Cannabis use, depression and suicidal ideation in adolescence: direction of associations in a population based cohort

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Abstract

Background: To clarify the direction of the association between frequency of cannabis use, depressive symptoms and suicidal ideation from 15 to 20 years using cross-lagged analyses.

Method: We included 1606 adolescents from the province of Québec followed since 1997 with information on frequency of cannabis use (none/monthly/weekly), depression (defined as being in the top 10% symptoms) and serious suicidal ideation at ages 15, 17 and 20 years.

Results: The prevalence of weekly cannabis use increased from 7.0% at age 15 years to 15.6% by age 20 years. Adolescents who reported using cannabis weekly at one age were 11 to 15 times more likely to continue using cannabis over time. In longitudinal cross-lagged analyses, weekly cannabis use at age 15 was associated with greater odds (OR:2.19, 95% CI:1.04-4.58) of suicidal ideation two years later. However, other substance use (alcohol, tobacco, other drugs) fully explained this association. Further, depression predicted subsequent weekly cannabis use, even after adjusting for comorbid other substance use (eg, for depression at 15 years predicting cannabis use at 17 years: OR:2.30, 95% CI:1.19-4.43).

Limitations: Quantity of cannabis consumed was not measured.

Conclusion: Findings suggest that depressive symptoms in adolescence may represent a risk factor for weekly cannabis consumption, which once initiated is likely to remain chronic. Weekly cannabis use increased risk for suicidal ideation, but not independently from other substance use including alcohol, tobacco and other drugs.

Key words: longitudinal, adolescence, cannabis, depression, suicidal ideation, substance use

Introduction

Cannabis is one of the most widely used psychoactive substances around the world (Degenhardt et al., 2013b) and its legalization in Canada and many states in the USA has raised concerns about its associations with mental health. Recent reviews and meta-analyses in adult populations suggest that cannabis use may be associated with depression and suicidal ideation (Borges et al., 2016; Lev-Ran and Feingold, 2017; Lev-Ran et al., 2014). However, our knowledge on associations between cannabis use and mental health in young people is more limited. Youths aged 15 to 24 years have the highest rates of mood disorders and suicidal ideation across the lifespan (Kessler et al., 2005; Nock et al., 2008), and represent the largest group of cannabis consumers worldwide (Degenhardt et al., 2016; Poulton et al., 1997), making adolescence a period of heightened vulnerability for comorbid mental health and substance use problems.

Adolescent cannabis use has been associated with depression and suicidal ideation cross-sectionally. For instance, prior studies have reported associations between the extent of cannabis consumption (ranging from any to heavy consumption) and higher odds of depression (odds ratio (ORs) ranging from 1.20 to 1.65) (Degenhardt et al., 2013a; Poulin et al., 2005b; Rasic et al., 2013; Rey et al., 2002) and suicidal ideation (ORs:1.30 to 2.45) (Carvalho et al., 2019; Huas et al., 2008; Sellers et al., 2019; Swahn et al., 2012). However, in cross-sectional studies, it is not possible to ascertain the developmental sequence of association; i.e., cannabis use preceding depression/suicidal ideation (secondary psychiatric disorder hypothesis) (Gobbi et al., 2019; Poorolajal et al., 2016) or depression/suicidal ideation preceding cannabis use (secondary substance use hypothesis) (Khantzian, 1987).

A recent meta-analysis of longitudinal studies (k=13) reported that weekly adolescent cannabis users were at increased odds for depression diagnosis and suicidal ideation and attempt in young adulthood (Gobbi et al., 2019), consistent with previous findings from large representative samples of youth (Fergusson et al., 2002; Silins et al., 2014). However, not all of the included studies in the meta-analysis adjusted for other substance use, including alcohol, despite its important overlap with cannabis use (Leatherdale and Burkhalter, 2012), and its associations with depression and suicidal ideation (Brière et al., 2014; Marschall-Lévesque et al., 2017; Poorolajal et al., 2016). Furthermore, their outcomes were assessed during young adulthood making it difficult to ascertain if acute effects of cannabis are detectable during adolescence. The investigation of such outcomes during adolescence are warranted given that the initiation of substance use typically occurs during this developmental period (Dick et al., 2000; Martin et al., 2002), with an increased risk of overall substance use peaking around mid-to-late adolescence (Patton et al., 2004).

Only few longitudinal studies have investigated the increased risk of cannabis use among youth with prior depression and/or suicidal ideation. Such studies have demonstrated that depression and suicidal ideation are associated with subsequent cannabis use (Rhew et al., 2017; Weinberger et al., 2020; Zhang and Wu, 2014), but most were based on small unrepresentative samples of adolescents (Rhew et al., 2017) and relied on a broad measure of cannabis use (ie, any or none) (Weinberger et al., 2020; Zhang and Wu, 2014). Therefore, there is a need to clarify the longitudinal associations between cannabis use, depression and suicidal ideation by assessing the bidirectionality of these associations.

The few studies that have investigated the bidirectional associations between cannabis use and depression in adolescence and/or young adulthood simultaneously (Hoffmann, 2018;

Wilkinson et al., 2016; Womack et al., 2016) have been limited by small unrepresentative samples (Hoffmann, 2018; Womack et al., 2016), with only one longitudinal study based on a representative sample (Wilkinson et al., 2016). Using data from the National Longitudinal Study of Adolescent to Adult Health in the US (data collection spanned from 1994 to 2009), this study supported an association from depressive symptoms to later cannabis use in both males and females from adolescence to young adulthood, but not from cannabis use to depressive symptoms (Wilkinson et al., 2016). However, given that the prevalence of cannabis consumption (Johnston et al., 2019), depression (Mojtabai et al., 2016), and suicidal ideation (Burstein et al., 2019) in adolescents has increased since then, it is important to study these associations in today's generations of adolescents. Further, to our knowledge, no prior longitudinal study has examined bidirectional associations between cannabis use and suicidal ideation.

