almost every day	15.8	15.1	-

1 Means and standard deviations are given, p-values refer to t-test for paired data.
[2] Percentages of use are given, p-values refer to related-samples Wilcoxon signed rank test.

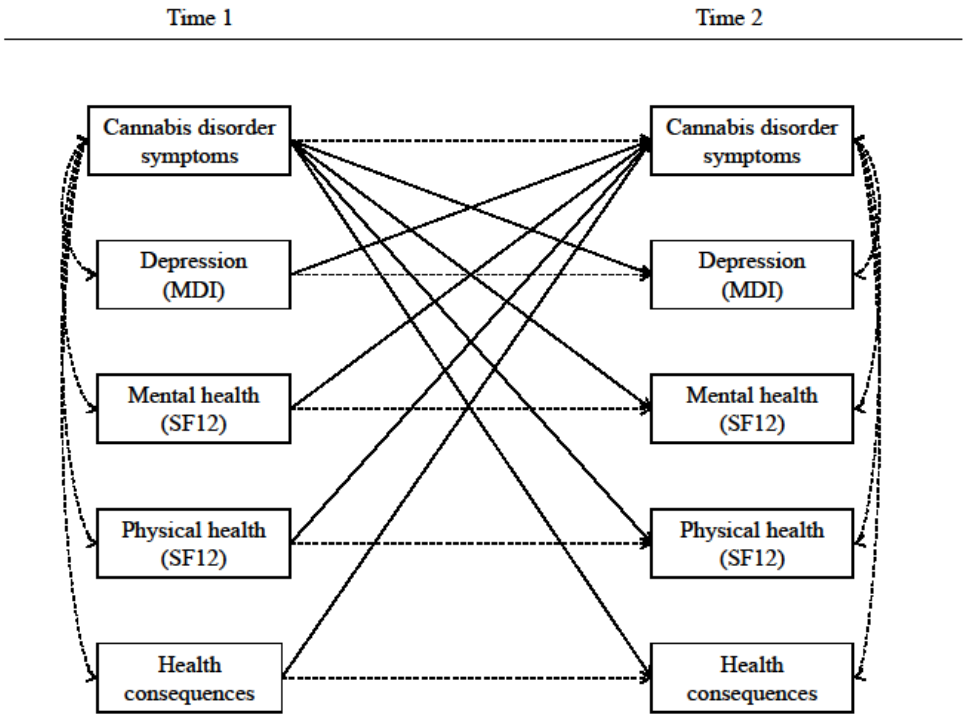
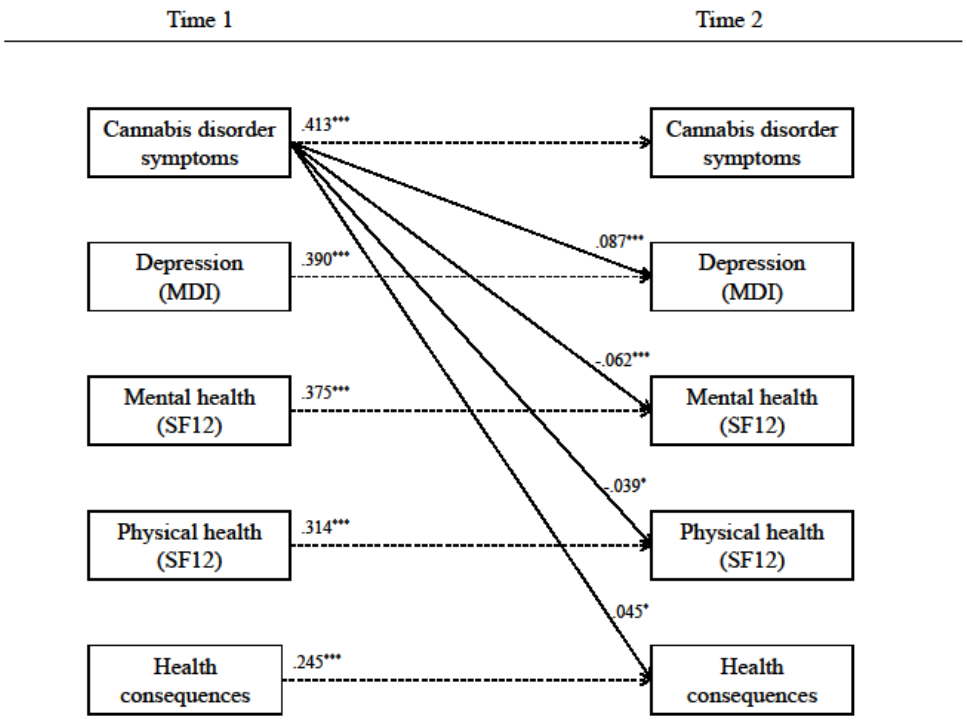


