HOW IS ANXIETY INVOLVED IN THE LINKS BETWEEN CANNABIS VARIABLES AND PSYCHOTIC-LIKE EXPERIENCES IN EMERGING ADULTS? INVESTIGATING TWO POTENTIAL MEDIATION MODELS IN A MULTI-SITE UNIVERSITY SAMPLE

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Dalhousie University is located in Mi'kma'ki, the ancestral and unceded territory of the Mi'kmaq. We are all Treaty people.

DEDICATION

Kaira, this one's for you. Thank you for 6 years of sunsets and a lifetime of love.

I promise I'll see you on the other side.

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ABSTRACT

Many Canadian emerging adult postsecondary students use cannabis, a known risk factor for developing psychotic-like experiences (PLEs). Anxiety has been independently linked to both cannabis use and PLEs and may partially explain the links between cannabis variables and PLEs. Study 1 of this thesis investigated and provided support for anxiety as a mediator of the link between cannabis use frequency and PLEs. Study 2 identified anxiety and cannabis coping-with-anxiety motives as sequential mediators of the link between PLEs and cannabis-related problems. Neither study supported moderation by biological sex, suggesting that anxiety explains the cannabis-to-PLEs trajectory; and anxiety and cannabis coping-with-anxiety motives explain the link between PLEs and cannabis-related problems for Canadian undergraduates regardless of sex. Anxiety and related anxiety-specific coping motives appear to be important targets of preventative and/or therapeutic interventions aimed at reducing emerging adult cannabis users' risks for mental health- and cannabis-related problems, including PLEs.

Keywords: cannabis, anxiety, psychotic-like experiences, cannabis coping-with-anxiety motives, cannabis-related problems, mediation, moderation, conditional process analysis, path analysis, emerging adulthood

LIST OF ABBREVIATIONS AND SYMBOLS USED

α	Cronbach's Alpha
APA	American Psychiatric Association
b	Regression coefficients of path models
BCAMM	Brief Cannabis Motives Measure
BMACQ	Brief Marijuana Consequences Questionnaire
CBT	Cognitive Behavioural Therapy
CI	Confidence Interval
COVID-19	Coronavirus (SARS-CoV-2) disease of 2019
GAD-7	Generalized Anxiety Disorder-7 scale
H1	Hypothesis 1
H2	Hypothesis 2
H3	Hypothesis 3
H4	Hypothesis 4
M	Mean
N	Sample size
OR	Odds ratio
PLEs	Psychotic-like experiences
PLEQ	Psychotic-Like Experiences Questionnaire
RR	Risk ratio
S1-5	Study sites 1-5

SD	Standard deviation
SE	Standard error
US	United States

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CHAPTER 1. GENERAL INTRODUCTION

Emerging adulthood is the label assigned to the developmentally vulnerable life stage situated between the ages of 18 to 25 years (Arnett, 2000). This developmental phase is characterized by five main features: the exploration of one's identity and ideals; the exploration of one's many possibilities; instability; a focus on the self; and feeling in-between the stages of adolescence and 'true' adulthood (Arnett, 2004). Emerging adults are demographically unique from other groups in that they are typically unconstrained by the societal norms that demarcate the period of adolescence (when the majority of adolescents live in a stable home with one or more caregiver(s), attend middle/high school, are unmarried and without children of their own), or the responsibilities and commitments of adulthood (i.e., domains of career, love, family). Emerging adulthood has been proposed as a developmentally distinct life stage created, in part, by large societal shifts that have occurred over the past several decades, including overall later median ages for getting married and starting families, and the ever more common pursuit of higher education (Arnett, 2000).

The pursuit of postsecondary education during this developmental stage is common: Statistics Canada (2022, October) reported that nearly half of all emerging adults in Canada – approximately 46% – attended postsecondary institutions in 2022. Unfortunately, those who attend postsecondary institutions tend to be at high risk for challenges related to both mental health (Canadian Alliance of Student Associations, 2022) and substance use (Health Canada, 2021, May). For example, a survey conducted with 2,000 Canadian postsecondary students in May 2022 found that three quarters of students reported struggling with mental health challenges during the course of their

education (Canadian Alliance of Student Associations, 2022). Additionally, 75% of respondents reported that the pandemic had a further negative impact on their mental health: 74% of students reported that their pre-existing mental health challenges had worsened, and 61% indicated that the pandemic had created new mental health struggles for them (Canadian Alliance of Student Associations, 2022). Furthermore, the most recent Canadian Postsecondary Education Alcohol and Drug Use Survey (2019/2020 academic year, pre-COVID-19-pandemic) reported that 84.3% and 48.4% of postsecondary students used alcohol and cannabis (the most commonly used substances) in the past year respectively (Health Canada, 2021, May). Thus, emerging adulthood is a period of time that is unique to both the development of mental health and substance use issues, including for those in post-secondary education.

Emerging adults who attend college or university are exposed to many new situations, influences, and experiences (Arnett, 2000). This includes transitions into states of increased freedom and independence (Arnett, 2000) as well as increased exposure to substances and potentially increased substance use behavior (Sussman & Arnett, 2014). While alcohol is consistently the most commonly used substance among members of this cohort (Health Canada, 2021, May), cannabis is the second most common. Cannabis use for medical and recreational purposes was legalized in Canada in 2001 and 2018/2019, respectively (Health Canada, 2021). As a result, there is much less research regarding cannabis use among emerging adults compared to alcohol. Therefore, cannabis use is the focus of this thesis.

While emerging adults in the general population increased their past-year cannabis use from 2018 to 2019 (44% versus 51%, respectively; Government of Canada,

2022), so too did emerging adults in pursuit of higher education. The 2019/2020 Canadian Postsecondary Education Alcohol and Drug Use Survey indicated that 25.3% of postsecondary students who used cannabis in the past year reported increased use since legalization (Health Canada, 2021, May). Furthermore, of the 48.4% of post-secondary students who used cannabis in the past year, 32.6% used within the past month, with approximately 9.3% of males and 5.8% of females reporting daily or almost daily cannabis use (i.e., five or more days per week; Health Canada, 2021, May).

Since the onset of the COVID-19 pandemic, rates of cannabis use among Canadian emerging adults have reportedly increased further: 40% of emerging adults reported increases in the quantities of cannabis used, and 38% reported increases in their frequency of cannabis use (Health Canada, 2021). Common reasons reported for increased cannabis use included elevated stress (60%), anxiety (55%), and loneliness (37%; Health Canada, 2021). Additionally, it has been reported that the self-isolation measures imposed during the pandemic resulted in 20% increases in cannabis use in a Canadian sample of emerging adults (Bartel et al., 2020). These high rates of cannabis use are concerning as high frequencies and quantities of cannabis use have been associated with increased risks for various mental health and other cannabis-related problems among emerging adults (Government of Canada, 2018).

Cannabis Use and Psychotic Symptom Development

One such cannabis-related mental health harm is the increased risk for psychotic disorders observed in those who engage in cannabis use. Research shows a complex association between cannabis use and the development of psychosis, defined by the experience of any or all of the following symptoms: abnormal delusions, hallucinations,

disorganized thoughts/speech, disorganized motor behavior, and/or negative symptoms (American Psychiatric Association [APA], 2022). Readers should note that this definition of psychosis is applied throughout the present thesis. In 1987, a seminal research article evaluating the role of cannabis as a causal factor for schizophrenia was published by Andréasson and colleagues; they followed over 45,000 Swedish Army conscripts in a 15-year longitudinal study. They found that those who had ever used cannabis at the time of conscription (majority aged 18-20 years) had a 2.4 times greater risk of developing schizophrenia compared to those who had never used cannabis (Andréasson et al., 1987). Furthermore, their results suggested a dose-dependent association wherein the relative risk for schizophrenia increased as the conscript's frequency of cannabis use increased. Specifically, those with high frequencies of cannabis use (i.e., more than 50 occasions of cannabis use) were at six times greater risk for the development of schizophrenia compared to non-using conscripts (Andréasson et al., 1987). While Andréasson et al. (1987) found a significant dose effect, this seminal study was conducted prior to the wide availability of the more potent THC products available today.

As such, since Andréasson and colleagues' seminal study (1987), other research teams have found additional support for the association between cannabis use and the development of psychosis (Di Forti et al., 2019; Hasan et al., 2020; Robinson et al., 2022; Sideli et al., 2020). For example, Robinson et al. (2022) conducted a systematic review and meta-analysis examining risk thresholds in the link between cannabis use frequency and the development of psychosis. They reported that the risk of psychosis significantly increased for weekly or more frequent cannabis users (weekly use risk ratio; RR = 1.35, 95% confidence interval (CI) = 1.19–1.52; daily use RR = 1.76, 95% CI = 1.47–2.12),

whereas less frequent users did not show an elevated risk for subsequently developing psychosis (yearly cannabis use RR = 1.01, 95% CI = 0.93–1.11; monthly use RR = 1.10, 95% CI = 0.97–1.25; Robinson et al., 2022). Additionally, more frequent cannabis use and use of high-potency THC products have been shown to be related to greater odds of developing a psychotic disorder relative to those who have never used cannabis (Di Forti et al., 2014). For example, the odds of developing psychosis were found to be over three times greater for those who used cannabis daily, which increased to nearly five times the risk when highly potent cannabis products were used (Di Forti et al., 2019). Furthermore, cannabis use has been shown to be associated with earlier onset of psychosis (Large et al., 2011). A recent systematic review of 26 meta-analyses and systematic reviews that evaluated the association between cannabis use and the subsequent risk for psychosis corroborated that the literature largely indicates a) that the most frequent cannabis users are at the greatest risk of psychosis compared to nonusers, b) that cannabis use has a dose-dependent link to the development of psychosis, and c) that those who use cannabis are at risk of earlier psychotic illness onset than non-users (Hasan et al., 2020). Given the high prevalence of cannabis use among emerging adults in Canada and cannabis' associations with the earlier development of psychosis, emerging adults are an important cohort to study, especially seeing as first episodes of psychosis tend to present most commonly during this developmentally vulnerable period (Moe & Breitborde., 2019).

The Psychosis Continuum Hypothesis

The investigation of processes occurring prior to the development of a psychotic disorder may be most beneficial for reducing cannabis-related risk for psychosis among emerging adults. The psychosis continuum hypothesis posits that psychosis occurs on a

spectrum that ranges from potentially transient subclinical symptoms (changes in perception and thought also known as 'psychotic-like experiences', or PLEs) to psychotic disorders such as schizophrenia (van Os et al., 2009). PLEs tend to occur in otherwise healthy members of the general population, are non-persistent, and do not impact upon one's overall functioning (Kelleher & Cannon, 2011; McGrath et al., 2015; van Os et al., 2009). PLEs are therefore considered to be positioned earlier along on the psychosis spectrum, as they do not qualify as symptoms of a primary psychotic disorder (Kelleher & Cannon, 2011; van Os et al., 2009).

Psychotic disorders tend to occur in the general population with a median prevalence of 1-3% (Kelleher & Cannon, 2011; van Os et al., 2009). PLEs, however, are more prevalent: the mean lifetime prevalence of ever having PLEs has been reported to be 5.8% in a sample of over 31,000 adults aged 18 years or older from 18 countries (McGrath et al., 2015). A meta-analysis of 61 epidemiological studies examining psychotic experiences found an even higher prevalence of PLEs at 7.2% (Linscott & van Os, 2013). Furthermore, a more recent systematic review and meta-analysis of the incidence and persistence of psychotic experiences in the general population reported that, among adults aged 18-64 years, two out of every hundred people would go on to develop PLEs in a given year (Staines et al., 2023). While PLEs are considered to fall earlier along the psychosis spectrum than a primary psychotic disorder, their presence may signify risk for impending progression along the psychosis continuum toward disorder (van Os et al., 2009). For example, a 15-year longitudinal study (Poulton et al., 2000) followed a cohort of 761 children from age 11 years until they turned 26 years old and found that those who reported PLEs at baseline were at significantly increased risk of

later developing schizophreniform disorder (odds ratio; OR = 16.4, 95% confidence interval (CI) = 3.9–67.8). Additionally, the aforementioned meta-analysis of 61 epidemiological studies reported that of those who had experienced PLEs, 20% progressed to experience persistent PLEs, while 7.4% went on to develop a psychotic disorder (Linscott & van Os., 2013). Furthermore, the most recent review by Staines et al. (2023) reported that 28.2% of adults reported persistent PLEs. Thus, those with PLEs have been shown to be at risk of developing psychosis, and therefore, it is important to understand the factors and risk pathways that increase the odds of developing PLEs, as well as understanding their adverse consequences among the developmentally vulnerable emerging adult cohort.

Cannabis Use and Anxiety

While it has been suggested that the same risk factors for psychosis exist across the spectrum from PLEs to psychotic disorders (Linscott & van Os, 2013; van Os et al., 2009), including cannabis use (Linscott & van Os., 2013; Ragazzi et al., 2018), the exact nature of the association between cannabis use and PLEs is not yet fully understood. One mechanism that may explain this cannabis-to-PLEs link is the user's experience of anxiety, a variable that has been independently linked to both cannabis use and PLEs.

Anxiety is a common experience among emerging adults, making it an important variable to consider when evaluating the links between cannabis use and PLEs. Prior to the onset of the COVID-19 pandemic, a longitudinal study sought to examine the development of psychopathology through childhood to emerging adulthood, following 1,420 children from ages 9, 11, and 13 to age 26 (Copeland et al., 2014). They observed the largest increases in anxiety disorders during the years of emerging adulthood, with

22.7% of all participants meeting criteria for an anxiety disorder by their early-to-mid-twenties per criteria listed in the fourth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-IV; APA, 1994; Copeland et al., 2014). Another longitudinal cohort study that collected data from first-year undergraduates at a Canadian university before the beginning of the pandemic (Time 1 collected September 2018; Time 2 collected March 2019) found that students' rates of clinically significant anxiety symptoms per the GAD-7 (Spitzer et al., 2006) increased over their first year of study (32.1% at Time 1; 37.0% at Time 2; Adams et al., 2021). According to a national survey on Canadian's mental health before and during the COVID-19 pandemic, anxiety symptoms have tended to increase since the arrival of the pandemic as well. For example, self-reported rates of high-to-extremely-high anxiety were shown to have quadrupled since the onset of the pandemic, going from 5% to 20% (Dozois & Mental Health Research Canada, 2021).

While there exists some mixed evidence in the literature (Gobbi et al., 2019; National Academies of Sciences, Engineering, and Medicine, 2017; Sideli et al., 2020), some studies have found support for an association between cannabis use and the development or worsening of anxiety symptoms in samples of adolescents and emerging adults (Duperrouzel et al., 2018; Hayatbakhsh et al., 2007; Kedzior & Laeber, 2014). For example, when compared to late onset and infrequent users, early onset and frequent cannabis users were reported to have worse anxiety symptoms in both adolescence (Duperrouzel et al., 2018) and in emerging adulthood (Hayatbakhsh et al., 2007). A systematic review examining the associations between cannabis use and subsequent mental health symptoms in emerging adult populations found that frequent cannabis use

(i.e., weekly or more) was associated with twice greater odds of future anxiety (OR = 1.9, 95% CI = 1.1–3.3; Hosseini & Oremus, 2019). Furthermore, cannabis has been reported to have a bi-phasic effect on anxiety wherein low frequency of cannabis use is reported to reduce one's experience of anxiety, whereas anxiety can be amplified at high frequencies of cannabis use (Crippa et al., 2009; Kedzior & Laeber, 2014; Sharpe et al., 2020). Given that cannabis use and anxiety are both prevalent among Canadian emerging adults, understanding their impacts on further mental health challenges (such as PLEs) and overall wellbeing is important.

Links Between Anxiety and Psychotic-Like Experiences

Just as cannabis use has been linked to the development of psychosis, so too has anxiety. McGrath et al. (2016) examined the bidirectionality of temporal associations between common DSM-IV mental disorders (APA, 1994) and PLEs. When controlling for age, gender, country, time-varying education, marital, and employment statuses, McGrath and colleagues (2016) found that anxiety was a significant temporally primary predictor of the subsequent onset of PLEs with a bivariate odds ratio (95% CI) of 2.4 (1.8–3.1). Furthermore, multivariate models with all temporally primary mental disorders entered simultaneously also found a significant odds ratio (95% CI) of 1.7 (1.2–2.3), signifying that anxiety preceded and approximately doubled the risk for developing PLEs in an international sample of over 31,000 adults (McGrath et al., 2016). Even stronger associations were found by Varghese et al. (2011) who reported that emerging adults with anxiety disorders were nearly five times more likely to be in the highest (compared to the lowest) quartile of scores on the Peters Delusion Inventory (PDI; Peters et al., 1999) compared to emerging adults without anxiety disorders. Furthermore, those with anxiety

disorders who reported current anxiety symptoms (i.e., within the past month) were at nearly six times the risk of scoring in the highest versus lowest PDI quartile compared to those with less frequent anxiety (Varghese et al., 2011).

While there is evidence for an anxiety-to-PLEs association, it can also be argued that PLEs are risk factors that increase one's chances of developing a non-psychotic disorder, including anxiety, in the general population (Lindgren et al., 2022). Although characteristically transitory, subclinical hallucinations or delusions may be overwhelming or distressing, leading to heightened anxiety. Indeed, frequent and distressing PLEs have recently been shown to be related to higher levels of psychological burden (defined as emotional and behavioral difficulties, assessed by the Strengths and Difficulties Questionnaire; Goodman, 1997) in a sample of adolescents (Mylona et al., 2022). As noted above, McGrath et al. (2016) evaluated the possible bidirectional associations between PLEs and DSM-IV mental disorders (APA, 1994) using data from an international sample of over 31,000 adults gleaned from the World Health Organizations' World Mental Health survey. When examining temporally primary PLEs and the subsequent onset of generalized anxiety disorder, those with PLEs were found to be at nearly twice the risk for developing anxiety than those without PLEs (OR = 1.9, 95% CI = 1.5–2.4; McGrath et al., 2016). When controlling for comorbid mental disorders, the adjusted odds ratio was still significant (AOR = 1.4, 95% CI = 1.1–1.8; McGrath et al., 2016). Also, in a sample of approximately 900 adolescents, Yamasaki et al. (2018) found that when followed over a year, those with incident cases of PLEs had significantly worse anxiety compared to those without PLEs. Which precedes the other and for whom, however, is still yet to be determined.

Maladaptive Coping and Cannabis-Related Problems

The self-medication hypothesis (Khantzian, 1985, 1997) suggests that people use substances to alleviate negative emotions and cope with their feelings of discomfort. While evidence in the literature is mixed (Gill et al., 2015; Pencer & Addington, 2008), individuals living with the distress and psychological burden of PLEs and/or anxiety may very well be motivated to turn to cannabis use in an effort to cope with their symptoms (Asselin et al., 2022; Mané et al., 2015; Schofield et al., 2006; Wallis et al., 2022). The self-medication hypothesis, therefore, has the potential to explain how those with PLEs (and heightened anxiety as a result of the PLEs) may experience greater cannabis-related problems.

Indeed, some studies have found support for the self-medication hypothesis in those with psychosis. For example, it has been reported that patients experiencing their first episode of psychosis used cannabis significantly more often with the goals of organizing their thoughts and decreasing their hallucinations and suspiciousness than did healthy control cannabis users (Mané et al., 2015). Furthermore, it was found that cannabis was used by those with psychotic disorders to relieve boredom (86%), improve sleep (58%), and decrease anxiety and agitation (49%; Schofield et al., 2006). It has also been reported that adolescents with psychosis tend to self-medicate with cannabis use not for management of the primary symptoms of psychosis, but to manage their experiences of negative affect (e.g., anxiety symptoms; Pencer, 2004).

Some studies have also found support for the self-medication hypothesis in those with anxiety. Individuals with anxiety have been shown to use cannabis in an attempt to alleviate their anxiety symptoms in a sample of Canadian adults (Asselin et al., 2022), a

sample of US emerging adults who frequently use cannabis (defined as three or more times a week; Wallis et al., 2022), and a sample of US college students during the COVID-19 pandemic (Dunaief et al., 2023). Furthermore, in a sample of over 2,500 current heavy (daily or almost daily past-month) cannabis users, those who were clinically anxious used significantly more cannabis compared to heavy cannabis using adults who were not anxious (Van Dam et al., 2012).

Unfortunately, cannabis use that is motivated by the desire to cope with or alleviate negative emotions like anxiety has been shown to be particularly hazardous, as it is related to greater cannabis use frequency (r = 0.35, 95% CI = 0.31–0.39), cannabis use quantity (r = 0.28, 95% CI = 0.08–0.46), and cannabis-related problems (r = 0.43, 95% CI = 0.38–0.48), including cannabis use disorder (r = 0.41, 95% CI = 0.23–0.56; Bresin & Mekawi, 2019). Furthermore, in a sample of current cannabis-using emerging adults, Moitra et al. (2015) reported that using cannabis to cope with negative emotions was associated with nearly twice greater odds of meeting cannabis use disorder criteria listed in the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5; APA, 2013; OR = 1.85, 95% CI = 1.31–2.62, $p < .01$).

Together, evidence exists suggesting that those who experience mental health challenges such as PLEs and anxiety may cope with their symptoms by self-medicating with cannabis. Coping motives for cannabis use are especially problematic, as they have been shown to increase the user's risk for greater cannabis use and cannabis-related problems. Unfortunately, cannabis-related problems are already a common concern among Canadian emerging adults who use cannabis. For example, the 2019-20 Canadian Postsecondary Education, Alcohol, and Drug Use survey reported that among those who

had used cannabis in the past three months, 60.3% experienced at least one of the listed cannabis-related harms (e.g., desire or urge to use; problems in health, social, legal, or financial domains; failed to meet expectations due to use; others expressed concern over use; and/or failed to control use; Health Canada, 2021, May). Furthermore, results from the Alcohol, Smoking and Substance Involvement Screening Test (Humeniuk et al., 2010) administered to current (i.e., past-three-months) emerging adult cannabis users revealed that 66.7% were at moderate-to-high risk of developing cannabis-related problems as a result of their current patterns of substance use; the 6% of past-three-month users who met high-risk criteria were considered likely to be dependent on cannabis (Health Canada, 2021, May). Finally, diagnoses of cannabis use disorder are also most common among the emerging adult cohort compared to all other developmental phases, with a prevalence of 6.9% (ages 18-29 years, APA, 2022).

While coping motives for cannabis use have been shown to increase risk for cannabis-related problems in general, they have been shown to be particularly risky during the COVID-19 pandemic. For example, Vedelago and colleagues (2022) found that, among a sample of Canadian adults, those with increased demand for cannabis (measured using the Marijuana Purchase Task; Aston & Meshesha, 2020, Collins et al., 2014) and those who tended to use cannabis as a means of coping were at increased risk of developing cannabis-related problems during the COVID-19 pandemic (data collected from April 30 until May 4, 2020). Furthermore, among a sample of US emerging adult college students, those who reported increased anxiety symptoms due to COVID-19 also reported greater coping-related motives for cannabis use compared to those whose anxiety symptoms had stayed the same (Dunaief et al., 2023). The link from increased

anxiety symptoms to greater cannabis-related adverse consequences was also shown to be explained by greater endorsement of coping motives for cannabis use in the same sample of US emerging adults (Dunaief et al., 2023). Evidently, coping (self-medication) motivations for cannabis use may be increasing the risk for Canadian emerging adults who experience PLEs and anxiety to develop cannabis-related problems throughout the pandemic. While cannabis-related problems certainly impact the individual user experiencing them, such problems also affect society overall as they utilize resources in the domains of healthcare, legal, and social services (Health Canada, 2021, May). Given both the potential personal and societal costs of increasing numbers of cannabis-related problems, uncovering what to target to mitigate risk for their development is important.

Summary

Emerging adulthood is a developmentally vulnerable period wherein cannabis use and anxiety are common, and when PLEs tend to emerge. Given the high prevalence of cannabis use among emerging adults in Canada, it is important to begin to understand its complex associations to mental health problems. Cannabis has been shown to be a risk factor for psychosis and may be associated with the development or worsening of anxiety. In turn, anxiety has been shown to be a risk factor for the later development of PLEs. However, a bidirectional association appears to exist between anxiety and PLEs where temporally primary PLEs have also been shown to predict later development of anxiety. This makes intuitive sense, as PLEs may be distressing experiences that give rise to greater symptoms of anxiety. Considering the evidence in support of the self-medication hypothesis, emerging adults with PLEs and resulting anxiety may, in turn, be motivated to attempt to cope with their psychological distress by increasing their

cannabis use. This possibility is especially problematic as coping motives for cannabis use have been shown to be associated with greater odds of experiencing cannabis-related harms, an already prevalent concern among the emerging adult population in Canada. Given the high prevalence of cannabis use among Canadian emerging adults and the potential seriousness of cannabis-related problems for both cannabis users and society overall, it is important to explore the potential impacts of common mental health challenges (e.g., anxiety) and using cannabis as a coping mechanism to manage unwanted symptoms (i.e., coping-with-anxiety motives for cannabis use) on the associations observed between cannabis variables and psychotic-like experiences, especially throughout the COVID-19 pandemic. Better understandings of these complex associations may help to identify the processes/mechanisms driving them, which, in turn, may inform potentially more effective targeted early intervention and prevention measures to mitigate risks for poor outcomes in Canadian emerging adults.

The Present Thesis

While some past research has examined the individual links described herein, the possible roles of anxiety and coping-with-anxiety motives for cannabis use as mediators of the links between cannabis use variables and PLEs have largely been overlooked. This thesis sought to address these gaps in the literature by examining two possible anxiety-mediation models to begin to understand anxiety's impact(s) on the complex associations that have been observed between cannabis variables and PLEs in Canadian emerging adult undergraduates.

Study 1

In the first study of my thesis, I sought to evaluate anxiety symptoms as a mediating variable explaining the link between cannabis use frequency and PLEs in a sample of Canadian emerging adults. Previous work has established that links exist between cannabis use and the development of psychosis; however, little work has examined the potential role of anxiety in explaining this trajectory. Reeves and colleagues (2014) were the first (and only) group to show that trait anxiety mediated the link between cannabis use and attenuated positive psychotic symptoms (APPS) in a US sample aged 17-35 years. Several opportunities for replication and extension of Reeves et al.'s (2014) study inspired the first study of my thesis.