Using data from a representative cohort of Canadian youth, we investigated the developmental sequence of association between cannabis use, depression and suicidal ideation from 15 to 20 years, using cross-lagged models, to allow for the simultaneous investigation of bidirectional associations.

Method

Participants

Participants were from the Québec Longitudinal Study of Child Development (QLSCD), conducted by the Institut de la statistique du Québec (ISQ; Québec Statistics Institute), which is a population-based cohort of 2120 individuals born in the Canadian province of Québec in 1997/98 who were followed up until 20 years of age. The original sample was selected from the Québec birth registry using a stratified procedure based on living area and birth rate. Single-birth

children were included if the mother could speak English or French. Data were collected annually or biannually from 1998 through 2018. For more details about the larger study design, please see: http://www.iamillbe.stat.gouv.qc.ca.

In the present study, we included 1606 participants who completed a confidential online questionnaire and for whom data were available at 15, 17 and 20 years, accounting for 76% of the original cohort. To account for attrition, we conducted analyses with inverse probability weights, where weights represented participants' probabilities of being included in the study sample conditional on variables related to attrition: males (39.5% v. 47.9%); internalizing behaviors in childhood (M=1.11 v. M=1.32); mothers with lower education (22.6% v.16.8%); and families with a single parent (11.1% v. 7.1%) (**See supplementary Table 1**).

Ethical Considerations

The QLSCD was approved by the Québec Statistics Institute and the St-Justine Hospital Research Center ethics committees, and informed consent was obtained at each data collection.

Measures at 15, 17 and 20 years

Cannabis Use

Cannabis use in the past-year was assessed using the following item: "During the past 12 months, how often did you use cannabis (marijuana/pot/hashish)?" Responses ranging from "I didn't" (1) to "everyday" (7) were grouped into three categories: Non-users, Monthly Users (1x to try/<1x/month/about1x/month), Weekly Users (1-2x/week/≥3x/week/everyday).

Depression

Depressive symptoms were self-reported by adolescents at ages 15 and 17 years using the Mental Health and Social Inadaptation Assessment (MIA) (Côté et al., 2017), and at 20 years using the Centre for Epidemiological Studies Depression Scale (CES-D) (Poulin et al., 2005a;

Radloff, 1977); see Appendix for a full list of items used. The MIA depression subscale consists of eight symptoms in the past year (eg, "I lost interest in things I usually like," α=.87 and .88 at ages 15 and 17 years, respectively); scored as 0 (never true), 1 (sometimes true) or 2 (often true). The CES-D short version (Poulin et al., 2005a) contains 12 items assessing symptoms that occurred in the past week (eg, "I felt depressed," α=.77) with response options ranging from 0 to 3. Adolescents in the top 10% of symptoms were identified as having elevated symptoms, which we refer to as depression and all models were also estimated using depressive symptoms treated as a continuous variable.

Suicidal ideation

We measured past year suicidal ideation (Côté et al., 2017; Geoffroy et al., 2016) with the following question, "Did you ever seriously think of attempting suicide?" Coded as *no* versus *yes* for serious suicidal ideation.

Other Substance Use (alcohol, tobacco and other drugs)

At each age, adolescents reported on their past-year other substance use in terms of: ***consuming alcohol*** (non-users/monthly users (<two drinks/week)/weekly users (≥two drinks/week); ***consuming tobacco*** (i.e., smoking cigarettes) (non-users/monthly/weekly users); and ***other drugs*** (cocaine/solvents/hallucinogens/heroin/amphetamines/methamphetamines/ medication without prescription (yes/no)).

Statistical Analyses

We first described the prevalence of cannabis use, depression and suicidal ideation and its associations with sex using chi-squared tests based on the maximum available number of cases for each variable at ages 15, 17 and 20 years. We then assessed concurrent associations between cannabis use and depression and suicidal ideation at each age using cross-tabulations and logistic

regressions. Finally, we used structural equation modelling to conduct an integrated cross-lagged model examining associations between cannabis use, depression and suicidal ideation across three time points using Mplus version 7.4 (Muthén and Muthén, 1998-2015). This type of analysis allows examining bidirectional effects between variables, while controlling for their stability over time. Regressed effects of cannabis use, depression and suicidal ideation were controlled for at ages 15 and 17 years. Given that alcohol, tobacco and other drug use were significantly correlated with cannabis use (see **supplementary Table 2**), they were added as baseline covariates at ages 15 and 17 years. Our two hypotheses were nested within the cross-lagged model allowing for them to be tested simultaneously. The model showed good fit to the data (Root Mean Square Error of Approximation=0.043, 90% CI=0.034-0.053; Comparative Fit Index=0.929). Full information maximum likelihood was used to handle missing data (Johnson and Young, 2011). This procedure was able to estimate the parameters of participants contributing to at least one data point (N=1606). Due to lack of statistical power, cross-lagged models were only estimated while combining males and females. Depression and suicidal ideation were entered simultaneously in the models. Finally, we undertook sensitivity analyses and re-estimated the cross-lagged models (a) using a continuous measure of depressive symptoms instead of top 10% of symptoms and (b) modeling depression and suicidal ideation separately.

Results

As shown in **Table 1**, overall prevalence of weekly cannabis use increased from 7.0% at age 15 years to 12.7% at age 17 years and 15.6% at age 20 years. The prevalence of weekly cannabis use was higher for males (15.1%-18.4%) compared to females (10.5%-13.5%) at ages 17 and 20 years, *p*s<.05. Similar trends were observed for monthly cannabis use. The prevalence

of depression was predefined at approximately 10.0%, but varied for males and females, such that the prevalence was slightly higher in females (12.9-15.4%) than males (4.2-8.6%) at all ages, *p*s<.05. The prevalence of suicidal ideation also varied by sexes: 8.7–9.1% for females and 3.1-4.1% for males at ages 15 and 17 years, *p*s<.05. Cannabis had significant overlap with alcohol, tobacco and other drug use at all ages, *p*s<.001 (see **supplementary Table 2**). For instance, of adolescents using cannabis weekly at age 15 years, 33.7%, 40.6% and 47.0% also used alcohol and tobacco weekly and other drugs, respectively.

