Characterizing poly-substance use and its associations with anxiety and depression among a sample of Canadian high school students

by

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This thesis consists of material all of which I authored or co-authored: see Statement of Contributions included in this thesis. This is a true copy of the thesis, including any required final revisions, as accepted by my examiners.

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

STATEMENT OF CONTRIBUTIONS

This thesis consists in part of three manuscripts that have been submitted for publication. Exceptions to sole authorship:

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As lead author of these three chapters, I was responsible for developing the research questions, conducting background research, leading the study designs, conducting statistical analyses, interpreting the results, and writing the initial drafts of the manuscripts. My co-authors provided guidance during each step of the research and provided feedback on draft manuscripts. Dr. Leatherdale provided significant direction throughout. Under Dr. Leatherdale's supervision, I also prepared the remaining chapters in this thesis, which were not written for publication.

ABSTRACT

In any given year, one in five Canadians experience mental illness. The majority of mental illnesses originate in adolescence or young adulthood. Many complex factors can contribute to this, including substance use. However, research does not accurately measure how students are using substances. Typically, researchers examine one substance at a time (e.g., alcohol, cannabis, or cigarettes) but 20% of youth use more than one, or poly-substance use. Poly-substance use is the concurrent use of more than one substance (e.g., alcohol, cannabis, or cigarettes) within a specified period (e.g., the past 30 days). To address this research gap, this thesis examined substance use classes among adolescents and how those classes were associated with anxiety and depression, both cross-sectionally and longitudinally. This research will help inform future surveillance, prevention, and treatment efforts for youth substance use and mental health.

Recent evidence indicates that one in five Canadian students in grades 9 to 12 engage in poly-substance use. Common patterns of substance use among adolescents have been identified, including a low use or no use group comprising most adolescents, a single or dual substance use group, a moderate poly-substance use group, and finally a higher poly-substance use group. Longitudinal research indicates that adolescents typically maintain substance use patterns over time but if they make a change, adolescents are more likely to increase rather than to decrease the number of substances they use over time. There is limited study of poly-substance use among Canadian youth and few studies have examined the role of recent increases in e-cigarette use among adolescents in poly-substance use over time.

Poly-substance use has been associated with elevated symptoms of depression and anxiety among adolescents in cross-sectional research. Previous longitudinal research has identified mixed results. Additionally, previous longitudinal studies have not explored sex differences, despite known differences being identified in cross-sectional research and the knowledge that patterns of poly-substance use, anxiety, and depression are known to differ between female and male adolescents.

The overall objective of this dissertation was to characterize poly-substance use and examine its associations with anxiety and depression among a sample of Canadian adolescents both cross-sectionally and longitudinally, stratified by sex. Specific objectives were to (1) determine the cross-sectional substance use classes among a sample of Canadian secondary school students and examine their associations with anxiety and depression symptoms, (2) examine the longitudinal bi-directional associations between poly-substance use and anxiety and depression among secondary school

students over time and, (3) examine the longitudinal associations between latent classes of substance use and anxiety and depression scores over time among youth who use substances. This thesis made use of data from 3 waves of the COMPASS study (Wave 1: 2017/18, Wave 2: 2018/19, and Wave 3: 2019/20). Students reported their substance use (alcohol, cannabis, cigarettes, and e-cigarettes) and anxiety and depression symptoms at each wave. The first manuscript made use of cross-sectional data (Wave 1: 2017/18) while the second two used longitudinal linked data from all three years (Wave 1: 2017/18, Wave 2: 2018/19, and Wave 3: 2019/20).

The first manuscript examined cross-sectional patterns of substance use among a sample of Canadian secondary school students and their associations with clinically relevant symptoms of anxiety and depression, or both in the 2017/18 school year. Results identified three classes of substance use: poly-use, dual use, and non-use. These results indicate that Canadian secondary school students are engaging in dual and poly-substance use. Those with anxiety, depression, or both had higher odds of being in the poly-use class compared to the non-use class. Symptomology was also associated with belonging to the dual use class except among males with anxiety symptoms only.

After identifying a cross-sectional association, the second manuscript used data from students linked over three years to examine the directionality of the association. The objective was to examine the bi-directional associations between (1) number of substances used and anxiety and depression among all students and (2) poly- versus single substance use and anxiety and depression among students who used substances. Among all male students, a uni-directional association was identified where an increase in the number of substances used was associated with reduced anxiety symptoms between Waves 1 and 2. Among students who used substances, uni-directional associations were identified between Waves 2 and 3 where poly-substance use was associated with increased depression among males and increased anxiety among females and males.

Finally, given that the previous manuscript provided evidence that poly-substance use preceded changes in anxiety and depression symptoms among students who used substances, the focus of the final manuscript was on this direction of effect. The third manuscript examined the longitudinal associations between latent classes of substance use over time and anxiety and depression scores among youth who used substances. These analyses identified three classes of substance use over time: occasional alcohol and e-cigarette use, escalating poly-substance use, and consistent poly-substance use. After controlling for relevant covariates, consistent poly-substance use was associated with depression but not anxiety. Additionally, escalating poly-substance use was associated with depression among male students.

This dissertation fills an important gap with respect to our knowledge of poly-substance use and its association with anxiety and depression among adolescents in Canada. The findings highlight the need to consider adolescent poly-substance use and have implications for practice and research. Given that many students reported poly-substance use, surveillance and prevention strategies should consider substance use patterns, including dual and poly-substance use. As this research identified substance use as a potentially modifiable behaviour associated with adolescent mental health, it may also be useful to consider a mental health component in substance use programming. Future research examining this association should additionally consider simultaneous poly-substance use, clinical measures of anxiety and depression, and capture reasons for substance use to further strengthen and understand the association between poly-substance use and anxiety and depression among adolescents.

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AIC	Akaike Information Criterion
BIC	Bayesian Information Criterion
CES-D-10	Centre for Epidemiological Studies Depression Scale
CFI	Comparative Fit Index
CI	Confidence Interval
COMPASS	Cannabis use, Obesity, Mental health, Physical activity, Alcohol use, Smoking, and Sedentary behaviour
COVID-19	Coronavirus Disease 2019
CSTADS	Canadian Student Tobacco, Alcohol and Drugs Survey
DF	Degrees of Freedom
FIML	Full-Information Maximum Likelihood
FP	Free Parameters
GAD	Generalized Anxiety Disorder
GAD-7	Generalized Anxiety Disorder 7 Scale
GLMM	Generalized Linear Mixed Model
HBSC	Health Behaviour in School-aged Children
LCA	Latent Class Analysis
LMRT	Lo-Mendell-Rubin adjusted likelihood ratio test
LST	Life Skills Training
MAR	Missing at Random
MCAR	Missing Completely at Random
MI	Measurement Invariance
MNAR	Missing Not at Random
PBT	Problem Behaviour Theory
RMLCA	Repeated Measures Latent Class Analysis
RMSEA	Root Mean Square Error of Approximation
SRMR	Standardized Root Mean Squared
WLSMV	Weighted Least Square Mean and Variance Adjusted

Chapter 1
General Introduction

Poly-substance use is the use of more than one substance (e.g., alcohol, cannabis, cigarettes) within a specified time period.(1) Poly-substance use is of public health relevance as recent evidence indicates that such use is prevalent among high school students.(2–4) Research to date has failed to consider e-cigarette use and frequency of substance use when examining poly-substance use.(2–5) In order to develop effective public health policies and interventions to target poly-substance use, we must have a better understanding of youth use.

Poly-substance use is associated with further risky behaviours and negative health outcomes above and beyond using each substance in isolation, including poor mental health.(6–10) For instance, poly-substance use has been associated with elevated symptoms of depression and anxiety among adolescents aged 11 to 18 in cross-sectional studies.(11–14) However, among studies that have examined this relationship longitudinally, findings have been mixed, few have identified significant effects after controlling for covariates, and only one study to date has examined anxiety.(15–20) Further longitudinal research is needed to determine the direction of effect.(6,14,21)

Additionally, previous longitudinal studies have not explored sex differences. Previous cross-sectional studies have identified important sex differences that should be further explored.(12) Patterns of poly-substance use, anxiety, and depression differ between female and male adolescents.(12,22) Female students report higher anxiety and depression symptoms(22–25) and these sex differences tend to increase across adolescence.(26,27) Conversely, male students typically report higher levels of poly-substance use, both more substances and higher frequency of use.(7,12,28–30) Having a better understanding of these relationships including any sex-based differences can help in tailoring prevention programming to different groups.

This thesis aimed to characterize poly-substance use and examine its associations with anxiety and depression among a sample of Canadian adolescents both cross-sectionally and longitudinally, stratified by sex. Adolescence is an important time to examine this relationship as it is a critical developmental period and over half of mental disorder symptoms are thought to initiate during this time.(31) The thesis contains three manuscripts where the objectives were to examine (1) the cross-sectionally associations, (2) the bi-directional associations, and (3) the longitudinal associations between poly-substance use and symptoms of anxiety and depression, stratified by sex.

This thesis made use of data from three waves of the COMPASS study (Wave 1: 2017/18, Wave 2: 2018/19, and Wave 3: 2019/20). The COMPASS Study (Cannabis use, Obesity, Mental health, Physical activity, Alcohol use, Smoking, Sedentary behaviour) (2012-2021) is a prospective cohort study that collects data from a convenience sample of high schools in British Columbia, Alberta, Ontario, and Quebec. Participating students completed the COMPASS survey during class time. Students reported their substance use (alcohol, cannabis, cigarettes, and e-cigarettes) and anxiety and depression symptoms at each wave. The first manuscript made use of cross-sectional data (Wave 1: 2017/18) while the second two used longitudinal linked data from all three waves (Wave 1: 2017/18, Wave 2: 2018/19, and Wave 3: 2019/20).

This thesis is organized as follows. Chapter 1 is an introduction and overview of the dissertation's topic and scope. Chapter 2 provides a background and review of the scientific literature pertaining to the dissertation's scope. It provides an overview of the poly-substance use literature both in Canada and around the world and its associations with anxiety and depression. Chapter 3 outlines the research questions that are included in this dissertation and provides hypotheses for each research question based on findings from previous literature. Chapter 4 outlines the general methods of the dissertation. It provides a brief overview of the COMPASS host study, details the measures included, and describes the statistical analyses that were completed. Chapters 5, 6, and 7 were dedicated to answering the research questions in the form of three manuscripts. Finally, Chapter 8 provides an overall discussion of the dissertation's results, implications for practice and future research, as well as strengths and limitations of the research.

Chapter 2
Literature Review

The following chapter provides a review of the literature for relevant studies of adolescents examining poly-substance use, anxiety and depression, and the relationships between them.

2.1 Adolescent poly-substance use

Poly-substance use is the use of more than one substance within a specified period.(1) Poly-substance use can either be simultaneous (i.e., using multiple substances in the same instance such as a party), or concurrent within a defined time period (i.e., past 30 day use of alcohol and cannabis but not necessarily at the same time).(1,32) While all simultaneous poly-substance users are also concurrent users, concurrent users may or may not be simultaneous users. Most substance use survey measures do not provide information on simultaneous substance use and therefore only concurrent poly-substance use will be considered in this document.(32) The following paragraphs describe the measurement of poly-substance use, trends in adolescent poly-substance use in Canada and around the world, correlates of use, and the health outcomes associated with this pattern of use.

2.1.1 Adolescent poly-substance use in Canada and globally

Adolescent substance use surveillance and prevention in North America (33,34) and around the world (35,36) typically focuses on single substance use. While it is important for surveillance purposes to monitor these trends, prevention efforts may be lacking context if we do not understand how adolescents are using substances in combination. Research suggests that a substantial minority of adolescents are engaging in poly-substance use and focusing on a single substance may obscure differences between users.(37) The following sections describe what is known about poly-substance use in Canada and around the world, which is primarily based on cross-sectional data.

2.1.1.1 Canada

Among students in grades 7 to 12 in the 2018 Canadian Student Tobacco, Alcohol and Drugs Survey (CSTADS) 44% reported past year alcohol use, 18% reported past year cannabis use, 19% reported ever trying a cigarette, 20% reported ever trying e-cigarettes.(38) 17% of students reported using both alcohol and cannabis in the past year.(38) There is limited information on adolescent poly-substance use in Canada.(3,4,39) Results from the nationally representative 2008-09 Canadian Youth Smoking

Survey indicated that 12% of students in grades 7-12 had engaged in single substance use and 12% had engaged in poly-substance use in the past 12 months.(4) However, while nationally representative, this work is now 10 years old. Recent work from the COMPASS study found in the 2017-18 school year, 61% of high school students reported no past 30-day substance use, 16% reported using one substance, and 18% reported using two or more substances.(7) An examination of these trends over the past 5 years indicates that while substance non-use has remained steady around 60% among high school students over the past 5 years, among adolescents who are using substances, poly-substance use is increasing with e-cigarette use being the probable cause.(2) Finally, a study of Canadian adolescents aged 12-18 in Victoria, BC asked about past year substance use and identified 3 substance use latent classes: low/no use (63%), co-use of primarily alcohol and cannabis (23%), and poly-substance use of alcohol, cannabis, cigarettes, and other illicit drugs (11%).(40)

2.1.1.2 Globally

Adolescent poly-substance use is well documented in other countries with the vast majority of research occurring in the United States.(41–47) In the US, prevalence of past 30-day poly-substance use of alcohol, cannabis, and cigarettes has declined since 1991, however there has been an increase in cannabis-only and dual alcohol and cannabis users among certain racial/ethnic minorities.(47) Among adolescents aged 12-18 in the US who reported past 30-day substance use from 2011-2014, 58% reported single substance use, and 42% reported the use of 2 or more substances.(44) Alcohol only (38%) followed by dual use of alcohol and cannabis (13%) were the most common combinations.(44) Other studies in the US have also examined poly-substance use, however, it is not always easy to compare results due differences in the number of substances considered and the time frame measured (i.e., past 30-day or past 12-month use). Silveira et al. considered past 12-month substance use among students aged 15-17 as part of the Population Assessment of Tobacco and Health (PATH) Study and found that 18% reported single substance use and 26% reported use of two or more substances in 2013-14.(46) This is the opposite of Banks et al. who found more single than poly-substance users when considering past 30-day use.(44) Silveira et al. also additionally considered e-cigarette use which was on-par with cigarette use at that time, which may have caused Banks et al. to underestimate poly-substance use among their sample as they did not consider e-cigarette use.(44,46) Other poly-substance use research from this time also identified e-cigarettes as driving dual substance use (alcohol and e-cigarette use) among high school students.(5)

Among adolescents aged 15 to 17 in Australia, more students reported single than poly-substance use: 20% reported the use of 1 substance, 7% reported dual use and 3% reported use of alcohol, cannabis, and tobacco in the past 30 days.(13) The most common combinations of use included alcohol and cigarettes followed by alcohol and cannabis.(13) Among adolescents aged 12 to 17 in Spain, 15% reported single substance use and 14% reported using two or more substance in the previous 6-months.(43) In 2009, the European Monitoring Centre for Drugs and Addiction identified poly-substance use as a problem among adolescents and found the most common patterns of use to be alcohol and cigarettes (20%) and cannabis with alcohol and/or cigarettes (6%).(48,49)

In summary, there is a lack of consistency among poly-substance use research in Canada and globally.(50) Substances and periods of use often vary by study and the studies examined in this literature review did not consider frequency of use, which may increase risks for adverse outcomes. Additionally, the majority of this research has not considered e-cigarette use (40) which is on the rise among adolescents and may be driving up poly-substance use.(2,5)

2.1.2 Measuring poly-substance use: Latent Class Analysis

The measurement of poly-substance use presents some statistical challenges. When considering poly-substance use above and beyond simply the number of substances consumed, there are many potential combinations of use.(7,51) To additionally consider frequency of use only intensifies this problem. Latent class analysis (LCA) is a solution that uses responses to two or more categorical variables to identify homogenous latent classes within the data that are mutually exclusive and exhaustive.(52) Latent class analysis is the most common method to measure poly-substance use (5,40,41,46,53–55) although it has also been measured by summing the total number of substances used within a designated time period.(2,7,13)

The majority of adolescent poly-substance use literature utilizing LCA has identified three or four classes of substance use among adolescents.(12,41) Common classes include no or low use, single or dual use, and moderate or high poly-substance use.(12,41) Most of these studies focus primarily on alcohol, cannabis, and tobacco use due to their high prevalence of use among adolescents. E-cigarettes have not been considered in many of these studies due to their novelty although their popularity has surged among adolescents in recent years and may be contributing to a rise in adolescent poly-substance use.(2,7,56) Morean et al. examined the co-occurrence of alcohol, cannabis, e-cigarettes and a variety of tobacco products among high school students in Connecticut, US.(5) They identified 4 classes of use: abstainers (82% of sample), alcohol and e-cigarette users

(5%), cannabis and alcohol users (7%), and users of all products (7%).(5) The fact that recent research is identifying classes of use that involve dual and poly-use of e-cigarettes with other substances indicates the importance of considering these devices when examining poly-substance use.(7)

2.1.3 Correlates of adolescent poly-substance use

Older students have been consistently identified at an increased risk of poly-substance use compared to their younger counterparts.(2,5,58–65,7,40,41,44–46,55,57) However, the relationship between sex and poly-substance use is more nuanced. The majority of studies have found male students generally to be more likely to be in a higher use category (2,4,60–63,5,7,28–30,42,44,59) but others have found no difference (13,45,66–68) or increased risk for females in certain poly-use classes.(46,69,70) Some literature has identified female youth who identified as lesbian or bisexual to be at increased risk compared to their heterosexual counterparts.(71–73) Additionally, some research has identified different latent classes for males and females.(53)

Findings for ethnic minorities and poly-substance use are also inconsistent. One study of a sample of nationally representative 10th graders in the US found no association.(42) Alternatively, identifying as Black, Hispanic or other in the nationally representative PATH (Population Assessment of Tobacco and Health) Study was associated with less tri-substance use (alcohol, marijuana, and tobacco) compared to white students in the US.(46) Hispanic and Other students were also less likely to engage in greater than 3 poly-substance use.(46) Other studies have also found Black students (8,62,74–76) or non-White students (63,64) to be less likely to be poly-substance users than white students. While others have identified specific groupings of substances popular among Black students: Banks et al. identified that Black students were more likely to engage in cannabis only use and dual alcohol and cannabis use compared to white students but less likely to engage in all other combinations.(44) Similarly, in this study, Hispanic students were more likely to engage in cannabis use only but less likely for all other combinations.(44) Indigenous students in the US,(58) Canada,(2,7) and New Zealand (77) are consistently at higher risk for poly-substance use while Asian students are consistently less likely to engage in poly-substance use.(7,44) Finally, some work has not found any differences between groups.(59)

Not all studies have assessed socioeconomic status, and results are mixed among those that have. Some studies have identified no effect (13,29,45,46,54,62) while others have identified that students in higher use classes are more likely to have higher family affluence or access to spending

money (7,53,67) while others have found lower socioeconomic status to be associated with increased poly-use.(68,78) Tangential to socioeconomic status, Rose et al. identified that high school students receiving free school lunches were more likely to be in a higher use class.(58) One study found that lower school-level SES predicted increased poly-substance use, while at the same time students who reported more spending money were also at higher risk.(77) Therefore, this relationship likely depends on the measures used (i.e., school level vs student level, or measure of family SES vs student spending money) and the location of the study.

Other individual level factors have been explored as well. Early alcohol, tobacco, or cannabis use has been identified as a risk factor for later poly-substance use.(28) Low social connectedness, high sensation seeking, and gambling have also been identified as risk factors for poly-substance use.(7,77,79,80) In contrast, adolescents' disapproval of substance use has been associated with lower likelihood of belonging to a higher use class.(81) Family, peer, and school factors also have an influence on adolescent substance use. Parental substance use (41,55,61,69,82–84) and peer substance use (15,41,88–91,55,61,68,70,81,85–87) have both been found to be positively associated with poly-substance use. While parental monitoring is a protective factor for poly-use.(15,67,69,77,81,82) Adolescents' sense of school connectedness has been found to have mixed results on poly-substance use. Some studies have found no effect of school connectedness or engagement (66,81) whereas other studies have found lower school connectedness associated with increased poly-use.(7,13,92) Residing in a non-urban setting has been found to be associated with poly-substance use involving predominantly tobacco use.(46)

2.1.4 Adolescent poly-substance use outcomes

Poly-substance use is associated with further risky behaviours and negative health outcomes above and beyond using each substance in isolation.(16,93) Firstly, adolescents who use multiple substances tend to continue to do so as they age and are more likely to increase the number of substances they use rather than to reduce over time.(54,57,94) These individuals are also at increased risk of substance use disorders (94–96) and reduced odds of cessation.(95) Second, these adolescents are less likely to do well academically. Those who engage in poly-substance use are more likely to have poorer grades (6,61,70) and less likely to complete secondary education.(97,98) Third, teen poly-substance use is associated with other risky behaviour including risky sexual behaviour (6,8,99) and involvement in violence.(9,10,100–102) It is not then surprising those who report poly-substance use also report poorer health overall than their peers, including mental illness.(6)

2.2 Adolescent mental illness

Mental illness refers to a wide range of disorders that affect mood, thinking, and behaviour and can be associated with mild to severe distress and/or impairment of functioning.(103) Examples include depression and anxiety disorders.(103) Adolescence is a critical juncture for addressing this issue as the majority of mental illnesses arise during adolescence and young adulthood.(104,105) It is a leading cause of disability in Canada and around the world and also presents a significant current and predicted economic burden.(106–109)

2.2.1 Anxiety and depression in Canada

Approximately 1 in 5 youth have a mental disorder (110) and this proportion has remained stable over time.(111) Two of the most common disorders include anxiety and depression. Results from the 2014 Canadian Community Health Survey indicate that 13% of youth aged 15 to 24 reported a lifetime mood disorder and 6% reported a lifetime generalized anxiety disorder.(112)

2.2.1.1 Anxiety

Generalized anxiety disorder (GAD) is characterized by generalized and persistent anxiety or worry that is accompanied by physical symptoms such as difficulty sleeping or muscle tension.(113) It is the broadest and most common anxiety disorder. In Canada in 2012, around 2% of young people reported past year GAD.(112)

2.2.1.2 Depression

Depression is a "mental disorder that presents with depressed mood, loss of interest or pleasure, decreased energy, feelings of guilt or low self-worth, disturbed sleep or appetite, and poor concentration."(114) In Canada in 2012 among youth people aged 15 to 24, 9% of females and 5% of males reported depression in the past 12 months.(115) Among the general population, 53% of those with GAD also met the criteria for depression (115). This co-occurrence has also been identified in other literature (116,117) and provides rationale for the examination of both depression and anxiety.

2.2.2 Measuring mental illness

There are two main methods to classify mental illness or disorders in epidemiologic research: diagnostic interviews and survey checklists.(118) Diagnostic interviews classify disorders based on disease classification manuals such as the Diagnostic and Statistical Manual of Mental Disorders (113) and the International Classification of Diseases.(119) Interviews can be structured where a

script is read by an interviewer, or unstructured where interviewers have the freedom to inquire about symptoms and make informed judgements.(118) Interviews are designed based on disease classification manuals whereas checklists might not be.(118) The presence of an interviewer removes potential issues of illiteracy and allows for complex questioning to clarify answers, however, they may encourage more socially acceptable responses.(118)

On the other hand, checklists are often in survey form and include brief descriptions of mental disorders and allow participants to rate the frequency or severity of said symptoms.(118) A score is computed and a standard cut point is used to determine if the individual has a disorder. Checklists take less time and are less expensive to implement than interviews. They are also less of a burden on participants and participants may feel more comfortable disclosing highly sensitive information.(118) Both diagnostic interviews and checklists can be used in epidemiological studies, however they have slightly different characteristics and objectives. This thesis made use of checklists to measure symptoms of anxiety and depression.

