

**Cannabis and mental health: prevalence of use, modes of administration, and adverse
outcomes by past 12-month mental health experience in Canada and the US.**

by

Jennifer Rup

A thesis

presented to the University of Waterloo

in fulfilment of the

thesis requirement for the degree of

Master of Science

in

Public Health and Health Systems

Waterloo, Ontario, Canada, 2020

© Jennifer Rup 2020

AUTHOR'S DECLARATION

I hereby declare that I am the sole author of this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

I understand that my thesis may be made electronically available to the public.

ABSTRACT

Background: Cannabis is among the most widely used drugs in the world. Although it is well established that cannabis may have an adverse impact on certain mental health conditions, there is relatively little data on how patterns of cannabis use differ by mental health status. The primary objective of this study was to examine cannabis use among consumers who reported a past 12-month experience of a mental condition, in regard to five specific outcomes: 1) prevalence of cannabis use; 2) types of products used by consumers; 3) medical help-seeking behaviours from adverse effects of cannabis use; 4) patterns of specific adverse health effects experienced; and 5) perceived impact of cannabis on friendships, physical health, mental health, family life, social life, work, and quality of life.

Methods: Data came from the 2018 International Cannabis Policy Study (Wave 1). Online surveys were conducted from Aug 27- Oct 7, 2018 with respondents aged 16-65 from Canada and the US. In Study 1, multinomial regression models examined differences in cannabis use prevalence (no use in the past 12 months/less than monthly/weekly or monthly/daily) among cannabis consumers with and without self-reported past 12-month experience of anxiety, depression, PTSD, bipolar disorder, and psychosis/schizophrenia. Binary logistic regression models tested differences in use of nine cannabis product types (dried herb, oils (oral/vaped), edibles, drinks, concentrates, hash, tinctures, topicals). In Study 2, binary logistic regression models examined differences in medical help-seeking, as well as adverse health effects reported by consumers (nausea, heart problems, dizziness, panic, hallucinations, flashbacks, depression, dissociation). In addition, multinomial models examined seven outcomes related to perceived impact of cannabis use (friendships or social life, physical and mental health, family life, work, studies, quality of life).

Results: In Study 1, respondents with each of the five mental health conditions reported more frequent cannabis use than those without a mental health condition ($p < .01$). Past 12-month cannabis consumers who experienced mental health conditions were also significantly more likely than those without a mental health condition to use the most potent products (solid concentrates, THC vape oils, and hash; $p < .05$), with fewer differences for dried flower, edibles, orally ingested oils, and other forms.

In Study 2, 4.3% of past 12-month consumers reported seeking medical help for an adverse effect of cannabis, particularly for panic, dizziness, and nausea/vomiting. Medical help-seeking was greater among those who experienced psychosis (22.4%: OR= 5.48; 3.20-9.37), bipolar disorder (9.4%: OR= 2.32; 1.44-3.74), and depression (6.0%: OR=1.71; 1.28-2.27). Additionally, 41.5% reported using cannabis to manage symptoms of mental health, with the highest rates among those with bipolar disorder (90.6%) and psychosis (90.8%). Consumers reporting >1 mental health condition were more likely to perceive positive impacts of cannabis use for each of the 7 categories (friendships or social life, physical and mental health, family life, work, studies, quality of life; $p < .001$ for all), whereas consumers with psychosis were most likely to perceive negative health effects across the 7 categories.

Conclusion: Individuals experiencing mental health conditions report more frequent cannabis use and use of more potent product types, despite public health warnings highlighting the potential risks of cannabis use among those susceptible to mental health conditions. For conditions with substantial evidence suggesting cannabis use is harmful (psychosis, bipolar disorder), greater medical help-seeking behaviours and self-perceived negative effects of cannabis use were observed. Consumers with mental health conditions were more likely to perceive cannabis to have a positive effect on their lives than those without. Thus, the

relationship between cannabis use and mental health is complex, disorder specific, and may include a combination of perceived benefits as well as harms.

ACKNOWLEDGEMENTS

I would first like to thank my supervisor, Dr. David Hammond, for his guidance and constant support. I have gained countless new skills through the valuable learning opportunities you have provided. I truly appreciate your commitment to providing exceptional mentorship, and it has been a great privilege to learn from you.

I am also grateful to my committee members- Dr. Tom Freeman and Dr. Chris Perlman- for their expertise, valuable feedback, and contributions to this research.

I would like to thank all the members of the Hammond Lab for their brilliance and encouragement. To my SPHHS friends and colleagues, thank you for your friendship and inspiration.

Finally, to my family and friends– thank you for your endless positivity and for supporting me over these past few years.

TABLE OF CONTENTS

AUTHOR'S DECLARATION	ii
ABSTRACT	iii
ACKNOWLEDGEMENTS	vi
1.0 BACKGROUND	1
1.1 Prevalence of cannabis use	1
1.2 Cannabis properties	1
1.3 Adverse effects & perceived impact of cannabis use	3
1.4 Therapeutic effects of cannabis	4
1.5 Cannabis and mental health conditions	5
1.5.1 Cannabis and psychosis	6
1.5.2 Cannabis and anxiety disorders.....	7
1.5.3 Cannabis and depression.....	8
1.5.4 Cannabis and bipolar disorder.....	9
1.5.5 Cannabis and post-traumatic stress disorder (PTSD).....	9
1.6 Types of cannabis products by mental health	10
2.0 STUDY RATIONALE	11
2.1 Research questions	12
3.0 METHODS	13
3.1 Data source and collection	13
3.2 Study sample	13
3.3 Measures	14
3.3.1 Study 1	15
3.3.2 Study 2.....	17
3.4 Analysis	18
3.4.1 Study 1	19
3.4.2 Study 2.....	20
4.0 RESULTS	23
4.1 Manuscript 1	23
4.2 Manuscript 2	44
5.0 DISCUSSION	69

6.0 STRENGTHS & LIMITATIONS	72
7.0 IMPLICATIONS	74
8.0 CONCLUSION	75
REFERENCES	77
Manuscript 1	85
Manuscript 2	90
APPENDICES	96
Appendix A: Manuscript 1 supplemental file	96
Appendix B: Manuscript 2 supplemental file	101

1.0 BACKGROUND

1.1 Prevalence of cannabis use

Cannabis is the most commonly used drug in the world.¹ In recent years, an increase in the prevalence of cannabis use has been observed in North America, a trend that appears to coincide with the increasing legalization of cannabis.² In Canada, medical cannabis has been legal since 2001, and non-medical cannabis was legalized in October 2018.³ National Cannabis Survey (NCS) data from 2018 revealed that approximately 15% of respondents aged 15 and older reported using cannabis in the past 3 months.⁴ Similar trends of increased use have also been observed in the US, where access to medical cannabis is legal in 33 states and non-medical cannabis is legal in 11 states.⁵ A 2018 national survey of adults aged 18 and over indicated that 16% of respondents used cannabis in the past year.⁶ The legalization of non-medical cannabis and rapid growth of cannabis markets have raised concerns about the public health impact of cannabis, including its use among vulnerable populations.

1.2 Cannabis properties

Cannabis affects the body by interacting with the endocannabinoid system (ECS), which is responsible for internal homeostatic processes. The system is involved in the regulation of many processes including mood, appetite, memory, pain, sleep, and motor control.⁷ In brief, the ECS is comprised of endocannabinoids (which are naturally produced in the body), cannabinoid receptors (such as CB1 and CB2), and enzymes that help break down endocannabinoids and cannabinoids.⁸ It is well established that the ECS plays an important role in emotional homeostasis, including the regulation of mood, anxiety and cognitive function; therefore,

deregulation of the different elements of the ECS through consumption of psychoactive drugs can contribute to the symptomatology of some mental conditions.⁸

The cannabis plant has various subspecies with roughly 100 cannabinoids. Research to date has focused on two primary cannabinoids: delta-9-tetrahydrocannabinol (THC) and cannabidiol (CBD). THC and CBD are structurally similar to endocannabinoids in the brain and body, and thus are able to bind to cannabinoid receptors and alter functions related to the ECS. THC primarily activates the CB1 receptors which are located in the central nervous system.⁸ It is responsible for producing the intoxicating effects of cannabis, which can include a ‘high’ or feelings of euphoria, and can also induce transient psychotic-like effects (e.g., hallucinations, delusions) and cognitive impairment (e.g., difficulty concentrating, disorganized thoughts).⁹ CBD follows a different pattern of activation compared to THC; it has minimal direct action at cannabinoid receptors but it has a broad range of actions both within and beyond the endocannabinoid system.⁷ CBD does not produce any intoxicating effects at typical doses, and is instead associated with potential therapeutic effects, including the treatment of psychotic and substance use disorders.^{10,11,12,13}

CBD and THC can produce opposite effects from each other on brain activation during a range of cognitive processes.¹⁴ Consequently, CBD has been shown to moderate some of the effects of THC when the cannabinoids are combined and administered together. For instance, CBD can reduce the acute effects of THC.¹⁵ Cannabis plant genetics give rise to three types of plant: THC dominant (high THC, low CBD), mixed THC/CBD (moderate THC and moderate CBD) and CBD dominant (high CBD, low THC), and the type of plant used determines the ratio of THC to CBD in cannabis products.¹⁶ The concentrations of THC and CBD in different cannabis products could have important implications for the health effects of cannabis use.

1.3 Adverse effects & perceived impact of cannabis use

Cannabis use can lead to acute adverse health outcomes by inducing unpleasant effects such as confusion, impaired ability to concentrate, anxiety, fear, panic, and psychotic episodes characterized by paranoia, delusions, and hallucinations.^{17,18,19} Cannabis can also induce acute effects for which some consumers seek medical attention, including acute intoxication, nausea and vomiting, cannabis hyperemesis syndrome, gastrointestinal and psychiatric complaints, and acute cardiovascular events.^{20,21,22} An increase in rates of cannabis-related emergency department (ED) visits has been observed over time in Canada and the US, especially among young people.^{23,24} Consumers visiting EDs for adverse effects from cannabis use are more likely to have an existing mental health diagnosis.²⁵ In Canada, the rate of hospitalizations for cannabis-related mental and behavioural disorders doubled between 2006 and 2015, and psychotic disorder was the most common condition among hospitalizations.²⁴ In addition, the proportions of patients with mental health conditions reporting cannabis use prior to admission to inpatient psychiatry in Ontario, Canada has increased between 2007 and 2017, with the greatest increases among those with psychotic disorders and non-cannabis substance use disorders.²⁶

The effects of chronic, long-term cannabis use develop gradually over time and could negatively impact functions related to memory, concentration, and intelligence, and lead to an increased risk of developing respiratory infections, withdrawal syndrome, and cannabis use disorder (CUD).¹⁷ Studies have shown that long-term cannabis use can lead to addiction, where the likelihood of developing an addiction increases among those who start using cannabis during adolescence, and those who smoke cannabis daily.^{18,27,28} An individual's response to cannabis is dependent on many factors such as age, sex, genes, pre-existing medical conditions, frequency and duration of use, previous experience with cannabis, and the potency and type of product

consumed, particularly with respect to the levels of THC and CBD.²⁹ In addition, risk factors for adverse mental health outcomes from cannabis use include frequent use over a long period of time, a younger age of initiation, and a family history of mental conditions.^{29,30}

Cannabis use can have a range of adverse outcomes that impact other areas of life, apart from mental or physical health. Common measures of problematic cannabis use assess the impact on areas such as social life, relationships, work, and school.^{31,32} Overall quality of life (QoL) can also be used to assess an individual's overall sense of health and wellbeing. Some evidence seems to support the existence of a positive dose-response relationship between frequency and amount of cannabis used, and QoL.³³ A systematic review examining the relationships between recreational cannabis use and self-reported QoL in those with and without CUD revealed that CUD is associated with reduced QoL, while abstinence and lower frequency of cannabis use are associated with higher QoL.³⁴ Among individuals with anxiety disorder, a lower QoL score was reported among regular, but not occasional, cannabis users.³⁵ Additionally, research has shown that those with severe mental illness consistently report lower QoL scores compared to the general population.³⁶ Therefore, it is important to further examine the perceived impact of cannabis among consumers who experience mental health conditions.

1.4 Therapeutic effects of cannabis

Research has demonstrated that cannabis and cannabinoids can have therapeutic effects in managing health conditions such as aches and pains, stress, sleep disturbances, and symptoms of some neurological and rheumatic conditions (e.g., multiple sclerosis, epilepsy, arthritis).^{37,38} Strong evidence supports the therapeutic use of cannabis for the alleviation of chronic pain and side effects associated with cancer chemotherapy.^{37,39} Cannabis and cannabinoids can also have the potential to manage symptoms associated psychiatric disorders, although current

evidence focused on recreational users is often contradictory. Varying results could be due to the lack of long-term data, inconsistent outcomes and measures, as well as a lack of evidence on sustained cannabinoid effects (e.g., tolerance, symptoms of withdrawal, cognition, quality of life, level of functioning).⁴⁰ Some studies suggest that cannabis use can alleviate symptoms associated with mental conditions, such as stress, negative mood, irritability, sleep disturbances, and the acute response to fear stimuli associated with PTSD.^{39,41} A systematic review and meta analysis of the effectiveness of medicinal cannabinoids as a treatment method revealed little evidence to suggest that it can improve mental health disorders.⁴² In addition, it has been shown that greater cannabis use can exacerbate the symptoms of psychosis, bipolar disorder, anxiety and depression.⁴³

1.5 Cannabis and mental health conditions

A high prevalence of comorbidity exists between regular cannabis use (weekly or more frequent use over periods of months or years), and the presence of mental conditions. Several theories have been postulated to provide an explanation for the relationship between mental conditions and substance use. The self-medication hypothesis suggests that the presence of a mental condition precedes substance use, and individuals use drugs to alleviate distress and regulate associated unpleasant symptoms.^{44,45} Alternatively, the shared-vulnerability hypothesis posits the idea that substance use can precipitate mental health conditions, as evidence has shown it can increase the risk of developing a condition, particularly with psychotic disorders.^{46,47,48} To fully explore the etiology of substance use within these populations, a multi-dimensional approach including biological, psychosocial, and environmental factors is favoured to conceptualize why those with mental conditions might use cannabis.

Numerous studies have been conducted examining the effect of cannabis on mental health. However, causality has not been established because it is difficult to determine whether cannabis use leads users to experience symptoms of mental conditions, or whether the presence of mental conditions leads to cannabis use.^{30,49} The consensus is that those who are already at risk of developing a mental health condition are more likely to suffer adverse effects from cannabis use, and the acute and long-term effects on mental health are dependent on many factors including age of initiation, frequency of cannabis use, dose and potency of product, duration of use, and individual and genetic differences.³⁰

Regular cannabis use is at least twice as common among individuals with schizophrenia, bipolar disorders, depressive and anxiety disorders, and PTSD, compared to the general population.⁶ National survey data from Canada in 2017 indicated that substance use disorder (patterns of symptoms resulting from continued use of a substance, despite experiencing problems) has a high comorbidity with mental illness.⁵⁰ In addition, rates of cannabis use disorder—defined as a problematic pattern of use leading to clinically significant impairment or distress—are higher among individuals reporting any lifetime psychiatric disorder, mood disorder or anxiety disorder.^{31,51} As described in the following sections, cannabis affects each mental health condition in different ways due to the varying neural pathways and physiological processes involved in different conditions.⁵²

1.5.1 Cannabis and psychosis

Schizophrenia spectrum and other psychotic disorders are characterized by psychosis (cognitive disengagement from reality that may involve delusions or hallucinations), and abnormalities in thinking, emotions, sense of self and behaviour.³¹ Schizophrenia affects approximately 1% of the general population.⁵³ There is substantial evidence linking chronic

cannabis use to an increased risk of developing psychotic disorders and schizophrenia, especially among individuals with an earlier age of initiation, family history, or genetic vulnerability to these conditions.^{27,50,54} Among those with schizophrenia, cannabis use has been shown to lead to earlier onset of psychosis, increased symptom severity, as well as poorer prognosis and quality of life.³⁰ Several longitudinal studies have reported a positive dose-response relationship between frequency of cannabis consumption and the risk of psychosis outcomes in the general population.^{55,56,57} In addition, a systematic review and meta-analyses that examined cannabis use and the risk of psychotic outcomes reported an increased risk of psychosis in individuals who had ever used cannabis compared to non-users.⁴⁷ Research shows that the ECS plays an important role in the pathophysiology of schizophrenia and psychosis.⁵⁸ Clinical studies investigating whether alterations in the cannabinoid system were present in those with schizophrenia have revealed that levels of anandamide (an endocannabinoid that is structurally similar to THC), were higher in the blood of patients with schizophrenia vs. those without.^{58,59} In addition, several studies have identified links between cannabis use and psychosis in those with pre-existing genetic risk factors related to variation in certain genotypes, supporting a biologically plausible association between cannabis use and the development of these conditions.^{60,61,62,63} Mendelian randomisation studies have provided some evidence of a causal role of cannabis use on psychotic disorders, though there is also some evidence that supports reverse causation.^{64,65,66}

1.5.2 Cannabis and anxiety disorders

Anxiety disorders exist in a variety of forms, including generalized anxiety, social anxiety, and panic disorders. The lifetime prevalence of any anxiety disorder in Canada is approximately 25%.⁵³ Studies on cannabis and anxiety disorders mostly focus on generalized

anxiety disorder, which is characterized by excessive worry about events or activities that persists for at least 6 months.^{31,50} Symptoms of generalized anxiety disorder include impaired concentration, restlessness, irritability, fatigue, muscle aches, and difficulty sleeping.³¹ In contrast to the strong association shown for cannabis use and psychosis, evidence is mixed with respect to the link between cannabis use and the development of anxiety disorders.^{50,67} A systematic review and meta-analysis from 10 countries looked at the relationship between anxiety diagnosis and cannabis use, and reported a small positive association between both anxiety and cannabis use, and comorbid anxiety/depression and cannabis use.⁶⁸ In addition, longitudinal studies have reported links between age of initiation of cannabis use and anxiety.⁶⁹ Individuals were more likely to report symptoms of anxiety when cannabis use was initiated before the age of 15 and continued to age 21, although, when controlling for confounding variables (e.g., other substance use, psychiatric illness, demographics), the relationship between anxiety and cannabis use is relatively small.^{70,71,72}

1.5.3 Cannabis and depression

Depression is characterized by persistent depressed mood or lack of interest or pleasure in all or most activities, and includes symptoms such as reduced energy, slowed thought and physical movement, changes in weight and sleep, feelings of worthlessness and guilt, and recurrent suicidal ideation.³¹ The lifetime prevalence of depression in Canada (including major depressive disorder) is 8%.⁵³ Depression and anxiety disorders are highly comorbid, and much like anxiety, research on the association between cannabis use and the development of depressive disorders is mixed. Several meta-analyses and systematic reviews show that cannabis use is associated with an increased risk of developing depression; however, the risk of developing depression among those who use cannabis regularly in the general population is relatively low

after accounting for sociodemographic factors.^{28,71} Evidence suggests that a moderate dose-response relationship exists between cannabis use and depressive symptoms.⁷³ In addition, it has been shown that for individuals younger than 25 years old, greater cannabis use is associated with more severe symptoms of depression, especially among those with a predisposition or existing vulnerability.²⁷

1.5.4 Cannabis and bipolar disorder

Research examining the association between cannabis use and bipolar disorders is limited. Bipolar disorders are typically characterized by periods of mania (symptoms include elevated mood, grandiosity, flights of ideas, distractibility), followed by episodes of depression.³¹ The estimated lifetime prevalence of bipolar disorder in Canada is 1%.⁷⁴ Evidence indicates that cannabis use has a negative impact on the course of the disorder, and heavy cannabis use might trigger the first episode of bipolar disorder.⁷⁵ Cannabis use typically worsens clinical outcomes in those with bipolar disorder, including greater symptom severity and duration of manic phases.^{76,77} National epidemiological surveys conducted in Canada from 2001-2002 revealed that individuals with bipolar disorder are more likely to use cannabis and develop CUD compared to the general population.^{31,78}

1.5.5 Cannabis and post-traumatic stress disorder (PTSD)

Evidence is limited regarding the risk of PTSD from cannabis use. PTSD is characterized by persistent re-experiencing of a traumatic event, either through intrusive memories, flashbacks, or nightmares, accompanied by intense emotional distress and physiological reactivity (e.g., elevated heart rate and blood pressure).³¹ The lifetime prevalence of PTSD in Canada is approximately 9.2%.⁷⁹ Results from longitudinal observational studies indicate that cannabis use among patients with PTSD is associated with poorer mental health outcomes, including

increased symptom severity.^{80,81} In addition, a systematic review of studies that assessed the longitudinal association between cannabis use and mood disorders demonstrates that recent cannabis use (within the last 6 months) was associated with negative outcomes over time among those with PTSD, panic disorder, bipolar disorder, and depressive disorder.⁷¹

1.6 Types of cannabis products by mental health

The rapid growth of legal markets has contributed to an increased availability of cannabis in a wide variety of forms, such as dried herb, edibles, oils, hash or kief, concentrates, drinks, tinctures, and lotions. These products differ in their modes of administration (e.g. smoked, vaporized, or orally ingested), which can have a direct influence on several aspects of the drug reaction, including the intensity of the high, duration of psychoactive effects, and the negative consequences associated with use.⁸² Products also differ in their range of THC and CBD concentrations. In recent years, there has been a shift toward the cultivation and consumption of dried herb with higher THC levels, and cannabis products with greater potencies. For example, the THC concentration of dried flower can range from less than 1% to 30%, whereas cannabis extract products such as oils can exceed 90% THC in many cases.^{39,83} CBD levels also vary across products, ranging from ‘CBD-rich’ products that contain little or no THC, to more ‘balanced’ products with similar concentrations. In Canada, the prevalence of past 12-month product use in 2019 revealed the most commonly used products were dried flower/leaf (77%), edible products (44%), and vape pens/cartridges (26%), and the prevalence of edibles, vaped oils, and orally ingested oils is increasing, particularly among younger consumers.^{4,84} Similarly, a study in the US looked at the prevalence of various modes of cannabis use using data from a 2014 national survey of adults aged 18 and older, and found that combusted modes of cannabis were most prevalent compared to edibles or vaporizers.⁸⁴

In relation to mental health, greater consumption of cannabis products with high levels of THC has been shown to be associated with risk of developing a psychotic disorder, which includes delusions, paranoia and dissociation.^{85,86} High THC products are also associated with an increased risk of relapse after a first episode of psychosis.⁸⁷ A multinational study across 11 sites revealed that daily users of high potency cannabis (10% THC or more) had a five-fold increased risk of psychosis compared to controls, and the prevalence of high potency cannabis use in controls was positively associated with the incidence of psychosis across sites.⁸⁸ Several studies have found more severe symptoms of cannabis use disorder in people using higher potency products; however, the extent to which consumers who experience mental health conditions self-select towards or away from these product categories remains unexplored.^{89,90,91,92}

2.0 STUDY RATIONALE

One of the goals of cannabis legalization in Canada is to minimize any negative public health impact. To achieve this goal, there is a need for greater understanding of the patterns of cannabis use and its health effects on vulnerable populations. A substantial amount of research exists investigating the potential link between cannabis use and the risk of developing or exacerbating symptoms related to certain mental health conditions. The strongest evidence of this link is demonstrated for psychosis and schizophrenia, while findings are mixed for anxiety, depression, bipolar disorder, and PTSD. However, cannabis use among these groups appears to be common. Overall, there is little population-level data and a lack of evidence on key factors related to cannabis use, such as the prevalence of use among mental health sub-populations, types of products used, adverse health effects experienced, and how consumers in these

populations perceive the impact of cannabis use on important indicators such as friendships or social life, physical and mental health, family life, work, studies, and general quality of life.

2.1 Research questions

The overall objective of this study was to examine cannabis use prevalence, product types, adverse effects, and the perceived impact of cannabis use among individuals who experienced any of the following mental conditions in the past 12 months: anxiety, depression, PTSD, bipolar disorder, and psychosis/schizophrenia. The following research questions were examined:

Study 1:

1. To what extent does the prevalence of cannabis use differ across individuals with and without past 12-month experience of a mental health condition?
2. Are there differences in the types of cannabis products being used by consumers with and without past 12-month experience of a mental health condition?

Study 2:

3. How does medical help-seeking for adverse effects from cannabis use differ across individuals with and without past 12-month experience of a mental health condition?
4. Do consumers with and without past 12-month experience of a mental health condition report different patterns of adverse effects from cannabis use?
5. How do consumers with and without past 12-month experience of a mental health condition perceive the overall impact of cannabis use on their friendships, physical health, mental health, family life, social life, work, and quality of life?

3.0 METHODS

3.1 Data source and collection

Cross-sectional data were examined from Wave 1 of the International Cannabis Policy Study (ICPS), conducted in Canada and the United States in 2018. Data were collected via self-completed web-based surveys conducted from August 27- October 7, 2018. Participants were recruited through the Nielsen Consumer Insights Global Panel and their partners' panels. Email invitations (with a unique link) were sent to a random sample of panelists (after targeting for age and country criteria); panelists known to be ineligible were not invited. Surveys were conducted in English in the United States and English or French in Canada (based on the panelist's known language preference). The ICPS study has been reviewed by and received ethics clearance through a University of Waterloo Research Ethics Committee (ORE#22392).

3.2 Study sample

Wave 1 of the ICPS study was conducted with participants aged 16–65 years living in Canada (n=10,057) and the USA (n=17,112) in three jurisdictions: Canada (all provinces); US states that had legalized non-medical cannabis (US 'legal' states) and those that had not (US 'illegal' states). Respondents were excluded if they selected "refuse to answer", "don't know" or did not provide valid responses to the questions of interest, including outcome measures, and covariates.

Post-stratification sample weights were constructed for respondents from Canada (age-by-sex-by-province and education groups) and the US (age-by-sex-by-legal state, education, and region-by-race groups), using population estimates from Statistics Canada and the US Census Bureau.^{93,94,95,96} A raking algorithm was applied to the full sample (n=27,169) to compute

weights that were calibrated to these groupings, and weights were rescaled to the final analytic sample size. A full profile of the ICPS sample and comparisons with national benchmark surveys is available in the ICPS Technical Report – Wave 2 (2019) and ICPS methodology paper.^{97,98} As described elsewhere, the ICPS sample provides comparable estimates of cannabis prevalence compared to national benchmark estimates in Canada, and moderately higher estimates than national estimates in the US in the National Survey on Drug Use and Health (NSDUH), with highly consistent estimates with respect to consumer patterns of frequency and type of products used.⁹⁷

3.3 Measures

The variables of interest for each study were identified based on a literature search, as well as preliminary analyses to determine which variables would be best suited to include as the predictor(s).

The ICPS survey included four self-reported indicators of mental health status: 1) family history of mental health (“Do you have a family history of mental health problems related to any of the following?”); 2) ever experienced mental health problems (“Have you ever experienced any of the following mental health problems, regardless of whether you were diagnosed?”); 3) experienced mental health problems in the last 12 months (“Have you experienced this/these mental health problem(s) in the past 12 months?”); and 4) ever diagnosed (“Have you ever been diagnosed with any of the following?”). Participants were presented with a list of mental conditions from which any applicable options could be selected.

Preliminary analyses were conducted to examine associations between each of these four measures and the primary outcome variables described below. The patterns of bivariate associations were highly consistent across all four of the ICPS mental health indicators;

therefore, the “past 12-month experience” measure was selected as the primary independent variable for both studies.

