Université de Montréal

# A CROSS-SECTIONAL STUDY OF THE ASSOCIATION BETWEEN POLYSUBSTANCE USE AND MENTAL HEALTH IN YOUNG ADULTS

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Mémoire présenté
en vue de l'obtention du grade de Maîtrise en Épidémiologie,

Avril 2023

Université de Montréal
Département de médecine sociale et préventive, École de santé publique de l'Université de Montréal

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*Ce mémoire intitulé*

# A CROSS-SECTIONAL STUDY OF THE ASSOCIATION BETWEEN POLYSUBSTANCE USE AND MENTAL HEALTH IN YOUNG ADULTS

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**RESUMÉ**

**Contexte :** Les études sur la consommation de substances en lien avec la santé mentale chez les jeunes adultes considèrent généralement chaque substance séparément et se concentrent sur les symptômes d'anxiété ou de dépression. Ce mémoire décrit les modes de consommation régulière (au moins hebdomadaire) d'alcool, de cannabis et de nicotine et estime l'association entre ces modes de consommation (séparément et en combinaison) et les symptômes de dépression, d'anxiété ainsi que la santé mentale positive (SMP) chez les jeunes adultes.

**Méthodes :** Les données de cette étude transversale sont tirées du cycle 23 (2017-20) de l'étude NDIT, lorsque les participants étaient âgés de 31 ans en moyenne. Une régression linéaire ajustée pour l'âge, le sexe et le niveau d'éducation modélise les associations entre: (i) le nombre de substances consommées; et (ii) les modes de consommation de plusieurs substances et chacun des indicateurs de santé mentale.

**Résultats :** 37 % des participants n'ont consommé aucune substance régulièrement; 42 %, 16 % et 5 % ont consommé une, deux et trois substances, respectivement. Il n'y avait pas d'association dose-réponse entre le nombre de substances et les indicateurs de santé mentale. La consommation de deux substances était associée aux symptômes d'anxiété ($\hat{\beta}$(IC95%) = 1,32(0,34;2,31) et à la SMP (-3,64(-6,34;-0,95)). La combinaison cannabis-nicotine était associée aux symptômes d'anxiété (2,58(1,06;4,10)) et à la SMP (-5,90(-10,04;-1,76)). La combinaison alcool-nicotine était associée à la SMP (-3,70(-7,30,-0,10)).

**Conclusion :** Les combinaisons de substances en plus des substances individuelles devraient être investiguées en lien avec la santé mentale.

**Mots clés :** consommation de plusieurs substances, cannabis, alcool, nicotine, santé mentale, jeunes adultes.

**ABSTRACT**

**Background:** Studies on substance use in relation to mental health among young adults generally consider each substance separately and in addition, they tend to focus on symptoms of anxiety or depression. This thesis describes the patterns of regular (at least weekly) use of alcohol, cannabis and nicotine, and estimates the association between these patterns and symptoms of depression, anxiety, as well as positive mental health (PMH) among young adults.

**Methods:** Data for this cross-sectional study were drawn from cycle 23 (2017-20) of the NDIT study when participants were age 31 years on average. The associations between: (i) number of substances used; and (ii) pattern of polysubstance use and each of the mental health indicators were modeled using linear regression adjusting for age, sex and level of education.

**Results:** 37% of participants did not consume any substances regularly; 42%, 16%, and 5% consumed one, two and three substances, respectively. There was no dose response association between number of substances and any of the mental health indicators. Use of two substances was associated with anxiety symptoms ($\hat{\beta}$(95% CI) = 1.32(0.34,2.31)) and PMH (-3.64(-6.34,-0.95)). The cannabis-nicotine combination was associated with anxiety symptoms (2.58(1.06,4.10)) and PMH (-5.90(-10.04,-1.76)). The alcohol-nicotine combination was associated with PMH (-3.70(-7.30,-0.10)).

**Conclusion:** Combinations of specific substances in addition to individual substances should be investigated in relation to mental health among young adults.

**Keywords:** polysubstance use, cannabis, alcohol, nicotine, mental health, young adults

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*I dedicate this work to my parents who have always been my source of inspiration, support, and guidance. I also dedicate this to the motherly eternal supreme power. All-knowing, you are the compassionate mother who nourishes and takes care of all. Your marvels are beyond comprehension. Salutations to my biggest strength.*

**LIST OF ACRONYMS**

AUD : Alcohol use disorder

CrCHUM: Centre de recherche du Centre hospitalier de l'Université de Montréal

CB1 : Cannabinoid receptor type 1

CB2 : Cannabinoid receptor type 2

CEGEP: Collège d'enseignement général et professionnel

COVID-19: Coronavirus Disease (2019)

DSM-III: Diagnostic and Statistical Manual of Mental Disorders, 3rd Edition

DSM-IV: Diagnostic and Statistical Manual of Mental Disorders, 4th Edition

DSM-V: Diagnostic and Statistical Manual of Mental Disorders, 5th Edition

GAD: Generalized Anxiety Disorder

GAD-7: Generalized Anxiety Disorder Assessment

CI: Confidence Interval

DA: Dopamine

GABA: Gamma-aminobutyric acid

ICD-10: International Classification of Diseases (Version 10)

IQR: Interquartile Range

MDD: Major Depressive Disorder

MDE: Major Depressive Episode

MDI: Major Depression Inventory

MHC-SF: Mental Health Continuum-Short Form

NDIT: Nicotine Dependence in Teens

nAChR: nicotinic ACh Receptor

SD: Standard Deviation

SEP: Socioeconomic Position

US: United States

VTA: Ventral Tegmental Area

**ACKNOWLEDGEMENTS**

I would like to sincerely thank my supervisors, Dr. Jennifer O'Loughlin and Dr. Marie-Pierre Sylvestre, for their unwavering support, encouragement, and assistance during the completion of this thesis. I am a great admirer of their listening abilities and humbleness. Without their assistance, I would not be here presenting this work. I feel very fortunate to have received guidance under two very experienced mentors that welcomed me into their great team of NDIT.

Next, I would like to express my gratitude towards all the professors and staff at the École de Santé Publique de Montréal for providing me with the necessary knowledge and skills for embarking on this journey of M.Sc. research.

Then, I wish to thank my family members for their unconditional support and love. They have constantly provided me with the confidence and encouragement to keep moving forward. Thank you for always being by my side.

Lastly, I would like to thank two great friends I made during my M.Sc. experience. I started this challenging journey during the peak of the COVID-19 pandemic. Classes were offered online only, and students, unfortunately, missed out on being present on campus. It was a tough time for students, and many missed on opportunities to make new friendships. Luckily, I got to meet Shayne and Mounia online. We worked together in the few online classes. The ideas and inputs we got to share really helped me perform well in those courses. I especially want to thank them for constantly motivating me in my thesis-writing journey.

## CHAPTER 1: INTRODUCTION

Young adults in Canada (and elsewhere) are generally considered physically healthier than older adults, but this is not the case for mental health. In 2019, relatively fewer younger than older Canadians reported excellent or very good mental health (Garriguet, 2021). The transition to adulthood involves demanding life changes such as job searching, career development and family planning, which can be mentally challenging for some. As defined by the World Health Organization (WHO), mental health is "a state of well-being in which the individual realizes his or her own abilities, can cope with the normal stresses of life, can work productively and fruitfully, and is able to make a contribution to his or her community" (Galderisi, 2015). In 2003, the percentage of Canadian youth that self-reported excellent or very good mental health was at its highest (76%). Since then, it declined to 73% in 2013-14 and, notably, to 60% in 2019 (Garriguet, 2021). Risk factors for declining mental health among young adults include early pregnancy, substance use, loneliness, poor work skills and habits, reading disabilities and stressful life events (Population Health and Wellness BC Ministry of Health, 2021). Mental health disorders, including depression and problematic substance use, are two leading and often linked causes of years lived with a mental health disability (Esmaeelzadeh, 2018).

People use alcohol and drugs for many reasons, including to relax and having fun, to celebrate an occasion, and to complement a meal. However, some use alcohol and drugs to cope with problems and to deal with negative feelings, stress, and loneliness (Garriguet, 2021), a phenomenon sometimes referred to as self-medication (Boileau-Falardeau et al., 2022). With the ubiquitous availability of alcohol, the recent legalization of cannabis in Canada in 2018, and the increasing popularity of e-cigarettes, polysubstance use has never been as accessible and national surveys suggest that the frequency of substance use has increased among adolescents and young adults (Zuckermann et al., 2019). Polysubstance use is defined as the use of different substances on the same or different occasions within the same timeframe (Konefal et al., 2022). Compared to individuals using one substance, polysubstance use is more reliably associated with mental illness, negative social and financial impacts, and poor treatment outcomes (Konefal et al., 2022). In 2018, Canada's Chief Public Health Officer's Report on Public Health highlighted the key concern of problematic substance use among Canadian youth and declining mental health (CPOH, 2018).

This traditional thesis has two primary aims. First, it describes patterns of past-year regular polysubstance use among young adults and second, it estimates the associations between patterns of polysubstance use and several indicators of mental health. Data for this project were drawn from the Nicotine Dependence in Teens (NDIT) study during the period between 2017 and 2020 (i.e., prior to the COVID-19 pandemic). This thesis includes seven chapters. Chapter 2 reviews the literature on mental health indicators (i.e., depression, general anxiety, flourishing positive mental health) and substance (i.e., alcohol, cannabis, nicotine) use. The section begins with definitions and a description of the epidemiology of the three mental health indicators, followed by a review of risk factors associated with declining mental health in young adulthood. The descriptive epidemiology of each of the three substances of interest in this thesis follows. The section then explores what is known about the association between substance use and mental health, before providing a summary of the section. Chapter 3 describes the objectives of this thesis. Chapter 4 describes the source of the data used in this thesis, the study design, the study variables, data analyses, and ethical considerations. Chapter 5 presents the results. Chapter 6 interprets the findings, describes the strengths and limitations of the study, and speculates on the implications of the findings. Chapter 7 presents the conclusions of this thesis.

# CHAPTER 2: LITERATURE REVIEW

## 2.1. Definitions and descriptive epidemiology of mental health indicators

*Depression*

The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) states that at least five symptoms must be present during a two-week period to diagnose a Major Depressive Episode (MDE), which is commonly referred to as depression (Tolentino et al., 2018). Anhedonia (i.e., loss of interest or pleasure) or a depressed mood should be at least one symptom. Secondary symptoms of depression include appetite or weight changes, sleep difficulties (i.e., insomnia or hypersomnia), psychomotor agitation/retardation, fatigue/loss of energy, diminished ability to think/concentrate, feelings of worthlessness/excessive guilt, and suicidality (Tolentino et al., 2018). These symptoms are graded in either all or none (0 or 1) fashion and then summed to assess the absence or presence of a MDE (Tolentino et al., 2018).

The primary type of depression is Major Depressive Disorder (MDD), which is characterized by recurrent depressive episodes (Malhi et al., 2018). Chronic depression is a pattern in which depressive episodes persist for extended periods. The condition is known as persistent depressive disorder or dysthymia if depressive symptoms have been present (on most days) for at least two years without any periods of remission lasting more than two months (Malhi et al., 2018). In the DSM-5, major depressive disorders are differentiated from bipolar disorders, with the main distinction being that manic symptoms occur only in bipolar disorders (Malhi et al., 2018).

The Global Burden of Disease Project listed major depression as Canada's second most important cause of disability-adjusted life years, making it one of the top priorities for global public health (Patten et al., 2016). A total of 322 million individuals around the globe suffer from depression, and the number of people living with depression increased by 18.4% between 2005 and 2015 (Friedrich, 2017). In 2015, depressive disorders were the leading cause of nonfatal health losses worldwide (Friedrich. 2017). Although a diagnosis of depression can strike anyone at any time in their life, women are 1.5 times more likely to experience depression than men (Friedrich, 2017). In 2012, major depressive episode was the most common type of mood disorder, with 4.7% of the population age 15 or older meeting the criteria (Statistics Canada, 2013). The most likely period for the first episode of major depression to begin is between mid-adolescence and mid-forties.

However, over 40% of people have their first episode before age 20, with an average age of onset in the mid-20s (Malhi et al., 2018).

*Generalized Anxiety Disorder*

Generalized Anxiety Disorder (GAD) is characterized by excessive worry and anxiety about a range of events or activities (e.g., work or academic performance), which a person finds challenging to control as per the DSM-5 (Patriquin et al., 2017). The worry is detrimental in various situations (e.g., work, home, and social interactions). Feeling restless, becoming tired easily, having difficulty concentrating or going blank, being irritable, having muscle tension, and having trouble sleeping are symptoms that must be present for diagnosis (Patriquin et al., 2017). The International Classification of Diseases, Version 10 (ICD-10) proposes diagnostic criteria for research and places greater weight on somatic symptoms: (i) at least six months of pronounced tension, worry, and feelings of apprehension about everyday routines and problems; and (ii) at least four symptoms in a list of 22 items, of which at least one of which is from a list of four autonomic arousal symptoms (i.e., palpitations/accelerated heart rate, sweating, trembling/shaking, dry mouth) (Crocq, 2017).

In the first survey to provide national population estimates for generalized anxiety disorder (GAD) in Canada in 2012, an estimated 2.4 million Canadians aged 15 years or older (8.7%) reported symptoms compatible with GAD during their lifetime (Pelletier, 2017). Among these individuals, 30% (2.6% of Canadians) reported symptoms in the 12 months (Pelletier, 2017). The Canadian data suggest that immigrant status is protective against GAD, consistent with findings in an Australia study (Pelletier, 2017). The survey also showed that a low household income was linked to anxiety disorders, particularly GAD (Pelletier, 2017). The cross-sectional design of the survey, however, renders studying etiology difficult because GAD may result in a lower income via poor work productivity or because poverty itself may be a risk factor (Watterson, 2016). Although people with GAD claim to experience anxiety every day of their lives, throughout the disorder, the primary sources of worry may change (Statistics Canada, 2015). GAD often begins in childhood or adolescence, and women are more likely than men to have the disorder (Statistics Canada, 2015). One of the major obstacles to early diagnosis of GAD is that those affected seek medical attention infrequently and usually only for excessive anxiety or worry (Pelletier, 2017).

*Positive mental health*

The Public Health Agency of Canada (PHAC) has defined mental health as "the capacity of each and all of us to feel, think, and act in ways that enhance our ability to enjoy life and deal with the challenges we face. It is a positive sense of emotional and spiritual well-being that respects the importance of culture, equity, social justice, interconnections, and personal dignity" (Orpana et al., 2017). The definition is consistent with that of the World Health Organization (WHO) which defines mental health as: "a state of well-being in which the individual realizes his or her own abilities, can cope with the normal stresses of life, can work productively and fruitfully, and is able to make a contribution to his or her community" (Orpana et al., 2017). These conceptualizations challenge the traditional belief that mental health is the absence of psychopathology (Lamers et al., 2010). The current definition is based on two enduring traditions in research on a life well lived: the *hedonic* tradition, which is concerned with feelings of happiness, and the *eudaimonic* tradition, which is concerned with optimal functioning at the individual level as well as in a social life context (Lamers et al., 2010). The *hedonic* tradition holds that happiness, and the experience of pleasurable emotions are essential components of well-being. Increased mental health results from boosting pleasant experiences while minimizing unpleasant ones. This affective side of the hedonistic ethos is reflected in research on *emotional well-being* (Lamers et al., 2010). Emotional well-being describes the degree to which a person feels good about themselves and is content with their life (Toronto Health Check, 2019). The *eudaimonic* tradition considers optimal psychological functioning in life and has been measured using two multidimensional models—*psychological well-being* and *social well-being* (Lamers et al., 2010). According to the positive mental health paradigm, one's sense of social well-being correlates with belonging to the local community (Toronto Health Check, 2019). Psychological well-being is a component of positive mental health that measures how accepting people are of who they are as individuals, how confident they are in expressing their opinions, how capable they are of handling day-to-day responsibilities, and how much they believe they can develop personally (Toronto Health Check, 2019).

In 2012, 76.9% of Canadians were categorized as having flourishing mental health (Statistics Canada, 2015). Compared to the range of 11.7% to 69.1% in the United States, the Netherlands, South Africa, France, and Korea, the proportion of people with flourishing mental health in Canada is higher (Statistics Canada. 2015). In relation to the *hedonic* emotional well-being factor, among

adults in Toronto, 71% rated their mental health as “excellent” or “very good” in 2015-16; 83% reported feeling happy “every day” or “almost every day” in the past month; and 84% reported being satisfied with their lives “every day” or “almost every day” (Toronto Health Check, 2019). In terms of the *eudaimonic* components of social well-being and psychological well-being, 68% reported a “very strong” or “somewhat strong” sense of belonging to their local community; and 75% scored highly on the psychological well-being scale (Toronto Health Check, 2019). Canadians in the lowest household income quintile, without a postsecondary education or a job, were less likely to report complete mental health (i.e., both flourishing and free of mental illness) (Statistics Canada, 2015). Seventy-two percent of people living in urban environments had complete mental health compared to 77% of rural residents (Statistics Canada, 2015). Finally, 76 % of those who reported strong spirituality had complete mental health versus 66 % of those without strong spirituality (Statistics Canada, 2015).

### 2.2 Risk factors for poor mental health in young adulthood

Risk factors for poor mental health in young adults include social isolation, loneliness, homelessness, sexual minority status, and migration (Sax Institute, 2019). In Canada, young persons feel lonely more frequently than older persons. Among 15–24-year-olds, about one in four felt lonely frequently or always compared to 15% of people ages 25-34 (Statistics Canada, 2021). Forty-nine percent of respondents who stated that they always or often felt lonely reported having fair or poor mental health (Statistics Canada, 2021). In comparison, 7% of individuals who indicated they rarely or never feel lonely, reported fair or poor mental health (Statistics Canada, 2021). Sleep is a fundamental physiological need that is disrupted during conditions of isolation (Wilkialis et al., 2021). Lack of sleep increased the risk for physiological deterioration and diminished immune function, as sleep is essential for healthy body maintenance and repair. Moreover, a sedentary lifestyle has a range of physiological impacts on the cardiovascular, metabolic, and endocrine systems, leading to other health issues (Wilkialis et al., 2021). Strain on insulin-related body systems results in body-wide inflammation and oxidative stress. A cascade of events can follow, which may lead to insulin resistance, neuro-inflammation, and oxidative stress resulting cognitive decline, decreased synaptic plasticity, decreased neuronal survival, increased cerebral degeneration, disruption of the hypothalamic-pituitary-adrenal (HPA) axis, and impairment of physiological mechanisms of reward, learning, and mood (Wilkialis et al., 2021).

Inflammation associated with the limbic system alters the performance of brain regions associated with symptoms of generalized anxiety (Wilkialis et al., 2021).

Many homeless young adults have had a troubled upbringing characterized by poverty, broken homes, histories of parental rejection, and physical or sexual abuse (Amore et al., 2012). Many experience foster care and have poor educational records. Common causes of running away from home include conflict, abuse, and pregnancies (Amore et al., 2012). In 2018, Canadians who had experienced both unsheltered and hidden homelessness were three times (28% compared to 9%) more likely to report fair or poor mental health than individuals who had not experienced homelessness (Uppal, 2022). Homeless young people are likely to engage in risky behaviours such as an early start to sexual activity, unprotected sex with multiple partners, drug abuse, and prostitution. Those who engage in such behaviours experience higher levels of depression and suicidality (Amore et al., 2012).

According to the Gay, Lesbian & Straight Education Network's (GLSEN) 2015 National School Climate Survey USA report on school climate, about 85% of LGBTQ teenagers experienced verbal abuse, 27% experienced physical harassment, and 13% experienced physical assault while in high school (McDonald, 2018). A Canadian study in 2015 found that sexual minority groups were more likely to have experienced mood or anxiety disorders or suicidality and were less likely to be in flourishing mental health (Gilmour, 2019). The predominant explanation for such disparities has been linked to the minority stress theory, which posits that members of minority groups suffer a higher risk of mental health disorders due to the unique chronic stressors they are exposed to through social stigma and discrimination (Scott et al., 2016).

In terms of migration status, the “Healthy Immigrant Effect” (HIE) suggests that immigrants, on average, are mentally healthier on arrival in Canada compared to their Canadian-born counterparts (Ng et al., 2020). The "Healthy Immigrant Effect" theory, also known as the "Immigrant Paradox," contends that immigrants have superior health than those who are native-born (Elshahat et al., 2021). Based on data from Canada-wide representative surveys, immigrants fare better in self-reported mental health (SRMH) and mental health disorders (Ng et al., 2020). Over time, the early health benefits tend to vanish, possibly because of stress and other difficulties integrating (i.e., the

"years since immigration effect (YSIE)" (Elshahat et al., 2021)). In contrast, recent immigrants or refugees from war-torn parts of the world are at a mental health disadvantage upon arrival in Canada (Ng et al., 2020).

### 2.3 Descriptive epidemiology of substance (alcohol, cannabis, and nicotine) use

Substance use among adolescents and young adults is a growing public health concern in Canada. Alcohol, cannabis, and nicotine-containing tobacco are the most frequently used substances by adolescents and young adults (Singh, 2019). Alcohol consumption is a leading contributor to the global disease burden and the most frequently consumed psychoactive substance among Canadians (Health Canada, 2020). The prevalence of alcohol consumption among Canadian adults ages 25 years or older was 79% in 2017 (Statistics Canada, 2017). Alcohol-related harm is on the rise in Canada (Spithoff, 2019). According to a report by Canada's Chief Public Health Officer, alcohol-related harms include suicide, accidents, pancreatitis, liver illness, psychological disorders, brain damage, and mortality. Between 2003 and 2016, the rate of alcohol-related emergency department visits in Ontario increased 4.4-fold (Spithoff, 2019). At the societal level, some experts describe alcohol as potentially just as harmful to users as cocaine (Spithoff, 2019). Alcohol use by Canadians resulted in 14,827 fatalities in 2014, with direct healthcare expenditures accounting for $11.1 billion of the $14.6 billion total cost to the public (Spithoff, 2019).

As of October 2018, Canada became the second country in the world to legalize the consumption of non-medical use of cannabis for adults (Rotermann, 2019). A fundamental justification for legalization was to allow users to switch from a long-established illegal market (i.e., valued at $6 billion in 2015) to legal sources to obtain regulated and quality-controlled cannabis products (Fischer et al., 2018). Cannabis is one of Canada's most widely used substances, with nearly half of all Canadians ages 15 years or older reporting consumption (Rotermann, 2019). In 2017, the prevalence of past-year cannabis use was 15%, an increase from 12% in 2015 (Statistics Canada, 2017). Age at initiation of cannabis use has become a strong predictor of many cannabis-related problems of public health concern. In 2019, among Canadian National Cannabis Survey respondents ages 15-24 years, one in four reported consuming cannabis in the previous three months, 14% reported driving within two hours of consuming cannabis, and 12% reported being a passenger in a vehicle driven by someone who had used cannabis in the previous two hours

(Brubacher et al., 2020). Epidemiological studies suggest a modest increase in crash risk after cannabis use, which tends to impair psychomotor skills required for safe driving (Brubacher et al., 2020). A California-based study (Gerberich et al., 2003) documented that compared to non-users of cannabis, all-cause hospitalization rates were 1.5 times higher among cannabis users (Gerberich et al., 2003). Recent American estimates also suggest that as many as one in three current users meet the criteria for a cannabis-use disorder (CUD) (Fischer et al., 2018), broadly defined as the inability to stop consuming cannabis even when it is causing physical and/or psychological harm (Connor et al., 2021).

In Canada, tobacco use remains the number one preventable cause of premature mortality (Callard, 2022). Despite a decline in tobacco consumption, many Canadians still smoke cigarettes, which causes 45,000 deaths in the country each year (Callard, 2022). In 2017, among adults ages 25 years or older, the prevalence of past-30-day use of at least one tobacco product was 18%, an increase from 15% in 2015 (Statistics Canada, 2017). Tobacco use increases the risk of cancer, cardiovascular disease, and pulmonary disease (Benowitz, 2010). Additionally, smoking increases the probability of developing diabetes, duodenal and gastric ulcers, osteoporosis, reproductive disorders, poor wound healing, and respiratory tract infections. Nicotine addiction is a direct cause of smoking-induced diseases (Benowitz, 2010). In addition to being highly addictive, nicotine adversely affects the heart, reproductive system, lungs, kidneys, etc. and has carcinogenic properties (Mishra et al., 2015). To reduce the staggering death and disease burden of tobacco use, the Government of Canada allocated a $330 million budget in 2018 to attain a goal of less than 5% tobacco use by 2035 (Callard, 2022). As policies are enacted to control tobacco use, young adults have instead taken up high nicotine and flavoured e-cigarettes, which also come with health concerns (i.e., addiction, headache, nausea, upper respiratory tract irritation, and the risk of lung cancer) (Al-Osaimi et al., 2015). In 2017, 15% of Canadians ages 15 years or older had ever tried an e-cigarette, representing an increase from 13% in 2015 (Statistics Canada, 2017).

It is common for individuals to report using these substances concurrently (Roche et al., 2019). Concurrent polysubstance use refers to when different psychoactive substances are consumed on separate occasions; simultaneous use refers to ingestion of two or more substances on a single occasion (Earleywine et al., 1997). In the US, over 75% of marijuana users reported alcohol use

(Roche et al., 2019). Longitudinal studies suggest that most users who report concurrent use of alcohol and marijuana consume these substances simultaneously - which is associated with increased heavy-drinking behaviour, drunk driving, other adverse social consequences, and self-harm (Roche et al., 2019). Cannabis dependence doubles the risk of long-term alcohol consequences (Yurasek et al., 2017). Among adults with no alcohol use disorder (AUD), cannabis use has been associated with an increased incidence of AUD three years later compared to non-cannabis users (Yurasek et al., 2017).

Concurrent marijuana and cigarette use is also highly prevalent. Recent findings indicate that more than two-thirds of current marijuana users use tobacco concurrently, and up to 53% of current tobacco users also consume marijuana (Roche et al., 2019). Tobacco and cannabis can be consumed simultaneously in what is referred to as "blunts" or "spliffs" (Jayakumar et al., 2019). Blunts are cannabis-filled cigar papers or rolled tobacco leaves that have been partially or totally hollowed out. Spliffs are joints (cannabis cigarettes) filled with loose-leaf tobacco and cannabis (Jayakumar et al., 2019). Spliff users claim that they mix tobacco with cannabis to lessen the latter's potency, lower the use cost, and enhance the burning properties (Jayakumar et al., 2019). In the US, in 2017, about 40.9 million people (15.0%) ages 12 or older used cannabis in the last year (Kumar et al., 2020). Also, in 2017, approximately one in 11 US cannabis users ages 15 or older developed dependent patterns of use, with 4.2 million people meeting diagnostic criteria for frequent or problematic use (Kumar et al., 2020).

