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# Gender Differences in the Associations Among Marijuana Use, Cigarette Use, and Symptoms of Depression During Adolescence and Young Adulthood

Natania A. Crane<sup>1,2,3</sup>, Scott A. Langenecker<sup>2</sup>, and Robin J. Mermelstein<sup>1,3</sup>

<sup>1</sup>Department of Psychology, University of Illinois at Chicago, 1007 West Harrison Street (M/C 285) Chicago, Illinois 60607, U.S.

<sup>2</sup>Department of Psychiatry and the Center for Cognitive Neuroscience, University of Illinois at Chicago, 1601 West Taylor Street (M/C 912) Chicago, Illinois 60612, U.S.

<sup>3</sup>Institute for Health Research and Policy, University of Illinois at Chicago, 1747 West Roosevelt Road (M/C 275) Chicago, Illinois 60608, U.S.

# Abstract

**Introduction**—As prevalence of marijuana use increases, it is important that we better understand how factors like gender, cigarette use, and depression are related to marijuana use during adolescence and young adulthood. We examined longitudinal relationships among these variables in adolescents moving into young adulthood who were studied longitudinally for six years.

**Methods**—1,263 individuals were included in the study. Participants were oversampled for eversmoking a cigarette at baseline, when they were 15-16 years old. Frequency of cigarette smoking and marijuana use, as well as depression symptoms were assessed at baseline, 6, 15-, 24-, 60- and 72- months.

**Results**—Cigarette use frequency and depression symptoms were associated with frequency of marijuana use (*p*-values <.001), particularly in adolescence, but there were important gender differences in these relationships. Specifically, symptoms of depression were related to marijuana use frequency among males (p<.001), but not females (p=.62). In addition, frequency of marijuana use was associated with increased cigarette use frequency, especially among males who had

#### Contributors

#### Conflict of Interest

The authors declare no conflicts of interest.

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Address correspondence to: Natania A. Crane, MA, 1007 W. Harrison Street (M/C 275) Chicago, IL 60607; phone: (312) 996-2236; fax: (312) 413-4122; ncrane3@uic.edu..

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higher symptoms of depression (p<.001). However, this effect was not seen among females. Exploratory analyses suggested relationships between frequency of use and depression are specific to marijuana, not cigarettes.

**Conclusions**—Marijuana use is strongly related to depression symptoms and cigarette use frequency in males, indicating that in males these detrimental factors converge, whereas in females they do not. Gender differences in the factors related to marijuana use may mean that there are different risks for and consequences from use and have implications for prevention and intervention efforts.

#### Keywords

cigarettes; depression; gender; marijuana; nicotine; sex differences

#### 1. Introduction

Marijuana and cigarettes, two commonly used substances among adolescents and young adults (Johnston et al., 2014) are often used concurrently (Kandel & Yamaguchi, 1993; Patton et al., 2006; Prince van Leeuwen et al., 2013; Rigotti et al., 2000; Silins et al., 2013), leading to escalating use and severity of dependence (Degenhardt et al., 2001; Kandel & Yamaguchi, 1993; Korhonen et al., 2008; Lynskey et al., 1998; Mathers et al., 2006; Patton et al., 2006). These substances are each associated with negative outcomes, including increased risk of depression (Brook et al., 2012; CDC, 2012, 2013; Cuijpers et al., 2007; Degenhardt et al., 2003; Hayatbakhsh et al., 2007; Klungsoyr et al., 2006; Mathers et al., 2006; Pedersen & von Soest, 2009; van Laar et al., 2007), especially if use is initiated in adolescence (Silins et al., 2014); but these relationships may differ by gender. Gender differences occur in prevalence, rate, and frequency of marijuana and cigarette use (Johnston et al., 2014; SAMSHA, 2013), and in prevalence of depression (Hankin & Abramson, 1999; Kuehner, 2003; Piccinelli & Wilkinson, 2000). Understanding how cigarette use, symptoms of depression, and gender are related to marijuana use during adolescence and young adulthood may help to develop better interventions.

Several studies have found a reciprocal relationship in the prevalence and severity of cigarette and marijuana use (Degenhardt et al., 2001; Kandel & Yamaguchi, 1993; Korhonen et al., 2008; Lynskey et al., 1998; Mathers et al., 2006; Patton et al., 2006). Cigarette users are more likely to engage in subsequent marijuana use (Kandel & Yamaguchi, 1993; Patton et al., 2006; Prince van Leeuwen et al., 2013; Rigotti et al., 2000; Silins et al., 2013), and cigarette users who also use marijuana are more likely to escalate cigarette use and develop nicotine dependence (Agrawal et al., 2008; Patton et al., 2005; Patton et al., 2006; Timberlake et al., 2007; Tullis et al., 2003). Males are more likely to use marijuana and cigarettes, and they use these substances in greater amounts than females (Johnston et al., 2014; SAMSHA, 2013). However, few studies have examined gender differences in marijuana and cigarette use over time. One recent longitudinal study found that adolescent females were more likely to use cigarettes than males, and while there was no difference in marijuana use during early adolescence, males escalated their marijuana use compared to females throughout adolescence (Mahalik et al., 2013). Males also escalated their cigarette use throughout adolescence, surpassing females' use, and remained heavier

cigarette smokers in young adulthood. Females "catch up" over time to males in marijuana use, and gender differences in amount of use may diminish in young adulthood (Mahalik et al., 2013).