Firstly, an important feature that applies to both of my thesis studies is the extension to/inclusion of the Canadian context. As previously mentioned, cannabis for both medicinal and recreational purposes is legal in Canada nationwide. This is a context which differs greatly from that in which Reeves et al. (2014) conducted their study: their sample was drawn nearly ten years ago from students at Temple University in Pennsylvania in the US, where the use of medicinal cannabis was only legalized post-publication in 2016, and where recreational cannabis use remains illegal to this day (Commonwealth of Pennsylvania, 2023). Although Reeves et al. (2014) gave their participants certificates of confidentiality in an effort to assure respondents that their identifiable information was being protected as confidential, students surveyed may still have been hesitant to respond truthfully about whether they were using cannabis (or their actual severity/frequency of use) due to its illegality and/or the variable influence of stigma and social desirability bias (Johnson, 2014; Johnson & Fendrich, 2005). This

difference in legal status also suggests likely differences in accessibility: access to cannabis in an earlier-tested Pennsylvanian sample is likely not comparable to that of a current Canadian one, which may have implications for results. For example, the presumed differential base rates of reported cannabis use may affect the nature of the links between the model's predictor (cannabis use frequency) and mediator (anxiety symptoms) and/or between the predictor and outcome (PLEs).

Secondly, while Reeves et al. (2014) specified trait anxiety as the mediating variable in their model, I opted to specify state anxiety symptoms as the mediator in my model. Trait anxiety refers to ones' overall tendency to be an anxious individual (a relatively stable personality trait; Endler & Kocovski, 2001), and although related, it can be argued that, conceptually, it is state anxiety, or rather, the *experience of symptoms of anxiety*, that is the relevant mediator of such models (Endler & Kocovski, 2001). For example, greater frequency of cannabis use is a risk factor for increasing the frequency of experiencing symptoms of anxiety (Duperrouzel et al., 2018; Hayatbakhsh et al., 2007; Hosseini & Oremus, 2019; Kedzior & Laeber, 2014), which, in turn, is a risk factor for psychotic symptoms (McGrath et al., 2016; Varghese et al., 2011). While being an inherently anxious individual may indeed impact upon the cannabis use-to-PLEs trajectory under study, the examination of state anxiety offers more potential avenues for intervention given that states of anxiety are relatively transient and may be managed in treatment, whereas trait anxiety is a relatively stable component of one's personality (theoretically harder to shift; Endler & Kocovski, 2001). Furthermore, Reeves and colleagues had some methodological limitations with their measurement of trait anxiety. Specifically, Reeves et al. (2014) made use of the seven-item Trait subscale of the State-

Trait Anxiety Inventory (STAI-T; Spielberger at al., 1983), which, when compared to other validated measures of anxiety, has been found to measure negative affect more broadly (Bados et al., 2010). In fact, it has been reported that the Trait subscale of the STAI-T actually correlates more strongly with measures of depression, as opposed to anxiety, as intended (Bados et al., 2010). Therefore, to increase the likelihood of capturing my participants' recent frequency of experiences of anxiety symptoms, I utilized the Generalized Anxiety Disorder-7 scale (Spitzer et al., 2007), as detailed in Chapter 2.

Thirdly, I extended Reeves et al.'s (2014) model by specifying PLEs as the outcome variable in lieu of their attenuated positive psychotic symptoms (APPS) variable. To capture their participant's experiences of APPS, Reeves et al. (2014) administered the 45-item positive symptoms subscale of the Prodromal Questionnaire (Loewy et al., 2005). The psychosis continuum hypothesis suggests that APPS and other prodromal symptoms are theoretically further along on the psychosis spectrum (closer toward psychotic disorder) than PLEs (Kelleher & Cannon, 2011; van Os et al., 2009). However, given that the same risk factors are expected to underlie the entire continuum (Linscott & van Os, 2013; van Os et al., 2009), similar anxiety-mediated results could be expected when examining processes earlier along on the spectrum (in this case, PLEs). This modification of specifying PLEs as the outcome variable is an advancement in Study 1 vs. the Reeves et al. (2014) study as PLEs are relevant for the possible earlier identification of those who may be at risk for the development of psychotic disorders and may potentially signal to those who may best benefit from early interventions to reduce their cannabis use and other prevalent risk factors such as anxiety.

Lastly, Reeves et al. (2014) did not evaluate the potential moderating impact of biological sex assigned at birth (male, female) on the proposed anxiety-mediated model. This was an important limitation to address in Study 1, as there appear to be differences across the sexes in the variables under study. For one, males and females are reported to use cannabis differently. Specifically, males have been reported to use cannabis more frequently and in higher quantities compared to females (Cuttler et al., 2016). Secondly, males and females also tend to differ in their experiences of mental health problems. For example, females are generally more anxious overall and carry at least twice greater odds for developing anxiety disorders compared to males (APA, 2022; LeBlanc et al., 2020). Furthermore, females who use cannabis frequently are more likely to have increased anxiety: daily female cannabis users were reported to have over five times the risk of developing anxiety compared to male cannabis users (Hosseini & Oremus, 2019). In contrast, males have been reported to experience earlier onset of psychosis symptoms than females (Li et al., 2016; Solmi et al., 2022) and have a harder time recovering from psychosis than females (Ayesa-Arriola et al., 2020); however, the evidence is mixed regarding sex differences in the prevalence of diagnoses of primary psychotic disorders (Ayesa-Arriola et al., 2020; Barajas et al.., 2015; Ochoa et al., 2012). This is due, in part, to the inconsistencies observed in research on sex/gender in psychosis, inconsistencies which are subsequently expressed in the literature. For example. while some research teams specify sex or gender and consistently use the appropriate definitions, others tend to combine the two terms into one seemingly interchangeable or equivalent concept. For instance, while Ayesa-Arriola et al. (2020) specified sex and reported in their longitudinal study that significantly more males than females in their first episodes of psychosis met

criteria for a schizophrenia diagnosis both at baseline (69% vs. 51%, $p = 0.009$) and ten-year follow-up (84% vs. 63%, $p = 0.002$), comprehensive literature reviews on 'gender differences' in individuals at high-risk of psychosis, first-episode psychosis, and schizophrenia used varying terminology and found evidence both in support of and refuting sex/gender differences in the prevalence of psychosis (Barajas et al., 2015; Ochoa et al., 2012). However, based on the body of evidence we have to date on gender/sex differences in this area, it stands to reason that the possible mediating role of anxiety symptoms in the link between cannabis use frequency and PLEs may also differ across sex.

Considering the limitations of the Reeves et al. (2014) study listed above, in the first study of my thesis, I aimed to replicate and extend their work using a larger sample of Canadian emerging adult undergraduates. In terms of replication, anxiety was expected to mediate the link between cannabis use frequency and psychosis symptoms. My first study also sought to extend Reeves et al.'s (2014) model in three ways: 1) by specifying state-like anxiety symptoms as the mediator, which may have important implications for interventions; 2) by specifying PLEs as the outcome variable (important for earlier risk mitigation as PLEs are earlier along the psychosis spectrum than APPS); and 3) by assessing the model for a possible moderating impact of biological sex (potential for nuanced differentiation between sexes).

Study 2

The second study of my thesis was more exploratory in nature. Study 2 sought to investigate the possibility that Canadian emerging adult undergraduates who have PLEs may find them anxiety-inducing, producing symptoms of anxiety with which they attempt

to cope by self-medicating with cannabis in an effort to reduce their emotional distress, but which ultimately increases their cannabis-related problems. While there exists evidence for each link of the present proposed model, extant literature has only evaluated coping motives broadly. While coping-with-anxiety and coping-with-depression motives have been identified as separate, unique motivations for alcohol use (Grant et al., 2007), this distinction has only recently been parsed out in cannabis use research (Bartel et al., 2023). As this study's first mediator was anxiety symptoms, coping-with-anxiety motives for cannabis use were specified as the second mediating variable over more general coping motives for cannabis use. This study was, therefore, the first to combine all previously described components into a single mediational model and testing for the chained-mediation effect that would be expected based on the self-medication hypothesis.

Consistent with Study 1, the second study of this thesis also sought to evaluate the chained anxiety-coping mediation model for the possible moderating impact of biological sex. As noted above, there are established sex differences between biological males and females regarding cannabis use, anxiety, and PLEs. The same can also be said for how males and females manage their anxiety symptoms. For example, females use cannabis significantly more often to treat symptoms of anxiety than males (66.6% versus 50.6%, respectively; Cuttler et al., 2016). Indeed, it has recently been reported that, compared to males, females are 3.3 times more likely to use cannabis to self-medicate their symptoms of anxiety (Wallis et al., 2022). Furthermore, males and females may experience cannabis-related problems differently: for example, according to the text revision of the fifth edition of the *Diagnostic and Statistical Manual of Mental Disorders* (DSM-5-TR; APA, 2022), males experience cannabis use disorder at twice the rate of females (3.5%

versus 1.7%, respectively), while females have been shown to be more likely to report symptoms of cannabis withdrawal and/or dependence, such as being less active, experiencing emotional problems, and using more cannabis than intended (National Academies of Sciences, Engineering, and Medicine, 2017).

It is for these reasons that I sought to explore the possibility of a more complex chained anxiety-coping mediation model for the first time in Study 2. Specifically, I attempted to evaluate the possible impact of PLEs on cannabis-related problems through a chained indirect association through anxiety symptoms and, in turn, coping-with-anxiety motives for cannabis use in a sample of Canadian emerging adult cannabis users. In keeping with Study 1, I also aimed to evaluate the model for variation across biological sex to determine if the proposed risk pathway was equally as relevant for both male and female emerging adult cannabis users.

Outline

Study 1 is presented in Chapter 2. Chapter 3 provides a transition between studies which discusses the potential bidirectionality of the links between anxiety and PLEs and the impact that PLEs have on the subsequent experience of cannabis-related problems. Study 2 is then presented in Chapter 4, followed by an integrative discussion of the two manuscripts, including theoretical and clinical implications emergent from this thesis in Chapter 5.

CHAPTER 2. STUDY 1: DO ANXIETY SYMPTOMS MEDIATE THE ASSOCIATION BETWEEN CANNABIS USE FREQUENCY AND PSYCHOTIC-LIKE EXPERIENCES IN EMERGING ADULT UNDERGRADUATES?

The first of two manuscripts on which this thesis is based appears in this chapter. Readers are advised that Haley Bernusky, under the co-supervision of Dr. Sherry Stewart and Dr. Phil Tibbo, was responsible for preparing the initial draft of the manuscript, incorporating feedback from her co-authors, and preparing the manuscript for submission. The manuscript underwent peer review at the *Canadian Journal of Psychiatry*. Haley incorporated suggested revisions from the reviewers with guidance from Dr. Sherry Stewart, Dr. Phil Tibbo, and her coauthors. The manuscript was accepted for publication on April 26th, 2023, and published on May 17th, 2023. Copyright permissions from the publisher to include this paper in this thesis are included in Appendix A. The full reference is as follows: Bernusky, H. C. R., Tibbo, P. G., Conrod, P. J., Yunus, F. M., Keough, M. T., Thompson, K. D., Krank, M. D., Hadwin, A. F., & Stewart, S. H. (2023). Do anxiety symptoms mediate the association between cannabis use frequency and psychotic-like experiences in emerging adult undergraduates? *Canadian Journal of Psychiatry.* doi:10.1177/07067437231176900

Abstract

Objective: Cannabis is commonly used by Canadian emerging adults (ages 18–25 years), many of whom attend post-secondary institutions. Frequent cannabis use is linked with psychotic-like experiences (PLEs); however, the exact nature of this association remains unclear. Anxiety symptoms may mediate this association, as they are prevalent in emerging adults and have been independently linked with both cannabis use and PLEs. Past work found that anxiety mediated the association between cannabis use frequency and attenuated positive psychotic symptoms (further along the psychosis continuum than PLEs), however this research had yet to be validated in the Canadian population, and trait rather than state anxiety (frequency of anxiety symptoms) was studied. Thus, our primary objective was to examine if anxiety symptoms mediated the association between cannabis use frequency and PLEs in Canadian emerging adult undergraduates. Despite known sex differences in cannabis use, expression of anxiety, and PLEs, past work did not evaluate the potential impact of biological sex on the anxiety-mediated model, and thus is the secondary objective of the present study. **Methods:** 1,266 first-/second-year emerging adult undergraduates from five Canadian universities provided cross-sectional, self-report survey data in fall 2021 semester. Validated measures of cannabis use frequency, anxiety, and PLEs were administered. **Results:** Path analyses supported mediation from cannabis use to PLEs through anxiety ($b = 0.07$, $P < 0.001$, 95% bootstrap CI [0.03, 0.10]). No direct effect was found ($P = 0.457$), suggesting that the cannabis-to-PLEs association was mediated by anxiety. Mediation did not depend on biological sex (i.e., bootstrapped 95% CIs crossed zero). **Conclusions:** Anxiety symptoms mediated the association between cannabis use and PLEs in emerging adults regardless of their biological sex. Assuming

replication in prospective research, results highlight anxiety as an important intervention target in frequent cannabis-using emerging adults, to potentially prevent development/worsening of PLEs, and in turn psychotic illness.

Keywords: Anxiety, Cannabis, Psychotic-Like Experiences, Mediation, Biological Sex, Moderation, Conditional Process Model, Path Analysis, Emerging Adults

Introduction

Many Canadian emerging adults (aged 18–25) use cannabis. In 2021, ~49% of those aged 20–24 years reported cannabis use (Health Canada, 2021); 26% of male and 24% of female emerging adult cannabis users reported daily/almost daily use (Health Canada, 2021). Of Canadian emerging adults attending post-secondary institutions pre-COVID-19 pandemic, 48% reported past-year cannabis use; 9% of all male and 6% of all female students reported past month daily/almost daily use (Health Canada, 2021, May).

Research shows an association between cannabis use and psychosis, with higher rates of use observed in patients with, versus without, psychosis (Kiburi et al., 2021). This association is dose-dependent, with higher frequency and THC potency of cannabis use significantly increasing the risk for psychosis (Di Forti et al., 2019; Kiburi et al., 2021; Sideli et al., 2020). Daily cannabis users are > three times more likely to develop a primary psychotic disorder compared to never users, increasing to nearly five-times the risk with higher potency cannabis (Di Forti et al., 2019). Cannabis risk mitigation strategies may benefit from examining processes earlier in psychotic illness development, specifically psychotic-like experiences (PLEs).

PLEs are defined as non-persistent changes in thoughts, perceptions, and behaviors that do not impede overall functioning (e.g., perceptual abnormalities, magical thinking), thus not qualifying as primary psychotic disorder symptoms (Kelleher & Cannon, 2011; van Os et al., 2009). According to the psychosis continuum hypothesis (van Os et al., 2009), the same factors that increase risk for psychotic disorders (e.g., frequent cannabis use) underlie the entire spectrum, thus also contributing to the prevalence of PLEs in the general population (Kelleher & Cannon, 2011; McGrath et al.,

2015; Ragazzi et al., 2018). Individuals with PLEs are at risk of developing psychotic disorders (McGrath et al., 2016; Poulton et al., 2000). As first episodes of psychosis tend to present in emerging adulthood (Moe & Breitborde, 2019), examining links between cannabis use and symptoms earlier along the psychosis continuum is important given the high prevalence of cannabis use in this cohort. Thus, it is important to expand our limited understanding of the link between cannabis use and the development of PLEs, including underlying mechanisms.

Anxiety is common in Canadian emerging adults: approximately 23% of those aged 18–24 reported moderate-to-severe anxiety (Statistics Canada, 2021), which typically increases in the first year of post-secondary education (LeBlanc et al., 2020). Frequent cannabis use is a risk factor for maintaining/worsening anxiety symptoms in adolescents and emerging adults. Early onset users, those using weekly or more, and those with greater lifetime cannabis exposure were all more likely to report elevated anxiety symptoms at later assessments compared to less frequent users (Crippa et al., 2009; Duperrouzel et al., 2018; Hosseini & Oremus, 2019; LeBlanc et al., 2020). Anxiety is also a risk factor for PLEs: emerging adults with anxiety disorders are approximately five times more likely to score in the highest (versus lowest) quartile of PLE scores compared to non-anxious peers (McGrath et al., 2016; Varghese et al., 2011). Given these established links, anxiety appears an important potential mediating variable in clarifying the cannabis use-to-PLEs association in emerging adults.

Reeves and colleagues demonstrated that the link between cannabis use frequency and attenuated positive psychotic symptoms (APPS) was mediated by trait anxiety in an American sample aged 17–35 years (Reeves et al., 2014). Their results require replication

and extension for four reasons. First, their data were collected in 2013 from a US sample in a state where recreational cannabis use remains illegal (Commonwealth of Pennsylvania, 2023), potentially limiting generalizability to the current Canadian undergraduate context. In Canada, recreational cannabis use was legalized in 2018 (Health Canada, 2021), increasing accessibility/normalization of cannabis, and potentially increasing participants' willingness to report actual cannabis use levels (Johnson, 2014; Johnson & Fendrich, 2005). Second, Reeves et al. (2014) measured trait anxiety (a stable personality trait; Endler & Kocovski, 2001) which is less conceptually relevant as a mediator of the cannabis use-to-PLEs association than anxiety symptom frequency. Their results warrant replication using a validated measure of anxiety symptoms, which would more accurately assess if higher frequency cannabis use is a risk factor for increased frequency of anxiety symptoms (Crippa et al., 2009; Duperrouzel et al., 2018; Hosseini & Oremus, 2019; LeBlanc et al., 2020), which, in turn, increases the risk for PLEs (McGrath et al., 2016; Varghese et al., 2011). Third, Reeves et al. (2014) specified their outcome as APPS (Loewy et al., 2005) which are further along on the psychosis continuum (i.e., closer to psychotic disorder) than PLEs (van Os et al., 2009). Keeping earlier risk mitigation for psychotic disorders in mind, it is important to examine if anxiety-mediation can be demonstrated earlier along the psychosis spectrum (Kelleher & Cannon, 2011; McGrath et al, 2015; Ragazzi et al., 2018; van Os et al., 2009).

Lastly, Reeves et al. (2014) did not evaluate the potential moderating impact of sex on the anxiety mediation model. Males use cannabis more frequently and in higher quantities, are more likely to have a cannabis use disorder, and are at higher risk for primary psychotic disorders than females (Cooper & Craft, 2018; Crocker & Tibbo,

2018; Hosseini & Oremus, 2019). Comparatively, females are at greater risk for developing anxiety disorders than males (APA, 2022; LeBlanc et al., 2020). Moreover, female versus male daily cannabis users have greater than five times the risk of developing anxiety (APA, 2022; Hosseini & Oremus, 2019). Anxiety mediation of the cannabis use-PLEs link suggested by Reeves et al. (2014) may also differ by sex.

Considering these gaps, we aimed to replicate previous mediational findings (Reeves et al., 2014) in a sample of Canadian emerging adult undergraduates. We also attempted to extend Reeves et al.'s (2014) model by specifying anxiety symptoms as the mediator and PLEs as the outcome, and by testing potential sex moderation. We hypothesized that (H1) more frequent cannabis use would be indirectly associated with greater PLEs through greater anxiety symptoms (Figure 1a). We hypothesized that sex would moderate this mediational model, with (H2) the cannabis-to-anxiety symptoms path (i.e., the *a*-path in the indirect effect) proving statistically stronger for females and (H3) the direct path from cannabis use frequency to PLEs proving stronger for males (Figure 2a).

Materials & Methods

Participants and Procedures

Hypotheses were tested using cross-sectional, self-report survey data collected in fall 2021 from first-/second-year emerging adult undergraduates aged 18–25 years. Students were recruited from five Canadian universities to participate in the UniVenture substance misuse prevention project[1]. All sites received research ethics board approval to

[1] UniVenture study sites are located across Canada in various rural, small, and large urban centres, labelled Sites 1-5 to preserve their privacy per an agreement between sites participating in the UniVenture Partnership (Thibault et al., 2023). Baseline UniVenture survey data analyzed in this study were collected

conduct the survey. Recruitment occurred via online undergraduate research participation pools, campus-/faculty-wide electronic communications, social media/website advertisements (e.g., Facebook, Instagram), and/or on-campus posters/information booths. Participants gave written, electronic informed consent before completing online surveys. Participants received partial credit for an eligible psychology course or a gift card as compensation for their participation.

Measures

Demographics

An author-compiled demographic measure identified emerging adult students (between 18 and 25 years; Arnett, 2000) and provided data on biological sex assigned at birth (male/female)[2] for the conditional process analysis. Site information was obtained to control for site effects.

Cannabis Use Frequency

The 20-item Co-Venture Drug Use Battery (O'Leary-Barrett; 2017), a shortened version of the psychometrically-sound Detection of Alcohol and Drug Problems in Adolescents (DEP-ADO) questionnaire (Germain et al., 2003; Landry et al., 2005), measured participants' frequency of use of several substances including cannabis (the

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during the COVID-19 pandemic (i.e., between September and November 2021). Infection rates during this time were highest in the community surrounding Site 5 (Quebec; 4,715.53 cases per 100,000 people), then Site 3 (Ontario; 3,942.67), Site 4 (British Columbia; 3,594.60), and lowest surrounding Sites 1 and 2 (Nova Scotia; 674.49) (Public Health Agency of Canada, 2022; Statistics Canada, 2022, September). Site differences in the number of cases and associated differences in public health restrictions may have differentially impacted the data collected, prompting sensitivity analyses controlling for site as described in the main body of the paper (site-specific data not shown).

[2] Biological sex and gender identity were largely congruent in the present sample (97.4%), thus precluding reliable analysis of subsamples beyond the gender binary (men, women). Our analyses focused on moderation by biological sex, promoting inclusivity by being able to retain data from those who identify differently.

predictor). The cannabis use item included other common terms such as “marijuana”, “hashish”, and “weed”, and included the use of vaped THC products). Alcohol and tobacco use (including cigarettes, e-cigarettes, vapes, chewing tobacco, etc.) was obtained to control for co-morbid substance use (common in cannabis users (Health Canada, 2021; 2021, May), posing additional risk for PLEs (Kiburi et al., 2021; Sideli et al., 2020)[3]. Participants responded using a 10-point frequency scale; the option *I prefer not to say* was treated as missing. For scoring, response options were recoded to match those of the first item of the AUDIT-C (Bush et al., 1998): 0 = *Never*, 1 = *Monthly or less*, 2 = *2–4 times a month*, 3 = *2–3 times a week*, 4 = *4 + times a week*. Those indicating daily/almost daily cannabis use were considered at highest risk for problematic cannabis use, including cannabis use disorder (APA, 2022).

Anxiety

The seven-item Generalized Anxiety Disorder scale (GAD-7; Spitzer et al., 2006) measured participants’ past-three-month frequency of anxiety symptoms, where higher scores reflected more frequent anxiety symptoms. Response options included: 0 = *Not at all*, 1 = *Several days*, 2 = *More than half the days*, 3 = *Nearly every day*, or *I prefer not to say* (treated as missing). Scores of 10 and 15 (out of a possible 21) are cut-offs signaling potentially clinically significant moderate and severe levels of anxiety, respectively (Spitzer et al., 2006). This study yielded Cronbach's $\alpha = 0.92$ for the GAD-7, consistent

[3] Emerging adults often consume cannabis and alcohol simultaneously (Health Canada, 2021, May). If participants indicated cannabis use within the past three months, they were prompted to respond to a single item which measured their frequency of cannabis and alcohol co-use (e.g., “During the past three months, when you used cannabis, how often did you combine it with alcohol?”). Response options were recoded to reflect endorsement of co-use, where 0 = *Never co-used*, 1 = *Co-used in the past three months*. *I don’t know* and *I prefer not to say* were treated as missing. Approximately 26.5% of the total sample reported that they had combined their cannabis use with alcohol at least once in the past three months.

with previous work (Spitzer et al., 2006). Total GAD-7 scores served as the mediator in our models.

Psychotic-Like Experiences

The Psychotic-Like Experiences Questionnaire (PLEQ; Laurens et al., 2007, 2012) is a validated measure of PLEs over the past three months in youth; higher scores reflect more severe symptoms. Five items predictive of schizophreniform disorder (Poulton et al., 2000) were adapted from the Diagnostic Interview Schedule for Children (Costello et al., 1982) (e.g., "Have you ever heard voices that other people could not hear?"). Four additional items assessed a broader range of PLEs (e.g., "Do you have any special powers that other people don't have?"; Laurens et al., 2007, 2012). Options included: 0 = *Not true*, 1 = *Somewhat true*, 2 = *Certainly true*, or *I prefer not to say* (treated as missing) for total scores from 0 to 18 (Laurens et al., 2007, 2012). Total scores of four or more indicate the presence of PLEs (Isaksson et al., 2022). This study yielded Cronbach's $\alpha = 0.78$ for the PLEQ, consistent with previous work (Laurens et al., 2012, 2017). Total PLEQ scores served as the outcome in our models.

Statistical Analysis

R version 4.2 (R Core Team, 2022) and SPSS Statistics version 28 (IBM Corp., 2021) were used to clean the data/obtain descriptive statistics. Two path models tested our hypotheses: in the simple mediation model, cannabis use frequency was specified as a predictor of PLEs (outcome) through anxiety (mediator); in the conditional process model, sex was examined as a moderator of the indirect (through anxiety) and direct pathways from cannabis use to PLEs. Here, cannabis use, sex, and the cannabis use by sex interaction term were specified as predictors of anxiety and of PLEs. Bias-corrected

bootstrapped 95% confidence intervals (CI) were used to determine the presence and magnitude of indirect effects. Mplus version 8.7 (Muthén & Muthén, 2017) was used to conduct the path analyses with FIML for missing data, and a maximum likelihood estimator robust to non-normal distributions (MLR), accounting for skewness. We considered both models supported if the relevant 95% CIs did not include zero (Hayes, 2022).

Sensitivity Analyses

Three additional models determined if any predicted effects supported in the main analyses remained significant after controlling for plausible confounds (i.e., study site, alcohol/tobacco use frequency).

Power and Sample Size

The 20-case-per-parameter rule of thumb (Kline, 2016) suggests that $N = 180$ participants would be needed to achieve 80% power. Thus, our much larger sample ($N = 1,266$) was sufficiently powered to detect sex moderation of the direct/indirect effects.