Past 12-month experience of a mental health condition

Participants were first asked “Have you ever experienced any of the following mental health problems (regardless of whether you were diagnosed)?” Participants were presented with a list from which they could select any of the conditions that were applicable to them. The options included: anxiety (including phobia, obsessive-compulsive disorder or panic disorder/depression (including or dysthymia)/post-traumatic stress disorder (PTSD)/bipolar disorder or mania/psychotic disorder (including schizophrenia)/substance use disorder/other/never received a mental health diagnosis/don’t know/refuse to answer. Those who selected ‘yes’ for any of the conditions were then asked the following question to determine past 12-month experience of a mental condition, “Have you experienced this/these mental health problem(s) in the past 12 months?” where the same list of conditions was presented. For the purpose of this study, substance use disorder and ‘other’ will be excluded from the list of disorders being examined. A response of ‘no’ to the initial “ever experienced” question will be recoded as “no experience in the past 12 months”.

An index variable for past 12-month experience of a mental condition was also created, where responses were recoded to “experienced no condition”, “experienced one condition” and “experienced more than one condition”.

3.3.1 Study 1

The following measures were used for Study 1:

Cannabis use frequency

A 6-level ‘cannabis use status’ variable (never used/used >12 months ago/used in past 12 months/monthly use/weekly use/daily or almost daily use) was derived from three survey questions: “Have you ever tried marijuana?” (yes/no); “When was the last time you used marijuana?” (more than 12 months ago/more than 3 months ago but less than 12 months ago/more than 30 days ago, but less than 3 months ago/within the past 30 days); and “How often do you use marijuana?” (less than once per month/ one or more times per month/one or more times per week/every day or almost every day). Responses in the ‘cannabis use status’ variable will be recoded into the following mutually exclusive categories: “no use in the past 12 months”, “used in the past 12 months”, “used less than monthly” “used weekly/monthly” and “used daily/almost daily”.

Cannabis products types

To assess use of specific cannabis product types, respondents who identified as past 12-month cannabis consumers were asked “Have you used marijuana in any of the following ways?” and were presented with a list of product types: dried herb (smoked or vaped)/cannabis oils or liquids taken orally (e.g., drops)/cannabis oils or liquids for vaping/Edibles or foods/drinks (e.g., marijuana cola, tea or coffee)/concentrates (e.g., wax, shatter, budder)/hash or kief/tinctures/topical ointments (e.g., skin lotions)/other. For each product type, respondents were asked to select one of the following options: no/yes but not in the past 12 months/yes in the past 12 months/don’t know. Responses will be recoded to “used in the past 12 months” and “did not use in the past 12 months”.

Covariates

The following sociodemographic characteristics will be included in this study: sex at birth (male/female), age group (15-25/26-35/36-45/46-55/56-65), ethnicity (white/other), country (Canada/USA), and education (less than high school, high school diploma or equivalent/some college or technical training/bachelor's degree or higher), and past 12-month cannabis use.

3.3.2 Study 2

The following measures were used for Study 2:

Sought medical help for adverse effects of cannabis use

Those who reported using cannabis in the past 12 months were asked “In the past 12 months, did you seek medical help for any adverse or negative health effects?” Response options included: yes/no/don't know/refuse to answer.

Adverse effects of cannabis use

Those who sought medical help for adverse or negative effects of cannabis were asked “In the past 12 months, which negative health effect(s) from marijuana use did you seek medical help for?” Respondents were presented with a list from which they could select any that were applicable to them: nausea or vomiting/heart or blood pressure/feeling faint or dizzy/panic reactions/hallucinations/flashbacks/depression/dissociation/depersonalization (feeling detached or disconnected from yourself)/other/never experienced any negative health effects from using marijuana/don't know/refuse to answer.

Perceived impact of cannabis use

To measure the perceived impact of cannabis use, those who identified as past 12-month cannabis consumers were asked “In the past 12 months, what effect did your marijuana use have

on your: friendships or social life, physical health, mental health, family life, work, studies, quality of life”. For each option, respondents were asked to identify the perceived impact by selecting from the following: (negative effect/no effect/positive effect/not applicable/don’t know/refuse to answer). A response of “not applicable” will be recoded as “missing”.

Ever used cannabis to manage/improve symptoms of a mental condition

Participants were asked “Have you ever used marijuana to improve or manage symptoms for any of the following?” and were presented with the following list from which they could select any of the conditions that were applicable to them: anxiety (including phobia, obsessive-compulsive disorder or panic disorder/depression (including or dysthymia)/post-traumatic stress disorder (PTSD)/bipolar disorder or mania/psychotic disorder (including schizophrenia)/substance use disorder/other/never received a mental health diagnosis/don’t know/refuse to answer. For the purpose of this study, substance use disorder and ‘other’ will be excluded from the list of disorders being examined.

Covariates

Similar to the first study, the covariates for this study included: sex at birth, age group, ethnicity, country, and education, and past 12-month cannabis use.

3.4 Analysis

All analyses were conducted using SAS Studio 9.4, using weighted data. To determine sample characteristics, descriptive statistics were conducted for the overall sample, stratified by mental conditions and covariate measures (sex, age, ethnicity, country, education, and past 12-month cannabis use. Frequency tables were generated to examine the prevalence of each

outcome of interest by mental health condition, as well as experience of one condition, >1 condition, or no condition.

3.4.1 Study 1

Unless otherwise stated, all models were adjusted for: sex, age, ethnicity, education, country, and past 12-month cannabis use. The research questions for each study, along with corresponding analyses and hypotheses are presented below:

Question 1: To what extent does the prevalence of cannabis use differ across individuals with and without past 12-month experience of a mental health condition?

Multinomial logistic regression models were fitted for each mental health condition (0= No experience, 1= Past 12-month experience) and the index variable (0= no condition, 1= one condition, 2= more than one condition), for frequency of cannabis use in each of the following mutually exclusive categories: no use in the past 12 months, used in the past 12 months, used less than monthly, and used daily/almost daily. The models were adjusted for sex, age, ethnicity, country, and education.

Given that problematic cannabis use is more prevalent among those with mental disorders, and cannabis use disorder is highly comorbid with mental conditions,⁵⁰ we hypothesize that:

H1.1 There will be greater cannabis use by those who experience more than one mental health condition vs. those who experience one condition or no condition.

Question 2: Are there differences in the types of cannabis products being used by consumers with and without past 12-month experience of a mental health condition?

Binary logistic regression models were fitted for each mental health condition and the index variable, in which use of each cannabis product served as the outcome (e.g. 1=used dried herb, 0=no dried herb use). Separate models were conducted for each of the following product types: dried herb, cannabis oils or liquids taken orally, cannabis oils or liquids for vaping, edibles or foods, drinks, concentrates, hash or kief, tinctures, topical ointment. Models only included respondents who reported consuming any cannabis in the past 12 months.

We hypothesized that:

H2.1 Those who experienced more than one mental health condition will be more likely to use each cannabis product compared to those who do not have a condition.

Evidence has shown that higher strength products (e.g. BHO, also oils and liquids) may be more likely to be used for medicinal purposes as they can deliver higher doses and are therefore more effective for symptom relief. Thus, we also hypothesized that:

H2.2 Those who experienced mental health conditions will be more likely to use products with high THC (vape oils, concentrates, hash or kief) compared to those with no condition.⁹⁹

3.4.2 Study 2

Question 3: How does medical help-seeking for health effects from cannabis use differ across individuals with and without past 12-month experience of a mental health condition?

Binary logistic regression models were fitted to examine differences between mental conditions in the prevalence of adverse effects and ‘seeking medical help’, where 1=sought

medical help for adverse events in the past 12 months; 0=did not seek medical help for adverse events in the past 12 months.

Evidence has shown that consumers visiting EDs for adverse effects from cannabis use are more likely to have an existing mental health diagnosis.⁶ Thus, we hypothesized that:

H3.1 Those with one or more than one mental health condition will be more likely to seek medical help compared to those with no condition.

Question 4: Do consumers with and without past 12-month experience of a mental health condition report different patterns of specific adverse effects from cannabis use?

Separate binary logistic regression models were fitted to examine differences between mental health conditions and specific adverse effects of interest, where 1=yes; 0=no for each of the following: nausea/vomiting, heart problems, feeling faint or dizzy, panic reactions, hallucinations, flashbacks, depression, dissociation, depersonalization, never experienced any negative health effects.

Since research has shown that cannabis use can exacerbate symptoms related to certain mental health conditions, we hypothesized that:

H4.1 Those with one or more than one mental health condition will be more likely to experience each specific adverse effect compared to those with no condition.

Question 5: How do consumers with and without past 12-month experience of a mental health condition perceive the overall impact of cannabis use on their physical health, mental health, family life, social life, work, and quality of life?

Seven multinomial logistic regression models were fitted to examine differences between mental health conditions for the categories related to perceived impact of cannabis use (friendships or social life, physical health, mental health, family life, work, studies, quality of life), each with 3 levels (negative effect, no effect, positive effect).

Evidence indicates that those with schizophrenia often exhibit impairments in social cognition and interactions (e.g., difficulties identifying and perceiving emotions in others).¹⁰² It is likely that this may be exacerbated by cannabis use, therefore we hypothesized that:

H5.1 Those with psychosis will be more likely to report negative perceived effects on friendships or social life compared to those with no condition.

H5.2 Those with mental health conditions more likely to report negative perceived effects across categories.

4.0 RESULTS

4.1 Manuscript 1

Cannabis and mental health: prevalence of use and modes of cannabis administration by mental health status.

Jennifer Rup, BA,¹ Tom P. Freeman, PhD,² Christopher Perlman, PhD,¹ David Hammond, PhD¹

¹School of Public Health & Health Systems, University of Waterloo, ON, Canada, N2L 3G1

²Addiction and Mental Health Group (AIM), Department of Psychology, University of Bath, Bath, UK.

Objective: To date, there is relatively little data on how patterns of cannabis use differ by mental health status. This study examined the prevalence of cannabis use and modes of cannabis administration among consumers who reported experiencing a mental condition in the past 12-months.

Methods: Data came from the International Cannabis Policy Study (Wave 1). Online surveys were conducted in Aug – Oct 2018 with 25,747 respondents aged 16-65 recruited from commercial panels in Canada and the US. Regression models were fitted to examine differences in cannabis prevalence and use of nine types of cannabis products among those with and without self-reported past 12-month experience of anxiety, depression, PTSD, bipolar disorder, and psychosis/schizophrenia.

Results: For each of the five mental health conditions, respondents with a mental health condition reported more frequent cannabis use than those without a mental health condition. Past 12-month cannabis consumers who experienced mental health conditions were significantly more likely than those without a mental health condition to use the most potent products (solid concentrates, THC vape oils, and hash), with fewer differences for dried flower, edibles, orally ingested oils, and other forms. Patterns of use were similar across specific mental health conditions, with some differences among respondents reporting psychosis and bipolar disorder.

Conclusion: Individuals experiencing mental health conditions report more frequent cannabis use and use of more potent product types. The findings highlight the need to target use of specific high potency products in prevention, treatment, and harm reduction among people with mental health disorders.

INTRODUCTION

Cannabis use is strongly associated with mental health status. Compared to the general population, regular cannabis use is substantially higher among individuals with schizophrenia, bipolar disorders, depressive and anxiety disorders, and post-traumatic stress disorder (PTSD).^{1,2} Rates of substance use disorder and cannabis use disorder are higher among individuals reporting any lifetime psychiatric disorder, mood disorder or anxiety disorder.^{2,3,4} Individuals who are already at risk of developing a mental health condition are also more likely to suffer adverse effects from cannabis use. The acute and long-term effects on mental health are dependent on several factors including age of initiation, frequency of cannabis use, dose and potency of product, duration of use, and individual and genetic differences.⁵

The self-medication hypothesis has been proposed to explain the relationship between mental health conditions and substance use.^{6,7} It suggests that the presence of a mental condition precedes substance use, and individuals use substances to alleviate distress and to regulate unpleasant symptoms associated with the condition.⁷ Alternatively, the shared-vulnerability hypothesis posits the idea that substance use can precipitate mental health conditions, as evidence has shown it can increase the risk of developing a condition, particularly with psychotic disorders.^{8,9,10} There is substantial evidence linking chronic cannabis use to an increased risk of developing psychotic disorders and schizophrenia, especially among individuals with an earlier age of initiation, family history, or genetic vulnerability to these conditions.^{9,11,12} Among those with schizophrenia, cannabis use has been shown to lead to earlier onset of psychosis, increased symptom severity, as well as poorer prognosis and quality of life.⁵ Greater frequency of cannabis consumption can also increase the risk of psychotic outcomes in the general population.^{13,14,15} In addition, several studies have identified an association with cannabis use and psychosis in those

with pre-existing genetic risk factors related to variation in certain genotypes, supporting a biologically plausible association between cannabis use and the development of these conditions.^{16,17,18,19} There is some evidence of a causal role of cannabis use on psychotic disorders established through Mendelian randomisation studies, however, there is also some evidence that supports reverse causation.^{20,21,22}

In contrast to the strong association shown for cannabis use and psychosis, evidence is mixed with respect to cannabis use and the development of anxiety disorders and depression.^{23,24} A systematic review and meta-analysis from 10 countries reported a small positive association between anxiety and cannabis use, and comorbid anxiety/depression and cannabis use.²⁵ For individuals younger than 25 years old, greater cannabis use was associated with more severe symptoms of depression, especially among those with a predisposition or existing vulnerability, and individuals were more likely to report symptoms of anxiety when cannabis use was initiated before the age of 15 and continued to age 21.^{11,23} In addition, several meta-analyses and systematic reviews show that cannabis use is associated with an increased risk of developing depression; however, the risk of developing either anxiety or depression among those who use cannabis regularly in the general population is relatively low after accounting for sociodemographic factors.^{26,27,28}

Research examining the association between cannabis use, bipolar disorders, and PTSD is limited. Evidence indicates that cannabis use has a negative impact on the course of bipolar disorders, and heavy cannabis use might trigger the first episode of the disorder.²⁹ Cannabis use adversely affects clinical outcomes in those with bipolar disorder, including greater symptom severity and duration of manic phases.^{4,30,31} In addition, cannabis use among patients with PTSD is associated with poorer mental health outcomes, including increased symptom severity, and

recent cannabis use (within the last 6 months) is associated with negative symptomatic outcomes over time among those with PTSD.^{27,32,33}

Cannabis is available in a wide variety of forms, such as dried herb, edibles, oils, hash or kief, concentrates, drinks, tinctures, and lotions. These products differ in their modes of administration (e.g. smoked, vaporized, or orally ingested), which can have an influence on the intensity of the high, duration of psychoactive effects, and potential adverse outcomes.³⁴ Products also differ in their range of THC and CBD concentrations. THC is responsible for producing the intoxicating effects of cannabis, including a ‘high’ or feelings of euphoria, and it can also induce transient psychotic-like effects (e.g., hallucinations, delusions) and cognitive impairment (e.g., difficulty concentrating, disorganized thoughts). CBD does not produce any intoxicating effects at typical doses, and is instead associated with potential therapeutic effects, including the treatment of psychotic and substance use disorders.^{35,36,37,38} In recent years, there has been a shift toward cannabis products with higher THC levels and greater potencies. For example, THC concentration of dried flower can range from less than 1% to 30%, whereas cannabis extract products such as oils can exceed 90% THC in many cases.^{39,40} CBD levels also vary across products, ranging from ‘CBD-rich’ products that contain little or no THC, to more ‘balanced’ products with similar concentrations. In Canada and the US, smoking dried flower remains the most common mode of administration; however, the prevalence of edibles, vaped oils, and orally ingested oils is increasing, particularly among younger consumers.⁴¹

Greater consumption of cannabis products with high levels of THC has been associated with the risk of developing a psychotic disorder, which includes delusions, paranoia and dissociation.^{42,43} High THC products are also associated with an increased risk of relapse after a first episode of psychosis.⁴⁴ A multinational study across 11 sites revealed that daily users of

high potency cannabis (10% THC or more) had a five-fold increased risk of psychosis compared to controls, and the prevalence of high potency cannabis use in controls was positively associated with the incidence of psychosis across sites.⁴⁵ In addition, those who reported a lifetime diagnosis of anxiety and depression, were more likely to use BHO (butane hash oil, a potent cannabis concentrate) than high potency herbal cannabis, and were more also likely to report stronger negative effects when using BHO.⁴⁶ However, we are unaware of any studies that have examined product preferences by mental health status for the wide range of product forms currently available on the cannabis market—including solid concentrates, orally administered oils, edibles, and vape/THC oils.⁴¹ Several studies have found more severe symptoms of cannabis use disorder in people using higher potency products; however, the extent to which consumers who experience mental health conditions self-select towards or away from these product categories remains unexplored.^{47,48,49,50}

The current study sought to examine the prevalence of cannabis use among those with mental health conditions, including anxiety, depression, bipolar disorder, PTSD, and psychosis. The study also examined the types of cannabis products used by consumers with a mental health condition compared to those without a condition.

METHODS

Cross-sectional data were examined from Wave 1 of the International Cannabis Policy Study (ICPS), conducted in Canada and the United States in 2018. The ICPS study seeks to evaluate the overall impact of cannabis legalization to examine the effectiveness of specific policy measures. Data were collected via self-completed web-based surveys conducted from August 27- October 7, 2018. Participants were recruited by the Nielsen Consumer Insights Global Panel and their partners' panels, which consist of non-probability based commercial

panels. Email invitations (with a unique link) were sent to a random sample of panelists (after targeting for age and country criteria); panelists known to be ineligible were not invited. Surveys were conducted in English in the United States and English or French in Canada (based on the panelist's known language preference). The ICPS study has been reviewed by and received ethics clearance through a University of Waterloo Research Ethics Committee (ORE#22392).

Participants

Wave 1 of the ICPS study was conducted with participants aged 16–65 years living in Canada (n=10,057) and the USA (n=17,112). For the current analysis, respondents were excluded if they either refused to answer or did not provide valid responses to the questions of interest (n=1,422).

Post-stratification sample weights were constructed for respondents from Canada (age-by-sex-by-province and education groups) and the US (age-by-sex-by-legal state, education, and region-by-race groups), using population estimates from Statistics Canada and the US Census Bureau.^{51,52,53,54} A raking algorithm was applied to the full sample (n=27,169) to compute weights that were calibrated to these groupings, and weights were rescaled to the final analytic sample size. A full profile of the ICPS sample and comparisons with national benchmark surveys is available in the ICPS Technical Report – Wave 2 (2019) and ICPS methodology paper.^{55,56} As described elsewhere, the ICPS sample provides comparable estimates of cannabis prevalence compared to national benchmark estimates in Canada, and moderately higher estimates than national estimates in the US in the National Survey on Drug Use and Health (NSDUH), with highly consistent estimates with respect to consumer patterns of frequency and type of products used.⁵⁵

Study measures

The ICPS survey included two measures to assess mental health status: “past 12-month experience of a mental health condition” and “ever been diagnosed with a mental health condition”. Analyses were conducted to examine bivariate associations between these measures and the primary outcome variables, and the patterns were highly consistent for both mental health measures. Given that mental health conditions can often go undiagnosed, the “past 12-month experience” measure was selected as the primary independent variable for this study. It also better aligns in temporality with the outcome measures, which were based on past 12-month cannabis use.

Past 12-month experience of mental health condition

Participants were asked “Have you ever experienced any of the following mental health problems (regardless of whether you were diagnosed)?” , and selected from the following options: anxiety (including phobia, obsessive-compulsive disorder or panic disorder/depression (including or dysthymia)/post-traumatic stress disorder (PTSD)/bipolar disorder or mania/psychotic disorder (including schizophrenia)/substance use disorder/other/never received a mental health diagnosis/don’t know/refuse to answer. Those who selected ‘yes’ for any of the conditions were then asked, “Have you experienced this/these mental health problem(s) in the past 12 months?” where the same list of conditions was presented. For the purpose of this study, substance use disorder and ‘other’ will be excluded from the list of disorders being examined.

An index variable for past 12-month experience of a mental condition was also created, where responses were recoded to “experienced no condition”, “experienced one condition” and “experienced >1 condition”.

Frequency of cannabis use

Frequency of cannabis use was analyzed with the following categories: “no use in the past 12 months”, “less than monthly”, “weekly/monthly” and “daily”.

Cannabis product types

Past 12-month cannabis consumers were asked if they had used the following product types within the past 12-months: dried herb (smoked or vaped)/cannabis oils or liquids taken orally (e.g., drops)/cannabis oils or liquids for vaping/edibles or foods/drinks (e.g., marijuana cola, tea or coffee)/concentrates (e.g., wax, shatter, budder)/hash or kief/tinctures/topical ointments (e.g., skin lotions)/other.

Covariates

The following sociodemographic characteristics were included in this study: sex at birth (male/female), age group (15-25/26-35/36-45/46-55/56-65), ethnicity (white/other), country (Canada/USA), and education (less than high school, high school diploma or equivalent/some college or technical training/bachelor’s degree or higher).

ANALYSIS

All analyses were conducted using SAS Studio 9.4, using weighted data. Descriptive statistics were used to determine the prevalence of cannabis use and product types used by past 12-month experience of each mental condition, as well as experience of one condition, >1 condition, or no condition. Multinomial logistic regression models were fitted for each mental condition (0= No experience, 1= Past 12-month experience) and the index variable (0= No condition, 1= One condition, 2= More than one condition), for frequency of cannabis use in each of the following mutually exclusive categories: daily, weekly or monthly, less than monthly, no

use in past 12-months. The full analytic sample was used for each model (n=25,747) and all models were adjusted for sex, age, ethnicity, country, and education.

Binary logistic regression models were fitted for each mental health condition (0= No experience, 1= Past 12-month experience) and the index variable (0= No condition, 1= One condition, 2= More than one condition), for use of each cannabis product in the past 12-months (e.g., 0= no dried herb use, 1= used dried herb). Separate models were conducted for each of the following product types: dried herb, oils (oral/vaped), edibles, drinks, concentrates, hash, tinctures, and topicals. The models only included respondents who reported consuming any cannabis in the past 12 months (n=5,749), and were adjusted for sex, age, ethnicity, country, education, and past 12-month cannabis use. Unless otherwise indicated, adjusted odds ratios (AORs) are reported with 95% confidence intervals.

RESULTS

Sample characteristics

Table 1 shows the weighted sample characteristics included in the current analyses from the ICPS 2018 (Wave 1) survey.

Prevalence of cannabis use

Figure 1 shows the prevalence of cannabis use by past 12-month experience of a mental health condition. As Table 2 indicates, the frequency of cannabis use was positively associated with the experience of a mental health condition. Compared to respondents who did not report experience of a mental health condition, those reporting one condition were more likely to use cannabis daily, weekly/monthly and less than monthly (Table 2). The odds of reporting frequent

cannabis use were greater among those who experienced more than one condition, including daily use, weekly/monthly use, and less than monthly use (Table 2). In addition, respondents who reported more than one mental health condition were more likely to use cannabis daily than those only reporting one condition (17.4%: AOR=1.72; 1.46-2.04).

Multinomial models were also conducted to examine differences in cannabis use by individual mental health condition (see Table 2). Compared to those who did not experience each condition, those who experienced anxiety, depression, PTSD, and bipolar disorder were more likely to report more frequent cannabis use vs. no use in the past 12-months (see Table 2). Additionally, respondents who experienced psychosis were more likely to use cannabis daily or weekly/monthly, but not less than monthly, versus no use in the past 12 months (see Table 2).

Cannabis product types

Figure 2 shows the type of products used among past 12-months cannabis consumers by mental health condition. For most product types, prevalence was consistently higher among those who reported experiencing one or more mental health conditions, with the exception of dried herb, where those with no condition and one condition reported similar use (Figure 2). Supplemental tables S1 to S9 show the results of binary logistic regression models for each specific mental health condition. Compared to ‘no mental condition’, those who experienced one condition were more likely to use the following: vaped oils, orally ingested oils, drinks, concentrates, tinctures, topicals, and edibles ($p<0.05$ for each product). Respondents reporting more than one mental health condition were also more likely to report using each product type ($p<0.05$ for each product).

Similar patterns were observed across individual mental conditions for the past 12-month use of cannabis concentrates and hash/kief. Compared to those with no experience, those with a past 12-month experience of each condition of interest were more likely to use concentrates: anxiety (21.4%: AOR=1.64; 1.37-1.95), depression (22.0%: AOR=1.76; 1.48-2.10), PTSD (25.9%: AOR=1.63; 1.28-2.09), bipolar disorder (29.1%: AOR=1.56; 1.15-2.14), or psychosis (34.9%: AOR=2.23; 1.39-3.59), and hash/kief: anxiety (23.1%: AOR=1.43; 1.21-1.69), depression (23.0%: AOR=1.38; 1.17-2.62), PTSD (29.2%: AOR=1.63; 1.29-2.06), bipolar disorder (32.9%: AOR=1.69; 1.25-2.28), or psychosis (36.0%: AOR=1.92; 1.20-3.06).

Less consistent patterns emerged for the use of other cannabis products. Those who experienced anxiety were more likely to use the following products compared to those who did not experience anxiety: dried herb (81.1%: AOR=1.19; 1.02-1.39), vaped oils (35.5%: AOR=1.59; 1.38-1.84), orally ingested oils (26.6%: AOR=1.38; 1.19-1.60), edibles (50.2%: AOR=1.20; CI 1.06-1.36), tinctures (10.5%: AOR=1.38; 1.11-1.72), and topicals (18.3%: AOR=1.40; 1.18-1.66), while there were no significant differences for cannabis drinks. Respondents who reported a past 12-month experience of depression were more likely to use the following products compared to those who did not: dried herb (81.9%: AOR=1.31; 1.12-1.53), vaped oils (32.2%: AOR=1.28; 1.10-1.47), drinks (11.0%: AOR=1.27; 1.03-1.56), topicals (17.6%: AOR=1.26; 1.06-1.49). There were no significant differences for orally ingested oils, edibles, and tinctures.

Past 12-month experience of PTSD was associated with higher odds of using the following product types: vaped oils (40.1%: AOR=1.65; 1.33-2.05), orally ingested oils (33.9%: AOR=1.64; 1.33-2.03), drinks (13.9%: AOR=1.51; 1.12-2.03), tinctures (14.0%: AOR=1.61; 1.20-2.16), topicals (23.5%: AOR=1.58; 1.24-2.01), while there were no significant differences

for dried herb or cannabis drinks. Compared to those without a past 12-month experience of bipolar disorder, those who reported an experience of bipolar disorder were more likely to use drinks (16.9%: AOR=1.72; 1.19-2.47), while there were no significant differences for dried herb, vaped oils, orally ingested oils, edibles, tinctures or topicals. Lastly, respondents who experienced psychosis were more likely to use drinks (27.5%: AOR=3.12; 1.92-5.07), tinctures (21.5%: AOR=3.10; 1.83-5.25), and topicals (26.3%: AOR=2.27; 1.39-3.70), compared to those who did not experience psychosis. There were no significant differences for dried herb, vaped oils, orally ingested oils, or edibles.

DISCUSSION

The current findings from population-based surveys in Canada and the United States add to the evidence that cannabis use is more prevalent and frequent among those who experience mental health conditions. These findings align with existing evidence that regular cannabis use is at least twice as common among individuals with schizophrenia, bipolar disorders, depressive and anxiety disorders, and PTSD, compared to the general population.¹ The findings are also consistent with the comorbidity of mental health conditions and substance use disorders.⁵⁷ Although the effects of cannabis use may differ across individual mental health conditions, the rate of cannabis use was similar across all conditions examined in the current study.

To our knowledge, the current study provides the most comprehensive assessment of how the types of cannabis products consumed differ by mental health condition. Most notably, high-potency products such as solid concentrates, THC vape oils, and hash, were more likely to be used by cannabis consumers reporting mental health conditions. This is consistent with a study which found that individuals with a diagnosis of anxiety and depression were more likely to use more potent cannabis products such as BHO.⁴⁶

Product preferences were largely similar across the five specific mental health conditions—particularly with respect to dried herb, which is the most commonly used product type across all populations.^{41,58} However, some differences were observed between mental health conditions. Anxiety and PTSD presented very similar patterns of product use, which could be attributed to the fact that anxiety and PTSD share overlapping symptoms and characteristics, and PTSD was categorized as being a form of anxiety disorder prior to the newer diagnostic criteria.^{4,59} Past 12-month experience of anxiety was associated with the use of more cannabis product types compared to other conditions. Product preferences were also more similar for anxiety, PTSD and depression, possibly reflecting the high comorbidity between these conditions. In contrast to the other conditions, bipolar disorder and psychosis presented no significant associations for more common modes of administration such as dried herb, vaped or orally ingested oils, and edibles.