Figure 1. Illustration of cross-lagged longitudinal model

Figure 2. Cross-lagged model examining the associations between cannabis disorder symptoms and health issues



For clarity, this figure only presents significant cross-lagged paths. However, all the cross-lagged paths depicted in Figure 1 were included in the final model, including within-time correlations between variables at both Time 1 and Time 2. Although not shown, the effect of age of onset of cannabis use disorder, language and frequency of cannabis use were controlled.

* $p < .05$, *** $p < .001$.

Standardized β are given.

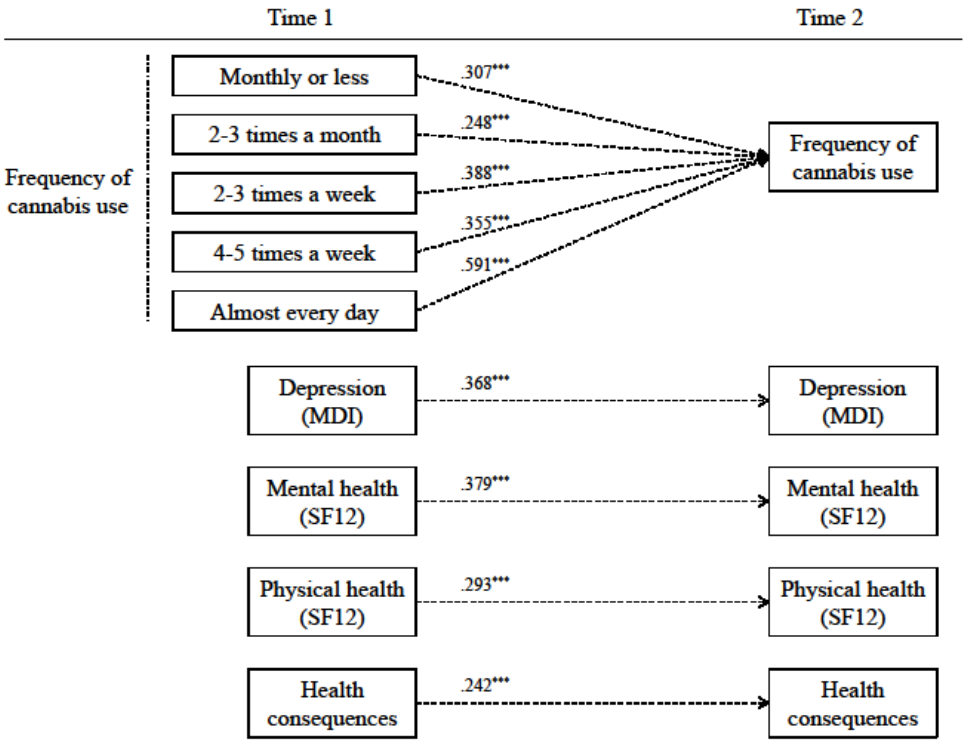


Figure 3. Cross-lagged model examining the associations between frequency of cannabis use and health issues

For clarity, this figure only presents significant cross-lagged paths. However, all the cross-lagged paths depicted in Figure 1 were included in the final model, including within-time correlations between variables at both Time 1 and Time 2. Although not shown, the effect of age of onset and language were controlled.

Frequency of cannabis use equal zero was used as the reference category.

*** $p < .001$.

Standardized β are given.