Results

Demographic Variables

Cross-site data were merged, scored, and cleaned: 1,875 participants were excluded, having withdrawn from participation ($n = 1,218$, i.e., closed browser prior to completion), ineligibility ($n = 504$, e.g., not 18–25 years), and unreliable responding ($n = 153$, e.g., inconsistent responses to similar items), resulting in a final sample of 1,266 participants (see Table 1 for demographics).

Clinical Variables

Table 2 provides the means and bivariate correlations of the clinically relevant variables under study and possible confounding variables. We found statistically significant positive correlations between cannabis use frequency and anxiety, and between anxiety and PLEs, the two paths constituting the hypothesized indirect effect.

Cannabis Use Frequency

Half (50.6%) of the sample reported lifetime cannabis use (48.6% never use, 0.8% missing). Of the total sample, 33.2% reported past-three-month use, and 6.5% daily/almost daily use. On average, participants used cannabis just less than once per month (Table 2). Approximately 43.5% of females and 47.0% of males reported having used cannabis in the past year. On average, females (M = 0.92 times per month, SD = 1.19) used cannabis significantly more frequently than males (M = 0.77 times per month, SD = 1.04), $t(914.56) = 2.29$, $P = 0.022$. Furthermore, cannabis use frequency differed significantly by site (S2 > all others, $P < 0.001$).

Anxiety

Of the total sample, 49.6% reported moderate, and 27.9% reported severe, anxiety over the past three months (Spitzer et al., 2006; Table 2). Females (M = 11.14, SD = 6.04) were significantly more anxious than males (M = 8.41, SD = 5.69), $t(844.10) = 7.77$, $P < 0.001$. Furthermore, anxiety levels differed significantly by site (S2 > S4, S5; S1 > S4, $P < 0.05$).

Psychotic-Like Experiences

Three-quarters (78.6%) of our sample reported any endorsement of PLEs in the past three months; 37.0% scored four or more, indicating the presence of PLEs (Isaksson

et al., 2022). On average, participants reported total PLEQ scores of 3.54/18 (Laurens et al., 2007, 2012) (Table 2), doubling the average total PLEQ score reported by emerging adults in a recent (pre-pandemic) cohort study (1.64/18 in the past year; Isaksson et al., 2022). Males (M = 3.29, SD = 3.28) and females (M = 3.65, SD = 3.26) did not differ significantly in PLEs (P = 0.073), but there was significant variation by site (S3 > all others, $P < 0.01$).

Simple Mediation Model

This model tested H1 that more frequent cannabis use would be associated with greater PLEs through greater anxiety symptoms. Both *a*- and *b*-paths constituting the indirect (mediated) effect were statistically significant at $P < 0.001$, as was the associated indirect effect (b = 0.07, $P < 0.001$, 95% CI [0.03, 0.10]); thus, we found support for H1. After accounting for the indirect effect, there was no evidence of a remaining direct effect of cannabis use frequency on PLEs (c' = −0.06, P = 0.457), suggesting anxiety symptoms fully mediate the cannabis-to-PLEs association in emerging adult undergraduates (see Figure 1b for full path diagram). The direction, magnitude, and significance of effects remained when controlling for study site and co-morbid alcohol and tobacco use.

Conditional Process Model

This model examined sex moderation of the simple mediation model (H2 and H3). The cannabis use frequency by sex interaction term did not predict anxiety symptoms or PLEs; thus, the anxiety mediation model did not depend on sex. Consistent with this lack of sex moderation effects, the 95% CIs crossed zero for both the indirect effect from the interaction term to PLEs through anxiety symptoms (95% CI = −0.093, 0.018], and the direct effect of the interaction term to PLEs [95% CI = −0.493, 0.303].

Inconsistent with H2 and H3, sex did not moderate the direct or indirect effects of cannabis use on PLEs (Figure 2b).[4,5]

Discussion

Our primary objective was to examine whether anxiety symptoms mediated the association between cannabis use frequency and PLEs. Results supported anxiety mediation of the link between cannabis use frequency and PLEs, consistent with H1. Our secondary objective was to examine the potential moderating effect of sex on the hypothesized anxiety-mediated model. Contrary to our hypotheses, there was no evidence of sex moderation.

Reeves et al. (2014) reported that the cannabis use-APPS association was mediated by trait anxiety in a US sample aged 17–35 years. We successfully replicated this anxiety-mediated model in the Canadian context (where cannabis is currently legal/widely available), and in a sample focused specifically on the developmentally vulnerable period of emerging adulthood (ages 18–25; Arnett, 2000) when cannabis use is common (Health Canada, 2021) and psychosis is most likely to onset (Moe &

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[4] Although not originally hypothesized, an anonymous reviewer asked us to examine the possibility of sex moderation on all paths in the model, specifically including the b-path from anxiety to PLEs. When we tested the fully moderated model, we found the same pattern of results: biological sex did not moderate any of the paths in the conditional process model, suggesting that anxiety is a relevant mediator of the link between cannabis use frequency and PLEs in Canadian emerging adult undergraduates regardless of their biological sex assigned at birth. We opted to retain the original, more parsimonious model described in the main text.

[5] Although not originally hypothesized, an anonymous reviewer asked us to investigate the possibility of gender as a moderator of the simple anxiety-mediated model. To do so, we dichotomized our gender variable, retaining only those who indicated “man” or “woman” as their gender identity since the sample size of non-binary participants was too small to permit reliable analyses. We ran the model with dichotomous gender specified as the moderator, and the same pattern of results were obtained—the mediation model did not depend on gender identity (binary: men vs. women), suggesting that anxiety is a relevant mediator explaining the link between cannabis use frequency and PLEs for both those who identify as men and those who identify as women. We have not included these analyses in the main text but are available upon request.

Breitborde, 2019). Moreover, results supported anxiety mediation despite changing both mediator and outcome variables relative to Reeves and colleagues (2014): mediation was supported when the mediator was current (past-three-month) anxiety symptoms, measured by the GAD-7 (Spitzer et al., 2006), rather than trait anxiety (Reeves et al., 2014). Conceptually, anxiety symptoms are more state-like (variable over time) than trait anxiety (a stable personality trait; Endler & Kocovski, 2001) and thus, a more relevant mediator in the cannabis use-PLE association. We also successfully extended Reeves et al.'s (2014) anxiety mediation model using PLEs as the outcome (versus APPS; Loewy et al., 2005). PLEs are less severe/earlier along the psychosis continuum (van Os et al., 2009), increasing the relevance of results to early identification and potential prevention of psychosis development in vulnerable emerging adults. This supported mediation model provides further evidence that frequent cannabis use and, in turn, heightened anxiety, are important potential risk factors for PLEs to target in interventions.

We extended Reeves et al. (2014) by testing the potential sex-moderation effects on the anxiety-mediation model. Results did not support our sex-moderation hypotheses, suggesting that anxiety mediates the trajectory from frequent cannabis use to PLEs in emerging adults regardless of sex.

Historically, research has supported that males tended to use cannabis more frequently and in higher quantities compared to females (Cooper & Craft, 2018; Crocker & Tibbo; 2018; Health Canada, 2021; 2021, May; Hosseini & Oremus, 2019). However, national cannabis surveys show that over time, the gap between sexes in cannabis use has narrowed, with rates of use in females rising to match that of males, a phenomenon known as convergence (Chapman et al., 2017; Rotermann, 2020). In the present sample,

females used cannabis significantly more frequently than males. This might be attributed to the growing social acceptability of cannabis use in young females in Canada (Rotermann, 2020). The COVID-19 pandemic may have influenced results: 40% of Canadian emerging adults reported increasing their quantity, and 38% their frequency, of cannabis use during the pandemic (Health Canada, 2021). Common reasons for increasing use were increased stress, anxiety, and isolation/loneliness (Health Canada, 2021); these predictors of greater cannabis use (Bartel et al., 2020; Crippa et al., 2009) were particularly elevated among Canadian female versus male undergraduates during the pandemic (Moyser, 2020; Prowse et al., 2021).

While anxiety symptoms were found to be moderately severe overall, females reported significantly more anxiety on the GAD-7 than males. This finding is consistent with literature showing that females are more anxious than males (APA, 2022; LeBlanc et al., 2020), and with reports that levels of anxiety have been significantly higher among females throughout the pandemic (Moyser, 2020; Prowse et al., 2021). Furthermore, PLEs were prevalent in this sample with students reporting an average of 3.54/18 on the PLEQ (Laurens et al., 2007; 2012), nearly doubling previous reports (1.64/18 in the past year; Isaksson et al., 2022). ~37% of the present sample scored four or more on the PLEQ, indicating the presence of PLEs (Isaksson et al., 2022). This rate is elevated compared to the 11.9% of a pre-pandemic sample of emerging adults who scored four or more found previously (Isaksson et al., 2022). As substance use, stress, anxiety, and isolation/loneliness increased during the pandemic (Health Canada, 2021), the elevation observed in PLE scores may also be explained by the present sample being taken during the pandemic. Indeed, a recent study compared inpatient psychiatric admissions during

the COVID-19 pandemic to an earlier comparator period and found significantly more admissions related to substance use during the pandemic than before (45% vs. 28%; Nejati et al., 2021). Contrasting literature showing males to be at higher risk for PLEs/primary psychotic disorders compared to females (Cooper & Craft, 2018; Crocker & Tibbo, 2018; Hosseini & Oremus, 2019), the number of PLEs reported herein did not vary by sex. Equivalent reports of PLEs by males and females in the present study may be due to females in our sample using cannabis significantly more frequently than the males, given the known links between cannabis use and symptoms along the psychosis continuum (Kelleher & Cannon, 2011; Kiburi et al., 2021; Ragazzi et al., 2018; van Os et al., 2009).

Limitations

Firstly, mediation is considered a causal process that unfolds over time (Hayes, 2022), however this study used cross-sectional data limiting causal inference (Chilcoat & Breslau, 1998). For example, this study assumed that anxiety symptoms preceded PLEs, however, it is possible that the experience of PLEs causes anxiety symptoms (McGrath et al., 2016). For this reason, some argue against testing mediation with cross-sectional data (Maxwell et al., 2011). Others suggest that cross-sectional studies are reasonable when evaluating newer mediational models while keeping directional inference limitations in mind (Chilcoat & Breslau, 1998; Hayes, 2022). Our results corroborate those found in a different sample using different measures (Reeves et al., 2014), supporting this study as a useful early step in increasing our understanding of anxiety's role in the link between cannabis use and psychosis-related outcomes.

Secondly, data were collected via online self-report measures which may be prone to biased responding. Furthermore, the Co-Venture Drug Use Battery (O'Leary-Barrett et al., 2017) is a shortened version of the psychometrically-sound DEP-ADO (Germain et al., 2003; Landry et al., 2005), yet the reliability/validity of some specific individual items (e.g., cannabis use frequency) are unavailable. Possible mitigating factors of these limitations include that self-reported substance use has been shown to be acceptably accurate when confidentiality is assured and there are no risks of adverse consequences for responding truthfully (both true for this study; Sobell & Sobell, 1990). Furthermore, online questionnaires have been shown to reliably capture emerging adults' self-reported substance use (Johnson, 2014). Future work would benefit from clinician-administered interviews or biological drug testing, for example, to support self-report measures.

This study did not include certain clinically relevant variables such as participants' family history of substance misuse, psychosis, and trauma (Kiburi et al., 2021). Future studies would benefit from inclusion and control of such variables, to allow a more nuanced interpretation of results.

Lastly, while our sensitivity analyses controlled for site effects and the substances most commonly co-used by cannabis users (Health Canada, 2021; 2021, May) and those at clinical high-risk for psychosis (Addington et al., 2014) other potential confounding variables may have impacted the study. For example, age of onset of cannabis use and other psychiatric comorbidities should be assessed and controlled for in future studies testing anxiety mediation (Kiburi et al., 2021; McGrath et al., 2016; Hosseini & Oremus, 2019).

Conclusion

The high frequency of cannabis use and high prevalence of moderate/severe anxiety and PLEs in this Canadian emerging adult undergraduate sample further supports the need to increase our understanding of the relationship between these variables. Our study moved toward clarifying one potential mechanism (anxiety symptoms) driving the link between cannabis use and PLEs, including assessing for sex moderation. Our results suggest the following possible clinical implications: that reducing anxiety symptoms in frequent cannabis-using emerging adults may help prevent the development/worsening of PLEs, and that anxiety symptoms as an intervention target may be relevant for psychosis risk-reduction among undergraduates regardless of sex.

Tables

Study 1 Table 1. Descriptive Statistics – Demographic Variables

Demographic Variable	Overall sample (N = 1,266)
Age (years), *M* (*SD*); [range]	19.13 (1.49); [18 – 25]
Sex assigned at birth, *n* (%)	Female = 849 (67.1%) Male = 414 (32.7%) Missing = 3 (0.2%)
Gender identity, *n* (%)	Woman = 825 (65.2%) Man = 409 (32.3%) Transgender = 3 (0.2%) Non-binary = 21 (1.7%) Two-spirit = 1 (0.1%) Other = 6 (0.5%) Missing = 1 (0.1%)
Year of study, *n* (%)	First-year undergraduate = 717 (56.6%)
International student status, *n* (%)	Yes = 170 (13.4%) No = 1,095 (86.5%) Missing = 1 (0.1%)
Visible minority status, *n* (%)	Yes = 337 (26.6%) No = 877 (69.3%) Missing = 51 (4.1%)
Parental status, *n* (%)	Yes, I have children = 3 (0.2%)
Employment status, *n* (%)	Full-time = 4 (0.3%) Part-time = 126 (10.0%) Unemployed = 455 (35.9%) I prefer not to say or Missing = 681 (53.8%)

Note. M = Mean. *SD* = Standard Deviation.

Study 1 Table 2. Descriptive Statistics and Bivariate Correlations – Clinical Variables

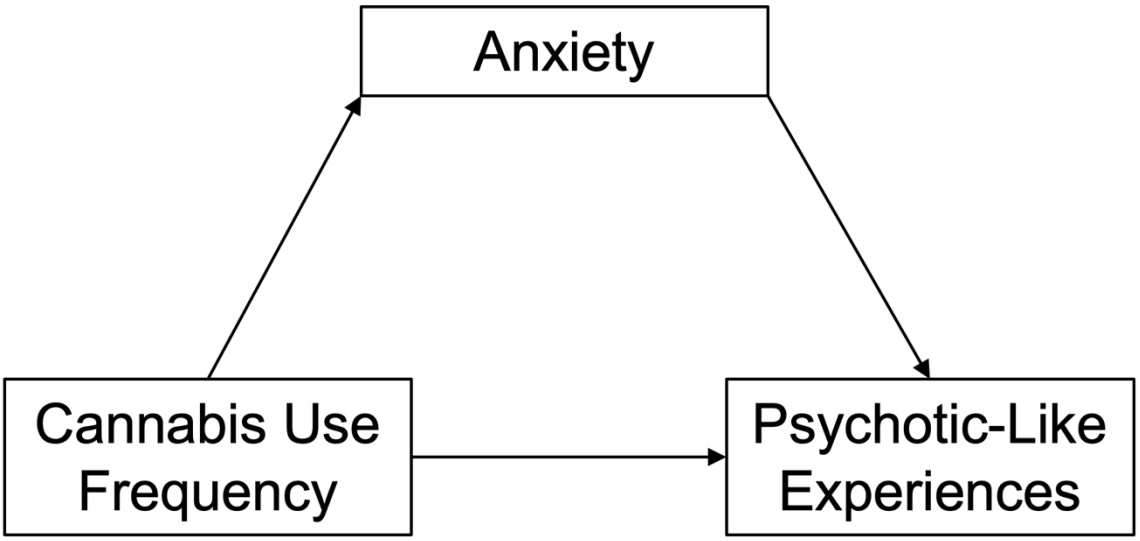
Variable	*M*	*SD*	Skew	Kurt	1.	2.	3.	4.
1. Cannabis Use Frequency	0.87	1.15	1.48	1.40				
2. Psychotic-Like Experiences	3.54	3.29	1.33	1.90	-.001			
3. Anxiety	10.26	6.06	0.19	-1.08	.145**	.157**		
4. Alcohol Use Frequency	1.44	1.07	0.34	-0.82	.501**	-.046	.071*	
5. Tobacco Use Frequency	0.75	1.24	1.78	1.95	.551**	.083**	.123**	.466**

Note. M = Mean. *SD* = Standard Deviation. Skew = skewness. Kurt = kurtosis.

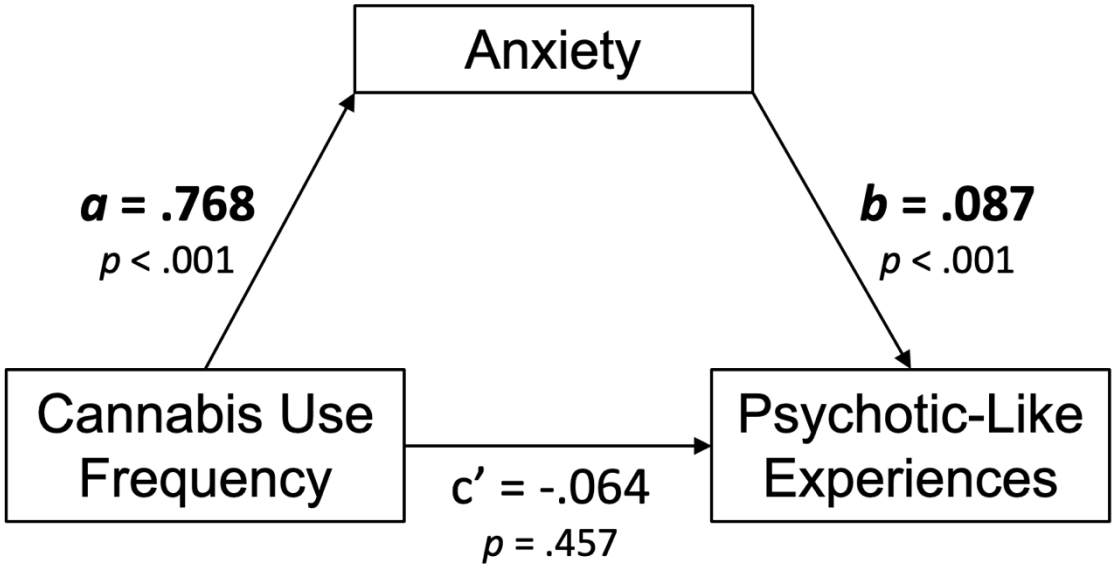
* Correlation significant at 0.05 level; ** Correlation significant at 0.01 level (2-tailed).

Figures

Study 1 Figure 1a. Conceptual model of the simple mediation model

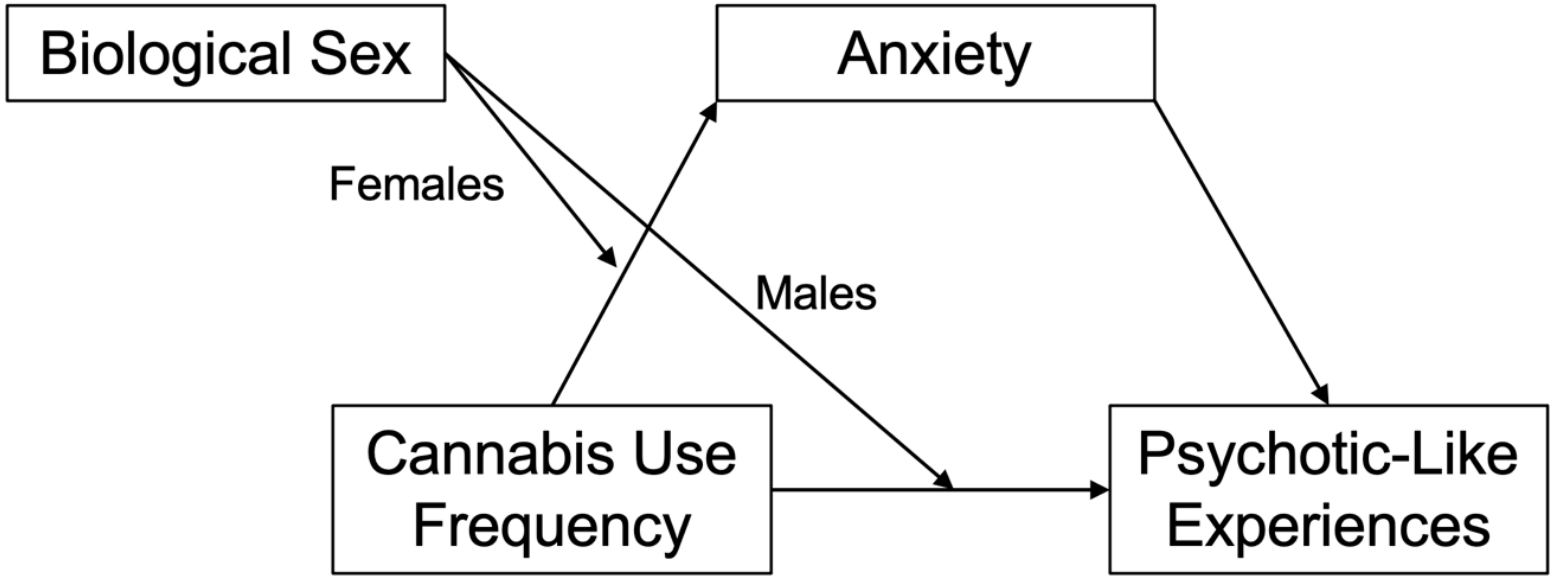


Study 1 Figure 1b. Path diagram of the simple mediation model

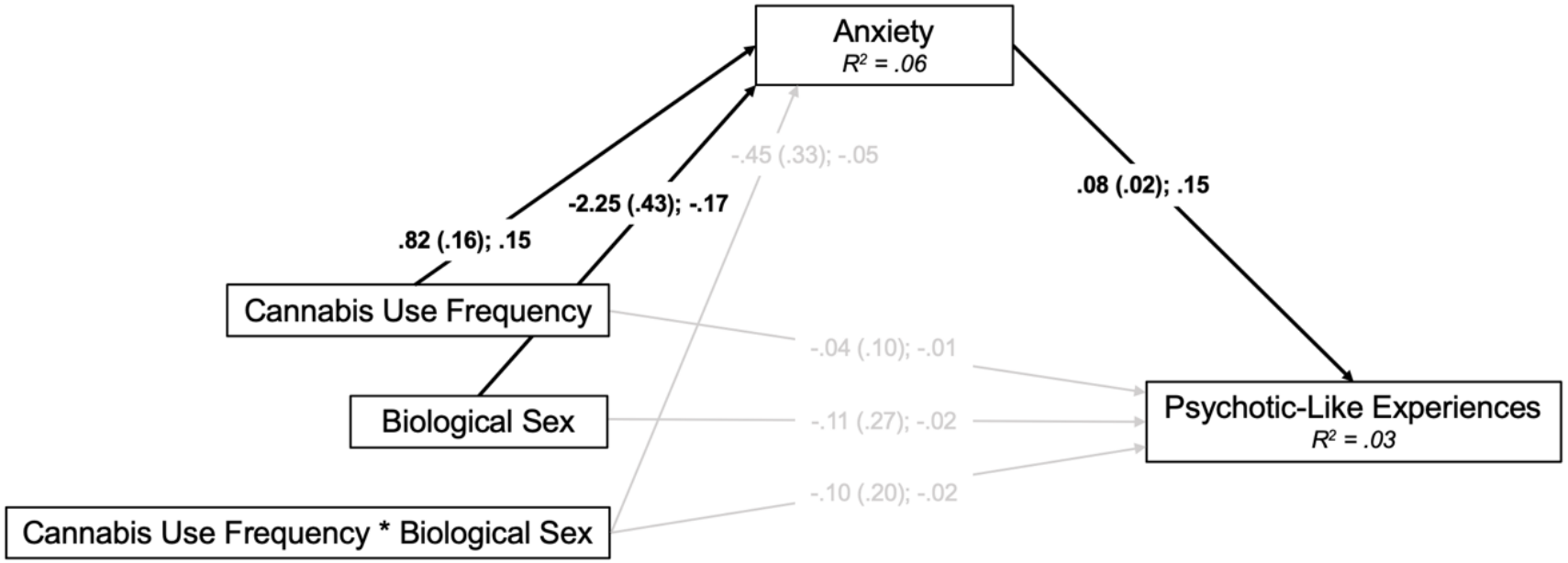


Note. N = 1,251.

Study 1 Figure 2a. Conceptual model of the conditional process (moderated mediation) model



Study 1 Figure 2b. Path diagram of the conditional process (moderated mediation) model



Note. Study 1 has a total sample of 1,266 with a biological sex split of 849 females and 414 males for analyses. Conditional process N = 1,248; with females coded = 0 and males coded = 1. Path estimates presented as unstandardized coefficient (standard error); standardized coefficient. Bold denotes specified paths that were statistically significant ($P < 0.05$). R^2 values represent the proportion of variance in the dependent variable that can be explained by the independent variables, significant at $P < 0.001$. MLR estimation was used to account for skewness.

CHAPTER 3: TRANSITION FROM STUDY 1 TO STUDY 2

The results of Study 1 demonstrated that anxiety mediated the link between cannabis use frequency and psychotic-like experiences in a Canadian sample of emerging adult undergraduates. When assessed for moderation by biological sex, no statistically significant variation in the model was observed, suggesting that anxiety appears to be a relevant target for interventions in cannabis-using emerging adults regardless of their sex assigned at birth. Targeting anxiety in those who use cannabis may mitigate risks for developing persistent PLEs or progression of symptoms along the psychosis continuum.

Reciprocal Associations Between Anxiety and PLEs

While there are several strengths to Study 1 including its large sample size and the examination of an exclusively emerging adult sample (aged 18-25 years), the study's limitations naturally left some questions unanswered. Primarily, as mentioned in the Limitations section of Study 1, the direction of effects cannot be ascertained. This is due to our proposed anxiety-mediational model being tested using cross-sectional data. Cross-sectional research designs capture a snapshot of what might be taking place by collecting all data from participants at a single point in time, with no time elapsing between the theorized cause and effect (Cain et al., 2018; O'Laughlin et al., 2018). Temporality is a mandatory requirement to establish causality (i.e., there must be evidence that the cause preceded the effect in time; Chilcoat & Breslau, 1998; Rothman & Greenland, 1998). Given that mediation is inherently a process that unfolds over time (Hayes, 2022; MacKinnon, 2008), some have argued against using cross-sectional data for testing mediation (Maxwell et al., 2011; Preacher, 2015). Others, however, have suggested that cross-sectional data are appropriate for testing mediational models that are early in their

conception, such as the model described in Study 1, so long as the limitations in our ability to determine temporal precedence/directionality are kept in mind (Hayes, 2022; Hayes & Rockwood, 2017). Thus, while Study 1 presumed that symptoms of anxiety preceded the onset of PLEs, we cannot be certain of this direction of effects.