Alcohol and nicotine dependence are strongly correlated, and alcohol and tobacco use are highly comorbid (Adams, 2017). The term "comorbidity," which was first used in 1970, is defined as any distinct clinical entity that may occur together with an index disorder, which is regarded as the "primary" condition of clinical or research interest (MacLean et al., 2018). People who are dependent on tobacco are four times more likely to be dependent on alcohol, and those who are dependent on alcohol are three times more likely to smoke than the general population (Adams, 2017). In Waves I and II of the National Epidemiologic Survey on Alcohol and Related Conditions (NESARC), US researchers found that among those with alcohol dependence, use of alcohol and tobacco together (32.5%) was more common than alcohol use alone (27.5%) (MacLean et al., 2018). Additionally, compared to non-alcohol-dependent smokers, alcohol-dependent smokers

have more severe nicotine dependence and a more challenging time quitting (Adams, 2017). In a recent study of US veterans, 58% of those with alcohol use disorder (AUD) also had tobacco use disorder (TUD) diagnoses (MacLean et al., 2018).

### 2.4 Substance use and mental health

*Alcohol consumption and mental health*

Numerous cross-sectional studies identify links between alcohol use and both anxiety and depression (Haynes et al., 2005). Data from four community-based studies conducted in Europe and the US demonstrate a 2-3-fold increase in the lifetime prevalence of anxiety and depression among those with DSM–III alcohol abuse or dependence (Haynes et al., 2005). A review by Madden (1993) discussed several potential "pathways" linking the physiological effects of heavy alcohol consumption to the induction of a depressed state which includes: depression as a component of a hangover state; withdrawal depression because of alcohol-induced neurochemical changes; and depression as a reaction to the psychological, social, and physical problems linked with alcoholism (Patten et al., 1998). Pietraszec et al. (1991) observed that whole-blood serotonin was reduced 45 minutes after drinking, and they postulated that alcohol-induced changes in mood might relate to changes in serotonin function. Cleare (1997) found that depressed subjects did indeed have lower whole blood serotonin (WBS) than controls. However, results of longitudinal studies are inconsistent (Haynes et al., 2005). An early meta-analysis of eight longitudinal studies found that baseline alcohol consumption was significantly associated with later depression (Haynes et al., 2005). In contrast, later studies have generally found no link between alcohol consumption and incident depressive illness (Haynes et al., 2005). Wang & Patten (2001) found that in a general population sample, alcohol consumption levels were not associated with major depression, while extreme patterns of alcohol consumption (which tend to characterize clinical samples) were associated with depression. Such drinking patterns, however, are relatively less common in the general population in Canada (Wang & Patten, 2001).

*Cannabis consumption and mental health*

A systematic review by Degenhardt et al. (2003) which investigated the association between cannabis use and the development of depression, concluded that longitudinal studies provided mixed evidence on the association between cannabis use and depression. It also emphasized that

although heavy cannabis use may increase depressive symptoms, uncontrolled confounding factors may underpin this relationship (Lev-Ran, 2013). A study linking cannabis use and depression by Lynskey et al. (2004) measured correlations between early cannabis use and lifetime cannabis dependence and each of Major Depressive Disorder (MDD), suicidal ideation, and suicide attempts among twins. The odds of MDD and suicidal ideation among individuals who met the lifetime criteria for cannabis dependence were 1.3 to 3.4 times higher than non–cannabis dependent twins. More importantly, there was evidence that shared genetic vulnerabilities could account for a substantial component of the link between cannabis dependence and MDD (Lynskey et al., 2004). A significant interaction between zygosity and cannabis dependence on the risk of MDD was reported, with cannabis dependence being significantly associated with elevated risks of MDD (compared to the non–cannabis-dependent twin) in dizygotic twins but not in monozygotic twins (Lynskey et al., 2014). In contrast, some preclinical studies suggest that cannabis may be therapeutically effective for depression (Adel et al., 2020). If blocking CB1 (cannabinoid receptors type 1) receptors produces depressive symptoms, activating CB1 receptors could alleviate the issue (i.e., marijuana might have antidepressant effects, with agonistic effects on the central CB1 receptors) (Stoner, 2017).

*Nicotine consumption and mental health*

Nicotine can both stimulate and inhibit the function of neuronal nicotinic ACh receptors (nAChRs) (Anderson & Brunzell, 2015). In fact, *in vitro* and *in vivo* studies have shown that nicotine can both activate and desensitize nAChR ion channels and that low concentrations can desensitize nAChRs, making them unavailable for further activation by nicotine (Anderson & Brunzell, 2015). Different psychotropic effects may result from this modulation of nAChRs in the brain (Anderson & Brunzell, 2015). However, uncertainties still exist regarding specific nAChR subtypes' roles in anxiety behaviours (Anderson & Brunzell, 2015). Studies based on rodent models of anxiety-like behaviour suggest that nicotine can dose-dependently activate or desensitize β2 subunit-containing nicotinic ACh receptors (β2*nAChRs) (Anderson & Brunzell, 2015). Thus, providing direct evidence that low-dose nicotine inhibits nAChRs. It also demonstrates that inhibition or stimulation of β2*nAChRs supports nicotine's corresponding anxiolytic-like or anxiogenic-like effects. Among traditional cigarette smokers, most common motives for continued smoking have been enjoyment and stress relief (Fidler and West, 2009). However, consistent with rodent-model

studies, high doses of nicotine or repeated exposure may also promote anxiety, as multiple studies suggest that smokers experience anxiety more intensely than non-smokers (Anderson & Brunzell, 2015).

*Polysubstance use and mental health*

Polysubstance use of alcohol, marijuana, and tobacco is widespread in populations with mental health and substance use problems, with the onset of these issues typically occurring during young adulthood (Cohn et al., 2018). A study by Cohn et al. (2018) reported strong associations between polysubstance use patterns and mental health problems among US adults. Interestingly, when used alone by young adults, alcohol and cigarettes were associated with poorer mental health than when used together. Mental health in the Cohn study, was assessed by capturing internalizing and externalizing disorders (two broad categories of behavioural problems) using the Global Appraisal of Individual Needs–Short Screener (GAIN-SS). Internalizing problems (i.e., withdrawal, anxiety, depression, emotional problems) are focused on the self, while externalizing problems (i.e., aggression, impulsivity, deviance, hyperactivity) occurs in interaction with the social environment (Nikstat et al., 2020). While polysubstance use is associated with poorer mental health among American adolescents (Banks et al., 2017), a review by Halladay et al. (2020) suggests that not all adolescents who use substances experience mental health issues. Rather, the review suggests for future studies to derive distinct patterns of substance use to study its relationship with mental health symptomatology (Halladay et al., 2020).

*Possible underpinnings linking polysubstance use and mental health.*

Compared to nicotine use alone, the chemistry of combined marijuana and nicotine use is characterized by upregulation of α4β2* nicotinic acetylcholine receptor (nAChR) availability in the prefrontal cortex and the thalamus (Brody et al., 2016). Animal models are beginning to shed light on the function of nAChRs in circuits regulating anxiety and mood, but the mechanisms underpinning how nicotine affects aggression-related behavioural states (ARBS) are still unclear (Picciotto et al., 2015). Numerous studies suggest that decreasing the activity of α4β2* nAChRs can improve symptoms of depression (Picciotto et al., 2015). Labarca et al. (2001) reported that mice with increased activity of α4β2* nAChRs showed increased anxiety-like behaviours. Functional magnetic resonance imaging (fMRI) assessments of the combined use of nicotine and

marijuana suggested increased connectivity disruptions in posterior cortical and frontoparietal regions (Vergara et al., 2017). Schultz et al. (2019) showed a negative correlation between the intensity of depressive symptoms and the frontoparietal network's between-network global connectivity. This suggests that higher levels of depressive symptoms may be associated with decreased connectivity between the frontoparietal network and the rest of the brain. These findings align with clinical studies supporting the hypothesis that global frontoparietal network connectivity plays a domain-general protective role against mental health symptoms (Schultz et al., 2019). Alterations in frontoparietal network functional connectivity have been linked to various mental disorders such as schizophrenia, anxiety, depression, attention deficit hyperactivity disorder (ADHD), and eating disorders (Schultz et al., 2019). Li et al. (2020) found that dysfunction of the right frontoparietal network and white matter fractional anisotropy in tracts to the right frontoparietal network were highly associated with comorbid-anxiety symptoms in late-life depression patients.

Combined alcohol and nicotine consumption also produces neurologic alterations that differ from single substance use, including that users become sensitive to the cognitive enhancement effects of nicotine (Vergara et al., 2017). The dopamine (DA) neuron activity induced by nicotine and alcohol correlates with increased DA release at target areas, including the nucleus accumbens (NAc) and ventral pallidum (Doyon et al., 2013). Nicotine and alcohol administered simultaneously produce an additive increase in DA release in the NAc compared to each drug alone (Doyon et al., 2013). Although the DA system in the NAc has been associated with emotion-related behaviours, the NAc acts as a common target in comorbid depression and addiction (Xu et al., 2020). The NAc and the dopaminergic inputs it receives from the ventral tegmental area (VTA) of the midbrain have been identified as one of the most significant anatomical substrates for drug-related rewards as well as for natural rewards like food, sex, and social interactions (Nestler et al., 2006). The possible involvement of the VTA-NAc pathway in mood regulation and depression, however, is not well studied, and the idea that the path may mediate depression-like behaviours was first proposed based on studies with dopamine receptor antagonists (Nestler et al., 2006). It is notable that the activation of dopaminergic neurons and other pathways within the mesolimbic dopaminergic system by nicotine and alcohol is dependent on nAChRs (Tarren & Bartlett, 2016). It is well documented that α4β2* and α7 nAChRs are located in DA cell bodies in the VTA (Tarren

& Bartlett, 2016). Moreover, high-affinity nAChRs (i.e., α4β2*) are located on GABAergic afferents projecting to key reward areas to regulate dopamine cell firing through the release of GABA. Ethanol (alcohol) potentiation in brain nAChRs is postulated to be the outcome of ethanol-induced stabilization of the open-channel state of the receptor (Tarren & Bartlett, 2016).

Both marijuana and alcohol consumption are linked to changes in structural connectivity in the brain, but affect functional connectivity in opposite directions (i.e., alcohol decreases and marijuana increases overall connectivity in the brain) (Vergara et al., 2017). The opposite trend between alcohol and cannabis does not indicate that detrimental neurocognitive effects will diminish because of concurrent use (Vergara et al., 2017). In a study comparing simultaneous versus concurrent use of alcohol and cannabis among high-school students in Quebec, Brière et al. (2011) reported that simultaneous use was associated with higher depressive symptoms. As neuro-inhibitory substances, both alcohol and cannabis cause many of the same behavioural effects, including euphoria, analgesia, drowsiness, hypothermia, cognitive and motor dysfunctions (Singh, 2019). Alcohol and marijuana use together may increase the severity of cognitive and motor deficits in occasional cannabis users. Chronic cannabis use, however, may lead to a tolerance to the impairing effects of alcohol or cannabis (Singh, 2019). Alcohol and cannabis both increase dopamine (DA) levels in the nucleus accubens (NAc) by activating DAergic neurons in the ventral tegmental area (VTA), where the mesoaccumbal DA-mediated pathway originates (Singh, 2019). Guillot et al. (2018) studied anxiety sensitivity components (i.e., physical, cognitive, and social concerns) with the use of cannabis and alcohol, which may also be interlinked with use of alcohol and cannabis. Fear of anxiety symptoms and possible adverse effects defines anxiety sensitivity (Guillot et al., 2018). The propensity to fear anxiety-related experiences intensifies unpleasantness and may cause more psychological suffering, possibly implicated in the development of several forms of psychopathology (e.g., panic, generalized anxiety, social anxiety, posttraumatic stress disorder, depression, and suicidal ideation) (Guillot et al., 2018). Although knowledge on the molecular basis of alcohol-cannabis interaction is limited, recent research has proposed epigenetic mechanisms: CB1 and CB2 receptors are both modulated by alcohol and cannabis activating the MAPK signalling pathways that further activate: (i) nuclear factors CREB and NF-κB, (ii) histone modifications, and (iii) DNA methylation mediated by the epigenetic enzymes (Singh, 2019). The

adverse effects of this pathway include synergetic augmentation of addictive response and depressive symptoms (Singh, 2019).

### 2.5 Gaps in knowledge

This review of the literature suggests a lack of studies describing patterns of polysubstance use among young adults. Further, few studies investigate the association between polysubstance use and mental health in this age group. To our knowledge, only Cohn et al. (2018) has reported patterns of polysubstance use including alcohol, marijuana, and tobacco, at a population-level among young adults. This thesis will provide one of the first population-level glimpses of polysubstance use among young adults in Canada. It also assesses the association between polysubstance use and several indicators of mental health including anxiety and depressive symptoms and in particular, flourishing positive mental health, which has been explored only infrequently.

## CHAPTER 3: OBJECTIVES

The aim of this MSc thesis is to better understand the association between polysubstance use and mental health among young adults. There are two specific objectives:

1. To describe patterns of regular (i.e., at least weekly) polysubstance use (i.e., use of two or more substances in the same timeframe) in the past year among young adults. Substances of interest include alcohol, cannabis, and nicotine.

2. To estimate the associations between patterns of regular polysubstance use and indicators of mental health including depressive symptoms, anxiety symptoms and flourishing positive mental health.

## CHAPTER 4: METHODS

This thesis is a secondary analysis of data drawn from the longitudinal Nicotine Dependence in Teens (NDIT) study. This section describes the source of the data, the study design, the methods used for data collection, the study variables, the data analysis plan, and ethical considerations.

### 4.1 Source of data

The ongoing longitudinal Nicotine Dependence in Teens recruited students in 1999–2000 from all grade 7 classes in a purposive sample of 10 high schools in Montreal, Canada (O'Loughlin et al., 2014). The primary goal of NDIT was to describe the natural course of cigarette smoking and nicotine dependence among youth and to identify individual-level and contextual predictors of the onset of smoking and nicotine dependence. NDIT, however, also includes investigations of blood pressure, adiposity, team sports, physical activity, sedentary behaviour, nutrition, genetics, alcohol consumption, use of cannabis, illegal drug use, second-hand smoke, gambling, sleep, and mental health (O'Loughlin et al., 2014).

Thirteen high schools in or near Montreal were selected in consultation with local school boards and school principals to include a mix of French- and English-language schools; urban, suburban, and rural schools; and schools situated in high, moderate, and low socioeconomic-status neighbourhoods (O'Loughlin et al., 2014). All grade 7 students in these schools (age 12-13 years) received a take-home information package that included a letter for their parents/legal guardians describing the research and a consent form for their parents/guardians to complete. One school was excluded because the school administration could not guarantee continued participation beyond the first year of the study, and two schools were excluded due to low returns of signed parental consent forms. Of 2,325 eligible students, 1,294 (56%) completed baseline questionnaires in autumn 1999 (nine schools) or in autumn 2000 (one school).

Follow-up questionnaires were completed at school by NDIT participants every three months during the 10-month school year for the next five years (i.e., from 1999-2005) until high school graduation, for a total of 20 cycles during high school. In cycle 21, which was undertaken post-high school in 2007-2008, participants (mean age 20 years) completed self-report questionnaires which were mailed to their homes. In cycle 22 which was undertaken in 2011-2012, participants

(mean age 24 years) completed self-report questionnaires administered in the NDIT research offices located at the *Centre de recherche du Centre Hospitalier de l'Université de Montréal* (CRCHUM). During cycle 23 (2017-2020), 99.3% of participants (mean age 31 years) who completed a questionnaire provided data before the declaration of a sanitary emergency (i.e., the COVID-19 pandemic) in Quebec on March 13, 2020, which resulted in the closure of daycares, schools, post-secondary institutions, and non-essential companies as well as restrictions on private gatherings. Data in cycle 24 were collected online from participants (mean age 34 years) during the COVID-19 lockdown in Canada from December 2020 to June 2021. Data collection for Cycle 25 ended in March 2023.

### 4.2 Study design

The study design to address the objectives of this thesis was cross-sectional. Data on all study variables including: (i) the substance use indicators (i.e., use of alcohol, cannabis, and/or nicotine at least weekly in the past year); (ii) the mental health indicators (i.e., depressive symptoms, anxiety symptoms, positive mental health); and (iii) the covariates (i.e., sex, age, level of education) were drawn from cycle 23 (2017-20), when participants were age 31 years on average. Note that although the study design was cross-sectional, the data for cycle 23 were collected over a 3-year time span. Appendix A includes a copy of the questionnaire used in cycle 23 and Appendix D describes each study variable including the questionnaire item(s) used to measure the variable, the response choices, re-coding of the response choices for analysis, and the psychometric properties of scales and references if applicable.

### 4.3 Study variables

*Regular alcohol use* - Frequency of alcohol consumption was determined by asking participants: "In the past 12 months, how often did you… drink alcoholic beverages?". Response options included: never; less than once a month; 1-3 times per month; 1-6 times per week; everyday. Regular alcohol use was coded "yes" if participants reported drinking alcoholic beverages 1-6 times per week or everyday. It was coded "no" if participants reported: never, less than once a month or 1-3 times per month.

*Regular cannabis use* - Frequency of cannabis consumption was determined by asking participants: “In the past 12 months, how often did you… use marijuana, cannabis or hashish without tobacco?” and “In the past 12 months, how often did you… use marijuana, cannabis or hashish mixed with tobacco?”. Response options for both items included: never; less than once a month; 1-3 times per month; 1-6 times per week; everyday. Regular cannabis use was coded “yes” if participants reported 1-6 times per week or everyday for either item. Regular cannabis user was coded “no” for all other responses.

*Regular nicotine use* - Frequency of nicotine consumption was determined by asking participants about their consumption of eight products containing nicotine: “In the past 12 months, how often did you… (i) use electronic cigarettes with nicotine, (ii) smoke flavored cigarettes or cigarillos, (iii) smoke cigars or pipe, (iv) use bidis, chewing tobacco and/or snuff, (v) smoke cigarillos, (vi) use a waterpipe, and (vii) use marijuana, cannabis or hashish mixed with tobacco”. Response options included: never; less than once a month; 1-3 times per month; 1-6 times per week; everyday. In addition, (viii) the frequency of cigarette use in the past year was determined by asking participants to: “Check the box that describes you best...”. Response options included: I have smoked cigarettes, but not at all in the past 12 months; I smoked cigarettes once or a couple of times in the past 12 months; I smoke cigarettes once or a couple of times each month; I smoke cigarettes once or a couple of times each week; I smoke cigarettes everyday. Regular nicotine use was coded “yes” if participants reported consuming nicotine from any source 1-6 times per week or everyday. Regular nicotine use was coded “no” for all other responses.

We used data on regular alcohol, cannabis and nicotine use in the past year to create two variables reflecting polysubstance use (i.e., number of substances used, pattern of polysubstance use). *Number of substances used* was computed as the sum of the number of the three substances of interest (i.e., alcohol, cannabis, nicotine) that were used regularly in the past year (range 0-3). A value of 0 denoted that the participant did not report any regular use of any of the three substances of interest in the past year. A value of 3 indicated that the participant reported regular use of all three substances in the past year.

*Pattern of polysubstance use* - To create the pattern of polysubstance use variable, we categorized participants into one of eight different patterns based on the number and type(s) of substances used regularly: (i) no-substance use included participants who did not report regular use of any of the three substances in the past year. Patterns representing regular use of one substance only included: (ii) alcohol only; (iii) cannabis only; and (iv) nicotine only. Regular use of two substances included: (v) alcohol-cannabis; (vi) alcohol-nicotine; and (vii) cannabis-nicotine. Finally, (viii) alcohol-cannabis-nicotine included participants who reported regular use of all three substances.

*Depressive symptoms* – Depressive symptoms were measured using the Major Depression Inventory (MDI), which is a 12-item self-report depression questionnaire that asks participants to report on a 6-point rating scale, how frequently they experienced each of 12 depressive symptoms in the past two weeks. Response options were: at no time; some of the time; slightly less than half of the time; slightly more than half of the time; most of the time; all the time scored 0-5. Items 8 and 10 had two sub-items (Appendix D), of which only the highest-scored sub-item was retained (Bech et al., 2001). Scores were summed across items to yield a score that ranged between 0 and 50, with higher scores indicative of more frequent depressive symptoms (Bech et al., 2001). Internal consistency of the MDI is high (Cronbach's $\alpha = 0.94$) (Bech et al., 2001).

*Anxiety symptoms* – Anxiety symptoms were measured using the Generalized Anxiety Disorder scale (GAD-7). The GAD-7 is a 7-item self-report questionnaire used as a diagnostic tool for a General Anxiety Disorder (GAD) diagnosis based on an initial 13-item questionnaire reflecting DSM-IV symptom criteria for GAD and earlier anxiety scales (Spitzer et al., 2006). The scale also quantifies the severity of anxiety symptoms (i.e., higher GAD-7 scores are closely correlated with several functional impairments and disability days (Spitzer et al., 2006)). GAD-7 asks participants to report, on a 4-point rating scale, how often each of the 7 anxiety-related issues had bothered them in the past two weeks. Response options included: not at all; several days; over half the days; and nearly every day scored 0 to 3. Scores ranged between 0 and 21, with higher scores indicative of more frequent anxiety symptoms; cut points of 5, 10, and 15 might be interpreted as representing mild, moderate, and severe levels of anxiety (Spitzer et al., 2006). Cronbach's $\alpha$ for internal consistency was 0.92 in earlier work (Spitzer et al., 2006).

*Flourishing positive mental health* – In accordance with the definition of the World Health Organization (WHO), flourishing positive mental health is defined as the presence of emotional, psychological, and social well-being (Lamers et al., 2010). Two longstanding traditions in studies on "life well-lived" were considered for the definition: the *hedonic* tradition (i.e., feelings of happiness) and the *eudaimonic* tradition, which focuses on optimal functioning in life (Lamers et al., 2010). Derived from several instruments that assess emotional, psychological and social well-being in the Survey on Midlife Development in the US, the self-report questionnaire of Mental Health Continuum-Short Form (MHC-SF) was developed to fully cover all three dimensions of mental health (Lamers et al., 2010). There are 14 items on the Positive Mental Health – Flourishing scale, which assesses the degree of (1) Emotional well-being (EWB) in items 1-3 - which relates to positive affect (PA) and satisfaction with life; (2) Social well-being (SWB) in items 4–8 – which relates to each of social acceptance, social actualization, social contribution, social coherence and social integration; and (3) Psychological well-being (PWB) in items 9–14 - which includes one item on each of the dimensions of autonomy, environmental mastery, personal growth, positive relations with others, purpose in life and self-acceptance (Keyes et al., 2008). Response options for all items included: never; rarely; sometimes; often; most of the time; always. Scores ranged from 0 to 70, with higher scores indicative of more psychological resources and strengths. The internal reliability of the MHC-SF as measured with Cronbach's $\alpha$ is 0.89 (Lamers et al., 2010).

*Covariates* - We based our selection of covariates primarily on an article which included both a systemic review and a meta-analysis (Esmaeelzadeh et al., 2018) on the association and directionality of the relationships between cannabis, alcohol, and tobacco use and mental health disorders among adolescents and young adults in the U.S. and Canada. Most studies in this review controlled for age, sex, ethnicity, parental education, household income and socioeconomic status (SES). The present analysis controlled for participant's age, sex and level of education. Ethnicity was not included because of low ethnic diversity in the NDIT sample (i.e., in Cycle 23, participants with Caucasian backgrounds represented 78.0% of the sample). Because the mean age of participants in our study was 31 years, participant's highest level of education attained (rather than parental education) was used as a covariate. In epidemiological studies, level of education is frequently used as an indicator of socioeconomic position (SEP) and is thought to capture knowledge-related assets (Galobardes et al., 2007). Other SEP indicators include household

income, household conditions, occupational social class, etc. (Galobardes et al., 2007). However, use of a single indicator (rather than several indicators) in this current study avoids the problem of overfitting in regression-type models, which can create uncertainty about the scientific validity of the findings. Overfitting can produce overly optimistic results that cannot be replicated (Babyak, 2004).

Sex - In 2019, higher proportions of men than women in Canada had consumed alcohol (78% vs. 75%), used cannabis (23% vs. 19%), and used tobacco (16% vs. 12%) (Statistics Canada, 2021). Similarly, in 2016, males were more likely than females in Canada to report polysubstance use (i.e., use of two or more of alcohol, cigarettes, cannabis, and e-cigarettes) (Zuckermann et al., 2019). Sex is also associated with symptoms of mental health problems. Prior to the COVID-19 pandemic, population health surveys in Canada indicated that women reported higher anxiety levels than men (Moyser, M., 2020). Similarly, the prevalence of depressive symptoms among Canadians in 2012, was 5.8% in women and 3.6% in men (Albert, P., 2015). Data on sex were collected in Cycles 1-11 by: "Are you a boy or a girl?" Response options included boy and girl.

Age - Age was also considered as a possible confounding variable in this study. Data from a nation-wide population survey in Canada (Statistics Canada, 2021) showed that use of alcohol, cannabis, and current cigarette smoking varied across age. For example, 44.6% of those age 20-24 had used cannabis in the past 12 months compared to 21.9% and 18.5% among 15-19 and ≥25-year-olds, respectively (Statistics Canada, 2021). Use of marijuana and cigarettes at age 18 predicts heavy drinking at age 35 (Merline et al., 2008). In a 2012 survey in Canada, 48.6% of those age 30-49 reported both a generalized anxiety disorder (GAD) and a major depressive episode (MDE) compared to 22.7% and 28.8% among those age 15-29 and ≥50, respectively (Pelletier et al., 2017). Compared to those with MDE only, those with GAD only were older (mean age = 38.0 and 43.8 years, respectively) (Pelletier et al., 2017). Age in this current study was computed based on the participants' birth date and the date when data were collected for the participant in cycle 23. Age was treated as a continuous variable in the analyses.

Level of education - Finally, level of education was considered as a possible confounding variable in this current analysis. Dropping out of high school is related to many adverse socioeconomic and

health outcomes. A report combining 2002 and 2014 data from the National Survey on Drug Use and Health (NSDUH) in the U.S (Tice et al., 2017) suggested that 12th grade dropouts were more likely than similarly aged youth still in school to have used a variety of substances (e.g., cigarettes, alcohol, binge alcohol use, marijuana, nonmedical use of prescription-type drugs, any illicit drugs) in the past month. Also, after considering a comprehensive set of socioeconomic measures across the life course in a nationally representative longitudinal cohort in the US, higher educational attainment was associated with a reduced risk of depression at age 40 (Cohen et al., 2020). Participants were asked in cycle 23: "How far have you gone in school…". Response options included: attended high school, but did not graduate; graduated high school; attended CEGEP, community/technical college but did not graduate; graduated CEGEP/technical college; attended university (or teachers college) but did not graduate; graduated university with a Bachelors degree; graduated university with a Masters degree; graduated university with a PhD; other. For analysis, high school graduate was coded yes (i.e., graduated high school; attended CEGEP, community/technical college but did not graduate; graduated CEGEP/technical college; attended university (or teachers' college) but did not graduate; graduated university with a Bachelors degree; graduated university with a Masters degree; graduated university with a PhD; other) or no (i.e., attended high school, but did not graduate).

### 4.4 Data Analysis

*Descriptive analyses*

Descriptive analyses were undertaken to identify missing data and outliers for all study variables and to check the distributions. We compared selected baseline characteristics (i.e., measured in NDIT cycle 1) of participants retained in the analytic sample and those not retained (i.e., participants who were lost-to-follow-up since cycle 1). Means (standard deviations (SD)) were computed for age, and percentages were computed for categorical variables (i.e., born in Canada, sex, mother graduated from high school, French-speaking).