Marijuana and cigarette use are often initiated during adolescence, a time when individuals are experiencing substantial neural, emotional, cognitive, physical, sex- and gender-related development and when many mental disorders, including depression, emerge (Copeland et al., 2011). As adolescents transition to young adulthood, they usually experience significant environmental changes (e.g., leaving home); social and relationship changes; school/work changes; and intrapersonal changes (e.g., self-concept, affect regulation strategies, etc.); which may all contribute to substance use changes (Brown et al., 2009). Due to the developmental and psychosocial differences between adolescence and young adulthood, we need to further understand marijuana and cigarette use patterns across these distinct periods.

Given the high comorbidity between marijuana and tobacco use and depression, symptoms of depression may be a key factor involved in initiation and continued use of these substances. Symptoms of depression are associated with marijuana and tobacco use (Boden et al., 2010; Brown et al., 1996; Libby et al., 2005; Volkow, 2004; Weinstein & Mermelstein, 2013) and heavy marijuana use may increase depressive symptoms over time and vice versa (Degenhardt et al., 2003; Patton et al., 2005). The relationship between marijuana use and depression may differ by gender, although the findings are mixed (Patton et al., 2002 versus Schepis et al, 2011). In an intriguing demographic juxtaposition, gender differences in depression (females higher) and substance use (males higher) emerge in adolescence, but this does not necessarily indicate that these problems are independent. Rather, these problems appear to be linked, but potentially in different ways for males and females. It is not yet clear if the relationship between heavier marijuana use and higher symptoms of depression varies over adolescence and young adulthood in males and females. In an earlier study with the same longitudinal cohort as the current study, our group found that more depression symptoms at baseline were associated with more frequent marijuana use two years later in adolescence for males, but not for females (Schuster et al., 2013). However, it remains unclear how the gender-specific relationship between depression and marijuana changes over time between adolescence and young adulthood.

The goal of the current study was to extend our previous findings of a gender-specific relationship between marijuana use frequency and depression symptoms in adolescence (Schuster et al., 2013) to now examine the relationship between gender, marijuana use, cigarette smoking, and depression symptoms during the transition from adolescence (<18 years old) to young adulthood ( 18 years old) in a longitudinal sample that has been followed for six years (Social and Emotional Contexts of Adolescent Smoking Patterns [SECASP] study). Consistent with prior literature and findings from earlier waves with this cohort, we expected that: marijuana use frequency would increase over time; males would use marijuana more frequently than females; and more frequent cigarette use would be related to more frequent marijuana use, especially among males. We also hypothesized that (1a) more symptoms of depression would be related to increased marijuana use frequency, (1b) especially for females, and (1c) this effect would increase over time. Furthermore, we

(2) hypothesized that more symptoms of depression and more frequent cigarette use would have an interactive effect, increasing marijuana use frequency.

### 2. Methods

#### 2.1 Participants

The sample was drawn from the longitudinal SECASP study, which has been described elsewhere (Dierker & Mermelstein, 2010; Dierker et al., 2013; Selya et al., 2013). The program project recruited a cohort of adolescents (mean baseline age=15 years) oversampled for ever-smoking a cigarette (83% ever-smoked), and thus at high risk for smoking escalation. Participants were 9<sup>th</sup> and 10<sup>th</sup> graders from 16 Chicago-area high schools, which were selected to reflect the area demographics. Of 3654 students invited, 1344 agreed to participate, and 1263 (94%) completed baseline measurements. Participants completed questionnaires assessing substance use and psychosocial factors at baseline, 6-, 15- months, and 2-, 5- and 6- years. Retention at 6 years was greater than 85%, and participants and nonparticipants at 6 years did not differ by gender, race/ethnicity, or age. For the present study, participants were included if they were assessed at three or more waves and were assessed at either 5- or 6-years (n=1108). The Institutional Review Board at the University of Illinois at Chicago approved the study and written informed consent was obtained.

#### 2.2 Demographics, Substance Use, and Depression

Demographic information was obtained through self-report questionnaires.

**2.2.1 Marijuana and Cigarette Use Frequency**—For each wave, participants reported frequency of marijuana use and cigarette use (number of days they used each substance) in the past month. Marijuana use frequency was measured using a single item question with 5 ordinal options coded as: 0= zero days; 1=one day a month or less; 3= more than one day a month but less than one day a week; 9=more than one day a week but less than daily; 27= every day. Cigarette use frequency was measured using a single item question with 9 ordinal options coded as: 0= zero days; 1=one day; 3= 2-3 days; 5= 4-5 days; 7= 6-7 days; 9= 8-10 days; 16= 11-20 days; 25= 21-29 days; 30= every day. Alcohol use frequency is included in supplement for comparison purposes (S.1 Figure) and relationships between alcohol use frequency and cigarette use and marijuana use frequency are shown in S.4 Table.

**2.2.2 Marijuana-Related Problems and Nicotine Dependence**—In order to describe the sample, participants completed the Cannabis Use Disorder Identification Test – Revised (CUDIT-R; Adamson et al., 2010) at 5- and 6-years, an 8-item self-report assessing marijuana-related problems that is accurate and reliable in adolescent and young adult populations (Annaheim et al., 2010). Total score was used, with higher values representing increased marijuana problems. At each wave, participants completed the modified Fagerstrom Questionnaire (mFTQ; Prokhorov et al., 1998; Prokhorov et al., 1996), measuring nicotine dependence and found to be accurate and reliable in adolescent and young adult populations (Prokhorov et al., 1996; Wilens et al., 2008). Total sum score was used.

**2.2.3 Depression**—For each wave, participants completed the Center for Epidemiological Scale-Depression (CES-D) scale (Radloff, 1977), with good reliability and validity in adolescent and young adult populations (Radloff, 1991). Total score was used.