Chapter 1 of this thesis detailed that there exist complex associations between cannabis use variables, PLEs, and anxiety. As previously mentioned, some evidence suggests that the association between anxiety and PLEs is bidirectional, meaning that, while anxiety is temporally primary to PLEs for some, PLEs may precede the onset of subsequent anxiety symptoms for others (McGrath et al., 2016). Alternatively, both may be true in a given individual: the bidirectionality of the PLEs-anxiety association may lead to the development of a vicious cycle wherein having PLEs heightens anxiety, which in turn increases one's PLEs, which increases anxiety, and so on. Chapter 1 further described how PLEs may be distressing events that can provoke feelings of anxiety, feelings with which emerging adults may then attempt to cope by increasing their cannabis use. This pattern of heightened substance use may then lead to greater experiences of cannabis-related problems such as the development of cannabis use disorder. This alternative hypothesized direction of effects is based in the self-medication hypothesis which suggests that individuals use substances to alleviate negative emotions such as anxiety (Khantzian, 1985, 1997). Thus, while Study 1 assumed that anxiety leads to PLEs, the possible reverse direction of effects from PLEs to anxiety is the focus of Study 2 of this thesis.

PLEs Lead to Cannabis Use and Related Problems

While PLEs have been shown to be associated with increased psychological burden (Mylona et al., 2022) and the possible development or worsening of anxiety symptoms (Lindgren et al., 2022; McGrath et al., 2016), PLEs have also been shown to be a risk factor for greater cannabis use and related problems. For example, PLEs have been shown to predict the subsequent onset of cannabis use with an odds ratio of 1.3 (95% CI = 1.0–1.5) in an international sample of over 30,000 adults (Degenhardt et al., 2018). Furthermore, Karcher et al. (2019) reported that PLEs were associated with both frequent cannabis use ($\beta = 0.11$, 95% CI = 0.08–0.14) and the development of cannabis use disorder ($\beta = 0.13$, 95% CI = 0.09–0.16) in a sample of adults aged 22-36 years and after adjusting for covariates.

While there appears to be a connection between having PLEs, subsequent cannabis use, and experiencing cannabis-related problems, little work has yet been done to uncover the potential psychological mechanisms that may underlie this link. The focus of Study 2, therefore, was to evaluate anxiety symptoms and specific coping-with-anxiety motivations for cannabis use as sequential (chained) mediators explaining the link between PLEs and cannabis-related problems in university students. Standardized questionnaires on PLEs, anxiety symptoms, cannabis coping-with-anxiety motives, and cannabis-related problems were administered to 413 emerging adult undergraduate cannabis users in their first or second year of study at five universities across Canada. Path analyses were used to test the hypothesized chained mediation and conditional process models.

CHAPTER 4: STUDY 2: DO ANXIETY SYMPTOMS AND COPING MOTIVES SERIALLY MEDIATE THE ASSOCIATION BETWEEN PSYCHOTIC-LIKE EXPERIENCES AND CANNABIS-RELATED PROBLEMS IN EMERGING ADULT UNDERGRADUTES?

The second of two manuscripts on which this thesis is based appears in this chapter. Readers are advised that Haley Bernusky, under the co-supervision of Dr. Sherry Stewart and Dr. Phil Tibbo, was responsible for preparing the initial draft of the manuscript, incorporating feedback from her co-authors, and preparing the manuscript for submission. The manuscript was submitted to *Addictive Behaviors* on May 20, 2023, where it is currently undergoing peer review. The full reference is as follows: Bernusky, H. C. R., Tibbo, P. G., Conrod, P. J., Yunus, F. M., Keough, M. T., Thompson, K. D., Krank, M. D., Hadwin, A. F., & Stewart, S. H. (under review). Do anxiety symptoms and coping motives serially mediate the association between psychotic-like experiences and cannabis-related problems in emerging adult undergraduates? *Addictive Behaviors.*

Abstract

Many Canadian emerging adults (ages 18-25 years) use cannabis, with 60% of past-three-month users experiencing one or more cannabis-related problems (i.e., adverse consequences of use). While psychotic-like experiences (PLEs) and cannabis problems overlap, little is known about the mechanisms explaining this link. One hypothesis is that PLEs are distressing and give rise to anxiety, with which emerging adults attempt to cope through increased cannabis use, in turn increasing their risk for cannabis-related problems. We tested a chained-mediational model to determine if anxiety and coping-with-anxiety motives for cannabis use sequentially mediated the link between PLEs and cannabis problems in emerging adult undergraduates; a conditional process model tested for moderation by sex. Emerging adult cannabis users (N = 413; mean [SD] age = 19.1 [1.5] years; 71.9% female) from five Canadian universities provided cross-sectional, self-report survey data in fall 2021. Validated measures of PLEs, anxiety, cannabis coping-with-anxiety motives, and cannabis-related problems were administered. Path analyses supported the hypothesized chained mediational indirect effect (b = .027, 95% bootstrap CI [.012, .050]). No direct effect was found (p = .698), suggesting that the PLEs-to-cannabis problems association is fully explained by anxiety and cannabis coping-with-anxiety motives. Inconsistent with hypotheses, mediation did not depend on sex (95% CIs crossed zero); therefore, anxiety and cannabis coping-with-anxiety motives explain the link between PLEs and cannabis problems in emerging adults regardless of their sex. Results highlight anxiety and cannabis coping-with-anxiety motives as potentially important intervention targets in cannabis-using emerging adults with PLEs, possibly preventing the development/worsening of cannabis-related problems.

Keywords. Psychotic-Like Experiences, Anxiety, Cannabis, Cannabis-Related Problems, Anxiety Coping Motives, Self-Medication

Introduction

Emerging adulthood (ages 18-25; Arnett, 2000) is a developmental phase when many Canadians use cannabis: ~50% of all 20-24-year-olds used cannabis in the past year (Health Canada, 2022). Many users experience cannabis-related problems (i.e., adverse social, health, legal, and psychological consequences of use): 60.3% of past-three-month users experienced at least one cannabis-related problem (Health Canada, 2021, May). Of the emerging adult cohort, 66.7% were at moderate-to-high risk for cannabis-related problems (Health Canada, 2021, May; Humeniuk et al., 2010). Indeed, rates of cannabis use disorder are highest among those aged 18-29-years (6.9%; APA, 2022). Therefore, it is important to identify risk factors, and the mechanisms linking risk factors to the development of cannabis-related problems, to develop effective prevention and early interventions to mitigate cannabis harms in emerging adults.

One possible risk factor for cannabis-related problems is psychotic-like experiences (PLEs, i.e., subclinical hallucinations/delusions that do not qualify as symptoms of primary psychotic disorders, occurring in the general population with a median prevalence of 5-8%; van Os et al., 2009). PLEs may lead to greater cannabis use and related problems (Degenhardt et al., 2018; Ferdinand et al., 2005; Karcher et al., 2019; Matheson et al., 2022). Results from the World Health Organizations' World Mental Health survey revealed that those aged 18+ with PLEs had 1.3 times greater odds of subsequently beginning to use cannabis compared to those without PLEs (Degenhardt et al., 2018). Furthermore, PLEs were positively associated with cannabis use disorder Karcher et al., 2019). Little work, however, has investigated the psychological mechanisms underlying the link between PLEs and cannabis-related problems.

One hypothesis is that PLEs are distressing, giving rise to anxiety symptoms, triggering coping-motivated cannabis use, in turn increasing the risk for cannabis-related problems. Each piece of this hypothesis has some support. First, PLEs are risk factors preceding the onset of anxiety (Bourgin et al., 2020; Lindgren et al., 2022; McGrath et al., 2016). Adults with PLEs have approximately 2.4 times the odds of developing later anxiety disorders compared to those without PLEs (McGrath et al., 2016). Furthermore, adolescents who reported PLEs at baseline showed significantly worse anxiety symptoms at follow-up than adolescents without baseline PLEs (Yamasaki et al., 2018).

Second, individuals experiencing anxiety resulting from their PLEs may be motivated to use cannabis to cope (Crippa et al., 2009; Knapp et al., 2021; Zvolensky et al., 2009). Indeed, 70.9% of an adult sample reported self-medicating with cannabis to manage their anxiety (Asselin et al., 2022). Among heavy cannabis using emerging adults, ~81.7% reported motivation to use cannabis to lessen their anxiety (Wallis et al., 2022). Clinically anxious heavy cannabis users have also been shown to use significantly more cannabis compared to non-anxious heavy-using individuals: a medium-to-large effect (*Cohen's d* = 0.73; Van Dam et al., 2012).

Lastly, cannabis use to cope may increase one's risk for more severe cannabis-related problems (Bresin & Mekawi, 2019; Cooper et al., 2015). A recent meta-analysis reported that coping motives are significantly related to cannabis problems ($r = 0.43$, 95% CI [0.38, 0.48]; Bresin & Mekawi, 2019). Yet to be determined, however, is whether specific cannabis coping-with-anxiety motives help to predict greater cannabis-related problems. Thus, anxiety and coping-with-anxiety motives for cannabis use have

been proposed in this study as potential chained mediators of the association between PLEs and cannabis-related problems.

The self-medication hypothesis (Khantzian 1985, 1997) offers a potential basis for understanding how PLEs and, in turn, anxiety may lead to increases in cannabis-related problems, in suggesting that people use substances to alleviate negative emotions (i.e., coping motives for cannabis use; Bresin & Mekawi, 2019; Cooper et al., 2015). It has been suggested that those with psychosis may use cannabis to self-medicate symptoms of psychosis (e.g., to allay hallucinations; Mané et al., 2015). However, there has been little support for this (Gill et al., 2015; Pencer & Addington, 2008). The version of the self-medication hypothesis with the most support in relation to psychosis is that those with psychosis self-medicate with cannabis to regulate negative affect (e.g., anxiety; Pencer, 2004). No study has directly tested the role of anxiety and cannabis coping-with-anxiety (self-medication) motives in explaining the PLEs to cannabis-related problems association as would be predicted by the self-medication hypothesis. Thus, the primary objective of this study was to fill this gap in the literature by combining PLEs, anxiety, cannabis coping-with-anxiety motives, and cannabis-related problems into a single cohesive model and testing the model in a single study.

We hypothesized that among a sample of emerging adult undergraduates, (H1) greater PLEs would be associated with more frequent anxiety symptoms, which, in turn, would be associated with greater cannabis coping-with-anxiety motives, which, in turn would be associated with greater cannabis-related problems (see Figure 1a), with a significant indirect effect through the chained mediational pathway. We also expected that (H2) the chained mediation pathway would be significantly stronger than the

constituent simple mediation pathways (e.g., PLEs to anxiety to cannabis-related problems, and PLEs to cannabis coping-with-anxiety motives to cannabis-related problems).

Our secondary, exploratory objective was to evaluate moderation of the chained-mediational model by biological sex (i.e., male, female). Historically, PLEs are more common in males than females (Ayesa-Arriola et al., 2020; Ochoa et al., 2012; van Os et al., 2009), and males use more cannabis/are at higher risk for related problems than females (Ayesa-Arriola et al., 2020; Ochoa et al., 2012). Females are more anxious than males (APA, 2022; LeBlanc et al., 2020), and are 3.3 times more likely than males to self-medicate anxiety with cannabis (Wallis et al., 2022). Given these differences, the chained-mediating roles of anxiety and coping-with-anxiety motives in the link between PLEs and cannabis-related problems may also differ by sex. We hypothesized that sex would moderate the chained-mediational model, with (H3) the a_1-path of the chained indirect effect (PLEs to anxiety path) proving stronger for females, and (H4) the direct path from PLEs to cannabis-related problems proving stronger for males (see Figure 2a).

Materials & Methods

Participants and Procedures

The dataset used in the present study has been described in full elsewhere[6]. In brief, cross-sectional online self-report survey data were collected (fall 2021) from first- and second-year emerging adult undergraduates at five Canadian universities as part of UniVenture, a substance misuse prevention project (Yunus et al., 2022). Each site

[6] See Bernusky et al. (2023) for: full details on the UniVenture study procedure; and impact of data collection during the COVID-19 pandemic, including pandemic-related site effects (Sites 1-5, anonymized per UniVenture partnership agreement).

received ethics approval; participants' electronic informed consent permitted the examination of associations between survey measures. Participants completed an author-compiled demographics measure and a battery of reliable and validated questionnaires. Cross-site data were merged, scored, and cleaned, producing a total sample of 1,266 participants (Bernusky et al., 2023); 853 participants were excluded as they were not recent (i.e., past-three-months) cannabis users and thus, were not asked to report on their cannabis use motivations. Thus, the present sample for hypothesis testing included N = 413 recent cannabis users (mean [SD] age = 19.1 [1.5] years; 71.9% female; 51.3% first-year undergraduates).

Measures

Demographics

An author-compiled measure of basic demographics was administered to ensure study eligibility criteria were met (e.g., first- and second-year undergraduates, 18-25 years of age). The demographics measure queried on biological sex assigned at birth (male/female)[7] for the conditional process analysis. Site information was obtained to control any site effects.

Cannabis Use Frequency

The Co-Venture Drug Use Battery (O'Leary-Barrett et al., 2017) captured frequency of use of various substances, including cannabis (also referred to as "marijuana", "hashish", and "weed"; included the use of vaped THC products). The

[7] Biological sex and gender identity were 97.0% congruent in the present sample, precluding any reliable analyses of subsamples beyond the gender binary (men; women). We focused on moderation by sex, thus promoting inclusivity by retaining data from those who identified their gender differently from their sex assigned at birth.

cannabis use frequency item was used to determine study eligibility, restricting the sample to past-three-month cannabis users, as a later measure under study (cannabis use motives) was only provided to recent (i.e., past three months) users (Health Canada, 2021, May). Cannabis, alcohol, and tobacco use (including cigarettes, e-cigarettes, vapes, chewing tobacco, etc.) information were gathered to assess for co-morbid substance use (common in cannabis users (Health Canada, 2022; 2021, May), posing additional risk for substance-related problems (Degenhardt et al., 2018; Health Canada, 2021, May). Sensitivity analyses were conducted, controlling for cannabis, alcohol, and tobacco use frequency (described below).

Psychotic-Like Experiences

The nine-item Psychotic-Like Experiences Questionnaire (PLEQ; Laurens et al., 2007, 2012) measured participants' PLEs; scores of 4+ indicate the presence of PLEs (Isaksson et al., 2022); higher scores reflect more severe symptoms. Response options included 0 = *Not true*, 1 = *Somewhat true*, 2 = *Certainly true,* or *I prefer not to say* (treated as missing). Internal consistency was acceptable ($\alpha = 0.76$) in the present sample, similar to previous work (Laurens et al., 2017). The PLEQ shows good construct validity (Laurens et al., 2012) and served as the predictor in the present models.

Anxiety Symptoms

The seven-item Generalized Anxiety Disorder (GAD-7; Spitzer et al., 2006) scale measured participants' anxiety symptoms; higher total scores reflected more frequent anxiety symptoms. Response options included: 0 = *Not at all*, 1 = *Several days*, 2 = *More than half the days*, 3 = *Nearly every day*, or *I prefer not to say* (treated as missing).

Internal consistency was excellent (α = 0.91) in the present sample, consistent with previous work (Spitzer et al., 2006). Total GAD-7 scores served as our first mediator.

Cannabis Use Motives

The Brief Cannabis Motives Measure (BCAMM; Bartel et al., 2023) is a six-item adaptation of the Marijuana Motives Measure (Simons et al., 1998), with separate coping-with-anxiety and -depression motives per the Modified Drinking Motives Questionnaire-Revised (Grant et al., 2007). The coping-with-anxiety motive item reads, "In the past 3 months, I've used cannabis because it helps me cope when I'm feeling nervous, anxious, or tense (e.g., to reduce my anxiety or to relax)." Participants responded using a visual analog scale (0 = *Never*, 100 = *Always*); higher scores reflected greater frequency of cannabis use to cope with anxiety. The BCAMM has good test-retest reliability, and content, concurrent, and predictive validity (Bartel et al., 2023), and has been used with emerging adults (Bartel et al., 2020). Cannabis coping-with-anxiety scores served as our second mediator.

Cannabis-Related Problems

The 21-item Brief Marijuana Consequences Questionnaire (B-MACQ; Simons et al., 2012) is a shortened, validated version of the 50-item Marijuana Consequences Questionnaire (Simons et al., 2012) and was used to evaluate cannabis-related problems. A sample item is "I have awakened the day after using cannabis and found that I could not remember a part of the evening before." Response options included 0 = *No*, 1 = *Yes*, or *I prefer not to say* (treated as missing). Scores could range from 0-21; higher scores indicated greater cannabis-related problems. The B-MACQ has good criterion validity with the 50-item MACQ, good test-retest reliability (r = 0.80) over 1-19 days (M = 6.24,

SD = 4.31), and significant positive correlations with other measures of cannabis-related problems, providing evidence of good convergent validity (Simons et al., 2012). The B-MACQ showed good internal consistency (α = 0.89) in the present sample, consistent with previous work (Simons et al., 2012), and served as our outcome.

Data Analysis

Descriptive statistics were obtained using IBM SPSS Statistics version 28 (IBM Corp, 2021). Two path models tested our hypotheses: in the chained mediational model, PLEs were specified as a predictor of cannabis-related problems (outcome) through two chained mediators: anxiety symptoms and cannabis coping-with-anxiety motives, respectively. In the conditional process model, biological sex served as moderator of the *a*-path (PLEs-to-anxiety), and the direct pathway (PLEs-to-cannabis-related problems). Here, PLEs, sex, and the PLEs by sex interaction term were specified as predictors of anxiety and cannabis-related problems. As all variables (except anxiety) were positively skewed, bias-corrected bootstrap 95% confidence intervals (CI) determined the presence and magnitude of indirect effects. Bootstrapping has stronger statistical power and lower risk of Type I error than more traditional methods but does not require normal sampling distributions (Hayes et al., 2022). Path analyses were conducted using Mplus version 8.7 (Muthén & Muthén, 2017) with FIML for missing data, and the MLR maximum likelihood estimator (also robust to non-normal sampling distributions). Both the chained mediation and the moderation by sex were considered supported if the corresponding bias-corrected bootstrap 95% CI did not include zero (Hayes et al., 2022).

Sensitivity Analysis

An additional model tested if the predicted effects supported in the main analyses remained significant when controlling important covariates (i.e., study site, cannabis, alcohol, and tobacco use frequency).

Results

Descriptive Statistics

Table 1 provides descriptives and bivariate correlations of the study variables and continuous covariates. Significant positive correlations were observed between PLEs and anxiety, anxiety and cannabis coping-with-anxiety motives, and cannabis coping-with-anxiety motives and cannabis-related problems, the three paths (a_1, d, b_2) constituting the hypothesized chained mediational indirect effect.

Psychotic-Like Experiences

Approximately 76.0% of our past-three-months cannabis users reported having experienced one or more PLEs in the past three months. Participants reported average total PLEQ scores of 3.51 out of a possible 18 (Table 1), nearly doubling the average reported by emerging adults in a pre-pandemic Swedish cohort study (M = 1.64 in the past year; Isaksson et al., 2022). There was significant cross-site variation in PLEs[8].

Anxiety

Using GAD-7 cut-offs (i.e., moderate = 10+; severe = 15+; Spitzer et al., 2006), 23.0% of our sample reported moderate and 35.4% reported severe anxiety over the past three months (Table 1). Females were more anxious than males (Ms *(SD*s*)* = 12.49 (5.72)

[8] Site 3 reported significantly more PLEs than Sites 1 and 5, and Site 4 reported significantly more PLEs than Site 1, all $p < .05$. These results were largely comparable to the site effects seen in the larger cohort reported and discussed in Bernusky et al. (2023).

vs. 8.45 (5.76), respectively; $t(206.31) = 6.39$, $p < .001$). There was significant cross-site variation in anxiety[9].

Cannabis Coping-with-Anxiety Motives

On average, the sample reported a score of 43.91, indicating that nearly half of the time participants used cannabis over the past three months, it was motivated, at least in part, by the desire to cope with anxiety (Table 1). Females used cannabis to cope with anxiety more often than males (*M*s *(SD*s*)* = 47.14 (37.13) vs. 35.63 (35.91), respectively; $t(216.47) = 2.90$, $p = .004$). Furthermore, cannabis use to cope with anxiety varied significantly by site (S2 > S1, $p = .022$).

Cannabis-Related Problems

Approximately 57.4% of our past-three-months cannabis users reported having experienced one or more cannabis-related problem(s) in the past three months. Participants reported average total BMACQ scores of 2.40 (Table 1). There was significant cross-site variation (S2 > S1, S5, both $p < .05$).

Chained Mediation Model

Analyses revealed that the a_1-, *d*-, and b_2-paths which constitute the indirect (chained-mediational) effect from PLEs to anxiety to coping-with-anxiety motives to cannabis-related problems were each statistically significant (*b's* = .366, 1.721, and .043, respectively, all $p < .001$). The associated indirect effect was also significant ($b = .027$ (bootSE = .010), 95% bias-corrected bootstrap CI [.012, .050]); thus, we found support for the hypothesized chained mediation (H1). After accounting for the indirect effects,

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[9] Sites 1, 3, and 4 reported significantly more anxiety than Site 5, all $p < .05$. Like above, these site effects were largely comparable to those seen in the larger cohort reported and discussed previously (Bernusky et al., 2023).

there was no evidence of a direct PLEs-to-cannabis-related problems effect (*c'* = -.020, *p* = .698). Figure 1b shows the path diagram. Our sensitivity analyses revealed the direction, magnitude, and significance of effects remained when controlling study site, cannabis, alcohol, and tobacco use (see Figure 1c for the adjusted path diagram).

Our second hypothesis (H2) that the chained mediation pathway would be statistically stronger than the constituent single mediator pathways (e.g., PLEs-to-anxiety-to-cannabis-related problems; PLEs-to-cannabis coping-with-anxiety motives-to-cannabis-related problems) was partially supported. Table 2 presents all three of the models' specific indirect effects and their pairwise comparisons, showing that the chained-mediational indirect effect through both anxiety and cannabis coping-with-anxiety motives was indeed stronger than the single mediational pathway through coping-with-anxiety motives alone. However, the chained-mediational pathway was not statistically stronger than the statistically significant single mediational pathway through anxiety alone. Nonetheless, the mediational pathway through anxiety alone was not stronger than the mediational pathway through coping-with-anxiety motives alone.

Conditional Process Model

The conditional process (moderated chained mediation) model revealed that the PLEs by sex interaction term was unexpectedly not a predictor of either anxiety or of cannabis-related problems. Moreover, the 95% CIs crossed zero for both the indirect effect from the interaction term to cannabis-related problems through the chained anxiety-mediated path [95% CI = -.024, .043], and for the direct effect [95% CI = -.245, .180]. These results counter H3 and H4: sex did not moderate the direct or indirect effects of PLEs on cannabis-related problems in our sample of emerging adult undergraduates.

There was, however, a significant main effect of sex with females being significantly more anxious than males (*b* = -4.15 (bootSE = 1.00), 95% bias-corrected bootstrap CI [-6.12, -2.19]); males and females did not differ in cannabis-related problems (*b* = .78 (bootSE = .545), 95% CI [-.285, .1.85]). Figure 2b shows the path diagram.

Discussion

Our primary objective was to examine if anxiety symptoms and cannabis coping-with-anxiety motives mediated the PLEs-to-cannabis-related problems association. Results were consistent with H1: greater PLEs were associated with more severe anxiety symptoms, which, in turn, were associated with greater cannabis coping-with-anxiety motives, which, in turn, were associated with greater cannabis-related problems, with a significant indirect effect through the chained mediational pathway. H2 was partially supported: the chained mediational indirect effect was stronger than the single mediation pathway through anxiety coping motives alone, but not the single mediation pathway through anxiety symptoms alone.

Our secondary objective was to evaluate the chained-mediational model for moderation by sex. We did not find support for either sex moderation hypothesis (H3 or H4). Thus, the chained mediational pathway through both anxiety symptoms and cannabis coping-with-anxiety motives appears to be relevant for both male and female Canadian emerging adult undergraduates.

While there exists previous evidence in support of each link within the present chained-mediation model, this study was the first to combine each link into a single, cohesive model, and test it in a sample of emerging adult cannabis users. Our preliminary results are consistent with the hypothesis that undergraduates with PLEs are self-

medicating by increasing their cannabis use to cope with the anxiety they are experiencing from their PLEs. This finding is in line with past work wherein those with psychosis (Mané et al., 2015; Pencer, 2004) and those with anxiety (Wallis et al., 2022) have been reported to self-medicate their symptoms with increased cannabis use. This pattern of use to cope, in turn, resulted in greater cannabis-related problems for both male and female undergraduates.

In our sample of past-three-month cannabis users, 76% reported having had at least one PLE. This is high compared to pre-pandemic general population (26.7%; Bourgin et al., 2020) and young adult (51.6%; Lindgren et al., 2022) samples. A recent case control study in a Turkish sample of adolescents found that those infected with COVID-19 had significantly more PLEs compared to healthy controls (40.7% and 31.6% respectively endorsed having at least one PLE "often" or "almost always"; Kafali et al., 2022). As described previously (Bernusky et al., 2023), the present sample was collected during the pandemic when isolation, anxiety, and substance use were noted to be increased (Statistics Canada, 2021), potentially explaining the high PLE scores in the present sample. Furthermore, while we expected males to score higher than females in PLEs, cannabis use, and cannabis-related problems, interestingly, we saw no sex differences. While research has historically shown that males tend to use more cannabis than females (Ayesa-Arriola et al., 2020; Health Canada, 2022; Ochoa et al., 2012; United Nations Office on Drugs and Crime, 2023), our findings fit with some work showing evidence of a phenomenon known as convergence, wherein female cannabis use has increased over time, narrowing the gap between the sexes to approach or even match the use of males (Chapman et al., 2017). Seeing as the rates of cannabis use were equal (monthly or less)

across males (M = 5.62, SD = 1.50) and females (M = 5.94, SD = 1.60) in our sample, and to the degree that cannabis use has been shown to contribute to PLEs (Di Forti et al., 2019; Ragazzi et al., 2018) and cannabis-related problems (Health Canada, 2021, May), the convergence seen across the sexes in cannabis use frequency may potentially explain the convergence also seen in PLEs and cannabis-related problems.