The popularity of high potency cannabis products observed in the current study reflects a general trend towards greater use of cannabis extracts and concentrates in the North American market. Whereas the average THC level of dried herb in the North American market is around 20%, products such as hash, vape oils, and solid concentrates have THC levels two to four times greater than dried herb. There are several potential factors that may account for the greater popularity of these products among consumers who experience mental health conditions. First, consumers who experience mental conditions may purposely select higher strength products to optimize the delivery of higher doses of THC, which may provide greater symptom relief.^{60,61} Alternatively, frequent cannabis use can also build tolerance, so higher strength products might also be sought out in order to maintain the desired outcomes and intoxication levels from cannabis use.⁶² The extent to which higher THC products ameliorate or worsen the experience of

mental health conditions has yet to be fully addressed; while emerging results suggest potential therapeutic effects for anxiety and depression, the existing evidence base highlights predominantly negative outcomes from higher THC products and mental health outcomes.^{47,49,46} For example, a recent study found that high-potency cannabis use was associated with a significant increase in the likelihood of anxiety disorder.⁵⁰ This trend may be of particular concern for those with psychosis, as substantial evidence suggests that greater consumption of cannabis products with high levels of THC is associated with risk of developing a psychotic disorder, which includes delusions, paranoia and dissociation.^{42,43} Overall, the use of high-potency cannabis products among consumers who experience mental health conditions warrants greater attention. A range of public health communications have sought to highlight the potential risks of cannabis use, particularly among those susceptible to psychosis. For example, two of the rotating warnings mandated by Health Canada that appear on cannabis packages focus on mental health: “frequent and prolonged use of cannabis containing THC can contribute to mental health problems over time”, and “daily or near-daily use increases the risk of dependence and may bring on or worsen disorders related to anxiety and depression.” Despite these efforts, there is a need to better understand patterns of use of cannabis products among those experiencing mental health conditions, including motivations for use and potential adverse and therapeutic effects.

STRENGTHS & LIMITATIONS

This study is subject to common limitations of survey research, including potential bias due to non-response. The ICPS sample was recruited using non probability-based sampling methods; therefore, the findings do not provide nationally representative estimates. As described elsewhere, the study uses post-stratification weights and comparisons with national benchmark surveys have been published.⁶³ Briefly, in Canada, the 2018 ICPS rate for ‘ever use’ was 56.5%

vs. 58.8% for the Canadian Cannabis Survey (CCS), and 8.9% for daily use vs. 9.1% for the NCS for the corresponding age groups.^{58,64} These differences are well within the variability in estimates between the CCS, National Cannabis Survey, and the Canadian Tobacco Alcohol and Drugs Survey, upon which the government relies for ‘official’ prevalence estimates.

The estimates are also subject to self-reported biases, including the measures of mental health status. The ICPS estimates for the prevalence of mental health diagnoses are generally lower compared to nationally representative surveys.^{65,66} In addition, compared to in-person surveys or telephone-assisted interviews, the online survey mode of the ICPS may provide greater anonymity and promote more truthful reporting on sensitive topics such as cannabis use and mental health. Finally, the cross-sectional design of this study does not allow conclusions to be drawn about the existence or direction of causality. Thus, it is not possible to infer the temporal association between mental health diagnosis and cannabis use or adverse events experienced.

CONCLUSION

The current study highlights greater frequency of cannabis use among consumers that have experienced mental health disorders and a disproportionately higher use of more potent forms of cannabis. Despite important differences in the etiology and experience of different mental health conditions, these patterns were largely consistent across the five specific conditions examined in the current study. The findings highlight the need to target use of specific high potency cannabis products in prevention, treatment, and harm reduction among people with mental health disorders.

TABLES & FIGURES

Table 1: Weighted sample characteristics by past 12-month experience of mental health condition (n=25,747)

	Anxiety		Depression		PTSD		Bipolar		Psychosis		Total sample
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	
	(n=3,606)	(n=22,141)	(n=3,740)	(n=22,007)	(n=862)	(n=24,885)	(n=495)	(n=25,252)	(n=191)	(n=25,556)	(n=25,747)
	% (n)	% (n)	% (n)	% (n)	% (n)	% (n)	% (n)	% (n)	% (n)	% (n)	% (n)
Age group											
16-20	21.5 (774)	14.2 (3,028)	18.1 (676)	14.2 (3,126)	15.2 (130)	14.8 (3,671)	19.4 (96)	14.7 (3,705)	23.0 (44)	14.7 (3,757)	14.8 (3,802)
21-35	21.9 (789)	12.4 (2,663)	19.4 (726)	12.4 (2,727)	20.6 (177)	13.2 (3,275)	20.3 (101)	13.3 (3,352)	29.1 (56)	13.3 (3,397)	13.4 (3,452)
36-45	18.3 (659)	14.5 (2,305)	17.7 (662)	14.5 (3,201)	19.1 (165)	14.9 (3,698)	19.1 (95)	15.0 (3,769)	16.1 (31)	15.0 (3,832)	15.0 (3,863)
46-55	21.4 (772)	21.3 (2,721)	21.9 (819)	21.2 (4,675)	24.1 (208)	21.2 (5,287)	22.8 (113)	21.3 (5,381)	18.3 (35)	21.4 (5,459)	21.3 (5,494)
56-65	17.0 (612)	38.5 (8,524)	22.9 (857)	37.6 (8,279)	21.1 (181)	36.0 (8,954)	18.4 (91)	35.8 (9,045)	13.3 (25)	35.6 (9,110)	35.5 (9,136)
Sex											
Male	25.1 (905)	42.7 (9,456)	27.8 (1,039)	42.4 (9,323)	20.3 (175)	40.9 (10,186)	30.2 (150)	40.4 (10,212)	48.5 (93)	40.2 (10,269)	40.2 (10,361)
Female	74.9 (2,701)	57.3 (12,685)	72.2 (2,701)	57.6 (12,685)	79.7 (687)	59.1 (14,698)	69.8 (346)	59.6 (15,040)	51.5 (99)	59.8 (15,287)	60.0 (15,386)
Ethnicity											
White	87.1 (3,141)	83.3 (18,443)	85.3 (3,190)	83.6 (18,393)	81.9 (707)	83.9 (20,877)	82.8 (410)	83.8 (21,173)	71.4 (137)	83.9 (21,336)	83.8 (21,583)
Other	12.9 (466)	16.7 (3,698)	14.7 (3,740)	16.4 (3,614)	18.1 (156)	16.1 (4,008)	17.2 (85)	16.2 (4,078)	28.6 (55)	16.1 (4,109)	16.2 (4,164)
Education											

Less than high school	10.7 (387)	10.4 (2,311)	8.8 (329)	10.8 (2,368)	8.1 (70)	10.6 (2,628)	8.4 (42)	10.5 (2,656)	15.0 (29)	10.4 (2,669)	10.5 (2,698)
High school or equivalent	18.6 (671)	14.5 (3,207)	18.5 (693)	14.5 (3,185)	19.0 (164)	15.0 (3,715)	23.0 (114)	14.9 (3,765)	25.6 (49)	15.0 (3,829)	15.1 (3,878)
Some college, tech. training	42.3 (1,525)	34.0 (7,537)	43.4 (1,622)	33.8 (7,439)	46.2 (398)	34.8 (8,663)	46.1 (228)	35.0 (8,833)	38.1 (73)	35.2 (8,988)	35.2 (9,061)
Bachelor's or higher	28.4 (1,024)	41.0 (9,086)	29.3 (1,095)	41.0 (9,014)	26.7 (231)	39.7 (9,879)	22.5 (111)	39.6 (9,998)	21.2 (41)	39.4 (10,069)	39.3 (10,110)
Country											
US	66.3 (2,390)	62.3 (12,784)	65.7 (2,458)	62.3 (13,716)	68.3 (589)	62.6 (15,585)	76.8 (380)	62.5 (12,793)	67.8 (130)	62.8 (16,044)	62.8 (12,174)
Canada	33.7 (1,217)	37.7 (8,356)	34.3 (1,282)	37.7 (8,291)	31.7 (273)	37.4 (9,300)	23.2 (115)	37.5 (9,458)	32.2 (62)	37.2 (9,511)	37.2 (9,573)

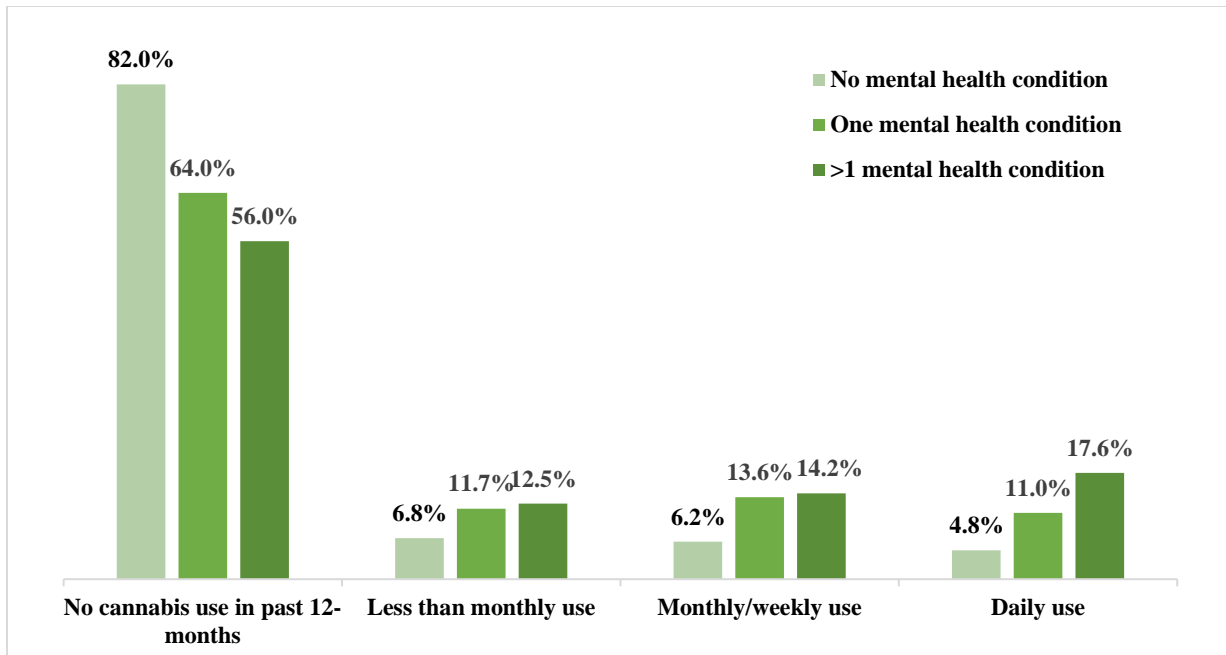


Figure 1: Frequency of cannabis use among those who experienced no mental condition, one condition, and >1 condition in the past 12 months (n=25,747)

Table 2: Multinomial regression results examining the association between past 12-month experience of mental health conditions and frequency of cannabis use* (n= 25,747)

	No use in past 12 months (ref)	Less than monthly cannabis use			Weekly/ monthly cannabis use			Daily cannabis use		
	% (n)	% (n)	AOR	95% CI	% (n)	AOR	95% CI	% (n)	AOR	95% CI
No anxiety	81.1 (17,958)	7.0 (1,549)	Ref		6.4 (1,471)	Ref		5.2 (1,165)	Ref	
Anxiety	56.6 (2,042)	13.2 (478)	2.26	(2.01-2.54)	14.2 (512)	2.79	(2.48-3.13)	16.0 (575)	4.06	(3.62-4.56)
No depression	80.6 (17,740)	7.2 (1,583)	Ref		6.8 (1,492)	Ref		5.4 (1,193)	Ref	
Depression	60.4 (2,258)	11.9 (444)	1.92	(1.71-2.16)	13.1 (491)	2.41	(2.15-2.71)	14.6 (547)	3.29	(2.93-3.69)
No PTSD	78.7 (19,591)	7.8 (1,934)	Ref		7.4 (1,838)	Ref		6.1 (1,522)	Ref	
PTSD	47.2 (407)	10.7 (92)	2.05	(1.62-2.58)	16.7 (144)	3.69	(3.02-4.51)	25.3 (218)	6.35	(5.31-7.59)
No bipolar	78.2 (19,747)	7.9 (1,984)	Ref		7.5 (1,901)	Ref		6.4 (1,619)	Ref	
Bipolar	50.7 (251)	8.5 (42)	1.40	(1.01-1.96)	16.5 (82)	2.91	(2.25-3.77)	24.4 (121)	4.81	(3.82-6.05)
No psychosis	77.9 (19,900)	7.9 (2,008)	Ref		7.6 (1,947)	Ref		6.7 (1,701)	Ref	
Psychosis	51.1 (98)	9.7 (19)	1.52	(0.92-2.51)	18.6 (36)	2.82	(1.91-4.18)	20.6 (39)	3.51	(2.40-5.14)
No conditions	82.2 (16,949)	6.8 (1,404)	Ref		6.2 (1,270)	Ref		4.8 (994)	Ref	
One condition	63.8 (1,504)	11.7 (275)	2.00	(1.73-2.29)	13.6 (320)	2.72	(2.37-3.11)	11.0 (259)	2.88	(2.48-3.36)
>1 condition	55.7 (1,546)	12.5 (347)	2.27	(1.99-2.59)	14.2 (393)	3.15	(2.77-3.59)	17.6 (488)	4.97	(4.38-5.64)

* Models adjusted for age, sex at birth, ethnicity, education, country. Separate models run for each condition and index variable.

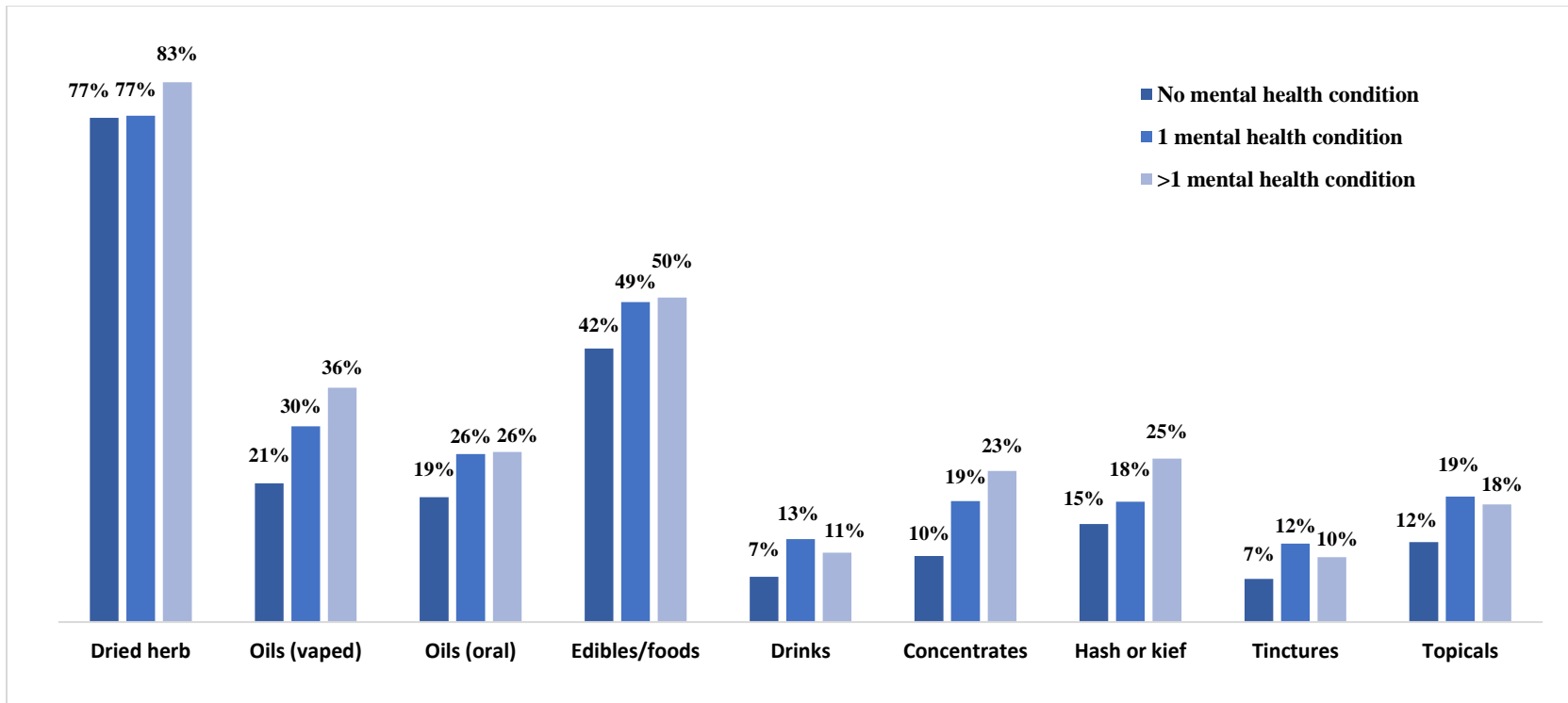


Figure 2: Product types used among past 12-month cannabis consumers by past 12-month experience of mental health conditions (5,749)

4.2 Manuscript 2

Cannabis and mental health: adverse outcomes and self-reported impact of cannabis use by mental health status.

Jennifer Rup, BA,¹ Tom P. Freeman, PhD,² Christopher Perlman, PhD,¹ David Hammond, PhD¹

¹School of Public Health & Health Systems, University of Waterloo, ON, Canada, N2L 3G1

²Addiction and Mental Health Group (AIM), Department of Psychology, University of Bath, Bath, UK

Objective: Cannabis can induce negative outcomes among consumers with mental health conditions. This study examined medical help-seeking behaviour, patterns of adverse effects, and perceived impacts of cannabis among consumers with and without mental health conditions.

Methods: Data came from the International Cannabis Policy Study, via online surveys conducted in 2018. Respondents included 5,749 past 12-month cannabis consumers aged 16-65, recruited from commercial panels in Canada and the US. Regression models examined differences in adverse health effects and perceived impact of cannabis among those with and without self-reported past 12-month experience of anxiety, depression, PTSD, bipolar disorder, psychosis.

Results: Overall, 4.3% of past 12-month consumers reported seeking medical help for adverse effects of cannabis, including panic, dizziness, nausea. Help-seeking was greater for those with psychosis (22.4%: OR= 5.48; 3.20-9.37), bipolar (9.4%: OR= 2.32; 1.44-3.74), depression (6.0%: OR= 1.71; 1.28-2.27). Additionally, 41.5% reported using cannabis to manage symptoms of mental health, with higher rates among those with psychosis (90.8%), bipolar (90.6%). Consumers reporting >1 condition were more likely to perceive positive impacts on friendships, physical/mental health, family life, work, studies, quality of life (all $p<.001$). Consumers with psychosis were most likely to perceive negative effects across categories.

Conclusion: For conditions with substantial evidence suggesting cannabis is harmful, greater help-seeking behaviours and self-perceived negative effects were observed. Consumers with mental health conditions generally perceive cannabis to have a positive impact on their lives. The relationship between cannabis and mental health is disorder specific and may include a combination of perceived benefits and harms.

INTRODUCTION

Cannabis use is associated with several acute and long-term effects on health. Cannabis can induce acute effects for which some consumers seek medical attention, including acute intoxication, nausea and vomiting, cannabis hyperemesis syndrome, gastrointestinal and psychiatric complaints, and acute cardiovascular events.^{20,21,22} An increase in rates of cannabis-related emergency department (ED) visits has been observed over time in Canada and the US, especially among young people.^{23,24} Consumers visiting EDs for adverse effects from cannabis use are more likely to have an existing mental health diagnosis.²⁵ In Canada, the rate of hospitalizations for cannabis-related mental and behavioural disorders doubled between 2006 and 2015, and psychotic disorder was the most common condition among hospitalizations.²⁴ In addition, the proportions of patients with mental health conditions reporting cannabis use prior to admission to inpatient psychiatry in Ontario, Canada has increased between 2007 and 2017, with the greatest increases among those with psychotic disorders and non-cannabis substance use disorders.²⁶

The potential impact of cannabis on mental health may depend on a range factors, including age, sex, genes, pre-existing medical conditions and family history of mental illness, frequency and duration of use, previous experience with cannabis, and potency and type of product consumed.³⁰ There is extensive evidence linking chronic cannabis use to an increased risk of developing psychotic disorders and schizophrenia, with greater susceptibility among individuals with an earlier age of initiation, heavier cannabis consumers and the use of higher potency products, and those with family history or genetic vulnerability to these conditions.^{57,88,103,54} Cannabis use can lead to earlier onset of psychosis, increased symptom severity, and poorer prognosis and quality of life among those with schizophrenia.³⁰ Additionally, several

studies have identified links between cannabis use and psychosis in those with pre-existing genetic risk factors related to certain gene variations.^{104,61,62,63} Mendelian randomisation studies have provided some evidence of a causal role of cannabis use on psychotic disorders, though there is also some evidence that supports reverse causation.^{64,65,66}

Evidence on the impact of cannabis use and the development anxiety disorders and depression is mixed.^{72,101} A systematic review and meta-analysis across 10 countries indicated the presence of a small positive association between anxiety and cannabis use, and comorbid anxiety/depression and cannabis use.⁶⁸ For individuals with an earlier age of initiation (younger than 25), and those with a predisposition or existing vulnerability, greater cannabis use was associated with more severe symptoms of depression and an increased likelihood of reporting symptoms of anxiety.^{27,72} In addition, several meta-analyses and systematic reviews demonstrate that cannabis use is associated with an increased risk of developing depression, though the risk of developing either anxiety or depression among those who use cannabis regularly in the general population is relatively low after accounting for sociodemographic factors.^{70,71,28}

Limited evidence exists for the effects of cannabis use on mental conditions such as bipolar disorders and post-traumatic stress disorder (PTSD). Research shows that cannabis use has a negative impact on the course of bipolar disorder, as it typically worsens clinical outcomes and leads to greater symptom severity and duration of manic phases.^{31,76,78} Heavy cannabis use may also trigger the first episode of bipolar disorder disorder.⁷⁵ Additionally, cannabis use is associated with poorer mental health outcomes and increased symptom severity among patients with PTSD.^{71,80,81}

Research has also examined the potential positive impact of cannabis use on mental health, though this literature is in the early stages. Some evidence suggests that cannabis use can

alleviate symptoms associated with mental conditions, such as stress, negative mood, irritability, sleep disturbances, and the acute response to fear stimuli associated with PTSD.^{39,41} However, a systematic review and meta analysis of the effectiveness of medicinal cannabinoids as a treatment method found little evidence to suggest that it can improve mental health conditions.⁴²

Cannabis use can have a range of adverse outcomes that impact other areas of life, apart from mental or physical health. Common measures of problematic cannabis use assess the impact on areas such as social life, relationships, work, and school.^{31,32} Overall quality of life (QoL) can also be used to assess an individual's overall sense of health and wellbeing. Heavy cannabis use and CUD are associated with reduced self-reported QoL scores, while abstinence and lower frequency of cannabis use are associated with higher QoL.^{33,34} Among individuals with anxiety, a lower QoL score was reported among regular, but not occasional, cannabis users.³⁵ Additionally, those with severe mental illness consistently report lower QoL scores compared to the general population.³⁶ Research to date has focused on mental health related QoL measures, particularly for recreational users or those with anxiety, depression, and CUD. However, there is limited evidence for other mental conditions and consumer perceptions of how cannabis impacts specific areas of life such as friendships or social life, family life, physical health, work, and studies.

The current study sought to: 1) examine the rate of cannabis consumers who seek medical help for adverse outcomes from cannabis, including the rate of specific adverse health effects experienced; 2) examine perceptions of positive and negative effects of cannabis use among cannabis consumers on seven outcomes: friendships or social life, physical and mental health, family life, work, studies, and general quality of life; and 3) to examine differences in adverse

outcomes and perceived effects by past 12-month experience of specific mental health conditions.

METHODS

Cross-sectional data were examined from Wave 1 of the International Cannabis Policy Study (ICPS), conducted in Canada and the United States in 2018. Data were collected via self-completed web-based surveys conducted from August 27- October 7, 2018. Participants were recruited through the Nielsen Consumer Insights Global Panel and their partners' panels, which consist of non-probability based commercial panels. Email invitations (with a unique link) were sent to a random sample of panelists (after targeting for age and country criteria); panelists known to be ineligible were not invited. Surveys were conducted in English in the United States and English or French in Canada (based on the panelist's known language preference). The ICPS study has been reviewed by and received ethics clearance through a University of Waterloo Research Ethics Committee (ORE#22392).

Participants

Wave 1 of the ICPS study was conducted with participants aged 16–65 years living in Canada (n=10,057) and the USA (n=17,112). For the current analysis, respondents were excluded if they refused to answer the questions of interest, did not provide valid responses, or did not use cannabis in the past 12-months (n=21,420). The final analytic sample included 5,749 respondents. A full profile of the ICPS sample and comparisons with national benchmark surveys is available in the ICPS Technical Report – Wave 2 (2019) and ICPS methodology paper.^{97,98}

Study measures

Participants were asked “Have you ever experienced any of the following mental health problems (regardless of whether you were diagnosed)?”, and selected from the following options: anxiety (including phobia, obsessive-compulsive disorder or panic disorder/depression (including or dysthymia)/post-traumatic stress disorder (PTSD)/bipolar disorder or mania/psychotic disorder (including schizophrenia)/substance use disorder/other/never received a mental health diagnosis/don’t know/refuse to answer. Those who selected ‘yes’ for any of the conditions were then asked, “Have you experienced this/these mental health problem(s) in the past 12 months?” where the same list of conditions was presented. For the purpose of this study, substance use disorder and ‘other’ will be excluded from the list of disorders being examined, as it was not possible to discern the type of substance consumed by those who reported experiencing ‘substance use disorder’ in the ICPS survey.

An index variable for past 12-month experience of a mental condition was also created, where responses were recoded to “experienced no condition”, “experienced one condition” and “experienced >1 condition”.

Sought medical help for adverse effects of cannabis use

Those who reported using cannabis in the past 12 months were asked “In the past 12 months, did you seek medical help for any adverse or negative health effects?” Response options included: yes/no/don’t know/refuse to answer.

Adverse effects of cannabis use

Consumers who sought medical help for adverse or negative effects of cannabis were asked “In the past 12 months, which negative health effect(s) from marijuana use did you seek medical help for?” Respondents were presented with a list from which they could select any that

were applicable to them: nausea or vomiting/heart or blood pressure/feeling faint or dizzy/panic reactions/hallucinations/flashbacks/depression/dissociation/depersonalization (feeling detached or disconnected from yourself)/other/never experienced any negative health effects from using marijuana/don't know/refuse to answer.

Perceived impact of cannabis use

To measure the perceived impact of cannabis use, past 12-month cannabis consumers were asked “In the past 12 months, what effect did your marijuana use have on your: friendships or social life, physical health, mental health, family life, work, studies, quality of life?”. For each option, respondents were asked to identify the perceived impact by selecting from the following: (negative effect/no effect/positive effect/not applicable/don't know/refuse to answer). A response of “not applicable” was recoded as “missing”.