Using cross-tabulations and logistic regressions, Table 2 indicated that cannabis use was concurrently associated with suicidal ideation and depression. Being a weekly cannabis user was associated with suicidal ideation at all ages, with Odds Ratios (ORs) ranging from 2.39 to 3.83. Similarly, weekly cannabis use was associated with depression at ages 15 and 17 years (ORs=2.35 and 2.56 respectively) although not at age 20 years. Patterns of associations were similar for monthly cannabis use, although ORs were smaller in magnitude. Interactions with sex were investigated by computing an interaction term between sex and cannabis use (non-user/monthly/weekly) which was entered as a continuous variable. All interactions with sex were non-significant (*p*s>.05); suggesting that concurrent associations did not differ for males and females.

Cross-lagged models are presented in **Figures 1** (unadjusted) and **2** (adjusted for sex and other substance use at baseline, i.e. 15y and 17y entered as continuous variables in the models).

Autoregressive effects of depression, suicidal ideation and cannabis use

Autoregressive effects describe the stability of the measures from one measurement point to the next. We found strong stability for all measures from ages 15 to 20 years. For example, weekly cannabis use at age 15 years was associated with an increased likelihood to carry this

behavior at age 17 years (OR=34.65, 95%CI=19.51-61.56), and subsequently at age 20 years (OR=21.01, 95%CI=12.40-35.59; see **Figure 1**). Additionally, monthly cannabis use was associated with weekly cannabis use at later time points: associations tend to be stronger for the period from ages 15 to 17 years (OR=6.39, 95%CI= 4.12-9.90; see **Figure 1**) than for the period from ages 17 to 20 years (OR=2.38, 95%CI=1.47-3.86).

Prediction from cannabis use to subsequent depression and suicidal ideation

As shown in **Figure 1**, adolescents who used cannabis weekly at age 15 years were at an increased risk of suicidal ideation at 17 years (OR=2.19, 95%CI=1.04-4.58), but not at 20 years (OR=0.72, 95%CI=0.15-1.30). However, adjustment for other substance use including alcohol, tobacco and other drugs at age 15 years abolished this association (OR=1.38, 95%CI=0.52-3.20; see **Figure 2**). Weekly cannabis use did not increase the risk of depression at ages 17 or 20 years.

Prediction from depression and suicidal ideation to subsequent cannabis use

Adolescents with depression at age 15 years were at increased risk of subsequent weekly cannabis use at age 17 years, and this association remained after adjusting for sex and other substance use (OR=2.30, 95%CI=1.19-4.43, see **Figure 2**). Moreover, depression at age 15 years indirectly increased risk of using cannabis weekly at age 20 years through weekly cannabis use at age 17 years (OR=7.55, 95%CI=1.36-42.05). In a further analysis, we adjusted for (in addition to sex and other substance use) family socioeconomic status (aggregate of annual gross income, parental education level and occupational prestige) (Willms and Shields, 1996) measured at age 15 years. Associations hardly changed after further adjustment for family socioeconomic status: depression at age 15 years was associated with weekly cannabis use at age 17 years (OR=2.41; 95%CI= 1.25-4.18; see **Supplementary Figure 1**). Depression at age 17 years was not

associated with cannabis use at age 20 years. Suicidal ideation was not associated with later cannabis use at any age.

Sensitivity analyses

The results were largely similar to those based on a categorical measure using a continuous measure of depressive symptoms in the cross-lagged models: (1) Weekly cannabis use at ages 15 and 17 years was not associated with greater depressive symptoms later on, and (2) Depressive symptoms were associated with later weekly cannabis use at ages 17 (β=0.21, 95%CI= 0.10-0.31), and 20 (β=0.13, 0.03-0.22) years. Further, patterns of results were similar while modeling depression and suicidal ideation separately (data not shown).

Discussion

This population-based study is the first, to our knowledge, to examine the temporal relation between cannabis use, depression and suicidal ideation simultaneously over five years during adolescence. Depression (but not suicidal ideation) predicted weekly cannabis use throughout adolescence. Weekly cannabis use predicted suicidal ideation (but not depression), but this association was no longer significant after taking into account other substance use including alcohol, tobacco and other drugs consumption. Associations observed for adolescents experiencing depression (defined as being in the top 10% of symptoms) were similar to those observed for the full spectrum of depressive symptoms. Compared to the few other studies (Hoffmann, 2018; Wilkinson et al., 2016; Womack et al., 2016) that have investigated the bidirectional associations between depression and cannabis use simultaneously, our study had the advantage of also examining suicidal ideation in the cross-lagged models and was based on a representative sample of today's adolescents.

Interpretation and comparison with other studies

Prediction from cannabis use to subsequent depression and suicidal ideation

In line with previous epidemiological findings (Degenhardt et al., 2013a; Rasic et al., 2013), the prevalence of weekly cannabis use for adolescents was 15.6% by age 20 years, and males were more likely to use cannabis compared to females. Cannabis use was concurrent with depression and suicidal ideation in the cohort, consistent with other studies including a Canadian cohort (Halladay et al., 2019). As such, it is of major interest to clarify the developmental sequence of association between these variables. Two previous longitudinal studies investigating bidirectional associations between cannabis use and depression in adolescence reported an association from cannabis use to depression (Hoffmann, 2018; Horwood et al., 2012), whereas another study failed to detect an association (Womack et al., 2016).