2.2.3 Correlates of anxiety and depression

Adolescence is a critical developmental period as over half of mental disorder symptoms are thought to initiate during this time.(31) The age of onset for anxiety symptoms is in early childhood, while depressive symptoms tend to emerge in early adolescence.(120) Evidence from checklist survey results in Canada and the United States has found that depressive symptoms among adolescents typically peak between ages of 15-18 years.(121–123) Although there may be subgroups of youth who experience this trajectory differently.(121,124) In contrast, studies have typically found a decrease in anxiety symptoms from childhood to adolescence.(125–129) Although there is evidence that among some subgroups of female adolescents, anxiety symptoms do not decrease over time.(125,126,130)

Another important correlate of anxiety and depression is sex. Female students report higher anxiety and depression symptoms (22–25,131–136) and these sex differences tend to increase across adolescence.(26,27) There is also some evidence of ethnic and sociodemographic differences among adolescents. Studies have identified that Hispanic and Black adolescents were more likely to report experiencing symptoms of anxiety and depression.(120,134,137,138) Lower socioeconomic status has been associated with symptoms of anxiety and depression.(139–142) However, some studies have found no association (136) or that not all measures of socioeconomic status have been consistent

correlates. For example, Merikangas et al found that poverty was not associated with mental disorder but lower parental education was.(120)

There is evidence for multifactorial causes of mental disorders among young people. Other correlates for anxiety and depression include family factors and other interpersonal factors. Parental symptoms of anxiety and depression are strongly associated with child and adolescent symptoms, even if the parent is not genetically related.(143–145) Lack of parental supervision has been associated with depressive symptoms (146) and divorce has been associated with higher anxiety.(120) Next, decreases in social support, feeling lonely, and being bullied have also been associated with depressive symptoms.(131,146,147) There are also emerging correlates of depressive symptoms. For example, some studies have identified a link between social media use and depressive symptoms.(148) It is also important to note that there is overlap between symptoms of anxiety and depression.(149) Symptoms of both frequently co-occur and symptoms of anxiety often precede symptoms of depression among children and youth.(150)

Finally, another correlate of anxiety and depression is substance use. The following section will discuss youth depression and anxiety symptoms and their relationship with substance use in more detail.

2.2.4 Substance use and anxiety and depression

Substance use has been associated with depression and anxiety among adolescents.(151–153) For example, binge drinking and alcohol use has been associated with feelings of depression and anxiety and general poor mental health.(146,154–157) Cannabis use, especially early, high frequency cannabis use, has been associated with symptoms of depression and internalizing symptoms (i.e., a combined measure of anxiety and depression symptoms in adolescence and later in life.(158–163) The associations between cannabis and anxiety are less established. Some research has established a link while other research has not.(164) Inconsistencies in the literature may be due to differences in samples, legal status of cannabis, the episodic nature of some mood disorders, concentrations of THC, age of onset, frequency/duration of use, and other co-occurring risks.(160,165) Research has also linked cigarette use and depressive symptoms (131,146,166–169) However, other research has suggested that high levels of cannabis use among students who use cigarettes potentially confounds this relationship.(170) Finally e-cigarette use and e-cigarette initiation has been associated with internalizing symptoms (171,172) and depression (173) although other research has found no significant association.(174)

2.3 Adolescent poly-substance use and depression and anxiety

Substance use has been associated with depression and anxiety among adolescents, however, the majority of this research has focused on the independent effects of substances on mental illness (e.g., the effects of cannabis alone on mental illness).(151–153) As the use of many of these substances are highly correlated and poly-substance use is prevalent among high school students it can be difficult to disentangle the independent effects of different substances (i.e., binge drinking, smoking, cannabis use) on mental illness.(175,176) The majority of the work examining adolescent poly-substance use and mental illness has focused on depression symptoms. However, due to the frequency of co-occurrence of these two mental illnesses (116) and the use of survey measures that do not differentiate between the two,(6,88) both will be examined in the following sections.

2.3.1 Cross-sectional evidence

A 2014 systematic review identified poly-substance use as a modifiable risk factor for depression among adolescents.(177) Since then, many cross-sectional studies have found that poly-substance users report higher instances of psychiatric symptoms including depression and anxiety.(7,14,60,178–183) For example, Kelly et al. found that membership in the poly-substance use class in comparison to the alcohol only class was associated with increased psychological distress (including both depression and anxiety symptoms) among teens in Australia.(88) Similarly, in the United States, membership in the poly-use class compared to the primarily cannabis class was associated with increased psychological distress (included items measuring depression and anxiety symptoms).(6) In the Monitoring the Future Study in the United States, depressive symptoms were associated with increased odds of poly-substance use compared to alcohol only use among 8th grade, 10th grade, and 12th grade students and symptoms of anxiety were not measured.(11) Similarly, among another sample of American adolescent cannabis users, those using additional illicit substances were at higher risk of depressive disorder symptoms compared to cannabis users only while no relationship was found for measures of anxiety or externalizing disorders.(184)

However, other research has identified opposite effects or null effects. Cranford et al. identified protective effects of internalizing problems, including depression and anxiety, on poly-substance group membership.(69) Among middle school and high school students in Michigan, US, those with internalizing problems were less likely to belong to the tobacco, alcohol, and cannabis class, the alcohol, nonmedical use of prescription medications, and excessive medical use of prescription medications class, or the multiple use class (encompassing all mentioned substances plus

other illicit drug use) compared to the low or no use class. In contrast, Connell et al. found no association between depression symptoms and substance use classes among grade 9 and 10 students in New England, US.(70) Finally, there is limited evidence examining the relationship between poly-substance use and anxiety alone. Among Dutch adolescents, hopelessness and sensation seeking were found to be associated with polys-substance use, but not anxiety.(185)

2.3.2 Longitudinal Evidence

Longitudinally, research has focused on depression or anxiety symptoms predicting poly-substance use among adolescents. Some studies have identified no effect of depression on poly-substance use. Brooks-Russell et al. examined the substance-use trajectories from grades 10-12 among adolescents in the NEXT Generation Health Study in the United States. They identified 4 classes of poly-substance users over time and depressive symptoms at baseline were associated with a higher likelihood of membership in 3 of these classes when only controlling for individual factors.(15) However, after controlling for parental monitoring, parental disapproval, and peer substance use, depressive symptoms were no longer significantly associated with group membership.(15) Fallu and colleagues measured depressive symptoms in grades 7-8 among students in Quebec, Canada (16) and found that depressive symptoms in grades 7-8 did not predict substance use class in grade 10.(16) Finally, among students in grades 7 to 12 in the US, Dierker et al found no association between depression at baseline and substance use classes one year later.(17)

In contrast, other studies have identified an effect. Among grade 9 and 10 students in Chicago the US, depression symptoms at baseline predicted poly-substance use over seven years as measured by a Z-score. (18) Carbonneau et al. studied a sample of low income boys in Montreal, Canada and anxiety symptoms at ages 10 to 12 were protective against belonging to poly-use classes at ages 13 to 17. (19) However, it should be noted the measures of anxiety in this study were assessed by a teacher rather than the student themselves.

Finally, one study examined the opposite direction of effect. A small cohort study (N=176) in San Francisco examined how poly-substance use was associated with future depression scores, specifically among smokers. They found that depression scores were more severe among smokers who engaged with multiple illicit substances (i.e., cocaine/crack, hallucinogens, ecstasy, and misused prescriptions) compared to those who used alcohol and cannabis only.(20) Longitudinally, this “hard” poly-substance use was also associated with future depression scores 2 and 3 years later although this study did not control for any other covariates.(20)

There are also findings that point to a co-occurring emergence of both substance use and depressive symptoms.(186) Felton et al. examined adolescents from the 2005 National Survey of Adolescents in the United States and identified that early depressive symptoms predicted increases poly-substance use but this relationship did not hold over time.(186) Later, poly-substance use predicted concurrent depressive symptoms over time.(186) These findings suggest that the relationship between poly-substance use and mental illness may not be as simple as one predicting the other over time.(186)

In conclusion, poly-substance use has primarily been associated with depression and a combination of depression and anxiety in cross-sectional studies among adolescents.(6,11,88,177,184) There is limited longitudinal evidence of the relationship between poly-substance use and depression (15–20,186) highlighting the challenge of determining temporality. Evidence generally supports the temporal precedence of mental disorders before substance use disorders (187) however directionality is less clear when considering lower levels of substance use as the majority of this research is based on cross-sectional studies.(186) There is also a lack of consistency in the mental health measures used (i.e., some examine depression and anxiety separately and others as a combined variable) and not all studies controlled for covariates. Further longitudinal studies are needed to examine the relationship between substance use and depression and anxiety among adolescents to establish temporality.

2.4 Summary and Implications

The evidence to date indicates that there is a lack of literature examining poly-substance use among adolescents in Canada, especially when considering e-cigarette use and frequency of substance use.(2–5) While limited, this literature indicates that poly-substance use is prevalent among high school students.(2–4) This is problematic as poly-substance use has been associated with numerous negative health outcomes including mental illness. However, there is much contradicting evidence on the direction and strength of this association.(6,11,15,16,20,88,177,184,186) Further longitudinal studies are needed to examine the relationship between substance use and mental illness outcomes among adolescents, particularly to establish temporality and with controls for confounders. Therefore, the overall goal of this thesis was to characterize poly-substance use among adolescents and examine its associations with depression and anxiety both cross sectionally and longitudinally.

Chapter 3
Study Rationale and Research Questions

This research project furthered our understanding of adolescent poly-substance use and its associations with symptoms of anxiety and depression through three studies and their corresponding three manuscripts. The research questions and implications for each study are described below.

3.1 Study 1

Recent evidence shows an estimated 23% of Canadian students in Grades 9 to 12 use more than one substance, also known as poly-substance use or poly-use.(7) While the prevalence of substance non-use has remained steady among high school students over the past five years, poly-use is increasing among adolescents, likely due to the emergence of e-cigarettes.(2) A recent systematic review identified strong evidence for the presence of subgroups of adolescent substance use, with common clusters being low use, single- or dual-substance use, moderate general multi-use and high multi-use.(12) Unfortunately, there is limited research examining patterns of substance use among Canadian adolescents and how e-cigarette use fits in.(5,12,40,54) This is concerning, as poly-use is associated with higher risks of negative social and health consequences.(6,188)

Furthermore, substance use has been associated with anxiety and depression symptoms among adolescents.(16,177) Generally, those who report poly-use have higher instances of poor mental health, including anxiety and depression.(6,11,88,184) Much of this work examining poly-use and poor mental health among adolescents has focused on depression. However, there is a high prevalence of comorbidity between symptoms of anxiety and depression and an estimated 25% to 50% of youth with depression also meeting the criteria for an anxiety disorder.(150) These youth have a higher risk of longer duration of symptoms, greater impairment, re-occurrence and greater utilization of mental health services.(150) Therefore, it is important to consider both depression and anxiety simultaneously in analyses.

There is limited previous research on adolescent poly-substance use in Canada.(2–4,7,40) This study was the first to examine poly-substance use using LCA and examine associations with anxiety and depression among secondary school students in multiple Canadian provinces. This study highlights the need to include poly-substance use in adolescent substance use surveillance and prevention efforts.

3.1.1 Study 1 research questions

The objective of Study 1 was to determine the latent classes of substance use among a sample of secondary students participating in Year 6 (2017/18) of the COMPASS study and then examine their cross-sectional associations with depression and anxiety scores. This first study answered the following research questions:

1. What are the homogenous latent classes of substance use among COMPASS secondary school students in 2017/18?
2. What are the associations between these latent classes and clinically relevant symptoms of anxiety, depression, or both?

3.1.2 Study 1 hypotheses

I expected the following results for these research questions:

1. I expected that the classes identified would include a group of non-users, single substance users, and multiple groups of poly-substance users (i.e., a low frequency and high frequency group).
2. I expected that students in groups representing a higher frequency and higher number of substances used would be more likely to have clinically relevant symptoms of anxiety or depression.

3.2 Study 2

There have been mixed results among studies that have examined the longitudinal relationship between poly-substance use and depression.(15,16,20,186) Thus, the direction of effect between these variables is unclear. Additionally, there are no longitudinal studies examining the relationship between poly-substance use and anxiety. This is problematic as some cross-sectional studies have identified a link between the two that should be further investigated to determine the direction of effect.(6,14,21)

Previous longitudinal studies have not explored sex differences even though cross-sectional studies have identified important sex differences.(12) Patterns of poly-substance use, anxiety, and depression differ between female and male adolescents.(12,22) Female students report higher anxiety and depression symptoms (22–25) and these sex differences tend to increase across adolescence.(26,27) Conversely, male students typically report higher levels of poly-substance use, both more substances and higher frequency of use.(7,12,28–30) Adolescence is a critical

developmental period as over half of mental disorder symptoms are thought to initiate during this time.(31) Having a better understanding of these relationships including any sex-based differences can help in tailoring prevention programming to different groups.

3.2.1 Study 2 research questions

The objective of this study was to better understand the longitudinal relationship between poly-substance use and anxiety and depression among a large sample of Canadian high school students stratified by sex. Specifically, this study answered the following research questions:

1. What are the longitudinal bi-directional associations between the number of substances used and anxiety and depression scores?
2. What are the longitudinal bi-directional associations between poly-substance use versus single substance use and anxiety and depression scores?

3.2.2 Study 2 hypotheses

I expected the following results for each research question:

1. I expected that an increasing number of substances would be associated with worse anxiety and depression scores, or worse anxiety and depression scores would be associated with increasing substance use.
2. I expected that poly-substance use would be associated with worse anxiety and depression scores, or worse anxiety and depression score would be associated with an increased risk of poly-substance use.

3.3 Study 3

Previous longitudinal research has often examined poly-substance simply by counting the total substances used rather than by investigating specific substances used.(186) Only two studies to date have considered classes of substance use over time and their relationship with symptoms of mental illness.(15,20) Additionally, previous longitudinal studies have not explored sex differences, despite differences being identified in cross-sectional research.(12,189) Patterns of poly-substance use, anxiety, and depression are known to differ between female and male adolescents.(12,22,189) Having a better understanding of these relationships, including any sex-based differences, can help in tailoring prevention programming to the potential uniqueness of different groups.

3.3.1 Study 3 research questions

The objective of Study 3 was to identify patterns of substance use over time and their associations with anxiety and depression symptoms among male and female students. Specifically, this study answered the following research questions:

1. What are the longitudinal patterns of substance use among a sample of grade 9 and 10 students across three years?
2. What are the associations between these substance use classes and anxiety and depression scores over time?

3.3.2 Study 3 hypotheses

I expected the following results for each research question:

1. I expected to identify patterns of substance use similar to those identified in Study 1 including a dual use group comprising alcohol and e-cigarette use as well as a poly-substance use group comprising alcohol, cannabis, cigarette, and e-cigarette use. As this study examined substance use over three years, I also expected to see a group that maintained their use over time, a group that increased their use, and potentially a group that also decreased their use over time.
2. I expected that substance use profiles representing a higher number of substances used and/or a higher frequency of use would be associated with poorer depression and anxiety scores over time.

Chapter 4
General Methodology

The following chapter presents an overview of the methods used to answer the previously described research questions. This chapter includes the theoretical frameworks guiding this project, the data source, the survey measures, and the statistical analysis techniques used.

4.1 Theoretical Framework

This dissertation was primarily driven by previous evidence and gaps in the literature but also is consistent with Problem Behaviour Theory (PBT). This section also explores theoretical explanations for the direction of association between substance use and mental illness. While theory can help focus and direct research by indicating factors that may be important to include in analyses, it should be noted that this dissertation was not designed to test theory.

4.1.1 Problem Behaviour Theory

PBT is a psychosocial theory that is used to understand and predict youth engagement in various problem behaviours.(190) Problem behaviours refer to transgressions of social or legal norms (e.g., alcohol or illicit drug use) that often elicit sanctions from others or larger society.(190) This is in contrast to health compromising behaviours (e.g., unhealthy dietary habits or insufficient exercise) which may compromise health but do not necessarily violate social or legal norms.(190) PBT rests upon the social-psychological relationships between three major systems: the personality system, the perceived environment system, and the behaviour system.(190) Each of these systems work together to predict the likelihood of occurrence of problem behaviour.(190)

The personality system includes sources of motivation (e.g., value on academic achievement, independence, and affection), personal beliefs (e.g., social criticism, alienation, and self-esteem), and personal control (e.g., tolerance of deviance, religiosity).(190) The environment system focuses on the perceived environment for the individual rather than the objective external environment including proximal (e.g., parent or friend approval of problem behaviour) and distal factors (e.g., parental support and controls, friend support and controls).(190) Finally, the behaviour system describes problem behaviours (e.g., alcohol or illicit drug use) which are balanced by conventional behaviours (e.g., church attendance and academic performance).(190) Each aspect of the personality, perceived environment, and behaviour systems work together to each positively or negatively affect the choice

to engage in problem behaviour.(190) Overall, PBT lends support for a "risk behaviour syndrome" where risk behaviours tend to cluster together and would benefit from wholistic prevention or treatment efforts.(191,192)

4.1.2 Explanatory relationship between substance use and mental illness

There are hypothesized explanations for these relationships seen in both directions between substance use and mental illness. The negative affect regulation model proposes that individuals use substances to cope with existing depressive symptoms and that this avoidance is the motive for addictive substance use.(193) This is supported by evidence that has found that depressive symptoms during adolescence predict future increased substance use, however, there are variations by gender and type of substance used.(15,194,195) However, as previously noted, the evidence does not always support this direction of effect.(16) On the other hand, the opponent process model hypothesizes that substance use in adolescence predicts future depressive symptoms.(196) The proposed pathway is through physiological changes experienced due to substance use including depressed mood. Specifically, substance use promotes an immediate mood boost ("appetitive process") followed by a slow decrease in mood ("opponent process"). After repeated use, it is proposed that the "opponent process" becomes stronger than the "appetitive process" and negatively affects mood over time. However, it is important to keep in mind that these are models of addiction and are often studied in adults which may not be relevant to initiation of substance use among youth.

4.2 The COMPASS Host Study

The COMPASS Study (Cannabis use, Obesity, Mental health, Physical activity, Alcohol use, Smoking, Sedentary behaviour) (2012-2021) is a prospective cohort study that collects data from a convenience sample of high schools in British Columbia, Alberta, Ontario, and Quebec. It is a research platform that was designed to examine and evaluate how changes in school programs, policies, and/or built environment characteristics are related to changes in multiple youth health behaviours and outcomes over time.(197) COMPASS collects data at both the student and school level, however only student-level data was considered for this thesis. Additional information about the COMPASS Study can be found online (https://uwaterloo.ca/compass-system/).

The COMPASS study began collecting data in the 2012-2013 school year and is currently funded until the 2020-2021 school year. Schools were purposively sampled from school boards in British Columbia, Alberta, Ontario, and Quebec that had secondary schools with grades 9 to 12

(Secondary I-V in Quebec), a student population of at least 100 students per grade, standard classroom settings, and permitted active-information passive consent parental permission protocols.(198) An active-information passive consent protocol involves sending parents information about the survey their student will be participating in and, rather than requiring a signature from every parent (i.e., active consent), asks that parents contact the research team or the school if they would prefer their child not participate.(199) Students were also able to decline participation on the day of the survey. Active-information passive consent was chosen for the COMPASS study as it has been shown to achieve higher participation rates, less biased sample demographics, and improved student confidentiality as student names are not recorded.(199)

4.2.1 Ethics

All procedures were approved by the University of Waterloo Office of Research Ethics (reference number 30118) and appropriate school board committees. The COMPASS study uses an active-information passive consent protocol. An active-information passive consent protocol involves sending parents information about the survey their student will be participating in and, rather than requiring a signature from every parent (i.e., active consent), asks that parents contact the research team or the school if they would prefer their child not participate.(199) Students also are able to decline participation on the day of the survey. An active-information passive-consent protocol was chosen for several reasons. Studies that use active-consent procedures in school-based research have lower response rates and more homogenous samples.(200) Additionally, the use of an active-information passive-consent protocol has been shown to encourage honest reporting which has been shown to be particularly important in substance use and mental health research.(197,199–201)

Student participants did not receive any compensation for participation in the study however, each participating school was provided with an honorarium as a token of appreciation.

4.2.2 COMPASS Student Questionnaire

The COMPASS paper-based student questionnaire (Cq) was a 15-page survey (see Appendix A) that took about 40 minutes to complete. The Cq included demographic questions, core measures (e.g., weight status, physical activity, and substance use questions), and supplementary measures of interest to school stakeholders (e.g., bullying and school outcomes).(202) In Year 6 of the COMPASS study (2017/18), a mental health module was added to the questionnaire to collect information pertaining to student mental health including depression and anxiety.(203)

The Cq was administered by teachers in the classroom.(204) Teachers were provided with detailed instructions on administering the survey to ensure consistency and student confidentiality.(204) All students in grades 9 to 12 (Secondary I-V in Quebec) who were present during the survey period, who gave consent to complete the survey, and whose parents had not refused consent completed the questionnaire during the designated class time. Students were given an envelope to seal their questionnaire in upon completion. A COMPASS data collector was present at the school throughout the survey completion to aid in the data collection and to return the surveys to the University of Waterloo for processing.

4.2.3 Longitudinal linkage methods

COMPASS is unique in its ability to link students longitudinally over time. To achieve this, the COMPASS questionnaire asked students 5 questions with single letter or number responses to create a unique self-generated code. This allowed for students to be linked over time within schools while maintaining student confidentiality.(205) Students were asked to answer the following questions: (1) The first letter of your middle name (if you have more than one middle name use your first middle name; if you don't have a middle name use "Z") (2) The name of the month in which you were born (3) The last letter of your full last name (4) The second letter of your full first name and (5) The first initial of your mother's first name (think about the mother you see the most). Students were also asked “Did you attend this school last year?” to confirm whether there should be matching data for a student in the previous year. Additional information describing COMPASS data linkage is described further elsewhere.(205,206)

4.3 Sample

This dissertation made use of data from three waves of the COMPASS study (Wave 1: 2017/18, Wave 2: 2018/19, and Wave 3: 2019/20) from students in British Columbia, Alberta, Ontario, and Quebec.

66,434 students participated in Wave 1 (81.7% response rate) of the survey from 122 schools: 16 in British Columbia, 8 in Alberta, 61 in Ontario, and 37 in Quebec. 74,501 students participated in Wave 2 (84.2% response rate) from 136 schools: 15 in British Columbia, 8 in Alberta, 61 in Ontario, and 52 in Quebec. In Wave 3, due to school closures resulting from the COVID-19 pandemic in March 2020, only 29 schools (British Columbia, n=5; Alberta, n=5; Ontario, n=17; and Quebec, n=2) completed the paper-based Cq and were included in this thesis. 29,770 students participated in Wave

3 (83.4% response rate). For manuscripts two and three, students in grades 9 and 10 at Wave 1 were linked over all three waves. 2,904 students were linked over time from 29 schools (5 in British Columbia, 5 in Alberta, 17 in Ontario, and 2 in Quebec).

4.4 Study Measures

4.4.1 Substance use measures

Alcohol use, cannabis use, cigarette use, and e-cigarette use were all assessed using the COMPASS Cq.