The distributions of the scores for the three mental health indicators were assessed in frequency distributions and quantile-quantile plots. Because the data for depressive and anxiety symptoms were not normally distributed, medians (interquartile ranges (IQR)) were reported in addition to means (standard deviations (SD)).

*Association between polysubstance use and mental health indicators*

We compared the means (SD) and medians (IQR) for depressive symptoms, anxiety symptoms and flourishing positive mental health according to the number of substances consumed regularly and patterns of polysubstance use. The association between: (i) number of substances consumed regularly; and (ii) pattern of polysubstance use and each of the three mental health indicators was then examined in multivariable linear regression models. Unadjusted models and models adjusting for age, sex, and level of education were considered. Analyses were undertaken to assess the normality of the residuals using quantile-quantile plots and the assumption of homoscedasticity by plotting residuals against fitted values. The residual analyses suggested that the normality assumption for the residuals was violated in the models for depressive and anxiety symptoms. In sensitivity analyses, a second set of models were estimated following a square root transformation of both the anxiety and depressive symptoms scores. A residual analysis of these models was also performed.

All analyses were undertaken using R software version 4.0.3 [RStudio version 1.4.1103] and *dplyr* R package [version 4.0.2] was used.

### 4.5 Ethical considerations

At inception, a package including a description of the NDIT study and a consent form (Appendix B), was sent home to parents or legal guardians with all eligible students. The Principal Investigator visited each study school before the first data collection to explain the research to teachers and students and to respond to questions (O'Loughlin et al., 2014). Participation was voluntary, and participants could decide to stop participating at any time without providing a reason and without any repercussions. In the post-high school data collections, participants were of legal age and therefore able to provide consent. They each received 50$ to cover any costs associated with participating in the study (O'Loughlin et al., 2014). This current project is embedded in the ongoing NDIT study which has received ethics approval (Appendix C) from the Montreal Department of Public Health Ethics Review Committee, the McGill University Faculty of Medicine Institutional Review Board, the Ethics Research Committee of the Centre de Recherche du Centre Hospitalier de l'Université de Montréal and the University of Toronto (O'Loughlin et al., 2014).

## CHAPTER 5: RESULTS

### 5.1 Response

A total of 1,267 students participated in cycle 1 of the NDIT study; 27 students joined the study in later cycles (i.e., primarily in cycles 2 to 4) for a total of 1,294 participants. Of the 1,294, 799 (61.7%) participated in cycle 23 which took place 23 years after the inception of the NDIT study. The primary reasons for non-participation include moving to a non-participating school during high school, lack of time, and loss of interest in the study (O'Loughlin et al., 2014).

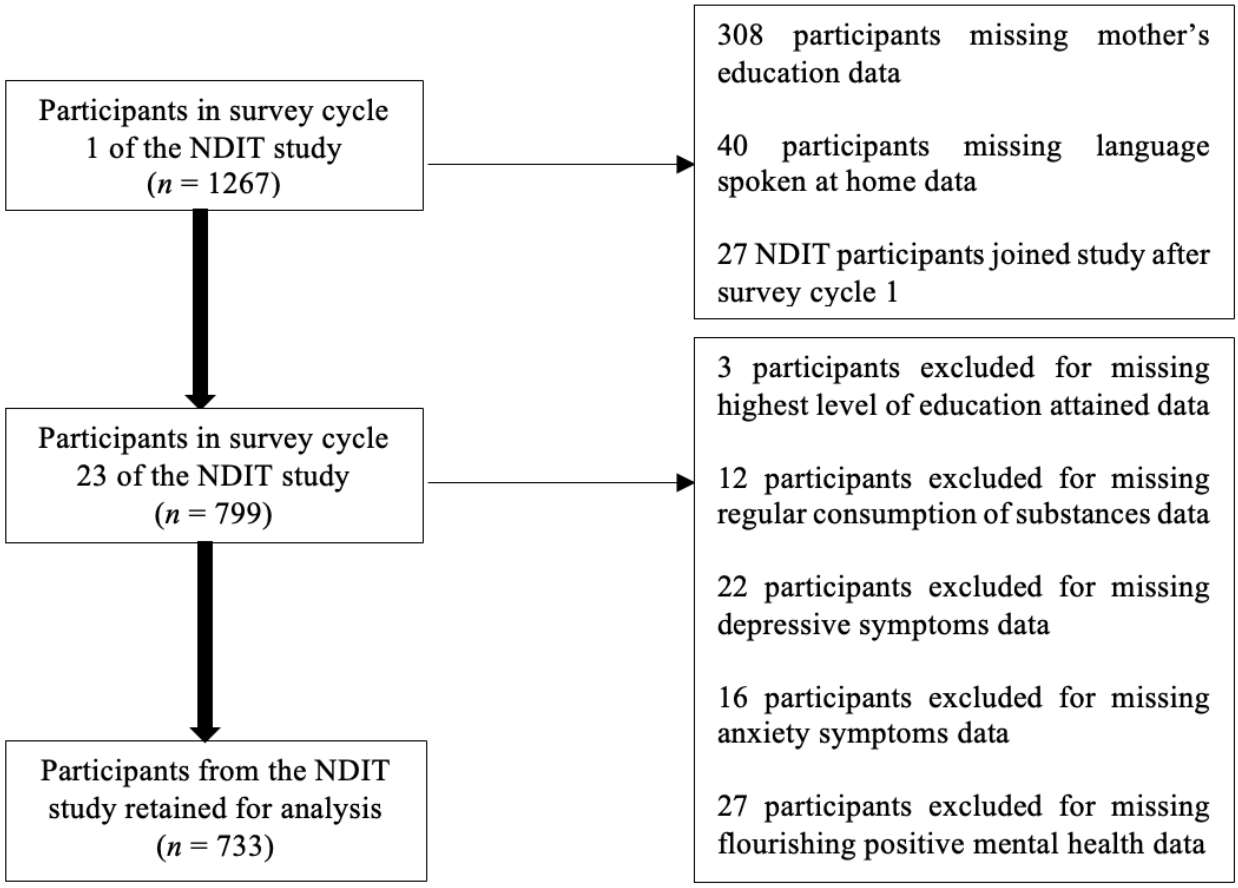


Figure 1. Flowchart describing the derivation of the analytical sample including the number of missing values for each study variable.

### 5.2 Comparison of cycle 23 participants and those lost-to-follow-up

Table 1 compares selected characteristics (measured in cycle 1) of participants who completed questionnaires in cycle 23 and those who did not (i.e., lost-to-follow-up). The proportion of males in the analytical sample was higher among those lost-to-follow-up than among participants who completed questionnaires in cycle 23. There were no notable differences in the proportions of Canadian-born participants, participants whose mothers had graduated from high school, or participants who were French-speaking.

Table 1. Selected characteristics (measured in NDIT cycle 1 (1999-2000)) of participants who completed cycle 23 (2017-2020) and those lost-to-follow-up, NDIT 1999-2020 (*n* = 1,294)

| | Participants who completed cycle 23 (*n* = 799) | Participants lost-to-follow-up (*n* = 495) |
|---|---|---|
| Age[1], y, mean (SD) | 12.7 (0.5) | 12.9 (0.6) |
| Born in Canada[1], % | 93.7 | 89.1 |
| Male[1], % | 44.0 | 55.9 |
| Mother graduated from high school[2], % | 90.2 | 91.5 |
| French-speaking[3], % | 31.3 | 30.5 |

[1]Data were available for 789 participants who completed NDIT cycle 23 questionnaire and 478 lost-to-follow-up participants (total = 1267 participants); [2]Data were available for 711 who completed NDIT cycle 23 questionnaire and 248 lost-to-follow-up participants (total = 959 participants); [3]Data were available for 774 who completed NDIT cycle 23 questionnaire and 453 lost-to-follow-up participants (total = 1227 participants).

Among the 799 participants who completed cycle 23 questionnaires, 66 were missing values for one or more study variables (i.e., 3 were missing data on level of education, 22 were missing data on depressive symptoms, 16 were missing data on anxiety symptoms, and 27 were missing data on flourishing positive mental health) (Table 2). A total of 733 of the 1,294 participants at inception (56.6%) were therefore retained for analysis.

Table 2. Number of participants missing data on study variables in Cycle 23 (n = 799), NDIT 2017-2020

| | Participants missing data | |
|---|---|---|
| | *n* | % |
| Age, y | 0 | 0.0 |
| Sex | 0 | 0.0 |
| Level of education of participant | 3 | 0.4 |
| Regular substance use | 12 | 1.5 |
| Depressive symptoms | 22 | 2.8 |
| Anxiety symptoms | 16 | 2.0 |
| Flourishing positive mental health | 27 | 3.4 |
| Total | 66 | 8.3 |

### 5.3 Distribution of scores for mental health indicators

Frequency distributions of the scores for the mental health indicators (Appendix E) suggested that scores for both depressive and anxiety symptoms were both right skewed. Quantile-quantile plots (Appendix F) concurred. A histogram of the distribution (Appendix E) and a quantile-quantile plot (Appendix F) both suggested that scores for flourishing positive mental health were normally distributed.

### 5.4 Patterns of substance use

One-third (36.7%) of cycle 23 participants reported that they had not use any of alcohol, cannabis or nicotine regularly in the past year; 42.0%, 16.0% and 5.3% reported regular use of one, two or three substances (Table 3). Most single-substance users reported regular use of alcohol only (34.0% of all participants). Only 2.6% of all participants used cannabis only, and 5.5% used nicotine only. Among participants who regularly used two substances, the most frequently reported combination was alcohol and nicotine (7.2% of all participants), followed by cannabis and nicotine (5.3%) and then alcohol and cannabis (3.4%).

Table 3. Proportion of participants and mean and median scores for depressive symptoms, anxiety symptoms and flourishing positive mental health, according to pattern of polysubstance use ($n$ = 733), NDIT 2017-2020

| No. substances used | Pattern of polysubstance use | Participants % ($n$ = 733) | Mental Health Indicators | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | | Depressive symptoms | | Anxiety symptoms | | Flourishing positive mental health | |
| | | | Mean (SD) | Median (IQR) | Mean (SD) | Median (IQR) | Mean (SD) | Median (IQR) |
| 0 | Not applicable | 36.7 | 10.2 (8.6) | 8.0 (9.0) | 4.7 (4.7) | 3.0 (5.0) | 43.8 (12.2) | 44.0 (18.0) |
| 1 | Alcohol only | 34.0 | 9.3 (8.6) | 8.0 (7.0) | 4.2 (4.2) | 3.0 (5.0) | 45.7 (11.3) | 45.0 (18.0) |
| | Cannabis only | 2.6 | 8.7 (8.1) | 9.0 (6.5) | 4.0 (3.2) | 4.0 (3.5) | 42.5 (11.0) | 43.0 (17.0) |
| | Nicotine only | 5.5 | 9.6 (9.3) | 8.5 (7.3) | 4.5 (4.9) | 3.0 (4.5) | 39.5 (11.8) | 38.5 (12.3) |
| | Total | 42.0 | 9.3 (8.7) | 8.0 (8.0) | 4.3 (4.2) | 3.0 (5.0) | 44.7 (11.5) | 44.0 (17.0) |
| 2 | Alcohol and cannabis | 3.4 | 9.8 (8.1) | 8.0 (7.0) | 5.2 (4.0) | 4.0 (5.0) | 43.6 (12.2) | 41.0 (21.0) |
| | Alcohol and nicotine | 7.2 | 11.5 (8.0) | 8.0 (10.0) | 5.1 (4.7) | 4.0 (6.0) | 39.9 (14.1) | 41.0 (20.0) |
| | Cannabis and nicotine | 5.3 | 12.5 (8.0) | 11.0 (11.5) | 7.3 (5.8) | 7.0 (8.0) | 37.2 (15.2) | 33.0 (25.0) |
| | Total | 16.0 | 11.5 (8.0) | 8.0 (10.0) | 5.8 (5.1) | 5.0 (6.0) | 39.8 (14.2) | 40.0 (21.0) |
| 3 | Alcohol, cannabis and nicotine | 5.3 | 11.9 (10.0) | 10.0 (8.5) | 4.4 (3.9) | 4.0 (6.0) | 41.8 (11.0) | 40.0 (17.5) |
| Total | | 100.0 | 10.1 (8.1) | 8.0 (7.0) | 4.7 (4.6) | 4.0 (6.0) | 43.4 (12.3) | 43.0 (18.0) |

**5.5 Mental health indicator scores by number and pattern of substances used**

Means (SD) and medians (IQR) of the scores for the three mental health indicators according to number and patterns of substance use are shown in Table 3. Because the data were right-skewed, medians (IQR) are presented for depressive and anxiety symptoms (although means (SD) are also presented for comparative purposes). Participants who reported regular use of three substances had the highest median (IQR) depressive symptoms scores (10.0 (8.5)). Participants who used two substances regularly had the highest median (IQR) for anxiety symptoms (5.0 (6.0)). Finally, participants who reported regular use of two substances reported the lowest median score for flourishing positive mental health (39.8 (14.2)).

Among single-substance users, participants who used cannabis only had the highest median score for both depressive and anxiety symptoms (9.0 (6.5) and 4.0 (3.5), respectively). Participants who used alcohol-only had the lowest median score for depressive symptoms (8.0 (7.0), as well as the

lowest median score for anxiety symptoms (3.0 (5.0)) (although the median score for anxiety symptoms was also 3.0 (3.5) among participants who used nicotine only). Participants who used alcohol-only had the highest median score for flourishing positive mental health (45.0 (18.0)); and participants who used nicotine-only had the lowest median score for flourishing positive mental health (38.5 (12.3)).

Among regular dual substance users, the median scores for depressive and anxiety symptoms were lowest among participants who reported regular alcohol-cannabis use (8.0 (7.0) and 4.0 (5.0), respectively) and regular alcohol-nicotine use (8.0 (10.0) and 4.0 (6.0), respectively). Participants with these two patterns also had the highest median scores for flourishing positive mental health (41.0 (21.0) and 41.0 (20.0), respectively). The highest median scores for depressive and anxiety symptoms were observed among participants who reported cannabis-nicotine use (11.0 (11.5) and 7.0 (8.0), respectively). These participants also had the lowest median score for flourishing positive mental health (33.0 (25.0)).

**5.6 Residual analyses**

Appendix G compares the residual versus fitted plots of the adjusted linear regression models for the mental health indicators according to number and pattern of polysubstance use. None of the models violated the assumption of homoscedasticity.

To assess the assumption of normality of the residuals, Appendix H presents the quantile-quantile plots of the adjusted linear regression models for mental health indicators according to the number and patterns of polysubstance. Quantile-quantile plots for the residuals of scores for depressive and anxiety symptoms for number of substances and patterns (Appendix H) suggested that the residuals were all right-skewed (positive-skewed). One treatment recommended to adjust right-skewed distributions to attain normality is the square root transformation (Lee, 2020). After applying the square root transformation, none of the residual versus fitted plots (Appendix G) violated the assumption of homoscedasticity and quantile-quantile plots (Appendix H) for each of the depressive and anxiety symptom scores suggested that both were now normally distributed. Quantile-quantile plots (Appendix H) for the residuals of adjusted linear regression model for

flourishing positive mental health score were normally distributed (i.e., prior to any transformation).

### 5.7 Sensitivity analyses

Table 4 presents the regression coefficients ($\widehat{\beta}$) and 95% confidence intervals (95% CI) from the multivariable linear regressions modelling the mental health indicators scores according to pattern of polysubstance use adjusting for age, sex, and level of education. Considering, the non-normality distributions of the scores for depressive and anxiety symptoms, the results for the adjusted linear regression model (i.e., prior to transformation) were compared with square root transformed linear regression models. Table S3 (Appendix I) presents regression coefficients and 95% CIs from multivariable linear regression models adjusting for sex, level of education and age for the square root transformed scores of the mental health indicators according to pattern of polysubstance use. The results were consistent with the findings for the non-transformed mental health indicators in terms of the sign of the estimated coefficients and the relative magnitude of estimated coefficients across patterns of substance use (Table 4). Similarly, all mental health indicator associations with number and pattern of polysubstance observed in Table 4 were consistent with the results of the unadjusted regression models (Table S1 & Table S2). For ease of analytical references, we consider the non-transformed adjusted linear regression models for interpretation of multivariable analyses.

Table 4. Regression coefficients and 95% confidence intervals from adjusted linear regression models for mental health indicators according to pattern of polysubstance use (n = 733), NDIT 2017-2020

| No. substances used | Pattern of polysubstance use | Mental Health Indicators | | |
|---|---|---|---|---|
| | | Depressive symptoms | Anxiety symptoms | Flourishing positive mental health |
| | | $\widehat{\beta}$ (95% CI) | $\widehat{\beta}$ (95% CI) | $\widehat{\beta}$ (95% CI) |
| 1 | Alcohol only | -0.43 (-1.83, 0.98) | -0.07 (-0.85, 0.72) | 1.77 (-0.36, 3.91) |
| | Cannabis only | -1.17 (-4.89, 2.56) | -0.53 (-2.60, 1.55) | -1.15 (-6.81, 4.51) |
| | Nicotine only | -0.80 (-3.46, 1.87) | -0.35 (-1.83, 1.14) | -3.99 (-8.04, 0.06) |
| | Total | -0.52 (-1.84, 0.81) | -0.13 (-0.87, 0.61) | 0.76 (-1.26, 2.79) |
| 2 | Alcohol and cannabis | 0.42 (-2.88, 3.73) | 1.01 (-0.82, 2.86) | -0.05 (-5.07, 4.97) |
| | Alcohol and nicotine | 1.63 (-0.74, 4.00) | 0.56 (-0.76, 1.88) | **-3.70 (-7.30, -0.10)** |
| | Cannabis and nicotine | 2.40 (-0.33, 5.13) | **2.58 (1.06, 4.10)** | **-5.90 (-10.04, -1.76)** |
| | Total | 1.63 (-0.13, 3.39) | **1.32 (0.34, 2.31)** | **-3.64 (-6.34, -0.95)** |
| 3 | Alcohol, cannabis and nicotine | 2.48 (-0.23, 5.19) | 0.32 (-1.19, 1.84) | -2.16 (-6.31, 1.99) |

*Linear regression model adjusted for sex, age, and level of education. Bold indicates that the CIs for the beta coefficient does not include the null value.

### 5.8 Multivariable analyses

Relative to no regular substance use, regular use of one substance, regardless of type, was not associated with any of the three mental health indicators (Table 4). Regular use of two substances was not associated with depressive symptoms, but was associated with higher anxiety symptoms scores ($\widehat{\beta}$ (95% CI) = 1.32 (0.34, 2.31)), and lower flourishing positive mental health scores (3.64 (-6.34, -0.95)). Regular use of all three substances was not associated with any of the mental health indicators.

We also examined the associations between regular use of specific pairs of substances (Table 4). Associations were detected between regular use of cannabis and nicotine and both anxiety symptoms scores (2.58 (1.06, 4.10)) and flourishing positive mental health scores (-3.70 (-7.30, -0.10)). In addition, regular use of alcohol and nicotine was associated with lower flourishing positive mental health (-5.90 (-10.04, -1.76)).

# CHAPTER 6: DISCUSSION

## 6.1 Overview of thesis

The extant literature lacks studies describing patterns of polysubstance use and how these patterns relate to mental health among young adults. Further, studies that do examine this association tend to examine alcohol, cannabis, or nicotine as single entities without carefully accounting for polysubstance use, and they focus either on anxiety or depressive symptoms. Results of this MSc thesis begin to address some of these gaps. Using a cross-sectional study design, this thesis describes patterns of regular substance use in the past year among young adults. Substances of interest included alcohol, cannabis, and nicotine. This study also estimated the associations between patterns of regular substance use and mental health indicators, including depressive symptoms, anxiety symptoms and, of particular interest, flourishing positive mental health, which has been less investigated in the literature. Specifically, we used multivariable linear regression to model the associations between number and patterns of substances used regularly in the past year and the three mental health indicators.

This discussion begins by comparing results obtained using NDIT data with the extant literature. Salient results pertaining to the two objectives of this thesis are then deliberated. Study limitations are described, and then research and public health implications of the findings are discussed.

## 6.2 Comparison of NDIT findings with the literature

*Patterns of regular polysubstance use*

Among participants retained for analysis in this study (mean age 31 years), no use of any substance and regular use of alcohol-only were the two most common substance use patterns. These two patterns were also observed to be the most prevalent among adults age ≥ 25 years in the study of Cohn et al. (2018), which described population-level patterns of alcohol, marijuana, and tobacco use among US young adults and adults. Aligned with the 2017 Canadian Statistics Survey, wherein 76% of participants reported consuming alcoholic beverages in the past year (Statistics Canada, 2017), alcohol use, whether alone or with other substances, was the most frequently consumed substance among NDIT participants in Cycle 23. Only 2.6% of all participants regularly used cannabis only, and 5.5% regularly used nicotine only. Among participants who used two substances, the most frequently observed combinations were alcohol and nicotine (7.2% of all

participants), followed by cannabis and nicotine (5.3%) and then alcohol and cannabis (3.4%). Only 5.3% of all participants used all three substances regularly.

One salient finding in our study is that nicotine is often used in combination with either alcohol and/or cannabis, suggesting that those who use nicotine may need to supplement their nicotine intake with other psychoactive substances. Kohut et al. (2016) described the ubiquitous presence of nAChRs in brain function and suggested that this may underpin polysubstance use among regular nicotine users. nAChRs are the primary targets for nicotine in the brain and are pentamers with α and β subunits which form several different nAChR subtypes in different brain areas (Picciotto et al., 2002). Subtypes α4 and β2 are the highest affinity nAChRs (Picciotto et al., 2002). Nicotine is known to reduce the sedative effects of alcohol, while alcohol potentiates the rewarding effects of nicotine (Adams, 2017). Despite notable differences in their neurobiological mechanisms, two main mechanisms may underpin their co-use. The first is cross-reinforcement via the mesolimbic dopamine pathway. Cross-reinforcement refers to the ability of one substance to enhance motivation to consume another substance by acting on shared neurobiological mechanisms that underpin the reinforcement of substance effects (Adams, 2017). Alcohol and nicotine both activate the mesolimbic dopamine pathway, amplifying the pleasurable effects of the other drug. This is known as a reward activation pathway (Adams, 2017). Dopamine is released with the sensation of reward and reward seeking in the mesolimbic pathway for natural rewards, such as food and sex (Adams, 2017). Alcohol has also been demonstrated to enhance and inhibit the ability of nAChR subtypes to transmit signals and nicotine-induced signalling, suggesting that common nAChR sites may influence the dual use of alcohol and nicotine (Adams, 2017).

The second mechanism is cross-tolerance via shared genetic and naChR interaction (Adams, 2017). Tolerance refers to the process of experiencing a lesser effect (i.e., euphoria, buzz) after repeated substance use. Regular consumption of both alcohol and nicotine induces tolerance to their pharmacological effects (Adams, 2017). A relatively higher proportion of regular cannabis users in NDIT also used nicotine. Epidemiological evidence suggests that cannabis use is more common among adults who smoke cigarettes than those who do not, and vice versa (Jayakumar et al., 2019). The conditioned place preference (CPP) paradigm is a standard preclinical behavioural model used to study the rewarding and aversive effects of substance use (Prus et al., 2009). Studies

suggest a relationship between nicotine and CB1Rs (Cannabinoid receptor type 1) and between cannabis and nAChRs (Rabin et al., 2015). For example, the CB1R antagonist rimonabant (SR141716) and AM251 have been shown to dose-dependently attenuate nicotine self-administration and block nicotine conditioned place preference (CPP) in rats (Rabin et al., 2015). Preclinical studies suggest that the α7 nAChR subtype may play a role in modulating both the reinforcing and discriminative stimulus effects of cannabis, while the α4β2* nAChR subtype may be involved in modulating the motor and sedative effects of cannabis (Buzzi et al., 2023). The results align with clinical studies such as Penetar et al. (2005), which demonstrated that pre-treatment with transdermal nicotine increased subjective cannabis ratings of "stimulated" and "high" on a visual analog scale among users. In sum, both preclinical and clinical studies support that tobacco products are often consumed with cannabis to prolong and increase the rewarding effects of cannabis (Rabin et al., 2015).

Overall, nicotine appears to interact with substances from other pharmacological classes in multiple ways mediated through the pharmacological activity of nicotine (Kohut, 2016). A likely common mechanism by which nicotine exposure alters the rewarding effects of other substances is the ability of nicotine to increase extracellular dopamine levels by activating nAChR in mesolimbic brain regions (Kohut, 2016). This may reinforce the gateway hypothesis first posited by Denise Kandel in 1975 (Rabin et al., 2015), which suggests a systematic sequencing in the use of psychoactive substances, which begins with alcohol and cigarettes, and then eventually progresses to cannabis and then to other "harder" illicit drugs (Rabin et al., 2015).

*Patterns of regular polysubstance use and mental health*

Another salient finding in our work is that there was no dose response between the number of substances used and any of the mental health indicators. The only associations observed were between use of two substances and each of anxiety symptoms and flourishing positive mental health. In contrast, Darke & Ross (1997) reported a strong linear relationship between dependence on multiple substances (i.e., opioids, alcohol, amphetamines, benzodiazepine, cannabis, cocaine, hallucinogens, and inhalants) and multiple mental health diagnoses (i.e., agoraphobia, panic attacks with agoraphobia, panic attacks, simple phobia, social phobia, GAD, major depression and

dysthymia). Differences across these two studies could relate to the limited number of substances considered in our investigation, as well as the fact that we did not study any illicit substances.

Our findings also did not align with those of Cohn et al. (2018), whose study was more similar to ours than that of Darke & Ross (1997). Cohn et al. (2018) studied use of alcohol, cannabis, and tobacco, and mental health was measured using the Global Appraisal of Individual Needs–Short Screener, which captures internalizing and externalizing disorders (i.e., two broad categories of behavioural problems). Internalizing problem behaviour (i.e., withdrawal, anxiety, depression, emotional problems) is focused on the self. Externalizing problem behaviour (i.e., aggression, impulsivity, deviance, hyperactivity) occurs in interaction with the social environment (Nikstat et al., 2020). Cohn et al (2018) found that mental health problems were most strongly associated with dual and polysubstance use patterns. In contrast, our findings did not support an association between number of substances used and mental health in population-based samples of young adults.

Among dual-substance users in the NDIT study, two patterns were associated with mental health issues (i.e., regular use of cannabis and nicotine related to higher anxiety and lower flourishing positive mental health scores; regular dual use of alcohol and nicotine was associated with lower flourishing positive mental health scores). Picciotto et al., 2015 reported that nAChrs involved in the reward activation pathway and associated with polysubstance use in regular nicotine users might also be involved in mood regulation. Pre-clinical rodent-based studies suggest that limiting nAChR signalling through α4β2* nAChRs can lead to positive effects on mood symptoms (Picciotto et al., 2015). Labarca et al. (2001) found that mice with increased activity of α4β2* nAChRs because of a point mutation in the α4 subunit, showed increased anxiety-like behaviour. Clinical studies on the role of nicotine in anxiety are challenged. However, they have been consistent with preclinical studies in showing that changes in nAChRs may provide relevant biomarkers for mood disorders (Picciotto et al., 2015). Thus, the negative association between mental health and dual use of alcohol-nicotine and of cannabis-nicotine may be associated with an increased number of nAChR stimulations through their molecular interactions. In fact, in comparison with single nicotine use, the chemistry of combined cannabis-nicotine use is characterized by upregulation of α4β2* nAChR availability in the prefrontal cortex and the

thalamus (Brody et al., 2016). Also, a recent preclinical study by Locker et al. (2015) provided support for previous findings (Ericson et al., (2003); Liu et al., (2012)) by demonstrating an increase in acetylcholine levels through activation of a greater number of nAChRs in regions of the reward pathway (specifically frontal cortex) due to alcohol-nicotine interactions compared to alcohol-use alone.