A previous meta-analysis (Gobbi et al., 2019) of longitudinal studies reported that weekly cannabis use predicted depression (OR=1.37) and suicidal ideation (OR=1.50) in young adulthood, whereas the association from depression and suicidal ideation to cannabis use was not investigated. Our study confirmed that weekly cannabis users had two times the odds of suicidal ideation at age 17 years only (but not depression) compared to non-cannabis users.

The specific association of cannabis use with suicidal ideation, but not depression, also contrasts with prior studies in adult populations showing increased risk of depression consecutive to cannabis use (Agrawal et al., 2017; Lev-Ran et al., 2014; Smolkina et al., 2017). In one study, initiation of cannabis before the age of 17 years was associated with depression in monozygotic twins discordant for cannabis use (Agrawal et al., 2017). It has also been documented that persistent and chronic cannabis use throughout adolescence is associated with depression later on (Horwood et al., 2012; Patton et al., 2002; Thompson et al., 2018). It could be that the consequences of cannabis use on mental health become apparent only after a certain duration of

using cannabis (Masten and Cicchetti, 2010). Comparatively, findings from the Dunedin Multidisciplinary Health and Development Study (McGee et al., 2000) demonstrated that cannabis use was associated with depression in young adulthood, but not during adolescence. These results shed light on the possibility that cannabis use may increase depression under certain conditions, such as an early age of onset or after a certain chronicity of use.

Similar to other studies (Tomczyk et al., 2016), we found that a large number of weekly cannabis users simultaneously use other drugs including, but not limited to, cocaine, hallucinogens and amphetamines, and consume alcohol and tobacco on a frequent basis. In our study, the association from weekly cannabis use to suicidal ideation was better explained by other substance use (alcohol, tobacco and other drugs) being associated with suicidal ideation in adolescence (Darvishi et al., 2015; Marschall-Lévesque et al., 2017; Poorolajal et al., 2016). This suggests that it may be other substance use (alone or in combination with cannabis use), rather than cannabis use alone, that increases the risk of suicidal ideation (Rasic et al., 2013). Prior studies included in the meta-analysis did not control for comorbid substance use (Gobbi et al., 2019). Further, their outcome measures of depression and suicidal ideation were measured in young adulthood (Gobbi et al., 2019), whereas our study measured these outcomes throughout adolescence.

Prediction from depression and suicidal ideation to subsequent cannabis use

As far as we are aware very few longitudinal studies have investigated associations from depression to cannabis use (Hoffmann, 2018; Hooshmand et al., 2012; Rhew et al., 2017; Wilkinson et al., 2016; Womack et al., 2016) and from suicidal ideation to cannabis use (Zhang and Wu, 2014). All studies (except (Hoffmann, 2018)) demonstrated that depression and suicidal ideation were associated with increased subsequent cannabis use during adolescence. Our study

extends the current body of knowledge by showing that today's adolescents experiencing depression were at an increased risk of using cannabis weekly, within cross-lagged models.

The associations in our study were also apparent while considering depressive symptoms instead of the top 10% of symptoms, suggesting that risk of using cannabis weekly is seen for the full spectrum of depressive symptoms. Further, our study demonstrated that depression at age 15 years indirectly increased the risk of using cannabis weekly at age 20 years through its association with weekly cannabis use at age 17 years.

Such associations from depression to cannabis use are in line with the secondary substance use hypothesis which posits that depression precedes cannabis use, whereby adolescents may use cannabis to alleviate distress (Khantzian, 1987). Specifically, cannabis has the ability to reduce negative mood states that exist prior to its use, but it does not resolve the underlying mood disturbances (Johns, 2001). As such, cannabis use may become reinforcing for vulnerable adolescents experiencing depression, as its ability to propagate euphoric mood states may be interpreted as therapeutic by the adolescent, where in fact the use of cannabis actually increases their vulnerability to substance use (Borodovsky and Budney, 2018).

Overall, about 16% of the adolescents in this study were weekly cannabis users by age 20 years, compared to 7% at age 15 years, suggesting that cannabis use increases throughout adolescence. Further, adolescents who used cannabis weekly and monthly were at heightened risk to use cannabis weekly later on, as shown elsewhere (Caldeira et al., 2012; Homel et al., 2014; Schulenberg et al., 2005).

Strengths and Limitations

This study relied on a large representative cohort of today's youth with repeated measurements of cannabis use, depression and suicidal ideation collected in 2013 (15 years),

2015 (17 years) and 2018 (20 years), which allowed for the modelling of all associations simultaneously. However, our study had some limitations. First, self-reported frequency of cannabis use may have been subject to response bias (eg, underreporting cannabis use) (Akinci et al., 2001; Delaney-Black et al., 2010). In a study by Kedzior et al, it was demonstrated that there is only moderate accuracy when self-reporting past-year cannabis use (Kedzior et al., 2006). Furthermore, there was no available information on the quantity and potency (eg, THC content) of cannabis consumed, although such information is challenging to quantify given the variation in the methods of cannabis consumption (eg, edibles v. joints), source and dosage (Gray et al., 2009). Further, it was not possible to disentangle between cannabis use and cannabis use disorder in the present study. Cannabis use disorder is characterized by dependence and abuse criteria as well as metrics on craving and withdrawal symptoms, whereas the item used in this study could not ascertain such a diagnosis. It has been demonstrated that cannabis use disorder is associated with worse outcomes including cognitive decline as well as poorer social functioning (Hasin et al., 2016), which may not be the case for cannabis use per se. Therefore, it may be that similar findings as those found in the present study would not hold for individuals with cannabis use disorder and as such, future research would be warranted. Moreover, although it has been documented that adolescent onset of cannabis use is associated with negative mental health outcomes (Rioux et al., 2018; Swahn et al., 2012), poor psychosocial adjustment (Fergusson and Horwood, 1997) and cognitive decline (Castellanos-Ryan et al., 2017; Meier et al., 2012) in adulthood, the present study did not evaluate the age of onset of cannabis use and its relation to depressive symptoms and suicidal ideation. Second, as in our previous work with this cohort (Geoffroy et al., 2018), our self-report questionnaires for depression did not provide a clinical diagnosis and we used an arbitrary cut-off to approximate individuals with the highest symptoms