Alcohol use was assessed by one question on the COMPASS Cq: “In the last 12 months, how often did you have 5 drinks of alcohol or more on one occasion?” In manuscripts one and three, students were categorized into four levels. Respondents who selected “I have never done this,” “I did not have 5 or more drinks on one occasion in the last 12 months,” were coded as “0” and acted as the reference group. Students who selected “Less than once a month,” were coded as “1” and categorized as less than monthly use. Students who responded "Once a month," or "2 to 3 times a month," were coded as “2” and categorized as monthly use. Finally, students who responded "Once a week," "2 to 5 times a week," or "Daily or almost daily" were coded as “3” and categorized as weekly use. In manuscript 2, reporting monthly use or more was considered current substance use.

Cannabis use was assessed by one question on the COMPASS Cq: “In the last 12 months, how often did you use marijuana or cannabis? (a joint, pot, weed, hash)” and had similar response options as alcohol use. In manuscripts one and three, students were categorized into four levels. Respondents who selected “I have never done this,” “I did not have 5 or more drinks on one occasion in the last 12 months,” were coded as “0” and acted as the reference group. Students who selected “Less than once a month,” were coded as “1” and categorized as less than monthly use. Students who responded "Once a month," or "2 to 3 times a month," were coded as “2” and categorized as monthly use. Finally, students who responded "Once a week," "2 to 5 times a week," or "Daily or almost daily" were coded as “3” and categorized as weekly use. In manuscript 2, reporting monthly use or more was considered current substance use.

Cigarette use was assessed on the COMPASS Cq by asking “Have you ever tried cigarette smoking, even just a few puffs?” and “On how many of the last 30 days did you smoke one or more cigarettes?” In manuscripts one and three, cigarette use was divided into four categories. Students who answered "No" to the first question were coded as “0” and considered the reference group.

Students who responded “Yes” to the first question but “None” to the second were coded as “1” and considered ever users. Students indicating "1 day," or "2 to 3 days," were considered monthly users and coded as “2”. Reporting "4 to 5 days" or more was considered weekly use and coded as “3.” In manuscript two, reporting any past 30-day use was considered current substance use.

E-cigarette use was assessed on the Cq by asking “Have you ever tried an electronic cigarette, also known as an e-cigarette?” and “On how many of the last 30 days did you use an e-cigarette?” In manuscripts one and three, e-cigarette use was divided into four categories. Students who answered "No" to the first question were coded as “0” and considered the reference group. Students who responded “Yes” to the first question but “None” to the second were coded as “1” and considered ever users. Students indicating "1 day," or "2 to 3 days," were considered monthly users and coded as “2”. Reporting "4 to 5 days" or more was considered weekly use and coded as “3.” In manuscript two, reporting any past 30-day use was considered current substance use.

4.4.2 Anxiety and Depression

The *Generalized Anxiety Disorder 7* (GAD-7) scale assesses symptoms of generalized anxiety and has been validated among adolescents.(207,208) It is designed primarily as a screening and severity measure for generalized anxiety disorder. Scores range from 0 to 21 and a recommended cut point for further evaluation is a score of 10 or greater, with scores of 5, 10, and 15 said to indicate mild, moderate, and severe levels of anxiety symptoms. Anxiety score was used as a categorical variable in Manuscript 1 and as a continuous variables in Manuscripts 2 and 3.

The *Centre for Epidemiological Studies Depression Scale* (CES-D-10) is one of the most well-known self-report scales for measuring depression risk and has been validated among adolescents.(209) Scores range from 0 to 30 with higher scores indicating more symptoms. Scores of 10 or above indicate significant depressive symptoms. Depression score was used as a categorical variable in Manuscript 1 and as a continuous variables in Manuscripts 2 and 3.

4.4.3 Covariates

Truancy was used as a measure of student risky behaviour. Students were asked “In the last 4 weeks, how many classes did you skip when you were not supposed to?” Students who responded “0 days” were coded as “0” and any other responses were coded as “1.”

To ascertain whether students felt supported by their friends or family respectively, they were asked how much they agreed with the statements “I can talk about my problems with my

family/friends" on a five-point scale ranging from "Strongly Agree" to "Strongly Disagree". These measures were categorized as a binary variable with students who responded "Agree" or "Strongly Agree" categorized as "1" and all other students categorized as "0."

4.4.4 Demographic variables

Sex, grade, ethnicity, and weekly spending money were also included as covariates. Students were asked, "Are you female or male", with response options of "male" or "female". Students were also asked to self-report what grade they were in, from grade 9 to 12 (Secondary I-V in Quebec, grades 7 to 11 equivalent). Students were also asked to self-report their ethnicity, with response options of "White", "Black", "Asian", "Aboriginal (First Nations, Metis, Inuit)", "Latin American/Hispanic" and "Other". Students were categorized as "White" or "non-White." Finally, students were asked, "About how much money do you usually get each week to spend on yourself or to save?", with response options ranging from "Zero" to "More than $100".

4.5 Statistical Analyses

This dissertation made use of multiple statistical methods to answer each research question. A full description of the analytic approach for each manuscript can be found in Chapter 5, Chapter 6, and Chapter 7. The following is an overview of the analyses conducted for each research question.

The objective of Chapter 5 was to determine the substance use classes among a sample of Canadian secondary school students and examine their cross-sectional associations with anxiety and depression symptoms. Latent Class Analysis (LCA) was first used to create substance use classes. LCA is a measurement model that uses categorical variables to identify homogenous latent classes within the data that are mutually exclusive and exhaustive.(52) After identifying substance use classes using LCA, a multinomial logistic regression was conducted to examine how anxiety and depression were associated with likelihood of membership in each class using the R3STEP command in Mplus.(210)

The objective of Chapter 6 was to examine the bi-directional associations between (1) number of substances used and anxiety and depression and (2) single versus poly-substance use and anxiety and depression among a sample of Canadian high school students. Auto-regressive cross-lagged models simultaneously tested the auto-regressive effects of number of substances used/poly-substance use, anxiety, and depression at each wave and the bi-directional relationships between them at each wave (i.e., whether the number of substances used at Wave 1 predicted subsequent anxiety

and depression scores at Wave 2 and vice versa). The auto-regressive cross-lagged analyses were performed using Mplus version 8.2 (Muthen & Muthen, Los Angeles, CA, USA). In part 1, these models were conducted in the full sample examining number of substances used using maximum likelihood estimation. In part 2, models were conducted in a substance use only subsample to examine single versus poly-substance use using robust mean and variance-adjusted weighted least-squares estimation (WLSMV).

Finally, the objective of Chapter 7 was to, first, examine the longitudinal latent classes of substance use using Repeated Measures Latent Class Analysis (RMLCA) and, second, to examine their associations with anxiety and depression scores among youth who used substances in three waves of the COMPASS study. To create substance use classes and examine their associations with anxiety and depression RMLCA (52) was implemented using Mplus 8.2 (Muthen & Muthen, Los Angeles, CA, USA). RMLCA is an application of Latent Class Analysis (LCA) that identifies latent classes over time.(52) Once the most parsimonious solution was determined, students were assigned to a latent class using most likely class membership (211). After the RMLCA was completed, the PROC MIXED function in SAS (SAS Institute Inc., Cary, NC) was used to fit linear mixed effects regression models. Using 3 years of data, the models tested the associations between classes of substance use and adolescents' anxiety and depression over time.

Chapter 5

Manuscript 1

Substance use classes and symptoms of anxiety and depression among Canadian secondary school students

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5.1 Overview

Introduction: Few studies have assessed patterns of substance use among Canadian adolescents. This cross-sectional study examined substance use classes among Canadian secondary school students and associations with anxiety and depression.

Methods: This study used data from Year 6 (2017/18) of the COMPASS study. Students (n = 51 767) reported their substance use (alcohol, cannabis, cigarette, and e-cigarette use) and anxiety and depression symptoms. We employed latent class analysis to identify substance use classes and multinomial logistic regression to examine how anxiety and depression were associated with class membership.

Results: Overall, 40% of students indicated having anxiety and/or depression (50% in females; 29% in males) and 60% of students reported substance use (60% in females; 61% in males). We identified three substance use classes: *poly-use*, *dual use*, and *non-use*. Females with both anxiety and depression had the highest odds of being in the poly-use class compared to the non-use class (OR = 4.09 [95% CI: 3.59–4.65]) followed by females with depression only (2.65 [2.31–3.04]) and males with both anxiety and depression (2.48 [2.19–2.80]). Symptomology was also associated with belonging to the dual use class except among males with anxiety only (1.13 [0.94–1.37]).

Conclusion: Canadian secondary school students are engaging in dual and poly-substance use, and anxiety and depression were associated with such use. Females had a higher prevalence of anxiety and depression and should be a priority population for mental health programming.

Keywords: anxiety, depression, alcohol drinking, cannabis smoking, cigarette smoking, vaping, latent class analyses, adolescent

5.2 Highlights

- 40% of students indicated anxiety and/or depression and 60% of students reported substance use.
- Females had a higher prevalence of anxiety and/or depression (50% vs. 29%).
- Overall, anxiety and/or depression were associated with dual use and poly-substance use.
- Females with both anxiety and depression had the highest odds of being in the poly-substance use class.

5.3 Introduction

In 2017, 57% of Canadians aged 15 to 19 years reported alcohol use, 19% reported cannabis use, 8% reported cigarette smoking and 23% reported trying e-cigarettes.(56) Such use is associated with adverse mental, physical and academic outcomes.(212,213) Notably, recent evidence shows an estimated 23% of Canadian students in Grades 9 to 12 use more than one substance, also known as poly-substance use or poly-use.(7)

While the prevalence of substance non-use has remained steady among high school students over the past five years, poly-use is increasing among adolescents, likely due to the emergence of e-cigarettes.(2) A recent systematic review identified strong evidence for the presence of subgroups of adolescent substance use, with common clusters being low use, single- or dual-substance use, moderate general multi-use and high multi-use.(12) Unfortunately, there is limited research examining patterns of substance use among Canadian adolescents and how e-cigarette use fits in.(5,12,40,54) This is concerning, as poly-use is associated with higher risks of negative social and health consequences.(6,188)

Age has been consistently identified as a risk factor for poly-substance use.(12,55) The relationship between sex and poly-substance use is more nuanced. Most studies found males more likely to be in higher use categories,(2,5,7,28–30,42,44,214) but others have found no difference(13,45,66,67) or increased risk for females in certain poly-use classes,(46,69) or different latent classes.(53) Other individual-level factors associated with poly-substance use include lower socioeconomic status, early-onset substance use, low social connectedness and parental and peer substance use.(12,15,85,87,215,28,41,55,69,77,81–83)

Substance use has also been associated with adolescent anxiety and depression.(16,177) This is a common problem among adolescents: one-third of Ontario high school students report moderate-to-severe symptoms of anxiety and/or depression.(22) Generally, those who report poly-use have higher instances of poor mental health, including anxiety and depression.(6,11,88,184) However, one study identified protective effects of internalizing problems (which is a measure capturing anxiety, depression and somatic symptoms) on poly-use class membership among adolescents.(69)
Most of the work examining poly-use and poor mental health among adolescents has focussed on depression. However, there is a high prevalence of comorbidity, with an estimated 25% to 50% of youth with depression also meeting the criteria for an anxiety disorder.(150) These youth have a higher risk of longer duration of symptoms, greater impairment, re-occurrence and greater utilization

of mental health services.(150) Therefore, it is important to consider both depression and anxiety simultaneously in analyses.

In the context of the limitations in the current knowledge base, our objectives were to determine the substance use classes among Canadian secondary school students and examine their cross-sectional associations with anxiety and depression symptoms.

5.4 Methods

5.4.1 Design

The COMPASS study is a prospective cohort study that annually collects data from students in Grades 9 to 12 in British Columbia, Alberta and Ontario, and Secondary I to V in Quebec (the equivalent of Grades 7 to 11) in Canada. Students in Grades 7 and 8 equivalent or with no assigned grade were categorized as being in "other" grade. To examine cross-sectional patterns of substance use, this study used student questionnaire data from Year 6 (Y6: 2017/18) of the COMPASS study from 122 schools in British Columbia (n = 16), Alberta (n = 8), Ontario (n = 61), and Quebec (n = 37). Schools were purposively sampled based on permitted use of passive consent protocols.(199) A full description of the COMPASS study can be found online (https://uwaterloo.ca/compass-system/) or in print.(197)

5.4.2 Participants

A total of 66 434 students participated in Y6 of the COMPASS study. Student response rate was 81.8% and the primary reason for non-response was absenteeism at the time of data collection. Among respondents, 51 767 had complete data (complete information for covariates and at least one substance use measure) and were included in the final sample. There were no significant differences in chi-square tests comparing those included and excluded based on missing outcome data (Appendix B, Supplementary Table 4).

5.4.3 Measures

5.4.3.1 Substance use

Students were asked to report *alcohol use* ("In the last 12 months, how often did you have a drink of alcohol that was more than just a sip?"); *cannabis use* ("In the last 12 months, how often did you use marijuana or cannabis? (a joint, pot, weed, hash)"); *cigarette use* ("Have you ever tried cigarette

smoking, even just a few puffs?" and "On how many of the last 30 days did you smoke one or more cigarettes?"); and *e-cigarette use* ("Have you ever tried an electronic cigarette, also known as an e-cigarette?" and "On how many of the last 30 days did you use an e-cigarette?"). It should be noted that these measures are not equivalent to problematic substance use and should not be interpreted as such.

5.4.3.2 Anxiety

The *Generalized Anxiety Disorder 7* (GAD-7) scale(207) was used to assess generalized *anxiety symptoms*. The GAD-7 reports on self-perceived feelings of worry, fear and irritability over a two-week period. Students were asked how often they were bothered by each symptom with the following response options: "Not at all," "Several days," "Over half the days" or "Nearly every day." The GAD-7 has been found to be reliable among adolescents ($\alpha = 0.91$)(208) and in the current study had an alpha coefficient of 0.91 for females and 0.90 for males. When screening for anxiety disorders, a score of 10 is used as recommended cut point for further evaluation and was used to categorize students as having clinically relevant anxiety symptomatology (herein "anxiety").(207)

5.4.3.3 Depression

The Center for Epidemiological Studies Depression Scale (CES-D-10)(209,216) was used to assess *depression symptoms*. Items assess characteristics of clinical depression, including negative affect, anhedonia and somatic symptoms, such as "I felt everything I did was an effort," or "I could not get 'going.'" Students were asked how often they experienced each symptom within the last 7 days, with the following response options: "None or less than 1 day," "1–2 days," "3–4 days," or "5–7 days." The CES-D-10 has been found to be reliable among adolescents ($\alpha = 0.85$) and in the current study had an alpha coefficient of 0.74 for females and 0.78 for males. A score of 10 or higher is indicative of clinically relevant depression symptomatology (herein "depression").(209)

5.4.3.4 Covariates

Poly-substance use is associated with other risky behaviour(6,8–10,100) as well as family and friend support.(7) *Truancy* was used as a measure of student risky behaviour. Students were asked, "In the last 4 weeks, how many classes did you skip when you were not supposed to?" Students who reported any number of classes skipped were categorized as truant. To ascertain whether students felt they had *family* or *friend support*, they were asked how much they agreed with the statement "I can talk about

my problems with my family/friends." Students who selected "Agree" or "Strongly agree" were categorized as having family or friend support.

Consistent with other adolescent health research,(217) *sex* (male, female), *grade* (9, 10, 11, 12, other), *ethnicity* (White, non-White), and *weekly spending money* (zero, $1–$20, $21–$100, $100+, don't know), were included as demographic covariates.

5.4.4 Analysis

Descriptive statistics were calculated for the entire sample. Chi-square statistics and Cramer's V were used to compare descriptive statistics by sex for categorical variables. Cramer's V is a measure of effect size from 0 to 1 where values greater than 0.1 indicate an effect.(218)

To create substance use classes and examine their associations with anxiety and depression, latent class analysis (LCA)(52) was implemented using Mplus version 8.2 (Muthen & Muthen, Los Angeles, CA, USA). LCA is a measurement model that uses categorical variables to identify homogenous latent classes within the data that are mutually exclusive and exhaustive.(52) First, a series of LCA models were fit to determine the number of classes to best fit the data. Categorical indicators of alcohol use, cannabis use, cigarette use and e-cigarette use were used as latent class indicators.

Using multiple group LCA, we evaluated whether there were statistically significant differences in class membership by sex ($p < 0.05$). Sex was first used as a grouping variable to explore differences among male and female students. Chi-square tests for measurement invariance compared models where classes were fixed and then allowed to vary by sex. Tests indicated significant differences in classes between males and females. AIC (Akaike Information Criterion) and BIC (Bayesian Information Criterion) values indicated better model fit when classes were allowed to vary by sex. Therefore, separate classes were created for male and female students and the following steps were carried out separately for males and females.

To establish the best-fitting LCA solution, we started with a one-class solution and added classes until good fit was no longer obtained. We used log-likelihood, AIC, BIC, and the Lo-Mendell-Rubin adjusted likelihood ratio test (LMRT) as indicators of model fit. Lower log-likelihood, AIC and BIC values indicate better model fit.(219) The LMRT tests whether a model with k classes fits better than a model with $k-1$ classes; a significant result indicates that it does.(220) These model selection criteria, combined with model interpretability, were used to place participants into the appropriate

latent classes. While entropy was not used for model selection, it is reported as an indicator of classification from zero to one, with larger values indicating better latent class separation.(52,221) After identifying substance use classes using LCA, we conducted multinomial logistic regression to examine how anxiety and depression were associated with likelihood of membership in each class using the R3STEP command in Mplus.(210) Covariates included in the model were sex, grade, ethnicity, weekly spending money, family support, friend support and truancy. The TYPE=COMPLEX and CLUSTER commands in MPlus were used to account for the nesting of students within schools.

5.5 Results

5.5.1 Descriptive statistics

About half the sample was female, and over two-thirds identified as White (Table 1). In 2017/18, 40% of students reported no substance use, 22% reported the use of one substance (i.e. past-year use of alcohol or cannabis or ever use of cigarettes or e-cigarettes) and 38% reported the use of two or more substances. Just over half of students reported having used alcohol in the past year (52%), whereas most had not used cannabis in the past year (77%). Overall, 23% of students reported trying cigarettes and 37% reported trying e-cigarettes. Most students reported having family (59%) and friend (76%) support and no truancy in the past four weeks (67%). Overall, 40% of students indicated having anxiety and/or depression. Chi-square tests indicated significant differences by sex for all variables except grade, while Cramer's V only indicated an effect for e-cigarette use (ever use: female 32%; male 41%) and anxiety and depression (anxiety and/or depression: female 50%; male 29%).

Table 1. Descriptive characteristics of the Year 6 (2017/18) COMPASS sample (n = 51 767), by sex (British Columbia, Alberta, Ontario and Quebec, Canada)

Variable	Total sample		Female (n = 26 308)		Male (n = 25 459)		Chi-square / *t* test *p*-value	Cramer's V
	n	%	n	%	n	%		
Grade								
9	12 197	23.6	6 212	23.6	5 985	23.5	0.91	0.00
10	12 767	24.7	6 493	24.7	6 274	24.6		
11	12 406	24.0	6 328	24.0	6 078	23.9		
12	8 168	15.8	4 111	15.6	4 057	15.9		
Other[a]	6 229	12.0	3 164	12.0	3 065	12.0		
Ethnicity								

White	34 890	67.4	17 859	67.9	17 031	66.9	0.02	0.01
Non-White	16 877	32.6	8 449	32.1	8 428	33.1		
Weekly spending money								
Zero	8 318	16.1	3 777	14.4	4 541	17.8	< 0 .01	0.08
$1–$20	13 029	25.2	6 750	25.7	6 279	24.7		
$21–$100	12 433	24.0	6 755	25.7	5 678	22.3		
$100+	9 819	19.0	4 545	17.3	5 274	20.7		
Don’t know	8 168	15.8	4 481	17.0	3 687	14.5		
Past-year alcohol use								
None	24 537	47.6	12 184	46.5	12 353	48.7	< 0.01	0.08
< 1 x /month	10 532	20.4	5 939	22.7	4 593	18.1		
1–3 x /month	11 930	23.1	6 256	23.9	5 674	22.4		
≥ 1 x /week	4 568	8.9	1 838	7.0	2 730	10.8		
Missing	200							
Past-year cannabis use								
None	39 808	77.1	20 459	77.9	19 349	76.2	< 0.01	0.06
< 1 x /month	4 959	9.6	2 724	10.4	2 235	8.8		
1–3 x /month	3 088	6.0	1 556	5.9	1 532	6.0		
≥ 1 x /week	3 790	7.3	1 515	5.8	2 275	9.0		
Missing	122							
Cigarette use								
None	39 820	77.0	20 456	77.8	19 364	76.1	< 0 .01	0.04
Ever use	7 049	13.6	3 609	13.7	3 440	13.5		
1–5 days (in past month)	2 790	5.4	1 358	5.2	1 432	5.6		
6+ days (in past month)	2 067	4.0	869	3.3	1 198	4.7		
Missing	41							
E-cigarette use								
None	32 616	63.4	17 733	67.7	14 883	58.9	< 0 .01	0.13
Ever use	7 522	14.6	3 741	14.3	3 781	15.0		
1–5 days (in past month)	6 844	13.3	3 278	12.5	3 566	14.1		
6+ days (in past month)	4 494	8.7	1 447	5.5	3 047	12.1		
Missing	291							
Family support								
No	21 245	41.0	11 632	44.2	9 613	37.8	< 0.01	0.07
Yes	30 522	59.0	14 676	55.8	15 846	62.2		
Friend support								
No	12 684	24.5	6 012	22.9	6 672	26.2	< 0.01	−0.04
Yes	39 083	75.5	20 296	77.2	18 787	73.8		
Truancy								
No	34 648	66.9	17 212	65.4	17 436	68.5	< 0.01	−0.03
Yes	17 119	33.1	9 096	34.6	8 023	31.5		
Anxiety and depression symptoms								
None	31 335	60.5	13 224	50.3	18 111	71.1	< 0.01	0.24

Anxiety only	2 209	4.3	1 450	5.5	759	3.0
Depression only	7 764	15.0	4 206	16.0	3 558	14.0
Both	10 459	20.2	7 428	28.2	3 031	11.9

Notes: Anxiety symptoms were assessed using the GAD-7 scale; depression symptoms were assessed using the CES-D-10. A score of ≥ 10 was used as the cut-off to indicate anxiety and depression. Family/friend support refers to students agreeing with the statement "I can talk about my problems with my family/friends."
[a] Primarily Grades 7 and 8 equivalents.

5.5.2 Substance use classes

A three-class model was selected as the best fitting model, as it had lower values for the model selection criteria and a more appropriate interpretation than its smaller and larger counterparts (Table 2).

Table 2. Model fit indices for 1 through 7 latent class models of substance use among female and male students in Year 6 (2017/18) of the COMPASS study

Number of classes	Log-likelihood	FP	AIC	BIC	LMRT *p*-value	Entropy
Female						
1	−96 491.1	12	193 006.2	193 066.2	—	1.00
2	−84 113.0	25	168 276.0	168 400.9	0.00	0.82
3	**−82 633.7**	**38**	**165 343.4**	**165 533.4**	**0.00**	**0.76**
4	−82 435.3	51	164 972.6	165 227.6	0.02	0.78
5	−82 247.2	64	164 622.4	164 942.3	0.77	0.74
6	−82 191.3	77	164 536.7	164 921.6	0.78	0.69
7	−82 157.8	90	164 495.5	164 945.5	0.79	0.72
Male						
1	−100 222.3	12	200 468.7	200 528.3	—	1.00
2	−86 759.7	25	173 569.5	173 693.6	0.00	0.84
3	**−85 059.5**	**38**	**170 195.0**	**170 383.7**	**0.00**	**0.76**
4	−84 853.8	51	169 810.0	170 062.9	0.06	0.73
5	−84 744.9	64	169 617.7	169 935.6	0.26	0.74
6	−84 706.9	77	169 567.8	169 950.2	0.66	0.74
7	Did not converge					

Abbreviations: AIC, Akaike information criterion; BIC, Bayesian information criterion; FP, free parameters; LMRT, Lo-Mendell-Rubin Test.
Notes: Bold typeface signifies class model selected. "—" signifies no value.