Ever used cannabis to manage/improve symptoms of a mental condition

Participants were asked “Have you ever used marijuana to improve or manage symptoms for any of the following?” and were presented with the following list from which they could select any of the conditions that were applicable to them: anxiety (including phobia, obsessive-compulsive disorder or panic disorder/depression (including or dysthymia)/post-traumatic stress disorder (PTSD)/bipolar disorder or mania/psychotic disorder (including schizophrenia)/substance use disorder/other/never received a mental health diagnosis/don't know/refuse to answer. For the purpose of this study, ‘substance use disorder’ and ‘other’ will be excluded from the list of disorders examined.

Covariates

Cannabis use frequency was analyzed as “less than monthly use”, “weekly/monthly use” and “daily use”. Other covariates included sex at birth (male/female), age group (15-25/26-35/36-45/46-55/56-65), ethnicity (white/other), education (less than high school, high school diploma or equivalent/some college or technical training/bachelor’s degree or higher), and country (Canada/USA).

ANALYSIS

All analyses were conducted using SAS Studio 9.4 and reported estimates are weighted. Post-stratification sample weights were constructed for respondents from Canada (age-by-sex-by-province and education groups) and the US (age-by-sex-by-legal state, education, and region-by-race groups), using population estimates from Statistics Canada and the US Census Bureau.^{93,94,95,96} A raking algorithm was applied to the full sample (n=27,169) to compute weights that were calibrated to these groupings, and weights were rescaled to the final analytic sample.

Binary logistic regression models were fitted to examine medical help-seeking for adverse effects in the past 12-months” (e.g., 0= Did not seek help, 1= Sought help). First, models were run with the index variable (0= No condition, 1= One condition, 2= More than one condition), and then separate models were run for each mental health condition (0= No experience, 1= Past 12-month experience). The same approach was used to examine the “used cannabis to manage/improve symptoms of mental health” outcome (e.g., 0= Did not use cannabis to manage symptoms, 1= Used cannabis to manage symptoms), as well as prevalence of help-seeking for specific health effects, with separate models for each of the 8 health effects (e.g., 0= Did not seek help for effect, 1= Sought help for effect).

Multinomial logistic regression models were also fitted to examine the 7 outcomes related to self-perceived impact of cannabis use, each with 3 levels (0=No effect, 1=Negative effect, 2=Positive effect). Models were run with the index variable (0= No condition, 1= One condition, 2= More than one condition), and then separate models were run for each mental health condition (0= No experience, 1= Past 12-month experience).

All models were adjusted for sex, age, ethnicity, country, education, and cannabis use frequency. Unless otherwise indicated, adjusted odds ratios (AORs) are reported with 95% confidence intervals.

RESULTS

Table 1 presents the weighted sample characteristics included in the current analyses from the ICPS 2018 (Wave 1) survey.

Medical help-seeking for adverse health effects

As Table 2 shows, 4.3% of all past 12-month cannabis consumers sought medical help for an adverse event, including 5% of monthly users and 4% of daily/near daily users. For specific mental health conditions, those with depression, bipolar disorder and psychosis were more likely to seek medical help compared to those who did not experience each condition. The association was strongest for psychosis (22.4%: AOR=5.48; 3.20-9.37), followed by bipolar disorder (9.4%: AOR=2.32; 1.44-3.74), and depression (6.0%: AOR=1.71; 1.28-2.27), while there were no significant differences for anxiety or PTSD. In addition, consumers who reported experiencing one mental health condition (10%), and more than one condition (5%) were more likely to seek medical help for adverse effects compared to those who did not experience a condition (2.7%).

As Figure 1 shows, panic, dizziness, and nausea/vomiting were the most commonly reported adverse effects. Compared to consumers with ‘no mental health condition’, those who experienced one condition were more likely to seek medical help for heart problems, dizziness and flashbacks ($p < .05$ for all), and respondents reporting more than one condition had higher odds of seeking help for nausea/vomiting, dizziness, panic reactions, flashbacks, and depression ($p < .05$ for all).

Supplemental tables S1 to S8 show the results of binary logistic regression models for each specific adverse health effect and the mental health conditions of interest. Briefly, consumers with anxiety were more likely to seek medical help for depression (24.7%: AOR=2.32; 1.07-5.06), while consumers with depression were more likely to seek help for panic reactions (36.1%: AOR=4.69; 2.13-10.29). Neither condition showed significant differences for any other adverse effects. Consumers with PTSD in the past 12-months were more likely to seek medical help for heart problems (39.1%: AOR=2.67; 1.01-7.03), panic reactions (16.5%: AOR=3.44; 1.28-9.25), flashbacks (26.4%: AOR=4.49; 1.45-13.92), and depression (37.7%: AOR=4.46; 1.56-12.75). Bipolar disorder was associated with seeking medical help for dizziness (53.3%: AOR=4.76; 1.74-12.97), hallucinations (28.8%: AOR=3.69; 1.15-11.86), and flashbacks (35.1%: AOR=7.53; 2.30-24.70). Finally, psychosis was associated with seeking medical help for flashbacks (30.5%: AOR=3.98; 1.30-12.21), and dissociation (24.6%: AOR=7.65; 1.90-30.75).

Perceived effects of cannabis use

Figure 2 shows the prevalence of perceived effects of past 12-month cannabis use. For all categories, the prevalence of negative and positive perceived effects of cannabis were generally lower among all past 12-month cannabis consumers and those with no mental health conditions

(Figure 3). Results of the multinomial logistic regression models examining the perceived effects of cannabis use by specific mental condition are presented in Supplemental tables S9-S15.

Friendships/social life

Among all past 12-month consumers, 21.2% reported positive effects of cannabis use on friendships/social life, and 4.0% reported negative effects. Consumers who reported experiencing each mental health condition in the past 12-months were more likely to report positive effects of cannabis use on friendships/social life vs. no effect, compared to those with no experience of each condition: anxiety (28.8%: AOR=1.65; 1.42-1.92), depression (27.3%: AOR=1.44; 1.23-1.68, PTSD (29.2%: AOR=1.46; 1.16-1.84), bipolar disorder (35.4%: AOR=1.76; 1.30-2.38), and psychosis (32.0%: AOR=1.66; 1.02-2.72). In addition, a past 12-month experience of psychosis was associated with higher odds of reporting negative effects on friendships/social life vs. no effect (16.2%: AOR=5.24; 2.77-9.89).

Physical health

Among all past 12-month consumers, 32.7% reported positive effects of cannabis use on physical health, and 4.3% reported negative effects. For each condition, those with a past 12-month experience were more likely to report positive effects of cannabis use on physical health vs. no effect, compared to those with no experience of each condition: anxiety (43.1%: AOR=1.88; 1.63-2.17), depression (43.1%: AOR=1.76; 1.53-2.03), PTSD (53.0%: AOR=1.93; 1.56-2.40), bipolar disorder (40.2%: AOR= 1.50; 1.12-2.00). Psychosis was not significantly associated with positive effect; however, it was associated with higher odds of reporting negative effects on physical health vs. no effect (3.2%: AOR=3.35; 1.65-6.81).

Mental health

For all conditions, those with a past 12-month experience were more likely to report positive effects of cannabis use on mental health ($p < .001$) vs. no effect. The association was strongest for anxiety (AOR= 4.83; 4.16-5.61) and weakest for psychosis (AOR= 2.97; 1.71-5.15). The odds of reporting negative perceived effects vs. no effect were also higher for those who experienced each condition ($p < .001$) compared to those who did not and conversely, the association was strongest for psychosis (AOR= 11.44; 5.74-22.78) and weakest for anxiety (AOR= 3.42; 2.48-4.73).

Family life

Among all past 12-month consumers, 39.4% reported positive effects of cannabis use on family life, and 3.8% reported negative effects. Those who reported a past 12-month experience of each condition were more likely to report positive effects on family life vs. no effect, compared to those with no experience of each condition: anxiety (24.3%: AOR=1.74; 1.47-2.06), depression (24.7%: AOR=1.75; 1.48-2.07), PTSD (33.2%: AOR=2.09; 1.64-2.65), bipolar disorder (29.9%: AOR= 1.69; 1.22-2.35), psychosis (33.3%: AOR= 2.48; 1.48-4.16). Past 12-month experience of bipolar disorder (8.8%: AOR=1.86; 1.10-3.13), and psychosis (17.4%: AOR=4.70; 2.48-8.92) were also associated with higher odds of reporting negative effects on family life vs. no effect.

Work

Among all past 12-month consumers, 17.0% reported positive effects of cannabis use on work, and 5.2% reported negative effects. Compared to those with no experience of each condition, those with a past 12-month experience were more likely to report positive effects of cannabis use on work vs. no effect: anxiety (17.7%: AOR=1.49; 1.22-1.82), depression (18.1%:

AOR=1.51; 1.22-2.19), PTSD (22.5%: AOR=1.63; 1.22-2.19), bipolar disorder (22.4%: AOR=1.49; 1.03-2.16), psychosis (35.9%: AOR=2.95; 1.74-5.00). Compared to no experience of each condition, a past 12-month experience of bipolar disorder (9.0%: AOR=2.13; 1.25-3.65), and psychosis (9.8%: AOR=2.94; 1.29-6.69) were associated with higher odds of reporting negative effects on work vs. no effect, while the other conditions presented no significant differences for negative effect.

Studies

Among all past 12-month consumers, 12.9% reported positive effects of cannabis use on physical health, and 4.3% reported negative effects. Respondents with a past 12-month experience of each condition were more likely to report positive effects of cannabis use on studies vs. no effect, compared to those with no experience of each condition: anxiety (17.2%: AOR=1.62; 1.31-2.00), depression (16.5%: AOR=1.41; 1.15-1.75), PTSD (23.7%: AOR=2.13; 1.58-2.87), bipolar disorder (24.9%: AOR= 1.79; 1.23-2.61), psychosis (32.8%: AOR=2.67; 1.57-4.55). Compared to no experience of each condition, a past 12-month experience of anxiety (6.7%: AOR=1.52; 1.12-2.04), PTSD (7.6%: AOR=1.89; 1.20-2.99), bipolar disorder (10.0%: AOR=1.94; 1.14-3.31), and psychosis (12.3%: AOR=2.90; 1.39-6.06) were associated with higher odds of reporting negative effects on studies vs. no effect.

Quality of life

Among all past 12-month consumers, 45.2% reported positive effects of cannabis use on physical health, and 3.0% reported negative effects. Those who reported a past 12-month experience of each condition were more likely to report positive effects of cannabis use on quality of life vs. no effect, compared to those with no experience of each condition: anxiety (61.8%: AOR=2.74; 2.37-3.16), depression (61.0%: AOR=2.40; 2.08-2.77), PTSD (68.4%:

AOR=2.32; 1.83-2.92), bipolar disorder (66.8%: AOR= 2.01; 1.48-2.73), psychosis (57.8%: AOR=2.00; 1.19-3.37). In addition, past 12-month experience of psychosis was strongly associated with higher odds of reporting negative effects on quality of life vs. no effect (13.9%: AOR=6.85; 3.27-14.33).

Used cannabis to improve or manage symptoms

As Figure 3 shows, 42% of all past 12-month consumers reported using cannabis to improve or manage any symptoms of a mental health condition. Consumers who reported experiencing >1 mental health condition—as well as each of the 5 specific mental health conditions— were significantly more likely to use cannabis to manage symptoms compared to those with one condition or no condition ($p<.001$; see Supplemental Table S16). The use of cannabis to manage symptoms of mental health was highest amongst consumers who experienced bipolar disorder and psychosis in the past 12-months (Figure 4).

DISCUSSION

The results from this study indicated that approximately 1 in 20 of all past 12-month cannabis consumers sought medical help for adverse effects from cannabis use. To our knowledge, this is the first population-based survey examining the rate of medical help seeking for adverse events from cannabis, as most previous research comes from hospitalization records or health administrative data. Medical help-seeking was more prevalent among those who experienced one or more mental health conditions, consistent with existing evidence on increased rates cannabis-related ED visits and hospitalizations among those with mental health diagnoses.^{25,24,37} In particular, consumers who experienced psychosis, bipolar disorder, and depression were more likely to seek medical help for cannabis use. This is unsurprising given the

negative effect that cannabis may have on these conditions, particularly among those with psychosis and bipolar disorder.^{47,78,73} For example, evidence has shown an increased risk of relapse to psychosis and longer hospital admissions following continued cannabis use after onset of psychosis.¹⁰⁵

Consumers with PTSD were more likely to report a greater number of adverse health effects (heart problems, panic reactions, flashbacks, depression), followed by bipolar disorder (panic reactions, hallucinations, flashbacks), and psychosis (flashbacks, dissociations). For these conditions, there is evidence indicating cannabis use is associated with increased symptom severity and negative symptomatic outcomes.^{47,78,75,81} However, it is unclear whether the adverse effects reported by consumers were elicited by cannabis use, or if the reactions were symptoms resulting from an existing mental condition.

Consumers who experienced mental health conditions consistently reported higher self-perceived positive effects of cannabis use across all seven categories. Interestingly, the perceived positive effects of cannabis use were greatest for the mental health (67%) and quality of life (64%) categories. The findings also indicate that a high proportion of consumers who experienced a mental health condition reported using cannabis to manage symptoms of a condition. This may reflect the increased sensitivity those with mental health conditions possess with regard to the benefits and harms of cannabis use.¹⁰⁶ A plausible explanation for the high prevalence of self-perceived positive effects could be that those with mental conditions use cannabis to manage symptoms that would otherwise impede on specific areas of their lives, and thus symptom alleviation would be viewed as a positive experience. For example, if one experiences difficulties with interpersonal relationships, stress, concentration, negative mood or irritability, cannabis may be used as a form of self-medication, as its acute effects may seemingly

provide relief in these areas depending on the dose and concentration (THC/CBD levels) consumed.^{39,42}

In contrast to self-reported ‘positive’ effects of cannabis use, perceptions of negative effects were substantially lower across all categories (3-7%), with fewer differences among consumers with and without experience of a mental health condition. Notably, consumers with psychosis were more likely to report negative effects of cannabis use across all seven categories. Overall, these results present a strong case that the risks related to cannabis use are worse for those who experience psychosis compared to other mental health conditions. Consumers who experienced bipolar disorder had negative self-perceived effects of cannabis on family life, work and studies, and those with anxiety and PTSD were more likely to report negative self-perceived effect on studies. This potentially adds to previous evidence which suggests links between heavy cannabis use and reduced educational attainment, lower income, and adverse consequences in the workplace.^{107,108} For each specific condition, consumers were also more likely to report negative perceived effects of cannabis on mental health. These findings are consistent with previous studies which demonstrated lower self-reported mental health related QoL scores among regular cannabis users with anxiety and depression.^{35,109} The negative effects could be attributed to the fact that although cannabis may be initially used for immediate relief of symptoms, its effects are only short-term. Over time, consumers might be left with an increased inability to regulate symptoms of distress, leading to an increased vulnerability to negative mental health related outcomes.^{26,30,110}

STRENGTHS & LIMITATIONS

The ICPS sample is not recruited using probability-based sampling, therefore, it cannot be assumed to be nationally representative. However, the 2018 ICPS sample has similar

prevalence of cannabis use than national benchmark surveys in Canada and the US.¹¹¹ For example, in Canada, the 2018 ICPS prevalence for ‘ever use’ was 56.5% vs. 58.8% for the Canadian Cannabis Survey (CCS), and 8.9% for daily prevalence vs. 9.1% for the NCS for the corresponding age groups.^{4,112} In addition, the patterns of cannabis use among consumers (e.g., the frequency of use and types of products used) are very similar to national benchmark studies.⁸⁴

This study is subject to common limitations of survey research including potential bias due to non-response and social desirability. In particular, the measure of mental health status used in the current paper (“past 12-month experience of a mental health condition”) is based on self-report rather than clinical interview and diagnosis. The ICPS survey also included a measure for self-reported diagnosis of a mental health condition. Preliminary analyses were conducted to examine bivariate associations between these measures with the primary outcome variables, and the patterns were highly consistent for both mental health measures. Given that mental health conditions can often go undiagnosed, the “past 12-month experience” measure was selected as the primary independent variable for this study. This measure also better aligns with our outcome measures, which were based on perceived effects and adverse effects of cannabis use in the past 12-months. Some sub-group analyses in this study had limited statistical power due to smaller sample sizes, such as analyses of specific adverse events by mental health condition.

It should be noted that ICPS estimates for prevalence of mental health diagnoses are generally lower compared to nationally representative surveys.^{113,114} In addition, compared to in-person surveys or telephone-assisted interviews, the online survey mode of the ICPS may provide greater anonymity and promote more truthful reporting on sensitive topics such as cannabis use or mental health.¹¹⁵ The cross-sectional design of this study does not allow

conclusions to be drawn about the existence or direction of causality. Thus, it is not possible to infer the temporal association between mental health diagnosis and cannabis use or adverse events experienced.

CONCLUSION

Almost half of past year consumers reported using cannabis to manage or improve mental health. In addition, consumers with mental health conditions were more likely to perceive that cannabis has a positive impact in most areas of their life, including mental health. For mental health conditions with more substantial evidence suggesting harmful effects of cannabis use (e.g., psychosis, bipolar disorder), greater self-reported use of cannabis to manage symptoms of mental health was observed, as well as greater help-seeking behaviours and self-perceived negative effects of cannabis use. Reports of negative effects from cannabis use were substantially lower than positive effects; nevertheless, almost 1 in 20 past 12-month cannabis users reported seeking medical help for adverse effects from cannabis, including 4% of daily/near daily users. Overall, the relationship between cannabis use and mental health is complex, disorder specific, and may include a combination of perceived benefits as well as harms.

TABLES & FIGURES

Table 1: Weighted sample characteristics by past 12-month experience of mental health condition (n=5,749)

	Anxiety		Depression		PTSD		Bipolar		Psychosis		Total Sample
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No	
	(n=1,564)	(n=4,184)	(n=1,481)	(n=4,267)	(n=455)	(n=5,294)	(n=244)	(n=5,505)	(n=94)	(n=5,655)	(n=5,749)
	% (n)	% (n)	% (n)	% (n)	% (n)	% (n)	% (n)	% (n)	% (n)	% (n)	% (n)
Age group											
16-20	23.7 (371)	16.5 (692)	22.4 (331)	17.1 (732)	16.9 (77)	18.6 (986)	28.0 (68)	18.1 (994)	26.5 (25)	18.4 (1,038)	18.5 (1,063)
21-35	27.0 (422)	17.4 (729)	24.4 (361)	18.5 (791)	25.9 (118)	19.5 (1,034)	21.6 (53)	20.0 (1,099)	32.7 (31)	19.8 (1,121)	20.0 (1,152)
36-45	18.3 (287)	14.3 (599)	17.4 (257)	14.7 (629)	18.1 (83)	15.2 (804)	17.6 (43)	15.3 (843)	16.4 (15)	15.4 (871)	15.4 (886)
46-55	18.8 (294)	20.3 (849)	20.5 (304)	19.7 (840)	21.7 (99)	19.7 (1,045)	21.3 (52)	19.8 (1,092)	17.1 (16)	20.0 (1,128)	19.9 (1,144)
56-65	12.1 (190)	31.4 (1,315)	15.4 (228)	29.9 (1,276)	17.4 (79)	26.9 (1,425)	11.5 (28)	26.8 (1,476)	7.2 (7)	26.5 (1,497)	26.2 (1,504)
Sex											
Female	73.1 (1,144)	51.2 (2,144)	71.4 (1,058)	52.2 (2,230)	77.5 (352)	55.4 (2,935)	66.3 (162)	56.8 (3,126)	55.9 (52)	57.2 (3,235)	57.2 (3,288)
Male	26.9 (420)	48.8 (2,041)	28.6 (423)	47.8 (2,038)	22.5 (103)	44.6 (2,359)	33.7 (82)	43.2 (2,379)	44.1 (41)	42.8 (2,420)	42.8 (2,461)
Ethnicity											
White	86.7 (1,356)	83.7 (3,503)	84.6 (1,253)	84.5 (3,606)	81.4 (371)	84.8 (4,489)	79.5 (194)	84.7 (4,665)	68.4 (64)	84.8 (4,795)	84.5 (4,859)
Other	13.3 (209)	16.3 (681)	15.4 (228)	15.5 (661)	18.6 (85)	15.2 (805)	20.5 (50)	15.2 (840)	31.6 (30)	15.2 (860)	15.5 (890)
Education level											
Less than high school	11.1 (173)	12.0 (501)	9.4 (140)	12.5 (534)	7.8 (36)	12.1 (638)	9.7 (24)	11.8 (651)	17.3 (16)	11.6 (658)	11.7 (674)

High school or equivalent	19.9 (312)	16.0 (671)	21.1 (312)	15.7 (670)	19.9 (91)	16.8 (892)	28.1 (69)	16.6 (914)	24.2 (23)	17.0 (960)	17.1 (982)
Some college, tech. training	42.2 (659)	38.1 (1,595)	42.6 (631)	38.0 (1,624)	48.3 (220)	38.4 (2,035)	46.3 (113)	38.9 (2,141)	38.3 (36)	39.2 (2,219)	39.2 (2,254)
Bachelor's higher	26.9 (420)	33.9 (1,418)	26.9 (398)	33.7 (1,439)	24.0 (109)	32.7 (1,729)	15.9 (39)	32.7 (1,799)	20.3 (19)	32.2 (1,819)	32.0 (1,838)
Country											
US	65.9 (1,031)	64.3 (2,690)	65.4 (969)	64.5 (2,752)	67.3 (306)	64.5 (3,415)	75.4 (184)	64.3 (3,537)	66.7 (62)	64.7 (3,659)	64.7 (3,721)
Canada	34.1 (533)	35.7 (1,495)	34.6 (512)	35.5 (1,516)	32.7 (149)	35.5 (1,879)	24.6 (60)	35.7 (1,968)	33.3 (31)	35.3 (1,997)	35.3 (2,028)
Cannabis use frequency											
Less than monthly	30.5 (478)	37.0 (1,549)	29.9 (444)	37.1 (1,573)	20.3 (92)	36.5 (1,934)	17.1 (42)	36.1 (1,984)	19.8 (19)	35.5 (2,008)	35.3 (2,026)
Weekly/monthly	32.7 (512)	35.1 (1,471)	33.1 (491)	35.0 (1,492)	31.7 (144)	34.7 (1,838)	33.4 (82)	34.5 (1,901)	38.0 (36)	34.4 (1,947)	34.5 (1,982)
Daily	36.7 (575)	27.8 (1,165)	36.9 (547)	28.0 (1,193)	48.0 (219)	28.7 (1,522)	49.4 (121)	29.4 (1,619)	42.2 (39)	30.1 (1,701)	30.3 (1,740)

Table 2: Binary logistic regression results examining the association between medical help seeking for adverse health effects among past 12-month cannabis consumers, by past 12-month experience of mental condition* (n=5,675)

	Sought medical help in past 12 months	AOR	95% CI	p value
	% (n)			
No anxiety	4.0 (167)	Ref		
Anxiety	4.8 (74)	1.17	(0.87-1.58)	0.296
No depression	3.6 (153)	Ref		
Depression	6.0 (88)	1.71	(1.28-2.27)	<0.001
No PTSD	4.1 (218)	Ref		
PTSD	5.3 (24)	1.26	(0.80-1.97)	0.324
No bipolar	4.0 (219)	Ref		
Bipolar	9.4 (23)	2.32	(1.44-3.74)	<0.001
No psychosis	3.9 (220)	Ref		
Psychosis	22.4 (21)	5.48	(3.20-9.37)	<0.001
No conditions	2.7 (97)	Ref		
One condition	10.0 (84)	3.89	(2.83-5.33)	<0.001
>1 condition	5.0 (60)	1.92	(1.36-2.72)	<0.001

* Models adjusted for age, sex at birth, ethnicity, cannabis use frequency, education, country. Separate models run for each condition and index variable.

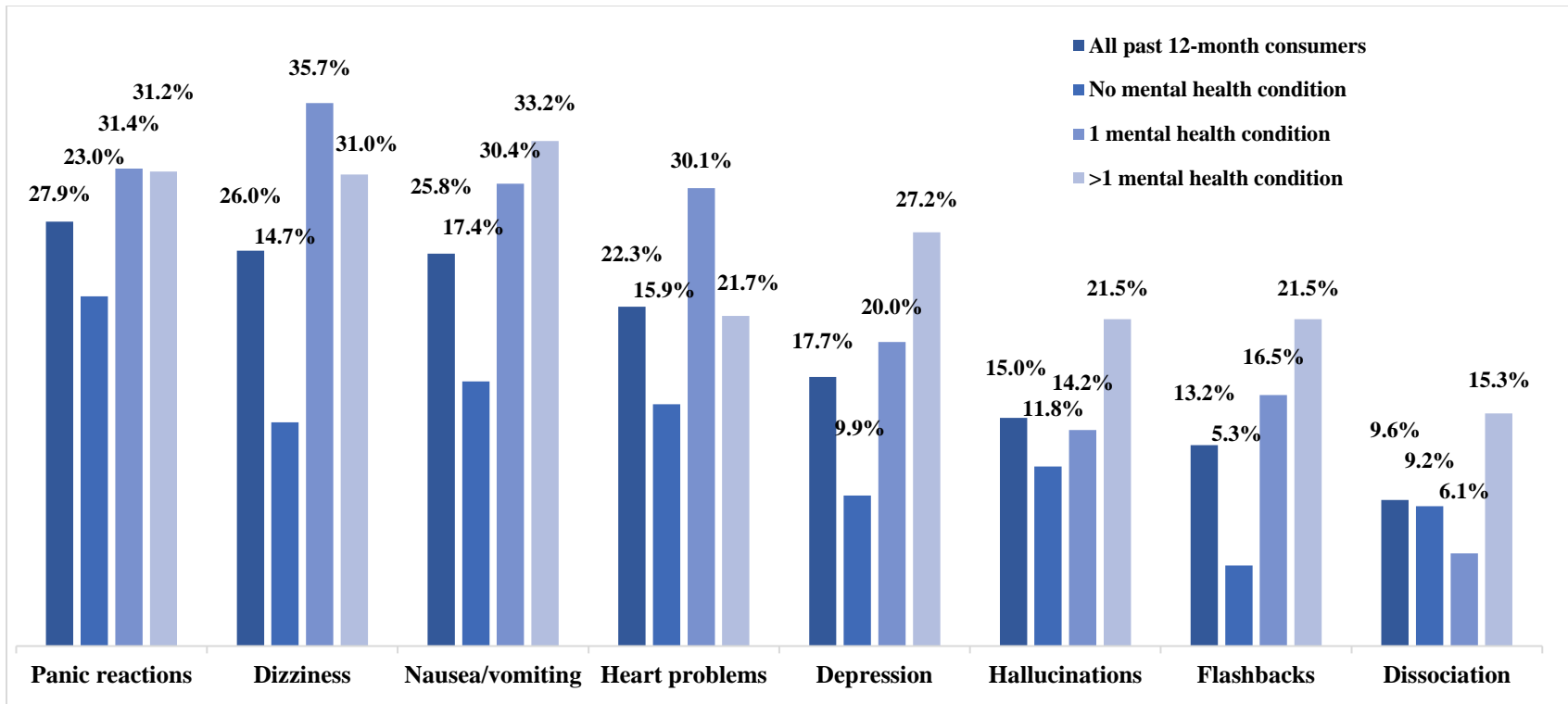


Figure 1: Medical help-seeking in past 12-months for specific adverse effects from cannabis use among all past 12-month consumers, and by experience of mental health conditions in the past 12-months (n=241)

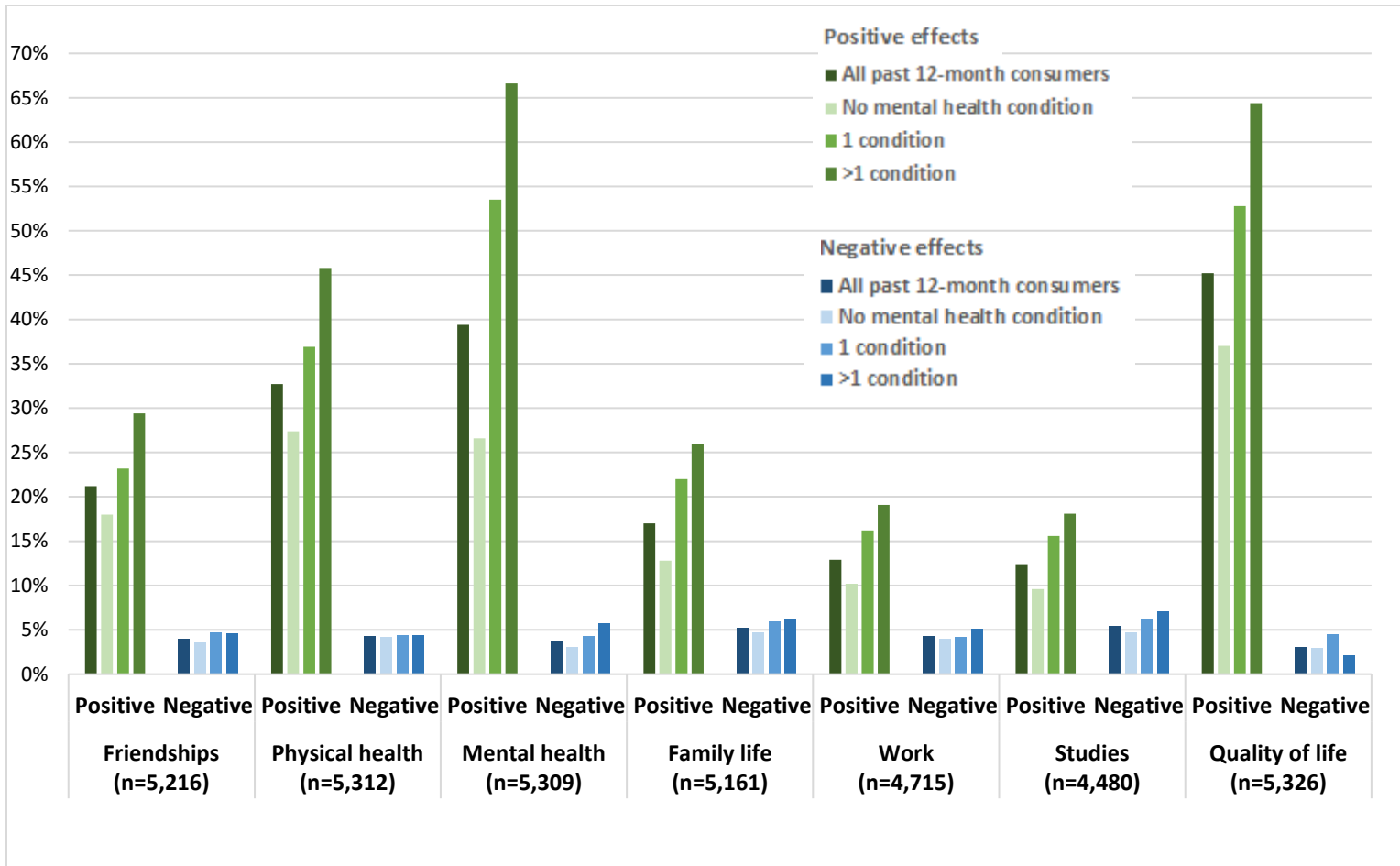


Figure 2: Perceived effects of past 12-month cannabis use among all past 12-month consumers, and by experience of mental health condition in the past 12-months.