at each age. However, cross-lagged models were re-estimated using depressive symptoms as a continuous variable, and patterns of results were largely similar. Third, although items assessing cannabis use and suicidal ideation were the same across all time points, depression was measured with the MIA at ages 15 and 17 years (assessing past-year depressive symptoms) and the CES-D at 20 years (assessing past two-weeks depressive symptoms). However, these measures capture similar symptoms, standardization of cut-off increased comparability across time-points, and cannabis use was not associated with depression at 17 years (MIA) nor 20 years (CES-D). Fourth, all measures were self-reported, potentially inflating strengths of associations due to shared method variance. Fifth, our study is observational in nature, and despite adjustments for time-sensitive covariates, we cannot rule out that unmeasured covariates may have accounted for some associations. For instance, it has been argued that genetic factors may contribute to the association between cannabis use and subsequent depression and suicidal ideation (Agrawal and Lynskey, 2014), although such variables were not available in the present sample. Sixth, as with all longitudinal surveys, attrition had occurred, with the most vulnerable participants more likely to be lost at follow-up. Nevertheless, our weighted analyses minimized such selective attrition bias.

Conclusion

Our findings suggest that cannabis use increases throughout adolescence and that once this behavior is initiated, cannabis use is likely to remain stable over time. We also found evidence for adolescents experiencing depressive symptoms to be at a greater risk of using cannabis on a weekly basis later on. These findings highlight the importance of targeting depressive symptoms during this sensitive developmental period in an attempt to offset the potential increased use of cannabis over time.

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Table 1. Prevalence, n (%) of cannabis use, depression and suicidal ideation in adolescence[a,b]

Variable	Total			Females			Males			P-value for sex differences[d]		
	15 y	17 y	20 y	15 y	17 y	20 y	15 y	17 y	20 y	15 y	17 y	20 y
Cannabis Use, n(%)										.282	.031	.045
Non-User	1097(76.3)	749(59.3)	702(56.4)	562(74.8)	407(59.6)	421(58.6)	535(78.0)	342(58.9)	281(53.4)			
Monthly User	239(16.6)	355(28.1)	349(28.0)	136(18.1)	204(29.9)	201(28.0)	103(15.0)	151(26.0)	148(28.1)			
Weekly User	101(7.0)	160(12.7)	194(15.6)	53(7.1)	72(10.5)	97(13.5)	48(7.0)	88(15.1)	97(18.4)			
Depression, n(%)[c]										<.001	<.001	.012
Depressed	146(10.1)	118(9.3)	137(11.1)	116(15.4)	94(13.7)	92(12.9)	30(4.4)	24(4.2)	45(8.6)			
Non-depressed	1296(89.9)	1146(90.7)	1101(88.9)	637(84.6)	592(86.3)	621(87.1)	659(95.6)	554(95.8)	480(91.4)			
Suicidal ideation n(%)										<.001	<.001	.891
Suicidal ideation	86(6.0)	84(6.8)	123(10.0)	65(8.7)	61(9.1)	70(9.9)	21(3.1)	23(4.1)	53(10.1)			
Non-suicidal ideation	1342(94.0)	1144(93.2)	1112(90.0)	682(91.3)	607(90.9)	640(90.1)	660(96.9)	537(95.9)	472(89.9)			

[a]Data were compiled from the final master file of the Québec Longitudinal Study of Child Development (1998-2018) ©Québec Gouvernement, Institut de la Statistique du Québec.

[b] The proportion of missing values at ages 15, 17 and 20 years for cannabis use: 35.4%, 43.1% and 44.0%, respectively; depression: 35.1%, 43.1% and 44.3%, respectively; and suicidal ideation: 35.8%, 44.8% and 44.4%, respectively.

[c]Depression scores were categorized as ≤90th percentile (not depressed) versus >90th percentile (depressed).

[d]*P* values are based on chi-square tests.

Note: The Mental Health and Social Inadaptation Scale (Côté et al., 2017) and Centre for Epidemiologic Studies Depression Scale (short-form) (Poulin et al., 2005a; Radloff, 1977) were used to assess depression, however, these measures did not provide clinical diagnoses of depression, but rather assessed the severity of symptoms.

Table 2. Odds ratios (ORs) and 95% confidence intervals (CIs) for cross-sectional associations of cannabis use with depression and suicidal ideation during adolescence[a] (N=1606).

	Depression[b]		Suicidal Ideation	
	N(%)	OR (95%CI)	N(%)	OR (95%CI)
Cannabis Use				
Monthly Users				
15 y	35(24.1)	1.99(1.28-2.97)	24(27.9)	2.60(1.53-4.31)
17 y	36(30.8)	1.39(0.88-2.17)	26(31.0)	1.37(0.80-2.31)
20 y	31(27.0)	0.97(0.61-1.52)	42(34.1)	1.66(1.13-2.72)
Weekly Users				
15 y	18(12.4)	2.35(1.31-4.04)	15(17.4)	3.83(1.88-7.02)
17 y	27(23.1)	2.56(1.54-4.19)	19(22.6)	2.39(1.32-4.21)
20 y	20(17.4)	1.12(0.64-1.88)	32(26.0)	2.57(1.58-4.12)

[a]Data were compiled from the final master file of the Québec Longitudinal Study of Child Development (1998-2018) ©Québec Government, Institut de la Statistique du Québec.

[b]Depression scores were categorized as ≤90th percentile (not depressed) versus >90th percentile (depressed).

Note: All models adjusted for sex. *p* for sex interaction = .459, .159, .504 for depression 15y, 17y and 20y, respectively; and .978, .471 and .366 for suicidal ideation at 15 y, 17 y and 20 y, respectively.