The three classes identified in this study were named *poly-use class*, *dual use class* and *non-use class* (Table 3; Figure 1). The high-use class, *poly-use*, made up 11% of the female sample and 15% of the male sample. This class had the highest probability of all forms of substance use. Female

students in this class were most likely to use alcohol one to three times per month and cannabis once per week or more often, to have tried cigarettes and to use e-cigarettes on six or more days in the past month. Male students in this class were most likely to use alcohol and cannabis once per week or more, to have used cigarettes one to five days in the past month and to have used e-cigarettes six or more days in the past month. The *dual use class* made up 26% of the female sample and 26% of the male sample. This class had a relatively high probability of alcohol and e-cigarette use, and a lower probability of cannabis and cigarette use. Finally, the *non-use class* represented the students reporting no or low use. This class made up 62% of the female sample and 59% of the male sample. All students in this class were most likely to report no past-year alcohol or cannabis use and never having tried cigarettes or e-cigarettes.

Table 3. Conditional item-response probabilities and the prevalence of latent classes of female and male substance use behaviours in Year 6 (2017/18) of the COMPASS study

	Female			Male		
Variable	**Class 1 Poly-use**	**Class 2 Dual use**	**Class 3 Non-use**	**Class 1 Poly-use**	**Class 2 Dual use**	**Class 3 Non-use**
Latent class prevalence	11.4%	26.2%	62.4%	14.7%	26.0%	59.3%
Past-year alcohol use						
None	0.04	0.10	0.73	0.05	0.15	0.76
< 1 x /month	0.11	0.35	0.19	0.09	0.32	0.14
1–3 x /month	0.49	0.47	0.08	0.40	0.43	0.08
≥ 1 x /week	0.36	0.08	0.01	0.47	0.10	0.02
Past-year cannabis use						
None	0.11	0.63	1.00	0.13	0.63	0.99
< 1 x /month	0.21	0.27	0.00	0.17	0.22	0.01
1–3 x /month	0.28	0.09	0.00	0.22	0.10	0.00
≥ 1 x /week	0.41	0.02	0.00	0.49	0.05	0.00
Cigarette use						
None	0.12	0.64	0.98	0.12	0.66	0.98
Ever use	0.33	0.31	0.02	0.29	0.29	0.02
Past month, 1–5 days	0.30	0.05	0.00	0.30	0.04	0.00
Past month, 6+ days	0.25	0.01	0.00	0.30	0.01	0.00
E-cigarette use						
None	0.15	0.35	0.95	0.06	0.23	0.90
Ever use	0.17	0.34	0.04	0.09	0.34	0.07
Past month, 1–5 days	0.33	0.27	0.01	0.27	0.32	0.02
Past month, 6+ days	0.35	0.04	0.00	0.58	0.11	0.00

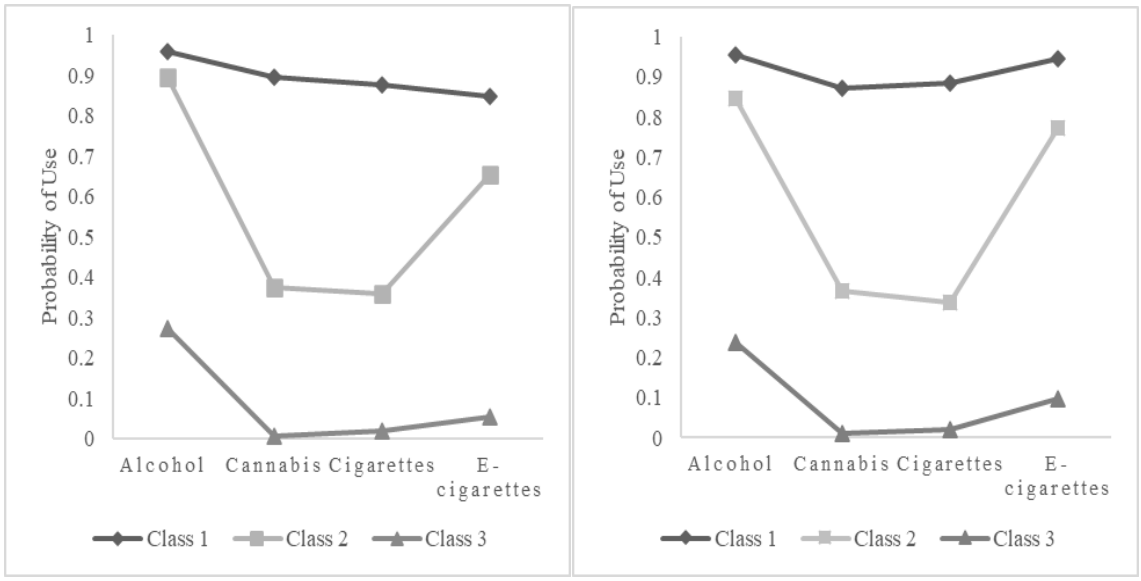

Figure 1. Substance use item probabilities for three-class latent class model for females (left) and males (right) in Year 6 (2017/18) of the COMPASS study

5.5.3 Mental illness and substance use classes

Anxiety and depression were first explored descriptively by substance use class in Figure 2. Among females, those with only anxiety had 1.48 (95% CI: 1.20–1.83) higher odds of being in the poly-use class and had 1.33 (1.16–1.51) higher odds of being in the dual use class than in the non-use class (Table 4). Those with only depression had 2.65 (2.31–3.04) higher odds of being in the poly-use class and 1.48 (1.34–1.64) higher odds of being in the dual use class compared to the non-use class. Finally, those with both anxiety and depression had 4.09 (3.59–4.65) higher odds of being in the poly-use class and 1.81 (1.65–1.99) higher odds of being in the dual use class than in the non-use class. Among males, those with only anxiety had 1.41 (1.14–1.73) higher odds of being in the poly-use class compared to the non-use class. Differences between the dual use and non-use class were not statistically significant. Those with only depression had 1.69 (1.52–1.87) higher odds of being in the poly-use class and 1.21 (1.10–1.34) higher odds of being in the dual use class compared to the non-use class. Finally, those with both anxiety and depression had 2.48 (2.19–2.80) higher odds of being in the poly-use class and 1.18 (1.05-1.32) higher odds of being in the dual use class.

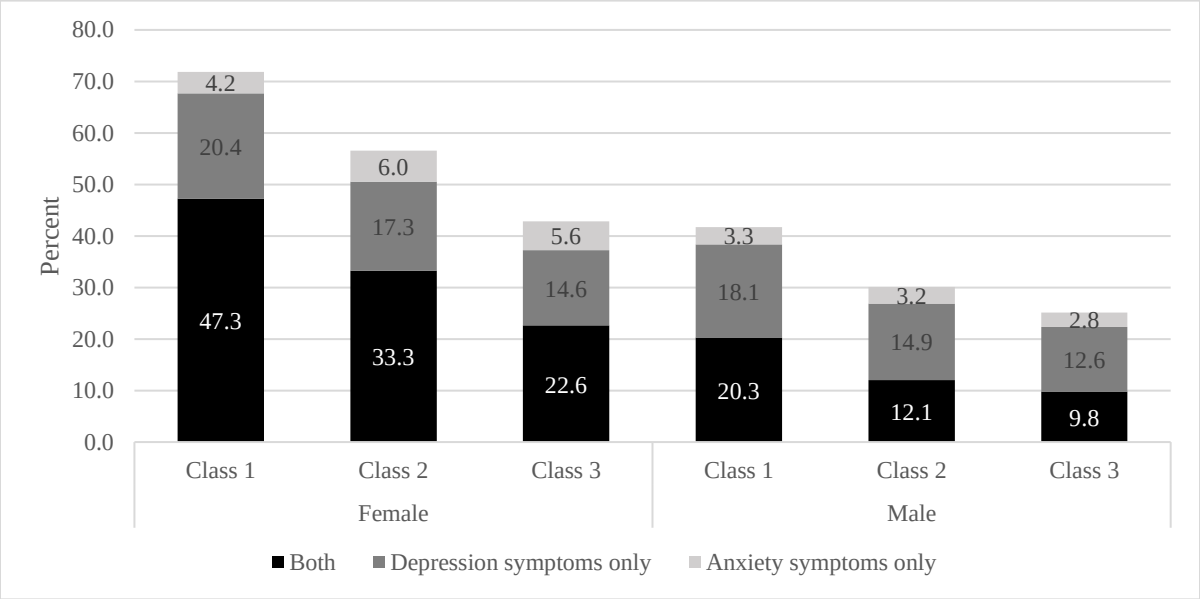

Figure 2. Estimated proportion of students reporting clinically meaningful symptoms of anxiety, depression or both in each of the three latent classes of substance use in Year 6 (2017/18) of the COMPASS study, by sex

Table 4. Substance use class membership by symptoms of anxiety and/or depression in Year 6 (2017/18) of the COMPASS study, by sex

Female students	Class 1 vs. Class 3	Class 2 vs. Class 3
None	1.00	1.00
Anxiety symptoms only	1.48 (1.20–1.83)	1.33 (1.16–1.51)
Depression symptoms only	2.65 (2.31–3.04)	1.48 (1.34–1.64)
Both	4.09 (3.59–4.65)	1.81 (1.65–1.99)
Male students	**n/a**	**n/a**
None	1.00	1.00
Anxiety symptoms only	1.41 (1.14–1.73)	1.13 (0.94–1.37)
Depression symptoms only	1.69 (1.52–1.87)	1.21 (1.10–1.34)
Both	2.48 (2.19–2.80)	1.18 (1.05–1.32)

Abbreviation: CI, confidence interval.
Note: Models adjusted for grade, ethnicity, weekly spending money, family support, friend support and truancy. Class 1 is poly-use, class 2 is dual use and class 3 is non-use

5.6 Discussion

This study examined a sample of Canadian adolescents from Alberta, British Columbia, Ontario and Quebec schools. We identified that three in five adolescents used one or more substances and two in five students experienced clinically relevant psychiatric symptomatology. Co-occurrence of anxiety and depression was high, especially among female students; few students identified as having anxiety alone. The high prevalence of substance use and symptoms of mental illness in this population during an important developmental period is a cause for concern.

Despite statistical tests indicating that classes differed by sex, similar classes were identified for female and male students. Results from the latent class analysis indicated three different patterns of substance use: poly-substance use, dual substance use and non-use. While similar classes were identified for female and male students, a higher proportion of male students were in the poly-substance use class and male students were more likely to use substances at a higher frequency. This result supports research that has found males more likely to belong to higher-use categories,(2,5,7,28–30,42,44,214) although others have found no difference(13,45,66,67) or increased risk for females in certain poly-use classes (e.g. nonmedical use of prescription medication, not measured in this study).(46,69) It should be noted that measures of substance use did not differentiate between simultaneous use (i.e. "true" co-use) and concurrent use (i.e. sequential use); therefore, students in the poly-substance use class did not necessarily use substances simultaneously.

These results are consistent with a recent systematic review that identified typical patterns of substance use among adolescents: a low-use or no-use class comprising the most adolescents, a predominantly alcohol-use class, and finally high multi-use groups.(12) Our study findings differed from that review in two main ways. First, we identified only one multi-use group, while other studies have identified a moderate and a high multi-use group;(42,63,69,72,75,222) although many of these surveys included additional illicit substances (i.e. ecstasy, amphetamines, cocaine),(42,69,222) which were not examined in this study. Second, rather than a predominantly alcohol-use class, we identified a dual use class that also included trying e-cigarettes. This is similar to a USA study that identified an alcohol and e-cigarette use class.(5) These findings highlight that adolescent prevention and treatment strategies should consider substance use patterns, including dual and poly-substance use.

The current study highlights the importance of including e-cigarette use or vaping when examining patterns of adolescent substance use. It is often included with cigarettes as a tobacco product; however, trends in use are diverging.(223) For example, in 2017/18, 13% of adolescents reported exclusive e-cigarette use while only 3% reported cigarette use and 5% reported dual use,

although e-cigarette use has been found to predict future dual use.(224) While previous studies have identified an “alcohol only” class,(53,63,102) that was not the case in this study. Our dual use class comprised a quarter of the students, and the presence of this class indicates that students who were previously only experimenting with alcohol a few times per month may now also be experimenting with e-cigarettes. In the poly-substance use class, e-cigarette use was more frequent. Due to the negative effects of nicotine on the developing brain (225) and the largely unknown long-term effects of e-cigarette use on lung health,(226) the prevalence of this dual use class is concerning and should be considered in future work examining adolescent substance use. It is important for surveillance work to be able to monitor the use of new substances that emerge in the marketplace and how new products and changes to regulations may impact substance use profiles among adolescents.

The descriptive statistics showed a gradient in mental illness symptom prevalence across classes. Those in the poly-use class had the highest prevalence of anxiety and depression, followed by the dual use class and the non-use class. While other studies have also identified this gradient, it has not been previously examined by sex.(6,88) Notably, prevalence of anxiety and depression in the lowest-risk group (i.e. non-use) among females (23%) was similar to prevalence in the highest-risk group (i.e. poly-substance use) among males (20%). Based on these findings, female students should be a priority population for mental health programming.

This study identified an association between substance use classes and anxiety and depression. These results are in line with many other studies that have examined adolescent substance use and anxiety and/or depression.(6,11,88) While the current research does not address direction of effect, some explanatory theories for this relationship have been proposed. First is the hypothesis that individuals use substances to cope with existing symptoms.(193) This is supported by evidence that has found that depression during adolescence predicts future increased substance use, although there are variations by sex and substances used.(15,194,195) Nevertheless, the evidence does not always support this direction of effect.(16) Other researchers hypothesize lowered mood is a direct result of substance use in adolescence.(196) Regardless of the direction of effect, these results emphasize the need to assess symptoms of anxiety and/or depression among students who are found to be using substances and vice versa.

It should be noted that, in contrast to our results, Halladay et al. (12) identified subgroups of adolescents with distinct substance use and mental health concerns. While we were not able to identify these students in regression analyses, they were present in our descriptive examination of our

sample. For example, 28% of females and 58% of males in the poly-substance use class did not report anxiety or depression.

5.6.1 Strengths and limitations

This study has several strengths. The COMPASS study has a large sample size and uses measures based on national surveillance tools.(217) The questionnaire uses an active-information passive-consent protocol to encourage participation and honest reporting, which has been shown to be particularly important in substance use and mental health research.(199–201) In addition, this study had a good participation rate, with data available for 78% of all participants. Finally, we made use of validated scales for anxiety and depression to assess students' symptoms.

This study was not without limitations. First, we made use of cross-sectional data, preventing causal inferences. Second, the COMPASS study was designed to evaluate changes in school programs and policies and therefore uses a convenience sample that is not representative of Canadian high school students. Third, there are limitations to the questionnaire used. There could be reporting bias in the substance use questions due to their illicit nature for underage youth, participants may have underreported substance use. Other illicit substances were not examined in this study, potentially further contributing to the underreporting of substance use. The questionnaire also lacked a definition of e-cigarette use and may have also captured some cannabis use in this measure. Additionally, measures of anxiety, depression and substance use were not indicative of diagnosed clinical disorders. These disorders are prevalent and have a large impact on health service use among young people.(110,227) Next, we were also lacking measures of peer or family substance use, which is associated with early initiation and escalating use through adolescence.(215) However, this study made use of variables indicating family and friends support, which have been positively and negatively associated with poly-substance use respectively.(7) Furthermore, there were no measures available of parental psychopathology, which is a significant risk factor for children.(144,145) Fourth, there was much missing data on the outcome in this study (19%); however, there were no significant differences in the outcome variable in chi-square tests comparing those included and those excluded based on missing data.

5.7 Conclusion

Half of female students and almost one-third of male students reported clinically relevant symptoms of anxiety and/or depression. Co-occurrence of anxiety and depression was common, and

few students reported anxiety only. We identified three substance use classes: poly-use, dual use and non-use. Those with both anxiety and depression or depression only were more likely to belong to the poly-substance use and dual use classes than the non-use class. Anxiety was associated with belonging to the poly-substance use class among female and male students and belonging to the dual use class among female students.

Chapter 6
Manuscript 2

Exploring the bi-directional associations between poly-substance use and symptoms of anxiety and depression among a large sample of Canadian adolescents

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6.1 Overview

Objective: Research has demonstrated a cross-sectional link between poly-substance use and anxiety and depression. However, there is limited evidence examining these relationships longitudinally. The objective of this study was to better understand the bi-directional relationship between poly-substance use and anxiety and depression among a large sample of Canadian high school students stratified by sex.

Methods: This study used data from 3 waves (Wave 1: 2017/18, Wave 2: 2018/19, and Wave 3: 2019/20) of the COMPASS study. Students in grades 9 and 10 (n=2179) were linked over time and reported their past month substance use (alcohol, cannabis, cigarettes, and e-cigarettes) and anxiety and depression symptoms at each wave. Using cross-lagged models, we explored bi-directional associations between 1) number of substances used and anxiety and depression among all students and 2) poly-substance use compared to single substance use and anxiety and depression among students who used substances (n=401), adjusting for relevant covariates.

Results: By Wave 3, 27% of students reported poly-substance use. We found uni-directional effects among youth who used substances from Wave 2 to Wave 3: poly-substance use was associated with anxiety symptoms (β=0.74 [95% CI: 0.20-1.27]) among female students and anxiety (β=0.82 [95% CI: 0.32-1.32]) and depression (β=1.08 [95% CI: 0.59-1.57]) symptoms among male students.

Conclusions: Our findings suggest that engaging in poly-substance use compared to single substance use may worsen anxiety and depression symptoms among high school students who use substances. These findings highlight the need for prevention programs to address poly-substance use and account for potential differences between female and male students.

Keywords: anxiety, depression, alcohol drinking, cannabis smoking, cigarette smoking, vaping, adolescent

6.2 Introduction

Poly-substance use is the use of more than one substance (e.g., alcohol, cannabis, cigarettes) within a specified period.(1) Recent evidence indicates that 23% of Canadian students in grades 9-12 engage in poly-substance use with alcohol and e-cigarette use being the most common combination of substances in recent years.(2,40,189) Generally, poly-substance use is associated with further risky behaviours (e.g., risky sexual behaviour, gambling) and negative health outcomes above and beyond using each substance in isolation, including poor mental health and mental ill-health.(6–10) For instance, poly-substance use has been associated with elevated symptoms of depression and anxiety among adolescents aged 11 to 18 in cross-sectional studies.(12,189)

However, among studies that have examined depression symptoms at baseline and poly-substance use at follow-up, none have identified significant effects after controlling for covariates.(15,16) A small cohort study examined the effect in the opposite direction and identified that youth that used the highest number of substances had the highest depression scores at follow-up, although this study did not control for covariates.(20) Another study identified a reciprocal relationship between poly-substance use and depression symptoms suggesting a more complex relationship between these two variables.(186) There is one study to date that has examined the longitudinal relationship between anxiety and poly-substance use and found higher anxiety to be protective against future poly-substance use.(19) This limited and contrasting research highlights the need for further exploration of the bidirectional associations between poly-substance use and anxiety and depression.

Additionally, previous longitudinal studies have not explored sex differences even though previous cross-sectional studies have identified important sex differences that should be further explored.(12,189) Patterns of poly-substance use, anxiety, and depression differ between female and male adolescents.(12,22,189) Female students report higher anxiety and depression symptoms(22–25) and these sex differences tend to increase across adolescence.(26,27) Conversely, male students typically report higher levels of poly-substance use, both more substances and higher frequency of use.(7,12,189) Adolescence is a critical developmental period as over half of mental disorder symptoms are thought to initiate during this time.(31) Having a better understanding of these relationships including any sex-based differences can help in tailoring prevention programming to different groups.

Therefore, the objective of this study was to examine the bi-directional associations between poly-substance use and symptoms of anxiety and depression among a sample of Canadian high school students stratified by sex.

6.3 Methods

6.3.1 Design

The COMPASS study is a prospective cohort study that collects data annually from students in British Columbia, Alberta, Ontario, and Quebec in grades 9 to 12 (Secondary I-V in Quebec). The current study used three waves of data from the COMPASS study (Wave 1: 2017/18, Wave 2: 2018/19, and Wave 3: 2019/20). All procedures were approved by the University of Waterloo Office of Research Ethics (reference number 30118) and appropriate school board committees. A more detailed description of the COMPASS study is available online (https://uwaterloo.ca/compass-system/) or in print.(197)

6.3.2 Participants

Overall, 122 schools (British Columbia, n=16; Alberta, n=8; Ontario, n=61; and Quebec, n=37) participated in the COMPASS study at Wave 1. Due to school closures because of COVID-19 in March 2020, only 29 schools (British Columbia, n=5; Alberta, n=5; Ontario, n=17; and Quebec, n=2) consistently completed the same questionnaire all 3 waves and were included in this study. In these schools, 7065 students in grades 9 and 10 (Secondary III in Quebec, grade 9 equivalent) participated at Wave 1. 2904 (41%) students were successfully linked across all three waves in the 29 schools. There were significant differences in substance use and anxiety and depression scores between linked and unlinked students (Supplementary Table 7). After missing data from independent variables was removed, 2179 (75%) had complete data for all three waves, making up our final sample. Those who were not linked had significantly higher depression scores (Supplementary Table 8).

6.3.3 Measures

6.3.3.1 Substance use

At each wave, students were asked about their *alcohol use* (“In the last 12 months, how often did you have a drink of alcohol that was more than just a sip?”), *cannabis use* (“In the last 12 months,

how often did you use marijuana or cannabis? (a joint, pot, weed, hash).”), *cigarette use* (“On how many of the last 30 days did you smoke one or more cigarettes?”), and *e-cigarette use* (“On how many of the last 30 days did you use an e-cigarette?”). Monthly use or more of alcohol and cannabis and past 30-day use of cigarettes or e-cigarettes was considered current substance use. We then calculated the number of substances currently used by summing current use of alcohol, cannabis, cigarettes, and e-cigarettes at each wave.

For part 2, a poly-substance use variable was calculated among the students who used at least one substance in every wave (n=401). Students were categorized as reporting single substance use (reported 1 substance in the past 30 days) or poly-substance use (reported 2+ substances in the past 30 days) at each wave.

6.3.3.2 Anxiety

The Generalized Anxiety Disorder 7 (GAD-7) scale(207) was used to assess generalized anxiety symptoms at each wave of the study. The GAD-7 reports on self-perceived feelings of worry, fear, and irritability over a 2-week period. Students were asked how often they were bothered by each symptom with the response options: “Not at all”, “Several days”, “Over half the days”, or “Nearly every day”. Responses were scored from 0 to 3, respectively, and summed. Total scores range from 0 to 21 and higher total scores indicate greater anxiety symptoms. The GAD-7 had an alpha coefficient of 0.91 for females and 0.87 for males at Wave 1.

6.3.3.3 Depression

The Centre for Epidemiological Studies Depression Scale (CES-D-10)(209,216) was used to assess depression symptoms at each wave of the study. Items assess characteristics of clinical depression, including negative affect, anhedonia, and somatic symptoms, such as “I felt everything I did was an effort” and “I could not get ‘going.’” Students were asked how often they experienced each symptom within the last 7 days, with the response options: “None or less than 1 day”, “1–2 days”, “3–4 days”, or “5–7 days”. Responses were scored from 0 to 3, respectively, and summed. Total scores range from 0 to 30 and higher total scores indicate greater depressive symptoms. The CES-D-10 had an alpha coefficient of 0.69 for females and 0.71 for males at Wave 1.