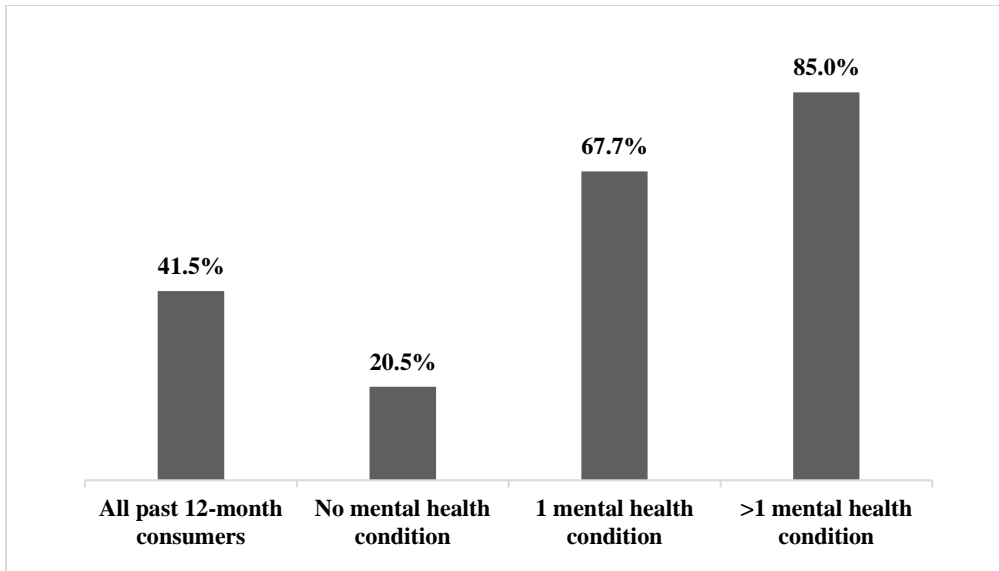


Figure 3: Use of cannabis use to improve/manage symptoms of mental health among all past 12-month consumers, and by experience of mental health conditions in the past 12-months (n=5,630)

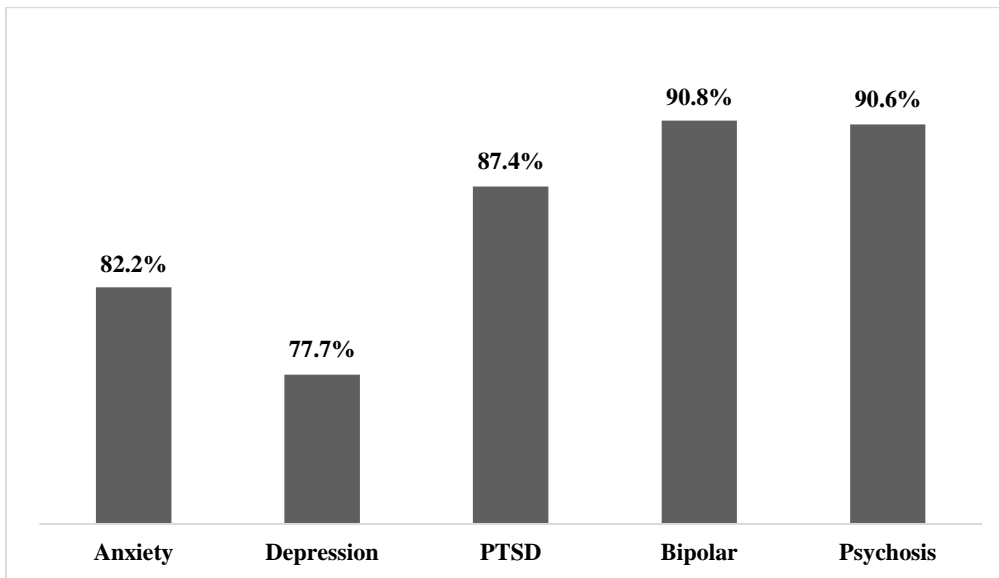


Figure 4: Use of cannabis to improve/manage any symptoms of mental health by experience of mental health condition in the past 12-months (n=5,630)

5.0 DISCUSSION

To our knowledge, the current studies provide among the most comprehensive assessments of how cannabis consumption differs by mental health condition at the population level. To our knowledge, the current study is also the first population-based survey examining the rate of medical help-seeking for adverse events from cannabis, as most previous research comes from hospitalization records or health administrative data. Overall, this research presents six primary findings. First, cannabis use is more prevalent and frequent among consumers who experience mental health conditions compared to those who do not, and these consumers are more likely to use high-potency products (e.g., solid concentrates, THC vape oils, and hash). Second, medical help-seeking is more prevalent among those who experience one or more mental health conditions compared to those without a condition. Third, consumers who experience psychosis, bipolar disorder, and depression are more likely to seek medical help from cannabis use. Consumers with PTSD, bipolar disorder and psychosis reported seeking medical help for a greater number of adverse effects compared to other conditions, including panic, dizziness, and nausea/vomiting. In addition, consumers who experienced mental health conditions reported higher perceived positive effects of cannabis use across all seven categories, and perceptions of negative effects were substantially lower across all categories (friendships or social life, physical health, mental health, family life, work, studies, quality of life). Finally, consumers with psychosis were more likely to report negative effects of cannabis use across all seven categories, while consumers with bipolar disorder reported negative perceived effects on family life, work and studies, and those with anxiety and PTSD reported negative perceived effect on studies.

The results from Study 1 indicate that the use of high-potency product types such as solid concentrates, THC vape oils, and hash is prevalent among those who experience mental health conditions. This reflects the general trend of cannabis consumption in the North American market, where greater use of more potent product types is being observed. Higher strength cannabis products with higher doses of THC might be sought out by consumers in order to relieve symptoms of a condition and maintain the desired intoxication levels from cannabis use.^{116,117} However, greater consumption of cannabis products with high levels of THC is associated with risk of developing psychotic disorders and may exacerbate symptoms of other conditions.^{85,86,92}

Public health communications such as mandated warnings from Health Canada that appear on cannabis packages, have sought to highlight the potential risks of cannabis use on mental health conditions, particularly for those with psychosis. These messages warn that frequent and prolonged use of cannabis with THC can increase the risk of mental health conditions and worsen symptoms. Evidently, frequent cannabis use and the preference for high potency cannabis products appears to be widespread among consumers with mental health conditions, despite substantial research and health warnings discouraging the use of these products.

Study 2 found that approximately 1 in 20 of all past 12-month cannabis consumers sought medical help for adverse effects from cannabis use. Medical help-seeking was more prevalent among those who experienced one or more mental health conditions and among consumers who experienced psychosis, bipolar disorder, and depression. This is unsurprising given the negative effect that cannabis may have on these conditions, particularly among those with psychosis and bipolar disorder.^{29,48,49}

Consumers who experienced mental health conditions consistently reported higher self-perceived positive effects of cannabis use across all seven categories, with the greatest perceived effects being shown for the mental health (67%) and quality of life (64%) categories. A high proportion of consumers who experienced a mental health condition reported using cannabis to manage symptoms of a condition, possibly reflecting the increased sensitivity those with mental health conditions possess with regard to the benefits and harms of cannabis use.⁵¹

In contrast to self-reported ‘positive’ effects of cannabis use, perceptions of negative effects were substantially lower. Notably, consumers with psychosis were more likely to report negative effects of cannabis use across all seven categories, presenting a strong case that the risks related to cannabis use are worse for those who experience psychosis compared to other mental health conditions. Consumers who experienced bipolar disorder had negative self-perceived effects of cannabis on family life, work and studies, and those with anxiety and PTSD were more likely to report negative self-perceived effect on studies. This potentially adds to previous evidence which suggests links between heavy cannabis use and reduced educational attainment, lower income, and adverse consequences in the workplace.^{52,53} For each specific condition, consumers were also more likely to report negative perceived effects of cannabis on mental health. The negative effects could be attributed to the fact that, although cannabis may be initially used for immediate relief of symptoms, its effects are only short-term. Over time, consumers might be left with an increased inability to regulate symptoms of distress, leading to an increased vulnerability to negative mental health related outcomes.^{7,8,55}

6.0 STRENGTHS & LIMITATIONS

Both studies are subject to common limitations of survey research. The ICPS sample was recruited using non probability-based sampling methods; therefore, generalizability of the findings may be limited as estimates are not nationally representative. The use of web panels also creates issues related to selection and non-responses biases. Participants are self-selected and may differ in meaningful ways from those who choose not to participate in panels.¹¹⁸ This may lead to the under-representation of certain groups, including those who do not have internet access.¹¹⁹ However, post-stratification sample weights were constructed for respondents from Canada (age-by-sex-by-province and education groups) and the US (age-by-sex-by-legal state, education, and region-by-race groups), using population estimates from Statistics Canada and the US Census Bureau, and survey weights were calibrated to match these groupings.^{93,94,95,96}

The 2018 ICPS sample has similar prevalence of cannabis use than national benchmark surveys in Canada and the US.¹¹¹ Briefly, in Canada, the 2018 ICPS rate for ‘ever use’ was 56.5% vs. 58.8% for the Canadian Cannabis Survey (CCS), and 8.9% for daily use vs. 9.1% for the NCS for the corresponding age groups.^{4,112} These differences are well within the variability in estimates between the CCS, National Cannabis Survey, and the Canadian Tobacco Alcohol and Drugs Survey, upon which the government relies for ‘official’ prevalence estimates. In addition, the patterns of cannabis use among consumers (e.g., the frequency of use and types of products used) are very similar to national benchmark studies.⁸⁴ Furthermore, compared to in-person surveys or telephone-assisted interviews, the online survey mode of the ICPS may provide greater anonymity and promote more truthful reporting on sensitive topics such as cannabis use or mental health.¹¹⁵

The measure of mental health status used in the current studies (“past 12-month experience of a mental health condition”) is based on self-report rather than clinical diagnoses. Self-report could increase social desirability and recall biases, as the ICPS survey also included a measure for self-reported diagnosis of a mental health condition, for which estimates are generally lower compared to nationally representative surveys.^{113,114} Preliminary analyses were conducted to examine bivariate associations between these measures with the primary outcome variables, and the patterns were highly consistent for both mental health measures. Given that mental health conditions can often go undiagnosed, the “past 12-month experience” measure was selected as the primary independent variable for this study. This measure also better aligns with our outcome measures, which were based on product use, perceived effects, and adverse effects of cannabis use in the past 12-months.

The “cannabis use frequency” measure included consumers who reported using cannabis in the past 12-months, but not those who have ‘ever tried’ cannabis. This would exclude consumers who experienced adverse effects prior to 12-months and ceased cannabis use as a result. The effect of this self-selection bias would be to underestimate the proportion of cannabis users who experience a negative adverse outcome. Additionally, the outcome measure for “cannabis product types” did not assess the concentrations of THC or CBD in the products that were consumed. Therefore, the relative potencies of product types were inferred based on previous literature and what is currently found in the cannabis market.

In Study 2, the sample size was relatively small for the analyses of specific adverse events by mental health condition. This may have impacted the power to detect significant differences between variables. Finally, the cross-sectional design of this study does not allow conclusions to be drawn about the existence or direction of causality. Thus, it is not possible to

infer the temporal association between mental health diagnosis and cannabis use or adverse events experienced.

7.0 IMPLICATIONS

Given the adverse outcomes associated with high potency products in relation to consumers with mental health conditions, future research should be conducted to assess the concentrations of THC and CBD in products that are being consumed to better determine relative potencies and draw comprehensive comparisons about product preferences. Longitudinal studies would also help to potentially establish causality regarding whether cannabis consumers with mental health conditions seek out certain products or if the use of certain products increases the risk for physiological dependence. Additionally, it is critical to assess public knowledge and awareness of labeling and health messages with cannabis products in legal markets, as there are discrepancies between public health warnings and consumer behaviour.

This study also provided novel findings regarding medical help seeking behaviour and self-perceived impact of cannabis use among those with mental health conditions. This research further demonstrate the complex nature of the relationship between cannabis and mental health, as consumers who experienced mental health conditions were more likely to rate cannabis as having a positive effect, but also were more likely to seek medical help related to adverse effects of cannabis use compared to those without a condition. Understanding the reasons and motivations behind its use could aid in developing targeted interventions or communications for consumers that may be sensitive to the potential harms associated with cannabis use. Future research should consider investigating adverse health effects in relation to cannabis product types

consumed, as well as the severity of symptoms experienced, to better detect problematic associations related to cannabis use for those with mental health conditions.

8.0 CONCLUSION

The current study highlights greater frequency of cannabis use among consumers that have experienced mental health disorders and a disproportionately higher use of more potent forms of cannabis. The use of these products is widespread despite public health communications advising against the use of higher potency products, which highlights a discrepancy between public health warnings and consumer behaviour.

In addition, almost half of past year consumers reported using cannabis to manage or improve mental health, with consumers indicating that cannabis has a positive impact in most areas of their life, including mental health. For mental health conditions with more substantial evidence suggesting harmful effects of cannabis use (e.g., psychosis, bipolar disorder), greater self-reported use of cannabis to manage symptoms of mental health was observed, as well as greater help-seeking behaviours and self-perceived negative effects of cannabis use. Reports of negative effects from cannabis use were substantially lower than positive effects; nevertheless, almost 1 in 20 past 12-month cannabis users reported seeking medical help for adverse effects from cannabis, including 4% of daily/near daily users.

Overall, the relationship between cannabis use and mental health is complex, disorder specific, and may include a combination of perceived benefits as well as harms. The findings highlight the critical need to assess public knowledge and awareness of labeling and health messages with cannabis products in legal markets, and target use of specific high potency

cannabis products in prevention, treatment, and harm reduction among people with mental health conditions.

REFERENCES

1. WHO. World Health Organization: Management of Substance Abuse. http://www.who.int/substance_abuse/publications/cannabis_report/en/index5.html. Published 2019.
2. UNODC Cannabis and Hallucinogens: World Drug Report. https://wdr.unodc.org/wdr2019/prelaunch/WDR19_Booklet_5_CANNABIS_HALLUCINOGENS.pdf. Published 2019.
3. Getting cannabis from a licensed producer. Government of Canada. <https://www.canada.ca/en/health-canada/services/getting-cannabis-from-licensed-producer.html>. Published 2019.
4. Canadian Cannabis Survey 2019 Summary. <https://www.canada.ca/en/health-canada/services/publications/drugs-health-products/canadian-cannabis-survey-2019-summary.html>. Published 2019.
5. National Conference of State Legislatures. State Medical Marijuana Laws. ncsl.org/research/health/state-medical-marijuana-laws.aspx#3. Published 2019.
6. SAMHSA Substance Abuse and Mental Health Services Administration. <https://www.samhsa.gov/data/sites/default/files/cbhsq-reports/NSDUHDetailedTabs2018R2/NSDUHDefTabsSect1pe2018.htm>. Published 2018.
7. Kaur R, R. Ambwani S, Singh S. Endocannabinoid System: A Multi-Facet Therapeutic Target. *Curr Clin Pharmacol*. 2016. doi:10.2174/1574884711666160418105339
8. Di Marzo V, Bifulco M, De Petrocellis L. The endocannabinoid system and its therapeutic exploitation. *Nat Rev Drug Discov*. 2004. doi:10.1038/nrd1495
9. Colizzi M, Bhattacharyya S. Does Cannabis Composition Matter? Differential Effects of Delta-9-tetrahydrocannabinol and Cannabidiol on Human Cognition. *Curr Addict Reports*. 2017. doi:10.1007/s40429-017-0142-2
10. Leweke FM, Piomelli D, Pahlisch F, et al. Cannabidiol enhances anandamide signaling and alleviates psychotic symptoms of schizophrenia. *Transl Psychiatry*. 2012. doi:10.1038/tp.2012.15
11. McGuire P, Robson P, Cubala WJ, et al. Cannabidiol (CBD) as an adjunctive therapy in schizophrenia: A multicenter randomized controlled trial. *Am J Psychiatry*. 2018. doi:10.1176/appi.ajp.2017.17030325
12. Hurd YL, Spriggs S, Alishayev J, et al. Cannabidiol for the reduction of cue-induced craving and anxiety in drug-abstinent individuals with heroin use disorder: A double-blind randomized placebo-controlled trial. *Am J Psychiatry*. 2019. doi:10.1176/appi.ajp.2019.18101191
13. Freeman TP, Hindocha C, Baio G, et al. Cannabidiol for the treatment of cannabis use disorder: a phase 2a, double-blind, placebo-controlled, randomised, adaptive Bayesian trial. *The Lancet Psychiatry*. 2020. doi:10.1016/s2215-0366(20)30290-x
14. Bhattacharyya S, Morrison PD, Fusar-Poli P, et al. Opposite effects of δ -9-

- tetrahydrocannabinol and cannabidiol on human brain function and psychopathology. *Neuropsychopharmacology*. 2010. doi:10.1038/npp.2009.184
15. Freeman AM, Petrilli K, Lees R, et al. How does cannabidiol (CBD) influence the acute effects of delta-9-tetrahydrocannabinol (THC) in humans? A systematic review. *Neurosci Biobehav Rev*. 2019. doi:10.1016/j.neubiorev.2019.09.036
 16. De Meijer EPM, Bagatta M, Carboni A, et al. The inheritance of chemical phenotype in *Cannabis sativa* L. *Genetics*. 2003.
 17. Karila L, Roux P, Rolland B, et al. Acute and Long-Term Effects of Cannabis Use: A Review. *Curr Pharm Des*. 2014. doi:10.2174/13816128113199990620
 18. Health Effects of Cannabis. Government of Canada. <https://www.canada.ca/en/health-canada/services/drugs-medication/cannabis/health-effects/effects.html>. Published 2018.
 19. Ford TC, Hayley AC, Downey LA, Parrott AC. Cannabis: An overview of its adverse acute and chronic effects and its implications. *Curr Drug Abuse Rev*. 2017. doi:10.2174/1874473710666170712113042
 20. Bollom A, Austrie J, Hirsch W, et al. Emergency Department Burden of Nausea and Vomiting Associated With Cannabis Use Disorder: US Trends From 2006 to 2013. *J Clin Gastroenterol*. 2018. doi:10.1097/MCG.0000000000000944
 21. Desai R, Fong HK, Shah K, et al. Rising trends in hospitalizations for cardiovascular events among young cannabis users (18–39 years) without other substance abuse. *Med*. 2019. doi:10.3390/medicina55080438
 22. Shearer FM, Bailey PM, Hicks BL, et al. Why do patients choose to attend a private emergency department? *EMA - Emerg Med Australas*. 2015. doi:10.1111/1742-6723.12330
 23. Zhu H, Wu LT. Trends and correlates of cannabis-involved emergency department visits: 2004 to 2011. *J Addict Med*. 2016. doi:10.1097/ADM.0000000000000256
 24. Maloney-Hall B, Wallingford SC, Konefal S, Young MM. Psychotic disorder and cannabis use: Canadian hospitalization trends, 2006–2015. *Heal Promot Chronic Dis Prev Canada*. 2020. doi:10.24095/hpcdp.40.5/6.06
 25. Hall KE, Monte AA, Chang T, et al. Mental Health–related Emergency Department Visits Associated With Cannabis in Colorado. *Acad Emerg Med*. 2018. doi:10.1111/acem.13393
 26. McGuckin T, Ferro M, Hammond D, et al. How high? Trends in Cannabis Use Prior to First Admission to Inpatient Psychiatry in Ontario, Canada between 2007 and 2017. *Can J Psychiatry*. 2020.
 27. Hosseini S, Oremus M. The Effect of Age of Initiation of Cannabis Use on Psychosis, Depression, and Anxiety among Youth under 25 Years. *Can J Psychiatry*. 2019. doi:10.1177/0706743718809339
 28. Gobbi G, Atkin T, Zytynski T, et al. Association of Cannabis Use in Adolescence and Risk of Depression, Anxiety, and Suicidality in Young Adulthood: A Systematic Review

- and Meta-analysis. *JAMA Psychiatry*. 2019. doi:10.1001/jamapsychiatry.2018.4500
29. Curran HV, Freeman TP, Mokrysz C, Lewis DA, Morgan CJA, Parsons LH. Keep off the grass? Cannabis, cognition and addiction. *Nat Rev Neurosci*. 2016. doi:10.1038/nrn.2016.28
 30. Lowe DJE, Sasiadek JD, Coles AS, George TP. Cannabis and mental illness: a review. *Eur Arch Psychiatry Clin Neurosci*. 2019. doi:10.1007/s00406-018-0970-7
 31. *Diagnostic and Statistical Manual of Mental Disorders: DSM-5TM (5th Ed.)*. Arlington VA: American Psychiatric Publishing Inc; 2013.
 32. WHO. *The Alcohol, Smoking and Substance Involvement Screening Test (ASSIST)*.; 2010. <https://www.who.int/management-of-substance-use/assist>.
 33. Goldenberg M, IsHak WW, Danovitch I. Quality of life and recreational cannabis use. *Am J Addict*. 2017. doi:10.1111/ajad.12486
 34. Brezing CA, Choi CJ, Pavlicova M, et al. Abstinence and reduced frequency of use are associated with improvements in quality of life among treatment-seekers with cannabis use disorder. *Am J Addict*. 2018. doi:10.1111/ajad.12660
 35. Lev-Ran S, Le Foll B, McKenzie K, Rehm J. Cannabis use and mental health-related quality of life among individuals with anxiety disorders. *J Anxiety Disord*. 2012. doi:10.1016/j.janxdis.2012.07.002
 36. Evans S, Banerjee S, Leese M, Huxley P. The impact of mental illness on quality of life: A comparison of severe mental illness, common mental disorder and healthy population samples. *Qual Life Res*. 2007. doi:10.1007/s11136-006-9002-6
 37. National Academies of Sciences, Engineering and M. *The Health Effects of Cannabis and Cannabinoids. The Current State of Evidence and Recommendations for Research*. Washington, DC: The National Academies Press; 2017.
 38. Whiting PF, Wolff RF, Deshpande S, et al. Cannabinoids for medical use: A systematic review and meta-analysis. *JAMA - J Am Med Assoc*. 2015. doi:10.1001/jama.2015.6358
 39. Abrams DI. The therapeutic effects of Cannabis and cannabinoids: An update from the National Academies of Sciences, Engineering and Medicine report. *Eur J Intern Med*. 2018. doi:10.1016/j.ejim.2018.01.003
 40. Hoch E, Niemann D, von Keller R, et al. How effective and safe is medical cannabis as a treatment of mental disorders? A systematic review. *Eur Arch Psychiatry Clin Neurosci*. 2019. doi:10.1007/s00406-019-00984-4
 41. Lim K, See YM, Lee J. A systematic review of the effectiveness of medical cannabis for psychiatric, movement and neurodegenerative disorders. *Clin Psychopharmacol Neurosci*. 2017. doi:10.9758/cpn.2017.15.4.301
 42. Black N, Stockings E, Campbell G, et al. Cannabinoids for the treatment of mental disorders and symptoms of mental disorders: a systematic review and meta-analysis. *The Lancet Psychiatry*. 2019. doi:10.1016/S2215-0366(19)30401-8