Note: The Mental Health and Social Inadaptation Scale (Côté et al., 2017) and Centre for Epidemiologic Studies Depression Scale (short-form) (Poulin et al., 2005a; Radloff, 1977) were used to assess depression, however, these measures did not provide clinical diagnoses of depression, but rather assessed the severity of symptoms.

Figure 1. Cross-lagged model at 15, 17 and 20 years for cannabis use, depression and suicidal ideation - non-adjusted model

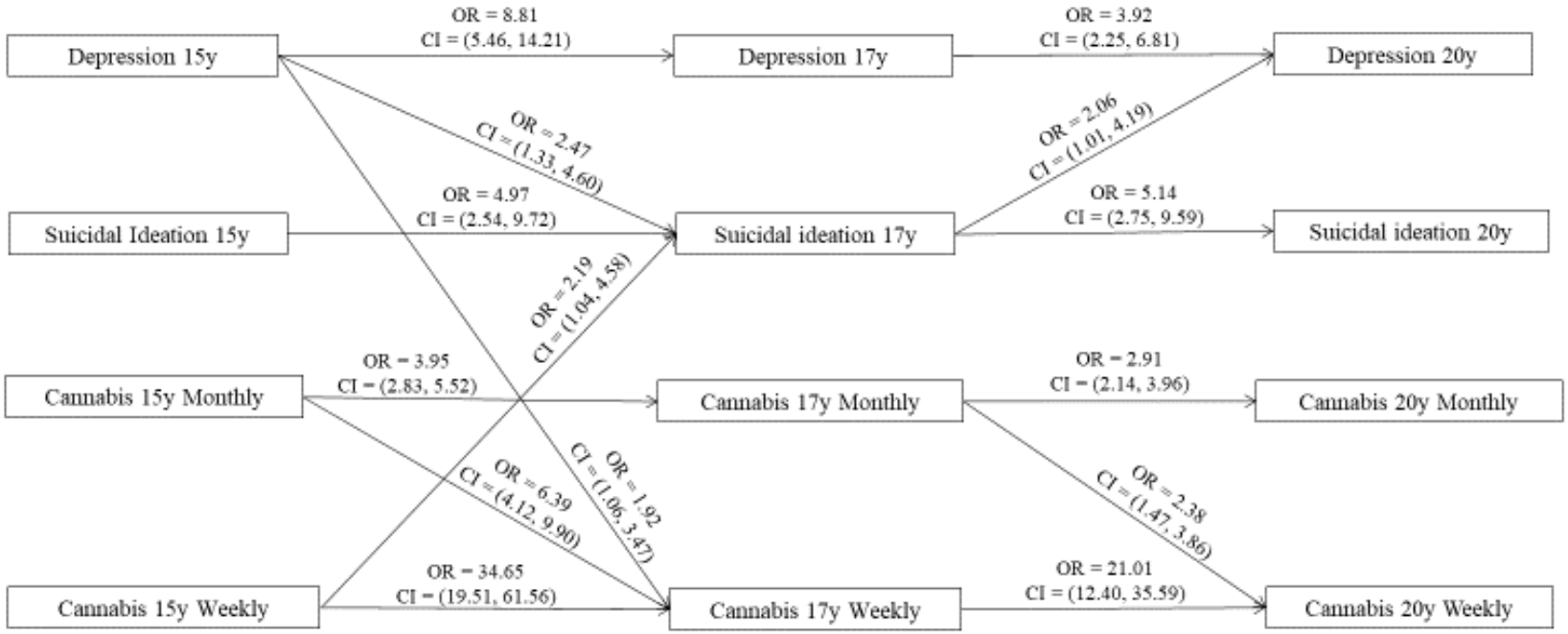

Figure 1. Results for the cross-lag at 15, 17 and 20 years (N=1606); Non-adjusted model. Using a continuous measure of depressive symptoms, depressive symptom model for cannabis use, depression and suicidal ideation ms were associated with later weekly cannabis use at ages 17 (β=0.122, 95%CI= 0.030-0.214), and 20 (β=0.095, 95%CI= 0.003-0.187) years. Note: Only significant paths ($p< 0.05$) are presented for clarity. OR and 95% CI=All values are Odds Ratio with 95% confidence intervals; 15y=15 years, 17y=17 years, 20y=20 years. Data were compiled from the final master file of the Québec Longitudinal Study of Child Development (1998-2018) ©Québec Government, Institut de la Statistique du Québec.

Figure 2. Cross-lagged model at 15, 17 and 20 years for cannabis use, depression and suicidal ideation - adjusted model