#### 2.3 Statistical Procedures

Analyses were carried out using SPSS 20.0 (IBM). Using frequency of marijuana use as the outcome, main effects and time-varying effects of symptoms of depression, frequency of cigarette use, gender, and their interactions were examined. Mixed-effects regression models using Generalized Linear Models in SPSS included both fixed effects of variables and random effects to account for the repeated measurements of participants over time. Random effects included intercepts (capturing individual differences in the frequency of marijuana use at baseline) and time trends (capturing individual differences in the rate of change in frequency of marijuana use across the years of the study), with an unstructured covariance structure.

Frequency of marijuana use (outcome), frequency of cigarette use, and symptoms of depression were all time-varying, while gender and ethnicity/race were static. Frequency of cigarette use and symptoms of depression were grand mean centered. Gender was effect coded (-0.5=female, 0.5=male). Time was measured continuously by the year of each assessment and centered at baseline. We investigated time-varying effects with interactions between each variable and time, and we also investigated interactions between the variables. Non-significant covariates and interactions were removed and the reduced model was rerun. Tables 2 and 3 show results from the full model and reduced models. Follow-up analyses of the simple slopes for significant 2-way interactions used linear regression to estimate the effects of depression and cigarette use frequency. Analyses with gender were run separately for males and females. Analyses with time used a median split based upon the participants' age to capture developmental and psychosocial differences before age 18 (years 0-2) and after age 18 (years 5-6). Follow-up analyses of the simple slopes for significant 3way interactions used linear regression with a median split of 16 for the CES-D, with scores 16 indicating higher depression symptoms and were run separately for males and females. Results were deemed statistically significant when p-values < .05.

## 3. Results

#### **3.1 Participant Characteristics**

Participant characteristics are shown in Table 1 (full sample participant characteristics and analyses were similar and are in the supplement). Marijuana and cigarette use frequency at 6 years are shown in Figure 1.

# 3.2 Relationships between Marijuana Use Frequency, Cigarette Use Frequency, and Depression

Marijuana use frequency significantly increased over time (Table 2). Males used marijuana significantly more frequently than females (Table 2). Ethnicity/race was not significantly associated with marijuana use frequency.

More symptoms of depression were significantly associated with a higher frequency of marijuana use (Table 2). Higher frequency of cigarette use was related to an increased frequency of marijuana use (Table 2).

The 3-way interactions of gender, depression, and cigarette use frequency and also time, gender, and cigarette use frequency on marijuana use frequency were significant (Table 2). The 3-way interaction of time, gender, and depression on marijuana frequency was not significant (Table 2). The 2-way interactions between time and cigarette frequency, gender and depression, gender and cigarette frequency, and depression and cigarette frequency were significant on marijuana use frequency (Table 2). The 2-way interaction between time and cigarette frequency were significant on marijuana use frequency (Table 2). The 2-way interaction between time and depression on marijuana use frequency was not significant (Table 2).

Follow-up of the simple slopes for the 3-way interactions demonstrated that for males, a higher frequency of cigarette use had a stronger relationship with an increased frequency of marijuana use among those with higher depression ( $\beta$ =.44, t(879)=14.79, *p*<.001) compared to those with lower depression,  $\beta$ =.31, t(1687)=13.14, *p*<.001. On the other hand, for females, the association between frequency of cigarette use and marijuana use was similar for those with higher depression ( $\beta$ =.32, t(1597)=13.66, *p*<.001) and those with lower depression,  $\beta$ =.33, t(2074)=16.06, *p*<.001. In addition, for males, a higher frequency of cigarette use had a stronger relationship with an increased frequency of marijuana use in adolescence (through the age of 18; baseline through 2 years) ( $\beta$ =.39, t(1737)=17.51, *p*<.001) than in young adulthood (after the age of 18; 4 years through 6 years),  $\beta$ =.28, t(2469)=19.30, *p*<.001) than in young adulthood,  $\beta$ =.26, t(1220)=9.31, *p*<.001.

Follow-up of the simples slopes for the 2-way interactions revealed that in adolescence, a higher frequency of cigarette use was strongly related to a higher frequency of marijuana use ( $\beta$ =.37, t(4208)=26.14, *p*<.001), but this effect lessened in young adulthood,  $\beta$ =.28, t(2063)=13.37, *p*<.001. In addition, more symptoms of depression were related to increased frequency of marijuana use in males ( $\beta$ =.13, t(2591)=6.57, *p*<.001), but not for females,  $\beta$ =. 01, t(3684)=0.50, *p*=.62. In addition, an increased frequency of cigarette use was associated with a slightly increased frequency of marijuana use in males ( $\beta$ =.33, t(3692)=21.07, *p*<.001), although this may not be a clinically significant difference given the small difference in beta weights.

#### 3.3 Exploratory Analyses

To understand if the observed relationships were specific to marijuana use or were also seen in cigarette use, we performed a mixed-effects regression model in which frequency of cigarette use (outcome), frequency of marijuana use, and symptoms of depression were all time-varying, while gender and ethnicity/race were static. Frequency of marijuana use and symptoms of depression were grand mean centered. The random effects included intercepts (capturing individual differences in the frequency of cigarette use at baseline) and time trends (capturing individual differences in the rate of change in frequency of cigarette use across the years of the study), with an unstructured covariance structure.

In general, cigarette use frequency increased over time, but there was no significant difference in the frequency of males' or females' cigarette use (Table 3). Ethnicity/race was significantly associated with frequency of cigarette use. Follow-up analyses using ANOVA with bonferroni correction found that individuals of Asian (M= 4.87, SD= 9.55), Black (M= 5.26, SD= 9.83), or Hispanic (M= 5.52, SD= 9.10) descent did not differ from one another, but they used cigarettes less frequently than Caucasians (M= 7.98, SD= 11.57), F(5, 6313)= 17.80, p<.001.