43. Walsh Z, Gonzalez R, Crosby K, S. Thiessen M, Carroll C, Bonn-Miller MO. Medical cannabis and mental health: A guided systematic review. *Clin Psychol Rev.* 2017. doi:10.1016/j.cpr.2016.10.002
44. Khantzian EJ. The self-medication hypothesis of substance use disorders: A reconsideration and recent applications. *Harv Rev Psychiatry.* 1997. doi:10.3109/10673229709030550
45. Smith LL, Yan F, Charles M, et al. Exploring the link between substance use and mental health status: What can we learn from the self-medication theory? *J Health Care Poor Underserved.* 2017. doi:10.1353/hpu.2017.0056
46. Mané A, Fernández-Expósito M, Bergé D, et al. Relationship between cannabis and psychosis: Reasons for use and associated clinical variables. *Psychiatry Res.* 2015. doi:10.1016/j.psychres.2015.07.070
47. Moore TH, Zammit S, Lingford-Hughes A, et al. Cannabis use and risk of psychotic or affective mental health outcomes: a systematic review. *Lancet.* 2007. doi:10.1016/S0140-6736(07)61162-3
48. Quello SB, Brady KT, Sonne SC. Mood disorders and substance use disorder: a complex comorbidity. *Sci Pract Perspect.* 2005. doi:10.1151/spp053113
49. National Institute on Drug Abuse Research Report Series. Comorbidity: Addiction and Other Mental Illnesses.
50. Konefal S, Gabrys R, Porath A. *Clearing the Smoke on Cannabis: Regular Use and Mental Health CCSA Report.*; 2019. <https://www.ccsa.ca/sites/default/files/2019-05/CCSA-Cannabis-Use-Mental-Health-Report-2019-en.pdf>.
51. Lev-Ran S, Le Foll B, McKenzie K, George TP, Rehm J. Cannabis use and cannabis use disorders among individuals with mental illness. *Compr Psychiatry.* 2013. doi:10.1016/j.comppsy.2012.12.021
52. Guttmanova K, Kosterman R, White HR, et al. The association between regular marijuana use and adult mental health outcomes. *Drug Alcohol Depend.* 2017. doi:10.1016/j.drugalcdep.2017.06.016
53. Canadian Mental Health Association: Mental Health Statistics. <https://ontario.cmha.ca/wp-content/uploads/2016/10/CMHA-Mental-health-factsheet.pdf>. Published 2016.
54. Wilkinson ST, Radhakrishnan R, D'Souza DC. Impact of Cannabis Use on the Development of Psychotic Disorders. *Curr Addict Reports.* 2014. doi:10.1007/s40429-014-0018-7
55. Andréasson S, Engström A, Allebeck P, Rydberg U. CANNABIS AND SCHIZOPHRENIA A Longitudinal Study of Swedish Conscripts. *Lancet.* 1987. doi:10.1016/S0140-6736(87)92620-1
56. Van Os J, Bak M, Hanssen M, Bijl R V., De Graaf R, Verdoux H. Cannabis use and psychosis: A longitudinal population-based study. *Am J Epidemiol.* 2002.

doi:10.1093/aje/kwf043

57. Marconi A, Di Forti M, Lewis CM, Murray RM, Vassos E. Meta-Analysis of the association between the level of cannabis use and risk of psychosis. *Schizophr Bull.* 2016. doi:10.1093/schbul/sbw003
58. Bossong MG, Jansma JM, Bhattacharyya S, Ramsey NF. Role of the endocannabinoid system in brain functions relevant for schizophrenia: An overview of human challenge studies with cannabis or {increment}9-tetrahydrocannabinol (THC). *Prog Neuro-Psychopharmacology Biol Psychiatry.* 2014. doi:10.1016/j.pnpbp.2013.11.017
59. De Marchi N, De Petrocellis L, Orlando P, Daniele F, Fezza F, Di Marzo V. Endocannabinoid signalling in the blood of patients with schizophrenia. *Lipids Health Dis.* 2003. doi:10.1186/1476-511X-2-1
60. Caspi A, Moffitt TE, Cannon M, et al. Moderation of the effect of adolescent-onset cannabis use on adult psychosis by a functional polymorphism in the catechol-O-methyltransferase gene: Longitudinal evidence of a gene X environment interaction. *Biol Psychiatry.* 2005. doi:10.1016/j.biopsych.2005.01.026
61. Van Winkel R, Kahn RS, Linszen DH, et al. Family-based analysis of genetic variation underlying psychosis-inducing effects of cannabis: Sibling analysis and proband follow-up. *Arch Gen Psychiatry.* 2011. doi:10.1001/archgenpsychiatry.2010.152
62. Di Forti M, Iyegbe C, Sallis H, et al. Confirmation that the AKT1 (rs2494732) genotype influences the risk of psychosis in cannabis users. *Biol Psychiatry.* 2012. doi:10.1016/j.biopsych.2012.06.020
63. Morgan CJA, Freeman TP, Powell J, Curran H V. AKT1 genotype moderates the acute psychotomimetic effects of naturalistically smoked cannabis in young cannabis smokers. *Transl Psychiatry.* 2016. doi:10.1038/tp.2015.219
64. Gage SH, Jones HJ, Burgess S, et al. Assessing causality in associations between cannabis use and schizophrenia risk: A two-sample Mendelian randomization study. *Psychol Med.* 2017. doi:10.1017/S0033291716003172
65. Vaucher J, Keating BJ, Lasserre AM, et al. Cannabis use and risk of schizophrenia: A Mendelian randomization study. *Mol Psychiatry.* 2018. doi:10.1038/mp.2016.252
66. Paskan J, Verweij K, Gerring Z, et al. Genome-wide association analysis of lifetime cannabis use (N=184,765) identifies new risk loci, genetic overlap with mental health, and a causal influence of schizophrenia on cannabis use. *bioRxiv.* 2018. doi:10.1101/234294
67. Government of Canada: Cannabis and mental health.
68. Kedzior KK, Laeber LT. 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.* 2014. doi:10.1186/1471-244X-14-136
69. Gage SH, Hickman M, Heron J, et al. Associations of cannabis and cigarette use with depression and anxiety at age 18: Findings from the Avon longitudinal study of parents and children. *PLoS One.* 2015. doi:10.1371/journal.pone.0122896

70. Twomey CD. Association of cannabis use with the development of elevated anxiety symptoms in the general population: A meta-analysis. *J Epidemiol Community Health*. 2017. doi:10.1136/jech-2016-208145
71. Mammen G, Rueda S, Roerecke M, Bonato S, Lev-Ran S, Rehm J. Association of cannabis with long-term clinical symptoms in anxiety and mood disorders: A systematic review of prospective studies. *J Clin Psychiatry*. 2018. doi:10.4088/JCP.17r11839
72. Botsford SL, Yang S, George TP. Cannabis and Cannabinoids in Mood and Anxiety Disorders: Impact on Illness Onset and Course, and Assessment of Therapeutic Potential. *Am J Addict*. 2019. doi:10.1111/ajad.12963
73. Lev-Ran S, Roerecke M, Le Foll B, George TP, McKenzie K, Rehm J. The association between cannabis use and depression: A systematic review and meta-analysis of longitudinal studies. *Psychol Med*. 2014. doi:10.1017/S0033291713001438
74. McDonald KC, Bulloch AGM, Duffy A, et al. Prevalence of bipolar I and II disorder in Canada. *Can J Psychiatry*. 2015. doi:10.1177/070674371506000310
75. Gibbs M, Winsper C, Marwaha S, Gilbert E, Broome M, Singh SP. Cannabis use and mania symptoms: A systematic review and meta-analysis. *J Affect Disord*. 2015. doi:10.1016/j.jad.2014.09.016
76. Van Rossum I, Boomsma M, Tenback D, Reed C, Van Os J. Does cannabis use affect treatment outcome in bipolar disorder?: A longitudinal analysis. *J Nerv Ment Dis*. 2009. doi:10.1097/NMD.0b013e31819292a6
77. Baethge C, Hennen J, Khalsa HMK, Salvatore P, Tohen M, Baldessarini RJ. Sequencing of substance use and affective morbidity in 166 first-episode bipolar I disorder patients. *Bipolar Disord*. 2008. doi:10.1111/j.1399-5618.2007.00575.x
78. Lev-Ran S, Le Foll B, McKenzie K, George TP, Rehm J. Bipolar disorder and co-occurring cannabis use disorders: Characteristics, co-morbidities and clinical correlates. *Psychiatry Res*. 2013. doi:10.1016/j.psychres.2012.12.014
79. Van Ameringen M, Mancini C, Patterson B, Boyle MH. Post-traumatic stress disorder in Canada. *CNS Neurosci Ther*. 2008. doi:10.1111/j.1755-5949.2008.00049.x
80. Gentes EL, Schry AR, Hicks TA, et al. Prevalence and correlates of cannabis use in an outpatient VA posttraumatic stress disorder clinic. *Psychol Addict Behav*. 2016. doi:10.1037/adb0000154
81. Wilkinson ST, Stefanovics E, Rosenheck RA. Marijuana use is associated with worse outcomes in symptom severity and violent behavior in patients with posttraumatic stress disorder. *J Clin Psychiatry*. 2015. doi:10.4088/JCP.14m09475
82. Grotenhermen F. Pharmacokinetics and pharmacodynamics of cannabinoids. *Clin Pharmacokinet*. 2003. doi:10.2165/00003088-200342040-00003
83. Chandra S, Radwan MM, Majumdar CG, Church JC, Freeman TP, ElSohly MA. New trends in cannabis potency in USA and Europe during the last decade (2008–2017). *Eur Arch Psychiatry Clin Neurosci*. 2019. doi:10.1007/s00406-019-00983-5

84. Goodman S, Wadsworth E, Leos-Toro C, Hammond D. Prevalence and forms of cannabis use in legal vs. illegal recreational cannabis markets. *Int J Drug Policy*. 2020. doi:10.1016/j.drugpo.2019.102658
85. Di Forti M, Morgan C, Dazzan P, et al. High-potency cannabis and the risk of psychosis. *Br J Psychiatry*. 2009. doi:10.1192/bjp.bp.109.064220
86. Di Forti M, Marconi A, Carra E, et al. Proportion of patients in south London with first-episode psychosis attributable to use of high potency cannabis: A case-control study. *The Lancet Psychiatry*. 2015. doi:10.1016/S2215-0366(14)00117-5
87. Schoeler T, Petros N, Di Forti M, et al. Effects of continuation, frequency, and type of cannabis use on relapse in the first 2 years after onset of psychosis: an observational study. *The Lancet Psychiatry*. 2016. doi:10.1016/S2215-0366(16)30188-2
88. Di Forti M, Quattrone D, Freeman TP, et al. 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*. 2019. doi:10.1016/S2215-0366(19)30048-3
89. Freeman TP, Winstock AR. Examining the profile of high-potency cannabis and its association with severity of cannabis dependence. *Psychol Med*. 2015. doi:10.1017/S0033291715001178
90. Meier MH. Associations between butane hash oil use and cannabis-related problems. *Drug Alcohol Depend*. 2017. doi:10.1016/j.drugalcdep.2017.06.015
91. Craft S, Winstock A, Ferris J, Mackie C, Lynskey MT, Freeman TP. Characterising heterogeneity in the use of different cannabis products: Latent class analysis with 55 000 people who use cannabis and associations with severity of cannabis dependence. *Psychol Med*. 2019. doi:10.1017/S0033291719002460
92. Hines LA, Freeman TP, Gage SH, et al. Association of High-Potency Cannabis Use with Mental Health and Substance Use in Adolescence. *JAMA Psychiatry*. 2020. doi:10.1001/jamapsychiatry.2020.1035
93. Statistics Canada, 2016 Census of Population, Statistics Canada Catalogue no. 98-400-X2016242. Highest Certificate, Diploma or Degree. <https://www12.statcan.gc.ca/census-recensement/2016/dp-pd/dt-td/Rp-eng.cfm?LANG=E&APATH=3&DETAIL=0&DIM=0&FL=A&FREE=0&GC=0&GID=0&GK=0&GRP=1&PID=110634&PRID=10&PTYPE=109445&S=0&SHOWALL=0&SUB=0&Temporal=2017&THEME=123&VID=0&VNAMEE=&VNAMEF>.
94. Statistics Canada. Table 17-10-0005-01 Population estimates on July 1st, by age and sex. <https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1710000501>. Published 2017.
95. U.S. Census Bureau, 2013-2017 American Community Survey 5-Year Estimates. https://factfinder.census.gov/faces/tableservices/jsf/pages/productview.xhtml?pid=ACS_17_5YR_S1501&src=pt.
96. U.S. Census Bureau, Population Division. Annual State Resident Population Estimates for 6 Race Groups (5 Race Alone Groups and Two or More Races) by Age, Sex, and Hispanic Origin: April 1, 2010 to July 1, 2017. File: 7/1/2017 State Characteristics Populat.

- <https://www.census.gov/data/datasets/2017/demo/popest/state-detail.html>.
97. Hammond D, Goodman S, Wadsworth E, Rynard V, Boudreau C, Hall W. Evaluating the impacts of cannabis legalization: The International Cannabis Policy Study. *Int J Drug Policy*. 2020. doi:10.1016/j.drugpo.2020.102698
 98. Goodman S, Burkhalter R, Hammond D. *International Cannabis Policy Study Technical Report - Wave 2 (2019)*. Waterloo, ON Canada; 2020. <http://cannabisproject.ca/methods/>.
 99. Bianconi F, Bonomo M, Marconi A, et al. Differences in cannabis-related experiences between patients with a first episode of psychosis and controls. *Psychol Med*. 2016. doi:10.1017/S0033291715002494
 100. Blessing EM, Steenkamp MM, Manzanares J, Marmar CR. Cannabidiol as a Potential Treatment for Anxiety Disorders. *Neurotherapeutics*. 2015. doi:10.1007/s13311-015-0387-1
 101. Crippa JA, Zuardi AW, Martín-Santos R, et al. Cannabis and anxiety: A critical review of the evidence. *Hum Psychopharmacol*. 2009. doi:10.1002/hup.1048
 102. Mondragón-Maya A, Ramos-Mastache D, Román PD, Yáñez-Téllez G. Social Cognition in Schizophrenia, Unaffected Relatives and Ultra- High Risk for Psychosis: What Do We Currently Know? *Actas Esp Psiquiatr*. 2017.
 103. Gage SH, Hickman M, Zammit S. Association between cannabis and psychosis: Epidemiologic evidence. *Biol Psychiatry*. 2016. doi:10.1016/j.biopsych.2015.08.001
 104. Saiz-Ruiz J, Cabrera B, Bernardo M, et al. Cannabis use, COMT, BDNF and age at first-episode psychosis. *Psychiatry Res*. 2017. doi:10.1016/j.psychres.2017.01.045
 105. Schoeler T, Monk A, Sami MB, et al. Continued versus discontinued cannabis use in patients with psychosis: A systematic review and meta-analysis. *The Lancet Psychiatry*. 2016. doi:10.1016/S2215-0366(15)00363-6
 106. Cousijn J, Núñez AE, Filbey FM. Time to acknowledge the mixed effects of cannabis on health: a summary and critical review of the NASEM 2017 report on the health effects of cannabis and cannabinoids. In: *Addiction*. ; 2018. doi:10.1111/add.14084
 107. Brook JS, Lee JY, Finch SJ, Seltzer N, Brook DW. Adult work commitment, financial stability, and social environment as related to trajectories of marijuana use beginning in adolescence. *Subst Abus*. 2013. doi:10.1080/08897077.2013.775092
 108. MacDonald S, Hall W, Roman P, Stockwell T, Coghlan M, Nesvaag S. Testing for cannabis in the work-place: A review of the evidence. *Addiction*. 2010. doi:10.1111/j.1360-0443.2009.02808.x
 109. Feingold D, Rehm J, Lev-Ran S. Cannabis use and the course and outcome of major depressive disorder: A population based longitudinal study. *Psychiatry Res*. 2017. doi:10.1016/j.psychres.2017.02.027
 110. Koob GF, Le Moal M. Drug addiction, dysregulation of reward, and allostasis. *Neuropsychopharmacology*. 2001. doi:10.1016/S0893-133X(00)00195-0

111. Hammond D, Goodman S, Wadsworth E, Rynard V, Boudreau C, Hall W. Evaluating the impact of cannabis legalization: The International Cannabis Policy Study. *Int J Drug Policy*. 2020;1(77).
112. Canadian Cannabis Survey 2018 Summary. Government of Canada. <https://www.canada.ca/en/services/health/publications/drugs-health-products/canadian-cannabis-survey-2018-summary.html>. Published 2018.
113. SAMHSA. Key substance use and mental health indicators in the United States: Results from the 2017 National Survey on Drug Use and Health (HHS Publication No. SMA 18-5068, NSUDH Series H-53). <https://www.samhsa.gov/data/sites/default/files/cbhsq-reports/NSDUHFFR2017/NSDUHFFR2017.pdf>. Published 2018.
114. Statistics Canada. Canadian Community Health Survey Information. <https://www23.statcan.gc.ca/imdb/p2SV.pl?Function=getSurvey&SDDS=3226&lang=en&db=imdb&adm=8&dis=2>. Published 2018.
115. Grucza RA, Agrawal A, Krauss MJ, Cavazos-Rehg PA, Bierut LJ. Recent trends in the prevalence of marijuana use and associated disorders in the United States. *JAMA Psychiatry*. 2016. doi:10.1001/jamapsychiatry.2015.3111
116. Stith SS, Vigil JM, Brockelman F, Keeling K, Hall B. The Association between Cannabis Product Characteristics and Symptom Relief. *Sci Rep*. 2019. doi:10.1038/s41598-019-39462-1
117. Colizzi M, Bhattacharyya S. Cannabis use and the development of tolerance: a systematic review of human evidence. *Neurosci Biobehav Rev*. 2018. doi:10.1016/j.neubiorev.2018.07.014
118. Hays RD, Liu H, Kapteyn A. Use of Internet panels to conduct surveys. *Behav Res Methods*. 2015. doi:10.3758/s13428-015-0617-9
119. Bethlehem J. Selection bias in web surveys. *Int Stat Rev*. 2010. doi:10.1111/j.1751-5823.2010.00112.x

Manuscript 1

1. Konefal S, Gabrys R, Porath A. *Clearing the Smoke on Cannabis: Regular Use and Mental Health CCSA Report.*; 2019. <https://www.ccsa.ca/sites/default/files/2019-05/CCSA-Cannabis-Use-Mental-Health-Report-2019-en.pdf>.
2. Lev-Ran S, Le Foll B, McKenzie K, George TP, Rehm J. Cannabis use and cannabis use disorders among individuals with mental illness. *Compr Psychiatry*. 2013. doi:10.1016/j.comppsy.2012.12.021
3. Khan S. Concurrent mental and substance use disorders in Canada. *Heal Reports*. 2017.
4. *Diagnostic and Statistical Manual of Mental Disorders: DSM-5TM (5th Ed.)*. Arlington VA: American Psychiatric Publishing Inc; 2013.
5. Lowe DJE, Sasiadek JD, Coles AS, George TP. Cannabis and mental illness: a review.

- Eur Arch Psychiatry Clin Neurosci.* 2019. doi:10.1007/s00406-018-0970-7
6. Khantzian EJ. The self-medication hypothesis of substance use disorders: A reconsideration and recent applications. *Harv Rev Psychiatry.* 1997. doi:10.3109/10673229709030550
 7. Khantzian EJ. The self medication hypothesis of addictive disorders: Focus on heroin and cocaine dependence. *Am J Psychiatry.* 1985. doi:10.1176/ajp.142.11.1259
 8. Mané A, Fernández-Expósito M, Bergé D, et al. Relationship between cannabis and psychosis: Reasons for use and associated clinical variables. *Psychiatry Res.* 2015. doi:10.1016/j.psychres.2015.07.070
 9. Moore TH, Zammit S, Lingford-Hughes A, et al. Cannabis use and risk of psychotic or affective mental health outcomes: a systematic review. *Lancet.* 2007. doi:10.1016/S0140-6736(07)61162-3
 10. Quello SB, Brady KT, Sonne SC. Mood disorders and substance use disorder: a complex comorbidity. *Sci Pract Perspect.* 2005. doi:10.1151/spp053113
 11. Hosseini S, Oremus M. The Effect of Age of Initiation of Cannabis Use on Psychosis, Depression, and Anxiety among Youth under 25 Years. *Can J Psychiatry.* 2019. doi:10.1177/0706743718809339
 12. Wilkinson ST, Radhakrishnan R, D'Souza DC. Impact of Cannabis Use on the Development of Psychotic Disorders. *Curr Addict Reports.* 2014. doi:10.1007/s40429-014-0018-7
 13. Andréasson S, Engström A, Allebeck P, Rydberg U. CANNABIS AND SCHIZOPHRENIA A Longitudinal Study of Swedish Conscripts. *Lancet.* 1987. doi:10.1016/S0140-6736(87)92620-1
 14. Van Os J, Bak M, Hanssen M, Bijl R V., De Graaf R, Verdoux H. Cannabis use and psychosis: A longitudinal population-based study. *Am J Epidemiol.* 2002. doi:10.1093/aje/kwf043
 15. Marconi A, Di Forti M, Lewis CM, Murray RM, Vassos E. Meta-Analysis of the association between the level of cannabis use and risk of psychosis. *Schizophr Bull.* 2016. doi:10.1093/schbul/sbw003
 16. Caspi A, Moffitt TE, Cannon M, et al. Moderation of the effect of adolescent-onset cannabis use on adult psychosis by a functional polymorphism in the catechol-O-methyltransferase gene: Longitudinal evidence of a gene X environment interaction. *Biol Psychiatry.* 2005. doi:10.1016/j.biopsych.2005.01.026
 17. Van Winkel R, Kahn RS, Linszen DH, et al. Family-based analysis of genetic variation underlying psychosis-inducing effects of cannabis: Sibling analysis and proband follow-up. *Arch Gen Psychiatry.* 2011. doi:10.1001/archgenpsychiatry.2010.152
 18. Di Forti M, Iyegbe C, Sallis H, et al. Confirmation that the AKT1 (rs2494732) genotype influences the risk of psychosis in cannabis users. *Biol Psychiatry.* 2012. doi:10.1016/j.biopsych.2012.06.020

19. Morgan CJA, Freeman TP, Powell J, Curran H V. AKT1 genotype moderates the acute psychotomimetic effects of naturalistically smoked cannabis in young cannabis smokers. *Transl Psychiatry*. 2016. doi:10.1038/tp.2015.219
20. Gage SH, Jones HJ, Burgess S, et al. Assessing causality in associations between cannabis use and schizophrenia risk: A two-sample Mendelian randomization study. *Psychol Med*. 2017. doi:10.1017/S0033291716003172
21. Vaucher J, Keating BJ, Lasserre AM, et al. Cannabis use and risk of schizophrenia: A Mendelian randomization study. *Mol Psychiatry*. 2018. doi:10.1038/mp.2016.252
22. Paskan J, Verweij K, Gerring Z, et al. Genome-wide association analysis of lifetime cannabis use (N=184,765) identifies new risk loci, genetic overlap with mental health, and a causal influence of schizophrenia on cannabis use. *bioRxiv*. 2018. doi:10.1101/234294
23. Botsford SL, Yang S, George TP. Cannabis and Cannabinoids in Mood and Anxiety Disorders: Impact on Illness Onset and Course, and Assessment of Therapeutic Potential. *Am J Addict*. 2019. doi:10.1111/ajad.12963
24. Crippa JA, Zuardi AW, Martín-Santos R, et al. Cannabis and anxiety: A critical review of the evidence. *Hum Psychopharmacol*. 2009. doi:10.1002/hup.1048
25. Kedzior KK, Laeber LT. 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*. 2014. doi:10.1186/1471-244X-14-136
26. Twomey CD. Association of cannabis use with the development of elevated anxiety symptoms in the general population: A meta-analysis. *J Epidemiol Community Health*. 2017. doi:10.1136/jech-2016-208145
27. Mammen G, Rueda S, Roerecke M, Bonato S, Lev-Ran S, Rehm J. Association of cannabis with long-term clinical symptoms in anxiety and mood disorders: A systematic review of prospective studies. *J Clin Psychiatry*. 2018. doi:10.4088/JCP.17r11839
28. Gobbi G, Atkin T, Zytynski T, et al. Association of Cannabis Use in Adolescence and Risk of Depression, Anxiety, and Suicidality in Young Adulthood: A Systematic Review and Meta-analysis. *JAMA Psychiatry*. 2019. doi:10.1001/jamapsychiatry.2018.4500
29. Gibbs M, Winsper C, Marwaha S, Gilbert E, Broome M, Singh SP. Cannabis use and mania symptoms: A systematic review and meta-analysis. *J Affect Disord*. 2015. doi:10.1016/j.jad.2014.09.016
30. Van Rossum I, Boomsma M, Tenback D, Reed C, Van Os J. Does cannabis use affect treatment outcome in bipolar disorder?: A longitudinal analysis. *J Nerv Ment Dis*. 2009. doi:10.1097/NMD.0b013e31819292a6
31. Lev-Ran S, Le Foll B, McKenzie K, George TP, Rehm J. Bipolar disorder and co-occurring cannabis use disorders: Characteristics, co-morbidities and clinical correlates. *Psychiatry Res*. 2013. doi:10.1016/j.psychres.2012.12.014
32. Gentes EL, Schry AR, Hicks TA, et al. Prevalence and correlates of cannabis use in an outpatient VA posttraumatic stress disorder clinic. *Psychol Addict Behav*. 2016.

doi:10.1037/adb0000154

33. Wilkinson ST, Stefanovics E, Rosenheck RA. Marijuana use is associated with worse outcomes in symptom severity and violent behavior in patients with posttraumatic stress disorder. *J Clin Psychiatry*. 2015. doi:10.4088/JCP.14m09475
34. Grotenhermen F. Pharmacokinetics and pharmacodynamics of cannabinoids. *Clin Pharmacokinet*. 2003. doi:10.2165/00003088-200342040-00003
35. Leweke FM, Piomelli D, Pahlisch F, et al. Cannabidiol enhances anandamide signaling and alleviates psychotic symptoms of schizophrenia. *Transl Psychiatry*. 2012. doi:10.1038/tp.2012.15
36. McGuire P, Robson P, Cubala WJ, et al. Cannabidiol (CBD) as an adjunctive therapy in schizophrenia: A multicenter randomized controlled trial. *Am J Psychiatry*. 2018. doi:10.1176/appi.ajp.2017.17030325
37. Hurd YL, Spriggs S, Alishayev J, et al. Cannabidiol for the reduction of cue-induced craving and anxiety in drug-abstinent individuals with heroin use disorder: A double-blind randomized placebo-controlled trial. *Am J Psychiatry*. 2019. doi:10.1176/appi.ajp.2019.18101191
38. Freeman TP, Hindocha C, Baio G, et al. Cannabidiol for the treatment of cannabis use disorder: a phase 2a, double-blind, placebo-controlled, randomised, adaptive Bayesian trial. *The Lancet Psychiatry*. 2020. doi:10.1016/s2215-0366(20)30290-x
39. Abrams DI. The therapeutic effects of Cannabis and cannabinoids: An update from the National Academies of Sciences, Engineering and Medicine report. *Eur J Intern Med*. 2018. doi:10.1016/j.ejim.2018.01.003
40. Chandra S, Radwan MM, Majumdar CG, Church JC, Freeman TP, ElSohly MA. New trends in cannabis potency in USA and Europe during the last decade (2008–2017). *Eur Arch Psychiatry Clin Neurosci*. 2019. doi:10.1007/s00406-019-00983-5
41. Goodman S, Wadsworth E, Leos-Toro C, Hammond D. Prevalence and forms of cannabis use in legal vs. illegal recreational cannabis markets. *Int J Drug Policy*. 2020. doi:10.1016/j.drugpo.2019.102658
42. Di Forti M, Morgan C, Dazzan P, et al. High-potency cannabis and the risk of psychosis. *Br J Psychiatry*. 2009. doi:10.1192/bjp.bp.109.064220
43. Di Forti M, Marconi A, Carra E, et al. Proportion of patients in south London with first-episode psychosis attributable to use of high potency cannabis: A case-control study. *The Lancet Psychiatry*. 2015. doi:10.1016/S2215-0366(14)00117-5
44. Schoeler T, Petros N, Di Forti M, et al. Effects of continuation, frequency, and type of cannabis use on relapse in the first 2 years after onset of psychosis: an observational study. *The Lancet Psychiatry*. 2016. doi:10.1016/S2215-0366(16)30188-2
45. Di Forti M, Quattrone D, Freeman TP, et al. 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*. 2019. doi:10.1016/S2215-0366(19)30048-3

46. Chan GCK, Hall W, Freeman TP, Ferris J, Kelly AB, Winstock A. User characteristics and effect profile of Butane Hash Oil: An extremely high-potency cannabis concentrate. *Drug Alcohol Depend.* 2017. doi:10.1016/j.drugalcdep.2017.04.014
47. Freeman TP, Winstock AR. Examining the profile of high-potency cannabis and its association with severity of cannabis dependence. *Psychol Med.* 2015. doi:10.1017/S0033291715001178
48. Meier MH. Associations between butane hash oil use and cannabis-related problems. *Drug Alcohol Depend.* 2017. doi:10.1016/j.drugalcdep.2017.06.015
49. Craft S, Winstock A, Ferris J, Mackie C, Lynskey MT, Freeman TP. Characterising heterogeneity in the use of different cannabis products: Latent class analysis with 55 000 people who use cannabis and associations with severity of cannabis dependence. *Psychol Med.* 2019. doi:10.1017/S0033291719002460
50. Hines LA, Freeman TP, Gage SH, et al. Association of High-Potency Cannabis Use with Mental Health and Substance Use in Adolescence. *JAMA Psychiatry.* 2020. doi:10.1001/jamapsychiatry.2020.1035
51. Statistics Canada, 2016 Census of Population, Statistics Canada Catalogue no. 98-400-X2016242. Highest Certificate, Diploma or Degree. <https://www12.statcan.gc.ca/census-recensement/2016/dp-pd/dt-td/Rp-eng.cfm?LANG=E&APATH=3&DETAIL=0&DIM=0&FL=A&FREE=0&GC=0&GID=0&GK=0&GRP=1&PID=110634&PRID=10&PTYPE=109445&S=0&SHOWALL=0&SUB=0&Temporal=2017&THEME=123&VID=0&VNAMEE=&VNAMEF>.
52. Statistics Canada. Table 17-10-0005-01 Population estimates on July 1st, by age and sex. <https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1710000501>. Published 2017.
53. U.S. Census Bureau, 2013-2017 American Community Survey 5-Year Estimates. https://factfinder.census.gov/faces/tableservices/jsf/pages/productview.xhtml?pid=ACS_17_5YR_S1501&src=pt.
54. U.S. Census Bureau, Population Division. Annual State Resident Population Estimates for 6 Race Groups (5 Race Alone Groups and Two or More Races) by Age, Sex, and Hispanic Origin: April 1, 2010 to July 1, 2017. File: 7/1/2017 State Characteristics Populat. <https://www.census.gov/data/datasets/2017/demo/popest/state-detail.html>.
55. Hammond D, Goodman S, Wadsworth E, Rynard V, Boudreau C, Hall W. Evaluating the impacts of cannabis legalization: The International Cannabis Policy Study. *Int J Drug Policy.* 2020. doi:10.1016/j.drugpo.2020.102698
56. Goodman S, Burkhalter R, Hammond D. *International Cannabis Policy Study Technical Report - Wave 2 (2019)*. Waterloo, ON Canada; 2020. <http://cannabisproject.ca/methods/>.
57. Kessler RC. The epidemiology of dual diagnosis. *Biol Psychiatry.* 2004. doi:10.1016/j.biopsych.2004.06.034
58. Canadian Cannabis Survey 2019 Summary. <https://www.canada.ca/en/health-canada/services/publications/drugs-health-products/canadian-cannabis-survey-2019-summary.html>. Published 2019.