6.3.3.4 Covariates

Poly-substance use, anxiety, and depression are associated with other risky behaviour and family and friend support.(6–10) Skipping school was used as a measure of student risky behaviour. Students were asked "In the last 4 weeks, how many classes did you skip when you were not supposed to?" Students who reported any number of classes skipped were categorized as truant. To ascertain whether students felt they had family or friend support, they were asked how much they agreed with the statements "I can talk about my problems with my family/friends." Students who selected "Agree" or "Strongly Agree" were categorized as having family or friend support. These variables were assessed each wave of the study.

Sex (male, female), grade (9, 10), ethnicity (White, non-White), and weekly spending money (zero, $1-$20, $21-$100, $100+, don't know/missing), were included as demographic covariates. Grade, sex, and ethnicity were assessed at Wave 1 and weekly spending money was assessed at each wave.

6.3.4 Analyses

Descriptive statistics were used to examine the Wave 1 characteristics of the linked longitudinal samples and the prevalence of number of substances used, poly-substance use, anxiety, and depression in each wave of the study. Chi-square statistics, Cramer's V, and T-tests were used to compare descriptive statistics by sex.

We also examined the number of substances used, poly-substance use, anxiety, and depression across waves. Statistical significance was set at $p=0.01$ to account for multiple comparisons. Wilcoxon signed-rank tests were used to compare difference scores over time for the number of substances used variable. McNemar's test was used to compare the binary poly-substance use variable over time. Paired t-tests were used to compare anxiety and depression scores over time.

Auto-regressive cross-lagged models simultaneously tested the auto-regressive effects of number of substances used/poly-substance use, anxiety, and depression at each wave and the bi-directional relationships between number of substances used/poly-substance use, anxiety, and depression at each wave (i.e., whether the number of substances used at Wave 1 predicted subsequent anxiety and depression scores at Wave 2 and vice versa). Based on previous evidence of sex differences, separate models were conducted for females and males.(12,189) The auto-regressive cross-lagged analyses were performed using Mplus version 8.2 (Muthen & Muthen, Los Angeles, CA, USA). In part 1, these models were conducted in the full sample examining number of

substances used using maximum likelihood estimation. However, these analyses were not able to differentiate between poly-substance use, single substance use, and no substance use. Therefore, a secondary analysis was completed to examine poly-substance use compared to single substance use. In part 2, models were conducted in a sample of those who reported single or poly-substance use each wave (n=401) to compare the two. Part 2 analyses were performed using robust mean and variance-adjusted weighted least-squares estimation (WLSMV). All models were adjusted for grade and ethnicity at Wave 1 and spending money, family and friend support, and skipping school at each wave. The TYPE=COMPLEX and CLUSTER commands in MPlus were used to account for the nesting of students within schools. Missing data on dependent variables in cross-lagged models was handled using Full Information Maximum Likelihood (FIML).

The fit of the cross-lagged models was assessed using the chi-square test of model fit ($p>0.05$), Root Mean Square Error of Approximation (RMSEA) (≤ 0.05), Comparative Fit Index (CFI) (>0.95), and Standardized Root Mean Square Residual (SRMR) (<0.08).(228) Models that met an a-priori threshold of 3 out of 4 tests were considered to have good model fit.(229)

6.4 Results

6.4.1 Descriptive characteristics

The sample (n=2179) was approximately half female (54%) and in grade 9 (54%) in Wave 1 (Table 5). Across waves, there were significant differences in number of substances used, anxiety, and depression (Supplementary Table 9). In Wave 1, 9% of students reported poly-substance use. By Wave 3, 27% of students reported poly-substance use. The most common pattern of poly-substance use was alcohol and e-cigarettes across all three waves (Supplementary Table 10).

Table 5. Characteristics at Wave 1 (2017/18) by sex, among high school students linked across 3 waves (2017/18-2019/20) of the COMPASS study (n=2179)

Wave 1 variables	Female (n=1187)		Male (n=992)		Chi-square / t-test p-value	Cramer's V
	n	%	n	%		
Grade						
9	662	55.77	521	52.5	0.1293	0.0325
10	525	44.23	471	47.5		
Ethnicity						
White	807	67.99	675	68.0	0.9770	-0.0006
Non-White	380	32.01	317	32.0		

Weekly spending money						
Zero	251	21.15	247	24.9	0.0422	0.0674
$1-$20	435	36.65	322	32.5		
$21-$100	216	18.20	187	18.9		
$100+	87	7.33	91	9.2		
Don't know/missing	198	16.68	145	14.6		
Number of substances used						
0	941	79.3	740	74.6	0.0151	0.0752
1	145	12.2	151	15.2		
2	64	5.4	53	5.3		
3	29	2.4	29	2.9		
4	8	0.7	19	1.9		
Family support						
No	487	41.3	321	32.7	<.0001	0.0890
Yes	692	58.7	662	67.3		
Missing	8		9			
Friend support						
No	304	25.6	292	29.6	0.0373	-0.0447
Yes	883	74.4	694	70.4		
Missing			6			
Skipping school						
No	990	84.5	839	85.8	0.4198	-0.0174
Yes	181	15.5	139	14.2		
Missing	16		14			
Anxiety score (GAD-7; mean, SD)	7.5	5.7	4.2	4.4	<.0001	
Depression score (CESD; mean, SD)	9.3	6.1	6.8	4.7	<.0001	

Note: Variables with missing values were included in models only in Waves 2 and 3 and missing values at those time points were removed

Among the sample of students who used at least one substance per wave (n=401) was approximately half female (49%) and had slightly more students in grade 10 (58%) (Supplementary

Table 11). Across waves, there were significant differences in poly-substance use, anxiety, and depression (Supplementary Table 12).

6.4.2 Part 1: Number of substances used

Figure 3 presents the results of the auto-regressive cross-lagged models among females and Figure 4 presents these results for males. The RMSEA, CFI, and SRMR showed adequate fit for these models (Female: RMSEA=0.043 [90% CI: 0.036-0.051], CFI=0.976, SRMR=0.025; Male: RMSEA=0.047 [90% CI: 0.039-0.055], CFI=0.970, SRMR=0.029).

Controlling for relevant covariates, we identified a significant uni-directional association between number of substances and anxiety from Wave 1 to Wave 2 among male students only: a 1-unit increase in the number of substances used was associated with a -0.39 decrease in anxiety score. Auto regressive and some bi-directional effects were also observed but were not the focus of this study (available in Supplementary Table 13).

6.4.3 Part 2: Poly-substance use versus single substance use

Figures 5 and 6 present the results of the auto-regressive cross-lagged models among students that used at least one substance in each wave to compare poly-substance use and single substance use. The chi-square test, RMSEA, and SRMR showed adequate fit for the female model (chi-square p-value= 0.2433, RMSEA=0.026 [90% CI: 0.000-0.054], SRMR=0.077) and the chi-square test, RMSEA, CFI, and SRMR showed adequate fit for the male model (chi-square p-value= 0.2025, RMSEA=0.028 [90% CI: 0.000-0.055], CFI=0.952, SRMR=0.077).

Controlling for relevant covariates, a significant uni-directional association was seen between poly-substance use and anxiety among female students from Wave 2 to Wave 3: after adjusting for covariates, compared to single substance use, poly-substance use in Wave 2 was associated with a 0.74 higher anxiety score in Wave 3 (95% CI: 0.20-1.27). Significant uni-directional associations were found between poly-substance use and anxiety and depression among male students from Wave 2 to Wave 3. Poly-substance use in Wave 2 was associated with a 0.82 higher anxiety score (95% CI: 0.32-1.32) and a 1.08 (95% CI: 0.59-1.57) higher depression score in Wave 3. Auto regressive and some bi-directional effects were also observed but were not the focus of this study (available in Supplementary Table 14).

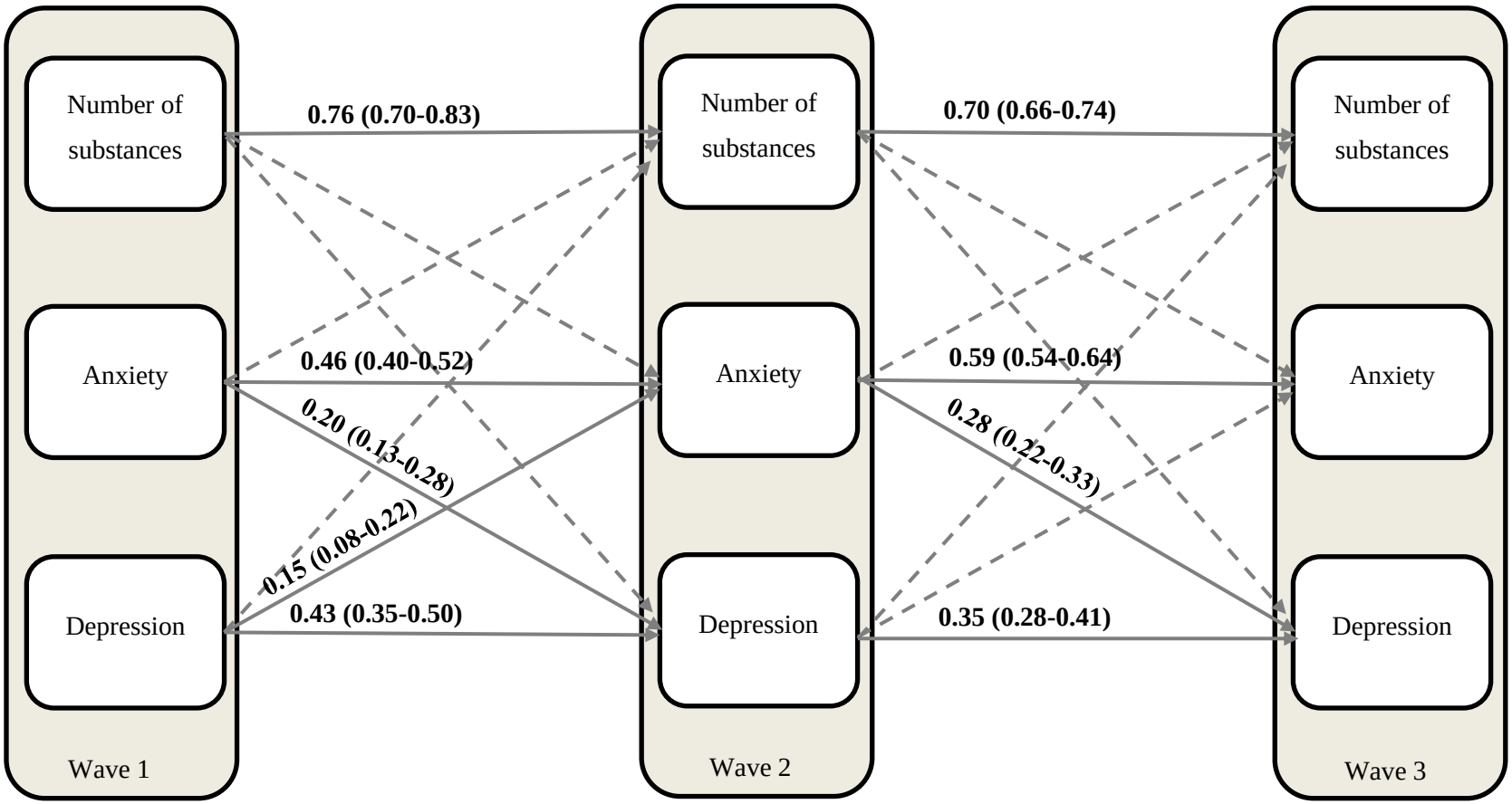

Figure 3. Cross-lag relationships between number of substances used and anxiety and depression scores among female students participating in all three waves of the study (n = 1187), adjusted for grade, ethnicity, weekly spending money, having friend and family support, and skipping school. Adjusted beta estimates and 95% confidence intervals are presented for pathways significant at p<0.05. The solid lines indicate significant effects ($p < 0.05$), while the dashed lines indicate non-significant effects ($p > 0.05$).

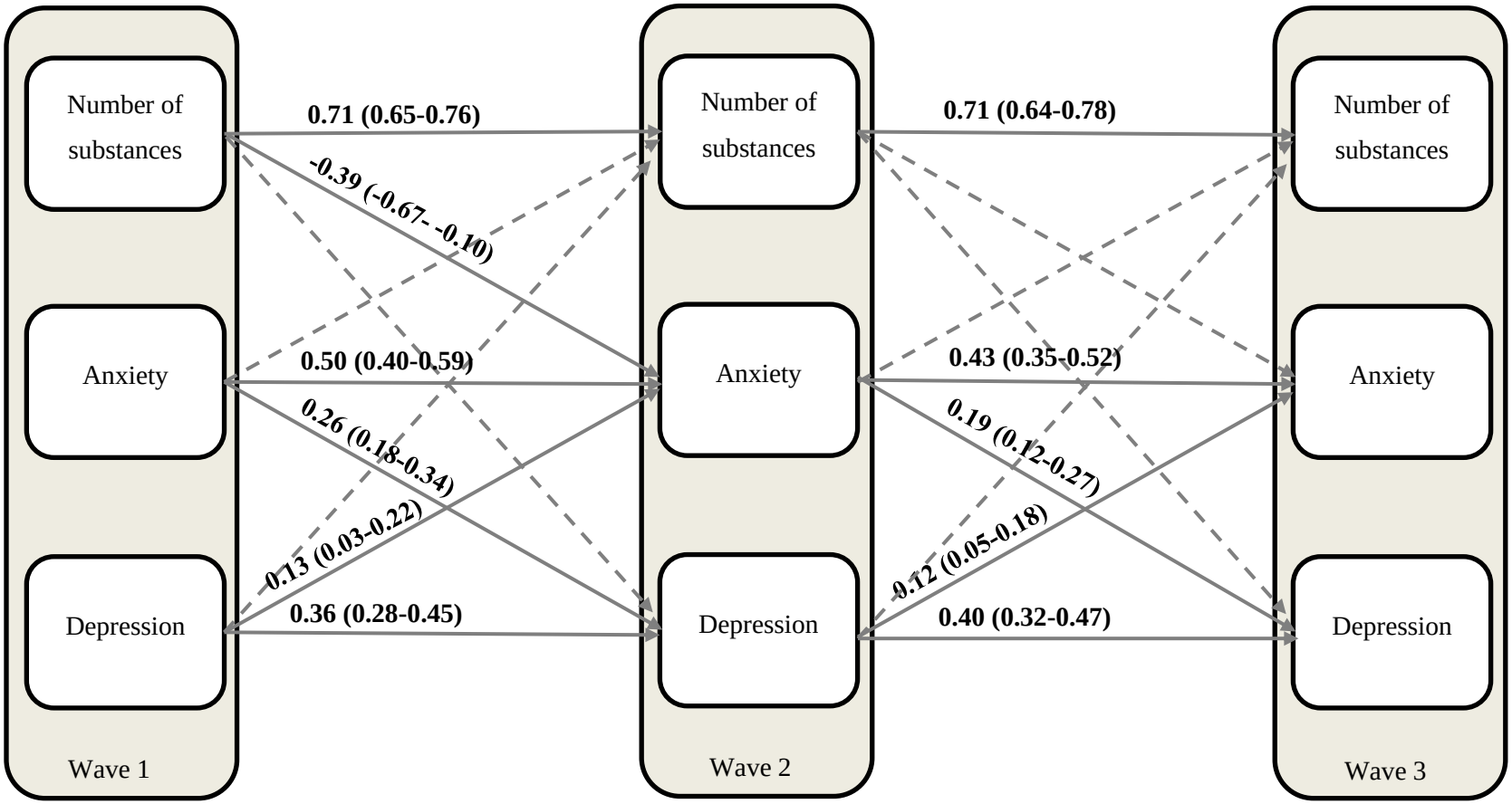

Figure 4. Cross-lag relationships between number of substances used and anxiety and depression among male students participating in all three waves of the study (n = 992), adjusted for grade, ethnicity, weekly spending money, having friend and family support, and skipping school. Adjusted beta estimates and 95% confidence intervals are presented for pathways significant at p<0.05. The solid lines indicate significant effects ($p < 0.05$), while the dashed lines indicate non-significant effects ($p > 0.05$).

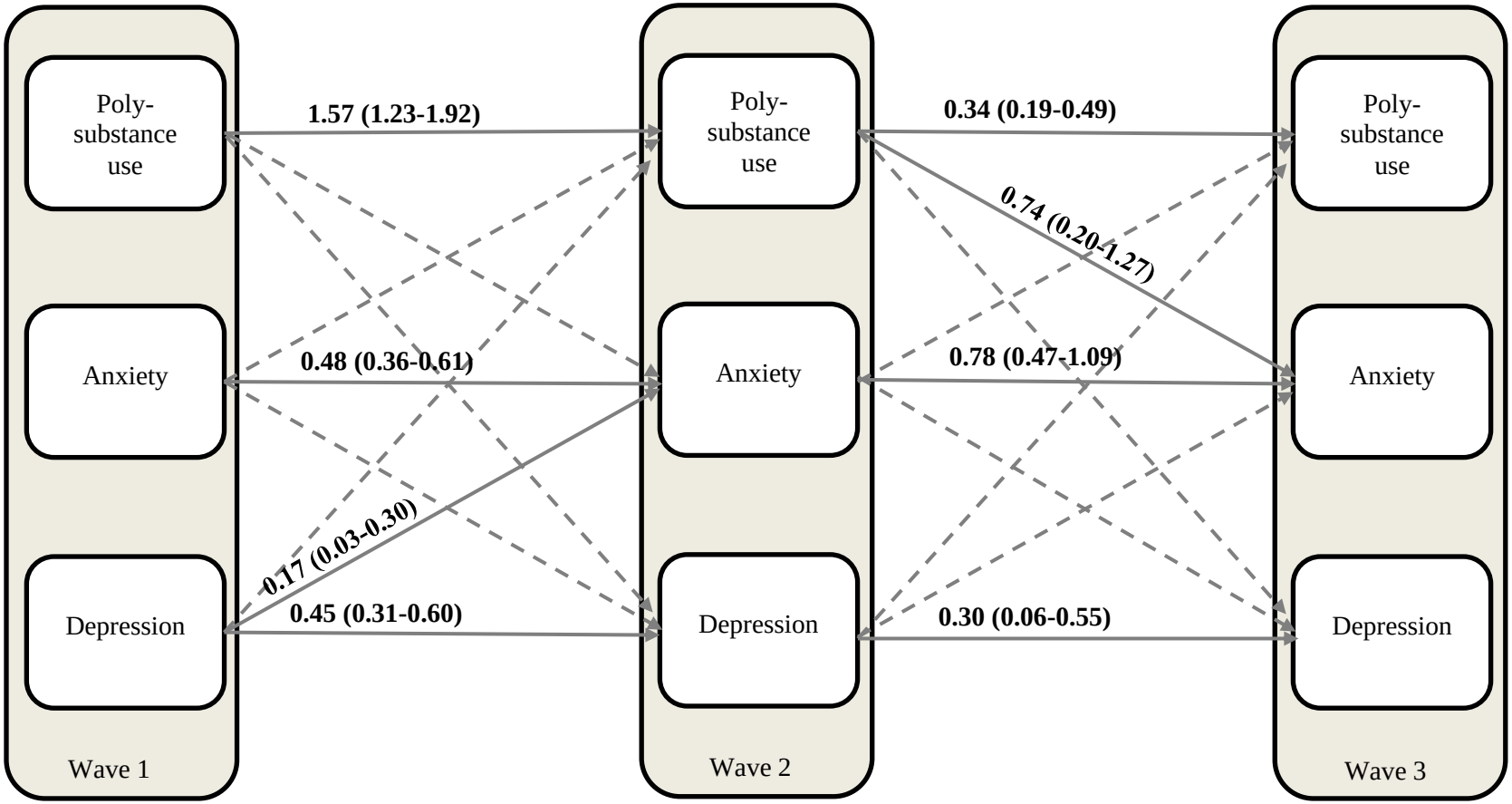

Figure 5. Cross-lag relationships between poly-substance use (versus single substance use) and anxiety and depression among female students who used substances in all three waves of the study (n = 195), adjusted for grade, ethnicity, weekly spending money, having friend and family support, and skipping school. Adjusted beta estimates and 95% confidence intervals are presented for pathways significant at p<0.05. The solid lines indicate significant effects ($p < 0.05$), while the dashed lines indicate non-significant effects ($p > 0.05$).

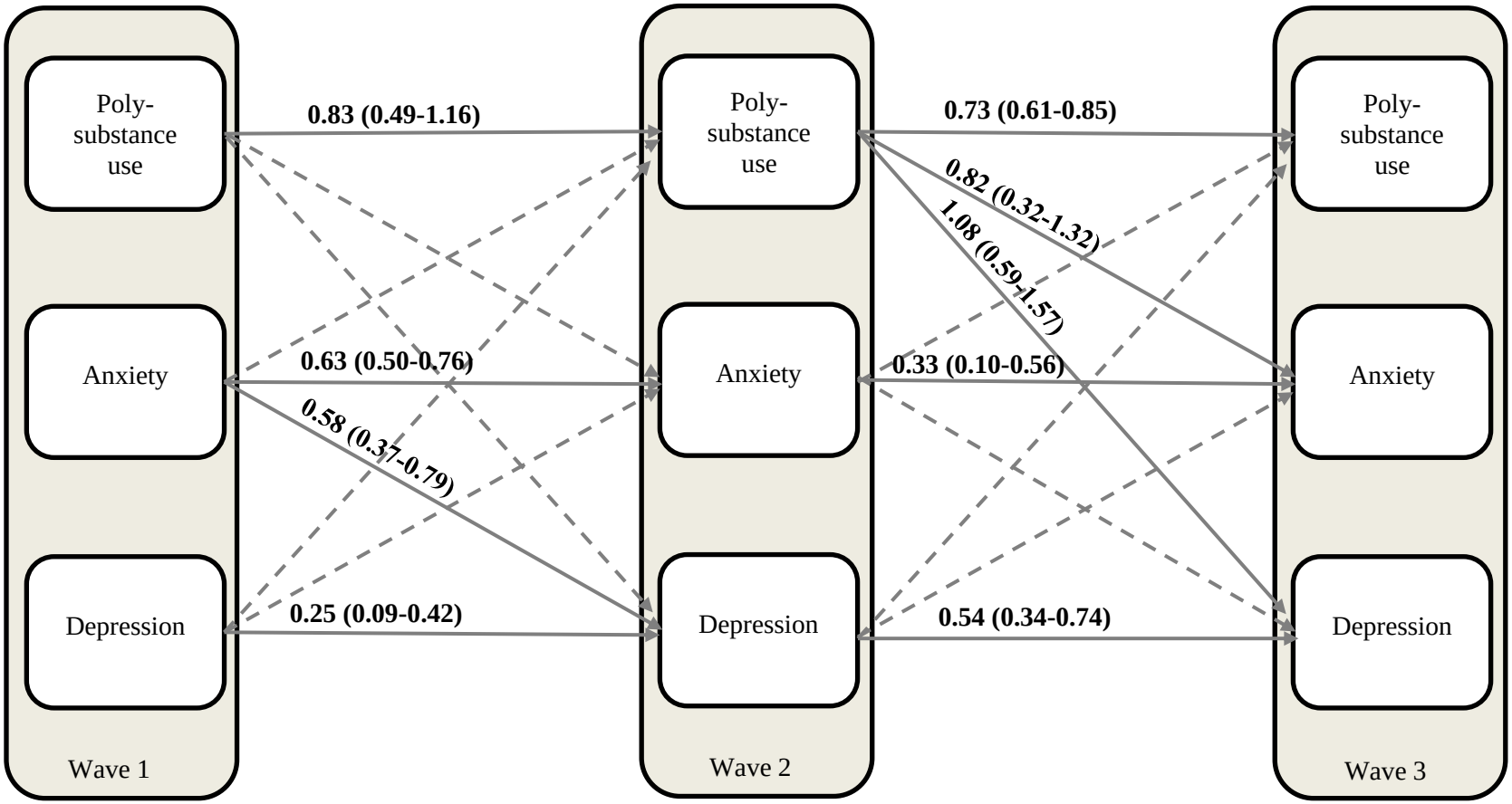

Figure 6. Cross-lag relationships between poly-substance use (versus single substance use) and anxiety and depression among male students who used substances in all three waves of the study (n = 206), adjusted for grade, ethnicity, weekly spending money, having friend and family support, and skipping school. Adjusted beta estimates and 95% confidence intervals are presented for pathways significant at p<0.05. The solid lines indicate significant effects ($p < 0.05$), while the dashed lines indicate non-significant effects ($p > 0.05$)

6.5 Discussion

This is the first Canadian study to examine bi-directional associations between poly-substance use and anxiety and depression using longitudinal data from a large sample of youth. Descriptively, we identified that a substantial number of adolescents are using substances. Substance use increased over time and by Wave 3, almost half of students reported using at least one substance and almost one third reported poly-substance use in the past month. We also saw a worsening of anxiety and depression symptoms over time. Among youth who used substances, we found uni-directional effects from Wave 2 to Wave 3 indicating that engaging in poly-substance use may worsen anxiety and depression symptoms in male students and anxiety in female students.