### 6.3 Limitations

*Study design*

Limitations of this study include that the cross-sectional study design limited causal inference (Wang & Cheng, 2020). Cross-sectional studies are subject to an antecedent-consequent bias (i.e., because both entities were measured at the same time, it is unknown whether the exposure preceded the outcome) (Wang & Cheng, 2020). In this current analysis, we could not study whetherthe association between polysubstance use and mental health indicators might be bidirectional because of the cross-sectional study design. Further, because of length-biased sampling, cross-sectional studies can overrepresent "cases" of long duration and underrepresent those of short duration (Qin, 2017; Rothman et al., 2008). Associations between substance use and mental health problems may differ depending on whether incident, prevalent or a mixture of both incident and prevalent "cases" are studied.

*Sample size*

Low statistical power associated with small sample sizes can reduce the probability of detecting associations (Button et al., 2013). Low statistical power resulting in wide confidence intervals may have limited our ability to detect associations in some of the analyses reported herein. For example, only 5.3% of participants used all three substances regularly, possibly limiting the ability to detect associations between polysubstance use and the three mental health indicators.

*Loss-to-follow-up*

Loss-to-follow-up since inception in NDIT could contribute to lack of generalizability of the findings to the source and target populations (Sedgwick, 2015). If differential across exposure groups, loss-to-follow-up could also contribute to selection bias in the associations estimated.

*Misclassification*

Although rapid, simple to use, and cost-effective, use of self-report questionnaires could result in misclassification error and possibly misclassification bias in the associations estimated. Latkin et al. (2017) reported differences in social desirability response bias by levels of depressive symptoms and substance use among opiate and cocaine users in Baltimore, Maryland. The recall period for the depression and anxiety indicators was two weeks; it was the past month for flourishing positive mental health; and substance use was reported for the past year. Participants may have provided erroneous responses depending on their ability to recall past events (Althubaiti, 2016). To minimize recall errors, a short recall period is preferable when participants are asked about routine or frequent events (Althubaiti, 2016). Differences in social desirability and recall error across exposure groups in NDIT could have resulted in misclassification bias in the associations estimated.

Concurrent substance use (i.e., when two or more substances are consumed on separate occasions within a specific timeframe such as one year) could not be distinguished in NDIT from simultaneous use (i.e., when multiple substances are consumed on the same occasion at the same time) (Earleywine et al., 1997). Brière et al. (2011) reported that, compared to concurrent alcohol and cannabis use, simultaneous use was associated with depressive symptoms. In the NDIT sample, an association between alcohol-cannabis use and mental health symptoms may not have been detected due to differences in concurrent vs. simultaneous polysubstance use.

Also, recreational use of cannabis could not be distinguished from medicinal use in this study. In the 2015 Canadian, Tobacco, Alcohol and Drug Survey, 47.2% of medicinal users reported daily cannabis use compared to 26.4% of exclusive recreational users and in addition, they reported worse physical and mental health and greater substance use (excluding alcohol) (Turna et al., 2020). Because we studied regular consumption, our sample may have included more medicinal than recreational users, which may have resulted in the appearance of stronger associations between cannabis use and the mental health indicators.

### 6.4 Implications

In the 2018 Chief Public Health Officer's report on the health status of Canadians, Dr. Theresa Tam described worrying trends in problematic substance use among young adults. Dr. Tam

encouraged research to identify the reasons for harmful substance use, as well as effective approaches to prevent problematic use. The report highlighted that major chronic diseases (i.e., cancer, cardiovascular diseases, neurological disorders, chronic respiratory diseases, and diabetes) continue to be the leading causes of all deaths, and that many can be prevented with public health approaches to reduce harmful substance use (CPHO Canada, 2018). Positive mental health, described in the report as equally important as physical and mental health (CPHO Canada, 2018) was associated with polysubstance use patterns in our study. The work described in this thesis is to our knowledge, one of the first population-based Canadian studies in the realm. Because this study was cross-sectional, our findings cannot inform causal relationships, but they can help generate hypotheses for future studies. For example, the notion that number of substances may not have a dose-response association with indicators of mental health is a natural upshot of our findings. Further, researchers may need to study the associations between combinations of specific substances separately (i.e., nicotine and cannabis, nicotine and alcohol, alcohol and cannabis) because these pairings appear to be important in terms of their associations with symptoms of depression, anxiety and flourishing positive mental health. In terms of implications for public health, we suggest that replication of our findings in longitudinal study designs with larger population-based datasets is needed, before exploring their utility in informing public health measures programming and policy.

## CHAPTER 7: CONCLUSION

In this M.Sc. thesis, we identified patterns of polysubstance use of alcohol, nicotine, and cannabis, and we examined the associations between number and patterns of substances consumed regularly and each of three mental health indicators (i.e., anxiety symptoms, depression symptoms, flourishing positive mental health). No dose-response association was detected between number of substances used and any of the three mental health indicators. However, use of two substances was associated with anxiety symptoms and flourishing positive mental health. Among the three possible combinations of two substances, the cannabis-nicotine combination was consistently associated with anxiety and positive mental health, and the combination of alcohol-nicotine was associated with the indicator of positive mental health. Future studies may need to investigate the associations between combinations of specific psychoactive substances separately because these pairings appear to be important in terms of their associations with mental health symptoms.

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# APPENDICES

## Appendix A: English questionnaire for NDIT Cycle 23, 2017-2020

étude NICO helping to understand NDIT study pour mieux comprendre

**Survey Cycle: 23**
By returning your completed questionnaire to us, **YOU CONSENT** to participate in the questionnaire component of the NDIT Study. If you do not wish to participate, please return the blank questionnaire to us, so that we know you have decided not to complete it. Thank you very much for your help!

**Name:** _____

**ID:**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| | | | | | | | |

**1. What is today's date?**

| Day | Month | Year |
|---|---|---|

**2. What is your home postal code?**

| | | | | | |
|---|---|---|---|---|---|
| | | | | | |

**3. Do you currently live alone?**

☐ Yes → **Go to question 5**
☐ No

**4. Do you live with your…? Check all that apply.**

| | Yes |
|---|---|
| Biological mother | ☐ |
| Biological father | ☐ |
| Step-mother | ☐ |
| Step-father | ☐ |
| Sister(s), step-sister(s), half-sister(s) | ☐ |
| Brother(s), step-brother(s), half-brother(s) | ☐ |
| Husband, wife | ☐ |
| Partner (girlfriend, boyfriend) | ☐ |
| Son(s), step-son(s) | ☐ |
| Daughter(s), step-daughter(s) | ☐ |
| Roommate(s) | ☐ |
| Other (specify) _____ | ☐ |

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**5. Does this person currently smoke cigarettes? Your….**

| | Yes |
|---|---|
| Biological mother | ☐ |
| Biological father | ☐ |
| Step-mother | ☐ |
| Step-father | ☐ |
| Any sister, step-sister, half-sisters | ☐ |
| Any brother, step-brother, half-brother | ☐ |
| Husband, wife | ☐ |
| Partner (girlfriend, boyfriend) | ☐ |
| Any son, step-son | ☐ |
| Any daughter, step-daughter | ☐ |
| Any roommate | ☐ |
| Other (specify) _____ | ☐ |

**6. How many close friends (people you feel at ease with and can talk to about what is on your mind) do you have?**

_____ Close friends

**7. How many of your close friends smoke cigarettes?**

_____ Close friends smoke

**8. Indicate your level of agreement with the following…**

| | Strongly disagree | Disagree | Neither agree nor disagree | Agree | Strongly agree |
|---|---|---|---|---|---|
| I feel a bond with my close friends | ☐ | ☐ | ☐ | ☐ | ☐ |
| I feel that I am similar to my close friends | ☐ | ☐ | ☐ | ☐ | ☐ |
| I have a sense of belonging with my close friends | ☐ | ☐ | ☐ | ☐ | ☐ |
| I have a lot in common with my close friends | ☐ | ☐ | ☐ | ☐ | ☐ |

**9. Even if you do not currently smoke cigarettes, how often do you…?**

| | Never | Rarely | Sometimes | Often |
|---|---|---|---|---|
| Want to smoke a cigarette | ☐ | ☐ | ☐ | ☐ |
| Need a cigarette | ☐ | ☐ | ☐ | ☐ |
| Crave a cigarette | ☐ | ☐ | ☐ | ☐ |

**10. Even if you do not currently smoke cigarettes, how addicted to smoking cigarettes are you…?**

| | Not at all | A little bit | Quite | Very |
|---|---|---|---|---|
| Physically | ☐ | ☐ | ☐ | ☐ |
| Mentally | ☐ | ☐ | ☐ | ☐ |

**11. Have you ever in your life smoked a cigarette, even just a puff (drag, hit, haul)?**

- ☐ No → **Go to question 43**
- ☐ Yes, 1 or 2 times
- ☐ Yes, 3 or 4 times
- ☐ Yes, 5 to 10 times
- ☐ Yes, more than 10 times

**12. Check the box that describes you best…**

- ☐ I have smoked cigarettes, but not at all in the past 12 months
- ☐ I smoked cigarettes once or a couple of times in the past 12 months
- ☐ I smoke cigarettes once or a couple of times each month
- ☐ I smoke cigarettes once or a couple of times each week
- ☐ I smoke cigarettes every day

**13. Have you smoked 100 or more whole cigarettes (4 packs of 25) in your life?**

- ☐ No
- ☐ Yes

**14. How old were you when you took cigarette smoke into your lungs for more than one puff?**

I was _____ years old

- ☐ I have never done this

**15. Did you smoke cigarettes (even just a puff) in the past three months?**

- ☐ No → **Go to question 22**
- ☐ Yes

**16. During _____ (last month), on how many days did you smoke cigarettes, even just a puff?**

- ☐ None → **Go to question 18**
- ☐ 1 day
- ☐ 2-3 days
- ☐ 4-5 days
- ☐ 6-10 days
- ☐ 11-15 days
- ☐ 16-20 days
- ☐ 21-30 days
- ☐ Every day
- ☐ Don't know

**17. On the days that you smoked during _____ (last month), how many cigarettes did you usually smoke each day?**

- ☐ Less than 1 cigarette (one or a few puffs)
- ☐ 1 cigarette
- ☐ 2-3 cigarettes
- ☐ 4-5 cigarettes
- ☐ 6-10 cigarettes
- ☐ 11-15 cigarettes
- ☐ 16-20 cigarettes
- ☐ 21-25 cigarettes
- ☐ More than 25
- ☐ Don't know

**18. During _____ (2 months ago), on how many days did you smoke cigarettes, even just a puff?**

- ☐ None → **Go to question 20**
- ☐ 1 day
- ☐ 2-3 days
- ☐ 4-5 days
- ☐ 6-10 days
- ☐ 11-15 days
- ☐ 16-20 days
- ☐ 21-30 days
- ☐ Every day
- ☐ Don't know

**19. On the days that you smoked during _____ (2 months ago), how many cigarettes did you usually smoke each day?**

- ☐ Less than 1 cigarette (one or a few puffs)
- ☐ 1 cigarette
- ☐ 2-3 cigarettes
- ☐ 4-5 cigarettes
- ☐ 6-10 cigarettes
- ☐ 11-15 cigarettes
- ☐ 16-20 cigarettes
- ☐ 21-25 cigarettes
- ☐ More than 25
- ☐ Don't know

**20. During _____ (3 months ago), on how many days did you smoke cigarettes, even just a puff?**

- ☐ None → **Go to question 22**
- ☐ 1 day
- ☐ 2-3 days
- ☐ 4-5 days
- ☐ 6-10 days
- ☐ 11-15 days
- ☐ 16-20 days
- ☐ 21-30 days
- ☐ Every day
- ☐ Don't know

**21. On the days that you smoked during _____ (3 months ago), how many cigarettes did you usually smoke each day?**

- ☐ Less than 1 cigarette (one or a few puffs)
- ☐ 1 cigarette
- ☐ 2-3 cigarettes
- ☐ 4-5 cigarettes
- ☐ 6-10 cigarettes
- ☐ 11-15 cigarettes
- ☐ 16-20 cigarettes
- ☐ 21-25 cigarettes
- ☐ More than 25
- ☐ Don't know

**22. Do you smoke cigarettes now because it is really hard to quit?**

- ☐ No
- ☐ Sometimes
- ☐ Often/always
- ☐ Never tried to quit
- ☐ Other (please explain) _____
- ☐ Don't know (I smoke so little)

**23. When you cut down or stop using cigarettes, or when you are not able to smoke for a long period (like most of the day), how often do you experience…?**

| | Never | Rarely | Sometimes | Often |
|---|---|---|---|---|
| Feeling irritable or angry | ☐ | ☐ | ☐ | ☐ |
| Feeling restless | ☐ | ☐ | ☐ | ☐ |
| Feeling nervous, anxious, or tense | ☐ | ☐ | ☐ | ☐ |
| Trouble concentrating | ☐ | ☐ | ☐ | ☐ |
| Feeling a strong urge or need to smoke | ☐ | ☐ | ☐ | ☐ |
| Trouble sleeping | ☐ | ☐ | ☐ | ☐ |

**24. How well do each of the following describe you?**

| | Describes me… | | | |
|---|---|---|---|---|
| | Not at all | A little | Pretty well | Very well |
| If I go too long without a cigarette, I begin to feel angry or irritable | ☐ | ☐ | ☐ | ☐ |
| If I go too long without a cigarette, I feel stressed | ☐ | ☐ | ☐ | ☐ |
| I usually want to smoke or use dip right after I wake up | ☐ | ☐ | ☐ | ☐ |
| If I go too long without smoking, the first thing I notice is a mild desire to smoke that I can ignore | ☐ | ☐ | ☐ | ☐ |
| If I go too long without smoking, the desire for a cigarette becomes so strong that it is hard to ignore and it interrupts my thinking | ☐ | ☐ | ☐ | ☐ |
| If I go too long without smoking, I just can't function right, and I know I will have to smoke just to feel normal again | ☐ | ☐ | ☐ | ☐ |

**25. When you see other people smoking cigarettes, how easy is it for you not to smoke?**

- ☐ Very easy
- ☐ Quite easy
- ☐ A bit difficult
- ☐ Very difficult

**26. How long can you go without smoking a cigarette before you feel a strong desire to smoke that is hard to ignore?**

- ☐ Less than an hour
- ☐ 1-2 hours
- ☐ 3-5 hours
- ☐ 6-10 hours
- ☐ 11-15 hours
- ☐ 16-23 hours
- ☐ 1 day
- ☐ 2 days
- ☐ More than 2 days, less than a week
- ☐ A week or more
- ☐ Other (specify) _____

**27. How deeply do you usually inhale?**

- ☐ Just into my mouth
- ☐ Back into my throat
- ☐ Into my lungs shallow
- ☐ Into my lungs deep
- ☐ Don't know (I smoke so little)

**28. On the days that you smoke, how soon after you wake up do you smoke your first cigarette?**

- ☐ Within 5 minutes
- ☐ 6 - 30 minutes after waking
- ☐ 31 - 60 minutes after waking
- ☐ More than 60 minutes after waking

**29. Do you find it difficult to refrain from smoking in places where it is forbidden?**

- ☐ Not at all difficult
- ☐ A bit difficult
- ☐ Very difficult

**30. Do you smoke more frequently during the first hours after waking, compared with the rest of the day?**

- ☐ No
- ☐ Yes

**31. If you are sick with a bad cold or sore throat, do you smoke?**

- ☐ No, I stop smoking when I'm sick
- ☐ Yes, but I cut down on the amount I smoke
- ☐ Yes, I smoke the same amount as when I'm not sick

**32. How true is each of the following for you?**

| | Not at all true | A bit true | Very true |
|---|---|---|---|
| Cigarettes are good for dealing with boredom | ☐ | ☐ | ☐ |
| A cigarette gives me energy when I'm tired | ☐ | ☐ | ☐ |
| When I'm feeling down, a cigarette makes me feel good | ☐ | ☐ | ☐ |
| Smoking cigarettes calms me down when I feel nervous | ☐ | ☐ | ☐ |
| Smoking cigarettes helps me control my weight | ☐ | ☐ | ☐ |
| Smoking cigarettes helps me concentrate on my work/homework | ☐ | ☐ | ☐ |
| Smoking cigarettes relieves tension when I am stressed | ☐ | ☐ | ☐ |
| I consider myself to be a social smoker | ☐ | ☐ | ☐ |
| I avoid going to a friend's house where you're not allowed to smoke even though I might enjoy hanging out with him/her | ☐ | ☐ | ☐ |
| In situations where I need to go outside to smoke, it's worth it even in cold or rainy weather | ☐ | ☐ | ☐ |
| I have cut down or stopped physical activities or sports because of my smoking | ☐ | ☐ | ☐ |
| I can function much better in the morning after I've had a cigarette | ☐ | ☐ | ☐ |
| Compared to when I first started smoking, I need to smoke a lot more now to be satisfied | ☐ | ☐ | ☐ |
| Compared to when I first started smoking, I can smoke much more now before I start to feel nauseated or ill<br>**OR**<br>☐ I've never felt nauseated or ill from smoking | ☐ | ☐ | ☐ |
| I often run out of cigarettes quicker than I thought I would | ☐ | ☐ | ☐ |
| I spend a lot of time getting cigarettes (going out of my way to buy cigarettes) | ☐ | ☐ | ☐ |
| I spend a lot of time smoking cigarettes (chain smoking, smoking a lot throughout the day) | ☐ | ☐ | ☐ |
| I've stopped hanging out with certain people because of my smoking | ☐ | ☐ | ☐ |

**33. How often do you have cravings to smoke cigarettes?**

- ☐ Never → **Go to question 35**
- ☐ Very rarely
- ☐ Sometimes
- ☐ Often
- ☐ Very often

**34. How strong are your cravings to smoke cigarettes?**

- ☐ Not at all strong
- ☐ A bit strong
- ☐ Quite strong
- ☐ Very strong

**35. Which cigarette would you most hate to give up?**

- ☐ The first one of the day
- ☐ Another one
- ☐ Don't know (I smoke so little)

**36. At this point in time, how much do you really want to quit smoking cigarettes completely and forever?**

- ☐ Not at all
- ☐ A little bit
- ☐ Quite a bit
- ☐ A whole lot

**37. In the last 12 months, did you seriously try to quit smoking cigarettes completely and forever?**

- ☐ No
- ☐ Yes, once
- ☐ Yes, two or more times

**38. When was the last time you made a serious attempt to quit smoking cigarettes?**

- ☐ Never made a serious attempt to quit smoking

_____ day(s) ago
_____ month(s) ago
_____ year(s) ago

**39. How confident are you that you can or that you have quit smoking cigarettes completely and forever?**

- ☐ Very confident
- ☐ Fairly confident
- ☐ Not very confident
- ☐ Not at all confident

**40. Think about the last time you tried to quit smoking cigarettes. Did you quit smoking completely (for a while)?**

- ☐ Never tried to quit
- ☐ No, but I cut down a lot
- ☐ No, but I cut down a little
- ☐ No, the amount I smoke didn't change at all
- ☐ Yes → I quit completely for _____days
- ☐ Yes → I quit completely and have remained non-smoking ever since

**41. How true for you are each of the following reasons to quit smoking cigarettes?**

| | Not at all true | A little true | Moderately true | Quite true | Extremely true |
|---|---|---|---|---|---|
| Because I am concerned that I will suffer from a serious illness if I don't quit smoking | ☐ | ☐ | ☐ | ☐ | ☐ |
| To show myself that I can quit smoking if I really want to | ☐ | ☐ | ☐ | ☐ | ☐ |
| So that my hair and clothes won't smell | ☐ | ☐ | ☐ | ☐ | ☐ |
| So that my spouse, children, or another person I am close to will stop nagging me | ☐ | ☐ | ☐ | ☐ | ☐ |
| Because I have noticed physical symptoms that smoking is hurting my health | ☐ | ☐ | ☐ | ☐ | ☐ |
| Because I will like myself better if I quit smoking | ☐ | ☐ | ☐ | ☐ | ☐ |
| So that I will save money on smoking-related costs such as dry cleaning | ☐ | ☐ | ☐ | ☐ | ☐ |
| Because someone has given me an ultimatum to quit (made a threat) | ☐ | ☐ | ☐ | ☐ | ☐ |
| Because I can graphically picture the effects that smoking has on my body | ☐ | ☐ | ☐ | ☐ | ☐ |
| So that I can feel in control of my life | ☐ | ☐ | ☐ | ☐ | ☐ |
| Because I won't burn holes in clothing or furniture | ☐ | ☐ | ☐ | ☐ | ☐ |
| Because I will receive a special gift if I quit | ☐ | ☐ | ☐ | ☐ | ☐ |
| Because I know other people who have died from serious illnesses caused by smoking | ☐ | ☐ | ☐ | ☐ | ☐ |
| Because quitting smoking will prove that I can accomplish other things that are important to me | ☐ | ☐ | ☐ | ☐ | ☐ |
| Because I want to save the money that I spend on cigarettes | ☐ | ☐ | ☐ | ☐ | ☐ |
| Because people I am close to will be upset with me if I don't quit | ☐ | ☐ | ☐ | ☐ | ☐ |
| Because I am concerned that smoking will shorten my life | ☐ | ☐ | ☐ | ☐ | ☐ |
| To prove to myself that I am not addicted to cigarettes | ☐ | ☐ | ☐ | ☐ | ☐ |
| So that I won't have to clean my house or car as often | ☐ | ☐ | ☐ | ☐ | ☐ |
| Because I will receive a financial reward (money from a friend or family member, bonus from work) for quitting | ☐ | ☐ | ☐ | ☐ | ☐ |
| Because I want to set a good example for my children | ☐ | ☐ | ☐ | ☐ | ☐ |
| Because I (or my partner) is pregnant or planning to become pregnant | ☐ | ☐ | ☐ | ☐ | ☐ |
| Because my doctor advised me to quit smoking | ☐ | ☐ | ☐ | ☐ | ☐ |

**42. Did you ever try any of the following to help you quit smoking cigarettes? If yes, was this in the past 12 months? Did it help you to quit?**

| | Ever tried<br>Yes | Tried in the past 12 months<br>Yes | Helped me quit<br>Yes |
|---|---|---|---|
| Nicotine patch | ☐ | ☐ | ☐ |
| Nicotine gum (Nicorette) | ☐ | ☐ | ☐ |
| Nicotine inhaler | ☐ | ☐ | ☐ |
| Zyban, Wellbutrin, Bupropion | ☐ | ☐ | ☐ |
| Varenicline (Champix) | ☐ | ☐ | ☐ |
| Electronic cigarettes with nicotine | ☐ | ☐ | ☐ |
| Electronic cigarettes without nicotine | ☐ | ☐ | ☐ |
| Cold Turkey | ☐ | ☐ | ☐ |
| Cutting down by only smoking at certain times or in certain situations | ☐ | ☐ | ☐ |
| Not having cigarettes with me (threw them out) | ☐ | ☐ | ☐ |
| Using other drugs (alcohol, marijuana, sleeping pills) more often | ☐ | ☐ | ☐ |
| Spending more time with friends who don't smoke | ☐ | ☐ | ☐ |
| Keeping myself occupied by doing other things | ☐ | ☐ | ☐ |
| Using a quit smoking APP | ☐ | ☐ | ☐ |
| Using a quit smoking SMS program (SMAT) | ☐ | ☐ | ☐ |
| Other (specify) _____ | ☐ | ☐ | ☐ |

**43. Are there any restrictions on smoking cigarettes in your home? Check all that apply.**

☐ No; smoking is permitted anywhere in my home anytime
☐ Yes; smoking is not permitted at all inside my home
☐ Yes; smoking is permitted in certain rooms only
☐ Yes; smoking is restricted in the presence of children
☐ Yes; other (specify) _____

**44. Are there any restrictions on smoking cigarettes in your car or in the car you travel in most often? Check all that apply.**

☐ No; smoking is permitted anytime
☐ Yes; smoking is not permitted at all in the car
☐ Yes; smoking is not permitted when there are children in the car
☐ Not applicable (I do not/infrequently travel by car)

**45. How many people smoke cigarettes inside your home every day or almost every day?**

☐ None OR _____ people

**46. In the past month, how often were you exposed to second-hand smoke...?**

| | Never | Rarely | Sometimes | Fairly often | Very often |
|---|---|---|---|---|---|
| Inside your home | ☐ | ☐ | ☐ | ☐ | ☐ |
| In a car or other private vehicle | ☐ | ☐ | ☐ | ☐ | ☐ |
| Inside public places (bars, restaurants, shopping malls, arenas) | ☐ | ☐ | ☐ | ☐ | ☐ |
| When visiting the homes of friends or relatives | ☐ | ☐ | ☐ | ☐ | ☐ |
| Outside a restaurant on a patio or terrace | ☐ | ☐ | ☐ | ☐ | ☐ |
| At work | ☐ | ☐ | ☐ | ☐ | ☐ |
| At school | ☐ | ☐ | ☐ | ☐ | ☐ |
| Other (specify)_____ | ☐ | ☐ | ☐ | ☐ | ☐ |

**47. In the past 12 months, how many organized sports teams did you belong to (where you practice with teammates or play against other teams)?**

☐ None OR _____ teams

**48. In the last 7 days, on how many days did you do <u>vigorous</u> physical activities (heavy lifting, digging, aerobics, fast bicycling) for at least 10 minutes at a time?**

☐ None → **Go to question 50**

_____ days in the last 7 days

**49. On the days that you did <u>vigorous</u> physical activities, how many minutes did you usually spend per day?**

_____ minutes per day

**50. In the last 7 days, on how many days did you do <u>moderate</u> physical activities (carrying light loads, bicycling at a regular pace, doubles tennis) for at least 10 minutes? Do not include walking.**