59. Zoellner LA, Rothbaum BO, Feeny NC. PTSD not an anxiety disorder? DSM committee proposal turns back the hands of time. *Depress Anxiety*. 2011. doi:10.1002/da.20899
60. Canadian Centre on Substance Use and Addiction: Policy and Regulations (Cannabis). <https://www.ccsa.ca/policy-and-regulations-cannabis>. Published 2019.
61. Stith SS, Vigil JM, Brockelman F, Keeling K, Hall B. The Association between Cannabis Product Characteristics and Symptom Relief. *Sci Rep*. 2019. doi:10.1038/s41598-019-39462-1
62. Colizzi M, Bhattacharyya S. Cannabis use and the development of tolerance: a systematic review of human evidence. *Neurosci Biobehav Rev*. 2018. doi:10.1016/j.neubiorev.2018.07.014
63. Hammond D, Goodman S, Wadsworth E, Rynard V, Boudreau C, Hall W. Evaluating the impact of cannabis legalization: The International Cannabis Policy Study. *Int J Drug Policy*. 2020;1(77).
64. Canadian Cannabis Survey 2018 Summary. Government of Canada. <https://www.canada.ca/en/services/health/publications/drugs-health-products/canadian-cannabis-survey-2018-summary.html>. Published 2018.
65. SAMHSA. Key substance use and mental health indicators in the United States: Results from the 2017 National Survey on Drug Use and Health (HHS Publication No. SMA 18-5068, NSUDH Series H-53). <https://www.samhsa.gov/data/sites/default/files/cbhsq-reports/NSDUHFFR2017/NSDUHFFR2017.pdf>. Published 2018.
66. Statistics Canada. Canadian Community Health Survey Information. <https://www23.statcan.gc.ca/imdb/p2SV.pl?Function=getSurvey&SDDS=3226&lang=en&db=imdb&adm=8&dis=2>. Published 2018.

Manuscript 2

1. Bollom A, Austrie J, Hirsch W, et al. Emergency Department Burden of Nausea and Vomiting Associated With Cannabis Use Disorder: US Trends From 2006 to 2013. *J Clin Gastroenterol*. 2018. doi:10.1097/MCG.0000000000000944
2. Desai R, Fong HK, Shah K, et al. Rising trends in hospitalizations for cardiovascular events among young cannabis users (18–39 years) without other substance abuse. *Med*. 2019. doi:10.3390/medicina55080438
3. Shearer FM, Bailey PM, Hicks BL, et al. Why do patients choose to attend a private emergency department? *EMA - Emerg Med Australas*. 2015. doi:10.1111/1742-6723.12330
4. Zhu H, Wu LT. Trends and correlates of cannabis-involved emergency department visits: 2004 to 2011. *J Addict Med*. 2016. doi:10.1097/ADM.0000000000000256
5. Maloney-Hall B, Wallingford SC, Konefal S, Young MM. Psychotic disorder and cannabis use: Canadian hospitalization trends, 2006–2015. *Heal Promot Chronic Dis Prev Canada*. 2020. doi:10.24095/hpcdp.40.5/6.06

6. Hall KE, Monte AA, Chang T, et al. Mental Health–related Emergency Department Visits Associated With Cannabis in Colorado. *Acad Emerg Med*. 2018. doi:10.1111/acem.13393
7. McGuckin T, Ferro M, Hammond D, et al. How high? Trends in Cannabis Use Prior to First Admission to Inpatient Psychiatry in Ontario, Canada between 2007 and 2017. *Can J Psychiatry*. 2020.
8. Lowe DJE, Sasiadek JD, Coles AS, George TP. Cannabis and mental illness: a review. *Eur Arch Psychiatry Clin Neurosci*. 2019. doi:10.1007/s00406-018-0970-7
9. Marconi A, Di Forti M, Lewis CM, Murray RM, Vassos E. Meta-Analysis of the association between the level of cannabis use and risk of psychosis. *Schizophr Bull*. 2016. doi:10.1093/schbul/sbw003
10. Di Forti M, Quattrone D, Freeman TP, et al. 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*. 2019. doi:10.1016/S2215-0366(19)30048-3
11. Gage SH, Hickman M, Zammit S. Association between cannabis and psychosis: Epidemiologic evidence. *Biol Psychiatry*. 2016. doi:10.1016/j.biopsych.2015.08.001
12. Wilkinson ST, Radhakrishnan R, D’Souza DC. Impact of Cannabis Use on the Development of Psychotic Disorders. *Curr Addict Reports*. 2014. doi:10.1007/s40429-014-0018-7
13. Saiz-Ruiz J, Cabrera B, Bernardo M, et al. Cannabis use, COMT, BDNF and age at first-episode psychosis. *Psychiatry Res*. 2017. doi:10.1016/j.psychres.2017.01.045
14. Van Winkel R, Kahn RS, Linszen DH, et al. Family-based analysis of genetic variation underlying psychosis-inducing effects of cannabis: Sibling analysis and proband follow-up. *Arch Gen Psychiatry*. 2011. doi:10.1001/archgenpsychiatry.2010.152
15. Di Forti M, Iyegbe C, Sallis H, et al. Confirmation that the AKT1 (rs2494732) genotype influences the risk of psychosis in cannabis users. *Biol Psychiatry*. 2012. doi:10.1016/j.biopsych.2012.06.020
16. Morgan CJA, Freeman TP, Powell J, Curran H V. AKT1 genotype moderates the acute psychotomimetic effects of naturalistically smoked cannabis in young cannabis smokers. *Transl Psychiatry*. 2016. doi:10.1038/tp.2015.219
17. Gage SH, Jones HJ, Burgess S, et al. Assessing causality in associations between cannabis use and schizophrenia risk: A two-sample Mendelian randomization study. *Psychol Med*. 2017. doi:10.1017/S0033291716003172
18. Vaucher J, Keating BJ, Lasserre AM, et al. Cannabis use and risk of schizophrenia: A Mendelian randomization study. *Mol Psychiatry*. 2018. doi:10.1038/mp.2016.252
19. Paskan J, Verweij K, Gerring Z, et al. Genome-wide association analysis of lifetime cannabis use (N=184,765) identifies new risk loci, genetic overlap with mental health, and a causal influence of schizophrenia on cannabis use. *bioRxiv*. 2018. doi:10.1101/234294
20. Botsford SL, Yang S, George TP. Cannabis and Cannabinoids in Mood and Anxiety

- Disorders: Impact on Illness Onset and Course, and Assessment of Therapeutic Potential. *Am J Addict*. 2019. doi:10.1111/ajad.12963
21. Crippa JA, Zuardi AW, Martín-Santos R, et al. Cannabis and anxiety: A critical review of the evidence. *Hum Psychopharmacol*. 2009. doi:10.1002/hup.1048
 22. Kedzior KK, Laeber LT. 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*. 2014. doi:10.1186/1471-244X-14-136
 23. Hosseini S, Oremus M. The Effect of Age of Initiation of Cannabis Use on Psychosis, Depression, and Anxiety among Youth under 25 Years. *Can J Psychiatry*. 2019. doi:10.1177/0706743718809339
 24. Twomey CD. Association of cannabis use with the development of elevated anxiety symptoms in the general population: A meta-analysis. *J Epidemiol Community Health*. 2017. doi:10.1136/jech-2016-208145
 25. Mammen G, Rueda S, Roerecke M, Bonato S, Lev-Ran S, Rehm J. Association of cannabis with long-term clinical symptoms in anxiety and mood disorders: A systematic review of prospective studies. *J Clin Psychiatry*. 2018. doi:10.4088/JCP.17r11839
 26. Gobbi G, Atkin T, Zytynski T, et al. Association of Cannabis Use in Adolescence and Risk of Depression, Anxiety, and Suicidality in Young Adulthood: A Systematic Review and Meta-analysis. *JAMA Psychiatry*. 2019. doi:10.1001/jamapsychiatry.2018.4500
 27. *Diagnostic and Statistical Manual of Mental Disorders: DSM-5™ (5th Ed.)*. Arlington VA: American Psychiatric Publishing Inc; 2013.
 28. Van Rossum I, Boomsma M, Tenback D, Reed C, Van Os J. Does cannabis use affect treatment outcome in bipolar disorder?: A longitudinal analysis. *J Nerv Ment Dis*. 2009. doi:10.1097/NMD.0b013e31819292a6
 29. Lev-Ran S, Le Foll B, McKenzie K, George TP, Rehm J. Bipolar disorder and co-occurring cannabis use disorders: Characteristics, co-morbidities and clinical correlates. *Psychiatry Res*. 2013. doi:10.1016/j.psychres.2012.12.014
 30. Gibbs M, Winsper C, Marwaha S, Gilbert E, Broome M, Singh SP. Cannabis use and mania symptoms: A systematic review and meta-analysis. *J Affect Disord*. 2015. doi:10.1016/j.jad.2014.09.016
 31. Gentes EL, Schry AR, Hicks TA, et al. Prevalence and correlates of cannabis use in an outpatient VA posttraumatic stress disorder clinic. *Psychol Addict Behav*. 2016. doi:10.1037/adb0000154
 32. Wilkinson ST, Stefanovics E, Rosenheck RA. Marijuana use is associated with worse outcomes in symptom severity and violent behavior in patients with posttraumatic stress disorder. *J Clin Psychiatry*. 2015. doi:10.4088/JCP.14m09475
 33. Abrams DI. The therapeutic effects of Cannabis and cannabinoids: An update from the National Academies of Sciences, Engineering and Medicine report. *Eur J Intern Med*. 2018. doi:10.1016/j.ejim.2018.01.003

34. Lim K, See YM, Lee J. A systematic review of the effectiveness of medical cannabis for psychiatric, movement and neurodegenerative disorders. *Clin Psychopharmacol Neurosci.* 2017. doi:10.9758/cpn.2017.15.4.301
35. Black N, Stockings E, Campbell G, et al. Cannabinoids for the treatment of mental disorders and symptoms of mental disorders: a systematic review and meta-analysis. *The Lancet Psychiatry.* 2019. doi:10.1016/S2215-0366(19)30401-8
36. WHO. *The Alcohol, Smoking and Substance Involvement Screening Test (ASSIST).*; 2010. <https://www.who.int/management-of-substance-use/assist>.
37. Goldenberg M, IsHak WW, Danovitch I. Quality of life and recreational cannabis use. *Am J Addict.* 2017. doi:10.1111/ajad.12486
38. Brezing CA, Choi CJ, Pavlicova M, et al. Abstinence and reduced frequency of use are associated with improvements in quality of life among treatment-seekers with cannabis use disorder. *Am J Addict.* 2018. doi:10.1111/ajad.12660
39. Lev-Ran S, Le Foll B, McKenzie K, Rehm J. Cannabis use and mental health-related quality of life among individuals with anxiety disorders. *J Anxiety Disord.* 2012. doi:10.1016/j.janxdis.2012.07.002
40. Evans S, Banerjee S, Leese M, Huxley P. The impact of mental illness on quality of life: A comparison of severe mental illness, common mental disorder and healthy population samples. *Qual Life Res.* 2007. doi:10.1007/s11136-006-9002-6
41. Hammond D, Goodman S, Wadsworth E, Rynard V, Boudreau C, Hall W. Evaluating the impacts of cannabis legalization: The International Cannabis Policy Study. *Int J Drug Policy.* 2020. doi:10.1016/j.drugpo.2020.102698
42. Goodman S, Burkhalter R, Hammond D. *International Cannabis Policy Study Technical Report - Wave 2 (2019).* Waterloo, ON Canada; 2020. <http://cannabisproject.ca/methods/>.
43. Statistics Canada, 2016 Census of Population, Statistics Canada Catalogue no. 98-400-X2016242. Highest Certificate, Diploma or Degree. <https://www12.statcan.gc.ca/census-recensement/2016/dp-pd/dt-td/Rp-eng.cfm?LANG=E&APATH=3&DETAIL=0&DIM=0&FL=A&FREE=0&GC=0&GID=0&GK=0&GRP=1&PID=110634&PRID=10&PTYPE=109445&S=0&SHOWALL=0&SUB=0&Temporal=2017&THEME=123&VID=0&VNAMEE=&VNAMEF>.
44. Statistics Canada. Table 17-10-0005-01 Population estimates on July 1st, by age and sex. <https://www150.statcan.gc.ca/t1/tbl1/en/tv.action?pid=1710000501>. Published 2017.
45. U.S. Census Bureau, 2013-2017 American Community Survey 5-Year Estimates. https://factfinder.census.gov/faces/tableservices/jsf/pages/productview.xhtml?pid=ACS_17_5YR_S1501&src=pt.
46. U.S. Census Bureau, Population Division. Annual State Resident Population Estimates for 6 Race Groups (5 Race Alone Groups and Two or More Races) by Age, Sex, and Hispanic Origin: April 1, 2010 to July 1, 2017. File: 7/1/2017 State Characteristics Populat. <https://www.census.gov/data/datasets/2017/demo/popest/state-detail.html>.

47. National Academies of Sciences, Engineering and M. *The Health Effects of Cannabis and Cannabinoids. The Current State of Evidence and Recommendations for Research.* Washington, DC: The National Academies Press; 2017.
48. Moore TH, Zammit S, Lingford-Hughes A, et al. Cannabis use and risk of psychotic or affective mental health outcomes: a systematic review. *Lancet.* 2007. doi:10.1016/S0140-6736(07)61162-3
49. Lev-Ran S, Roerecke M, Le Foll B, George TP, McKenzie K, Rehm J. The association between cannabis use and depression: A systematic review and meta-analysis of longitudinal studies. *Psychol Med.* 2014. doi:10.1017/S0033291713001438
50. Schoeler T, Monk A, Sami MB, et al. Continued versus discontinued cannabis use in patients with psychosis: A systematic review and meta-analysis. *The Lancet Psychiatry.* 2016. doi:10.1016/S2215-0366(15)00363-6
51. Cousijn J, Núñez AE, Filbey FM. Time to acknowledge the mixed effects of cannabis on health: a summary and critical review of the NASEM 2017 report on the health effects of cannabis and cannabinoids. In: *Addiction.* ; 2018. doi:10.1111/add.14084
52. Brook JS, Lee JY, Finch SJ, Seltzer N, Brook DW. Adult work commitment, financial stability, and social environment as related to trajectories of marijuana use beginning in adolescence. *Subst Abus.* 2013. doi:10.1080/08897077.2013.775092
53. MacDonald S, Hall W, Roman P, Stockwell T, Coghlan M, Nesvaag S. Testing for cannabis in the work-place: A review of the evidence. *Addiction.* 2010. doi:10.1111/j.1360-0443.2009.02808.x
54. Feingold D, Rehm J, Lev-Ran S. Cannabis use and the course and outcome of major depressive disorder: A population based longitudinal study. *Psychiatry Res.* 2017. doi:10.1016/j.psychres.2017.02.027
55. Koob GF, Le Moal M. Drug addiction, dysregulation of reward, and allostasis. *Neuropsychopharmacology.* 2001. doi:10.1016/S0893-133X(00)00195-0
56. Hammond D, Goodman S, Wadsworth E, Rynard V, Boudreau C, Hall W. Evaluating the impact of cannabis legalization: The International Cannabis Policy Study. *Int J Drug Policy.* 2020;1(77).
57. Canadian Cannabis Survey 2019 Summary. <https://www.canada.ca/en/health-canada/services/publications/drugs-health-products/canadian-cannabis-survey-2019-summary.html>. Published 2019.
58. Canadian Cannabis Survey 2018 Summary. Government of Canada. <https://www.canada.ca/en/services/health/publications/drugs-health-products/canadian-cannabis-survey-2018-summary.html>. Published 2018.
59. Goodman S, Wadsworth E, Leos-Toro C, Hammond D. Prevalence and forms of cannabis use in legal vs. illegal recreational cannabis markets. *Int J Drug Policy.* 2020. doi:10.1016/j.drugpo.2019.102658
60. SAMHSA. Key substance use and mental health indicators in the United States: Results

from the 2017 National Survey on Drug Use and Health (HHS Publication No. SMA 18-5068, NSUDH Series H-53). <https://www.samhsa.gov/data/sites/default/files/cbhsq-reports/NSDUHFFR2017/NSDUHFFR2017.pdf>. Published 2018.

61. Statistics Canada. Canadian Community Health Survey Information. <https://www23.statcan.gc.ca/imdb/p2SV.pl?Function=getSurvey&SDDS=3226&lang=en&db=imdb&adm=8&dis=2>. Published 2018.
62. Gruzca RA, Agrawal A, Krauss MJ, Cavazos-Rehg PA, Bierut LJ. Recent trends in the prevalence of marijuana use and associated disorders in the United States. *JAMA Psychiatry*. 2016. doi:10.1001/jamapsychiatry.2015.3111

APPENDICES

Appendix A: Manuscript 1 supplemental file

Table S1: Prevalence and correlates of past 12-month use of ‘solid’ cannabis concentrates among past 12-month cannabis consumers, by past 12-month experience of mental condition* (n=5,749)

Used concentrates in past 12 months		AOR	95% CI	p-value
	% (n)			
No anxiety	11.4 (477)	Ref		
Anxiety	21.4 (334)	1.64	(1.37, 1.95)	<0.001
No depression	11.4 (486)	Ref		
Depression	22.0 (326)	1.76	(1.48, 2.10)	<0.001
No PTSD	13.1 (694)	Ref		
PTSD	25.9 (118)	1.63	(1.28, 2.09)	<0.001
No bipolar	13.5 (740)	Ref		
Bipolar	29.1 (71)	1.56	(1.15, 2.14)	0.005
No psychosis	13.8 (779)	Ref		
Psychosis	34.9 (33)	2.23	(1.39, 3.59)	0.001
No conditions	10.1 (369)	Ref		
One condition	18.5 (158)	1.87	(1.50, 2.33)	<0.001
>1 condition	23.1 (284)	2.00	(1.65, 2.42)	<0.001

*Binary logistic models adjusted for age, sex at birth, ethnicity, education, country, past 12-month use.

Table S2: Prevalence and correlates of past 12-month use of hash or kief among past 12-month cannabis consumers, by past 12-month experience of mental condition* (n=5,749)

Used hash or kief in past 12 months		AOR	95% CI	p-value
	% (n)			
No anxiety	15.7 (656)	Ref		
Anxiety	23.1 (361)	1.43	(1.21, 1.69)	<0.001
No depression	15.9 (677)	Ref		
Depression	23.0 (341)	1.38	(1.17, 1.62)	<0.001
No PTSD	16.7 (885)	Ref		
PTSD	29.2 (133)	1.63	(1.29, 2.06)	<0.001
No bipolar	17.0 (937)	Ref		
Bipolar	32.9 (80)	1.69	(1.25, 2.28)	0.001
No psychosis	17.4 (984)	Ref		
Psychosis	36.0 (34)	1.92	(1.20, 3.06)	0.007
No conditions	15.0 (554)	Ref		
One condition	18.4 (158)	1.19	(0.97, 1.48)	0.100
>1 condition	25.0 (306)	1.57	(1.31, 1.87)	<0.001

*Binary logistic models adjusted for age, sex at birth, ethnicity, education, country, past 12-month use.

Table S3: Prevalence and correlates of past 12-month use of dried herb among past 12-month cannabis consumers, by past 12-month experience of mental condition* (n=5,749)

Used dried herb in past 12 months		AOR	95% CI	p-value
	% (n)			
No anxiety	77.3 (3,234)	Ref		
Anxiety	81.1 (1,269)	1.19	(1.02, 1.39)	0.029
No depression	77.1 (3,289)	Ref		
Depression	81.9 (1,213)	1.31	(1.12, 1.53)	<0.001
No PTSD	77.9 (4,126)	Ref		
PTSD	82.6 (376)	1.24	(0.96, 1.61)	0.099
No bipolar	78.0 (4,295)	Ref		
Bipolar	84.8 (207)	1.29	(0.89, 1.85)	0.176
No psychosis	78.2 (4,424)	Ref		
Psychosis	83.5 (78)	1.16	(0.66, 2.03)	0.608
No conditions	77.1 (2,829)	Ref		
One condition	77.4 (660)	1.01	(0.84, 1.21)	0.959
>1 condition	82.5 (1,013)	1.31	(1.10, 1.56)	0.003

*Binary logistic models adjusted for age, sex at birth, ethnicity, education, country, past 12-month use.

Table S4: Prevalence and correlates of past 12-month use of vaped cannabis oils among past 12-month cannabis consumers, by past 12-month experience of mental condition* (n=5,749)

Used vaped oils in past 12 months		AOR	95% CI	p-value
	% (n)			
No anxiety	21.9 (918)	Ref		
Anxiety	35.5 (555)	1.59	(1.38, 1.84)	<0.001
No depression	23.3 (996)	Ref		
Depression	32.2 (477)	1.28	(1.10, 1.47)	<0.001
No PTSD	24.4 (1,291)	Ref		
PTSD	40.1 (182)	1.65	(1.33, 2.05)	<0.001
No bipolar	25.1 (1,380)	Ref		
Bipolar	37.9 (93)	1.15	(0.87, 1.54)	0.332
No psychosis	25.5 (1,441)	Ref		
Psychosis	33.8 (32)	0.996	(0.63, 1.58)	0.985
No conditions	21.2 (778)	Ref		
One condition	29.9 (255)	1.37	(1.15, 1.64)	<0.001
>1 condition	35.8 (440)	1.61	(1.38, 1.89)	<0.001

*Binary logistic models adjusted for age, sex at birth, ethnicity, education, country, past 12-month use.

Table S5: Prevalence and correlates of past 12-month use of orally ingested cannabis oils or liquids among past 12-month cannabis consumers, by past 12-month experience of mental condition* (n=5,749)

Used orally ingested oils in past 12 months		AOR	95% CI	p-value
	% (n)			
No anxiety	19.7 (824)	Ref		
Anxiety	26.6 (416)	1.38	(1.19, 1.60)	<0.001
No depression	20.6 (880)	Ref		
Depression	24.3 (360)	1.12	(0.97, 1.30)	0.133
No PTSD	20.5 (1,086)	Ref		
PTSD	33.9 (154)	1.64	(1.33, 2.03)	<0.001
No bipolar	21.4 (1,178)	Ref		
Bipolar	25.2 (61)	1.06	(0.78, 1.44)	0.699
No psychosis	21.5 (1,215)	Ref		
Psychosis	27.0 (25)	1.25	(0.78, 2.00)	0.361
No conditions	19.1 (701)	Ref		
One condition	25.7 (219)	1.36	(1.14, 1.63)	<0.001
>1 condition	26.0 (320)	1.34	(1.14, 1.58)	<0.001

*Binary logistic models adjusted for age, sex at birth, ethnicity, education, country, past 12-month use.

Table S6: Prevalence and correlates of past 12-month use of edibles/foods among past 12-month cannabis consumers, by past 12-month experience of mental condition* (n=5,749)

Used edibles/foods in past 12 months		AOR	95% CI	p-value
	% (n)			
No anxiety	42.4 (1,775)	Ref		
Anxiety	50.2 (785)	1.20	(1.06, 1.36)	0.005
No depression	42.9 (1,832)	Ref		
Depression	49.1 (727)	1.13	(0.99, 1.28)	0.062
No PTSD	44.0 (2,329)	Ref		
PTSD	50.6 (230)	1.08	(0.89, 1.32)	0.449
No bipolar	44.5 (2,448)	Ref		
Bipolar	45.7 (112)	0.87	(0.67, 1.13)	0.301
No psychosis	44.4 (2,513)	Ref		
Psychosis	49.6 (46)	1.09	(0.72, 1.66)	0.681
No conditions	41.8 (1,534)	Ref		
One condition	48.9 (417)	1.20	(1.03, 1.40)	0.021
>1 condition	49.6 (609)	1.16	(1.01, 1.33)	0.037

*Binary logistic models adjusted for age, sex at birth, ethnicity, education, country, past 12-month use.

Table S7: Prevalence and correlates of past 12-month use of drinks among past 12-month cannabis consumers, by past 12-month experience of mental condition (n=5,749)

Used cannabis drinks in past 12 months		AOR	95% CI	p-value
	% (n)			
No anxiety	7.9 (331)	Ref		
Anxiety	10.3 (161)	1.08	(0.87, 1.34)	0.483
No depression	7.7 (328)	Ref		
Depression	11.0 (163)	1.27	(1.03, 1.56)	0.028
No PTSD	8.1 (428)	Ref		
PTSD	13.9 (63)	1.51	(1.12, 2.03)	0.007
No bipolar	8.2 (450)	Ref		
Bipolar	16.9 (41)	1.72	(1.19, 2.47)	0.004
No psychosis	8.2 (466)	Ref		
Psychosis	27.5 (26)	3.12	(1.92, 5.07)	<0.001
No conditions	6.9 (253)	Ref		
One condition	12.7 (109)	1.75	(1.36, 2.24)	<0.001
>1 condition	10.6 (130)	1.28	(1.01, 1.63)	0.042

*Binary logistic models adjusted for age, sex at birth, ethnicity, education, country, past 12-month use.