Depression was not significantly associated with cigarette use frequency, and this effect neither changed over time, nor did it differ by gender (Table 3). However, a higher frequency of marijuana use was related to an increased frequency of cigarette use, and this effect lessened over time so that the effect was not as strong after the age of 18 (in the same manner as described above), but did not differ by gender (Table 3).

# 4. Discussion

This study examined longitudinal relationships among marijuana use frequency, cigarette use frequency, and depression and whether these relationships differed for males and females among a sample of young adults followed over six years. We replicated prior findings that males used marijuana more frequently than females (Johnston et al., 2014; SAMSHA, 2013; Schepis et al., 2011); higher levels of cigarette use were related to increased frequency of marijuana use (Ramo et al., 2013; Ramo & Prochaska, 2012); and more depression symptoms were significantly associated with higher frequency of marijuana use (Degenhardt et al., 2003). The association between cigarette use frequency and marijuana use frequency diminished over time, suggesting cigarette use frequency is more strongly related to marijuana use frequency in adolescence than in young adulthood and vice-versa.

We also found gender differences in these relationships. We replicated previous findings from this sample that more symptoms of depression were related to increased frequency of marijuana use in males, but not in females (Schuster et al., 2013), and notably, this effect did not change as individuals transitioned into young adulthood. In addition, higher frequency of cigarette use was more strongly associated with higher frequency of marijuana use in males, and this effect did not change over time. Among males, higher symptoms of depression and a higher frequency of cigarette use were more strongly related to increased frequency of marijuana use than lower symptoms of depression and a higher frequency of cigarette use. Depression did not, however, alter the relationship between higher frequency of cigarette use and increased frequency of marijuana use for females. These findings were specific to marijuana use frequency, as we did not find gender differences or significant influence of symptoms of depression on cigarette use frequency.

Our findings indicate that marijuana use frequency is strongly related to depression and cigarette use frequency in males, suggesting that males may be particularly vulnerable to the negative consequences not only of marijuana use, but also of depression and cigarette use. It may be that marijuana is a coping mechanism for males to deal with symptoms of depression (Schuster et al., 2013). Other studies have similarly found that males are more

likely to cope with negative affect by using external avoidance-based coping strategies, like using substances (Hankin et al., 2007), while females are more likely to cope with negative affect by using strategies like rumination and isolation (Copeland & Hess, 1995; Hankin et al., 2007). In addition, marijuana and cigarettes differ in psychopharmacological properties and also in the environmental context in which they are used by males and females (Caggiula et al., 2002; Crane et al., 2013; Shrier et al., 2012), which may contribute to these differential relationships. It is also possible that marijuana use and depression share common environmental and biological vulnerabilities, especially among males.

Although it is tempting to speculate on the temporal order of the relationship between marijuana use, cigarette use, and depression, doing so would be misrepresenting the true developmental course of these behaviors. Our sample was 14-15 years old at baseline, and many had already smoked at least one cigarette; 38% used marijuana at least once in the past three months; and 25% had clinically significant depression score based on the CES-D at that time. Therefore, many of the behaviors and symptoms of interest had already been expressed prior to the start of the longitudinal study, making causal interpretations difficult. Participants were oversampled for prior cigarette use to maximize chances to observe escalation (and not for marijuana use or symptoms of depression); however, the high number of individuals who use marijuana and who have high depression scores suggests that adolescents who have ever tried a cigarette by 15 are at high-risk for not only cigarette smoking, but also marijuana use, and higher symptoms of depression. Our findings suggest that this may be especially true for males.

Developmental transitions in the late adolescent to adult period bring many environmental changes as well. Our study is one of only handful to address this important transition, allowing us to provide suggestive hypotheses about whether the relationships between cigarettes, marijuana, and depression remain stable even through these transitions. The fact that the relationship between cigarette and marijuana use diminishes over time is suggestive that one or both of these substances are influenced by environmental features such as peers, family, or maturation. Unlike the changing relationship between cigarette and marijuana use during adolescence-adult transition, relationships between higher symptoms of depression and increased frequency of marijuana use in males remained stable. Therefore, males with higher symptoms of depression in adolescence have fewer changes in environment or peer networks during the adolescence-adult transition. It is also possible that their patterns of use may become entrenched in adolescence, creating a negative feedback loop in which they use marijuana to relieve symptoms of depression, which in turn contributes to higher symptoms of depression via endogenous mechanisms (see Chadwick et al., 2013) and environmental factors (isolation, school or employment problems, etc.); and this pattern is difficult to change in young adulthood for males.

The lack of a relationship between marijuana use frequency and symptoms of depression in females, in comparison to males, is intriguing. As depression is more common in females, and substance use is more common in males, these findings require further pursuit. It may be that depression in females is more heterogeneous, and there may be a subgroup of females for whom marijuana use frequency and depression symptoms are more closely linked, like we found among males. Longitudinal studies of individuals at an early age can more closely

disentangle the semiology of substance use and depression, and whether another underlying phenotype might predict risk for both conditions in some significant portion of substance users. It will be important for future studies to better understand factors that influence the link between marijuana and cigarette use in adolescence.