The present sample was also highly anxious: approximately 23.0% reported moderate and 35.4% reported severe anxiety in the past three months. A national survey assessed Canadians' levels of anxiety during the COVID-19 pandemic and found that the percentage of people reporting high-to-extremely-high anxiety quadrupled from 5% pre-pandemic to 20% in the first year of the pandemic (Dozois & Mental Health Research Canada, 2021). Our high rates of anxiety might also be explained by this being a first-/second-year university sample, a cohort known for high anxiety levels increasing during the transition to university (LeBlanc et al., 2020). Additionally, it could be due to our majority female sample as females have been reported to experience the negative emotional effects of the pandemic to a greater extent than males (Moyser, 2020). Consistent with the literature (APA, 2022; LeBlanc et al., 2020), females in the present sample were significantly more anxious than males. Additionally, females in the present sample were more likely than males to use cannabis to cope with anxiety, consistent with previous findings (Wallis et al., 2022).

Limitations

This study has limitations to consider when interpreting results. Our results may be more largely applicable to female than male cannabis users due to the predominantly female sample. Furthermore, generalizability of our results beyond emerging adult

undergraduates in their first or second year of study may be limited as all emerging adult participants were recruited from universities. However, since our data collection sites were located across Canada and included both small and large and rural- and urban-based universities, our study may have captured a largely representative sample. While the present study explored the possibility of cannabis coping-with-anxiety motives operating as the second of two chained mediators in the present models, coping-with-anxiety motives were assessed using only a single item which may be less reliable than a multi-item measure of the construct (Allen et al., 2022) possibly reducing the strength of the chained mediation effect and potentially impacting our ability to fully support H2. The UniVenture team, however, opted to include the BCAMM items over multi-item motives questionnaires like the Marijuana Motives Measure (Simons et al., 1998) in order to reduce participant burden in an already long survey. Lastly, the present study utilized cross-sectional survey data collected at a single point in time, thus limiting our ability to establish causality or even temporality.

Conclusion

Together, our results suggest possible clinical implications, including that early interventions and prevention measures should target both anxiety symptoms and coping-with-anxiety motives for cannabis use to reduce the development/progression of cannabis-related problems in Canadian cannabis-using emerging adults with PLEs.

Tables

Study 2 Table 1. Descriptive Statistics and Bivariate Correlations

Variable	*M*	*SD*	Skew	Kurt	1.	2.	3.	4.	5.	6.	7.
1. Psychotic-Like Experiences	3.51	3.19	1.09	0.91	–						
2. Anxiety	11.36	6.01	-0.03	-1.13	.183*	–					
3. Anxiety Coping Motive	43.91	37.11	0.10	-1.54	-.018	.280*	–				
4. Cannabis-Related Problems	2.40	3.54	1.88	2.99	-.011	.214*	.464*	–			
5. Cannabis Use Frequency	5.85	1.58	0.38	-1.00	.008	.077	.498*	.556*	–		
6. Alcohol Use Frequency	5.95	1.33	-1.21	1.75	-.055	.038	-.046	.021	.170*	–	
7. Tobacco Use Frequency	3.95	3.03	.583	-1.22	.142*	.058	.172*	.294*	.427*	.291*	–

Note. M = Mean. *SD* = Standard Deviation. Skew = skewness. Kurt = kurtosis. * Correlation significant at $p < 0.01$ level (2-tailed).

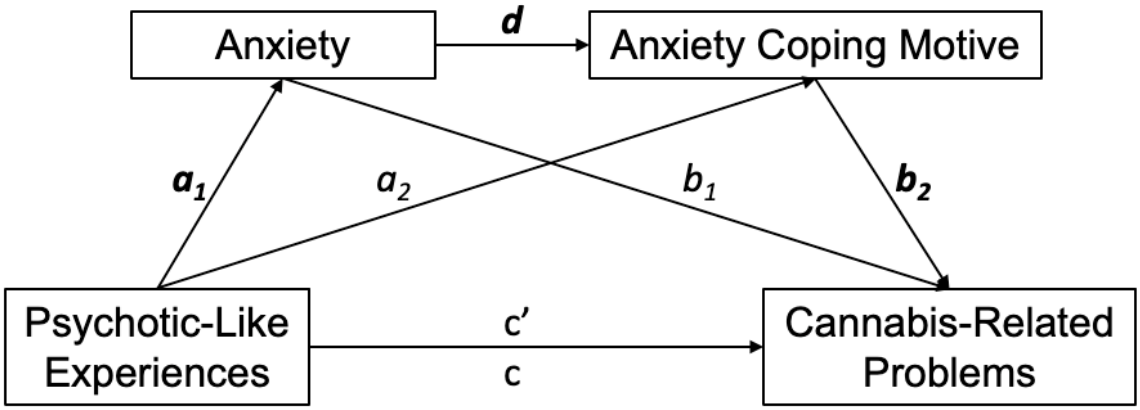
Study 2 Table 2. Specific Indirect Effects of Psychotic-Like Experiences on Cannabis-Related Problems Through Mediators and their Comparisons

Effects	β	SE	95% bootstrapped CI
Total indirect	.010	.028	-.045 – .064
1) PLEs → Anxiety → Cannabis-Related Problems (a_1b_1)*	.017	.011	.001 – .044
2) PLEs → Coping with Anxiety → Cannabis-Related Problems (a_2b_2)	-.034	.027	-.090 – .017
3) PLEs → Anxiety → Coping with Anxiety → Cannabis-Related Problems (a_1db_2)*	.027	.010	.012 – .050
Contrasts			
Model 1 vs Model 2 (a_1b_1 minus a_2b_2)	.051	.030	-.004 – .113
Model 1 vs Model 3 (a_1b_1 minus a_1db_2)	-.010	.011	-.037 – .009
Model 2 vs Model 3 (a_2b_2 minus a_1db_2)*	-.061	.031	-.127 – -.004

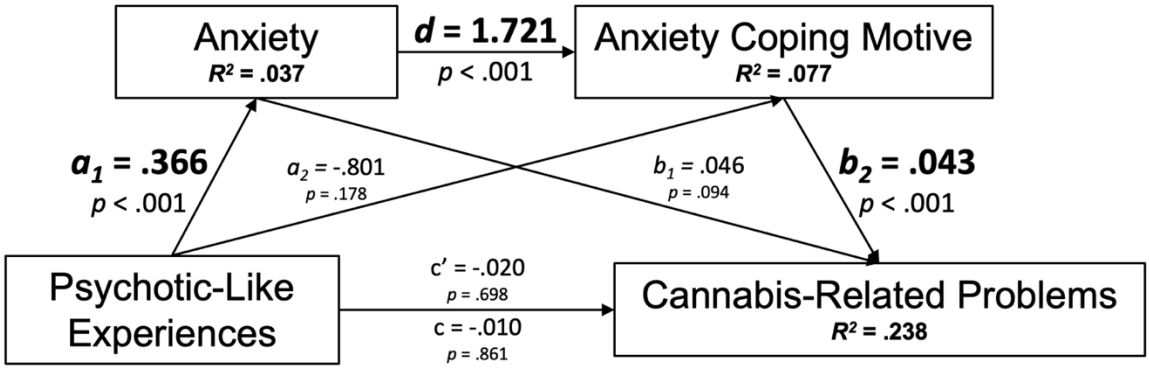
Note. PLEs = Psychotic-Like Experiences. Indirect effects where the 95% bias-corrected bootstrapped confidence intervals do not include zero are considered statistically significantly different from zero and are indicated with an asterisk (*). Model comparisons where the 95% CIs do not include zero are considered statistically significant contrasts and are indicated with an asterisk (*).

Figures

Study 2 Figure 1a. Statistical model showing paths of the chained anxiety mediation model

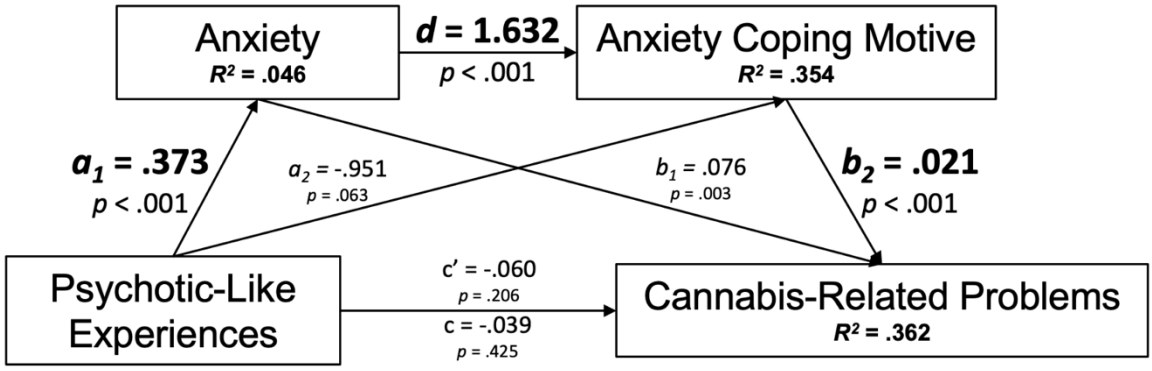


Study 2 Figure 1b. Path diagram of the chained anxiety mediation model



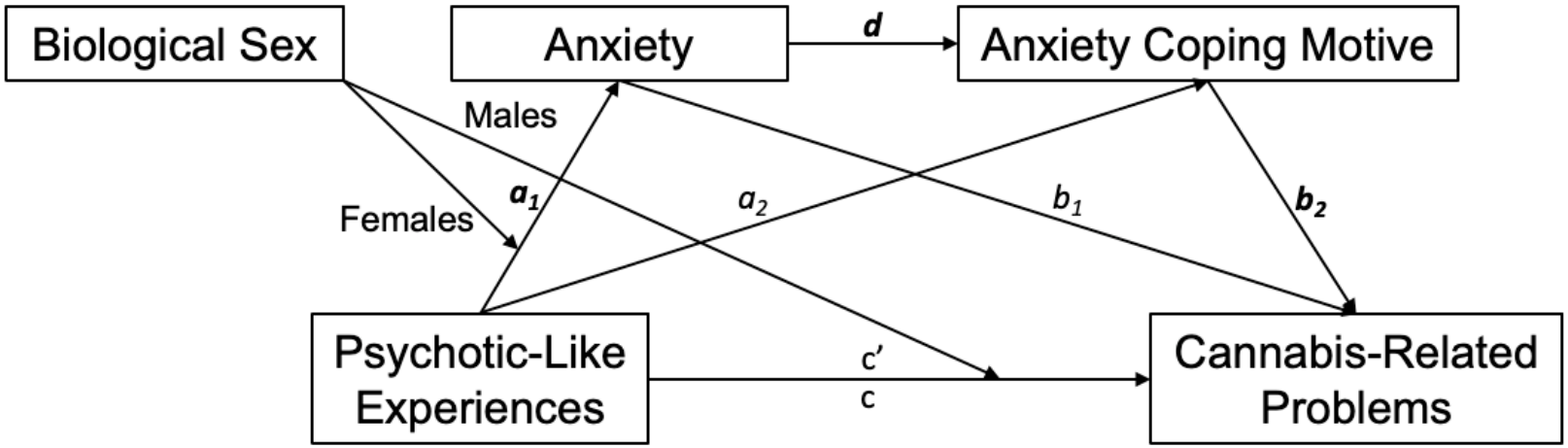
Note. $N = 366$.

Study 2 Figure 1c. Path diagram of the chained anxiety mediation model with study site, cannabis, alcohol, and tobacco use frequency held constant as covariates

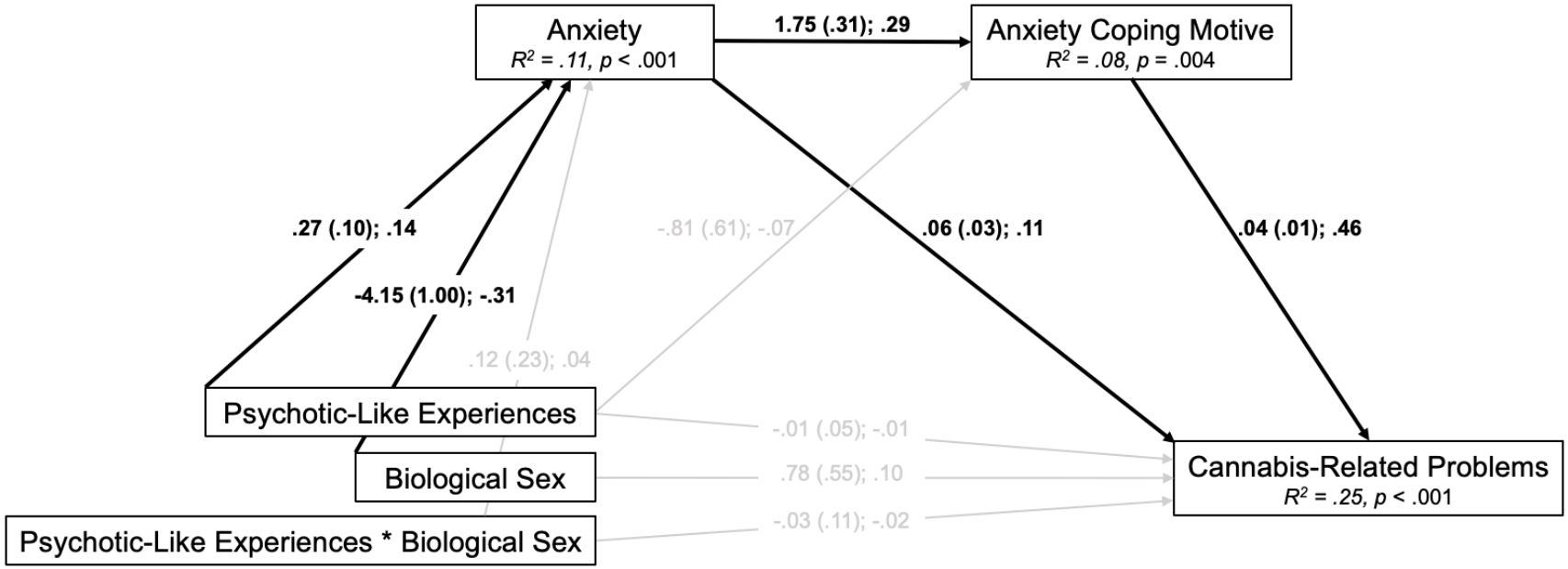


Note. $N = 365$.

Study 2 Figure 2a. Statistical model showing paths of the conditional process (moderated chained mediation) model



Study 2 Figure 2b. Path diagram of the conditional process (moderated chained mediation) model



Note. Study 2 has a total sample of 413 with a biological sex split of 297 females and 116 males for analyses. Conditional process N = 377; with females coded = 0 and males coded = 1. Path estimates presented as unstandardized coefficient (standard error); standardized coefficient. Bolding denotes specified paths that were statistically significant ($p < .01$). R^2 values represent the proportion of variance in the dependent variable that can be explained by the independent variable(s). MLR estimation was used to account for skewness.

CHAPTER 5: GENERAL DISCUSSION

My Masters' thesis investigated two potential anxiety-mediated models of the associations between cannabis variables and psychotic-like experiences (PLEs) in a multi-site sample of Canadian emerging adult undergraduate students. Through this research, I sought to determine whether anxiety might be a relevant target for intervention among emerging adult university students who use cannabis, to potentially help mitigate their risks of developing cannabis-related mental health problems such as PLEs and substance use problems such as cannabis use disorder. The following sections summarize and integrate the findings of my two studies as they pertain to the extant literature and to the overarching goal of earlier risk reduction for adverse cannabis-related mental health and substance use outcomes in emerging adults. Discussion of both the theoretical and clinical implications and the strengths and limitations of this thesis are included, concluding with my suggestions for related future research.

Summaries and Integration of Findings

Summary: Study 1

Study 1 (Chapter 2) of this thesis, entitled "Do anxiety symptoms mediate the association between cannabis use frequency and psychotic-like experiences in emerging adult undergraduates?", sought to replicate and extend upon previous work which demonstrated that trait anxiety mediated the link between cannabis use frequency and attenuated positive psychotic symptoms (APPS; Reeves et al., 2014). As this previous work was conducted almost a decade ago in Pennsylvania where the use of recreational cannabis was (and as of June 2023, still is) illegal, replication in the current Canadian context where cannabis is legal and more readily accessible was warranted. However, the

mediational model hypothesized and tested in Study 1 differed from that of Reeves et al. (2014) in three major ways.

Firstly, while cannabis use frequency remained the predictor variable in my model, I opted to specify state-like anxiety symptoms as the mediating variable instead of trait anxiety. This was done as supported mediational models identify the mechanisms to target with preventative and treatment interventions to influence an outcome (Lee et al., 2021). While trait anxiety may indeed likely be relevant to the links observed between cannabis use and the development of symptoms along the psychosis continuum on a personality level, states of anxiety may be more readily targeted with interventions in cannabis-using emerging adults to mitigate their risks for developing symptoms or experiences along the psychosis continuum.

Secondly, considering the psychosis continuum hypothesis (van Os et al., 2009), I elected to specify PLEs as the outcome variable in lieu of the APPS variable specified previously by Reeves et al. (2014). This choice was made because APPS are found further along the psychosis continuum (closer to psychotic disorder) than PLEs (van Os et al., 2009). Therefore, replication of the anxiety-mediated results reported by Reeves et al. (2014), but with PLEs as the outcome, would provide evidence that Reeves et al.'s (2014) previously reported results extend to this potential earlier manifestation of psychosis (PLEs).

Thirdly, this study is original in that it was the first in the literature to examine the hypothesized anxiety-mediational model for moderation by biological sex (a facet not examined by Reeves et al., 2014). I expected some variation in the model across sexes as evidence suggests that males tend to use cannabis more often, in greater quantities, and

have greater risks for developing primary psychotic disorders than females (Cooper & Craft, 2018; Crocker & Tibbo, 2018; Hosseini & Oremus, 2019). These findings suggest that the males of our sample may experience a stronger direct effect of cannabis use frequency on PLEs than the females. Furthermore, as females tend to be at greater risk for experiencing anxiety and developing anxiety-related disorders than males (APA, 2022; LeBlanc et al., 2020), I expected that the path from cannabis use frequency to anxiety symptoms would be stronger in females.

Cross-sectional survey data was collected in fall 2021 from 1,266 emerging adult undergraduate students aged 18-25 years enrolled in their first or second year of study at one of five universities across Canada, as part of the UniVenture substance misuse prevention project. Validated questionnaires were administered which measured participants' frequency of cannabis use (Co-Venture Drug Use Battery; O'Leary-Barrett et al., 2017), the frequency with which they experienced anxiety symptoms (GAD-7; Spitzer et al., 2006), and the number of PLEs they had experienced in the past three months (PLEQ; Laurens et al., 2007, 2012). The simple mediation and conditional process models were tested using path analyses in Mplus (Muthén & Muthén, 2017). Analyses revealed that our results successfully replicated those previously reported by Reeves et al. (2014) and provided support for my first hypothesis, demonstrating that state-like symptoms of anxiety mediated the link between cannabis use frequency and PLEs in this Canadian emerging adult sample. This means that anxiety symptoms help to explain the link commonly observed between cannabis use frequency and PLEs: we found that more cannabis use led to more symptoms of anxiety, which in turn led to greater numbers of PLEs. Despite hypothesized sex differences (H2 and H3), analyses

revealed no statistical variation in the model between biological males and females. This lack of variation suggests that anxiety indeed appears to be a potentially relevant target for prevention and early intervention measures in cannabis-using Canadian emerging adult undergraduates, regardless of their sex. Such measures may help to mitigate these emerging adults' risks for developing PLEs.

Summary: Study 2

Study 2 (Chapter 4) of this thesis, entitled "Do anxiety symptoms and coping motives serially mediate the association between psychotic-like experiences and cannabis-related problems in emerging adult undergraduates?", sought to explore for the first time, the possibility of a more complex chained mediational model (than Study 1) in a sample of Canadian emerging adults who currently use cannabis (i.e., reported use within the past three months). More specifically, while Study 1 assumed (and supported) a causal pathway leading from cannabis use to PLEs through anxiety (as cannabis use is a known risk factor for developing symptoms along the psychosis continuum; Di Forti et al., 2019; Hasan et al., 2020; Robinson et al., 2022; Sideli et al., 2020), Study 2 sought to investigate the reverse causal sequence. Specifically, in Study 2, PLEs were specified as the predictor of cannabis-related problems (the outcome) through two chained mediators (i.e., anxiety symptoms and, in turn, specific coping-with anxiety motivations for cannabis use).

The chained mediation model hypothesized and tested in Study 2 was designed as such for four main reasons. Firstly, some research has suggested that the link between cannabis variables and symptoms along the psychosis continuum is bidirectional, meaning that while cannabis use indeed increases the user's risk for experiencing PLEs,

having PLEs may also lead to greater cannabis use and the development of cannabis-related problems (Degenhardt et al., 2018; Karcher et al., 2019). Secondly, this hypothesized inverse causal sequence (with anxiety as a mediator) is supported, in theory, by research showing possible bidirectional associations between PLEs and anxiety (Lindgren et al., 2022; McGrath et al., 2016). This work suggests that while anxiety may indeed lead to greater PLEs (as supported in Study 1), having PLEs may also precede and lead to the onset or worsening of one's symptoms of anxiety. Thirdly, the self-medication hypothesis (Khantzian 1985; 1997) suggests that people use substances to relieve negative emotions such as anxiety. Thus, based on this hypothesis, I expected that cannabis-using emerging adults with PLEs and subsequent anxiety would attempt to cope with the heightened anxiety symptoms emerging from their experiences of PLEs by increasing their cannabis use. Lastly, based on substance use motivations literature (Bresin & Mekawi, 2019; Cooper et al., 2015), maladaptive motives for substance use, particularly coping motives, have been shown to lead to substance-related problems including the development of cannabis use disorder (Bresin & Mekawi, 2019; Cooper et al., 2015; Moitra et al., 2015). Furthermore, after first being validated in alcohol research (Grant et al., 2007), specific anxiety-coping and depression-coping motives were recently identified as distinct motivations for substance use in cannabis research (Bartel et al., 2023). Thus, in Study 2, I wanted to take advantage of this methodological advancement by specifying anxiety-specific coping motivations for cannabis use as the second of two chained mediators (following anxiety symptoms), with cannabis-related problems specified as the outcome of Study 2.

Consistent with Study 1, the hypothesized chained anxiety-mediational model of Study 2 was evaluated for moderation by biological sex. Variation in the model across the sexes was expected for the same reasons outlined in Study 1 (i.e., greater cannabis use and risk for PLEs typically reported for males [Cooper & Craft, 2018; Crocker & Tibbo, 2018; Hosseini & Oremus, 2019] and greater risk for anxiety reported for females [APA, 2022; LeBlanc et al., 2020]). Moreover, evidence suggests that females use cannabis to alleviate symptoms of anxiety significantly more often than males (Cuttler et al., 2016; Wallis et al., 2022). Even the experience of cannabis-related problems may vary across sexes, as males tend to be more prone to developing cannabis use disorder than females (APA, 2022), while females tend to experience more emotional problems and symptoms of cannabis withdrawal and/or dependence than males (National Academies of Sciences, Engineering, and Medicine, 2017). Therefore, due to these documented sex differences, I had expected that current cannabis-using male emerging adult undergraduates would have a stronger direct effect from PLEs to the development of cannabis-related problems, whereas their female counterparts would experience a stronger association between PLEs and anxiety, which would contribute to a stronger overall indirect effect from PLEs to cannabis-related problems via anxiety symptoms and coping-with-anxiety motives for cannabis use among females compared to males.

As detailed in Chapter 4, Study 2 used a subsample of the cross-sectional survey dataset used and described in Study 1, restricting the sample for Study 2 to those 413 emerging adult undergraduates who reported current cannabis use (i.e., use within the past three months). As mentioned in Chapter 4, this reduction in sample size compared to Study 1 was due to the additional requirement that participants be current (past-three-

months) cannabis users in order to report on their recent motivations for use on the BCAMM (Bartel et al., 2023). Consistent with Study 1, the chained mediation and conditional process models of Study 2 were tested with Mplus path analyses (Muthén & Muthén, 2017). Analyses provided support for my first hypothesis: anxiety symptoms and specific coping-with-anxiety motives for cannabis use were supported as chained mediators of the link between PLEs and cannabis-related problems in this sample of Canadian emerging adult current cannabis-using undergraduates. However, once again, hypothesized sex differences in the model between biological males and females were not observed. As supported mediational models provide insight into the processes to be targeted with preventative and treatment interventions (Lee et al., 2021), these results suggest that anxiety symptoms and anxiety-specific coping motives for cannabis use appear to be important and relevant targets for prevention measures/treatments aimed at reducing risks for development of cannabis-related problems in Canadian cannabis-using emerging adult undergraduates who experience PLEs, regardless of their sex. Such measures would potentially have an impact on the development of cannabis-related problems in emerging adults by decreasing their levels of anxiety. Decreased anxiety resultant from PLEs would thereby reduce emerging adults' need to use cannabis to cope, resulting in decreased cannabis use which, in turn, reduces their risk for developing cannabis-related problems. This reduction of cannabis use and related problems would impede the exacerbation of the vicious cycle (described in full below) that could develop between mental health challenges and substance misuse when self-medicating to cope with anxiety (Stewart & Conrod, 2008).