☐ None → **Go to question 52**

_____ days in the last 7 days

**51. On the days that you did <u>moderate</u> physical activities, how many minutes did you usually spend per day?**

_____ minutes per day

**52. In the last 7 days, on how many days did you walk for at least 10 minutes at a time?**

☐ None → **Go to question 54**

_____ days in the last 7 days

**53. On the days that you walked, how many minutes did you usually spend walking per day?**

_____ minutes per day

**54. To what extent is each of the following true for you?**

| | Not true | Rarely true | Sometimes true | Often true | Very often true |
|---|---|---|---|---|---|
| It's important to me to exercise regularly | ☐ | ☐ | ☐ | ☐ | ☐ |
| I don't see why I should have to exercise | ☐ | ☐ | ☐ | ☐ | ☐ |
| I exercise because it's fun | ☐ | ☐ | ☐ | ☐ | ☐ |
| I feel guilty when I don't exercise | ☐ | ☐ | ☐ | ☐ | ☐ |
| I exercise because it's consistent with my life goals | ☐ | ☐ | ☐ | ☐ | ☐ |
| I exercise because other people say I should | ☐ | ☐ | ☐ | ☐ | ☐ |
| I value the benefits of exercise | ☐ | ☐ | ☐ | ☐ | ☐ |
| I can't see why I should bother exercising | ☐ | ☐ | ☐ | ☐ | ☐ |
| I enjoy my exercise sessions | ☐ | ☐ | ☐ | ☐ | ☐ |
| I feel ashamed when I miss an exercise session | ☐ | ☐ | ☐ | ☐ | ☐ |
| I consider exercise part of my identity | ☐ | ☐ | ☐ | ☐ | ☐ |
| I take part in exercise because my friends/family/partner say I should | ☐ | ☐ | ☐ | ☐ | ☐ |
| I think it's important to make the effort to exercise regularly | ☐ | ☐ | ☐ | ☐ | ☐ |
| I don't see the point in exercising | ☐ | ☐ | ☐ | ☐ | ☐ |
| I find exercise a pleasurable activity | ☐ | ☐ | ☐ | ☐ | ☐ |
| I feel like a failure when I haven't exercised in a while | ☐ | ☐ | ☐ | ☐ | ☐ |
| I consider exercise a fundamental part of who I am | ☐ | ☐ | ☐ | ☐ | ☐ |
| I exercise because others will not be pleased with me if I don't | ☐ | ☐ | ☐ | ☐ | ☐ |
| I get restless if I don't exercise regularly | ☐ | ☐ | ☐ | ☐ | ☐ |
| I think exercising is a waste of time | ☐ | ☐ | ☐ | ☐ | ☐ |
| I get pleasure and satisfaction from participating in exercise | ☐ | ☐ | ☐ | ☐ | ☐ |
| I would feel bad about myself if I was not making time to exercise | ☐ | ☐ | ☐ | ☐ | ☐ |
| I consider exercise consistent with my values | ☐ | ☐ | ☐ | ☐ | ☐ |
| I feel under pressure from my friends/family to exercise | ☐ | ☐ | ☐ | ☐ | ☐ |

**55. How true are each of the following for you? When I exercise, I feel like…**

| | False | Mostly false | More false than true | More true than false | Mostly true | True |
|---|---|---|---|---|---|---|
| I engage in a variety of exercises | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| I try a range of exercises | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| I change the type of exercise that I do | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| My exercise program is varied | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| I experience variety in my exercise | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |

**56. How many of your close friends …?**

| | None | A few | Some | Most | All |
|---|---|---|---|---|---|
| Exercise most days of the week | ☐ | ☐ | ☐ | ☐ | ☐ |
| Are physically active | ☐ | ☐ | ☐ | ☐ | ☐ |

**57. How important is it for your close friends to…?**

| | Not very important | Somewhat important | Very important |
|---|---|---|---|
| Exercise most days of the week | ☐ | ☐ | ☐ |
| Be physically active | ☐ | ☐ | ☐ |

**58. Indicate your level of agreement with the following. My close friends …**

| | Strongly disagree | Disagree | Neither agree nor disagree | Agree | Strongly agree |
|---|---|---|---|---|---|
| Encourage me to be physically active | ☐ | ☐ | ☐ | ☐ | ☐ |
| Would disapprove if they saw me just sitting around | ☐ | ☐ | ☐ | ☐ | ☐ |
| Think I should exercise most days of the week | ☐ | ☐ | ☐ | ☐ | ☐ |
| Think I should be physically active | ☐ | ☐ | ☐ | ☐ | ☐ |

**59. During one hour of sitting in a typical 7-hour (work)day, how many breaks from sitting (standing up, stretching, taking a short walk) do you usually take? Write "0" if you usually do not take any breaks.**

_____ break(s)

**60. In a typical 7-hour (work)day, how many minutes do you spend in short physical activity breaks? Write "0" if you usually do not take any breaks.**

_____ minute(s)

**61. Which statement best describes your usual daily activities or work habits in the past 3 months?**

- ☐ Usually sit during the day and don't walk around very much
- ☐ Stand or walk quite a lot during the day but don't have to carry or lift things very often
- ☐ Usually lift or carry light loads, or have to climb stairs or hills often
- ☐ Do heavy work or carry very heavy loads

**62. Do you consider yourself….?**

- ☐ Too thin
- ☐ Just about right
- ☐ A little too heavy
- ☐ Much too heavy

**63. How much do you weigh?**

_____ pounds **OR** _____ kilograms

**64. How tall are you without your shoes on?**

____ feet ____inches **OR** ____ meters ____cm

**65. Currently, what are you doing about your weight?**

- ☐ I'm trying to lose weight
- ☐ I'm trying to gain weight
- ☐ I want to maintain my weight
- ☐ I'm not doing anything about my weight

**66. Are you or your partner currently pregnant?**

- ☐ No/Not applicable → **Go to question 68**
- ☐ Yes, I am pregnant
- ☐ Yes, my partner is pregnant

**67. How many weeks pregnant are you or your partner?**

_____ week(s) pregnant

**68. How often do you overeat (eat more than usual, more than you wanted, more than you think is good for you)?**

- ☐ Never → **Go to question 70**
- ☐ Rarely
- ☐ Sometimes
- ☐ Often
- ☐ Very often

**69. Do you do any of the following to compensate for overeating during the 24 hours after overeating?**

| | Never | Rarely | Sometimes | Often | Very often |
|---|---|---|---|---|---|
| Exercise or go for a walk | ☐ | ☐ | ☐ | ☐ | ☐ |
| Purge (vomit) or use laxatives | ☐ | ☐ | ☐ | ☐ | ☐ |
| Skip meals | ☐ | ☐ | ☐ | ☐ | ☐ |
| Give up on my diet for the rest of the day | ☐ | ☐ | ☐ | ☐ | ☐ |
| Eat fruits | ☐ | ☐ | ☐ | ☐ | ☐ |
| Eat vegetables | ☐ | ☐ | ☐ | ☐ | ☐ |
| Eat more high-protein foods | ☐ | ☐ | ☐ | ☐ | ☐ |
| Eat fewer fried foods | ☐ | ☐ | ☐ | ☐ | ☐ |
| Eat fewer sweets | ☐ | ☐ | ☐ | ☐ | ☐ |
| Eat foods that are low in calories | ☐ | ☐ | ☐ | ☐ | ☐ |
| Eat more because I blew my diet for the day | ☐ | ☐ | ☐ | ☐ | ☐ |
| Do nothing differently | ☐ | ☐ | ☐ | ☐ | ☐ |

**70. In the past 2 years, how often did people in your life…?**

| | Never | Rarely | Sometimes | Often | Always |
|---|---|---|---|---|---|
| Make negative comments about your weight | ☐ | ☐ | ☐ | ☐ | ☐ |
| Encourage you to lose weight | ☐ | ☐ | ☐ | ☐ | ☐ |
| Encourage you to gain weight | ☐ | ☐ | ☐ | ☐ | ☐ |

**71. How many hours per day do you usually spend in front of a screen (computer, hand-held device) for work or for school? Write "0" if none. Write "LT ½" if less than ½ hour.**

On weekdays, I usually spend _____ hour(s) per day in front of a screen for work or school

On weekends, I usually spend _____ hour(s) per day in front of a screen for work or school

**72. How many hours per day, during your leisure time, do you usually spend in front of a screen (computer, TV, hand-held device)? Write "0" if none. Write "LT ½" if less than ½ hour.**

On weekdays, I usually spend _____ hour(s) per day in front of a screen in my leisure time

On weekends, I usually spend _____ hour(s) per day in front of a screen in my leisure time

**73. How many minutes per day do you usually spend on social media (Facebook, Twitter, Instagram, Snapchat) posting or browsing? Write "0" if none. Write "LT ½" if less than ½ hour.**

On weekdays, I usually spend_____ minute(s) per day posting or browsing on social media

On weekends, I usually spend _____ minute(s) per day posting or browsing on social media

**74. How many times per day OR per week OR per month (ANSWER ONLY ONE) do you eat or drink the following foods?**

| | Never | | Times per day | | Times per week | | Times per month |
|---|---|---|---|---|---|---|---|
| Donuts or cakes or pastries | ☐ | or | | or | | or | |
| Candy or chocolate bars | ☐ | or | | or | | or | |
| Ice cream/frozen yogurt | ☐ | or | | or | | or | |
| Potato chips, Fritos, Doritos | ☐ | or | | or | | or | |
| Diet soft drinks | ☐ | or | | or | | or | |
| Regular soft drinks | ☐ | or | | or | | or | |
| Deli or charcuterie meats | ☐ | or | | or | | or | |
| Fried chicken (Kentucky) | ☐ | or | | or | | or | |
| Hot dogs | ☐ | or | | or | | or | |
| Hamburgers | ☐ | or | | or | | or | |
| French fries or poutine | ☐ | or | | or | | or | |
| Bacon or sausages | ☐ | or | | or | | or | |
| 100% fruit juice (orange, grapefruit, or tomato juice) | ☐ | or | | or | | or | |
| Fruit (not including juice) | ☐ | or | | or | | or | |
| Green salad | ☐ | or | | or | | or | |
| Potatoes (not including French fries, fried potatoes, potato chips) | ☐ | or | | or | | or | |
| Carrots | ☐ | or | | or | | or | |
| Other vegetables (not including carrots, potatoes, green salad) | ☐ | or | | or | | or | |
| Walnuts, seeds or other nuts and nut butters (including peanuts or peanut butter) | ☐ | or | | or | | or | |
| Milk (including chocolate milk, hot chocolate, café au lait, in cereal) | ☐ | or | | or | | or | |
| Milk alternatives (almond, soy, rice) | ☐ | or | | or | | or | |
| Yogurt, kefir, excluding frozen yogurt | ☐ | or | | or | | or | |
| Processed cheese slices or spreads (Kraft slices, Vache Qui Rit, Cheez Wiz, Velveeta) | ☐ | or | | or | | or | |
| Other cheeses | ☐ | or | | or | | or | |
| Cereal (hot or cold) | ☐ | or | | or | | or | |
| Rice and other grains (quinoa) | ☐ | or | | or | | or | |

| | Never | | Times per day | | Times per week | | Times per month |
|---|---|---|---|---|---|---|---|
| Pasta, couscous | ☐ | or | | or | | or | |
| Bread, bagels, pita, tortilla wraps | ☐ | or | | or | | or | |
| Red Meat (beef, pork, lamb, horse, veal) | ☐ | or | | or | | or | |
| Chicken/poultry | ☐ | or | | or | | or | |
| Fresh/frozen fish and fish products (canned tuna) | ☐ | or | | or | | or | |
| Seafood (shrimp, lobster, scallops) | ☐ | or | | or | | or | |
| Tofu, Veggie burgers, Veggie hot dogs, TVP | ☐ | or | | or | | or | |
| Eggs and egg dishes | ☐ | or | | or | | or | |
| Cooked/canned dried peas, lentils, beans, Falafel, Hummus | ☐ | or | | or | | or | |
| Pizza (frozen, fast-food or delivery) | ☐ | or | | or | | or | |
| Frozen meals | ☐ | or | | or | | or | |
| Tea and tisanes | ☐ | or | | or | | or | |
| Coffee | ☐ | or | | or | | or | |

**75. Have you ever exergamed (played an active videogame) that uses a console (Nintendo WII, XBOX 360, Kinect, Sony Play Station Move, Sony Eye Toy: Kinetic), a cell phone or a mobile APP (RUN!, Nike+ Running APP, Pokémon Go)?**

☐ No→ **Go to question 83**
☐ Yes

**76. In the past 12 months, how often did you exergame…?**

| | Never | Less than once a month | 1-3 times per month | 1-3 times a week | 4-6 times per week | Every day |
|---|---|---|---|---|---|---|
| Using a console | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| Using a cellphone or mobile APP | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |

**77. In the past month, how many days per week did you exergame?**

☐ None → **Go to question 80**

_____ days per week

**78. On average, how many minutes did you spend each time you exergamed?**

_____ minutes on average

**79. In the past month, what was your usual level of effort when you exergamed?**

- ☐ Light
- ☐ Moderate
- ☐ Intense

**80. How true is each of the following for you?**

| | Completely false | Slightly false | Neither true nor false | Slightly True | Completely true |
|---|---|---|---|---|---|
| I like to exergame | ☐ | ☐ | ☐ | ☐ | ☐ |
| I prefer exergaming over outdoor sports | ☐ | ☐ | ☐ | ☐ | ☐ |
| I prefer exergaming over indoor sports | ☐ | ☐ | ☐ | ☐ | ☐ |
| I like to exergame with friends | ☐ | ☐ | ☐ | ☐ | ☐ |
| I like to exergame with my family | ☐ | ☐ | ☐ | ☐ | ☐ |
| I think that exergaming is a good way to integrate physical activity into my life | ☐ | ☐ | ☐ | ☐ | ☐ |
| I think that I will exergame for many years | ☐ | ☐ | ☐ | ☐ | ☐ |
| Given the chance I would exergame in my free time | ☐ | ☐ | ☐ | ☐ | ☐ |
| Exergaming is boring | ☐ | ☐ | ☐ | ☐ | ☐ |
| I prefer exergaming over traditional video games | ☐ | ☐ | ☐ | ☐ | ☐ |
| Exergames are irritating to play | ☐ | ☐ | ☐ | ☐ | ☐ |
| Exergames are calming to play | ☐ | ☐ | ☐ | ☐ | ☐ |
| I prefer exergaming over watching TV | ☐ | ☐ | ☐ | ☐ | ☐ |
| I prefer exergaming over being on social media (facebook, instagram, snapchat) | ☐ | ☐ | ☐ | ☐ | ☐ |
| Exergaming is exciting | ☐ | ☐ | ☐ | ☐ | ☐ |
| I exergame to be more active | ☐ | ☐ | ☐ | ☐ | ☐ |
| I exergame to lose weight | ☐ | ☐ | ☐ | ☐ | ☐ |
| I exergame to maintain my weight | ☐ | ☐ | ☐ | ☐ | ☐ |
| I exergame to maintain my level of fitness | ☐ | ☐ | ☐ | ☐ | ☐ |
| I exergame to gain strength | ☐ | ☐ | ☐ | ☐ | ☐ |
| I exergame to “bulk up” | ☐ | ☐ | ☐ | ☐ | ☐ |
| I exergame to gain flexibility | ☐ | ☐ | ☐ | ☐ | ☐ |
| I exergame to gain balance | ☐ | ☐ | ☐ | ☐ | ☐ |
| I exergame just for fun | ☐ | ☐ | ☐ | ☐ | ☐ |
| I exergame to be social | ☐ | ☐ | ☐ | ☐ | ☐ |
| Exergaming is the only type of videogame I like | ☐ | ☐ | ☐ | ☐ | ☐ |
| Videogames other than exergames bore me | ☐ | ☐ | ☐ | ☐ | ☐ |

**81. How often do you exergame…?**

| | Never | Rarely | Sometimes | Often | Very often |
|---|---|---|---|---|---|
| Alone | ☐ | ☐ | ☐ | ☐ | ☐ |
| With friends | ☐ | ☐ | ☐ | ☐ | ☐ |
| With family | ☐ | ☐ | ☐ | ☐ | ☐ |

**82. How important are the following in motivating you to continue exergaming…?**

| | Very important | Important | Neither important nor unimportant | Unimportant | Very unimportant |
|---|---|---|---|---|---|
| I am able to play well | ☐ | ☐ | ☐ | ☐ | ☐ |
| The game gets harder as you progress | ☐ | ☐ | ☐ | ☐ | ☐ |
| The goal of the game (winning, scoring high point totals) is easy to understand | ☐ | ☐ | ☐ | ☐ | ☐ |
| Tips in the game help me play better | ☐ | ☐ | ☐ | ☐ | ☐ |
| The game provides feedback on how to improve my play | ☐ | ☐ | ☐ | ☐ | ☐ |
| I like the sound effects in the game | ☐ | ☐ | ☐ | ☐ | ☐ |
| I feel like I am really part of what is happening | ☐ | ☐ | ☐ | ☐ | ☐ |
| The game is addictive | ☐ | ☐ | ☐ | ☐ | ☐ |
| I lose track of time while playing | ☐ | ☐ | ☐ | ☐ | ☐ |
| The game provides interesting options and choices | ☐ | ☐ | ☐ | ☐ | ☐ |
| I try to figure out new ways to play the game | ☐ | ☐ | ☐ | ☐ | ☐ |
| I feel like I can control what is happening | ☐ | ☐ | ☐ | ☐ | ☐ |
| Learning the game controls (Wii-mote, Kinect, PS Move) is easy | ☐ | ☐ | ☐ | ☐ | ☐ |
| I feel like my movements control the game | ☐ | ☐ | ☐ | ☐ | ☐ |
| The game is challenging | ☐ | ☐ | ☐ | ☐ | ☐ |
| The game keeps me on my toes, but does not overwhelm me | ☐ | ☐ | ☐ | ☐ | ☐ |
| The game includes challenges within each level | ☐ | ☐ | ☐ | ☐ | ☐ |
| I know what I have to do to win | ☐ | ☐ | ☐ | ☐ | ☐ |
| The game provides feedback on how I am doing | ☐ | ☐ | ☐ | ☐ | ☐ |
| I am able to practice skills within a game, which helps me play better | ☐ | ☐ | ☐ | ☐ | ☐ |
| I like the graphics | ☐ | ☐ | ☐ | ☐ | ☐ |

| | Very important | Important | Neither important nor unimportant | Unimportant | Very unimportant |
|---|---|---|---|---|---|
| I discover new things about the game the more I play | ☐ | ☐ | ☐ | ☐ | ☐ |
| I find myself getting totally absorbed in the game | ☐ | ☐ | ☐ | ☐ | ☐ |
| The game allows me to do interesting things | ☐ | ☐ | ☐ | ☐ | ☐ |
| I am able to play the game the way I want to | ☐ | ☐ | ☐ | ☐ | ☐ |
| The game controller (tennis racquet, bowling ball) tracks my movements well | ☐ | ☐ | ☐ | ☐ | ☐ |
| If I want to do something in the game, it is easy to remember the correct control (Wii-mote, Kinect, PS Move) | ☐ | ☐ | ☐ | ☐ | ☐ |

**83. In general, how would you rate…?**

| | Poor | Fair | Good | Very good | Excellent |
|---|---|---|---|---|---|
| Your health | ☐ | ☐ | ☐ | ☐ | ☐ |
| Your mental health | ☐ | ☐ | ☐ | ☐ | ☐ |
| Your ability to handle unexpected and difficult problems (a family or personal crisis) | ☐ | ☐ | ☐ | ☐ | ☐ |
| Your ability to handle day-to-day demands in your life (work, family responsibilities) | ☐ | ☐ | ☐ | ☐ | ☐ |
| The overall quality of your sleep at night | ☐ | ☐ | ☐ | ☐ | ☐ |
| The quality of your sleep in the past month | ☐ | ☐ | ☐ | ☐ | ☐ |

**84. How often do you feel…?**

| | Never | Rarely | Sometimes | Often | Always |
|---|---|---|---|---|---|
| Ashamed of the way you look | ☐ | ☐ | ☐ | ☐ | ☐ |
| Proud that you are more attractive than others | ☐ | ☐ | ☐ | ☐ | ☐ |
| Proud that you are a good-looking person | ☐ | ☐ | ☐ | ☐ | ☐ |
| Inadequate when you think about your appearance | ☐ | ☐ | ☐ | ☐ | ☐ |
| Ashamed of your appearance | ☐ | ☐ | ☐ | ☐ | ☐ |
| Proud of your superior appearance | ☐ | ☐ | ☐ | ☐ | ☐ |
| Proud of the effort you place on maintaining your appearance | ☐ | ☐ | ☐ | ☐ | ☐ |
| Proud of your efforts to improve the way you look | ☐ | ☐ | ☐ | ☐ | ☐ |
| Proud that you have achieved your appearance goals | ☐ | ☐ | ☐ | ☐ | ☐ |
| Proud of your appearance efforts | ☐ | ☐ | ☐ | ☐ | ☐ |
| Ashamed that you are a person who is unattractive | ☐ | ☐ | ☐ | ☐ | ☐ |
| Guilty that you do not do enough to improve the way you look | ☐ | ☐ | ☐ | ☐ | ☐ |
| Guilty that you look the way you do | ☐ | ☐ | ☐ | ☐ | ☐ |
| Regret that you do not work on improving your appearance | ☐ | ☐ | ☐ | ☐ | ☐ |
| Regret that you do not put effort into your appearance | ☐ | ☐ | ☐ | ☐ | ☐ |
| Proud that you are an attractive person | ☐ | ☐ | ☐ | ☐ | ☐ |
| Envious of another person's appearance | ☐ | ☐ | ☐ | ☐ | ☐ |
| Inferior when you think about your appearance | ☐ | ☐ | ☐ | ☐ | ☐ |
| Frustrated to see some people who have a great appearance with little effort | ☐ | ☐ | ☐ | ☐ | ☐ |
| Unfair that some people have the "perfect" appearance | ☐ | ☐ | ☐ | ☐ | ☐ |
| Embarrassed about your appearance | ☐ | ☐ | ☐ | ☐ | ☐ |
| Foolish when your body and appearance are on display | ☐ | ☐ | ☐ | ☐ | ☐ |
| Awkward when you are trying to improve your appearance | ☐ | ☐ | ☐ | ☐ | ☐ |
| Nervous when you think about others seeing your appearance | ☐ | ☐ | ☐ | ☐ | ☐ |

**85. Indicate your level of agreement with the following…**

| | Strongly agree | Agree | Disagree | Strongly disagree |
|---|---|---|---|---|
| On the whole, I am satisfied with myself | ☐ | ☐ | ☐ | ☐ |
| At times, I think I am no good at all | ☐ | ☐ | ☐ | ☐ |
| I feel that I have a number of good qualities | ☐ | ☐ | ☐ | ☐ |
| I am able to do things as well as most other people | ☐ | ☐ | ☐ | ☐ |
| I feel I do not have much to be proud of | ☐ | ☐ | ☐ | ☐ |
| I certainly feel useless at times | ☐ | ☐ | ☐ | ☐ |
| I feel that I'm a person of worth, at least on an equal place with others | ☐ | ☐ | ☐ | ☐ |
| I wish I could have more respect for myself | ☐ | ☐ | ☐ | ☐ |
| All in all, I am inclined to feel that I am a failure | ☐ | ☐ | ☐ | ☐ |
| I take a positive attitude toward myself | ☐ | ☐ | ☐ | ☐ |

**86. Has a health professional ever diagnosed you with the following? How old were you when first diagnosed?**

| | Yes | Age first diagnosed |
|---|---|---|
| Asthma | ☐ | ____ years |
| Migraine headaches | ☐ | ____ years |
| Food allergies | ☐ | ____ years |
| Other allergies | ☐ | ____ years |
| Thyroid condition | ☐ | ____ years |
| Mood disorder (depression, bipolar disorder) | ☐ | ____ years |
| Anxiety disorder (phobia, fear of social situations, obsessive-compulsive disorder, panic disorder, generalized anxiety disorder) | ☐ | ____ years |
| Learning disability (attention deficit disorder, dyslexia) | ☐ | ____ years |
| Eating disorder (anorexia, bulimia) | ☐ | ____ years |
| Back problems | ☐ | ____ years |
| Intestinal or stomach ulcers | ☐ | ____ years |
| Bowel disorder (Crohn's disease, ulcerative colitis, irritable bowel) | ☐ | ____ years |
| Cholesterol or lipid problems | ☐ | ____ years |
| Diabetes (type 1) | ☐ | ____ years |
| Diabetes (type 2) | ☐ | ____ years |
| High blood pressure (hypertension) | ☐ | ____ years |
| Insomnia | ☐ | ____ years |
| Obstructive sleep apnea | ☐ | ____ years |
| Other sleep disorder | ☐ | ____ years |
| Concussion | ☐ | ____ years |
| Other (specify)_____ | ☐ | ____ years |

**87. In the past month, did you take any of the following medications, either prescription or over-the-counter?**

| | Yes |
|---|---|
| Pain relievers (aspirin, Tylenol, arthritis medicine, anti-inflammatories) | ☐ |
| Tranquilizers (Valium, Ativan) | ☐ |
| Diet pills (Ponderal, Fastin) | ☐ |
| Anti-depressants (Prozac, Paxil, Effexor) | ☐ |
| Codeine, Demerol or morphine | ☐ |
| Allergy medicine (Allegra, Reactine) | ☐ |
| Asthma medications (inhalers, nebulizers) | ☐ |
| Cough or cold remedies | ☐ |
| Penicillin or other antibiotics | ☐ |
| Mood stabilizers (Lithium, Epival) | ☐ |
| Major tranquilizers, anti-psychotics, neuroleptics (Risperidol, Olanzapine, Seroquel) | ☐ |
| Thyroid medication (Synthroid, Levothyroxine) | ☐ |
| Steroids | ☐ |
| Insulin | ☐ |
| Pills to control blood sugar levels | ☐ |
| Sleeping pills (Imovane, Nytol, Starnoc, melatonin) | ☐ |
| Stomach remedies | ☐ |
| Laxatives | ☐ |
| Birth control pills | ☐ |
| Blood pressure medication | ☐ |
| Cholesterol pills (Lipitor, Statins) | ☐ |
| Other (specify)_____ | ☐ |

**88. Thinking about the amount of stress in your life, would you say that most days are…?**

- ☐ Not at all stressful
- ☐ Not very stressful
- ☐ A bit stressful
- ☐ Quite stressful
- ☐ Extremely stressful

**89. In the past two weeks, how much of the time have you…?**

| | At no time | Some of the time | Slightly less than half of the time | Slightly more than half of the time | Most of the time | All the time |
|---|---|---|---|---|---|---|
| Felt low in spirits or sad | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| Lost interest in, or could no longer enjoy your daily activities | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| Felt lacking in energy and strength | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| Felt less self-confident | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| Had a bad conscience or feelings of guilt | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| Felt that life wasn't worth living | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| Had difficulty concentrating (when reading the newspaper or watching TV) | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| Felt very restless | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| Felt subdued or slowed down | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| Had trouble sleeping at night or waking up too early | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| Suffered from reduced appetite | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| Suffered from increased appetite | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |

**90. Have you ever…?**

| | Yes |
|---|---|
| Seriously considered committing suicide (taking your own life) | ☐ |
| Attempted to commit suicide (tried taking your own life) | ☐ |
| Spoken to a health professional about your suicidal thoughts | ☐ |

**91. In the past 2 weeks, how often have you been bothered by …?**

| | Not at all | Several days | Over half the days | Nearly every day |
|---|---|---|---|---|
| Feeling nervous, anxious, or on edge | ☐ | ☐ | ☐ | ☐ |
| Not being able to stop or control worrying | ☐ | ☐ | ☐ | ☐ |
| Worrying too much about different things | ☐ | ☐ | ☐ | ☐ |
| Trouble relaxing | ☐ | ☐ | ☐ | ☐ |
| Being so restless that it's hard to sit still | ☐ | ☐ | ☐ | ☐ |
| Becoming easily annoyed or irritable | ☐ | ☐ | ☐ | ☐ |
| Feeling afraid as if something awful might happen | ☐ | ☐ | ☐ | ☐ |