Table S8: Prevalence and correlates of past 12-month use of tinctures among past 12-month cannabis consumers, by past 12-month experience of mental condition (n=5,749)

Used tinctures in past 12 months		AOR	95% CI	p-value
	% (n)			
No anxiety	7.3 (304)	Ref		
Anxiety	10.5 (165)	1.38	(1.11, 1.72)	0.003
No depression	7.8 (333)	Ref		
Depression	9.2 (136)	1.08	(0.87, 1.35)	0.482
No PTSD	7.7 (405)	Ref		
PTSD	14.0 (64)	1.61	(1.20, 2.16)	0.002
No bipolar	8.0 (442)	Ref		
Bipolar	11.1 (27)	1.16	(0.76, 1.78)	0.493
No psychosis	7.9 (449)	Ref		
Psychosis	21.5 (20)	3.10	(1.83, 5.25)	<0.001
No conditions	6.6 (242)	Ref		
One condition	12.3 (105)	1.82	(1.42, 2.35)	<0.001
>1 condition	9.9 (122)	1.40	(1.10, 1.79)	0.007

*Binary logistic models adjusted for age, sex at birth, ethnicity, education, country, past 12-month use.

Table S9: Prevalence and correlates of past 12-month use of topicals among past 12-month cannabis consumers, by past 12-month experience of mental condition (n=5,749)

Used topicals in past 12 months		AOR	95% CI	p-value
	% (n)			
No anxiety	13.1 (546)	Ref		
Anxiety	18.3 (287)	1.40	(1.18, 1.66)	<0.001
No depression	13.4 (573)	Ref		
Depression	17.6 (260)	1.26	(1.06, 1.49)	0.009
No PTSD	13.7 (726)	Ref		
PTSD	23.5 (107)	1.58	(1.24, 2.01)	<0.001
No bipolar	14.4 (793)	Ref		
Bipolar	16.3 (40)	0.94	(0.66, 1.36)	0.756
No psychosis	14.3 (808)	Ref		
Psychosis	26.3 (25)	2.27	(1.39, 3.70)	<0.001
No conditions	12.2 (449)	Ref		
One condition	19.2 (164)	1.59	(1.29, 1.95)	<0.001
>1 condition	18.0 (221)	1.42	(1.17, 1.72)	0.004

*Binary logistic models adjusted for age, sex at birth, ethnicity, education, country, past 12-month use.

Appendix B: Manuscript 2 supplemental file

Table S1: Binary logistic regression results examining medical help-seeking for nausea/vomiting among past 12-month cannabis consumers, by past 12-month experience of mental condition* (n=241)

Sought medical help for nausea/vomiting in past 12 months		AOR	95% CI	p value
	% (n)			
No anxiety	23.5 (39)	Ref		
Anxiety	31.0 (23)	1.39	(0.71, 2.72)	0.343
No depression	26.2 (40)	Ref		
Depression	25.1 (22)	0.88	(0.45, 1.72)	0.717
No PTSD	24.6 (53)	Ref		
PTSD	37.0 (9)	1.92	(0.74, 4.94)	0.179
No bipolar	25.1 (55)	Ref		
Bipolar	32.8 (7)	1.44	(0.51, 4.06)	0.488
No psychosis	24.2 (53)	Ref		
Psychosis	42.8 (9)	2.46	(0.93, 6.50)	0.070
No conditions	17.4 (17)	Ref		
One condition	30.4 (26)	1.90	(0.91, 3.97)	0.090
>1 condition	33.2 (20)	2.50	(1.08, 5.78)	0.033

* Models adjusted for age, sex at birth, ethnicity, cannabis use frequency, education, country.

Table S2: Binary logistic regression results examining medical help-seeking for heart problems among past 12-month cannabis consumers, by past 12-month experience of mental condition* (n=241)

Sought medical help for heart problems in past 12 months				
	% (n)	AOR	95% CI	p value
No anxiety	23.7 (40)	Ref		
Anxiety	19.1 (14)	0.85	(0.40, 1.78)	0.662
No depression	23.3 (36)	Ref		
Depression	20.5 (18)	1.00	(0.50, 2.00)	0.999
No PTSD	20.5 (45)	Ref		
PTSD	39.1 (9)	2.67	(1.01, 7.03)	0.047
No bipolar	21.4 (47)	Ref		
Bipolar	31.3 (7)	2.04	(0.72, 5.80)	0.179
No psychosis	21.2 (47)	Ref		
Psychosis	33.9 (7)	1.92	(0.70, 5.28)	0.208
No conditions	15.9 (16)	Ref		
One condition	30.1 (25)	2.42	(1.14, 5.16)	0.022
>1 condition	21.7 (13)	1.80	(0.73, 4.47)	0.203

* Models adjusted for age, sex at birth, ethnicity, cannabis use frequency, education, country.

Table S3: Binary logistic regression results examining medical help-seeking for feeling faint or dizzy among past 12-month cannabis consumers, by past 12-month experience of mental condition* (n=241)

Sought medical help for feeling faint or dizzy in past 12 months				
	% (n)	AOR	95% CI	p value
No anxiety	25.7 (43)	Ref		
Anxiety	26.8 (20)	1.33	(0.67, 2.66)	0.420
No depression	25.4 (39)	Ref		
Depression	27.2 (24)	1.57	(0.81, 3.05)	0.181
No PTSD	24.6 (53)	Ref		
PTSD	39.8 (9)	2.28	(0.89, 5.89)	0.088
No bipolar	23.2 (51)	Ref		
Bipolar	53.3 (12)	4.76	(1.74, 12.97)	0.002
No psychosis	24.1 (53)	Ref		
Psychosis	46.3 (10)	2.40	(0.91, 6.35)	0.079
No conditions	14.7 (14)	Ref		
One condition	35.7 (30)	4.72	(2.15, 10.37)	<0.001
>1 condition	31.0 (18)	4.42	(1.79, 10.92)	0.001

* Models adjusted for age, sex at birth, ethnicity, cannabis use frequency, education, country.

Table S4: Binary logistic regression results examining medical help-seeking for panic reactions among past 12-month cannabis consumers, by past 12-month experience of mental condition* (n=241)

Sought medical help for panic reactions in past 12 months				
	% (n)	AOR	95% CI	p value
No anxiety	29.1 (49)	Ref		
Anxiety	25.3 (19)	1.33	(0.62, 2.86)	0.463
No depression	23.3 (36)	Ref		
Depression	36.1 (32)	4.69	(2.13, 10.29)	<0.001
No PTSD	25.5 (56)	Ref		
PTSD	50.0 (12)	3.44	(1.28, 9.25)	0.015
No bipolar	29.1 (64)	Ref		
Bipolar	16.5 (4)	0.48	(0.13, 1.75)	0.268
No psychosis	28.7 (63)	Ref		
Psychosis	19.4 (4)	0.63	(0.18, 2.20)	0.465
No conditions	23.0 (22)	Ref		
One condition	31.4 (26)	1.84	(0.85, 4.01)	0.124
>1 condition	31.2 (19)	4.07	(1.57, 10.50)	0.004

* Models adjusted for age, sex at birth, ethnicity, cannabis use frequency, education, country.

Table S5: Binary logistic regression results examining medical help-seeking for hallucinations among past 12-month cannabis consumers, by past 12-month experience of mental condition* (n=241)

Sought medical help for hallucinations in past 12 months				
	% (n)	AOR	95% CI	p value
No anxiety	14.6 (24)	Ref		
Anxiety	16.0 (12)	0.94	(0.41, 2.16)	0.882
No depression	15.4 (24)	Ref		
Depression	14.3 (13)	0.95	(0.41, 2.20)	0.909
No PTSD	13.6 (30)	Ref		
PTSD	28.5 (7)	2.40	(0.83, 7.00)	0.108
No bipolar	13.6 (30)	Ref		
Bipolar	28.8 (7)	3.69	(1.15, 11.86)	0.028
No psychosis	14.0 (31)	Ref		
Psychosis	25.8 (5)	1.79	(0.56, 5.77)	0.330
No conditions	11.8 (12)	Ref		
One condition	14.2 (12)	1.15	(0.45, 2.95)	0.776
>1 condition	21.5 (13)	2.27	(0.93, 6.21)	0.112

* Models adjusted for age, sex at birth, ethnicity, cannabis use frequency, education, country.

Table S6: Binary logistic regression results examining medical help-seeking for flashbacks among past 12-month cannabis consumers, by past 12-month experience of mental condition* (n=241)

Sought medical help for flashbacks in past 12 months				
	% (n)	AOR	95% CI	p value
No anxiety	12.1 (20)	Ref		
Anxiety	15.8 (12)	2.15	(0.88, 5.23)	0.093
No depression	13.7 (21)	Ref		
Depression	12.4 (77)	1.15	(0.49, 2.70)	0.748
No PTSD	11.8 (26)	Ref		
PTSD	26.4 (6)	4.49	(1.45, 13.92)	0.009
No bipolar	11.0 (24)	Ref		
Bipolar	35.1 (8)	7.53	(2.30, 24.70)	<0.001
No psychosis	11.6 (25)	Ref		
Psychosis	30.5 (6)	3.98	(1.30, 12.21)	0.016
No conditions	5.3 (5)	Ref		
One condition	16.5 (14)	4.99	(1.58, 15.71)	0.006
>1 condition	21.5 (13)	13.02	(3.63, 46.70)	<0.001

* Models adjusted for age, sex at birth, ethnicity, cannabis use frequency, education, country.

Table S7: Binary logistic regression results examining medical help-seeking for depression among past 12-month cannabis consumers, by past 12-month experience of mental condition* (n=241)

Sought medical help for depression in past 12 months				
	% (n)	AOR	95% CI	p value
No anxiety	14.6 (24)	Ref		
Anxiety	24.7 (18)	2.32	(1.07, 5.06)	0.034
No depression	14.6 (22)	Ref		
Depression	23.2 (20)	2.06	(0.97, 4.39)	0.061
No PTSD	15.6 (34)	Ref		
PTSD	37.7 (9)	4.46	(1.56, 12.75)	0.005
No bipolar	18.4 (40)	Ref		
Bipolar	11.5 (3)	0.81	(0.19, 3.46)	0.776
No psychosis	16.8 (37)	Ref		
Psychosis	27.3 (6)	1.96	(0.65, 5.99)	0.235
No conditions	9.9 (10)	Ref		
One condition	20.0 (17)	2.15	(0.86, 5.34)	0.101
>1 condition	27.2 (16)	5.54	(2.00, 15.35)	0.001

* Models adjusted for age, sex at birth, ethnicity, cannabis use frequency, education, country.

Table S8: Binary logistic regression results examining medical help-seeking for dissociations or depersonalization among past 12-month cannabis consumers, by past 12-month experience of mental condition* (n=241)

Sought medical help for dissociation in past 12 months		AOR	95% CI	p value
	% (n)			
No anxiety	11.1 (18)	Ref		
Anxiety	6.4 (5)	0.54	(0.15, 1.89)	0.335
No depression	9.8 (15)	Ref		
Depression	9.4 (8)	0.86	(0.28, 2.68)	0.798
No PTSD	9.2 (20)	Ref		
PTSD	14.0 (3)	4.44	(0.95, 20.66)	0.058
No bipolar	8.8 (19)	Ref		
Bipolar	18.0 (4)	3.63	(0.77, 17.18)	0.104
No psychosis	8.2 (18)	Ref		
Psychosis	24.6 (5)	7.65	(1.90, 30.75)	0.004
No conditions	9.2 (9)	Ref		
One condition	6.1 (5)	0.64	(0.17, 2.44)	0.510
>1 condition	15.3 (9)	3.37	(0.90, 12.67)	0.071

* Models adjusted for age, sex at birth, ethnicity, cannabis use frequency, education, country

Table S9: Correlates of perceived effect of cannabis use on friendships or social life among past 12-month cannabis consumers, by past 12-month experience of mental condition* (n= 5,216)

	No effect (ref) % (n)	Positive effect % (n)	AOR	95% CI	p value	Negative effect % (n)	AOR	95% CI	p value
No anxiety	77.7 (2,939)	18.4 (696)	Ref			3.9 (147)	Ref		
Anxiety	67.0 (960)	28.8 (412)	1.65	(1.42, 1.92)	<0.001	4.2 (60)	1.34	(0.96, 1.84)	0.091
No depression	76.8 (2,984)	19.1 (746)	Ref			4.0 (155)	Ref		
Depression	68.8 (914)	27.3 (364)	1.44	(1.23, 1.68)	<0.001	3.9 (52)	1.13	(0.81, 1.58)	0.475
No PTSD	75.5 (3,622)	20.6 (987)	Ref			3.9 (188)	Ref		
PTSD	66.2 (277)	29.2 (122)	1.46	(1.16, 1.84)	0.002	4.6 (19)	1.48	(0.90, 2.45)	0.121
No bipolar	75.5 (3,722)	20.7 (1,032)	Ref			3.9 (194)	Ref		
Bipolar	58.6 (127)	35.4 (77)	1.76	(1.30, 2.38)	<0.001	5.9 (13)	1.73	(0.94, 3.17)	0.078
No psychosis	75.1 (3,855)	21.1 (1,082)	Ref			3.8 (193)	Ref		
Psychosis	51.9 (45)	32.0 (27)	1.66	(1.02, 2.72)	0.043	16.2 (14)	5.24	(2.77, 9.89)	<0.001
No conditions	78.3 (2,613)	18.0 (603)	Ref			3.6 (120)	Ref		
One condition	72.2 (549)	23.2 (176)	1.31	(1.08, 1.60)	0.007	4.7 (35)	1.49	(1.00, 2.20)	0.048
>1 condition	65.9 (738)	29.4 (330)	1.73	(1.46, 2.05)	<0.001	4.6 (52)	1.67	(1.17, 2.39)	0.005

* Multinomial logistic models adjusted for age, sex at birth, ethnicity, cannabis use frequency, education, country.

Table S10: Correlates of effect of cannabis use on physical health among past 12-month cannabis consumers, by past 12-month experience of mental condition* (n= 5,312)

	No effect (ref) % (n)	Positive effect % (n)	AOR	95% CI	p value	Negative effect % (n)	AOR	95% CI	p value
No anxiety	67.0 (2,584)	28.8 (1,113)	Ref			4.3 (165)	Ref		
Anxiety	52.6 (762)	43.1 (625)	1.88	(1.63, 2.17)	<0.001	4.3 (62)	1.28	(0.93, 1.76)	0.133
No depression	66.5 (2,622)	29.1 (1,147)	Ref			4.3 (171)	Ref		
Depression	52.8 (724)	43.1 (591)	1.76	(1.53, 2.03)	<0.001	4.1 (56)	1.16	(0.84, 1.60)	0.371
No PTSD	64.7 (3,159)	31.0 (1,512)	Ref			4.4 (214)	Ref		
PTSD	43.8 (187)	53.0 (226)	1.93	(1.56, 2.40)	<0.001	3.2 (14)	0.99	(0.55, 1.76)	0.960
No bipolar	63.2 (3,234)	32.6 (1,631)	Ref			4.2 (216)	Ref		
Bipolar	47.8 (112)	40.2 (107)	1.50	(1.12, 2.00)	0.006	12.0 (11)	1.21	(0.63, 2.31)	0.567
No psychosis	64.7 (3,305)	31.0 (1,704)	Ref			4.4 (217)	Ref		
Psychosis	43.8 (41)	53.0 (34)	1.44	(0.90, 2.40)	0.131	3.2 (10)	3.35	(1.65, 6.81)	0.001
No conditions	68.4 (2,316)	27.4 (926)	Ref			4.2 (143)	Ref		
One condition	58.7 (462)	36.9 (290)	1.57	(1.32, 1.89)	<0.001	4.4 (35)	1.24	(0.84, 1.83)	0.287
>1 condition	49.8 (568)	45.8 (522)	2.18	(1.86, 2.55)	<0.001	4.4 (50)	1.39	(0.98, 1.99)	0.067

* Multinomial logistic models adjusted for age, sex at birth, ethnicity, cannabis use frequency, education, country.

Table S11: Correlates of effect of cannabis use on mental health among past 12-month cannabis consumers, by past 12-month experience of mental condition* (n= 5,309)

	No effect (ref) % (n)	Positive effect % (n)	AOR	95% CI	p value	Negative effect % (n)	AOR	95% CI	p value
No anxiety	66.9 (2,561)	29.8 (1,143)	Ref			3.3 (126)	Ref		
Anxiety	30.9 (456)	64.0 (948)	4.83	(4.16, 5.61)	<0.001	5.0 (75)	3.42	(2.48, 4.73)	<0.001
No depression	65.4 (2,563)	31.0 (1,218)	Ref			3.5 (137)	Ref		
Depression	32.7 (455)	62.7 (872)	3.92	(3.39, 4.54)	<0.001	4.6 (64)	3.58	(1.86, 3.57)	<0.001
No PTSD	59.8 (2,915)	36.7 (1,788)	Ref			3.5 (173)	Ref		
PTSD	23.7 (102)	69.9 (302)	3.71	(2.90, 4.74)	<0.001	6.5 (28)	4.81	(3.04, 7.62)	<0.001
No bipolar	58.3 (2,956)	38.1 (1,929)	Ref			3.6 (184)	Ref		
Bipolar	25.8 (62)	67.1 (161)	2.94	(2.14, 4.04)	<0.001	7.1 (17)	3.47	(1.96, 6.14)	<0.001
No psychosis	57.4 (2,998)	39.1 (2,039)	Ref			3.5 (184)	Ref		
Psychosis	22.2 (19)	58.8 (51)	2.97	(1.71, 5.15)	<0.001	19.1 (17)	11.44	(5.74, 22.78)	<0.001
No conditions	70.4 (2,362)	26.6 (892)	Ref			3.0 (100)	Ref		
One condition	41.2 (332)	53.5 (421)	3.56	(3.98, 4.25)	<0.001	4.3 (34)	2.51	(1.66, 3.79)	<0.001
>1 condition	27.7 (324)	66.6 (778)	6.43	(5.43, 7.62)	<0.001	5.7 (67)	6.43	(5.43, 7.62)	<0.001

* Multinomial logistic models adjusted for age, sex at birth, ethnicity, cannabis use frequency, education, country.

Table S12: Correlates of effect of cannabis use on family life among past 12-month cannabis consumers, by past 12-month experience of mental condition* (n= 5,161)

	No effect (ref) % (n)	Positive effect % (n)	AOR	95% CI	p value	Negative effect % (n)	AOR	95% CI	p value
No anxiety	80.8 (3,045)	14.2 (536)	Ref			5.0 (188)	Ref		
Anxiety	69.9 (974)	24.3 (339)	1.74	(1.47, 2.06)	<0.001	5.7 (80)	1.28	(0.96, 1.71)	0.096
No depression	80.7 (3,119)	14.4 (555)	Ref			5.0 (192)	Ref		
Depression	69.5 (900)	24.7 (320)	1.75	(1.48, 2.07)	<0.001	5.8 (76)	1.33	(1.00, 1.79)	0.053
No PTSD	79.2 (3,773)	15.6 (742)	Ref			5.2 (256)	Ref		
PTSD	61.4 (246)	33.2 (133)	2.09	(1.64, 2.65)	<0.001	5.5 (22)	1.47	(0.92, 2.35)	0.111
No bipolar	78.6 (3,889)	16.4 (812)	Ref			5.0 (249)	Ref		
Bipolar	61.4 (130)	29.9 (63)	1.69	(1.22, 2.35)	0.002	8.8 (19)	1.86	(1.10, 3.13)	0.020
No psychosis	78.3 (3,979)	16.7 (848)	Ref			5.0 (253)	Ref		
Psychosis	49.2 (40)	33.3 (27)	2.48	(1.48, 4.16)	0.001	17.4 (14)	4.70	(2.48, 8.92)	<0.001
No conditions	82.5 (2,738)	12.8 (426)	Ref			4.7 (155)	Ref		
One condition	72.0 (552)	22.0 (168)	1.90	(1.54, 2.34)	<0.001	5.9 (46)	1.45	(1.02, 2.07)	0.040
>1 condition	67.7 (729)	26.0 (281)	2.10	(1.74, 2.54)	<0.001	6.2 (67)	1.63	(1.18, 2.24)	0.003

* Multinomial logistic models adjusted for age, sex at birth, ethnicity, cannabis use frequency, education, country.

S13: Correlates of effect of cannabis use on work among past 12-month cannabis consumers, by past 12-month experience of mental condition* (n= 4,715)

	No effect (ref) % (n)	Positive effect % (n)	AOR	95% CI	p value	Negative effect % (n)	AOR	95% CI	p value
No anxiety	84.8 (2,938)	11.1 (386)	Ref			4.0 (140)	Ref		
Anxiety	77.4 (968)	17.7 (222)	1.49	(1.22, 1.82)	<0.001	4.9 (61)	1.35	(0.97, 1.88)	0.075
No depression	84.5 (3,000)	11.2 (397)	Ref			4.4 (155)	Ref		
Depression	77.9 (907)	18.1 (210)	1.51	(1.24, 1.85)	<0.001	4.0 (46)	0.95	(0.67, 1.35)	0.771
No PTSD	83.6 (3,664)	12.2 (533)	Ref			4.2 (185)	Ref		
PTSD	77.8 (243)	22.5 (75)	1.63	(1.22, 2.19)	<0.001	4.7 (16)	1.27	(0.73, 2.19)	0.397
No bipolar	83.5 (3,773)	12.5 (564)	Ref			4.1 (183)	Ref		
Bipolar	68.4 (134)	22.4 (44)	1.49	(1.03, 2.16)	0.035	9.0 (18)	2.13	(1.25, 3.65)	0.006
No psychosis	83.3 (3,867)	12.5 (582)	Ref			4.2 (194)	Ref		
Psychosis	54.3 (40)	35.9 (26)	2.95	(1.74, 5.00)	<0.001	9.8 (7)	2.94	(1.29, 6.69)	0.010
No conditions	85.8 (2,622)	10.2 (311)	Ref			4.0 (123)	Ref		
One condition	79.7 (558)	16.2 (113)	1.62	(1.26, 2.08)	<0.001	4.2 (29)	1.17	(0.77, 1.78)	0.475
>1 condition	75.8 (727)	19.1 (183)	1.74	(1.39, 2.17)	<0.001	5.1 (48)	1.40	(0.97, 2.02)	0.074

* Multinomial logistic models adjusted for age, sex at birth, ethnicity, cannabis use frequency, education, country.

Table S14: Correlates of effect of cannabis use on studies among past 12-month cannabis consumers, by past 12-month experience of mental condition* (n= 4,480)

	No effect (ref) % (n)	Positive effect % (n)	AOR	95% CI	p value	Negative effect % (n)	AOR	95% CI	p value
No anxiety	84.5 (2,776)	10.6 (348)	Ref			4.9 (162)	Ref		
Anxiety	76.0 (908)	17.2 (206)	1.62	(1.31, 2.00)	<0.001	6.7 (80)	1.52	(1.12, 2.04)	0.006
No depression	83.8 (2,835)	11.0 (373)	Ref			5.2 (174)	Ref		
Depression	77.3 (848)	16.5 (181)	1.41	(1.15, 1.75)	0.001	6.2 (68)	1.26	(0.93, 1.72)	0.134
No PTSD	83.3 (3,463)	11.5 (478)	Ref			5.2 (218)	Ref		
PTSD	68.7 (220)	23.7 (76)	2.13	(1.58, 2.87)	<0.001	7.6 (24)	1.89	(1.20, 2.99)	0.006
No bipolar	83.0 (3,566)	11.8 (509)	Ref			5.2 (223)	Ref		
Bipolar	65.2 (118)	24.9 (45)	1.79	(1.23, 2.61)	0.003	10.0 (18)	1.94	(1.14, 3.31)	0.014
No psychosis	82.7 (3,642)	12.0 (529)	Ref			5.3 (233)	Ref		
Psychosis	54.9 (42)	32.8 (25)	2.67	(1.57, 4.55)	<0.001	12.3 (9)	2.90	(1.39, 6.06)	0.005
No conditions	85.7 (2,493)	9.6 (280)	Ref			4.7 (137)	Ref		
One condition	77.3 (510)	15.6 (109)	1.89	(1.46, 2.44)	<0.001	6.1 (41)	1.46	(1.00, 2.12)	0.048
>1 condition	74.8 (680)	18.1 (164)	1.84	(1.46, 2.33)	<0.001	7.1 (65)	1.75	(1.26, 2.44)	0.001

* Multinomial logistic models adjusted for age, sex at birth, ethnicity, cannabis use frequency, education, country.

Table S15: Correlates of effect of cannabis use on quality of life among past 12-month cannabis consumers, by past 12-month experience of mental condition* (n= 5,326)

	No effect (ref) % (n)	Positive effect % (n)	AOR	95% CI	p value	Negative effect % (n)	AOR	95% CI	p value
No anxiety	57.8 (2,236)	39.0 (1,507)	Ref			3.2 (124)	Ref		
Anxiety	35.9 (523)	61.8 (901)	2.74	(2.37, 3.16)	<0.001	2.4 (34)	1.20	(0.80, 1.80)	0.389
No depression	57.1 (2,259)	40.0 (1,571)	Ref			3.2 (125)	Ref		
Depression	36.5 (500)	61.0 (836)	2.40	(2.08, 2.77)	<0.001	2.5 (34)	1.23	(0.82, 1.85)	0.315
No PTSD	53.8 (2,633)	43.2 (2,114)	Ref			3.1 (150)	Ref		
PTSD	29.5 (126)	68.4 (293)	2.32	(1.83, 2.92)	<0.001	2.0 (9)	1.12	(0.55, 2.30)	0.749
No bipolar	52.8 (2,688)	44.2 (2,250)	Ref			3.0 (152)	Ref		
Bipolar	30.5 (72)	66.8 (157)	2.01	(1.48, 2.73)	<0.001	2.7 (6)	1.25	(0.54, 2.90)	0.609
No psychosis	52.2 (2,736)	45.0 (2,358)	Ref			2.8 (147)	Ref		
Psychosis	28.2 (24)	57.8 (49)	2.00	(1.19, 3.37)	0.009	13.9 (12)	6.85	(3.27, 14.33)	<0.001
No conditions	60.1 (2,039)	37.0 (1,253)	Ref			2.9 (98)	Ref		
One condition	42.7 (339)	52.8 (418)	2.13	(1.79, 2.53)	<0.001	4.5 (36)	2.21	(1.47, 3.33)	<0.001
>1 condition	33.5 (382)	64.4 (736)	3.23	(2.75, 3.79)	<0.001	2.1 (24)	1.33	(0.83, 2.15)	0.237

* Multinomial logistic models adjusted for age, sex at birth, ethnicity, cannabis use frequency, education, country.

Table S16: Correlates of past 12-month cannabis use to improve/manage any mental health symptoms, by past 12-month experience of mental condition* (n=5,630)

Used cannabis to manage/improve any symptoms				
	% (n)	AOR	95% CI	p value
No anxiety	26.0 (1,059)	Ref		
Anxiety	82.2 (1,279)	13.26	(11.27, 15.61)	<0.001
No depression	28.8 (1,200)	Ref		
Depression	77.7 (1,138)	8.21	(7.05, 9.55)	<0.001
No PTSD	37.5 (1,944)	Ref		
PTSD	87.4 (394)	9.55	(7.11, 12.83)	<0.001
No bipolar	39.3 (2,120)	Ref		
Bipolar	90.8 (218)	11.56	(7.31, 18.28)	<0.001
No psychosis	40.7 (2,255)	Ref		
Psychosis	90.6 (83)	10.85	(5.28, 22.31)	<0.001
No conditions	20.5 (730)	Ref		
One condition	67.7 (570)	8.81	(7.36, 10.55)	<0.001
>1 condition	85.0 (1,038)	22.30	(18.37, 27.07)	<0.001

* Binary logistic models adjusted for age, sex at birth, ethnicity, cannabis use frequency, education, country.