In the full sample, we identified a uni-directional association between the number of substances used and anxiety between Waves 1 and 2 in males. No significant effect was seen in the reverse direction. This result is in contrast to previous cross-sectional evidence.(11–14,189) While no previous prospective studies have examined the relationship between poly-substance use and anxiety, research examining poly-substance use and depression has typically found increasing substance use to be associated with greater symptoms.(20,186) This surprising finding could be due to some potential social benefits of substance use experienced through a third factor. For example, physical activity, and particularly team sport participation, have been associated with improved mental health including anxiety and depression among adolescents.(230,231) However, team sports participation has also been associated with binge drinking, e-cigarette use, and poly-substance use.(232–235) Future research should further explore this association. It is also notable that no bi-directional or uni-directional effects were seen between number of substances used and anxiety or depression among female students, even though female students had worse anxiety and depression scores at baseline and consistently over time.

In contrast to our findings in the full sample, among students who used substances each year, we identified uni-directional effects with poly-substance being associated with increased anxiety in female students and increased anxiety and depression in male students from Wave 2 to Wave 3. These results are in part consistent with previous longitudinal research.(20,186) McKelvey et al. found that that, among youth smokers, high poly-substance use was associated with worse depression scores at follow-up compared to low poly-substance use. Felton et al. identified a reciprocal relationship between poly-substance use and depression symptoms where poly-substance use at an early age was

associated with early depression symptoms, which were then associated with increasing poly-substance use over time, which was in turn associated with increasing depression symptoms over time.(186) In contrast, our results did not identify anxiety or depression predicting future poly-substance use and were significant in later, rather than earlier, waves.

Our study provides novel insights and has important implications for youth health. This study expands on current longitudinal research examining relationships between mental ill-health and poly-substance use, as the first longitudinal study to include a measure of anxiety in addition to depression.(15,16,20,186) We identified uni-directional effects suggesting that engaging in poly-substance versus single substance use may worsen anxiety and depression symptoms among high school students. This study also highlights some sex differences. Although female students began with worse anxiety and depression scores, we only found an association between poly-substance use and anxiety among female students whereas we found an association between number of substances and anxiety, poly-substance and anxiety, and poly-substance use and depression for male students. Finally, this research indicates that youth prevention programs should address poly-substance use in addition to focusing on single substances, given the high prevalence and escalation of polysubstance use over secondary school, and prospective associations with symptoms of anxiety and depression among students who engaged in poly-substance use compared to single substance use over time. Future research should examine how specific combinations of substances are associated with anxiety and depression over time to further inform potential programming.

6.5.1 Strengths and Limitations

This study has numerous strengths. To start, this study made use of a large longitudinal sample. In addition, the COMPASS study utilizes an active-information passive-consent protocol to encourage participation and honest reporting. This has been shown to be particularly important in substance use and mental health research.(197,199–201) Finally, we made use of validated scales for our measures of anxiety and depression symptoms.(208,209)

However, this study was not without limitations. First, the COMPASS study is not representative of all Canadian secondary school students. Second, the COMPASS survey measured concurrent (i.e., multiple substances being used in the same period such as the past 30 days), not simultaneous (i.e., multiple substances being used in the same instance) poly-substance use and therefore we can not draw any conclusions about simultaneous substance use. Third, there are several

limitations with the questionnaire that could result in participants under-reporting their substance use including the illicit nature of the substances for underage youth, a limited number of substances included on the questionnaire, and in Waves 1 and 2, the lack of a definition of an e-cigarette or listing of brands on the questionnaire. Fourth, we were lacking measures of peer or family substance use which have been associated with early initiation and escalating use through adolescence.(86) However, this study made use of variables indicating family and friends support which have been positively and negatively associated with poly-substance use respectively.(7) Additionally, there were no measures available of parental psychopathology, which is a significant risk factor for children.(144,145) Finally, there were limitations with the study sample. Less than half of participants were linked over time and there were missing data for one-quarter of participants. Consistent with previous research students who were linked over time were more likely to be younger, female, and less likely to use substances.(206,236) We also identified that those with higher anxiety and depression scores were less likely to be linked over time. This may have resulted in an underestimation of substance use rates and the association with anxiety and depression scores.

6.6 Conclusions

This study expands on current longitudinal research examining relationships between poly-substance use and anxiety and depression. Among all students, we found that substance use, anxiety and depression increased over time. By grades 11 and 12 almost half of students used at least one substance in the past month. Our findings suggest that engaging in poly-substance use may worsen anxiety and depression symptoms among high school students who consistently use substances. These findings highlight the need for youth prevention programs to address poly-substance use and account for potential differences between females and males.

Chapter 7

Manuscript 3

Associations between longitudinal patterns of substance use and anxiety and depression symptoms among a sample of Canadian secondary school students

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7.1 Overview

The objective of this study was to examine the longitudinal associations between latent classes of substance use and anxiety and depression scores among youth who use substances. This study used data from 3 waves (Wave 1: 2017/18, Wave 2: 2018/19, and Wave 3: 2019/20) of the COMPASS study. Students in grades 9 and 10 who reported substance use at baseline (n=738) reported their substance use (alcohol, cannabis, cigarettes, and e-cigarettes) and anxiety and depression symptoms at each wave. Repeated Measures Latent Class Analysis (RMLCA) was used to determine substance use classes and mixed models were used to examine the associations between substance use classes and anxiety and depression. We identified three classes of substance use: (1) Occasional alcohol and e-cigarette use, (2) Escalating poly-substance use, and (3) Consistent poly-substance use. After controlling for relevant covariates, consistent poly-substance use was associated with depression (Female OR: 1.24 [95%CI: 0.46, 2.02]; Male OR 1.13 [95%CI: 0.38, 1.87]) but not anxiety. Escalating poly-substance use was associated with depression among males (OR 0.72 [95%CI: 0.10, 1.33]). These findings should be taken into consideration when creating prevention programming and treatment strategies for adolescents. Substance use programming should be comprehensive and consider multiple substances and be cognizant of symptoms of mental ill-health, particularly depression.

Keywords: anxiety; depression; alcohol drinking; cannabis smoking; cigarette smoking; vaping; adolescent

7.2 Introduction

Risk factors and negative outcomes associated with substance use have been well studied for individual substances in isolation (i.e., alcohol, cigarettes, cannabis) (225,237,238). However, recent evidence indicates that 23% of Canadian students in grades 9-12 engage in poly-substance use, defined as the concurrent use of more than one substance within a specified period (1). Prior cross-sectional research has consistently identified common patterns of substance use among adolescents, including a low use or no use group comprising the majority of adolescents, a single or dual substance use group, a moderate poly-substance use group, and finally a higher poly-substance use group (12). Longitudinal research indicates that adolescents typically maintain substance use patterns over time but if they make a change, adolescents are more likely to increase than decrease the number of substances they use over time (15,54,57,239). No studies to date have examined the role of recent increases in e-cigarette use among adolescents (223) in poly-substance use over time. This knowledge is vital to better understand the reality of youth substance use and to plan appropriate interventions and prevention programming.

Poly-substance use has also been linked with risk behaviours other than substance use (e.g., risky sexual behaviour, gambling) and negative health outcomes above and beyond using each substance in isolation, including poor mental health and mental ill-health (6–10,16,88,95,100,186). Of note, poly-substance use has been associated with elevated symptoms of depression and anxiety among adolescents aged 11 to 18 in cross-sectional research (11–14,189), although previous longitudinal research has identified mixed results. A large US study found no associations between poly-substance use and depressive symptoms after controlling for other variables (15). However, another study found that the onset of poly-substance use may worsen anxiety and depression symptoms among secondary school students who use substances (240), and yet another identified a transactional relationship between poly-substance use and depression symptoms, suggesting a more complex relationship between these two variables (186). Adolescence is a critical juncture for addressing poor mental health and mental ill-health as the majority of mental illnesses arise during adolescence and young adulthood (105). Mental illnesses are a leading cause of disability in Canada and also present a significant current and predicted economic burden (106–108). Early prevention and interventions may help maximize benefits to improve population mental health (241–243).

Previous longitudinal research has often examined poly-substance simply by counting the total substances used rather than by investigating specific substances used (186,240). Only two

studies to date have considered classes of substance use over time and their relationship with symptoms of mental illness (15,20). For example, Brooks-Russell and colleagues used a Repeated Measures Latent Class Analysis (RMLCA) to examine substance use classes across grades 10 to 12 and their associations with depression symptoms (15). Additionally, previous longitudinal studies have not explored sex differences, despite differences being identified in cross-sectional research (12,189). Patterns of poly-substance use, anxiety, and depression are known to differ between female and male adolescents (12,22,189). Female students report higher anxiety and depression symptoms than male students (22–25), and these sex differences tend to increase across adolescence (26,27). Conversely, male students typically report higher levels of poly-substance use, both more substances and higher frequencies of use (7,12,28–30,189). Having a better understanding of these relationships, including any sex-based differences, can help in tailoring prevention programming to the potential uniqueness of different groups.

Our research addresses these gaps in the existing literature by identifying patterns of substance use over time and their associations with anxiety and depression symptoms among male and female students. The study objectives were to, first, examine the longitudinal latent classes of substance use using RMLCA and, second, to examine their associations with anxiety and depression scores among youth who used substances in three waves of the COMPASS study (Wave 1: 2017/18, Wave 2: 2018/19, and Wave 3: 2019/20).

7.3 Materials and Methods

7.3.1 Design

The COMPASS study is a prospective cohort study that collects data annually from a convenience sample of students in British Columbia, Alberta, Ontario, and Quebec in grades 9 to 12 (Secondary I-V in Quebec). The current study used three waves of data from the COMPASS study. All procedures were approved by the University of Waterloo Office of Research Ethics (reference number 30118) and appropriate school board committees. A more detailed description of the COMPASS study is available online (https://uwaterloo.ca/compass-system/) or in print (197).

7.3.2 Participants

Overall, 122 schools (British Columbia, n=16; Alberta, n=8; Ontario, n=61; and Quebec, n=37) participated in the COMPASS study at Wave 1. Due to school closures because of COVID-19

in March 2020, only 29 schools (British Columbia, n=5; Alberta, n=5; Ontario, n=17; and Quebec, n=2) consistently completed the same questionnaire all 3 waves and were included in this study. In these schools, 7084 students in grades 9 and 10 (Secondary III in Quebec, grade 9 equivalent) participated at Wave 1. Using an anonymous self-generated identification code,(206) 2904 (41%) students were successfully linked across all three waves in the 29 schools. Among the linked sample, there were a higher proportion of students who were in grade 9 and female and a lower proportion who reported substance use (Supplementary Table 15). After missing data were removed, 1852 (64%) had complete data for all three waves. There were no significant differences between students with complete data and students who were removed due to incomplete data (Supplementary Table 16). Finally, students who did not report any substance use at baseline (n=1114, 60%) were removed for a final sample of 738 students.

7.3.3 Measures

7.3.3.1 Substance Use

Substance use measures were consistent with national surveillance measures (217). At each wave, students were asked to report *alcohol use* ("In the last 12 months, how often did you have a drink of alcohol that was more than just a sip?"), *cannabis use* ("In the last 12 months, how often did you use marijuana or cannabis? (a joint, pot, weed, hash)."), *cigarette use* ("Have you ever tried cigarette smoking, even just a few puffs?" and "On how many of the last 30 days did you smoke one or more cigarettes?"), and *e-cigarette use* ("Have you ever tried an electronic cigarette, also known as an e-cigarette?" and "On how many of the last 30 days did you use an e-cigarette?"). Each substance was categorized into one of four categories: No use, Ever/less than monthly use, Monthly use, or Weekly use. Students who had missing data for all four substances were removed from the analyses.

7.3.3.2 Anxiety

The Generalized Anxiety Disorder 7 (GAD-7) scale (207) was used to assess generalized anxiety symptoms at each wave of the study. The GAD-7 reports on self-perceived feelings of worry, fear, and irritability over a 2-week period. Students were asked how often they were bothered by each symptom with the response options: "Not at all", "Several days", "Over half the days", or "Nearly every day". Responses were scored from 0 to 3, respectively, and summed. Total scores range from 0 to 21 and higher total scores indicate greater anxiety symptoms. The GAD-7 had an alpha coefficient

of 0.91 for females and 0.89 for males at Wave 1. As anxiety scores were used as both independent and dependent variables, students with missing scores were removed from the sample.

7.3.3.3 Depression

The Centre for Epidemiological Studies Depression Scale (CES-D-10) (209,216) was used to assess depression symptoms at each wave of the study. Items assess characteristics of clinical depression, including negative affect, anhedonia, and somatic symptoms, such as "I felt everything I did was an effort" and "I could not get 'going.'" Students were asked how often they experienced each symptom within the last 7 days, with the response options: "None or less than 1 day", "1–2 days", "3–4 days", or "5–7 days". Responses were scored from 0 to 3, respectively, and summed. Total scores range from 0 to 30 and higher total scores indicate greater depressive symptoms. The CES-D-10 had an alpha coefficient of 0.70 for females and 0.75 for males at Wave 1. As depression scores were used as both independent and dependent variables, students with missing scores were removed from the sample.

7.3.3.4 Covariates

Poly-substance use, anxiety, and depression are associated with other risky behaviour and family and friend support (6–10,100,146,244–246). Skipping school was used as a measure of student risky behaviour. Students were asked "In the last 4 weeks, how many classes did you skip when you were not supposed to?" Students who reported any number of classes skipped were categorized as truant. To ascertain whether students felt they had family or friend support, they were asked how much they agreed with the statements "I can talk about my problems with my family/friends." Students who selected "Agree" or "Strongly Agree" were categorized as having family or friend support. These variables were assessed at Wave 1.

Consistent with other Canadian adolescent health research (217), sex (male, female), grade (9, 10), ethnicity (White, non-White), and weekly spending money (zero, $1-$20, $21-$100, $100+, don't know/missing), were assessed at Wave 1 and included as demographic covariates.

7.3.4 Analyses

To create substance use classes and examine their associations with anxiety and depression, Repeated Measures Latent Class Analysis (RMLCA) (52) was implemented using Mplus 8.2 (Muthen & Muthen, Los Angeles, CA, USA). RMLCA is an application of Latent Class Analysis (LCA) that

identifies latent classes over time (52). First, a series of RMLCA models were fit to determine the number of classes to best fit the data. Categorical indicators of alcohol use, cannabis use, cigarette use, and e-cigarette use were used as latent class indicators. To establish the best fitting solution, we started with a 1 class solution and added classes until good fit was no longer obtained. We used log-likelihood, AIC, BIC, and the Lo-Mendell-Rubin adjusted likelihood ratio test (LMRT) as indicators of model fit. Lower log-likelihood, AIC, and BIC values indicate better model fit (219). The LMRT tests whether a model with *k* classes fits better than a model with *k-1* classes where a significant result indicates that it is (220). These model selection criteria, combined with model interpretability were used to place participants into the appropriate latent classes. While entropy was not used for model selection, it is reported as an indicator of classification from 0 to 1 with larger values indicating better latent class separation (52,221). The TYPE=COMPLEX and CLUSTER commands were used account for the nesting of students within schools. Based on previous evidence of sex differences, separate models were conducted for females and males (12,189). Once the most parsimonious solution was determined, students were assigned to a latent class using most likely class membership (211).

Descriptive statistics were used to examine the Wave 1 characteristics of the linked longitudinal sample by substance use class and the prevalence of number of substances used, poly-substance use, anxiety, and depression in each wave of the study.

After the RMLCA was completed, we used the PROC MIXED function in SAS (SAS Institute Inc., Cary, NC) to fit linear mixed effects regression models. Using 3 years of data, the models tested the effects of engaging in the different classes of substance use on adolescents' anxiety and depression trajectories over time. All mixed effects models included a random intercept term to account for the within-student correlation of response over time as well as student nesting within schools. For models where a significant main effect was seen, an interaction with wave was tested, however, no significant effects were found. Two sets of models were run, the first controlled for grade, ethnicity, weekly spending money, friend support, family support, and skipping school. The second set of models controlled for depression in the anxiety models and vice versa.

7.4 Results

Approximately half of the sample was female (53%) and in grade 9 (46%). At Wave 1, the sample had a mean anxiety score of 6.8 (SD 5.8), and a mean depression score of 9.2 (SD 6.2).

To determine the best model, we examined model fit statistics for one to six latent classes (Table 6). A three-class model was selected as the best fitting model as it had lower values for the model selection criteria and the best interpretability. The three classes identified in this study were (1) Occasional alcohol and e-cigarette use (*occasional*), (2) Escalating poly-substance use (*escalating*), and (3) Consistent poly-substance use (*consistent*). While classes were similar among females and males, they had slightly different interpretations and are described in Figures 7 and 8 and Table 7.

Table 6. Model fit indices for 1 through 6 latent class models of substance use among female and male substance users in 3 waves of the COMPASS study (Wave 1: 2017/18, Wave 2: 2018/19, Wave 3: 2019/20) in British Columbia, Alberta, Ontario, and Quebec, Canada.

Number of classes	Log-likelihood	FP	AIC	BIC	LMRT p-value	Entropy
Female (n=388)						
1	-5194.0	36	10459.9	10602.5	-	1.00
2	-4665.3	73	9476.7	9765.8	0.00	0.90
3	-4535.5	110	9291.0	9726.7	0.80	0.86
4	-4432.2	147	9158.4	9740.7	0.77	0.88
5	-4371.6	184	9111.3	9840.1	0.78	0.89
6	-4317.8	221	9077.6	9953.0	0.78	0.90
Male (n=350)						
1	-4847.1	36	9766.3	9905.2	-	1.00
2	-4400.3	73	8946.6	9228.2	0.07	0.87
3	-4287.1	110	8794.3	9218.6	0.77	0.86
4	-4187.2	147	8668.4	9235.6	0.60	0.88
5	-4103.8	184	8575.7	9285.5	0.76	0.91
6	-4055.1	221	8552.2	9404.8	0.77	0.93

FP=Free Parameters; AIC = Akaike information criterion; BIC = Bayesian information criterion; LMRT = Lo-Mendell-Rubin Test;

Among female students (Figure 7), the occasional class (45%) was characterized by consistent less than monthly alcohol use and increasing ever e-cigarette use across waves. The escalating class (29%) was characterized by increasing monthly alcohol use, increasing less than monthly cannabis use, and increasing monthly and weekly e-cigarette use. Students in the escalating class were primarily using alcohol and e-cigarettes at Wave 1 and by Wave 3 were engaging in some cannabis and cigarette use. The consistent class (26%) was characterized by regular monthly alcohol use, increasing ever and monthly cannabis use, regular ever and monthly cigarette use, and increasing monthly and weekly e-cigarette use. Students in the consistent class were engaging with all four substances at Wave 1 and this remained consistent over time.

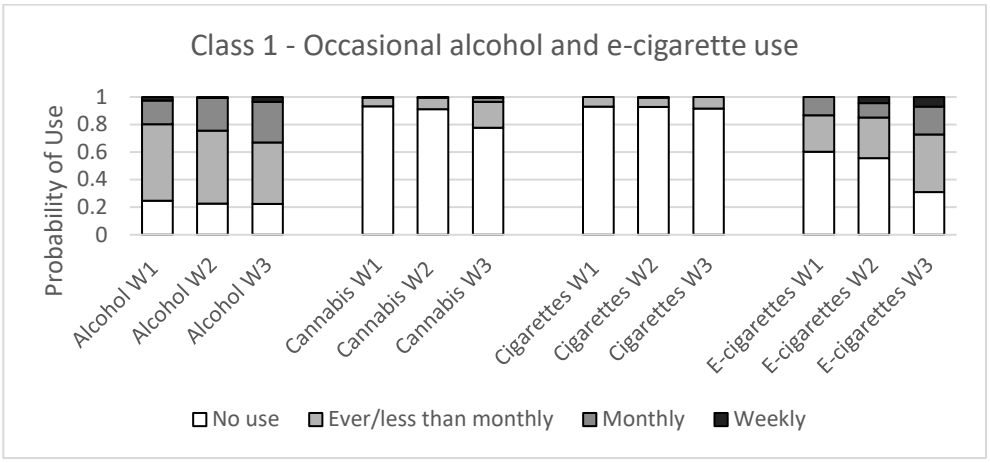
Table 7. Wave 1 characteristics of the linked longitudinal sample of adolescents participating in 3 waves of the COMPASS study (Wave 1: 2017/18, Wave 2: 2018/19, Wave 3: 2019/20) in British Columbia, Alberta, Ontario, and Quebec, Canada. (n=738).