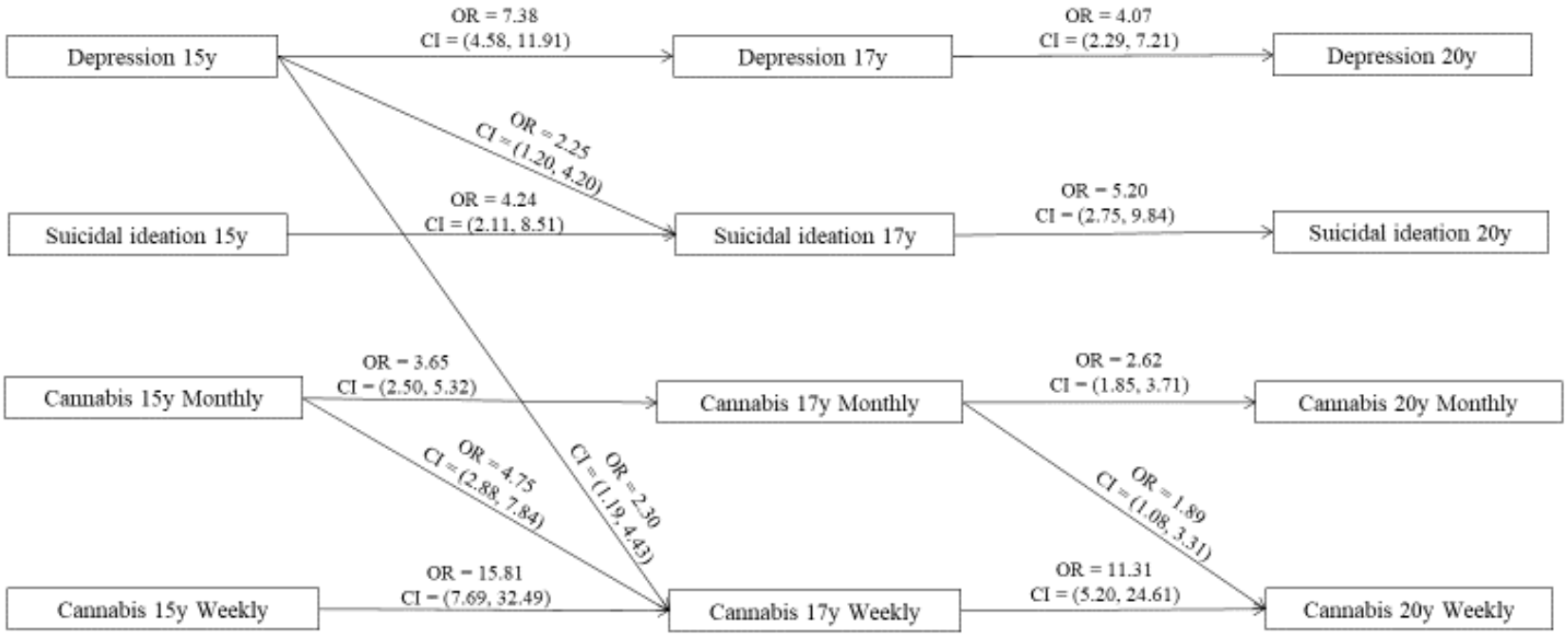

Figure 2. Results for the cross-lag model for cannabis use, depression and suicidal ideation at 15, 17 and 20 years (N=1606); Adjusted for sex and other substance use (alcohol, tobacco and other drugs) at15 and 17 years. Using a continuous measure of depressive symptoms, depressive symptoms were associated with later weekly cannabis use at ages 17 (β=0.208, 95%CI= 0.104-0.312), and 20 (β=0.126, 95%CI=0.030-0.222) years. Note: Only significant paths (p< .05) are presented for clarity. OR and 95% CI= All values are Odds Ratio with 95% confidence intervals; 15y=15 years, 17y=17 years, 20y=20 years. Data were compiled from the final master file of the Québec Longitudinal Study of Child Development (1998-2018) ©Québec Government, Institut de la Statistique du Québec.

Appendix

DEPRESSION SYMPTOMS

Depression subscale from Mental Health and Social Inadaptation Assessment for Adolescents (MIA); 8 items; 15 and 17 years

Nothing was fun for me, I wasn't interested in anything.
I felt sad and unhappy.
I lacked energy or felt tired.
I lost interest in things I usually like.
I felt I couldn't do anything well.
I felt I wasn't as good-looking or as smart as other people.
Doing even little things made me feel really tired.
I had trouble thinking clearly.

Center for Epidemiologic Studies Depression Scale (CES-D); 13 items; 20 years

I did not feel like eating; my appetite was poor.
I felt that I could not shake off the blues even with help from my family or friends.
I had trouble keeping my mind on what I was doing.
I felt depressed.
I felt that everything I did was an effort.
I felt hopeful about the future.
My sleep was restless.
I was happy.
I felt lonely.
I enjoyed life.
I had crying spells.
I felt that people disliked me.
I have felt scared or panicky for no very good reason.

Table S1. Sociodemographic Characteristics of Participants Versus Non-Participants[a]

Characteristics	Participants (*n*=1606)	Nonparticipants (*n*=514)	*p-value*[b]
Child Sex, N(%)			<.001
Male	769(47.9)	203(39.5)	
Socioeconomic status, mean (SD)[c]	0.06(.99)	0.21(.99)	.346
Maternal education, N(%)			
No high school diploma	269(16.8)	116(22.6)	.003
Maternal age at child birth, mean (SD)	29.39(5.15)	28.98(5.44)	.072
Family composition, N(%)			.024
Biological parents	1304(81.2)	402(78.2)	
Single parent	114(7.1)	57(11.1)	
Blended	183(11.4)	52(10.1)	
Maternal depression[d], mean (SD)	0.99(.94)	1.03(1.03)	.296
Child externalizing behaviour[e] (up to age 6), mean (SD)	2.73(1.60)	2.63(1.23)	.149
Child internalizing behaviour[e] (up to age 6), mean (SD)	1.32(.96)	1.11(1.01)	<.001

[a]Variables were measures when the child was 5 months of age, otherwise indicated. Data were compiled from the final master file of the Québec Longitudinal Study of Child Development (1998-2018), ©Québec Government, Québec Statistics Institute.

[b]*p*-values are based on independent t test for continuous variables and chi-square test for categorical variables.

[c]Assessed with an aggregate of 5 items regarding parental educational level, parental occupation, and annual gross income (range, -3 to 3, centered at 0, with higher scores indicating higher socioeconomic status)[1].

[d]Assessed using a short version of the Center for Epidemiological Study Depression Scale [2]. Scores range from 0 to 10, with higher scores indicating higher depressive symptoms.

[e]Assessed using the Children's Social Behaviour Questionnaire (reported by mothers)[3]. Scores range from 0 to 10, with higher scores indicating higher internalizing and externalizing behaviours.