**92. In the past month, how often did you feel…?**

| | Never | Rarely | Sometimes | Often | Most of the time | Always |
|---|---|---|---|---|---|---|
| Happy | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| Interested in life | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| Satisfied | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| You had something important to contribute to society | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| You belonged to a community (like a social group, or your neighborhood) | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| That our society is becoming a better place for people like you | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| That people are basically good | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| That the way our society works makes sense to you | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| That you liked most parts of your personality | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| Good at managing the responsibilities of your daily life | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| You had warm and trusting relationships with others | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| You had experiences that challenged you to grow and become a better person | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| Confident to think or express your own ideas and opinions | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |
| Your life has a sense of direction or meaning to it | ☐ | ☐ | ☐ | ☐ | ☐ | ☐ |

**93. In the past 12 months, how often did you…?**

| | Never | Less than once a month | 1-3 times per month | 1-6 times per week | Every day |
|---|---|---|---|---|---|
| Use electronic cigarettes without nicotine | ☐ | ☐ | ☐ | ☐ | ☐ |
| Use electronic cigarettes with nicotine | ☐ | ☐ | ☐ | ☐ | ☐ |
| Use electronic cigarettes to smoke marijuana, hash oil, liquid or wax | ☐ | ☐ | ☐ | ☐ | ☐ |
| Smoke flavored cigarettes or cigarillos | ☐ | ☐ | ☐ | ☐ | ☐ |
| Smoke cigars or a pipe, use bidis, chewing tobacco and/or snuff | ☐ | ☐ | ☐ | ☐ | ☐ |
| Smoke cigarillos | ☐ | ☐ | ☐ | ☐ | ☐ |
| Use a waterpipe (hubble bubble, nargilé, shisha) | ☐ | ☐ | ☐ | ☐ | ☐ |
| Drink energy drinks (Red Bull, Monster) without alcohol | ☐ | ☐ | ☐ | ☐ | ☐ |
| Drink energy drinks mixed with alcohol | ☐ | ☐ | ☐ | ☐ | ☐ |
| Drink alcoholic beverages (beer, wine, liquor) | ☐ | ☐ | ☐ | ☐ | ☐ |
| Drink 5 or more alcoholic beverages on one occasion | ☐ | ☐ | ☐ | ☐ | ☐ |
| Use pain relief pills (Percocet, Percodan, Demerol, OxyNeo, OxyCotin, codeine) without a prescription or without a doctor telling you to take them | ☐ | ☐ | ☐ | ☐ | ☐ |
| Use marijuana, cannabis or hashish without tobacco | ☐ | ☐ | ☐ | ☐ | ☐ |
| Use marijuana, cannabis or hashish mixed with tobacco | ☐ | ☐ | ☐ | ☐ | ☐ |
| Use cocaine | ☐ | ☐ | ☐ | ☐ | ☐ |
| Use speed (amphetamines) | ☐ | ☐ | ☐ | ☐ | ☐ |
| Use ecstasy (MDMA) or other similar drugs | ☐ | ☐ | ☐ | ☐ | ☐ |
| Use hallucinogens (PCP, LSD (acid), mushrooms) | ☐ | ☐ | ☐ | ☐ | ☐ |
| Use inhalants (glue, gasoline) | ☐ | ☐ | ☐ | ☐ | ☐ |
| Use heroin (smack, junk) | ☐ | ☐ | ☐ | ☐ | ☐ |
| Use another illicit drug | ☐ | ☐ | ☐ | ☐ | ☐ |
| Play games (cards, bingo, dice) for money | ☐ | ☐ | ☐ | ☐ | ☐ |
| Bet money (slot machines, sports pool, casino, over the Internet) | ☐ | ☐ | ☐ | ☐ | ☐ |
| Buy lottery tickets (6-49, Sports Select, Instant lottery, Scratch and win) | ☐ | ☐ | ☐ | ☐ | ☐ |
| Use a smartphone APP (Moves and Strava) that monitors your physical activity | ☐ | ☐ | ☐ | ☐ | ☐ |
| Wear a fitness device (Fitbit, Jawbone, Apple Watch) that monitors your physical activity | ☐ | ☐ | ☐ | ☐ | ☐ |

**94. In the past month, what time did you usually go to bed at night?**

_____

**95. In the past month, how long has it usually taken you to fall asleep at night?**

_____ minutes

**96. In the past month, what time did you usually get up in the morning?**

_____

**97. In the past month, how many hours of actual sleep did you usually get at night?**

_____ hours of sleep

**98. In the past month, how often did you experience each of the following?**

| | Never | Less than once a week | 1-2 times per week | 3 or more times per week |
|---|---|---|---|---|
| Unable to get to sleep within 30 minutes | ☐ | ☐ | ☐ | ☐ |
| Woke up in the middle of the night or early morning | ☐ | ☐ | ☐ | ☐ |
| Had to get up to use the bathroom | ☐ | ☐ | ☐ | ☐ |
| Could not breathe comfortably while sleeping | ☐ | ☐ | ☐ | ☐ |
| Coughed or snored loudly | ☐ | ☐ | ☐ | ☐ |
| Felt too cold while sleeping | ☐ | ☐ | ☐ | ☐ |
| Felt too hot while sleeping | ☐ | ☐ | ☐ | ☐ |
| Had bad dreams | ☐ | ☐ | ☐ | ☐ |
| Had pain while sleeping | ☐ | ☐ | ☐ | ☐ |
| Took prescribed or "over the counter" medicine to help you sleep | ☐ | ☐ | ☐ | ☐ |
| Had trouble staying awake while driving, eating meals, engaging in social activities | ☐ | ☐ | ☐ | ☐ |

**99. In the past month, has it been a problem for you to keep up enough enthusiasm to get things done?**

- ☐ No problem at all
- ☐ Only a very slight problem
- ☐ Somewhat of a problem
- ☐ A very big problem

**100. How long before going to bed at night do you usually…?**

| | Less than 30 minutes | Between 30-59 minutes | Between 1-2 hours | More than 2 hours | Not applicable |
|---|---|---|---|---|---|
| Smoke cigarettes | ☐ | ☐ | ☐ | ☐ | ☐ |
| Do physical activity | ☐ | ☐ | ☐ | ☐ | ☐ |
| Drink coffee | ☐ | ☐ | ☐ | ☐ | ☐ |
| Drink alcohol | ☐ | ☐ | ☐ | ☐ | ☐ |
| Use marijuana | ☐ | ☐ | ☐ | ☐ | ☐ |
| Use screens (TV, iPad, reading tablet, smartphone) | ☐ | ☐ | ☐ | ☐ | ☐ |
| Meditate or do yoga | ☐ | ☐ | ☐ | ☐ | ☐ |

**101. How true are each of the following for you…?**

| | Not at all true | A bit true | Very true |
|---|---|---|---|
| Cigarette ads are 'cool' | ☐ | ☐ | ☐ |
| Ads in magazines tell the truth | ☐ | ☐ | ☐ |
| TV ads are boring | ☐ | ☐ | ☐ |
| TV beer commercials make me want to be like the people in them | ☐ | ☐ | ☐ |
| I like to read ads in magazines | ☐ | ☐ | ☐ |
| Warnings on cigarettes packages make me afraid to smoke | ☐ | ☐ | ☐ |
| I like to watch TV ads | ☐ | ☐ | ☐ |
| Cigarette ads make me want to smoke | ☐ | ☐ | ☐ |
| Ads make us buy things we don't really need | ☐ | ☐ | ☐ |
| People who smoke are very influenced by cigarette ads | ☐ | ☐ | ☐ |
| Ads help keep people up to date about new products | ☐ | ☐ | ☐ |
| I usually want the products advertised on TV | ☐ | ☐ | ☐ |

**102. People living in Canada come from many backgrounds. Are you…?**

- ☐ White (British, French, Italian, Portuguese, Ukrainian, Russian, Israeli)
- ☐ Chinese
- ☐ South Asian (East Indian, Pakistani, Bangladeshi, Sri Lankan)
- ☐ Black
- ☐ Latin American, Central American, South American (Mexican, Brazilian, Chilean, Guatemalan, Venezuelan, Colombian, Argentinian, Salvadorian, Costa Rican)
- ☐ Southeast Asian (Cambodian, Indonesian, Laotian, Vietnamese, Malaysian)
- ☐ Arabic
- ☐ West Asian (Afghan, Iranian)
- ☐ Aboriginal (First Nations, Inuit, Métis, non-status Indian)
- ☐ Japanese
- ☐ Other (specify)_____

**103. How far have you gone in school?**

- ☐ Attended high school, but did not graduate
- ☐ Graduated high school
- ☐ Attended CEGEP, community/technical college, but did not graduate
- ☐ Graduated CEGEP, community/technical college
- ☐ Attended university (or teacher's college), but did not graduate
- ☐ Graduated university with a Bachelor's degree
- ☐ Graduated university with a Master's degree
- ☐ Graduated university with a PhD
- ☐ Other (specify) _____

**104. What is your current marital status?**

- ☐ Single
- ☐ Married
- ☐ Common-law
- ☐ Divorced
- ☐ Separated
- ☐ Other (specify) _____

**105. Are you currently enrolled as a full- or part-time student?**

- ☐ No
- ☐ Yes, Full-time. Where?_____
- ☐ Yes, Part-time. Where?_____

**106. Are you currently working at a job or business (paid or unpaid)?**

- ☐ No → **Go to question 108**
- ☐ Yes

**107. About how many hours per week do you usually work at your job/business (paid or unpaid)?**

_____hours per week

**108. What is your best estimate of the total income, before taxes and deductions, of all household members from all sources in the past 12 months?**

- ☐ Less than $20 000
- ☐ 20 000$ - 29 999$
- ☐ 30 000$ - 39 999$
- ☐ 40 000$ - 49 999$
- ☐ 50 000$ - 59 999$
- ☐ 60 000$ - 69 999$
- ☐ 70 000$ - 79 999$
- ☐ 80 000$ - 99 999$
- ☐ 100 000$ - 119 999$
- ☐ 120 000$ - 149 999$
- ☐ 150 000$ or more
- ☐ Don't know

**109. Please complete this chart about your residential history beginning with where you currently live and working back to where you last lived in high school (13-14 years ago).**

| | | Number and Street | City | Number of years lived at this address (if less than 12, write LT12) |
|---|---|---|---|---|
| 1 | Current address | | | |
| 2 | Address prior to 1 | | | |
| 3 | Address prior to 2 | | | |
| 4 | Address prior to 3 | | | |
| 5 | Address prior to 4 | | | |
| 6 | Address prior to 5 | | | |

**110. To help us locate you for the next follow-up, what is your….?**

Home telephone number _____

Cell phone number _____

E-mail address _____

**Comments for us:**

_____

_____

_____

_____

**END OF QUESTIONS**
**THANK YOU SO MUCH FOR RESPONDING!**

## Appendix B: NDIT consent form used at study inception in 1999-2000

RÉGIE RÉGIONALE
DE LA SANTÉ ET DES
SERVICES SOCIAUX
DE MONTRÉAL-CENTRE

November 18, 1999

**MCGILL UNIVERSITY STUDY ON NICOTINE DEPENDENCE IN TEENS**

Investigators: J. O'Loughlin, PhD., G. Paradis, MD, P. Clarke, PhD., J. Hanley, PhD, R. Tyndale, PhD., J. DiFranza, MD

Dear Parent/Guardian:

The Public Health Directorate of Montréal-Centre in collaboration with McGill University, and the Universities of Toronto and Massachusetts, is undertaking a 3-year study among Secondary I students in 12-15 Montreal high schools to study how smoking becomes an established habit in certain adolescents. All Secondary I students in your child's school have been asked to participate because we need to study children who smoke, as well as children who do not smoke. The ultimate purpose of this research is to help us develop more effective strategies to prevent the onset of smoking in children, as well as to help youth who want to quit smoking. In addition, this study will examine the relationship between smoking, weight, and blood pressure during adolescence. The study has 2 parts:

**Part I -** In the next few weeks, our research team will visit your child's classroom. Two interviewers will administer a 45-minute in-class questionnaire to all students about their smoking experiences. The interviewers will visit your child's class again 3-4 months later and every 3-4 months after that for the next 3 years (in Secondary I, II and III) to re-administer the questionnaire in order to collect updated information on the students' smoking experiences. Trained technicians will measure your child's height, weight, skinfold thickness, waist circumference and blood pressure once a year. All data will be stored in locked storage areas at the Public Health Directorate.

**Part II -** An important aspect of this study is to investigate if genetic factors are involved in smoking uptake. To explore this possibility, we will collect a blood sample from each student for genetic analysis. During data collection in March 2002, a nurse will draw 10 ml of blood (2 teaspoons) for genetic analysis. The samples will be analyzed and stored at the University of Toronto, which specializes in this type of genetic analysis. The blood samples will be labeled only by number and the results of the genetic test will remain completely confidential. A master list linking the child and the identification number will be stored securely at the Public Health Directorate. Only the principal investigator and the project coordinator will have access to the list. This list will be destroyed at the end of the study. It will be impossible to provide any individual results of the genetic testing to anyone because they will never be linked to a particular name. After the list is destroyed, all blood samples will be completely anonymous. The samples will be stored for a maximum of ten (10) years for future genetic analysis exclusively related to smoking.

**Request for your consent -** We are now asking for your and your child's consent for Part I of the study (the in-class questionnaire and the anthropometric measures). In February or March 2002, we will ask you separately and specifically for a consent for the blood sample. Both your school board and school principal fully support this project and have agreed that your child's class can participate. However your child's participation is completely voluntary, and it is entirely up to you and your child whether or not he/she participates. Your child can decide not to participate in the blood sample portion of the study and participate only in the questionnaires and anthropometric measures. Also, your child can withdraw from the study at any time and/or ask that his/her blood sample be destroyed before the end of the study by contacting the Project Coordinator (telephone number shown below). If you decide not to allow his/her participation, or if he/she withdraws from the study before it is completed, there will be no prejudice against your child.

Please complete the attached form to indicate whether or not your child will participate in Part I of the study, and return it to your child's teacher in the next 3 days. If you have any questions, please contact the Project Coordinator, Mrs. Elizabeth MacMillan-Davey at 528-2400 local 3976. We thank you and your child for your help in this important project.

[redacted]

Jennifer O'Loughlin, Ph.D.
Principal Investigator

[redacted]

Gilles Paradis, M.D.
Co-Investigator

*Santé physique*
1301, rue Sherbrooke Est
Montréal (Québec) H2L 1M3
Téléphone : (514) 528-2400
Télécopieur : (514) 528-2512
http://www.santepub-mtl.qc.ca

Hôpital général de Montréal
*mandataire*

DIRECTION DE LA SANTÉ PUBLIQUE
*Garder notre monde en santé*

RÉGIE RÉGIONALE
DE LA SANTÉ ET DES
SERVICES SOCIAUX
DE MONTRÉAL-CENTRE

## MCGILL UNIVERSITY STUDY ON NICOTINE DEPENDENCE IN TEENS

Investigators: J. O'Loughlin, PhD., G. Paradis, MD, P. Clarke, PhD., J. Hanley, PhD, R. Tyndale, PhD., J. DiFranza, MD

### CONSENT FORM - PART I

(In-class questionnaire and anthropometric measures)

**Please complete and return this form to your child's teacher within 3 days.**

**Child's name:**

First name (please print clearly) Last name (please print clearly)

☐ **Yes,** my child will participate in Part I of this study (i.e. the classroom questionnaire and the measurement of height, weight, skinfold thickness, waist circumference and blood pressure).

☐ **No,** my child will not participate in this study.

**PLEASE NOTE**: You are not consenting to the blood sample at this time. You will receive a separate consent form to sign for Part II (blood sample) in February or March 2002, just before the blood sample will be taken.

**Signatures**

Parent's name (please print) Parent's signature Date

Child's name (please print) Child's signature Date

*Santé physique*
1301, rue Sherbrooke Est
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DIRECTION
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**Appendix C: Original ethics approval of the NDIT Study**

RÉGIE RÉGIONALE DE LA SANTÉ ET DES SERVICES SOCIAUX
DE MONTRÉAL-CENTRE

## APPROBATION DU PROJET PAR LE COMITÉ D'ÉTHIQUE

Le Comité d'éthique de santé publique de la Régie régionale de Montréal-Centre a examiné le projet de recherche :

**A prospective study on the natural history of nicotine dependence**

Soumis par: *Madame Jennifer O'Loughlin*

Le comité d'éthique a conclu que la recherche proposée respecte les règles éthiques en santé publique définies par la Régie régionale de Montréal-Centre.

*Membres du comité*:

| | |
|---|---|
| *M. Denis Allard* | *Agent de recherche* |
| *Dr. Robert Allard* | *Médecin* |
| *Mme Lorraine Bernier* | *Agente de recherche sociosanitaire* |
| *Dr. Nicole-Hébert-Croteau* | *Médecin-conseil* |
| *M. Alain Gauthier* | *Secrétaire général, C.S. Marguerite Bourgeois* |
| *Mme Marie Hirtle* | *Avocate* |
| *Mme Marcelle Monette* | *Conseillère à la recherche et au développement professionnel* |
| *Mme Francine Tardif* | *Sociologue consultante* |
| *M. Claudio Zanchettin* | *Professeur en philosophie* |
| *Dr. Bernard Heneman* | *Médecin-conseil et président du comité* |

[redacted]

*Président du comité*

99-04-07
*Date*

*Note:* Le présent certificat n'est valide que si une preuve d'acceptation du protocole pour son évaluation scientifique a été déposée auprès du comité d'éthique de la santé publique.

certifica.eth

**Appendix D: Description of study variables including name of variable, item(s) in the NDIT questionnaire used to measure the study variable, response choices, re-coding of response choices for analysis, and psychometric properties and references if applicable and available**

| Name of variable | Questionnaire item | Response choices | Re-coding of response choices for analysis | Psychometric properties and references, if applicable and available |
|---|---|---|---|---|
| Regular alcohol use in the past 12 months | In the past 12 months, how often did you drink alcoholic beverages? | 1. Never<br>2. Less than once a month<br>3.1-3 times per month<br>4. 1-6 times per month<br>5. Everyday | Yes (1-6 times per week; everyday)<br><br>No (Never, less than once a month; 1-3 times per month | Not applicable |
| Regular cannabis use in the past 12 months | 1. In the past 12 months, how often did you use marijuana, cannabis, or hashish without tobacco?<br>2. In the past 12 months, how often did you use marijuana, cannabis, or hashish with tobacco? | 1. Never<br>2. Less than once a month<br>3.1-3 times per month<br>4. 1-6 times per month<br>5. Everyday | Yes (marijuana, cannabis, or hashish with or without tobacco 1-6 times per week; everyday)<br><br>No (marijuana, cannabis, or hashish with or without tobacco never, less than once a month; 1-3 times per month | Not applicable |
| Regular nicotine use in the past 12 months | 1. Check the box that describes you best | 1. I have smoked cigarettes, but not at all in the past 12 months<br>2. I smoked cigarettes once or a couple of times in the past 12 months<br>3. I smoke cigarettes once or a couple of times each month<br>4. I smoke cigarettes once or a couple of times each week<br>5. I smoke cigarettes everyday | Yes (participant reported consuming nicotine from any source 1-6 times per week or everyday)<br><br>No (all other responses) | Not applicable |
| | 2. In the past 12 months, how often did you use electronic cigarettes with nicotine?<br>3. In the past 12 months, how often did you smoke flavored cigarettes or cigarillos?<br>4. In the past 12 months, how often did you smoke cigars or pipe, use bidis, chewing tobacco and/or snuff?<br>5. In the past 12 months, how often did you smoke cigarillos? | For each substance:<br>1. Never<br>2. Less than once a month<br>3.1-3 times per month<br>4. 1-6 times per month<br>5. Everyday | | |

| | | | | |
|---|---|---|---|---|
| | 6. In the past 12 months, how often did you use a waterpipe?<br>7. In the past 12 months, how often did you use marijuana, cannabis or hashish mixed with tobacco? | | | |
| Depression Symptoms (MDI) | 1. In the past two weeks, how much of the time have you… felt low in spirits or sad?<br>2. In the past two weeks, how much of the time have you… lost interest in, or could no longer enjoy your daily activities?<br>3. In the past two weeks, how much of the time have you… felt lacking in energy and strength?<br>4. In the past two weeks, how much of the time have you… felt less self-confident?<br>5. In the past two weeks, how much of the time have you… had a bad conscience or feelings of guilt?<br>6. In the past two weeks, how much of the time have you… felt that life wasn't worth living?<br>7. In the past two weeks, how much of the time have you… had difficulty concentrating (when reading the newspaper or watching TV)?<br>8. In the past two weeks, how much of the time have you… felt very restless?<br>9. In the past two weeks, how much of the time have you… felt subdued or slowed down?<br>10. In the past two weeks, how much of the time have you… had trouble sleeping at night or waking up too early? | 1. At no time<br>2. Some of the time<br>3. Slightly less than half of the time<br>4. Slightly more than half of the time<br>5. Most of the time<br>6. All the time | | Cronbach's $\alpha = 0.94$)<br>(Bech et al., 2001) |

| | | | | |
|---|---|---|---|---|
| | 11. In the past two weeks, how much of the time have you… suffered from reduced appetite?<br>12. In the past two weeks, how much of the time have you… suffered from increased appetite? | | | |
| Generalized Anxiety Disorder (GAD-7 Scale) | 1. Over the last 2 weeks, how often have you been bothered by the following … Feeling nervous, anxious, or on edge?<br>2. Over the last 2 weeks, how often have you been bothered by the following … Not being able to stop or control worrying?<br>3. Over the last 2 weeks, how often have you been bothered by the following … Worrying too much about different things?<br>4. Over the last 2 weeks, how often have you been bothered by the following … Trouble relaxing?<br>5. Over the last 2 weeks, how often have you been bothered by the following … Being so restless that it's hard to sit still?<br>6. Over the last 2 weeks, how often have you been bothered by the following … Becoming easily annoyed or irritable?<br>7. Over the last 2 weeks, how often have you been bothered by the following … Feeling afraid as if something awful might happen? | 1. Not at all<br>2. Several days<br>3. Over half the days<br>4. Nearly every day | | Cronbach's $\alpha = 0.92$)<br>(Spitzer et al., 2006) |
| Positive mental health (flourishing) | 1. In the past month, how often did you feel happy?<br>2. In the past month, how often did you feel interested in life?<br>3. In the past month, how often did you feel satisfied with life? | 1. Never<br>2. Rarely<br>3. Sometimes<br>4. Often<br>5. Most of the time<br>6. Always | | Cronbach's $\alpha = 0.89$<br>(Lamers et al., 2010). |

| | | | | |
|---|---|---|---|---|
| | 4. In the past month, how often did you feel that you had something important to contribute to society?<br>5. In the past month, how often did you feel that you belonged to a community (like a social group, or your neighborhood)?<br>6. In the past month, how often did you feel that our society is becoming a better place for people like you?<br>7. In the past month, how often did you feel that people are basically good?<br>8. In the past month, how often did you feel that the way our society works makes sense to you?<br>9. In the past month, how often did you feel that you liked most parts of your personality?<br>10. In the past month, how often did you feel good at managing the responsibilities of your daily life?<br>11. In the past month, how often did you feel that you had warm and trusting relationships with others?<br>12. In the past month, how often did you feel that you had experiences that challenged you to grow and become a better person?<br>13. In the past month, how often did you feel confident to think or express your own ideas and opinions?<br>14. In the past month, how often did you feel that your life has a sense of direction or meaning to it? | | | |

**Appendix E: Distributions of mental health indicators' scores among young adults (*n* = 733), NDIT 2017-2020**

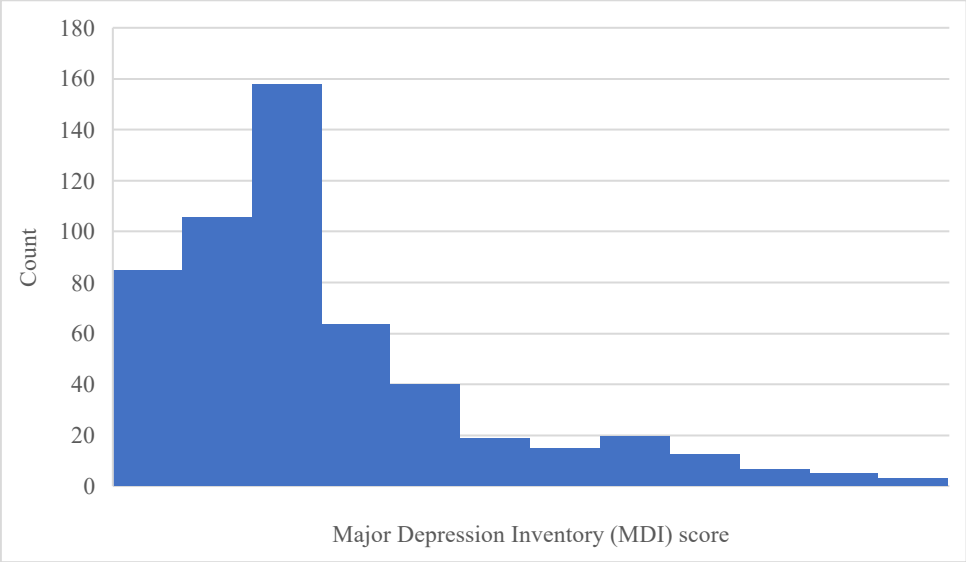



Figure 2. Distribution of depressive symptoms' scores among young adults (*n* = 733), NDIT 2017-2020

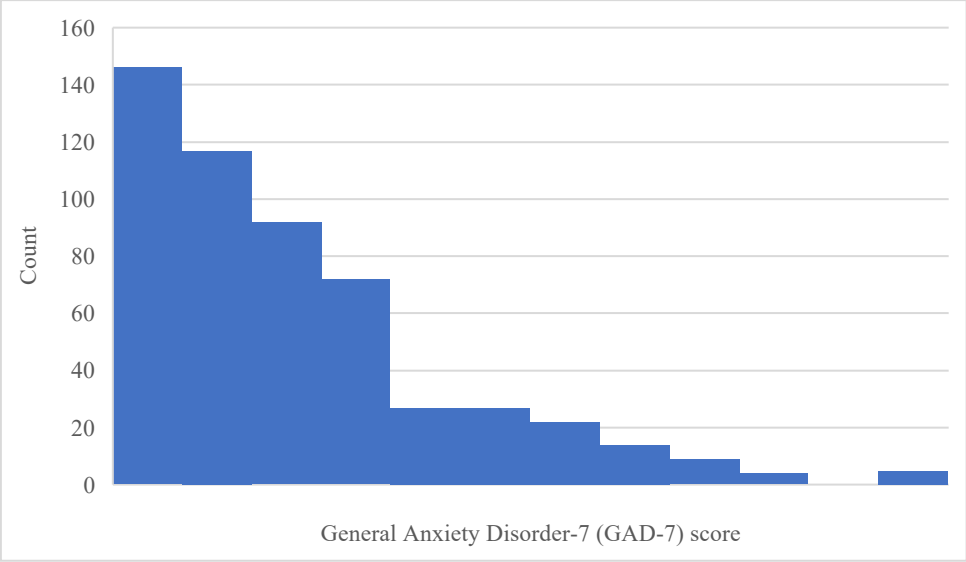



Figure 3. Distribution of anxiety symptoms' scores among young adults (*n* = 733), NDIT 2017-2020