Although the study has a large and diverse sample and captures individuals at different levels of marijuana and cigarette use, the current findings should be considered in the context of limitations. Most of the participants were selected for having ever smoked a cigarette at baseline, limiting the generalizability of our findings. However, it is important to note that marijuana and cigarettes are often used concurrently, and previous evidence indicates cigarette users are more likely to engage in subsequent marijuana use (Kandel & Yamaguchi, 1993; Patton et al., 2006; Prince van Leeuwen et al., 2013; Rigotti et al., 2000; Silins et al., 2013), making this an important group to study. In addition, data on marijuana use frequency and depression symptoms were not captured between years 2 and 5, diminishing our ability to understand the relationships between marijuana use, cigarette use, depression symptoms, and gender during this time. The relationships between marijuana use, cigarette use, and depression symptoms are associational, not causal. However, the fact that we found a gender-specific relationship for marijuana use and depression symptoms, but not for cigarette use and depression symptoms or for gender differences in cigarette use frequency, suggests specificity in these relationships. Finally, the present analyses did not consider alcohol use. The supplement includes the frequency of alcohol use and its relationship to cigarette smoking and to marijuana use frequency. As was true for the relationship between marijuana and cigarettes, we found that there was a stronger relationship between alcohol and cigarette use during adolescence, and that this relationship diminished over time as the frequency of alcohol use increased for the full sample and normatively with age. This also was true for the relationship between marijuana use and alcohol use. Given the almost universal use of any alcohol among the sample by the 6-year follow-up, examining relationships between alcohol and cigarettes, marijuana, and depression are less informative, and hence we did not include alcohol in our present analyses. Future work is planned to look at combined substance use and effects on and relationships with depression.

# 5. Conclusions

Our study expands previously reported relationships between marijuana use, cigarette use, and depression, finding important gender differences in these relationships among a sample of adolescents transitioning into young adulthood. Results indicate that depression symptoms and cigarette use frequency may be key factors that contribute to marijuana use in males. Thus depression and cigarette use may be early treatment targets to decrease marijuana use in adolescent males. Cigarette use also seems to be linked to females' marijuana use, so interventions for adolescent cigarette use may decrease marijuana use among females as well. More broadly, cigarette use and depression are key factors that contribute to marijuana use over time. However, our findings underscore the importance of examining the impact of other substance use and depression on marijuana use separately for males and females. These gender differences may mean different functional consequences from use and have important implications for intervention efforts. Future longitudinal

studies that begin collecting data at an earlier age are needed to better understand if symptoms of depression are a key factor involved in initiation and continued use of marijuana among males and what risk factors are involved in initiation and continued use among females.

### **Supplementary Material**

Refer to Web version on PubMed Central for supplementary material.

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#### References

- Adamson SJ, Kay-Lambkin FJ, Baker AL, Lewin TJ, Thornton L, Kelly BJ, Sellman JD. An improved brief measure of cannabis misuse: the Cannabis Use Disorders Identification Test-Revised (CUDIT-R). Drug Alcohol Depend. 2010; 110:137–143. [PubMed: 20347232]
- Agrawal A, Madden PA, Bucholz KK, Heath AC, Lynskey MT. Transitions to regular smoking and to nicotine dependence in women using cannabis. Drug Alcohol Depend. 2008; 95:107–114. [PubMed: 18325694]
- Annaheim B, Scotto TJ, Gmel G. Revising the Cannabis Use Disorders Identification Test (CUDIT) by means of Item Response Therory. Int J Methods Psychiatr Res. 2010; 19:142–155. [PubMed: 20812291]
- Boden JM, Fergusson DM, Horwood LJ. Cigarette smoking and depression: tests of causal linkages using a longitudinal birth cohort. Br J Psychiatry. 2010; 196:440–446. [PubMed: 20513853]
- Brook JS, Lee JY, Brown EN, Finch SJ. Comorbid trajectories of tobacco and marijuana use as related to psychological outcomes. Subst Abus. 2012; 33:156–167. [PubMed: 22489588]
- Brown RA, Lewinsohn PM, Seeley JR, Wagner EF. Cigarette smoking, major depression, and other psychiatric disorders among adolescents. J Am Acad Child Adolesc Psychiatry. 1996; 35:1602– 1610. [PubMed: 8973066]
- Brown SA, McGue M, Maggs J, Schulenberg J, Hingson R, Swartzwelder S, Martin C, Chung T, Tapert SF, Sher K, Winters KC, Lowman C, Murphy S. A Developmental Perspective on Alcohol and Youths 16 to 20 Years of Age. Pediatrics. 2008; 121:S290–S310. [PubMed: 18381495]
- Caggiula AR, Donny EC, Chaudhri N, Perkins KA, Evans-Martin FF, Sved AF. Importance of nonpharmacological factors in nicotine self-administration. Physiol Behav. 2002; 77:683–687. [PubMed: 12527019]
- CDC. Fact Sheets: Alcohol Use and Health. 2012. Retrieved November 22, 2013, from http:// www.cdc.gov/alcohol/fact-sheets/alcohol-use.htm
- CDC. Fact Sheet: Health Effects of Cigarette Smoking. 2013. Retrieved November 22, 2013, from http://www.cdc.gov/tobacco/data\_statistics/fact\_sheets/health\_effects/effects\_cig\_smoking/
- Chadwick B, Miller ML, Hurd YL. Cannabis use during adolescent development: susceptibility to psychiatric illness. Front Psychiatry. 4:129. [PubMed: 24133461]
- Copeland EP, Hess RS. Differences in young adolescents' coping strategies based on gender and ethnicity. Journal of Early Adolescence. 1995; 15:203–219.