Table S2. Cross-tabulation of cannabis and other substance use at ages 15, 17 and 20 years[a,b]

	Cannabis Use, n(%)											
	15 years				17 years				20 years			
	Non-User	Monthly User	Weekly User	*p*-value[c]	Non-user	Monthly User	Weekly User	*p*-value	Non-User	Monthly User	Weekly User	*p*-value
Alcohol, n(%)												
Non-Users	537(49)	17(7.1%)	2(2.0)	< .001	198(26.9)	7(2.0)	3(1.9)	< .001	121(17.3)	9(2.6)	11(5.7)	< .001
Monthly Users	519(47.4)	195(81.6)	65(64.4)	< .001	466(63.4)	243(68.5)	88(55.0)	< .001	511(73.0)	266(76.2)	121(62.4)	< .001
Weekly Users	40(3.6)	27(11.3)	34(33.7)	< .001	71(9.7)	105(29.6)	69(43.1)	< .001	68(9.7)	74(21.2)	62(32.0)	< .001
Tobacco, n(%)												
Non-Users	1079(98.7)	211(88.7)	52(51.5)	< .001	728(97.5)	320(90.9)	77(48.1)	< .001	631(90.1)	241(69.1)	68(35.1)	< .001
Monthly Users	2(0.2)	9(3.8)	8(7.9)	< .001	3(0.4)	12(3.4)	21(13.1)	< .001	37(5.3)	69(19.8)	49(25.3)	< .001
Weekly Users	12(1.1)	18(7.6)	41(40.6)	< .001	16(2.1)	20(5.7)	62(38.8)	< .001	32(4.6)	39(11.2)	77(39.7)	< .001
Other Drug Use, n(%)												
Yes	7(0.6)	34(14.3)	47(47.0)	< .001	4(0.5)	54(15.5)	82(51.6)	< .001	19(2.7)	69(19.8)	97(50.0)	< .001
No	1090(99.4)	203(85.7)	53(53.0)		745(99.5)	295(84.5)	77(48.4)		683(97.3)	280(80.2)	97(50.0)	

[a]Data were compiled from the final master file of the Québec Longitudinal Study of Child Development (1998-2018) ©Québec Government, Institut de la Statistique du Québec.

[b]Sample size was N = 1606 based on participants included in the longitudinal analyses.

[c] All *p*-values are based on chi-square test for categorical variables.

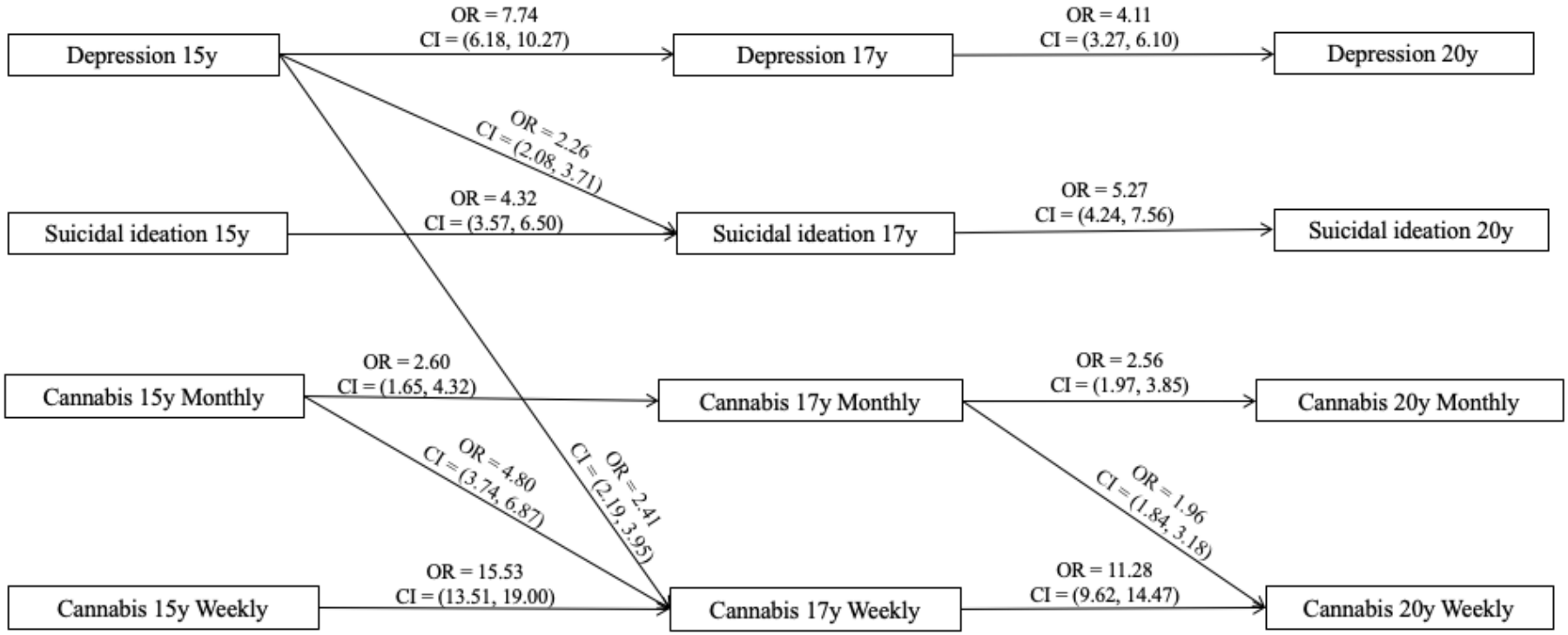

Figure S1. Results for the cross-lag model for cannabis use, depression and suicidal ideation at 15, 17 and 20 years (N=1606); Adjusted for sex, socioeconomic status and other substance use (alcohol, tobacco and other drugs) at 15 and 17 years. Note: Only significant paths ($p < .05$) are presented for clarity. OR and 95% CI= All values are Odds Ratio with 95% confidence intervals; 15y=15 years, 17y=17 years, 20y=20 years. Data were compiled from the final master file of the Québec Longitudinal Study of Child Development (1998-2018) ©Québec Government, Institut de la Statistique du Québec.

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