	Female (n=388)						Male (n=350)					
Wave 1 variables	**Class 1 (n=175)**		**Class 2 (n=113)**		**Class 3 (n=100)**		**Class 1 (n=146)**		**Class 2 (n=124)**		**Class 3 (n=80)**	
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Grade												
9	87	49.7	54	47.8	43	43.0	73	50.0	55	44.4	26	32.5
10	88	50.3	59	52.2	57	57.0	73	50.0	69	55.6	54	67.5
Ethnicity												
White	118	67.4	93	82.3	79	79.0	100	68.5	98	79.0	48	60.0
Non-White	57	32.6	20	17.7	21	21.0	46	31.5	26	21.0	32	40.0
Weekly spending money												
Zero	32	18.3	14	12.4	15	15.0	32	21.9	17	13.7	11	13.8
$1-$20	69	39.4	38	33.6	25	25.0	45	30.8	39	31.5	19	23.8
$21-$100	32	18.3	26	23.0	24	24.0	40	27.4	34	27.4	22	27.5
$100+	17	9.7	17	15.0	22	22.0	12	8.2	18	14.5	19	23.8
Don't know/missing	25	14.3	18	15.9	14	14.0	17	11.6	16	12.9	9	11.3
Anxiety score (GAD-7; mean, SD)	8.3	5.9	7.2	5.2	10.5	6.3	4.3	4.5	5.0	5.0	6.2	5.4
Depression score (CESD; mean, SD)	9.9	6.7	9.1	5.0	13.7	7.2	6.6	4.5	7.6	5.5	9.2	5.8

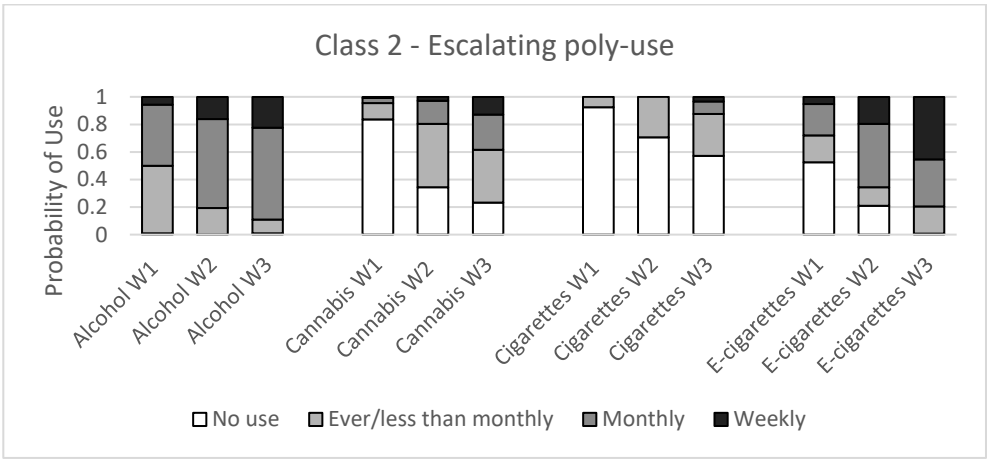
Note: Class 1=Occasional alcohol and e-cigarette use, Class 2=Escalating poly-substance use, and Class 3=Consistent poly-substance use.

Among male students (Figure 8), the occasional class (42%) was characterized by consistent less than monthly alcohol use and ever e-cigarette use. The escalating class (35%) was characterized by increasing monthly alcohol use, increasing less than monthly cannabis use, and increasing monthly and weekly e-cigarette use. Students in the escalating class were primarily using alcohol and e-cigarettes at Wave 1 and by Wave 3 were engaging in some cannabis and cigarette use. Finally, the consistent class (23%) was characterized by consistent monthly alcohol use, increasing weekly cannabis use, consistent ever and monthly cigarette use, and increasing weekly e-cigarette use. Students in the consistent class were engaging with all four substances at Wave 1 and this remained consistent over time.

(a)



(b)



(c)

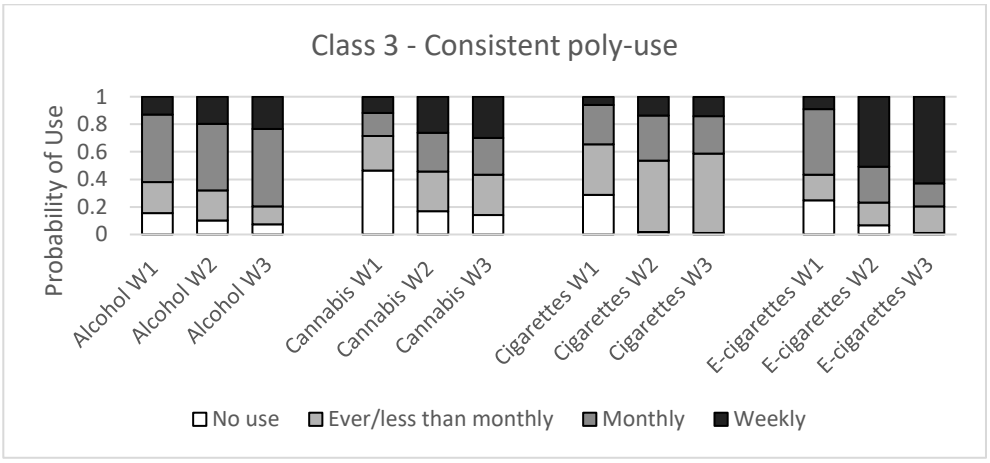
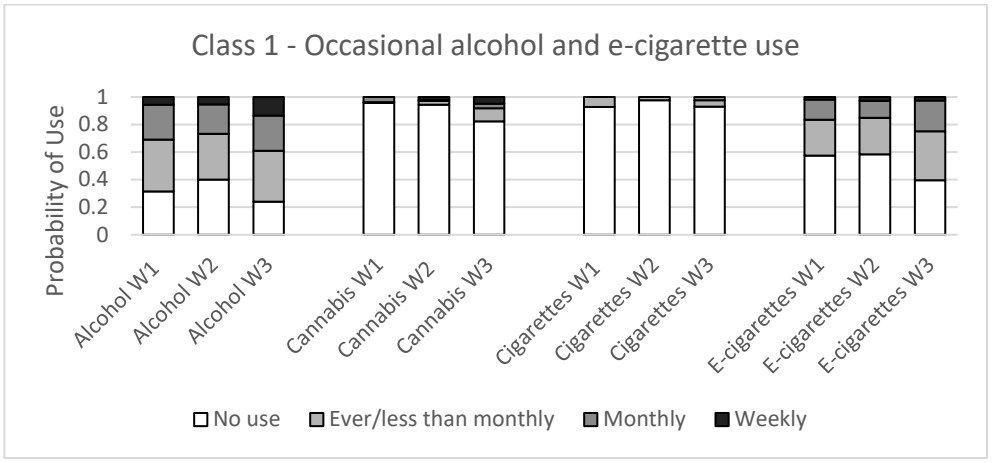
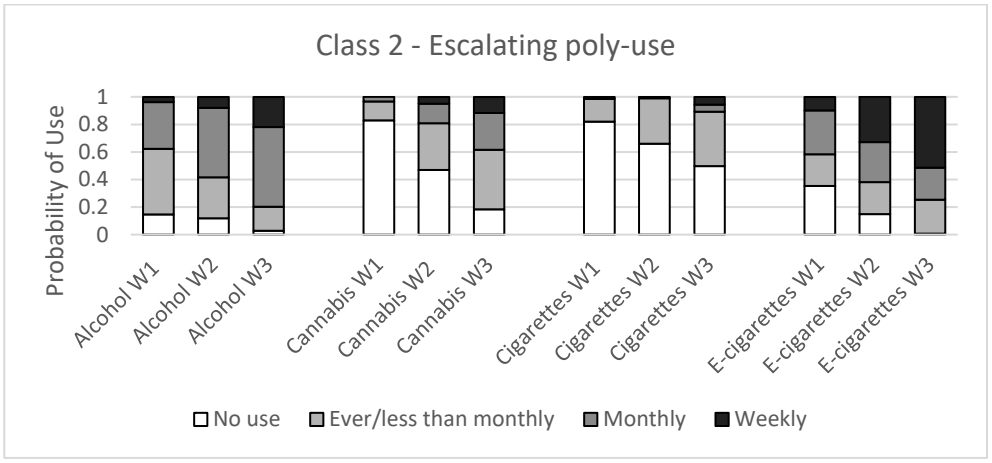


Figure 7. Substance use item probabilities for a three-class latent class model for females in 3 waves of the COMPASS study (Wave 1: 2017/18, Wave 2: 2018/19, Wave 3: 2019/20) in British Columbia, Alberta, Ontario, and Quebec, Canada. (a) Class 1 - Occasional alcohol and e-cigarette use, (b) Class 2 - Escalating poly-use (c) Class 3 - Consistent poly-use.

(a)



(b)



(c)

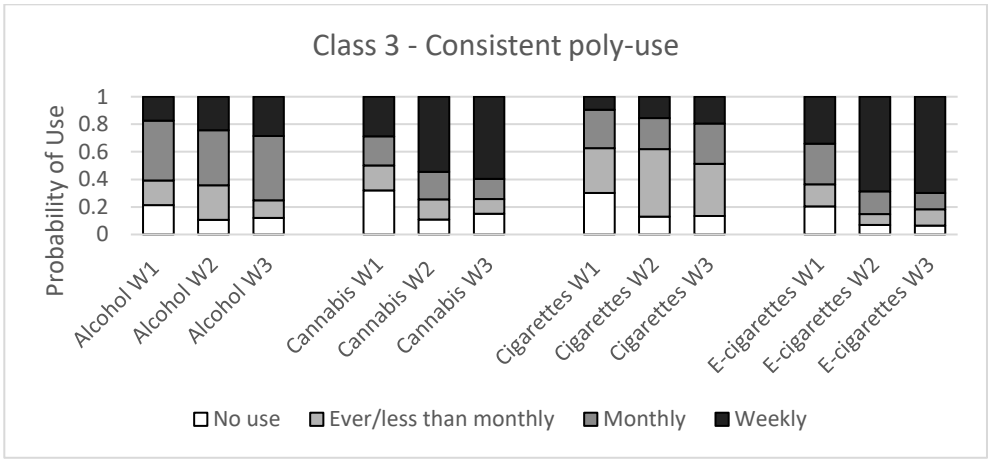


Figure 8. Substance use item probabilities for a four-class latent class model for males in 3 waves of the COMPASS study (Wave 1: 2017/18, Wave 2: 2018/19, Wave 3: 2019/20) in British Columbia, Alberta, Ontario, and Quebec, Canada.(a) Class 1 - Experimental alcohol and e-cigarette use, (b) Class 2 - Escalating poly-use (c) Class 3 - Consistent poly-use.

7.4.1 Regression Results

Regression coefficients for all models are found in Table 8. Among female students, results from Anxiety Model 1 suggested that the consistent class had significantly higher anxiety scores than the occasional class. However, after for controlling for depression score, this relationship was no longer significant. Results from Depression Model 1 indicated that the consistent class had significantly higher anxiety scores than the occasional class and this relationship held after controlling for anxiety in Model 2 (β=1.24; 95% CI: 0.46, 2.02).

Table 8. Mixed effects regression coefficients between substance use class and anxiety and depression scores over time among of adolescents participating in 3 waves of the COMPASS study (Wave 1: 2017/18, Wave 2: 2018/19, Wave 3: 2019/20)in British Columbia, Alberta, Ontario, and Quebec, Canada. (n=738).

Variables	Anxiety Model 1 β (95% CI)	Anxiety Model 2 β (95% CI)	Depression Model 1 β (95% CI)	Depression Model 2 β (95% CI)
Female				
Year				
Wave 1	0.00	0.00	0.00	0.00
Wave 2	**0.65 (0.11, 1.20)**	0.04 (-0.40, 0.48)	**0.98 (0.39, 1.57)**	**0.50 (0.02, 0.97)**
Wave 3	**0.98 (0.43, 1.53)**	0.41 (-0.03, 0.86)	**0.90 (0.31, 1.49)**	0.18 (-0.30, 0.65)
Substance Use Class				
Occasional alcohol and e-cigarette use	0.00	0.00	0.00	0.00
Escalating poly-use	-0.45 (-1.53, 0.63)	-0.10 (-0.78, 0.59)	-0.56 (-1.72, 0.60)	-0.23 (-0.97, 0.51)
Consistent poly-use	**2.07 (0.94, 3.20)**	0.33 (-0.39, 1.06)	**2.76 (1.54, 3.98)**	**1.24 (0.46, 2.02)**
Depression score	-	**0.63 (0.59, 0.67)**	-	-
Anxiety Score	-	-	-	**0.74 (0.69, 0.78)**
Male				
Year				
Wave 1	0.00	0.00	0.00	0.00
Wave 2	0.15 (-0.39, 0.69)	-0.09 (-0.55, 0.37)	0.38 (-0.19, 0.95)	0.27 (-0.22, 0.76)
Wave 3	**0.57 (0.03, 1.11)**	-0.09 (-0.56, 0.37)	**1.04 (0.47, 1.61)**	**0.64 (0.15, 1.12)**
Substance Use Class				
Occasional alcohol and e-cigarette use	0.00	0.00	0.00	0.00
Escalating poly-use	**1.00 (0.02, 1.98)**	0.09 (-0.50, 0.69)	**1.42 (0.41, 2.43)**	**0.72 (0.10, 1.33)**
Consistent poly-use	**1.28 (0.10, 2.47)**	-0.02 (-0.74, 0.71)	**2.03 (0.80, 3.26)**	**1.13 (0.38, 1.87)**
Depression score	-	**0.64 (0.60, 0.68)**	-	-
Anxiety Score	-	-	-	**0.70 (0.66, 0.74)**

Anxiety Model 1 and Depression Model 1 also controlled for grade, ethnicity, weekly spending money, friend support, family support, and skipping school. Anxiety Model 2 additionally controlled

for depression score. Depression Model 2 additionally controlled for anxiety score. Bold indicates significance <0.05.

Among male students, the escalating class and consistent class had significantly higher anxiety scores than the occasional alcohol and e-cigarette use class in Anxiety Model 1. However, this relationship was no longer significant after controlling for depression in Anxiety Model 2. The escalating class and consistent class had significantly higher depression scores than the occasional class in both Depression Model 1 and Depression Model 2. This result indicates that after controlling for all other variables, those in the escalating class had 0.72 higher depression scores (95% CI: 0.10, 1.33) and those in the consistent class had 1.13 higher depression scores (95% CI: 0.38, 1.87) than those in the occasional class.

7.5 Discussion

The purpose of this study was to examine how latent classes of substance use were associated with anxiety and depression scores over time among adolescents who used substances. We identified three unique classes of substance use: occasional alcohol and e-cigarette use, escalating poly-substance use, and consistent poly-substance use. The occasional group was the largest class representing just under half of our sample, whereas the escalating and consistent groups were roughly the same size at around a quarter of our sample each. Notably, there were no significant interactions between substance use classes and time indicating that any differences in depression and anxiety scores were consistent across time. After controlling for depression, substance use classes were not associated with anxiety among female or male students. In contrast, after controlling for anxiety, the escalating poly-use class among males and the consistent poly-use class among both females and males were associated with higher depression scores than the occasional class. As such, our data suggests that while poly-substance use may have a role in the worsening of depression symptoms, depression plays a larger role in the worsening of anxiety symptoms than poly-substance use, although additional investigation is required to strengthen the evidence on the temporality of these associations.

The longitudinal classes of substance use identified in this study differed from existing research, however there were significant differences in samples and methodology that could explain these differences. For example, in the US, Brooks-Russell et al identified a 4-class model that included (1) alcohol and other drug use, (2) tobacco, alcohol, and other drug use, (3) increasing multiple substance use, and (4) decreasing multiple substance use (15). There are some similarities

with this work including identifying students who maintained their substance use over time and those who increased their substance use over time. However, we did not include as many substances (i.e., ecstasy, amphetamines, cocaine) in our analyses. Additionally, we did not identify a decreasing use group over time. While some students in our study did decrease their use over time (17%), it may not have been a common enough pattern to be identified as a unique class. McKelvey et al also used a similar approach and their LCA results identified two distinct classes of substance use:(1) a limited range group that reported use of tobacco, alcohol, and cannabis and (2) an extended range group that also reported use of additional substances (i.e., cocaine, ecstasy, misused prescriptions) (20). However, their sample comprised only smokers, so results are not necessarily comparable as only 4% of adolescents in the current study reported current smoking. Notably, both of these studies are older and did not examine the recent increase in e-cigarette use among adolescents (223). Our results indicate that e-cigarette use was a consistent component of each substance use class and therefore is important to include in future work examining poly-substance use over time.

Next, we identified a notable difference between female and male substance use classes. Male students in the consistent poly-use class had a higher probability of weekly cannabis and e-cigarette use. Over half of males in this class reported weekly cannabis use and over two thirds reported weekly e-cigarette use by Wave 3 whereas these number were approximately one-third and one-half respectively among female students. The high prevalence of weekly use of both substances warrants further investigation into whether they are being used simultaneously and the preferred mode of cannabis use in this group. As these students are regularly using e-cigarettes, they may also be consuming cannabis by vaping.

In regression analyses, we found that after controlling for depression symptoms, consistent poly-substance use was no longer associated with anxiety symptoms. This is in contrast to previous findings where poly-substance use was associated with elevated anxiety symptoms compared to single substance use (240). Instead, we found that over time anxiety symptoms were primarily explained by depression symptoms. Specifically, we identified that a 10-unit increase in depression symptoms (indicative of clinically relevant depression symptoms) (209) was associated with a 6.3-unit increase in anxiety score among females and a 6.4-unit increase in anxiety score among males. This observed comorbidity was expected as it is common to have overlapping symptoms (189). In a previous examination of the baseline sample of this study, 51% of those who reported clinically

relevant symptoms of anxiety or depression, reported clinically relevant symptoms of both and few reported symptoms of anxiety alone (11%) (189).

Finally, we found that consistent poly-substance use was associated with depressive symptoms even after controlling for anxiety symptoms. This is consistent with the majority of previous literature (20,186,240), however, one study found no association after adjusting for peer substance use (15). This finding is consistent with the opponent process model of addiction which hypothesizes that substance use in adolescence predicts future depressive symptoms (196). It has been proposed that substance use promotes an immediate mood boost ("appetitive process") followed by a slow decrease in mood ("opponent process") which over time becomes stronger than the "appetitive process" and negatively affects mood over time. However, it is important to note that we did not see significant interactions with time meaning that baseline differences between groups held over time. This means that increased substance use over time did not result in increasingly worse depression symptoms compared to the lowest use class. Additionally, the increasing poly-substance use class was associated with depression symptoms among male students only. This was surprising as female students began with worse anxiety and depression scores, perhaps indicating a ceiling effect of anxiety and depression symptoms among female students.

7.5.1 Strengths and Limitations

This study made use of a longitudinal sample. The COMPASS study also uses an active-information passive-consent protocol to encourage participation and honest reporting which has been shown to be particularly important in substance use and mental health research.(197,199–201) Finally, we made use of validated scales to measure anxiety and depression symptoms.(208,209)

However, this study was not without limitations. First, the COMPASS survey measured concurrent (i.e., multiple substances being used over the same time period such as the past 30 days or past 12 months), not simultaneous (i.e., multiple substances being used in the same instance) poly-substance use and therefore we can not draw any conclusions about simultaneous substance use. Second, the COMPASS study is not representative of all Canadian secondary school students limiting the generalizability of results. Third, there are several limitations with the questionnaire that could result in participants under-reporting their substance use. These include the illicit nature of the substances for underage youth, a limited number of substances included on the questionnaire, and in Waves 1 and 2, the lack of a definition of an e-cigarette or listing of brands on the questionnaire.

Fourth, we were lacking measures of peer or family substance use which have been associated with early initiation and escalating use through adolescence (86). However, this study made use of variables indicating family and friends support which have been positively and negatively associated with poly-substance use respectively (7). Additionally, there were no measures available of parental psychopathology, which is a significant risk factor for children (144,145). Finally, only two fifths of participants were linked over time. This is consistent with previous research findings where older, male, and youth who use substances are less likely to be linked over time (206,236). We also identified that those with higher anxiety and depression scores were less likely to be linked over time. This may have resulted in an underestimation of substance use rates and their associations with anxiety and depression scores.

7.6 Conclusions

This research gives novel insights into how Canadian adolescents use substances over time. Three classes of substance use emerged among those who used substances: (1) Occasional alcohol and e-cigarette use, (2) Escalating poly-substance use, and (3) Consistent poly-substance use. We did not identify significant interactions between time and group membership; however, we did identify a link between poly-substance use and depression. Over time, consistent poly-substance use was associated with depression but not anxiety and escalating poly-substance use was associated with depression among males. These findings should be taken into consideration when creating prevention programming and treatment strategies for adolescents. Substance use programming should be comprehensive and consider multiple substances and be cognizant of symptoms of mental ill-health, particularly depression. Future research should continue to include e-cigarette use and consider modes of cannabis use when examining poly-substance use.

Chapter 8
General Discussion

8.1 Overview

Risk factors and negative outcomes associated with substance use have been well studied for individual substances in isolation (i.e., alcohol, cigarettes, cannabis).(225,237,238) However, recent evidence indicates that over 1 in 5 of Canadian secondary school students engage in poly-substance use, defined as the concurrent use of more than one substance within a specified period.(1) Additionally, there has been a rapid increase in e-cigarette use among adolescents in recent years which has changed the substance use context among this group.(2,223) Poly-substance use has been linked with risk behaviours other than substance use and negative health outcomes above and beyond using each substance in isolation, including poor mental health.(6–10,16,88,95,100,186) Of note, poly-substance use has been associated with elevated symptoms of depression and anxiety among adolescents in cross-sectional research (11–14) and previous longitudinal research has identified mixed results.(15,186) Adolescence is a critical juncture for addressing mental health as the majority of mental illnesses arise during adolescence and young adulthood.(105) Mental illnesses are a leading cause of disability in Canada and also present a significant current and predicted economic burden.(106–108) Early prevention and interventions may help maximize benefits to improve population mental health.(241–243)

Overall, this dissertation characterized poly-substance use and examined its associations with anxiety and depression cross-sectionally and longitudinally among a sample of Canadian secondary school students. The main objectives were to (1) determine the cross-sectional substance use classes among a sample of Canadian secondary school students and examine their associations with clinically relevant anxiety and depression symptoms, (2) examine the bi-directional associations between poly-substance use and anxiety and depression symptoms among secondary school students and, (3) examine the longitudinal associations between latent classes of substance use and anxiety and depression symptoms over time among youth who use substances.

This thesis fills an important gap with respect to our knowledge of poly-substance use and its association with anxiety and depression among adolescents in Canada. The inclusion of e-cigarettes

in measuring poly-substance use is novel and timely in the Canadian literature. E-cigarettes are a relatively new product on the market and have seen an increase in use among adolescents in recent years.(223) This thesis was also able to examine recent poly-substance use trends both cross-sectionally and longitudinally. These findings update previous Canadian research that was completed prior to the emergence of e-cigarettes.(4,40,54) Finally, due to the longitudinal design of the COMPASS study, this thesis was able to include three waves of data to examine the longitudinal associations between poly-substance use and anxiety and depression which few studies have done to date.(15,16,20,186) The following sections present key findings of this research, implications for practice, and directions for future research.

8.2 Summary of Key Findings

Chapter 5 examined cross-sectional patterns of substance use among a sample of Canadian secondary school students and their associations with clinically relevant symptoms of anxiety and depression. Results identified three classes of substance use: poly-use, dual use, and non-use. These results indicate that Canadian secondary school students are engaging in dual and poly-substance use. Those with anxiety, depression, or both had higher odds of being in the poly-use class compared to the non-use class. Symptomology was also associated with belonging to the dual use class except among males with anxiety symptoms only. This is consistent with previous research, that has found depressive symptoms and psychological distress (i.e., a combined measure of anxiety and depression) to be associated with poly-use.(6,11,88) This chapter also highlighted sex differences: female students had a higher prevalence of anxiety and depression and female students with both anxiety and depression had the highest odds of being in the poly-use class compared to the non-use class.

Chapter 6 examined the bi-directional associations between, first, number of substances used and anxiety and depression among all students and, second, single versus poly-substance use and anxiety and depression among students who used substances. Among all male students, uni-directional associations were identified where an increase in the number of substances used was associated with reduced anxiety symptoms between Waves 1 and 2. This result was in contrast to previous cross-sectional (11–14) and longitudinal (19)evidence. In addition, previous research examining poly-substance use and depression has typically found increasing substance use to be associated with greater symptoms.(20,186) Among students who used substances each year, uni-directional effects were identified from Wave 2 to Wave 3: poly-substance use was associated with

increased anxiety symptoms among female students and increased anxiety and depression symptoms among male students. These results are more consistent with previous longitudinal research.(20,186) This study also highlighted some sex differences. Although female students began with worse anxiety and depression scores, we found more significant results for male students, perhaps indicating a ceiling effect for female students.