Integration of Findings

As the above summaries of my thesis studies have highlighted, using cross-sectional mediational path analyses, my thesis results helped to provide early evidence in support of anxiety variables as mediating or explanatory mechanisms underlying the previously evidenced associations between cannabis use variables and PLEs. Taken together, the results of this thesis support the previously described bidirectional associations observed between both cannabis use variables and PLEs, and between PLEs and anxiety. Specifically, Study 1 found evidence supporting a causal pathway from cannabis use frequency to PLEs through anxiety symptoms. This model supports a substance-induced mental health symptom enhancement (i.e., worsening) process, as described in earlier anxiety and substance use disorder co-morbidity research (Stewart & Conrod, 2008), wherein the use of substances (e.g., cannabis) promotes the development of adverse mental health outcomes (e.g., anxiety, PLEs). Furthermore, Study 2 found evidence in support of a chained causal pathway from PLEs to cannabis-related problems through anxiety symptoms and coping-with-anxiety motives for cannabis use. This second model, on the other hand, supports a self-medication process (Stewart & Conrod, 2008) wherein those with PLEs who experience subsequent anxiety symptoms increase their cannabis use to cope with these heightened symptoms, thereby increasing their risk for developing cannabis-related problems. Finding evidence consistent with both these causal directions supports the idea of a vicious cycle, also known as a mutual maintenance model, wherein both the substance-induced anxiety-intensification and self-medication processes operate together to maintain (or even exacerbate) co-morbid mental health issues and substance use/problems (Stewart & Conrod, 2008; **see Figure 1**).

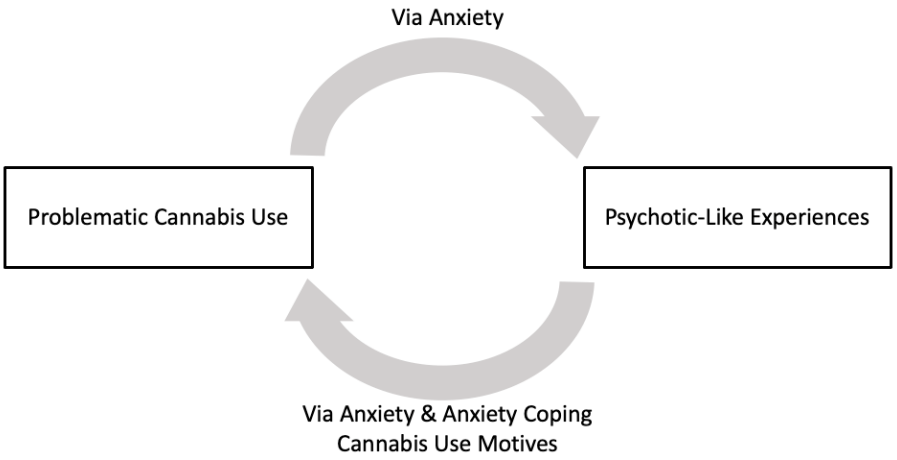


Figure 1. Diagram of the theorized vicious cycle between the substance-induced mental health symptom enhancement process of Study 1 and the self-medication process of Study 2. At the top of the diagram: frequent cannabis use leads to PLEs through cannabis-induced anxiety. At the bottom: having PLEs leads to greater anxiety and related coping motives for cannabis use, leading to an increase in cannabis-related problems including the development of cannabis use disorder. Through this theorized vicious cycle, increased cannabis use motivated by the desire to cope with anxiety triggered by the PLEs may, in the long term, exacerbate the very mental health problems (i.e., anxiety and in turn PLEs) that the cannabis use was originally intended to alleviate.

As this work was done with cross-sectional self-report survey data, neither of these directions of effects can be ascertained at this stage since temporality, a necessary component of causality, cannot be established (Chilcoat & Breslau, 1998). Longitudinal study designs are recommended for future work interested in testing for bidirectional influences, determining causality and the possibility of whether a vicious cycle may be at play among Canadian cannabis-using emerging adult undergraduates. Such replication and/or extension in longitudinal designs is required prior to influencing clinical prevention measures or early interventions. However, this work succeeded in its goal of providing support for anxiety and anxiety-specific coping motives for cannabis use as relevant targets for intervention among cannabis-using emerging adult university students. Once longitudinally validated, these results will help influence measures to earlier mitigate the development of cannabis-related mental health and substance use problems, such as PLEs (which may progress along the psychosis continuum) or the development of cannabis use disorder.

Both studies of this thesis are important as they are useful replications of and extensions upon existing literature, bringing supported work from other areas of substance use research into the sphere of research on cannabis use, supporting two different anxiety-mediated models specifically in an emerging adult sample of Canadian undergraduates. As described earlier, the inspiration for Study 1 came from Reeves et al. (2014) who found that trait anxiety mediated the link between cannabis use frequency and attenuated positive psychotic symptoms (APPS). I successfully replicated their anxiety-mediated model, providing support for their previous results with an earlier manifestation of psychotic symptoms (PLEs), compared to their focus on APPS, and when the mediator was changed to the more conceptually relevant state-like symptoms of anxiety, compared to their focus on the theoretically less malleable trait anxiety.

The model tested in Study 2 was inspired theoretically by Khantzian's (1985, 1997) self-medication hypothesis and motivational models of substance use (Cooper, 1994; Cooper et al., 2015) which state that people use substances for a purpose, to achieve a desired outcome. From the alcohol literature, Cooper (1994) established four drinking motives based on desired outcomes: enhancement of positive affect and social motivations (positive reinforcement motives), conformity in social situations and coping with negative affect (negative reinforcement motives). It was determined that the coping motive for alcohol use most reliably predicted later alcohol-related problems (Cooper et al., 2015). More recent work from the cannabis literature has also provided support for strong links between cannabis use motivated by the desire to cope with negative affect and the development of later cannabis-related problems such as cannabis use disorder (Bresin & Mekawi, 2019; Moitra et al., 2015).

Substance use motivational theorists have posited that one's reasons for using substances constitute the final common pathway through which more distal risk factors impact upon and result in substance misuse and related problems (Comeau et al., 2001; Cooper, 1994; Cooper et al., 2015). Previous works have examined the impacts of various distal risk factors on the development of substance-related problems through the chained mediators of emotional symptoms and negative reinforcement substance use motives, influencing the development of the model hypothesized and tested in Study 2 of this thesis. For example, again from alcohol research, Allan et al. (2015) tested the impact of anxiety sensitivity on alcohol problems, finding support for a chained indirect effect through generalized anxiety symptoms and drinking to cope with negative affect as sequential mediators. To replicate and extend upon this previous work, Chinneck et al. (2018) made use of previously mentioned methodological advancements in the measurement of coping drinking motives (Grant et al., 2007), which had parsed out drinking to cope with anxiety and drinking to cope with depression as separate motives for alcohol use. Results from the study by Chinneck et al. (2018) supported anxiety sensitivity's indirect effect on alcohol-related problems through the more specific chained mediators of anxiety disorder symptoms and coping-with-anxiety motives for alcohol use. More recently, cannabis research emergent from the Mood, Anxiety, and Addiction Co-morbidity Lab at Dalhousie University found support for the distal risk factor of trauma exposure on the subsequent development of cannabis use disorder through the chained mediators of emotional disorder symptoms (i.e., post-traumatic stress disorder; PTSD) and coping motives for cannabis use (Stewart et al., 2023).

Study 2 clearly replicates and extends upon existing supported chained mediational models that have considered a distal risk factor for the development of adverse substance-related outcomes through the underlying sequential mechanisms of emotional problems and maladaptive motives for substance use. Specifically, Study 2 drew inspiration from work by Allan et al. (2015) and Chinneck et al. (2018), bringing supported chained mediation models tested in alcohol users into emergent cannabis use research. Like Chinneck et al. (2018) did for alcohol use motives, Study 2 also took advantage of recent advancements in the measurement of cannabis use coping motives (Bartel et al., 2023) and further extended upon a supported model by Stewart et al. (2023) involving trauma exposure leading to cannabis problems through PTSD symptoms and coping motivations for cannabis use. This extension was achieved in Study 1 by specifying anxiety symptoms and specific coping-with-anxiety motivations for cannabis use as the chained mediators linking PLEs to the development of cannabis-related problems.

Theoretical Implications

Psychosis Continuum Hypothesis

The results from Study 1 of this thesis provide theoretical support for the psychosis continuum hypothesis (van Os et al., 2009) in that the same factors that increase risk for psychotic disorders (e.g., frequent cannabis use) do indeed appear to underlie the entire spectrum, from the earliest manifestations of psychosis continuum symptoms (PLEs; Chapter 2; Bernusky et al., 2023), to APPS (Reeves et al., 2014), through to high-risk for psychosis populations (Carney et al., 2017) and those with psychotic disorders (Di Forti et al., 2019). Previous work by Reeves et al. (2014)

suggested that anxiety explained the link between cannabis use and the development of APPS, later along the psychosis continuum than PLEs. Again, extending to the earlier manifestations along the continuum, the results of Study 1 support that anxiety symptoms are indeed an important underlying psychological mechanism for explaining the link between cannabis use and development of PLEs in Canadian emerging adult males and females. Together, these results support anxiety as a relevant mediator to be considered in future work examining the links between cannabis use variables and the development of symptoms along the psychosis continuum.

Self-Medication Hypothesis

The results of Study 2 add to existing work showing that PLEs increase the risk for cannabis-related problems (Degenhardt et al., 2018; Karcher et al., 2019); however, Study 2 went further by exploring the mechanisms that may explain how PLEs impact upon cannabis-related problems in a self-medication-based model. The traditional concept of the self-medication hypothesis suggests that those who experience symptoms along the psychosis continuum use substances to help alleviate the psychotic symptoms themselves (Khantzian, 1985, 1997). While little support for this original idea has been found (Gill et al., 2015; Pencer & Addington, 2008), some research has indicated that adolescents self-medicate the affective symptoms (such as anxiety) that result from their experiences of psychotic symptoms (Pencer, 2004; Pencer & Addington, 2008). The results of Study 2 provide support for the latter self-medication concept in emerging adults with PLEs: evidence suggests that PLEs lead to anxiety symptoms with which emerging adults are indeed motivated to cope by increasing their cannabis use, ultimately leading to the development of more cannabis-related problems. This finding is consistent

with some past work that has supported the self-medication hypothesis in those with anxiety (Asselin et al., 2022; Dunaief et al., 2023; Wallis et al., 2022) and those with psychosis for the management of their subsequent anxiety symptoms (Pencer, 2004). This thesis has, therefore, supported both the psychosis continuum hypothesis and the self-medication hypothesis, suggesting that PLEs are an important symptom to monitor clinically and to evaluate in research in emerging adults who use cannabis. Furthermore, this thesis supports the importance of anxiety symptoms and coping-with-anxiety motives for cannabis use as targets for early intervention in emerging adults caught in the links between cannabis variables and PLEs.

Clinical Implications

Cannabis Use Considerations in Emerging Adults by Biological Sex

In Study 1 of this thesis, cannabis use was shown to be significantly more frequent in females compared to males, and in Study 2 (in current cannabis users), rates of cannabis use were equal across the sexes. These patterns of results differ from extant literature which supported greater cannabis use in males than females (Ayesa-Arriola et al., 2020; Cooper & Craft, 2018; Crocker & Tibbo, 2018; Health Canada, 2021; 2021, May; 2022; Hosseini & Oremus, 2019; Ochoa et al., 2012; United Nations Office on Drugs and Crime, 2023). A pre-pandemic systematic review and meta-regression found evidence for sex convergence in the prevalence of cannabis use, meaning that the gap between the sexes in the rates of their cannabis use appears to be narrowing (Chapman et al., 2017). It is possible that the present sample captured this convergence, with females increasing their cannabis use to match (Study 2) and even exceed (Study 1) the use reported by the males.

As mentioned in Chapter 1, this pattern of increased cannabis use among females compared to males in more recent years might be attributable to the occurrence of the COVID-19 pandemic. For example, the 2021 Canadian Cannabis Survey reported that 40% of emerging adults increased the quantity of cannabis they used due to the pandemic, and 38% reported increased frequency of cannabis use (Health Canada, 2021). The most cited reasons for increased cannabis use during the pandemic included the increased amounts of stress, anxiety, isolation, and loneliness that emerging adults had experienced resulting from the COVID-19 pandemic public health lockdown orders (Health Canada, 2021). Of note is that stress, anxiety, isolation, and loneliness are common predictors of greater cannabis use (Bartel et al., 2020; Crippa et al., 2009), and these risk factors tended to be particularly elevated among Canadian female versus male undergraduates during the COVID-19 pandemic (Moyser, 2020; Prowse et al., 2021).

Furthermore, it is also important to acknowledge that perhaps we have simply captured an unusual sample with females using significantly more cannabis than males. As mentioned in Chapter 2, 43.5% of females and 37.0% of males reported cannabis use in the past year. Both sexes' rates of cannabis use are high compared to the 25% and 30% reported for females and males, respectively, in the 2022 Canadian Cannabis Survey (Health Canada, 2022). Given cannabis' connections to both mental health problems including anxiety (Duperrouzel et al., 2018; Hayatbakhsh et al., 2007) and symptoms along the psychosis continuum (Di Forti et al., 2019; Hasan et al., 2020; Robinson et al., 2022; Sideli et al., 2020) and the development of cannabis-related problems such as cannabis use disorder (APA, 2022; Health Canada, 2021, May), results suggest that cannabis use is an important risk factor to monitor in both emerging adult males and

females alike. Female emerging adult cannabis use should not be overlooked in prevention measures or early interventions, as results show cannabis use is occurring in both emerging adult males and females.

PLE Considerations in Emerging Adults by Biological Sex

Seeing as rates of cannabis use were (near) equal across biological sex in the present studies and given cannabis' links to the development of symptoms along the psychosis continuum (Kelleher & Cannon, 2011; Kiburi et al., 2021; Ragazzi et al., 2018; van Os et al., 2009), it follows that reported rates of PLEs were equal across emerging adult male and female undergraduates of the present sample as well. These equal rates of PLEs contrast extant literature suggesting that the prevalence of PLEs and the risk for developing primary psychotic disorders are higher in males compared to females (Cooper & Craft, 2018; Crocker & Tibbo, 2018; Hosseini & Oremus, 2019). As indicated in Chapter 2, the equal rates of PLEs across males and females of our sample may be partially explained by the occurrence of the COVID-19 pandemic: substance use, stress, anxiety, isolation, and feelings of loneliness were elevated during the pandemic (Health Canada, 2021), and these risk factors were particularly high among Canadian female versus male undergraduates (Moyser, 2020; Prowse et al., 2021). Thus, perhaps the females of the present sample experienced equal rates of PLEs to those of the males due to this increased pandemic-related distress.

As PLEs were the outcome of Study 1 and the predictor of Study 2, results suggest that PLEs, like cannabis use, are important symptoms to evaluate and monitor in emerging adults who use cannabis, regardless of their biological sex assigned at birth. Results suggest that both male and female emerging adults are at risk for developing

PLEs, and once acquired, PLEs may lead to the development of cannabis-related problems in both sexes alike. PLEs, like cannabis use, ought not to be overlooked for females. PLEs are important to prevent or manage as early as possible, as those individuals experiencing PLEs may be at risk of progressing along the psychosis continuum toward psychotic disorders. Furthermore, having PLEs may signal those who are at risk for development of other cannabis-related problems, including cannabis use disorder, for both males and females.

Lessons Learned from Anxiety

Finally, the most important clinical implications from this thesis come from the evaluation of anxiety variables as mediators in both Study 1, which supported the link from cannabis use to PLEs through anxiety symptoms, and Study 2, which supported PLEs to cannabis-related problems through anxiety symptoms and coping-with-anxiety motives for cannabis use. Consistent with literature (APA, 2022; LeBlanc et al., 2020; Moyser, 2020; Prowse et al., 2021), both studies found that females were significantly more anxious than males. Despite this marked sex difference, however, neither conditional process model assessing for moderation of the cannabis-PLE relation by biological sex was supported.

In the first study, this finding suggests that anxiety symptoms explain the link between cannabis use frequency and PLEs, independent of sex. Therefore, anxiety symptoms are an important mental health concern to monitor in frequent cannabis-using emerging adult undergraduates for earlier risk reduction for psychosis, regardless of the sex they were assigned at birth. Those emerging adults who frequently use cannabis and subsequently experience significant anxiety symptoms may benefit from the earlier

implementation of preventative measures or treatments designed to reduce their anxiety such as the UniVenture workshops described below, which in turn, would reduce their risk for developing PLEs.

In the second study, the supported chained mediation and the non-significant moderation analyses suggest that anxiety symptoms, and in turn, anxiety-specific coping motives for cannabis use, sequentially mediate the link between PLEs and cannabis-related problems in Canadian emerging adult undergraduate cannabis users, again independent of their biological sex. Therefore, anxiety symptoms and specific anxiety-coping motives for cannabis use are important psychological mechanisms to monitor in frequent cannabis-using emerging adult university students who have PLEs for earlier mitigation of the development of cannabis-related problems, regardless of the sex they were assigned at birth. Those cannabis-using emerging adults who have PLEs and subsequent anxiety problems may also benefit from the implementation of prevention measures or early treatments designed to reduce their anxiety and their associated desire to use cannabis to cope with their anxiety (described next), which in turn, would help prevent the development of greater cannabis-related problems.

Suggested Actions

As previously mentioned, mediational analyses that employ cross-sectional data cannot establish temporal precedence as all measurements were taken at a single point in time, not allowing for the passage of time required for determining causality (Cain et al., 2018; O'Laughlin et al., 2018). Seeing as mediation unfolds over time, the results of this thesis ought to be replicated in longitudinal research designs over several waves of data collection prior to influencing current prevention measures or intervention techniques.

Taken together as is, however, the results of this thesis showed a linear association between cannabis use frequency and PLEs (through anxiety variables), suggesting that by limiting cannabis use frequency, young people might reduce their risk for developing symptoms along the psychosis spectrum, consistent with recent risk reduction recommendations (Fischer et al., 2023). Results also provide early cross-sectional support for anxiety variables as targets in frequent cannabis-using emerging adult undergraduates in Canada to lower their risks for developing a) PLEs which may progress along the psychosis continuum toward disorder and/or b) cannabis-related problems which may progress to cannabis use disorder. Anxiety symptoms appear to be a relevant intervention target for both psychosis risk reduction and the prevention of cannabis-related problems; additionally, anxiety-specific coping motives for cannabis use appears to be a relevant intervention target for the prevention of cannabis-related problems in those experiencing PLEs.

Results of this thesis have already been published in the *Canadian Journal of Psychiatry* (Study 1; Bernusky et al., 2023) or are currently under review with *Addictive Behaviors* (Study 2; Bernusky et al., under review). Dissemination of these results to a local clinical audience first occurred in April 2023 when presented at Dalhousie University's Department of Psychiatry Grand Rounds. Furthermore, as mentioned throughout the chapters of this thesis, the dataset used herein was collected as part of the UniVenture substance misuse prevention project. This is important to note as UniVenture is a partnership project with collaborative connections established between the five Canadian universities involved in data collection, the corresponding Student Affairs Units from each university, various student-led organizations, and on-campus psychology

clinics. UniVenture is also supported by other influential methodological and knowledge translation partner organizations including each region's Strategy for Patient-Oriented Research (SPOR) SUPPORT Unit, the Canadian Research Initiative in Substance Misuse (CRISM), the Canadian Centre on Substance Use and Addiction (CCSA), and the Mental Health Commission of Canada (MHCC). As the goal of the project is to test, adapt, and share an effective and sustainable personality-targeted wellness program (UniVenture Project, 2023), dissemination of my thesis results to these important stakeholders at UniVenture Partner Meetings may be valuable. Results may potentially influence Canadian universities' approaches to student health services and education campaigns and may impact the development of future iterations of the UniVenture program itself.

Students may participate in UniVenture in two ways: first, they complete a battery of surveys at baseline. Questionnaires included those measures mentioned in Study 1 and 2, plus measures of participants' personalities, mental health and wellbeing, academic outcomes, and more. Participants receive the questionnaire battery again at follow-up both six- and 12-months later. Second, following completion of the baseline surveys, participants are placed in one of four groups based on their personality type (anxiety sensitive, negative thinking, sensation seeking, impulsive; Substance Use Risk Profile Scale; Woicik et al., 2009). Participants are then randomly assigned to either a control group or one of two treatment groups (online or in-person). Those assigned to receive treatment are invited to participate in two 90-minute workshops targeted to their dominant personality trait. These workshops aim to develop skills useful to emerging adults in their transitions to university, including emotional distress management and dealing with challenges related to substance misuse. Students learn how to set short- and

long-term goals and how to harness their unique personalities to achieve those goals (UniVenture Project, 2023).

Based on the results of this thesis showing high rates of both anxiety and PLEs in our sample, as well as supported links between PLEs and cannabis variables via anxiety, two recommendations may be made. Firstly, we ought to test the anxiety sensitivity UniVenture study arm to see if it may potentially be effective for reducing psychosis risk in those emerging adults who use cannabis and/or cannabis risk in those who have PLEs, given this intervention's focus on CBT skills for anxiety management. With appropriate sample size, it would be useful to see if the benefits of this anxiety management-focused intervention would be particularly strong among those who score high on the PLEQ (Laurens et al., 2007, 2012) or if those scoring high on the PLEQ benefit most from the anxiety management-focused UniVenture intervention (i.e., for AS students) relative to the other three interventions. Alternatively, we could develop a new, separate, fifth arm of UniVenture focused on preventing cannabis use and related consequences in those particularly at-risk for developing psychosis (e.g., those scoring high in the PLEQ). In fact, the development of such an additional program is already underway, titled PsyVenture (VentureLab, 2023). The results of this thesis may inform the content necessary for PsyVenture to be effective: this might include anxiety symptom management material, the reinforcement of the importance of developing healthy anxiety-specific coping strategies, and PLE psychoeducation content designed to reduce the degree to which emerging adults may misinterpret the symptoms as a threat, thus reducing their anxiety response. Once validated, this program could be offered to those with high scores on the PLEQ to strengthen their anxiety-coping abilities aside from

turning to cannabis use to cope. This would presumably reduce their cannabis use and prevent the development of cannabis-related problems including potential mental health (i.e., anxiety, PLEs) and substance use (i.e., cannabis use disorder) problems.

Similar emphases can be made to the universities themselves and their Student Affairs offices including Student Health Services. These stakeholders ought to be informed that PLEs and anxiety rates are high across Canada and that targeting anxiety variables in both females and males is important for promoting student's overall wellbeing, limiting development of PLEs and cannabis-related problems. Shorter workshops in addition to/separate from UniVenture aimed exclusively at developing anxiety-specific coping skills in those current cannabis users already experiencing PLEs may be developed in collaboration with the Student Health Services and Student Affairs units of the participating universities. Ideally, these sessions would reach the wider undergraduate population, expanding beyond the psychology student participant pool UniVenture draws from. These workshops may be promoted by on-campus student-led organizations and facilitated through on-campus psychology clinics.

Strengths and Limitations

Chapters 2 and 4 of this thesis have discussed the specific strengths and limitations corresponding to each study. However, I will briefly review them here along with some general observations as they pertain to the thesis overall. I will begin with strengths and conclude with the limitations of this research.

Strengths

This thesis has several important strengths. Methodologically, our statistical analyses made use of robust techniques to manage variable skewness, increasing both the

suitability of our dataset for use in regression-based analyses and the interpretability of our results. Importantly, this work was conducted in a large sample of Canadian emerging adult undergraduates. This sample is a notable strength for four main reasons. First, both studies were done in the Canadian context where cannabis use is legal and readily accessible (Health Canada, 2021) and where stigma surrounding use is relatively low (Charlebois et al., 2020). This is a strength as previous research was conducted in an American sample from a state where cannabis use is illegal (Reeves et al., 2014), and therefore, results may not have been generalizable to Canadian emerging adult undergraduates. Study 1 supported that previous results do in fact generalize to Canadian emerging adult undergraduates. Second, while our sample was restricted to first- and second-year university students, potentially limiting the generalizability of our results, our sample may be largely representative of the overall Canadian undergraduate population as data were collected from variable rural and urban university settings spanning from the West to East coasts of Canada. Furthermore, this restriction is relevant as first and second year of university is a time of transition when anxiety has been shown to increase (LeBlanc et al., 2020). A third strength of the sample is that we restricted participation to those within the developmentally important years of emerging adulthood (ages 18-25 years; Arnett, 2000). This is a strength as emerging adulthood has been shown to be a time of many transitions and new experiences, including increased exposure to substance use (Arnett, 2000; Sussman & Arnett, 2014), and is a time of increased risk for developing symptoms along the psychosis continuum (Moe & Breitborde, 2019). Given cannabis' popularity among Canadian emerging adult undergraduates (Health Canada, 2021, May) and its evidenced links to the development

of mental health (e.g., anxiety [Duperrouzel et al., 2018; Hayatbakhsh et al., 2007], psychosis continuum [Di Forti et al., 2019; Hasan et al., 2020; Robinson et al., 2022; Sideli et al., 2020]), and substance use problems (e.g., cannabis use disorder; APA, 2022; Health Canada, 2021, May), emerging adulthood is a specific time period worth investigating.

Lastly, seeing as this research made use of archival survey data (i.e., the UniVenture study protocol and procedures were already in place and recruitment was underway well before the conceptualization of the included studies), a priori sample size and power calculations could not be completed. However, due to the large sample sizes of both studies, they are each believed to be appropriately powered. This was assessed using Kline's (2016) 20-case-per-parameter rule-of-thumb. For example, as mentioned in Chapter 2, the simple mediation model of Study 1 required only 180 participants to achieve 80% power. Therefore, we concluded that our larger sample of 1,266 participants had enough power to detect direct/indirect effects and any moderation of those effects by biological sex should the hypothesized moderation truly be taking place in the population. In Study 2, we had a more complicated model with two chained mediators and a total of 13 parameters to estimate. Kline's (2016) rule-of-thumb suggests that a sample size of 260 participants would be required to achieve 80% power. As our sample of 413 participants was larger than this estimation, like Study 1, we concluded that we had enough power to detect sex moderation of the chained anxiety-mediational model.

Limitations

As mentioned previously, a primary limitation of this thesis is the use of cross-sectional survey data to test mediational models, prohibiting causal inference. This means

that while Study 1 is consistent with a substance-induced anxiety-enhancement process from cannabis use to PLEs through anxiety and Study 2 is consistent with a self-medication process from PLEs to cannabis-related problems through anxiety and anxiety coping motives for cannabis use, these directions of effects are not certain. Additionally, the design of Study 1 precluded the parsing out of the effects of cannabis and alcohol co-use (Linden-Carmichael & Wardell, 2021), which was shown to be occurring in 26.5% of our total sample. Although alcohol use frequency was controlled for in analyses, this does not account for when the two substances are used together (i.e., where cannabis and alcohol may have additive or synergistic effects; Linden-Carmichael & Wardell, 2021). Thus, we cannot be certain that the observed effects in Study 1 were due to cannabis use only. Future studies ought to employ longitudinal research designs to replicate these results over time, allowing for the testing of possible bidirectional influences and the development of a vicious cycle as alluded to in these early results. Future work should also attempt to parse out the presumed differential effects of cannabis use alone versus cannabis co-used with alcohol on the development of mental health problems like anxiety and PLEs.