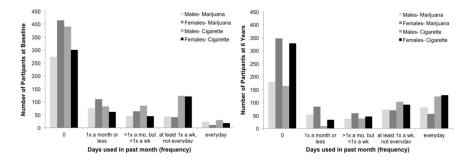
- Copeland W, Shanahan L, Costello E, Angold A. Culumative prevalence of psychiatric disorders by young adulthood: a prospective cohort analysis from the Great Smoky Mountains Study. J Am Acad Child Adolesc Psychiatry. 2011; 50:252–261. [PubMed: 21334565]
- Crane NA, Schuster RM, Fusar-Poli P, Gonzalez R. Effects of cannabis on neurocognitive functioning: recent advances, neurodevelopmental influences, and sex differences. Neuropsychol Rev. 2013; 23:117–137. [PubMed: 23129391]
- Cuijpers P, Smit F, ten Have M, de Graaf R. Smoking is associated with first-ever incidence of mental disorders: a prospective population-based study. Addiction. 2007; 102:1303–1309. [PubMed: 17624980]
- Degenhardt L, Hall W, Lynskey M. The relationship between cannabis use and other substance use in the general population. Drug Alcohol Depend. 2001; 64:319–327. [PubMed: 11672946]
- Degenhardt L, Hall W, Lynskey M. Exploring the association between cannabis use and depression. Addiction. 2003; 98:1493–1504. [PubMed: 14616175]
- Dierker L, Mermelstein R. Early emerging nicotine-dependence symptoms: a signal of propensity for chronic smoking behavior in adolescents. J Pediatr. 2010; 156:818–822. [PubMed: 20097354]
- Dierker L, Selya A, Piasecki T, Rose J, Mermelstein R. Alcohol problems as a signal for sensitivity to nicotine dependence and future smoking. Drug Alcohol Depend. 2013; 132:688–693. [PubMed: 23660243]
- Hankin BL, Abramson LY. Development of gender differences in depression: description and possible explanations. Ann Med. 1999; 31:372–379. [PubMed: 10680851]
- Hankin BL, Mermelstein R, Roesch L. Sex differences in adolescent depression: stress exposure and reactivity models. Child Dev. 2007; 78:279–295. [PubMed: 17328705]
- Hayatbakhsh MR, Najman JM, Jamrozik K, Mamun AA, 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. [PubMed: 17314727]
- Johnston, LD.; O'Malley, PM.; Miech, RA.; Bachman, JG.; Schulenberg, JE. Monitoring the Future national results on adolescent drug use: Overview of key findings. Institute for Social Research, The University of Michigan; Ann Arbor: 2014. 2013. p. 90
- Kandel D, Yamaguchi K. From beer to crack: developmental patterns of drug involvement. Am J Public Health. 1993; 83:851–855. [PubMed: 8498623]
- Klungsoyr O, Nygard JF, Sorensen T, Sandanger I. Cigarette smoking and incidence of first depressive episode: an 11-year, population-based follow-up study. Am J Epidemiol. 2006; 163:421–432. [PubMed: 16394201]
- Korhonen T, Huizink AC, Dick DM, Pulkkinen L, Rose RJ, Kaprio J. Role of individual, peer and family factors in the use of cannabis and other illicit drugs: a longitudinal analysis among Finnish adolescent twins. Drug Alcohol Depend. 2008; 97:33–43. [PubMed: 18455885]
- Kuehner C. Gender differences in unipolar depression: An update of epidemiological findings and possible explanations. Acta Psychiatrica Scandinavica. 2003; 108:163–174. [PubMed: 12890270]
- Libby AM, Orton HD, Stover SK, Riggs PD. What came first, major depression or substance use disorder? Clinical characteristics and substance use comparing teens in a treatment cohort. Addict Behav. 2005; 30:1649–1662. [PubMed: 16098679]
- Lynskey MT, Fergusson DM, Horwood LJ. The origins of the correlations between tobacco, alcohol, and cannabis use during adolescence. J Child Psychol Psychiatry. 1998; 39:995–1005. [PubMed: 9804032]
- Mahalik JR, Levine Coley R, McPherran Lombardi C, Doyle Lynch A, Markowitz AJ, Jaffee SR. Changes in health risk behaviors for males and females from early adolescence through early adulthood. Health Psychol. 2013; 32:685–694. [PubMed: 23477574]
- Mathers M, Toumbourou JW, Catalano RF, Williams J, Patton GC. Consequences of youth tobacco use: a review of prospective behavioural studies. Addiction. 2006; 101:948–958. [PubMed: 16771887]
- Patton GC, Coffey C, Carlin JB, Degenhardt L, Lynskey M, Hall W. Cannabis use and mental health in young people: cohort study. BMJ. 2002; 325:1195–1198. [PubMed: 12446533]