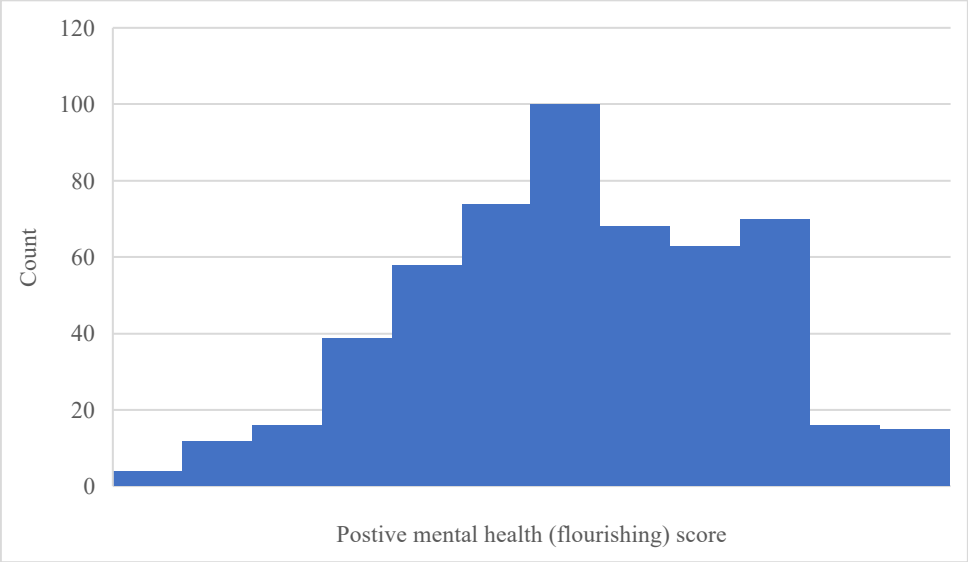



Figure 4. Distribution of flourishing positive mental health scores among young adults (*n* = 733), NDIT 2017-2020

**Appendix F: Quantile-Quantile plots of mental health indicators' scores among young adults (*n* = 733), NDIT 2017-2020**

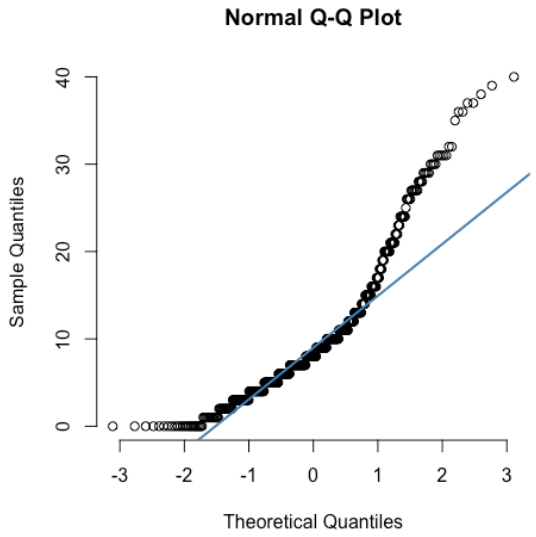



Figure 5. Quantile-Quantile (Q-Q) plot of the distribution of depressive symptoms' scores among young adults (*n* = 733), NDIT 2017-2020

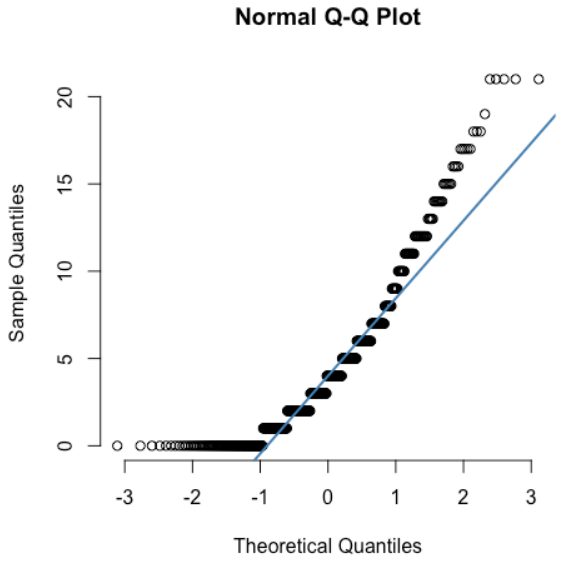



Figure 6. Quantile-Quantile plot (Q-Q plot) of the distribution of the anxiety symptoms' scores among young adults (*n* = 733), NDIT 2017-2020

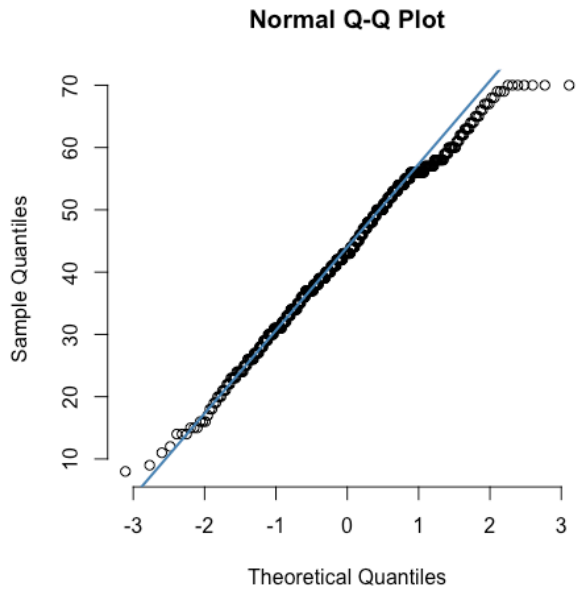



Figure 7. Quantile-Quantile (Q-Q plot) for the distribution of flourishing positive mental health scores among young adults (*n* = 733), NDIT 2017-2020

**Appendix G: Residual analyses – residuals versus fitted plots for linear regression models for mental health indicators according to the number and pattern of polysubstance use (n = 733), NDIT 2017-2020**

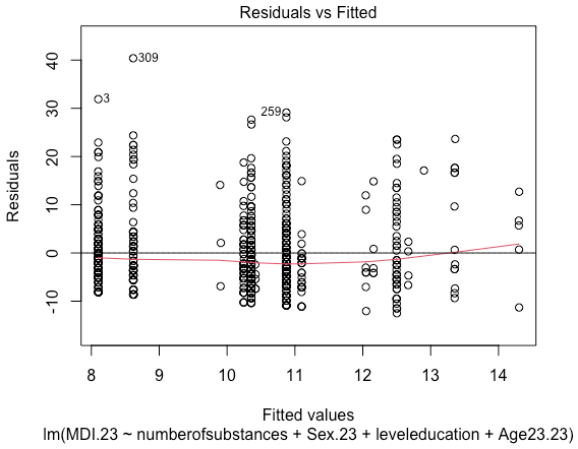



Figure 8. Residuals versus fitted plot for adjusted linear regression model for depressive symptoms according to the number of substances consumed by young adults (*n* = 733), NDIT 2017-2020

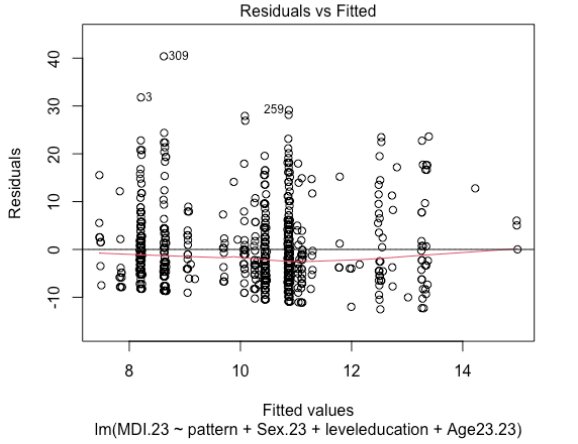



Figure 9. Residuals versus fitted plot for adjusted linear regression model for depressive symptoms according to pattern of polysubstance consumed by young adults (*n* = 733), NDIT 2017-2020

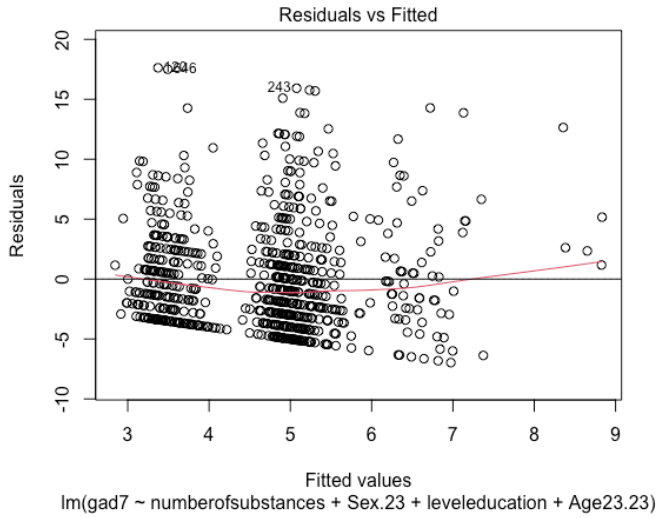



Figure 10. Residuals versus fitted plot for adjusted linear regression model for anxiety symptoms according to number of substances consumed by young adults (*n* = 733), NDIT 2017-2020


Figure 11. Residuals versus fitted plot for adjusted linear regression model for anxiety symptoms according to pattern of polysubstance consumed by young adults (*n* = 733), NDIT 2017-2020

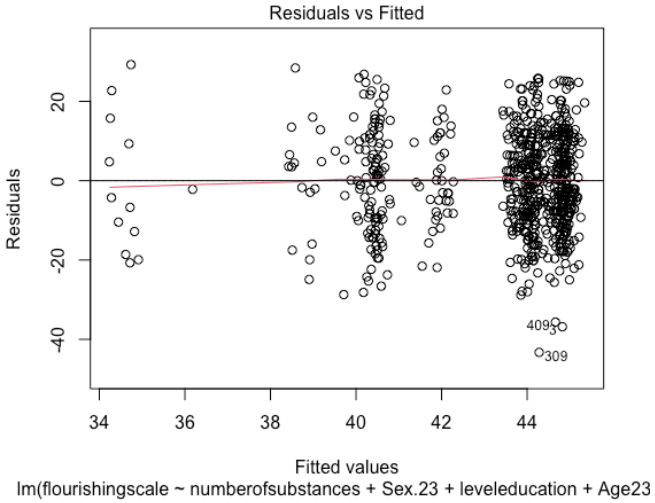



Figure 12. Residuals versus fitted plot for adjusted linear regression model for positive flourishing mental health scores according to number of substances consumed by young adults (*n* = 733), NDIT 2017-2020

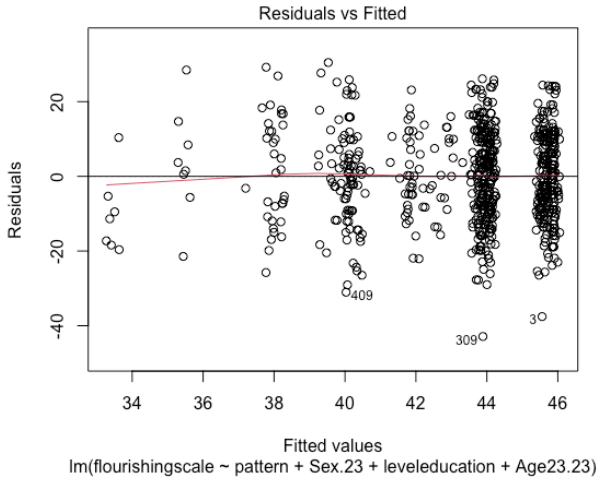



Figure 13. Residuals versus fitted plot for adjusted linear regression model for positive flourishing mental health scores according to pattern of polysubstance consumed by young adults (*n* = 733), NDIT 2017-2020

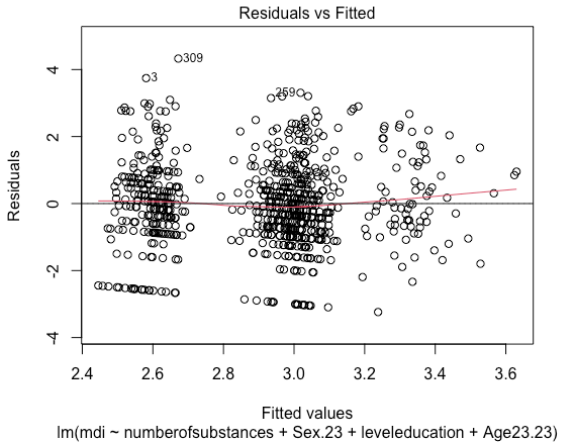



Figure 14. Residuals versus fitted plot for adjusted square root transformed linear regression model for depressive symptoms according to the number of substances consumed by young adults ($n$ = 733), NDIT 2017-2020

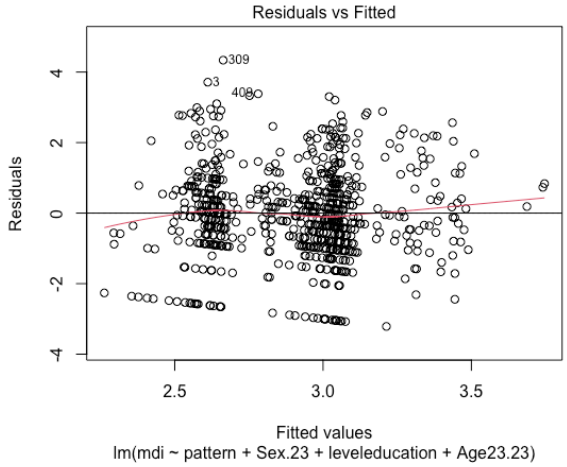



Figure 15. Residuals versus fitted plot for adjusted square root transformed linear regression model for depressive symptoms according to pattern of polysubstance consumed by young adults ($n$ = 733), NDIT 2017-2020

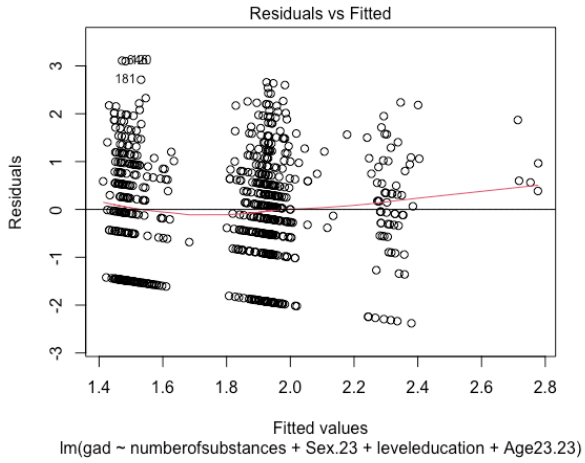



Figure 16. Residuals versus fitted plot for adjusted square root transformed linear regression model for anxiety symptoms according to the number of substances consumed by young adults ($n$ = 733), NDIT 2017-2020

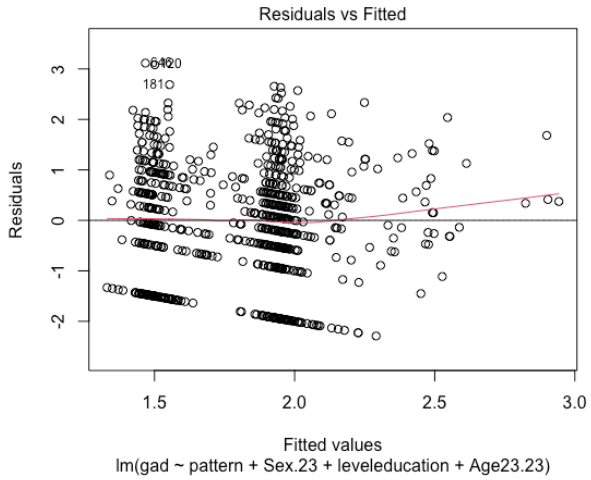



Figure 17. Residuals versus fitted plot for adjusted square root transformed linear regression model for anxiety symptoms according to pattern of polysubstance consumed by young adults ($n$ = 733), NDIT 2017-2020

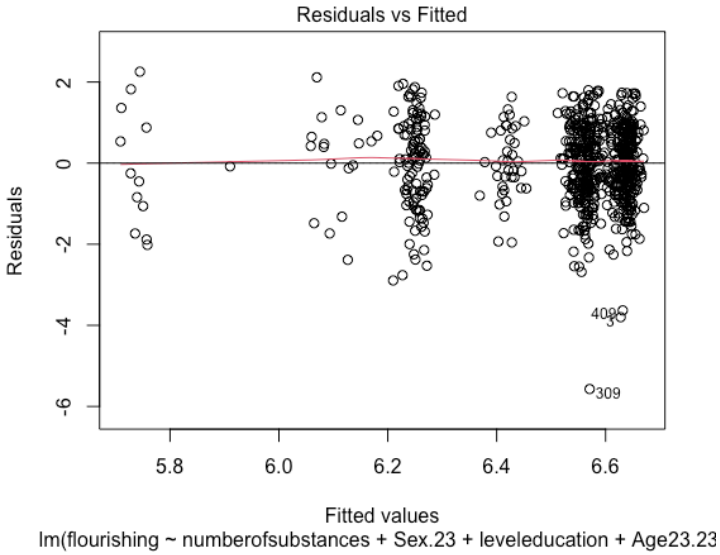



Figure 18. Residuals versus fitted plot for adjusted square root transformed linear regression model for positive flourishing mental health scores according to the number of substances consumed by young adults ($n$ = 733), NDIT 2017-2020

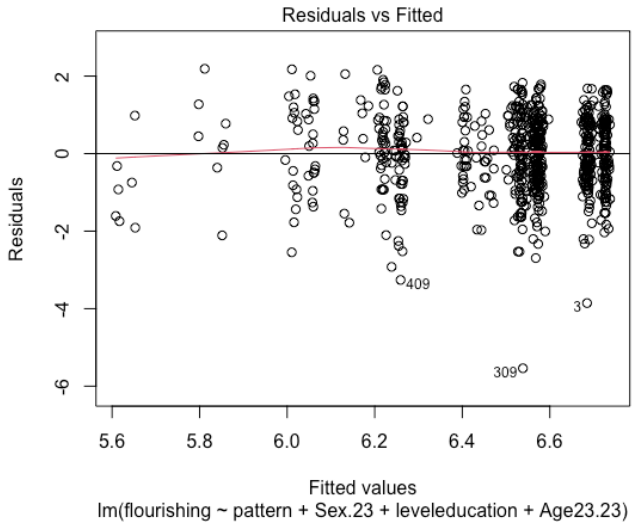



Figure 19. Residuals versus fitted plot for adjusted square root transformed linear regression model for positive flourishing mental health scores according to pattern of polysubstance consumed by young adults ($n$ = 733), NDIT 2017-2020

**Appendix H: Residual analyses – quantile-quantile plots for the residuals of linear regression models for mental health indicators according to the number and pattern of polysubstance use (*n* = 733), NDIT 2017-2020**

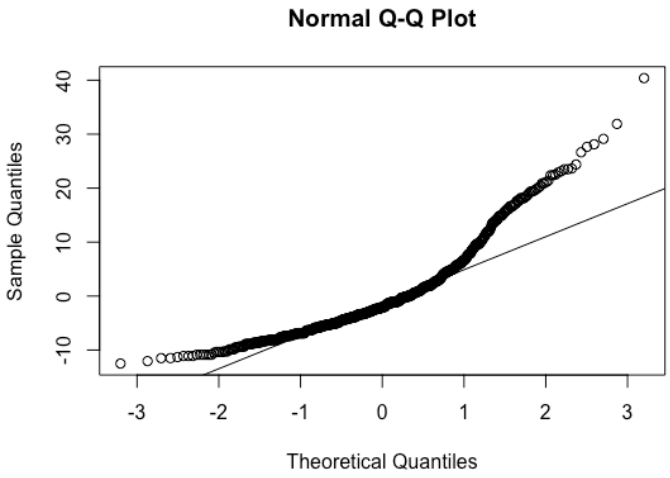



Figure 20. Residuals' quantile-quantile plot for adjusted linear regression model for depressive symptoms according to the number of substances consumed by young adults (*n* = 733), NDIT 2017-2020

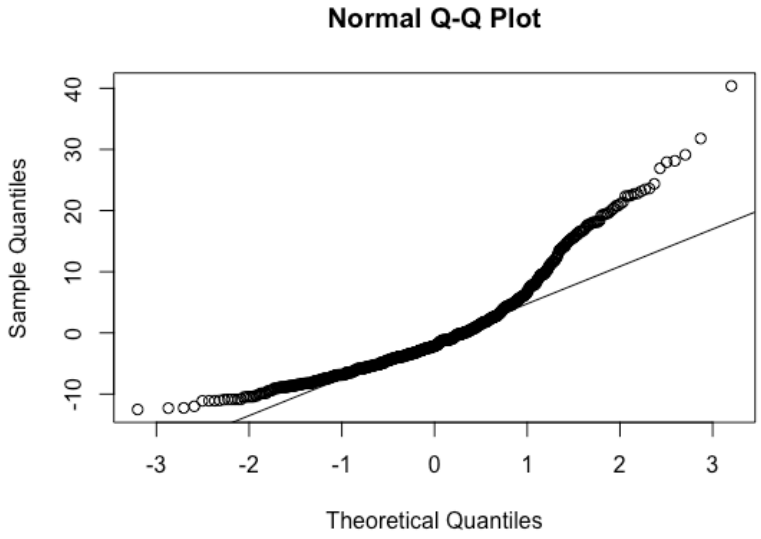



Figure 21. Residuals' quantile-quantile plot for adjusted linear regression model for depressive symptoms according to pattern of polysubstance consumed by young adults (*n* = 733), NDIT 2017-2020

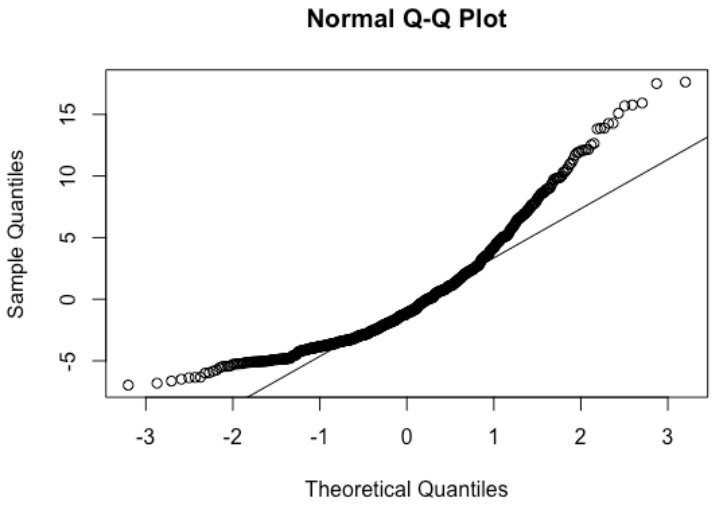



Figure 22. Residuals' quantile-quantile plot for adjusted linear regression model for anxiety symptoms according to the number of substances consumed by young adults (*n* = 733), NDIT 2017-2020

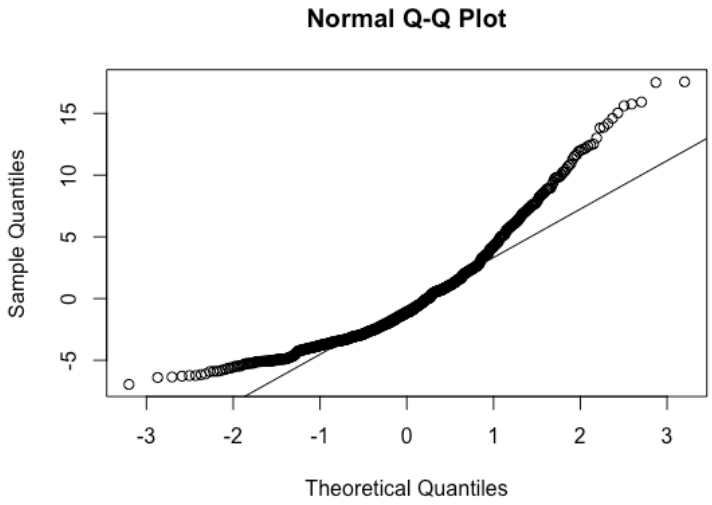



Figure 23. Residuals' quantile-quantile plot for adjusted linear regression model for anxiety symptoms according to pattern of polysubstance consumed by young adults (*n* = 733), NDIT 2017-2020

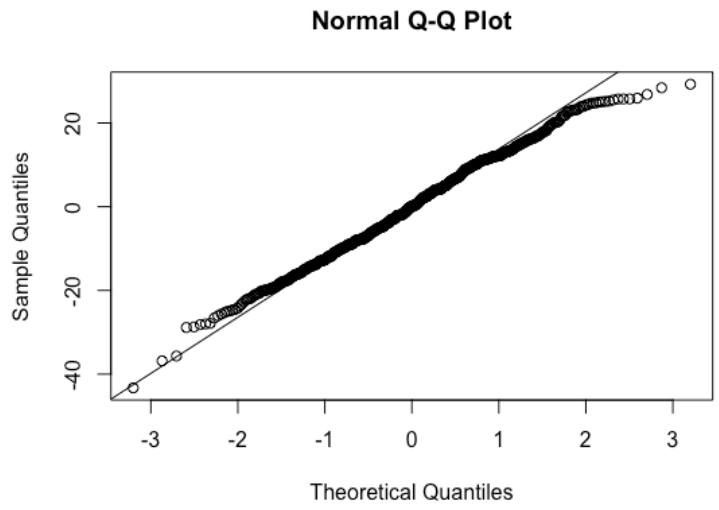



Figure 24. Residuals' quantile-quantile plot for adjusted linear regression model for flourishing positive mental health according to the number of substances consumed by young adults (*n* = 733), NDIT 2017-2020

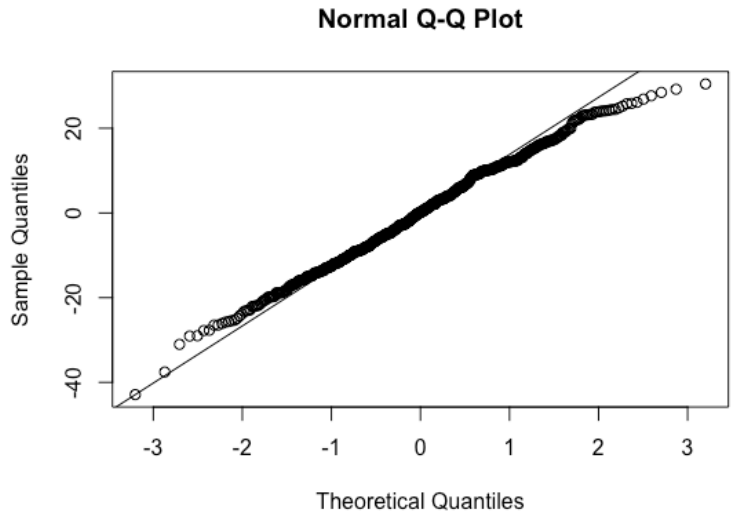



Figure 25. Residuals' quantile-quantile plot for adjusted linear regression model for flourishing positive mental health according to pattern of polysubstance consumed by young adults (*n* = 733), NDIT 2017-2020