A further limitation is that our reported effect sizes (R^2 values), which represent the proportion of variance in the dependent variable that can be explained by the independent variables, were small, so again we cannot be certain of our conclusions. While effect sizes of small magnitude tend to limit the impact of the findings for changing current practice, some (e.g., Götz et al., 2022) argue that any individual cause of a complex psychological phenomenon is likely to have only a small effect, and that replicated small effects together can contribute to a cumulative understanding of complex

phenomena such as the association between cannabis use and PLEs. Should future studies replicate our achieved effects, we may more reliably recommend the implementation of changes to current practice described previously.

The battery of questionnaires given to participants of the UniVenture project did not include items that would capture more clinically relevant variables such as age of onset of cannabis use, participant's family histories of substance use or psychosis, or their personal and family histories of trauma. These types of variables could dramatically impact one's relationship with substances and the development of mental health- and substance-related problems (Kiburi et al., 2021). Furthermore, participants may have been experiencing other psychiatric symptoms which may have confounded results. Future work would benefit from gathering more of this information, and controlling for in analyses, to provide greater context to our sample and to allow for a more nuanced interpretation of results.

The GAD-7 scale (Spitzer et al., 2006) was originally validated to inquire about symptoms experienced over the past two weeks. In this thesis, however, the GAD-7 was used to measure participant's frequency of anxiety symptoms over the past three months. This change in timeframe was due to my thesis studies being embedded within a clinical trial (UniVenture), which captured all measurements within a past-three-months timeframe. Extending the timeframe for which we asked participants to recall their anxiety symptoms may be a limitation that could have impacted results as the GAD-7 questionnaire may not be as reliable or valid for longer periods of time, and participant's ability to recall their symptoms over longer durations may be limited. Future studies might consider the use of measures validated for use within the timeframe of interest.

Lastly, in both studies of this thesis, our samples were predominantly female. Unequal group sizes across sexes may have impacted our ability to determine if the simple and chained mediational models were indeed moderated by sex. Furthermore, it is for this reason that the results of this thesis may ultimately be most applicable to female emerging adult undergraduates who use cannabis.

Future Directions

This thesis represents an early step for identifying the psychological mechanisms of action underlying the commonly observed trajectories between cannabis use variables and psychotic-like experiences (PLEs). As previously discussed, this work has limitations that may inform the design and conduct of future studies. For example, this work ought to be replicated in longitudinal research designs and analyzed through cross-lagged panel analyses to test the theorized bidirectional effects. Future studies should also attempt to parse out the effects of cannabis alone and cannabis-alcohol co-use. The reported associations should also be replicated using data collected after the termination of the COVID-19 pandemic to determine if there are lasting effects of the pandemic such as the continued elevation of cannabis use in females and the high rates of anxiety/PLEs in emerging adults overall. The UniVenture Questionnaire Battery is already quite lengthy, taking approximately 45 minutes to complete (Yunus et al., 2022). Future research must consider if the benefits of adding further clinically relevant questionnaires outweigh the possible fatigue that respondents may experience if the length of the questionnaire battery was extended, also possibly increasing the amount of compensation required per participant. Furthermore, future work should strive to recruit large equal samples of

males and females to more reliably confirm that these hypothesized mediational models are not moderated by biological sex.

Conclusion

In conclusion, my Masters' thesis succeeded in providing early support for two anxiety-mediated models of the links between cannabis variables and psychotic-like experiences (PLEs) in a multi-site sample of Canadian emerging adult undergraduate students. Through this research, I determined that anxiety symptoms (and related coping motives) indeed appear to be relevant targets for interventions aimed at helping cannabis-using emerging adult undergraduates to mitigate their risks of developing cannabis-related mental health and substance use problems such as PLEs or cannabis use disorder, respectively. Furthermore, the results of this thesis suggest anxiety variables are important targets for earlier psychosis risk reduction among undergraduates regardless of their sex. Once replicated longitudinally, this thesis may have clinical implications for both the future iterations of the UniVenture program questionnaires and workshops, and for the services offered by psychology clinics and Student Affairs/Health Services offices on Canadian university campuses (i.e., tailored focus to those highly anxious cannabis users with PLEs and maladaptive related coping strategies).

REFERENCES

Adams, K. L., Saunders, K. E., Keown-Stoneman, C. D. G., & Duffy, A. C. (2021). Mental health trajectories in undergraduate students over the first year of university: A longitudinal cohort study. *BMJ Open*, *11*(12), e047393. https://doi.org/10.1136/bmjopen-2020-047393

Addington, J., Case, N., Saleem, M. M., Auther, A. M., Cornblatt, B. A., & Cadenhead, K. S. (2014). Substance use in clinical high risk for psychosis: A review of the literature. *Early Intervention in Psychiatry*, *8*(2), 104–112. https://doi.org/10.1111/eip.12100

Allan, N. P., Albanese, B. J., Norr, A. M., Zvolensky, M. J., & Schmidt, N. B. (2015). Effects of anxiety sensitivity on alcohol problems: Evaluating chained mediation through generalized anxiety, depression and drinking motives: Mechanisms of anxiety sensitivity and alcohol. *Addiction*, *110*(2), 260–268. https://doi.org/10.1111/add.12739

Allen, M. S., Iliescu, D., & Greiff, S. (2022). Single item measures in psychological science. *European Journal of Psychological Assessment*, *38*(1), 1–5. https://doi.org/10.1027/1015-5759/a000699

American Psychiatric Association (1994). *Diagnostic and statistical manual of mental disorders: DSM-IV* (4th ed.). American Psychiatric Association Publishing.

American Psychiatric Association (2013). *Diagnostic and statistical manual of mental disorders: DSM-5* (5th ed.). American Psychiatric Association Publishing.

American Psychiatric Association. (2022). *Diagnostic and statistical manual of mental disorders: DSM-5-TR* (5th ed., text revision.). American Psychiatric Association Publishing.

Andréasson, S., Engström, A., Allebeck, P., & Rydberg, U. (1987). Cannabis and schizophrenia: A longitudinal study of Swedish conscripts. *The Lancet*, *330*(8574), 1483–1486. https://doi.org/10.1016/S0140-6736(87)92620-1

Arnett, J. J. (2000). Emerging adulthood: A theory of development from the late teens through the twenties. *American Psychologist*, *55*(5), 469–480. https://doi.org/10.1037/0003-066X.55.5.469

Arnett, J. J. (2004). Emerging adulthood: The winding road from the late teens through the twenties. New York: Oxford University Press.

Asselin, A., Lamarre, O. B., Chamberland, R., McNeil, S.-J., Demers, E., & Zongo, A. (2022). A description of self-medication with cannabis among adults with legal access to cannabis in Quebec, Canada. *Journal of Cannabis Research*, *4*(1), 26. https://doi.org/10.1186/s42238-022-00135-y

Aston, E. R., & Meshesha, L. Z. (2020). Assessing cannabis demand: A comprehensive review of the Marijuana Purchase Task. *Neurotherapeutics*, *17*(1), 87–99. https://doi.org/10.1007/s13311-019-00819-z

Ayesa-Arriola, R., de la Foz, V. O.-G., Setién-Suero, E., Ramírez-Bonilla, M. L., Suárez-Pinilla, P., Son, J. M., Vázquez-Bourgon, J., Juncal-Ruiz, M., Gómez-Revuelta, M., Tordesillas-Gutiérrez, D., & Crespo-Facorro, B. (2020). Understanding sex differences in long-term outcomes after a first episode of psychosis. *Npj Schizophrenia*, *6*(1), Article 1. https://doi.org/10.1038/s41537-020-00120-5

Bados, A., Gómez-Benito, J., & Balaguer, G. (2010). The State-Trait Anxiety Inventory, Trait Version: Does it really measure anxiety? *Journal of Personality Assessment*, *92*(6), 560–567. https://doi.org/10.1080/00223891.2010.513295

Barajas, A., Ochoa, S., Obiols, J. E., & Lalucat-Jo, L. (2015). Gender differences in individuals at high-risk of psychosis: A comprehensive literature review. *The Scientific World Journal*, *2015*, e430735. https://doi.org/10.1155/2015/430735

Bartel, S., Sherry, S., Mahu, I., & Stewart, S. (2023). Development of Brief Alcohol and Cannabis Motives Measures: Psychometric evaluation using expert feedback and longitudinal methods. *Cannabis*, *6*(1), 34–49. doi:10.26828/cannabis/2023.01.004

Bartel, S. J., Sherry, S. B., & Stewart, S. H. (2020). Self-isolation: A significant contributor to cannabis use during the COVID-19 pandemic. *Substance Abuse*, *41*(4), 409–412. doi:10.1080/08897077.2020.1823550

Bernusky, H. C. R., Tibbo, P. G., Conrod, P. J., Yunus, F., Keough, M. T., Thompson, K. D., Krank, M. D., Hadwin, A. F., & Stewart, S. H. (2023). Do anxiety symptoms mediate the association between cannabis use frequency and psychotic-like experiences in emerging adult undergraduates? *The Canadian Journal of Psychiatry*. doi:10.1177/07067437231176900

Bernusky, H. C. R., Tibbo, P. G., Conrod, P. J., Yunus, F. M., Keough, M. T., Thompson, K. D., Krank, M. D., Hadwin, A. F., & Stewart, S. H. (under review). Do anxiety symptoms and coping motives serially mediate the association between psychotic-like experiences and cannabis-related problems in emerging adult undergraduates? *Addictive Behaviors.*

Bourgin, J., Tebeka, S., Mallet, J., Mazer, N., Dubertret, C., & Le Strat, Y. (2020). Prevalence and correlates of psychotic-like experiences in the general population. *Schizophrenia Research*, *215*, 371–377. https://doi.org/10.1016/j.schres.2019.08.024

Bresin, K., & Mekawi, Y. (2019). Do marijuana use motives matter? Meta-analytic associations with marijuana use frequency and problems. *Addictive Behaviors*, *99*, 106102. https://doi.org/10.1016/j.addbeh.2019.106102

Bush, K., Kivlahan, D. R., McDonell, M. B., Fihn, S. D., Bradley, K. A., & for the Ambulatory Care Quality Improvement Project (ACQUIP). (1998). The AUDIT Alcohol Consumption Questions (AUDIT-C): An effective brief screening test for problem drinking. *Archives of Internal Medicine*, *158*(16), 1789–1795. https://doi.org/10.1001/archinte.158.16.1789

Cain, M. K., Zhang, Z., & Bergeman, C. S. (2018). Time and other considerations in mediation design. *Educational and Psychological Measurement*, *78*(6), 952–972. https://doi.org/10.1177/0013164417743003

Canadian Alliance of Student Associations. (2022, September 25). *The new abnormal: Student mental health two years into COVID-19.* https://www.casa-acae.com/the_new_abnormal_report

Carney, R., Cotter, J., Firth, J., Bradshaw, T., & Yung, A. R. (2017). Cannabis use and symptom severity in individuals at ultra-high risk for psychosis: A meta-analysis. *Acta Psychiatrica Scandinavica*, *136*(1), 5–15. https://doi.org/10.1111/acps.12699

Chapman, C., Slade, T., Swift, W., Keyes, K., Tonks, Z., & Teesson, M. (2017). Evidence for sex convergence in prevalence of cannabis use: A systematic review and meta-regression. *Journal of Studies on Alcohol and Drugs*, *78*(3), 344–352. https://doi.org/10.15288/jsad.2017.78.344

Charlebois, S., Music, J., Sterling, B., & Somogyi, S. (2020). Edibles and Canadian consumers' willingness to consider recreational cannabis in food or beverage products: A second assessment. *Trends in Food Science & Technology*, *98*, 25–29. https://doi.org/10.1016/j.tifs.2019.12.025

Chilcoat, H. D., & Breslau, N. (1998). Investigations of causal pathways between ptsd and drug use disorders. *Addictive Behaviors*, *23*(6), 827–840. https://doi.org/10.1016/S0306-4603(98)00069-0

Chinneck, A., Thompson, K., Dobson, K. S., Stuart, H., Teehan, M., Stewart, S. H., & The Caring Campus Team. (2018). Neurotic personality traits and risk for adverse alcohol outcomes: Chained mediation through emotional disorder symptoms and drinking to cope. *Substance Use & Misuse*, *53*(10), 1730–1741. https://doi.org/10.1080/10826084.2018.1432647

Collins, R. L., Vincent, P. C., Yu, J., Liu, L., & Epstein, L. H. (2014). A behavioral economic approach to assessing demand for marijuana. *Experimental and Clinical Psychopharmacology*, *22*(3), 211–221. https://doi.org/10.1037/a0035318

Comeau, N., Stewart, S. H., & Loba, P. (2001). The relations of trait anxiety, anxiety sensitivity, and sensation seeking to adolescents' motivations for alcohol, cigarette, and marijuana use. *Addictive Behaviors*, *26*(6), 803–825. https://doi.org/10.1016/S0306-4603(01)00238-6

Commonwealth of Pennsylvania. (2023). *Getting medical marijuana in Pennsylvania.* https://www.pa.gov/guides/pennsylvania-medical-marijuana-program/

Cooper, Z. D., & Craft, R. M. (2018). Sex-dependent effects of cannabis and cannabinoids: A translational perspective. *Neuropsychopharmacology*, *43*(1), 34–51. https://doi.org/10.1038/npp.2017.140

Cooper, M. L. (1994). Motivations for alcohol use among adolescents: Development and validation of a four-factor model. *Psychological Assessment*, *6*(2), 117–128. https://doi.org/10.1037/1040-3590.6.2.117

Cooper, M. L., Kuntsche, E., Levitt, A., Barber, L. L., & Wolf, S. (2015). *Motivational Models of Substance Use* (K. J. Sher, Ed.; Vol. 1). Oxford University Press. https://doi.org/10.1093/oxfordhb/9780199381678.013.017

Copeland, W. E., Angold, A., Shanahan, L., & Costello, E. J. (2014). Longitudinal patterns of anxiety from childhood to adulthood: The Great Smoky Mountains study. *Journal of the American Academy of Child & Adolescent Psychiatry*, *53*(1), 21–33. https://doi.org/10.1016/j.jaac.2013.09.017

Costello, A. J., Edelbrock, C. S., Kalas, R., Kessler, M. K., & Klaric, S. A. (1982). *NIMH Diagnostic Interview Schedule for Children: Child Version (DIS-C).* Bethesda, MD: National Institute of Mental Health.

Crippa, J. A., Zuardi, A. W., Martín-Santos, R., Bhattacharyya, S., Atakan, Z., McGuire, P., & Fusar-Poli, P. (2009). Cannabis and anxiety: A critical review of the evidence. *Human Psychopharmacology: Clinical and Experimental*, *24*(7), 515–523. https://doi.org/10.1002/hup.1048

Crocker, C. E., & Tibbo, P. G. (2018). The interaction of gender and cannabis in early phase psychosis. *Schizophrenia Research*, *194*, 18–25. https://doi.org/10.1016/j.schres.2017.04.046

Cuttler, C., Mischley, L. K., & Sexton, M. (2016). Sex differences in cannabis use and effects: A cross-sectional survey of cannabis users. *Cannabis and Cannabinoid Research*, *1*(1), 166–175. https://doi.org/10.1089/can.2016.0010

Degenhardt, L., Saha, S., Lim, C. C. W., Aguilar-Gaxiola, S., Al-Hamzawi, A., Alonso, J., Andrade, L. H., Bromet, E. J., Bruffaerts, R., Caldas-de-Almeida, J. M., de Girolamo, G., Florescu, S., Gureje, O., Haro, J. M., Karam, E. G., Karam, G., Kovess-Masfety, V., Lee, S., Lepine, J.-P., … Collaborators, on behalf of the W. W. M. H. S. (2018). The associations between psychotic experiences and substance use and substance use disorders: Findings from the World Health Organization World Mental Health surveys. *Addiction*, *113*(5), 924–934. https://doi.org/10.1111/add.14145

Di Forti, M., Quattrone, D., Freeman, T. P., Tripoli, G., Gayer-Anderson, C., Quigley, H., Rodriguez, V., Jongsma, H. E., Ferraro, L., La Cascia, C., La Barbera, D., Tarricone, I., Berardi, D., Szöke, A., Arango, C., Tortelli, A., Velthorst, E., Bernardo, M., Del-Ben, C. M., … van der Ven, E. (2019). The contribution of cannabis use to variation in the incidence of psychotic disorder across Europe (EU-GEI): A multicentre case-control study. *The Lancet Psychiatry*, *6*(5), 427–436. https://doi.org/10.1016/S2215-0366(19)30048-3

Di Forti, M., Sallis, H., Allegri, F., Trotta, A., Ferraro, L., Stilo, S. A., Marconi, A., La Cascia, C., Reis Marques, T., Pariante, C., Dazzan, P., Mondelli, V., Paparelli, A., Kolliakou, A., Prata, D., Gaughran, F., David, A. S., Morgan, C., Stahl, D., … Murray, R. M. (2014). Daily use, especially of high-potency cannabis, drives the earlier onset of psychosis in cannabis users. *Schizophrenia Bulletin*, *40*(6), 1509–1517. https://doi.org/10.1093/schbul/sbt181

Dozois, D. J. A. & Mental Health Research Canada. (2021). Anxiety and depression in Canada during the COVID-19 pandemic: A national survey. *Canadian Psychology/Psychologie Canadienne*, *62*(1), 136–142. https://doi.org/10.1037/cap0000251

Dunaief, R., Bravo, A. J., & Henson, J. (2023). Changes in mental health as a predictor of cannabis coping motives and consequences: Examining the impact of COVID-19 among college students. *Cannabis*. https://publications.sciences.ucf.edu/cannabis/index.php/Cannabis/article/view/163

Duperrouzel, J., Hawes, S. W., Lopez-Quintero, C., Pacheco-Colón, I., Comer, J., & Gonzalez, R. (2018). The association between adolescent cannabis use and anxiety: A parallel process analysis. *Addictive Behaviors*, *78*, 107–113. https://doi.org/10.1016/j.addbeh.2017.11.005

Endler, N. S., & Kocovski, N. L. (2001). State and trait anxiety revisited. *Journal of Anxiety Disorders*, *15*(3), 231–245. https://doi.org/10.1016/S0887-6185(01)00060-3

Ferdinand, R. F., Sondeijker, F., Van Der Ende, J., Selten, J.-P., Huizink, A., & Verhulst, F. C. (2005). Cannabis use predicts future psychotic symptoms, and vice versa. *Addiction*, *100*(5), 612–618. https://doi.org/10.1111/j.1360-0443.2005.01070.x

Fischer, B., Hall, W., Fidalgo, T. M., Hoch, E., Foll, B. L., Medina-Mora, M.-E., Reimer, J., Tibbo, P. G., & Jutras-Aswad, D. (2023). Recommendations for reducing the risk of cannabis use-related adverse psychosis outcomes: A public mental health-oriented evidence review. *Journal of Dual Diagnosis*, *19*(2–3), 71–96. https://doi.org/10.1080/15504263.2023.2226588

Gage, S. H., Jones, H. J., Burgess, S., Bowden, J., Smith, G. D., Zammit, S., & Munafò, M. R. (2017). Assessing causality in associations between cannabis use and schizophrenia risk: A two-sample Mendelian randomization study. *Psychological Medicine*, *47*(5), 971–980. https://doi.org/10.1017/S0033291716003172

Germain, M., Guyon, L., Landry, M., Tremblay, J., Brunelle, N., & Bergeron, J. (2003). Grille de dépistage de consommation problématique d'alcool et de drogues chez les adolescents et les adolescentes – DEP-ADO, Version 3.1. *Montréal, QC: Recherche et intervention sur les substances psychoactives - Québec (RISQ)*. https://apimed-pl.org/contenu/uploads/2019/11/Grille-RISQ.2003-d%C3%A9pistage-alcool-drogues-ado.pdf

Gill, K. E., Poe, L., Azimov, N., Ben-David, S., Vadhan, N. P., Girgis, R., Moore, H., Cressman, V., & Corcoran, C. M. (2015). Reasons for cannabis use among youths at ultra-high risk for psychosis. *Early Intervention in Psychiatry*, *9*(3), 207–210. https://doi.org/10.1111/eip.12112

Gobbi, G., Atkin, T., Zytynski, T., Wang, S., Askari, S., Boruff, J., Ware, M., Marmorstein, N., Cipriani, A., Dendukuri, N., & Mayo, N. (2019). Association of cannabis use in adolescence and risk of depression, anxiety, and suicidality in young adulthood: A systematic review and meta-analysis. *JAMA Psychiatry*, *76*(4), 426. https://doi.org/10.1001/jamapsychiatry.2018.4500

Goodman, R. (1997). The Strengths and Difficulties Questionnaire: A research note. *Journal of Child Psychology and Psychiatry, and Allied Disciplines, 38*(5), 581–586. https://doi.org/10.1111/j.1469-7610.1997.tb01545.x

Götz, F. M., Gosling, S. D., & Rentfrow, P. J. (2022). Small effects: The indispensable foundation for a cumulative psychological science. *Perspectives on Psychological Science*, *17*(1), 205–215. https://doi.org/10.1177/1745691620984483

Government of Canada. (2018, August 6). *Is cannabis safe to use? Facts for young adults aged 18-25 years.* https://www.canada.ca/en/health-canada/services/publications/drugs-health-products/is-cannabis-safe-use-facts-young-adults.html

Government of Canada. (2022). *Cannabis use for non-medical purposes among Canadians (aged 16+).* https://health-infobase.canada.ca/cannabis/index.html

Grant, V. V., Stewart, S. H., O'Connor, R. M., Blackwell, E., & Conrod, P. J. (2007). Psychometric evaluation of the five-factor Modified Drinking Motives Questionnaire—Revised in undergraduates. *Addictive Behaviors*, *32*(11), 2611–2632. https://doi.org/10.1016/j.addbeh.2007.07.004

Hasan, A., Von Keller, R., Friemel, C. M., Hall, W., Schneider, M., Koethe, D., Leweke, F. M., Strube, W., & Hoch, E. (2020). Cannabis use and psychosis: A review of reviews. *European Archives of Psychiatry and Clinical Neuroscience*, *270*(4), 403–412. https://doi.org/10.1007/s00406-019-01068-z

Hayatbakhsh, M. R., Najman, J. M., Jamrozik, K., Mamun, A. A., Alati, R., & Bor, W. (2007). Cannabis and anxiety and depression in young adults: A large prospective study. *Journal of the American Academy of Child & Adolescent Psychiatry*, *46*(3), 408–417. https://doi.org/10.1097/chi.0b013e31802dc54d

Hayes, A. F. (2022). *Introduction to mediation, moderation, and conditional process analysis a regression-based approach* (3rd ed.). The Guilford Press.

Hayes, A. F., & Rockwood, N. J. (2017). Regression-based statistical mediation and moderation analysis in clinical research: Observations, recommendations, and implementation. *Behaviour Research and Therapy*, *98*, 39–57. https://doi.org/10.1016/j.brat.2016.11.001

Health Canada. (2021). *Canadian cannabis survey 2021: Summary. 2021.* https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/research-data/canadian-cannabis-survey-2021-summary.html

Health Canada. (2021, May 10). *Canadian postsecondary education alcohol and drug use survey, 2019/2020.* https://health-infobase.canada.ca/alcohol/cpads/

Health Canada. (2022). *Canadian cannabis survey 2022: Summary. 2022.* https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/research-data/canadian-cannabis-survey-2022-summary.html

Hosseini, S., & Oremus, M. (2019). The effect of age of initiation of cannabis use on psychosis, depression, and anxiety among youth under 25 years. *The Canadian Journal of Psychiatry*, *64*(5), 304–312. https://doi.org/10.1177/0706743718809339

Humeniuk, R. E., Henry-Edwards, S., Ali, R. L., Poznyak, V., & Monteiro, M. G. (2010). *The Alcohol, Smoking and Substance Involvement Screening Test (ASSIST): Manual for use in primary care*. Geneva, World Health Organization.

IBM Corp. (2021). *IBM SPSS Statistics for Macintosh* (Version 28.0). IBM Corp.

Isaksson, J., Angenfelt, M., Frick, M. A., Olofsdotter, S., & Vadlin, S. (2022). Psychotic-like experiences from adolescence to adulthood: A longitudinal study. *Schizophrenia Research*, *248*, 1–7. https://doi.org/10.1016/j.schres.2022.07.010

Johnson, E. C., Colbert, S. M. C., Jeffries, P. W., Tillman, R., Bigdeli, T. B., Karcher, N. R., Chan, G., Kuperman, S., Meyers, J. L., Nurnberger, J. I., Plawecki, M. H., Degenhardt, L., Martin, N. G., Kamarajan, C., Schuckit, M. A., Murray, R. M., Dick, D. M., Edenberg, H. J., D'Souza, D. C., … Agrawal, A. (2023). Associations between cannabis use, polygenic liability for schizophrenia, and cannabis-related experiences in a sample of cannabis users. *Schizophrenia Bulletin*, *49*(3), 778–787. https://doi.org/10.1093/schbul/sbac196

Johnson, T. P. (2014). Sources of error in substance use prevalence surveys. *International Scholarly Research Notices*, *2014*, e923290. https://doi.org/10.1155/2014/923290

Johnson, T., & Fendrich, M. (2005). Modeling sources of self-report bias in a survey of drug use epidemiology. *Annals of Epidemiology*, *15*(5), 381–389. https://doi.org/10.1016/j.annepidem.2004.09.004

Kafali, H. Y., Turan, S., Akpınar, S., Mutlu, M., Özkaya Parlakay, A., Çöp, E., & Toulopoulou, T. (2022). Correlates of psychotic like experiences (PLEs) during pandemic: An online study investigating a possible link between the SARS-CoV-2 infection and PLEs among adolescents. *Schizophrenia Research*, *241*, 36–43. https://doi.org/10.1016/j.schres.2021.12.049

Karcher, N. R., Barch, D. M., Demers, C. H., Baranger, D. A. A., Heath, A. C., Lynskey, M. T., & Agrawal, A. (2019). Genetic predisposition vs individual-specific processes in the association between psychotic-like experiences and cannabis use. *JAMA Psychiatry*, *76*(1), 87–94. https://doi.org/10.1001/jamapsychiatry.2018.2546

Kedzior, K. K., & Laeber, L. T. (2014). A positive association between anxiety disorders and cannabis use or cannabis use disorders in the general population—A meta-analysis of 31 studies. *BMC Psychiatry*, *14*, 136. http://dx.doi.org/10.1186/1471-244X-14-136

Kelleher, I., & Cannon, M. (2011). Psychotic-like experiences in the general population: Characterizing a high-risk group for psychosis. *Psychological Medicine*, *41*(1), 1–6. https://doi.org/10.1017/S0033291710001005

Khantzian, E. J. (1985). The self-medication hypothesis of addictive disorders: Focus on heroin and cocaine dependence. *American Journal of Psychiatry, 142*(11), 1259–1264. doi:10.1176/ajp.142.11.1259

Khantzian, E. J. (1997). The self-medication hypothesis of substance use disorders: A reconsideration and recent applications. *Harvard Review of Psychiatry*, *4*(5), 231–244. https://doi.org/10.3109/10673229709030550

Kiburi, S. K., Molebatsi, K., Ntlantsana, V., & Lynskey, M. T. (2021). Cannabis use in adolescence and risk of psychosis: Are there factors that moderate this relationship? A systematic review and meta-analysis. *Substance Abuse*, 1–25. https://doi.org/10.1080/08897077.2021.1876200

Kline, R. B. (2016). *Principles and practice of structural equation modeling* (4th ed.). The Guilford Press.