- Patton GC, Coffey C, Carlin JB, Sawyer SM, Lynskey M. Reverse gateways? Frequent cannabis use as a predictor of tobacco initiation and nicotine dependence. Addiction. 2005; 100:1518–1525. [PubMed: 16185213]
- Patton GC, Coffey C, Carlin JB, Sawyer SM, Wakefield M. Teen smokers reach their mid twenties. J Adolesc Health. 2006; 39:214–220. [PubMed: 16857533]
- Pedersen W, von Soest T. Smoking, nicotine dependence and mental health among young adults: a 13year population-based longitudinal study. Addiction. 2009; 104:129–137. [PubMed: 19133898]
- Piccinelli M, Wilkinson G. Gender differences in depression. Critical review. Br J Psychiatry. 2000; 177:486–492. [PubMed: 11102321]
- Prince van Leeuwen A, Creemers HE, Verhulst FC, Vollebergh WA, Ormel J, van Oort F, Huizink AC. Legal substance use and the development of a DSM-IV cannabis use disorder during adolescence: the TRAILS study. Addiction. 2013; 109:303–311. [PubMed: 24033662]
- Prokhorov AV, Koehly LM, Pallonen UE, Hudmon KS. Adolescent nicotine dependence measuring by the modified Fagerstrom Tolerance Questionnaire at two time points. J Child Adolesc Subst Abuse. 1998; 7:35–47.
- Prokhorov AV, Pallonen UE, Fava JL, Ding L, Niaura R. Measuring nicotine dependence among highrisk adolescent smokers. Addict Behav. 1996; 21:117–127. [PubMed: 8729713]
- Radloff LS. The CES-D scale: A self report depression scale for research in the general population. Applied Psychological Measurements. 1977; 1:385–401.
- Radloff LS. The use of the Center for Epidemiologic Studies Depression Scale in adolescents and young adults. J Youth Adolesc. 1991; 2:149–166. [PubMed: 24265004]
- Ramo DE, Delucchi KL, Hall SM, Liu H, Prochaska JJ. Marijuana and tobacco co-use in young adults: patterns and thoughts about use. J Stud Alcohol Drugs. 2013; 74:301–310. [PubMed: 23384378]
- Ramo DE, Prochaska JJ. Prevalence and co-use of marijuana among young adult cigarette smokers: An anonymous online national survey. Addict Sci Clin Pract. 2012; 7:5. [PubMed: 23186143]
- Rigotti NA, Lee JE, Wechsler H. US college students' use of tobacco products: results of a national survey. JAMA. 2000; 284:699–705. [PubMed: 10927777]
- SAMSHA. Results from the 2012 National Survey on Drug Use and Health: Summary of National Findings. 2013:13–4795. NSDUH Series H-46, HHS Publication No. (SMA).
- Schepis TS, Desai RA, Cavallo DA, Smith AE, McFetridge A, Liss TB, Krishnan-Sarin S. Gender differences in adolescent marijuana use and associated psychosocial characteristics. J Addict Med. 2011; 5:65–73. [PubMed: 21769049]
- Schuster RM, Mermelstein R, Wakschlag L. Gender-specific relationships between depressive symptoms, marijuana use, parental communication and risky sexual behavior in adolescence. J Youth Adolesc. 2013; 42:1194–1209. [PubMed: 22927009]
- Selya AS, Dierker LC, Rose JS, Hedeker D, Tan X, Li R, Mermelstein RJ. Time-varying effects of smoking quantity and nicotine dependence on adolescent smoking regularity. Drug Alcohol Depend. 2013; 128:230–237. [PubMed: 22995764]
- Shrier LA, Walls CE, Kendall AD, Blood EA. The context of desire to use marijuana: momentary assessment of young people who frequently use marijuana. Psychol Addict Behav. 2012; 26:821– 829. [PubMed: 22823544]
- Silins E, Horwood JL, Patton GC, Fergusson DM, Olsson CA, Hutchinson DM, Spry E, Toumbourou JW, Degenhardt L, Swift W, Coffey C, Tait RJ, Letcher P, Copeland J, Mattick RP. Young adult sequelae of adolescent cannabis use: an integrative analysis. Lancet Psychiatry. 2014; 1:286–293.
- Silins E, Hutchinson D, Swift W, Slade T, Toson B, Rodgers B. Factors associated with variability and stability of cannabis use in young adulthood. Drug Alcohol Depend. 2013; 133:452–458. [PubMed: 23916322]
- Timberlake DS, Haberstick BC, Hopfer CJ, Bricker J, Sakai JT, Lessem JM, Hewitt JK. Progression from marijuana use to daily smoking and nicotine dependence in a national sample of U.S. adolescents. Drug Alcohol Depend. 2007; 88:272–281. [PubMed: 17174040]
- Tullis LM, Dupont R, Frost-Pineda K, Gold MS. Marijuana and tobacco: a major connection? J Addict Dis. 2003; 22:51–62. [PubMed: 14621344]

- 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. [PubMed: 17624975]
- Volkow ND. The reality of comorbidity: depression and drug abuse. Biol Psychiatry. 2004; 56:714–717. [PubMed: 15556111]
- Weinstein SM, Mermelstein RJ. Influences of Mood Variability, Negative Moods, and Depression on Adolescent Cigarette Smoking. Psychol Addict Behav. 2013; 27:1068–1078. [PubMed: 23438244]
- Wilens TE, Vitulano BA, Upadhyaya H, Adamson J, Parcell T, Westerberg D, Biederman J. Concordance Between Cigarette Smoking and the Modified Fagerstrom Tolerance Questionnaire in Controlled Studies of ADHD. Am J Addict. 17:491–496. [PubMed: 19034741]

### Highlights

- We examined longitudinal relationships among gender, marijuana use, cigarette use, and symptoms of depression
- Higher symptoms of depression were related to increased marijuana use frequency in males, but not in females
- More frequent marijuana use was associated with increased cigarette use frequency, especially among males who had higher symptoms of depression
- Cigarette use frequency is more strongly related to marijuana use frequency in adolescence than in young adulthood
- Exploratory analyses suggested relationships between frequency of use and depression are specific to marijuana, not cigarettes