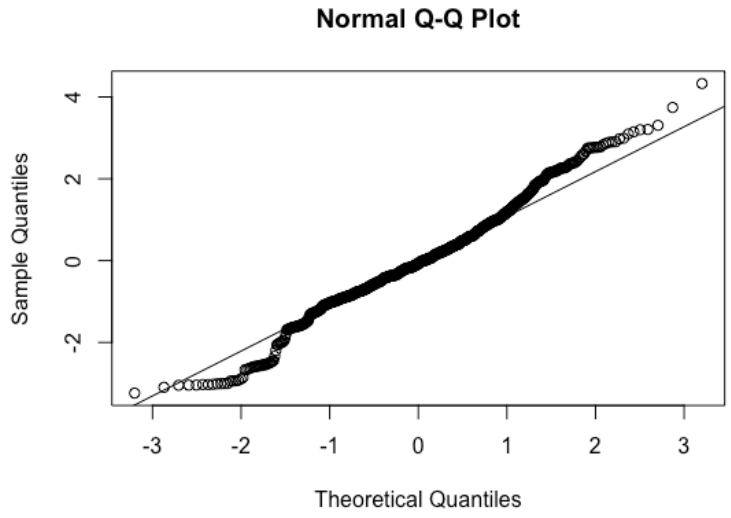



Figure 26. Residuals' quantile-quantile plot for adjusted square root transformed linear regression model for depressive symptoms according to the number of substances consumed by young adults (*n* = 733), NDIT 2017-2020

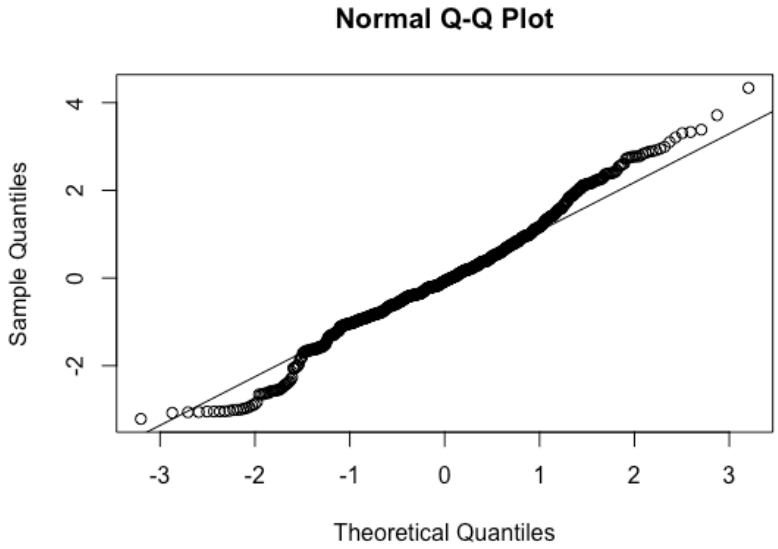



Figure 27. Residuals' quantile-quantile plot for adjusted square root transformed linear regression model for depressive symptoms according to pattern of polysubstance consumed by young adults (*n* = 733), NDIT 2017-2020

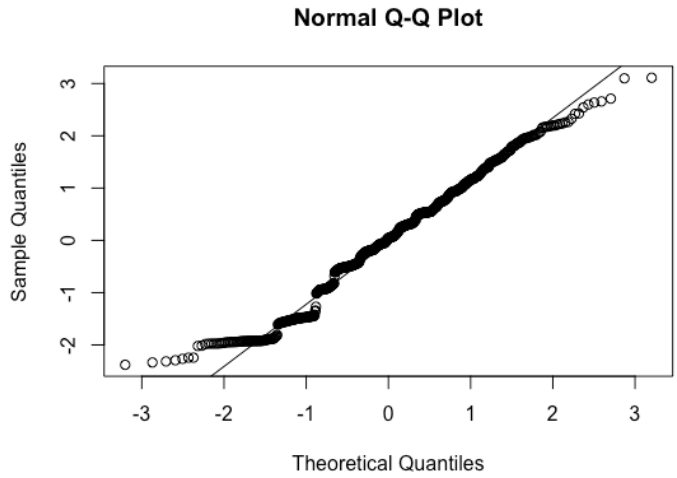



Figure 28. Residuals' quantile-quantile plot for adjusted square root transformed linear regression model for anxiety symptoms according to the number of substances consumed by young adults (*n* = 733), NDIT 2017-2020

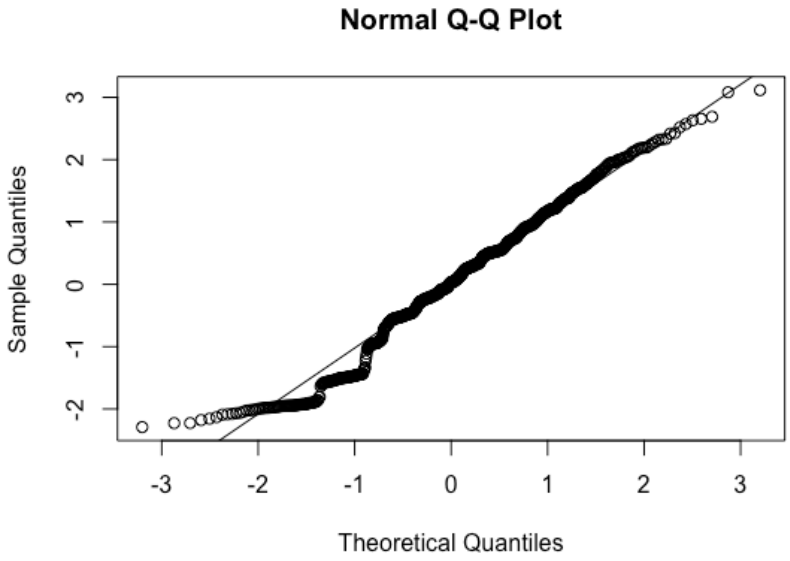



Figure 29. Residuals' quantile-quantile plot for adjusted square root transformed linear regression model for depressive symptoms according to pattern of polysubstance consumed by young adults (*n* = 733), NDIT 2017-2020

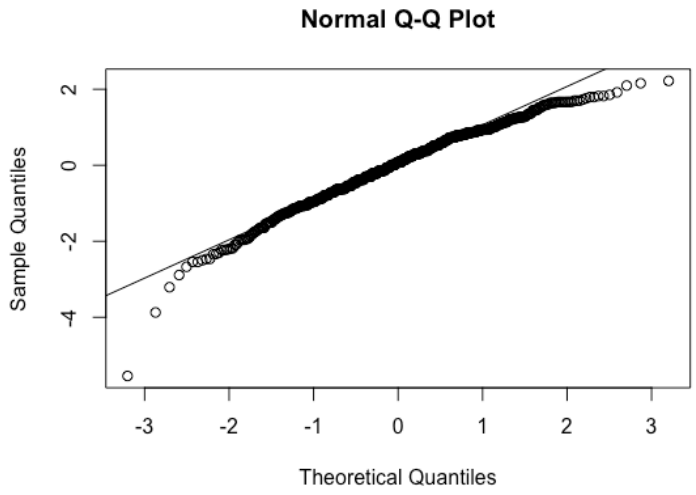



Figure 30. Residuals' quantile-quantile plot for adjusted square root transformed linear regression model for flourishing positive mental health according to the number of substances consumed by young adults (*n* = 733), NDIT 2017-2020

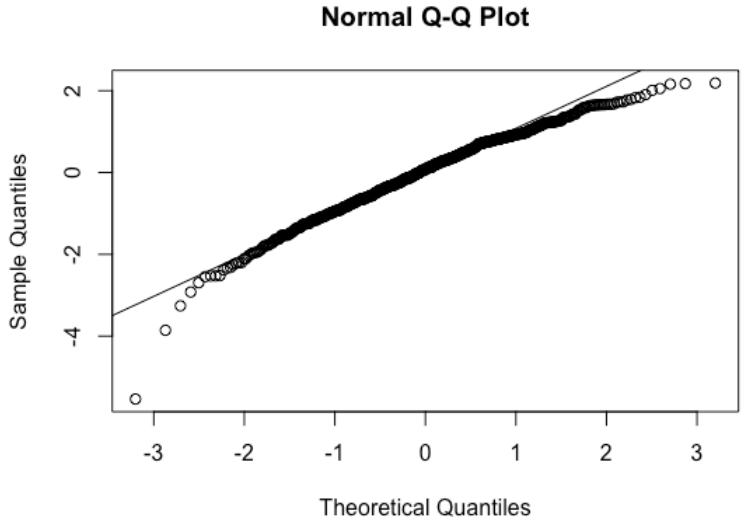



Figure 31. Residuals' quantile-quantile plot for adjusted square root transformed linear regression model for flourishing positive mental health according to the pattern of polysubstance consumed by young adults (*n* = 733), NDIT 2017-2020

**Appendix I: Sensitivity analyses - regression coefficients and 95% confidence intervals from linear regression models for mental health indicators according to the number and pattern of polysubstance use (*n* = 733), NDIT 2017-2020**

Table S1. Regression coefficients and 95% confidence intervals from unadjusted linear regression models for the mental health indicators according to pattern of polysubstance use (*n* = 733), NDIT, 2017-2020

| No. substances used | Pattern of polysubstance use | Mental Health Indicators | | |
|---|---|---|---|---|
| | | Depressive symptoms | Anxiety symptoms | Flourishing positive mental health |
| | | $\widehat{\beta}$ (95% CI) | $\widehat{\beta}$ (95% CI) | $\widehat{\beta}$ (95% CI) |
| 1 | Alcohol only | -0.83 (-2.22, 0.56) | -0.43 (-1.21, 0.35) | 1.85 (-0.24, 3.95) |
| | Cannabis only | -1.43 (-5.19, 2.32) | -0.68 (-2.78, 1.43) | -1.29 (-6.95, 4.37) |
| | Nicotine only | -0.60 (-3.27, 2.08) | -0.15 (-1.66, 1.35) | -4.29 (-8.33, -0.25) |
| | Total | -0.84 (-2.15, 0.48) | -0.41 (-1.15, 0.33) | 0.86 (-1.14, 2.86) |
| 2 | Alcohol and cannabis | -0.33 (-3.64, 2.97) | 0.48 (-1.37, 2.34) | -0.17 (-5.16, 4.81) |
| | Alcohol and nicotine | 1.32 (-1.06, 3.70) | 0.38 (-0.95, 1.71) | **-3.95 (-7.53, -0.36)** |
| | Cannabis and nicotine | 2.32 (-0.39, 5.02) | **2.61 (1.08, 4.13)** | **-6.61 (-10.69, -2.52)** |
| | Total | 1.30 (-0.45, 3.05) | **1.14 (0.16, 2.13)** | **-4.03 (-6.69, 1.37)** |
| 3 | Alcohol, cannabis and nicotine | 1.73 (-0.98, 4.43) | -0.27 (-1.79, 1.26) | -2.04 (-6.16, 2.07) |

*Linear regression model adjusted for sex, age, and level of education. Bold indicates that the CIs for the beta coefficient does not include the null value.

Table S2. Regression coefficients and 95% confidence intervals from unadjusted square-root transformed linear regression models for the mental health indicators according to pattern of polysubstance use ($n$ = 733), NDIT, 2017-2020

| No. substances used | Pattern of polysubstance use | Mental Health Indicators | | |
|---|---|---|---|---|
| | | Depressive symptoms | Anxiety symptoms | Flourishing positive mental health |
| | | $\widehat{\beta}$ (95% CI) | $\widehat{\beta}$ (95% CI) | $\widehat{\beta}$ (95% CI) |
| 1 | Alcohol only | -0.06 (-0.29, 0.16) | -0.06 (-0.26, 0.14) | 0.16 (-0.40, 0.40) |
| | Cannabis only | -0.13 (-0.73, 0.47) | -0.05 (-0.59, 0.49) | -0.08 (-0.53, 0.38) |
| | Nicotine only | -0.19 (-0.62, 0.24) | -0.07 (-0.45, 0.32) | -0.34 (-0.66, -0.01) |
| | Total | -0.08 (-0.30, 0.13) | -0.06 (-0.25, 0.13) | 0.08 (-0.08, 0.24) |
| 2 | Alcohol and cannabis | 0.05 (-0.48, 0.58) | 0.27 (-0.21, 0.75) | -0.00 (-0.40, 0.40) |
| | Alcohol and nicotine | 0.19 (-0.19, 0.57) | 0.16 (-0.19, 0.50) | **-0.34 (-0.63, -0.05)** |
| | Cannabis and nicotine | 0.38 (-0.05, 0.81) | **0.56 (0.17, 0.95)** | **-0.58 (-0.91, -0.25)** |
| | Total | 0.22 (-0.06, 0.50) | **0.32 (0.06, 0.57)** | **-0.35 (-0.56, -0.13)** |
| 3 | Alcohol, cannabis and nicotine | 0.21 (-0.22, 0.65) | -0.03 (-0.42, 0.36) | -0.13 (-0.47, 0.19) |

*Bold indicates that the CIs for the beta coefficient does not include the null value. the absence of value of zero within the 95 % confidence interval associated with respective beta coefficients.

Table S3. Regression coefficients and 95% confidence intervals from adjusted square root transformed linear regression models for the mental health indicators according to pattern of polysubstance use ($n$ = 733), NDIT, 2017-2020

| No. substances used | Pattern of polysubstance use | Mental Health Indicators | | |
|---|---|---|---|---|
| | | Depressive symptoms | Anxiety symptoms | Flourishing positive mental health |
| | | $\widehat{\beta}$ (95% CI) | $\widehat{\beta}$ (95% CI) | $\widehat{\beta}$ (95% CI) |
| 1 | Alcohol only | -0.00 (-0.23, 0.22) | 0.03 (-0.17, 0.23) | 0.15 (-0.02, 0.32) |
| | Cannabis only | -0.07 (-0.67, 0.52) | -0.00 (-0.53, 0.53) | -0.06 (-0.52, 0.39) |
| | Nicotine only | -0.23 (-0.65, 0.20) | -0.11 (-0.49, 0.27) | -0.31 (-0.64, 0.02) |
| | Total | -0.04 (-0.25, 0.17) | 0.01 (-0.18, 0.20) | 0.07 (-0.09, 0.24) |
| 2 | Alcohol and cannabis | 0.19 (-0.34, 0.71) | 0.43 (-0.05, 0.90) | 0.01 (-0.39, 0.42) |
| | Alcohol and nicotine | 0.25 (-0.12, 0.63) | 0.22 (-0.12, 0.55) | **-0.32 (-0.60, -0.03)** |
| | Cannabis and nicotine | 0.40 (-0.04, 0.83) | **0.57 (0.18, 0.96)** | **-0.51 (-0.85, -0.18)** |
| | Total | 0.29 (0.01, 0.57) | **0.38 (0.13, 0.63)** | **-0.31 (-0.53, -0.09)** |
| 3 | Alcohol, cannabis and nicotine | 0.36 (-0.09, 0.77) | 0.13 (-0.26, 0.52) | -0.14 (-0.48, 0.19) |

*Linear regression model adjusting for sex, age, and level of education. Bold indicates that the CIs for the beta coefficient does not include the null value. the absence of value of zero within the 95 % confidence interval associated with respective beta coefficients.

**SUPPLEMENTARY MATERIAL**

**Copy of mini protocol (submitted 01-10-2021)**

**Context, literature review and rationale** Substance use is on the rise in Canada among young adults. 25% of Canadian population sample in 2019 said they had used cannabis in the preceding 12 months, which was up from 22 percent the cycle before [1]. In 2017, 15% of Canadians aged 15 and over had used an e-cigarette, up from 13% in 2015[2]. With increasing popularity of substances, co-use, referring to use of two or more substances (polysubstance) within the same-time frame (i.e. as in past year) has also increased. According to several longitudinal studies, greater drug use has been linked to increased depressive symptoms in adolescence and young adulthood that can persist in later years as well [3]. Crane et al. (2021) reports that while females have higher symptoms and rates of both depression and anxiety that emerge during childhood and adolescence and males have higher substance use frequency, depressive and anxiety symptoms pertaining to polysubstance use was more significant in males [3]. This contradicted the findings from the recent longitudinal study of the Add Health nationally representative sample of 7th-12th graders (recruited in 1994–1995) [3]. Bailey et al. (2019) found that among adults aged 25 and more, alcohol/ cigarette co-use was the most common pattern of polysubstance followed by alcohol/cigarette/e-cigarette co-use. It was also determined on the same paper that polysubstance use patterns were more prevalent than single-use patterns [4]. With legalization of recreational cannabis use in Canada in addition to ever-changing product availability, there is a compelling need to monitor the different patterns of substance use in young adults as well as to describe the physical and mental health outcomes associated with polysubstance use.

**Objectives**

1. To describe patterns of concurrent psychoactive substance use (within the past year) among young adults. Substances of interest include binge drinking, cannabis, cigarette smoking, other tobacco products, electronic cigarettes, and opioids
2. To estimate the association between patterns of concurrent substance use and mental health problems (depressive symptoms, symptoms of anxiety)
3. To assess effect modification by sex in the association between patterns of concurrent substance use and mental health problems.

**Study specifications and study population** Data are available in the context of the ongoing Nicotine Dependence in Teens (NDIT) study, a longitudinal investigation of the natural course of cigarette smoking and nicotine dependence among 1294 students recruited in 1999–2000 from all grade 7 classes in a purposive sample of ten Montreal-area high schools. Data were collected in self-report questionnaires administered at school every 3–4 months from grade 7 to 11, and in four cycles post-high school when participants were age 20.4, 24.0, 30.5 and 33.6 years on average. This current cross-sectional study will use data collected in 2017–20 when participants were age 30.5 years on average.

**Study variables** *Binge drinking* was measured by: "In the past 12 months, how often did you… drink 5 or more alcoholic beverages on one occasion". Response options *were never, less than once a month, 1-3 times per month, 1-6 times per week, everyday*. Participants who reported engaging in binge drinking once a month or more often will be classified as current binge drinkers. *Cannabis use* **-** participants were asked "In the past 12 months, how often did you… use marijuana, cannabis or hashish mixed without tobacco?" and "In the past 12 months, how often did you… use marijuana, cannabis or hashish mixed with tobacco?". Response options included

*were never, less than once a month, 1-3 times per month, 1-6 times per week, everyday*. Reports of engaging in one or more of these behaviours once a month or more often will be classified as current cannabis users. *Cigarette smoking* was measured by: "Check the box that describes you best…" Response options included I have smoked cigarettes, but not at all in the past 12 months; I smoked cigarettes once or a couple of times in the past 12 months; I smoke cigarettes once or a couple of times each month; I smoke cigarettes once or a couple of times each week; I smoke cigarettes everyday. Reports of engaging in one or more of these behaviours once a month or more often will be classified as current use of cigarettes. *E-cigarette use* Students were asked "In the past 12 months, how often did you… use electronic cigarettes without nicotine" and "In the past 12 months, how often did you… use electronic cigarettes with nicotine". Response options included *were never, less than once a month, 1-3 times per month, 1-6 times per week, everyday*. Reports of engaging in one or more of these behaviours once a month or more often will be classified as current e-cigarette users. *Opioid use* was measured by: "In the past month, did you take any of the following medications, either prescription or over the counter… codeine, Demerol or morphine". Participants who answered "Yes" will be classified as using opioids. *Other tobacco products use* was measured by: "In the past 12 months, how often did you… smoke cigars or pipe, use bidis, chewing tobacco and/or snuff" and "In the past 12 months, how often did you… smoke cigarillos". Reports of engaging in one or more of these behaviours once a month or more often will be classified as current other tobacco product users. *Number of substances used* will be calculated by summing the number of substances (i.e., binge drinking, cannabis use, smoking, vaping, opioids, other tobacco products) participants currently use. *Positive mental health* was assessed using the Flourishing Scale, a summary measure of perceived success in relationships, self-esteem, purpose, and optimism (i.e., Below are 8 statements with which you may agree or disagree…….) Scores range from 0 to 70 with higher scores indicative of more psychological resources and strengths. *Anxiety* was assessed using the Generalized Anxiety Disorder 7 (GAD-7) scale. Scores range from 0 to 21 with higher scores indicative of more frequent symptoms of anxiety. *Depressive symptoms* was assessed using the Major Depression Inventory (MDI) scale. Score range from 0 to 50 with higher scores indicative of more frequent depressive symptoms. *Sex, age, ethnicity, annual household income*, *education*, *sleep quality* will be used to describe the sample and/or as potential confounders.

**Data management and analysis strategy** Preliminary analyses will involve descriptive statistics to understand the distributions of each study variable according to sex and to describe the patterns of missing data. The "exposure" will be studied as the proportion of males and females using 1, 2, 3, 4 or more substances and as the frequency of all possible combinations of substance use. The distributions of the "outcomes" (i.e., the mental health variables) will also be described according to sex. Comparison of two means using t-test will be accomplished comparing the mental health indicators for polysubstance users (yes/no) to monosubstance users. A linear regression model will be estimated to examine mean differences in the mental health indicators according to the number of substances used. Linear regression models will also be used to examine the association between the top 5 most prevalent polysubstance patterns with each of the mental health indicators. Effect modification by sex will be investigated by including an interaction term between sex and substance use in the models. All models will include sex, age, ethnicity, annual household income, education, and sleep quality as potential confounders. Model assumptions (normality of errors, linearity of associations, homoscedasticity) will be checked using a residual analysis.

**Statistical power and sample size considerations** Calculations were performed for the second objective, as objective 1 is descriptive and objective 3 is exploratory. We calculated the detectable

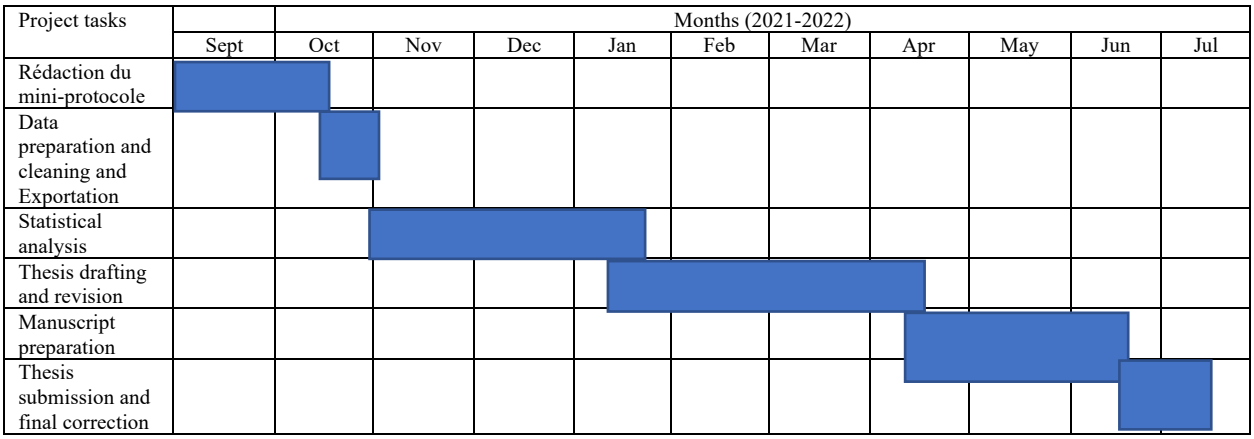
differences between two independent means (mental health of polysubstance users vs. others) assuming a statistical power of 80% and a significance level of 5%. The mean GAD-7 score found in the literature for young adults in the province of Quebec in 2018 was of 4.73, and the minimal difference in means was calculated to be ± 0.65 (SD = 4.61) [5]. As for the mean MDI score found in the literature for young adults from Montreal in 2011-2012 was of 8.48, and the minimal difference in means was calculated to be of ± 1.12 (SD = 7.96) [6]. Finally, for the flourishing scale, the mean score found for adults across Canada in 2015 was of 56.5, and the minimal difference in means was calculated to be of ±1.8 (SD = 12.5) [7].

**Potential bias considerations** Self-report measures can be affected by social desirability and other reporting errors increasing the potential for misclassification. NDIT did not differentiate simultaneous (i.e., in the same session) and concurrent substance use (i.e., within the same time reference period). Opioid use may be underestimated because of an incomplete list of opioids. Loss-to-follow-up since NDIT inception may also resulted in selection bias and the relatively small sample could result in lack of statistical power. The cross-sectional study design limits causal inference.

**Ethical considerations and Feasibility**

Parents provided informed consent during high school. Participants (who had attained legal age) provided informed consent post high school. All data necessary for the conduct of the study are available. The team brings together expertise in biostatistics (Marie-Pierre Sylvestre, ESPUM) and epidemiology (Jennifer O'Loughlin, ESPUM).

**Calendar**

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**Appendix**

| Question | Response options | Coding for analyses |
|---|---|---|
| *Binge drinking* | | |
| *In the past 12 months, how often did you… Drink 5 or* | *1. Never*<br>*2. Less than once a month*<br>*3. 1-3 times per month* | *2,3,4,5 = current binge drinker* |

| | | |
|---|---|---|
| *more alcoholic beverages on one occasion* | *4. 1-6 times per week*<br>*5. Everyday* | *1 = excluded* |
| *Cannabis use* | | |
| *In the past 12 months, how often did you… use marijuana, cannabis or hashish without tobacco*<br><br>*Or*<br><br>*In the past 12 months, how often did you… use marijuana, cannabis or hashish mixed with tobacco* | *1. Never*<br>*2. Less than once a month*<br>*3. 1-3 times per month*<br>*4. 1-6 times per week*<br>*5. Everyday* | *3,4,5 = current cannabis user*<br>*1,2 = excluded* |
| *Cigarette smoking* | | |
| *Check the box that describes you best…* | *1. I have smoked cigarettes, but not at all in the past 12 months*<br>*2. I smoked cigarettes once or a couple of times in the past 12 months*<br>*3. I smoke cigarettes once or a couple of times each month*<br>*4. I smoke cigarettes once or a couple of times each week*<br>*5. I smoke cigarettes everyday* | *3,4,5 = current cigarette smokers*<br>*1,2 = excluded* |
| *E-cigarette smoking* | | |
| *In the past 12 months, how often did you… use electronic cigarettes without nicotine*<br><br>*Or*<br><br>*In the past 12 months, how often did you… use electronic cigarettes with nicotine* | *1. Never*<br>*2. Less than once a month*<br>*3. 1-3 times per month*<br>*4. 1-6 times per week*<br>*5. Everyday* | *3,4,5 = current e-cigarette smoker*<br>*1,2 = excluded* |
| *Opioid use* | | |
| *In the past month, did you take any of the following medications, either prescription or over-the-counter… codeine, Demerol or morphine* | *1. No*<br>*2. Yes* | *2 = current opioid user*<br>*1 = excluded* |
| *Other tobacco products* | | |

| | | |
|---|---|---|
| *In the past 12 months, how often did you… smoke cigars or pipe, use bidis, chewing tobacco and/or snuff* | *1. Never*<br>*2. Less than once a month*<br>*3. 1-3 times per month*<br>*4. 1-6 times per week*<br>*5. Everyday* | *3,4,5 = current other tobacco products user*<br>*1,2 = excluded* |