Knapp, A. A., Allan, N. P., Cloutier, R., Blumenthal, H., Moradi, S., Budney, A. J., & Lord, S. E. (2021). Effects of anxiety sensitivity on cannabis, alcohol, and nicotine use among adolescents: Evaluating pathways through anxiety, withdrawal symptoms, and coping motives. *Journal of Behavioral Medicine*, *44*(2), 187–201. https://doi.org/10.1007/s10865-020-00182-x

Landry, M., Tremblay, J., Guyon, L., Bergeron, J., & Brunelle, N. (2005). La Grille de dépistage de la consommation problématique d'alcool et de drogues chez les adolescents et les adolescentes (DEP-ADO): Développement et qualités psychométriques. *Drogues, santé et société*, *3*(1), 20–37. https://doi.org/10.7202/010517ar

Large, M., Sharma, S., Compton, M. T., Slade, T., & Nielssen, O. (2011). Cannabis use and earlier onset of psychosis: A systematic meta-analysis. *Archives of General Psychiatry*, *68*(6), 555–561. https://doi.org/10.1001/archgenpsychiatry.2011.5

Laurens, K., Hodgins, S., Maughan, B., Murray, R., Rutter, M., & Taylor, E. (2007). Community screening for psychotic-like experiences and other putative antecedents of schizophrenia in children aged 9–12 years. *Schizophrenia Research*, *90*(1–3), 130–146. https://doi.org/10.1016/j.schres.2006.11.006

Laurens, K. R., Hobbs, M. J., Sunderland, M., Green, M. J., & Mould, G. L. (2012). Psychotic-like experiences in a community sample of 8000 children aged 9 to 11 years: An item response theory analysis. *Psychological Medicine*, *42*(7), 1495–1506. https://doi.org/10.1017/S0033291711002108

Laurens, K. R., Tzoumakis, S., Dean, K., Brinkman, S. A., Bore, M., Lenroot, R. K., Smith, M., Holbrook, A., Robinson, K. M., Stevens, R., Harris, F., Carr, V. J., & Green, M. J. (2017). The 2015 Middle Childhood Survey (MCS) of mental health and well-being at age 11 years in an Australian population cohort. *BMJ (Open)*, *7*(6). https://doi.org/10.1136/bmjopen-2017-016244

LeBlanc, N. J., Brown, M., & Henin, A. (2020). Anxiety disorders in emerging adulthood. In *Clinical handbook of anxiety disorders: From theory to practice.* (pp. 157–173). Humana Press/Springer Nature. https://doi.org/10.1007/978-3-030-30687-8_8

Lee, H., Cashin, A. G., Lamb, S. E., Hopewell, S., Vansteelandt, S., VanderWeele, T. J., MacKinnon, D. P., Mansell, G., Collins, G. S., Golub, R. M., McAuley, J. H., & AGReMA group. (2021). A guideline for reporting mediation analyses of randomized trials and observational studies: The AGReMA Statement. *JAMA*, *326*(11), 1045–1056. https://doi.org/10.1001/jama.2021.14075

Li, R., Ma, X., Wang, G., Yang, J., & Wang, C. (2016). Why sex differences in schizophrenia? *Journal of Translational Neuroscience*, *1*(1), 37–42.

Linden-Carmichael, A. N., & Wardell, J. D. (2021). Combined use of alcohol and cannabis: Introduction to the special issue. *Psychology of Addictive Behaviors*, *35*(6), 621–627. https://doi.org/10.1037/adb0000772

Lindgren, M., Numminen, L., Holm, M., Therman, S., & Tuulio-Henriksson, A. (2022). Psychotic-like experiences of young adults in the general population predict mental disorders. *Psychiatry Research*, *312*, 114543. https://doi.org/10.1016/j.psychres.2022.114543

Linscott, R. J., & van Os, J. (2013). An updated and conservative systematic review and meta-analysis of epidemiological evidence on psychotic experiences in children and adults: On the pathway from proneness to persistence to dimensional expression across mental disorders. *Psychological Medicine*, *43*(6), 1133–1149. https://doi.org/10.1017/S0033291712001626

Loewy, R. L., Bearden, C. E., Johnson, J. K., Raine, A., & Cannon, T. D. (2005). The prodromal questionnaire (PQ): Preliminary validation of a self-report screening measure for prodromal and psychotic syndromes. *Schizophrenia Research*, *79*(1), 117–125. https://doi.org/10.1016/j.schres.2005.03.007

MacKinnon, D. P. (2008). *Introduction to statistical mediation analysis*. Taylor & Francis Group.

Mané, A., Fernández-Expósito, M., Bergé, D., Gómez-Pérez, L., Sabaté, A., Toll, A., Diaz, L., Diez-Aja, C., & Perez, V. (2015). Relationship between cannabis and psychosis: Reasons for use and associated clinical variables. *Psychiatry Research*, *229*(1), 70–74. https://doi.org/10.1016/j.psychres.2015.07.070

Matheson, S. L., Laurie, M., & Laurens, K. R. (2022). Substance use and psychotic-like experiences in young people: A systematic review and meta-analysis. *Psychological Medicine*, 1–15. https://doi.org/10.1017/S0033291722003440

Maxwell, S. E., Cole, D. A., & Mitchell, M. A. (2011). Bias in cross-sectional analyses of longitudinal mediation: Partial and complete mediation under an autoregressive model. *Multivariate Behavioral Research*, *46*(5), 816–841. doi:10.1080/00273171.2011.606716

McGrath, J. J., Saha, S., Al-Hamzawi, A., Alonso, J., Bromet, E. J., Bruffaerts, R., Caldas-de-Almeida, J. M., Chiu, W. T., de Jonge, P., Fayyad, J., Florescu, S., Gureje, O., Haro, J. M., Hu, C., Kovess-Masfety, V., Lepine, J. P., Lim, C. C. W., Mora, M. E. M., Navarro-Mateu, F., … Kessler, R. C. (2015). Psychotic experiences in the general population: A cross-national analysis based on 31,261 respondents from 18 countries. *JAMA Psychiatry*, *72*(7), 697–705. https://doi.org/10.1001/jamapsychiatry.2015.0575

McGrath, J. J., Saha, S., Al-Hamzawi, A., Andrade, L., Benjet, C., Bromet, E. J., Browne, M. O., Almeida, J. M. C. de, Chiu, W. T., Demyttenaere, K., Fayyad, J., Florescu, S., Girolamo, G. de, Gureje, O., Haro, J. M., Have, M. ten, Hu, C., Kovess-Masfety, V., Lim, C. C. W., … Kessler, R. C. (2016). The bidirectional associations between psychotic experiences and DSM-IV mental disorders. *American Journal of Psychiatry*. https://doi.org/10.1176/appi.ajp.2016.15101293

Moe, A. M., & Breitborde, N. J. K. (2019). Psychosis in emerging adulthood: Phenomenological, diagnostic, and clinical considerations. *Evidence-Based Practice in Child and Adolescent Mental Health*, *4*(2), 141–156. https://doi.org/10.1080/23794925.2018.1509032

Moitra, E., Christopher, P. P., Anderson, B. J., & Stein, M. D. (2015). Coping-motivated marijuana use correlates with DSM-5 cannabis use disorder and psychological distress among emerging adults. *Psychology of Addictive Behaviors: Journal of the Society of Psychologists in Addictive Behaviors*, *29*(3), 627–632. https://doi.org/10.1037/adb0000083

Moyser, M. (2020, June 9). *Gender differences in mental health during the COVID-19 pandemic.* https://www150.statcan.gc.ca/n1/pub/45-28-0001/2020001/article/00047-eng.htm

Muthén, L. K., & Muthén, B. O. (2017). *Mplus (version 8).* Los Angeles: Muthén & Muthén; 1998-2017. https://www.statmodel.com/download/usersguide/MplusUserGuideVer_8.pdf

Mylona, S., Triantafyllou, K., Papanikolaou, K., Tzavara, C., Skopeliti, N., & Kolaitis, G. (2022). Psychotic- like experiences (PLEs) and trauma in adolescents: The role of PLEs' persistence and distress in overall psychological burden. *Psychosis*, *14*(3), 270–280. https://doi.org/10.1080/17522439.2021.1961010

National Academies of Sciences, Engineering, and Medicine. (2017). *The health effects of cannabis and cannabinoids: The current state of evidence and recommendations for research.* Washington, DC: The National Academies Press. doi: 10.17226/24625.

Nejati, N., Crocker, C., Kolajova, M., Morrison, J., Simon, P., Sridharan, S., & Tibbo, P. (2021). Examination of the impact of COVID-19 public health quarantine measures on acute mental health care services: A retrospective observational study. *Psychiatry Research*, *302*, 113999. https://doi.org/10.1016/j.psychres.2021.113999

Ochoa, S., Usall, J., Cobo, J., Labad, X., & Kulkarni, J. (2012). Gender differences in schizophrenia and first-episode psychosis: A comprehensive literature review. *Schizophrenia Research and Treatment*, *2012*, 916198. https://doi.org/10.1155/2012/916198

O'Laughlin, K. D., Martin, M. J., & Ferrer, E. (2018). Cross-sectional analysis of longitudinal mediation processes. *Multivariate Behavioral Research*, *53*(3), 375–402. https://doi.org/10.1080/00273171.2018.1454822

O'Leary-Barrett, M., Mâsse, B., Pihl, R. O., Stewart, S. H., Séguin, J. R., & Conrod, P. J. (2017). A cluster-randomized controlled trial evaluating the effects of delaying onset of adolescent substance abuse on cognitive development and addiction following a selective, personality-targeted intervention programme: The Co-Venture trial: Adolescent substance use, cognition and addiction. *Addiction*, *112*(10), 1871–1881. https://doi.org/10.1111/add.13876

Pasman, J. A., Verweij, K. J. H., Gerring, Z., Stringer, S., Sanchez-Roige, S., Treur, J. L., Abdellaoui, A., Nivard, M. G., Baselmans, B. M. L., Ong, J.-S., Ip, H. F., van der Zee, M. D., Bartels, M., Day, F. R., Fontanillas, P., Elson, S. L., de Wit, H., Davis, L. K., MacKillop, J., … Vink, J. M. (2018). GWAS of lifetime cannabis use reveals new risk loci, genetic overlap with psychiatric traits, and a causal effect of schizophrenia liability. *Nature Neuroscience*, *21*(9), 1161–1170. https://doi.org/10.1038/s41593-018-0206-1

Pencer, A. (2004). *Adolescent substance use in first episode psychosis: A test of three models*. [Unpublished doctoral dissertation, University of Calgary]. PRISM. https://doi.org/10.11575/PRISM/21147

Pencer, A., & Addington, J. (2008). Reasons for using substances in adolescents with and without psychosis. *Early Intervention in Psychiatry*, *2*(1), 42–44. https://doi.org/10.1111/j.1751-7893.2007.00055.x

Peters, E. R., Joseph, S. A., & Garety, P. A. (1999). Measurement of delusional ideation in the normal population: Introducing the PDI (Peters et al. Delusions Inventory). *Schizophrenia Bulletin*, *25*(3), 553–576. https://doi.org/10.1093/oxfordjournals.schbul.a033401

Poulton, R., Caspi, A., Moffitt, T. E., Cannon, M., Murray, R., & Harrington, H. (2000). Children's Self-Reported Psychotic Symptoms and Adult Schizophreniform Disorder: A 15-Year Longitudinal Study. *Archives of General Psychiatry*, *57*(11), 1053. https://doi.org/10.1001/archpsyc.57.11.1053

Preacher, K. J. (2015). Advances in mediation analysis: A survey and synthesis of new developments. *Annual Review of Psychology*, *66*(1), 825–852. https://doi.org/10.1146/annurev-psych-010814-015258

Prowse, R., Sherratt, F., Abizaid, A., Gabrys, R. L., Hellemans, K. G. C., Patterson, Z. R., & McQuaid, R. J. (2021). Coping with the COVID-19 pandemic: Examining gender differences in stress and mental health among university students. *Frontiers in Psychiatry*, *12*, 650759. https://doi.org/10.3389/fpsyt.2021.650759

Public Health Agency of Canada. (2022, July 28). *Public Health Infobase – Data on COVID-19 in Canada – Open Government Portal.* https://open.canada.ca/data/en/dataset/261c32ab-4cfd-4f81-9dea-7b64065690dc

R Core Team. (2022). *R: A language and environment for statistical computing* (Version 4.2.0). R Foundation for Statistical Computing. 2022. https://www.R-project.org/

Ragazzi, T. C. C., Shuhama, R., Menezes, P. R., & Del-Ben, C. M. (2018). Cannabis use as a risk factor for psychotic-like experiences: A systematic review of non-clinical populations evaluated with the Community Assessment of Psychic Experiences. *Early Intervention in Psychiatry*, *12*(6), 1013–1023. https://doi.org/10.1111/eip.12693

Reeves, L. E., Anglin, D. M., Heimberg, R. G., Gibson, L. E., Fineberg, A. M., Maxwell, S. D., Kerns, C. M., & Ellman, L. M. (2014). Anxiety mediates the association between cannabis use and attenuated positive psychotic symptoms. *Psychiatry Research*, *218*(1–2), 180–186. https://doi.org/10.1016/j.psychres.2014.03.040

Robinson, T., Ali, M. U., Easterbrook, B., Hall, W., Jutras-Aswad, D., & Fischer, B. (2022). Risk-thresholds for the association between frequency of cannabis use and the development of psychosis: A systematic review and meta-analysis. *Psychological Medicine*, 1–11. https://doi.org/10.1017/S0033291722000502

Rotermann, M. (2020). Looking back from 2020, how cannabis use and related behaviours changed in Canada. *Health Reports*, *32*(82), 14. https://www150.statcan.gc.ca/n1/pub/82-003-x/2021004/article/00001-eng.htm

Rothman, K., & Greenland, S. (1998). *Modern epidemiology* (2nd ed.). Lippincott-Raven.

Schofield D, Tennant C, Nash L, Degenhardt L, Cornish A, Hobbs C, & Brennan G. (2006). Reasons for cannabis use in psychosis. *Australian & New Zealand Journal of Psychiatry*, *40*(6/7), 570–574. https://doi.org/10.1080/j.1440-1614.2006.01840.x

Sharpe, L., Sinclair, J., Kramer, A., de Manincor, M., & Sarris, J. (2020). Cannabis, a cause for anxiety? A critical appraisal of the anxiogenic and anxiolytic properties. *Journal of Translational Medicine*, *18*(1), 374. https://doi.org/10.1186/s12967-020-02518-2

Sideli, L., Quigley, H., La Cascia, C., & Murray, R. M. (2020). Cannabis use and the risk for psychosis and affective disorders. *Journal of Dual Diagnosis*, *16*(1), 22–42. https://doi.org/10.1080/15504263.2019.1674991

Simons, J., Correia, C. J., Carey, K. B., & Borsari, B. E. (1998). Validating a five-factor marijuana motives measure: Relations with use, problems, and alcohol motives. *Journal of Counselling Psychology, 45*(3), 265–273. doi:10.1037/0022-0167.45.3.265

Simons, J. S., Dvorak, R. D., Merrill, J. E., & Read, J. P. (2012). Dimensions and severity of marijuana consequences: Development and validation of the Marijuana Consequences Questionnaire (MACQ). *Addictive Behaviors*, *37*(5), 613–621. https://doi.org/10.1016/j.addbeh.2012.01.008

Sobell, L. C., & Sobell, M. B. (1990). Self-report issues in alcohol abuse: State of the art and future directions. *Behavioral Assessment, 12*(1), 77–90.

Solmi, M., Radua, J., Olivola, M., Croce, E., Soardo, L., Salazar de Pablo, G., Il Shin, J., Kirkbride, J. B., Jones, P., Kim, J. H., Kim, J. Y., Carvalho, A. F., Seeman, M. V., Correll, C. U., & Fusar-Poli, P. (2022). Age at onset of mental disorders worldwide: Large-scale meta-analysis of 192 epidemiological studies. *Molecular Psychiatry*, *27*(1), 281–295. https://doi.org/10.1038/s41380-021-01161-7

Spielberger, C. D., Gorsuch, R. L., Lushene, R., Vagg, P. R., & Jacobs, G. A. (1983). *Manual for the State-Trait Anxiety Inventory*. Palo Alto, CA: Consulting Psychologists Press.

Spitzer, R. L., Kroenke, K., Williams, J. B. W., & Löwe, B. (2006). A brief measure for assessing generalized anxiety disorder: The GAD-7. *Archives of Internal Medicine*, *166*(10), 1092. https://doi.org/10.1001/archinte.166.10.1092

Staines, L., Healy, C., Murphy, F., Byrne, J., Murphy, J., Kelleher, I., Cotter, D., & Cannon, M. (2023). Incidence and persistence of psychotic experiences in the general population: Systematic review and meta-analysis. *Schizophrenia Bulletin*, sbad056. https://doi.org/10.1093/schbul/sbad056

Statistics Canada. (2021, September 27). *Survey on COVID-19 and mental health, February to May 2021.* https://www150.statcan.gc.ca/n1/daily-quotidien/210927/dq210927a-eng.pdf

Statistics Canada. (2022, September 28). *Table 17-10-0009-01 Population estimates, quarterly, Q4 October 1, 2021.* https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1710000901

Statistics Canada. (2022, October 18). *Table 37-10-0103-01. Participation rate in education, population aged 18 to 34, by age group and type of institution attended.* https://doi.org/10.25318/3710010301-eng

Stewart, S. H., & Conrod, P. J. (Eds.). (2008). *Anxiety and substance use disorders: The vicious cycle of comorbidity.* Springer Science + Business Media. https://doi.org/10.1007/978-0-387-74290-8

Stewart, S. H., McKee, K., Maguire, K., & Carleton, R. N. (2023, June 1). *Trauma exposure is linked to problematic cannabis use through posttraumatic stress symptoms and cannabis use to cope in Canadian public safety personnel.* [Poster presentation]. Society for Prevention Research (SPR) Annual Meeting, Washington, DC, United States.

Sussman, S., & Arnett, J. J. (2014). Emerging adulthood: Developmental period facilitative of the addictions. *Evaluation & the Health Professions*, *37*(2), 147–155. https://doi.org/10.1177/0163278714521812

Thibault, T., Thompson, K., Keough, M., Krank, M., Conrod, P., Moore, M., & Stewart, S. H. (2023). Psychometric properties of a brief version of the COVID-19 Stress Scales (CSS-B) in young adult undergraduates. *Stress and Health: Journal of the International Society for the Investigation of Stress*, *39*(1), 154–161. https://doi.org/10.1002/smi.3175

United Nations Office on Drugs and Crime. (2023). *World Drug Report 2023*. https://www.unodc.org/unodc/en/data-and-analysis/world-drug-report-2023.html

UniVenture Project. (2023). *About the study.* https://www.univentureproject.org/about

Van Dam, N. T., Bedi, G., & Earleywine, M. (2012). Characteristics of clinically anxious versus non-anxious regular, heavy marijuana users. *Addictive Behaviors*, *37*(11), 1217–1223. https://doi.org/10.1016/j.addbeh.2012.05.021

van Os, J., Linscott, R. J., Myin-Germeys, I., Delespaul, P., & Krabbendam, L. (2009). A systematic review and meta-analysis of the psychosis continuum: Evidence for a psychosis proneness–persistence–impairment model of psychotic disorder. *Psychological Medicine*, *39*(2), 179–195. https://doi.org/10.1017/S0033291708003814

Varghese, D., Scott, J., Welham, J., Bor, W., Najman, J., O'Callaghan, M., Williams, G., & McGrath, J. (2011). Psychotic-like experiences in major depression and anxiety disorders: A population-based survey in young adults. *Schizophrenia Bulletin*, *37*(2), 389–393. https://doi.org/10.1093/schbul/sbp083

Vedelago, L., Wardell, J. D., Kempe, T., Patel, H., Amlung, M., MacKillop, J., & Keough, M. T. (2022). Getting high to cope with COVID-19: Modelling the associations between cannabis demand, coping motives, and cannabis use and problems. *Addictive Behaviors*, *124*, 107092. https://doi.org/10.1016/j.addbeh.2021.107092

VentureLab. (2023). *PsyVenture*. https://www.conrodventurelab.com/projets/psyventure

Wallis, D., Coatsworth, J. D., Mennis, J., Riggs, N. R., Zaharakis, N., Russell, M. A., Brown, A. R., Rayburn, S., Radford, A., Hale, C., & Mason, M. J. (2022). Predicting self-medication with cannabis in young adults with hazardous cannabis use. *International Journal of Environmental Research and Public Health*, *19*(3), 1850. https://doi.org/10.3390/ijerph19031850

Woicik, P. A., Stewart, S. H., Pihl, R. O., & Conrod, P. J. (2009). The substance use risk profile scale: A scale measuring traits linked to reinforcement-specific substance use profiles. *Addictive Behaviors*, *34*(12), 1042–1055. https://doi.org/10.1016/j.addbeh.2009.07.001

Yamasaki, S., Usami, S., Sasaki, R., Koike, S., Ando, S., Kitagawa, Y., Matamura, M., Fukushima, M., Yonehara, H., Foo, J. C., Nishida, A., & Sasaki, T. (2018). The association between changes in depression/anxiety and trajectories of psychotic-like experiences over a year in adolescence. *Schizophrenia Research*, *195*, 149–153. https://doi.org/10.1016/j.schres.2017.10.019

Yunus, F. Md., Livet, A., Mahmoud, A., Moore, M., Murphy, C. B., Nogueira-Arjona, R., Thompson, K., Keough, M. T., Krank, M. D., Conrod, P. J., & Stewart, S. H. (2022). Is anxiety sensitivity associated with COVID-19 related distress and adherence among emerging adults? *Psych*, *4*(4), 934–951. https://doi.org/10.3390/psych4040069

Zvolensky, M. J., Marshall, E. C., Johnson, K., Hogan, J., Bernstein, A., & Bonn-Miller, M. O. (2009). Relations between anxiety sensitivity, distress tolerance, and fear reactivity to bodily sensations to coping and conformity marijuana use motives among young adult marijuana users. *Experimental and Clinical Psychopharmacology*, *17*(1), 31–42. https://doi.org/10.1037/a0014961

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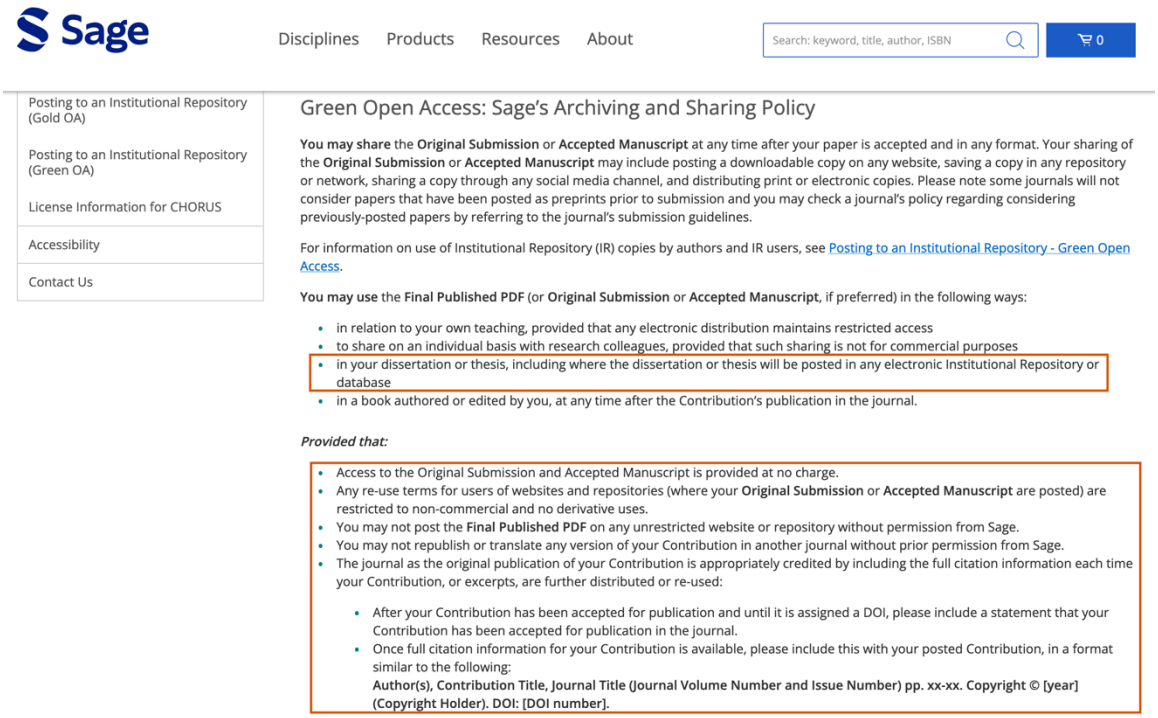

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