**Figure 1.** Prevalence of Marijuana and Cigarette Use at Baseline and at 6 Years

#### Table 1

#### Participant Characteristics

	Baseline (n=1108)	6 months (n=1052)	15 months (n=1037)	2 years (n=1061)	5 years (n=1027)	6 years (n=1064)
Demographics						
Age	15.63 (0.61)	16.14 (0.62)	16.89 (0.62)	17.59 (0.60)	21.38 (0.81)	22.40 (0.83)
Gender (% female)	58%	58%	59%	59%	59%	59%
Years of Education	9.49 (0.50)	10.47 (0.52)	11.14 (0.73)	11.46 (0.55)	13.11 (1.05)	13.59 (1.42)
Ethnicity/Race						
Caucasian	57%	57%	57%	57%	58%	57%
Black	17%	17%	17%	17%	17%	17%
Hispanic	17%	16%	16%	16%	16%	16%
Asian	4%	4%	4%	4%	4%	4%
Other	5%	6%	6%	6%	5%	6%
CES-D Total Score						
Males	14.32 (8.65)	14.25 (8.72)	13.52 (8.90)	13.43 (9.05)	12.96 (9.89)	12.26 (9.50)
Females	18.84 (10.32)	17.93 (10.49)	15.37 (9.38)	16.15 (9.62)	13.74 (9.82)	13.14 (9.82)
Substance Use						
Frequency of marijuana use	e in past month (days)					
Males	2.71 (6.27)	3.23 (6.93)	3.85 (7.55)	5.24 (8.75)	6.81 (9.91)	7.14 (10.23)
Females	1.51 (4.06)	1.92 (4.92)	2.24 (5.73)	2.84 (6.34)	4.34 (8.05)	3.89 (7.83)
Marijuana-Related Problen	ns (CUDIT-R)					
Males					7.73 (8.08)	7.09 (7.42)
Females					4.66 (6.38)	4.27 (6.04)
Frequency of cigarette use	in past month (days)					
Males	4.01 (7.80)	4.97 (8.87)	6.33 (10.52)	7.48 (11.16)	12.73 (13.23)	12.31 (12.93)
Females	3.88 (7.85)	4.38 (8.38)	5.26 (9.65)	5.94 (10.23)	9.31 (12.12)	8.47 (12.22)
Nicotine Dependence (mF)	ΓQ)					
Males	1.41 (1.18)	1.63 (1.39)	1.79 (1.49)	1.87 (1.53)	2.78 (1.65)	2.85 (1.63)
Females	1.41 (1.22)	1.42 (1.31)	1.57 (1.39)	1.62 (1.39)	2.40 (1.40)	2.51 (1.53)

*Note:* all values are means or standard deviations unless otherwise noted; CES-D, Center for Epidemiological Scale-Depression; CUDIT-R, Cannabis Use Disorders Identification Test-Revised; mFTQ, modified Fagerstrom Questionnaire.

#### Table 2

Longitudinal Multilevel Regression Model with Frequency of Marijuana Use as the Dependent Variable

Predictor	Frequency of Marijuana Use (days used in last month)						
	Est. (SE)	df	t	p-value			
Intercept	2.89 (0.15)	1152.43	19.65	<.001			
Time (linear)	0.38 (0.05)	1200.96	7.77	<.001			
Gender	1.62 (0.26)	1145.73	6.17	<.001			
Ethnicity/Race+	-0.04 (0.11)	1090.69	-0.40	.69			
Time-varying predictors							
Depression (CES-D Total)	0.04 (0.01)	5768.75	4.03	<.001			
Cigarette use (frequency of use in last month)	0.22 (0.01)	3410.61	16.22	<.001			
Interactions							
Time*Depression <sup>+</sup>	0.00 (0.00)	4720.97	-1.06	.29			
Time*Cigarette Use	-0.01 (0.00)	3628.37	-3.47	.001			
Gender*Depression	0.05 (0.02)	5827.08	2.72	.007			
Gender*Cigarette Use	0.09 (0.03)	3425.48	3.31	.001			
Depression*Cigarette Use	0.00 (0.00)	5982.25	5.90	<.001			
Time*Gender*Depression+	0.00 (0.01)	4694.69	-0.38	.70			
Time*Gender*Cigarette Use	-0.02 (0.01)	3641.69	-2.07	.04			
Gender*Depression*Cigarette Use	0.01 (0.00)	5982.35	4.02	<.001			

Note. CES-D, Center for Epidemiological Scale-Depression.

#### Table 3

Longitudinal Multilevel Regression Model with Frequency of Cigarette Use as the Dependent Variable

Predictor	Frequency of Cigarette Use (days used in last month)					
	Est. (SE)	df	t	p-value		
Intercept	1.25 (0.80)	1093.60	1.55	.12		
Time (linear)	0.99 (0.06)	1109.96	15.48	<.001		
Gender <sup>+</sup>	0.54 (0.45)	1106.02	1.21	.23		
Ethnicity/Race	0.81 (0.19)	1071.98	4.35	<.001		
Time-varying predictors						
Depression (CES-D Total) <sup>+</sup>	0.01 (0.02)	5086.99	0.26	.61		
Marijuana use (frequency of use in last month)	0.32 (0.02)	5078.23	13.51	<.001		
Interactions						
Time*Depression <sup>+</sup>	0.01 (0.01)	4751.40	1.88	.06		
Time*Marijuana Use	-0.02 (0.01)	4784.57	-2.62	.01		
Gender*Depression <sup>+</sup>	0.01 (0.03)	5058.98	0.21	.83		
Gender*Marijuana Use <sup>+</sup>	-0.05 (0.05)	5122.14	-0.90	.37		
Depression*Marijuana Use <sup>+</sup>	0.00 (0.00)	5213.23	-0.04	.97		
Time*Gender*Depression <sup>+</sup>	0.00 (0.01)	4751.02	-0.08	.94		
Time*Gender*Marijuana Use <sup>+</sup>	-0.01 (0.01)	4831.76	-0.46	.65		
Gender*Depression*Marijuana Use <sup>+</sup>	0.00 (0.00)	5207.02	0.35	.72		

Note. CES-D, Center for Epidemiological Scale-Depression;

<sup>+</sup>variable removed from final reduced model.