Chapter 7 examined the longitudinal associations between latent classes of substance use and anxiety and depression scores among youth who used substances. Given that the previous chapter provided evidence that poly-substance use preceded changes in anxiety and depression symptoms among students who used substances, the focus of this chapter was on this direction of effect. These analyses identified three classes of substance use over time: occasional alcohol and e-cigarette use, escalating poly-substance use, and consistent poly-substance use. The longitudinal classes of substance use identified in this study differed from existing research, however, there were significant differences in samples and methodology that could explain these differences.(15,20) After controlling for relevant covariates, consistent poly-substance use was associated with depression but not anxiety. Additionally, escalating poly-substance use was associated with depression among male students but not female students.

There were three main themes that were consistent across all studies. The first was that Canadian adolescents engaged in poly-substance use. This thesis was the first to examine poly-substance use using LCA among secondary school students in multiple Canadian provinces. These findings are consistent with the limited previous research on adolescent poly-substance use in Canada.(2–4,7,40) A study of Canadian adolescents aged 12-18 in Victoria, BC in 2003 identified 3 substance use latent classes: low/no use (63%), co-use of primarily alcohol and cannabis (23%), and poly-substance use of alcohol, cannabis, cigarettes, and other illicit drugs (11%).(40) In Chapter 5, similar classes were identified using data from the 2017/18 school year, however the dual use class was made up of students engaging in alcohol and e-cigarette use rather than alcohol and cannabis use. Approximately 26% of adolescents belonged to the dual use class and 13% belonged to the poly-use class (11% among females, 15% among males). Recent work from the COMPASS study found that in the 2017/18 school year, 16% of students reported using one substance in the past 30 days, and 18% reported using two or more substances.(7) In Chapter 6, lower numbers were calculated, likely owing to the use of a linked longitudinal sample. In Wave 1 (2017/18), 12% of adolescents reported past 30-day use of one substance and 9% reported past 30-day poly-substance use. By Wave 3 (2019/20),

20% of students reported single substance use and 27% reported poly-substance use. This thesis highlights that Canadian adolescents are engaging in poly-substance use and that such use increases with age.

The second theme in the findings of this thesis was the consistent role of e-cigarettes in adolescent poly-substance use. This study was the first among adolescents in Canada to include e-cigarettes in examining poly-substance use. Since 2016, e-cigarette use has been increasing among adolescents in Canada.(223,247) Across all chapters in this thesis, e-cigarette use was a consistent component of all substance use classes. This is consistent with other recent literature. The majority of adolescents who report e-cigarette use also report other substance use (248) and e-cigarette use has been associated with incident poly-substance use.(249) Other studies that have included e-cigarettes and used LCA to examine substance use classes have found e-cigarette use to be a part of the majority of substance use classes (5,60,62,63) or at least the highest use class.(79,181)

Thirdly, poly-substance use was consistently associated with worse depression symptoms. In Chapter 5, both the dual use and poly-use classes were associated with clinically relevant symptoms of depression. This is consistent with the majority of previous cross-sectional research.(6,7,182–184,11,14,60,88,178–181) Limited studies have identified no effect or the opposite direction of effect.(69,70) Next, in Chapter 6, among adolescents who used substances, poly-substance use was associated with increased depression symptoms among male students from Wave 2 to 3. This evidence supports poly-substance predicting subsequent depression symptoms. This direction of effect is consistent with the opponent process model of substance use addiction.(196) Finally, in Chapter 7, among adolescents who used substances, the consistent poly-use class was associated with higher depression symptoms compared to the occasional use class even after controlling for anxiety. There is limited longitudinal research examining poly-substance use and depression and one study to date has found results consistent with this direction of effect. McKelvey and colleagues found that poly-substance use was associated with future depression scores 2 and 3 years later, although this study did not control for any covariates.(20) Other research has identified a co-occurring emergence of both poly-substance use and depressive symptoms.(186)

There were also findings across this thesis that were more nuanced. The first were the differences identified in substance use patterns between female and male students. In Chapter 5, a higher proportion of male students were in the poly-substance use class and male students were more likely to use substances at a higher frequency. This was in line with current literature (2,4,60–

63,5,7,28–30,42,44,59) and findings from Chapter 7. In Chapter 7, similar classes were identified for both females and males at baseline, but over time, male students in the consistent use class reported higher frequency cannabis and e-cigarette use. One difference between Chapters 5 and 7 was that in Chapter 5 there were more male students in the highest use class (poly-use) compared to female students whereas in Chapter 7, slightly more female students were in the highest use class (consistent poly-use) than male students. This is in contrast to previous longitudinal evidence: two US-based studies found no sex differences in adolescence,(17,20) while another identified that males were more likely to use more substances.(18)

Next, there were also distinctions in the association between substance use and anxiety and depression among females and males. Cross-sectionally, in Chapter 5, symptomology was associated with belonging to the poly-use class and dual use class, except among males with anxiety only. Anxiety has not always been associated with polys-substance use cross-sectionally (183,184) although neither study examined sex differences and psychological distress, a measure of both anxiety and depression, has consistently been associated with poly-substance use.(6,88) Longitudinally, in Chapter 6, there were two main differences between results for female and male students. First, among all male students, an increase in the number of substances used was associated with less anxiety symptoms between Waves 1 and 2 and this result was not found among female students. This result is in contrast to previous cross-sectional evidence (12–14) and the limited longitudinal literature.(19) Previous longitudinal research found anxiety symptoms to be protective against poly-use.(19) However, no studies to date have examined interactions with sex.(13,14,19) Second, among male students who used substances, poly-substance use was associated with worse depression symptoms, in addition to worse anxiety symptoms seen among both male and female students. These results were more consistent with previous longitudinal research.(20,186) Similar to Chapter 6, in Chapter 7, there was also an association between escalating poly-substance use and depression in addition to the association between consistent poly-substance use and depression found among both female and male students. The fact that there were more significant associations for male students in the longitudinal studies were surprising given that female students began with worse anxiety and depression symptoms. These findings indicate that perhaps there is a ceiling effect for the relationship between poly-substance use and anxiety and depression among female students.

The final more inconsistent findings were between poly-substance use and anxiety symptoms. Anxiety symptoms were associated with dual use and poly-substance use cross-sectionally among

female students, and among all students when in parallel with depression. However, a more complicated relationship emerged longitudinally. In Chapter 6, among all males, increasing substance use was associated with less anxiety symptoms between Waves 1 and 2. This result is in contrast to previous cross-sectional evidence (12–14) and research examining poly-substance use and depression has typically found increasing substance use to be associated with greater symptoms.(20,186) This surprising finding could be due to some potential benefits of substance use such as social acceptance by peers that may have temporarily resulted in reduced symptoms of anxiety as we no longer saw this association from Waves 2 to 3. In contrast, among adolescents who used substances, poly-use was associated with worse anxiety symptoms compared to single substance use between Waves 2 and 3. These contrasting findings indicate a perhaps complicated relationship between poly-substance use and anxiety that warrants further examination. In contrast, in Chapter 7, when examining the relationship between specific substances and anxiety and depression, this relationship was no longer significant after controlling for depressions symptoms. This suggests that depression plays a larger role in the worsening of anxiety symptoms than poly-substance use.

8.3 Implications for Practice

The results of this dissertation present implications and directions for future practice. First, this thesis highlights the need to include poly-substance use in adolescent substance use surveillance efforts. There is limited information on youth poly-substance use in Canada.(2–4,7,40) The most recent study of poly-substance use among Canadian adolescents using nationally representative surveillance data is now over 10 years old.(4) In this thesis, I found that by grades 11 and 12, almost half of students reported substance use in the past month and over 1 in 4 reported poly-substance use. Future youth substance use surveillance should consider examining poly-substance use and reporting those numbers as to better capture substance use trends among youth. For instance, the Canadian Student Tobacco, Alcohol, and Drugs Survey (CSTADS) and the Health Behaviour in School-aged Children (HBSC) are nationally representative cross-sectional studies that collect data on adolescent substance use and could report on poly-substance use.(38,250) CSTADS currently reports concurrent and simultaneous alcohol and cannabis use and could benefit from also including e-cigarette use in that reporting.(38)

The second consideration for public health practice is the provision of consistent, multi-substance use programming throughout adolescence. The results of this dissertation provide support

for a “risk behaviour syndrome” where risk behaviours tend to cluster together (191) and multi-substance use programming. Prevention efforts and strategy tend to be substance specific. Based on the results of this thesis, adolescent prevention and treatment strategies should consider substance use patterns, including the dual use of alcohol and e-cigarettes and poly-substance use. While many programs do consider multiple substances, they may not address poly-substance use directly.(251,252) Additionally, programs to address new substances, such as e-cigarettes, should take into consideration that these new products may not be used in isolation.(253) Given the increase in poly-substance use over time, programming throughout adolescence is likely warranted. Within Canada, substance use prevention programming is only mandated as part of the physical education curriculum of which students are not required to take throughout secondary school. To target those youth who were found to escalate their poly-substance use over time, programming should be provided every year.

Finally, it may be useful to consider a mental health component in substance use programming. A recent systematic review indicates that there is limited mental health programming included in adolescent substance use prevention programs.(251) Some programs address stress management and coping strategies, however this is not consistent across programs and this aspect of programming is typically not evaluated.(251) Two studies to date have found positive effects of the Life Skills Training (LST) program on improving anxiety management skills.(254,255) The LST program is a school-based program designed to prevent adolescent substance use and consists of three major components: (1) personal competence that teaches self-management skills, including coping with stress and anxiety, (2) social competence that teaches an array of social skills, and (3) drug resistance which teaches resistance skills and health related content.(256) This program has demonstrated effectiveness in the reduction of numerous substances including alcohol, cannabis, and other drugs.(251) This thesis identified a consistent link between poly-substance use and depression symptoms. Therefore, ensuring students understand how substance use may influence their mental health, including depression symptoms, is important. Some youth identify using substances such as alcohol and cannabis to cope with symptoms of anxiety and depression or as being beneficial for their mental health.(257–260) These youth may benefit from support in developing more healthy coping strategies (261) and gaining a better understanding of the potential long term effects of substance use on their mental health.(257,262) Students should understand symptoms to be mindful of if they choose to engage in substance use and who they can approach for help should such symptoms arise. It

may also be helpful to assess symptoms of anxiety and/or depression among students who are found to be using substances and vice versa.

8.4 Implications for Research

The results of this dissertation also present implications and directions for future research. First, future examinations of poly-substance use should include e-cigarettes as a substance of interest. Except for the non-use classes, e-cigarettes were a consistent component of all substance use classes in both cross-sectional and longitudinal research. Promisingly many more recent studies of poly-substance use have included e-cigarette use and this trend should continue in the future.(5,60,62,63,79,181) On this note, it is important to ensure that surveillance systems are adaptive as new products come onto the market. For example, including brand names and current terminology in surveys is recommended to obtain a more accurate picture of e-cigarette use rates.(263) As the e-cigarette market rapidly evolves, surveillance systems may need to be updated regularly to accurately capture e-cigarette use.

Second, future studies should further examine the link between poly-substance use and anxiety and depression. While this thesis demonstrates an association, it is important to strengthen the evidence on the temporality of these associations with the use of more frequent questionnaires (i.e., greater frequency than once per year). This would allow for a greater examination of which came first and for whom. Next, stronger measures of poly-substance use and anxiety and depression could also be used. This study was unable to differentiate between simultaneous and concurrent poly-substance use and should be examined in future work. It is also important to note, that while this research used validated scales to examine symptoms of anxiety and depression,(208,209) these measures are not indicative of clinical diagnoses. Future research could benefit from examining clinical diagnoses of anxiety and depression.

Third, future research should explore why youth are using multiple substances and how they feel it impacts their mental health. Understanding why youth are engaging in poly-substance use would help determine potential causal associations between poly-substance use and anxiety and depression. For example, using a more in-depth questionnaire or qualitative research methods could help determine whether adolescents are using multiple substances to help cope with their anxiety or depression or if they felt their anxiety or depression symptoms were a result of their substance use.

Finally, it will also be important to examine the impact of the COVID-19 pandemic on these relationships. Early research indicates that there was no evidence of an adverse effect of the early stages of the COVID-19 pandemic period on cannabis use among a sample of youth in Ontario and Quebec, Canada, however, it is unclear how the pandemic may affect poly-substance use.(264) Additionally, the pandemic-related lockdowns and school closures have negatively affected adolescents' mental health.(265–268) While the current research did not find evidence for students using substances to cope with symptoms of anxiety and depression, it will be important to monitor youth to understand if they are using substances to cope with COVID-19 related stress. Moving forward it will be important to continue to closely follow these trends to ensure students have the appropriate supports to cope in subsequent waves of COVID-19 and succeed as they move forward from this traumatic event.

8.5 Overall Strengths and Limitations

8.5.1 Strengths

This dissertation project had several strengths. First, it provided important information to fill a research gap in Canada and internationally. This study was the first to examine substance use using LCA in multiple provinces across Canada. This thesis is also the first study in Canada to include e-cigarettes as a substance when considering poly-substance use and to examine the longitudinal relationship between poly-substance use and anxiety and depression.

Secondly, the COMPASS questionnaire collected data on a range of substance use and health risk behaviours that allowed for the timely exploration of the relationships of interest. This dissertation made use of substance use questions that were consistent with national youth health surveillance research (217) and measures of anxiety and depression symptoms were captured using validated scales.(208,209) Additionally, the format of the COMPASS study allowed for a timely investigation of current substance use patterns. The emergence of e-cigarettes and their recent increase in use among adolescents makes much of the Canadian evidence on poly-substance use outdated.(3,4,40,223)

Thirdly, the longitudinal design of the COMPASS study provided a unique opportunity to answer the research questions. A strength of this study design was the inclusion of three waves of data from the COMPASS study to examine the temporal associations between poly-substance use and

anxiety and depression. Additionally, the COMPASS study utilizes an active-information passive-consent protocol to encourage participation and honest reporting. This recruitment method has been shown to limit self-selection and response biases and generate more robust results which has been shown to be particularly important in substance use and mental health research.(197,199–201)

Finally, the use of LCA was a strength of this thesis. Using LCA, I was able to create substance use groupings that considered the number of substances used and frequency of use.(52) Additionally, without the use of LCA, this thesis would have been more limited by student missing data. LCA makes use of the full-information maximum likelihood (FIML) estimate technique which is beneficial because of how missing data is handled. If an individual is missing one observed variable, they will still be assigned a latent class based on their other responses. Without the FIML estimation technique, students who were missing any substance use data would have been excluded from the analyses.

8.5.2 Limitations

Although there were many strengths to this project, there were also some limitations. The largest limitation was with the substance use measures. The COMPASS questionnaire did not collect information about whether substances were used individually or in combination. Therefore, this research was only able to capture concurrent poly-substance use (i.e., multiple substances being used in the same period such as the past 30 days), not simultaneous poly-substance use (i.e., multiple substances being used in the same instance) and therefore we could not draw any conclusions about simultaneous substance use. However, nationally representative survey results found that 74% of Canadian students in grades 7 to 12 who reported both alcohol and cannabis use in the past year reported simultaneous use indicating that some simultaneous use was likely.(38)

There are also some limitations to the questionnaire that may have resulted in students under-reporting their substance use. Firstly, due to the illicit nature of the substances for underage youth, students may not have felt comfortable reporting their substance use on the COMPASS questionnaire. However, the COMPASS study does employ a passive consent procedure to encourage participation and honest reporting.(199) Second, there were a limited number of substances included on the questionnaire and students may be using other substances that were not captured (e.g., stimulants, sedatives/tranquilizers, hallucinogens). However, less than 5% of students in grades 7 to 12 report use of these substances.(38) Finally in Waves 1 and 2, there was a lack of a definition of an e-cigarette

provided and no brands were listed on the questionnaire. This has been found to result in students under-reporting their e-cigarette use.(263) The COMPASS study is also lacking measures of peer or family substance use which have been associated with early initiation and escalating use through adolescence.(86) However, this study made use of variables indicating family and friends support which have been positively and negatively associated with poly-substance use respectively.(7) Additionally, there were no measures available of parental psychopathology, which is a significant risk factor for children.(144,145)

The COMPASS study was designed to evaluate changes in school programs and policies and therefore uses a convenience sample that is not representative of all Canadian secondary school students. Additional limitations in the study design included that data collection only occurred once annually. Annual data collections reduce school and participant burden; however, they may miss important developments in substance use or anxiety and depression symptoms. Therefore, this data collection schedule may not have adequately captured the temporality of the relationships investigated in this thesis. Another limitation with longitudinal research is participant drop-out. Students who use substances and have worse mental health are less likely to be followed-up over time.(206,236) As a result, the results reported here may underestimate poly-substance use and its relationship with anxiety and depression.

There were also some limitations to the use of LCA as an analysis method. In LCA, missing data on latent class indicators are assumed to be missing at random (MAR).(269) However, in practice, data can be a combination of missing completely at random (MCAR), MAR, and missing not at random (MNAR). If data is MCAR or MAR, it can be handled by the model, however if data is MNAR the model cannot adjust for it and may produce biased results. This could lead to a potential misrepresentation of the classes.(52,270) However, the use of the full-information maximum likelihood (FIML) estimate technique minimizes the removal of data.

There was also a disadvantage to using a generalized linear mixed model (GLMM) in conjunction with RMLCA in Chapter 7. GLMM does not take into account the uncertainty in classification of the latent classes, which is based on probability.(52) In other words, there is an assumption that the assigned latent classes reflect groupings that exist in the population; this assumption may or may not be valid, and this limitation can affect any inferences made from the analysis. However, an entropy value of >.80 is considered sufficient to indicate certainty in the

classes and the RMLCA models in Chapter 7 had entropy values of 0.86; therefore, this should not impact the validity of results.(211)

8.6 Conclusions

This dissertation fills an important gap with respect to our knowledge of poly-substance use and its associations with anxiety and depression among adolescents in Canada. The findings highlight the need to consider adolescent poly-substance use and have implications for practice and research. Given that many students reported poly-substance use, surveillance, prevention, and treatment strategies should consider substance use patterns, including dual and poly-substance use. As this research identified substance use as a potentially modifiable behaviour associated with adolescent mental health, it may also be useful to consider a mental health component in substance use programming. Future research examining this relationship should additionally consider simultaneous poly-substance use, clinical measures of anxiety and depression, and capture reasons for substance use to further strengthen and understand the relationship between poly-substance use and anxiety and depression among adolescents.

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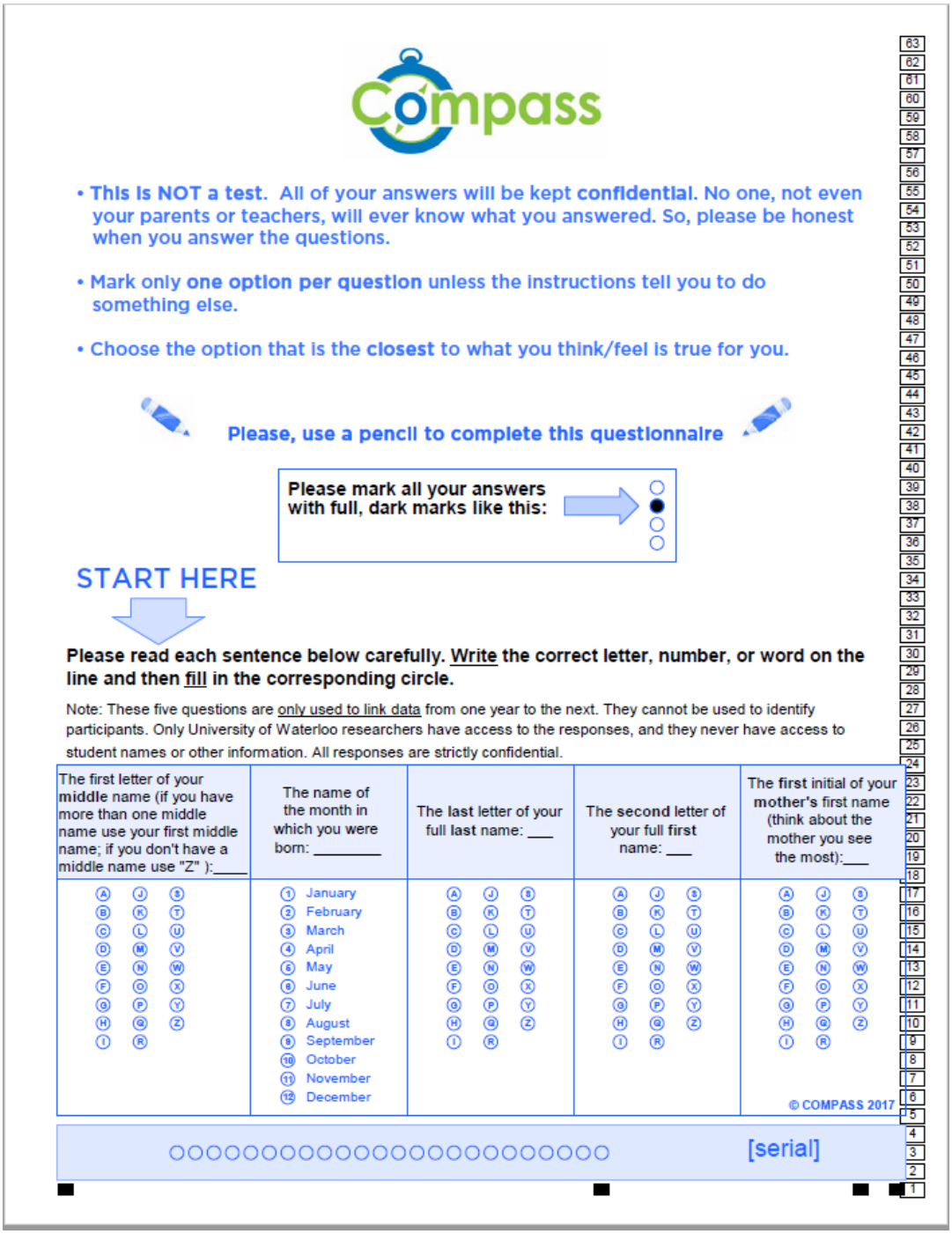
Appendix A

Year 6 (2017-2018) COMPASS Questionnaire



Compass

- **This is NOT a test.** All of your answers will be kept **confidential**. No one, not even your parents or teachers, will ever know what you answered. So, please be honest when you answer the questions.
- Mark only **one option per question** unless the instructions tell you to do something else.
- Choose the option that is the **closest** to what you think/feel is true for you.

Please, use a pencil to complete this questionnaire

Please mark all your answers with full, dark marks like this:

START HERE

Please read each sentence below carefully. Write the correct letter, number, or word on the line and then fill in the corresponding circle.

Note: These five questions are only used to link data from one year to the next. They cannot be used to identify participants. Only University of Waterloo researchers have access to the responses, and they never have access to student names or other information. All responses are strictly confidential.

The first letter of your **middle** name (if you have more than one middle name use your first middle name; if you don't have a middle name use "Z"):____	The name of the month in which you were born: _____	The **last** letter of your full **last** name: ___	The **second** letter of your full **first** name: ___	The **first** initial of your **mother's** first name (think about the mother you see the most):___
A J S B K T C L U D M V E N W F O X G P Y H Q Z I R	1 January 2 February 3 March 4 April 5 May 6 June 7 July 8 August 9 September 10 October 11 November 12 December	A J S B K T C L U D M V E N W F O X G P Y H Q Z I R	A J S B K T C L U D M V E N W F O X G P Y H Q Z I R	A J S B K T C L U D M V E N W F O X G P Y H Q Z I R

[serial]

About You

1. What grade are you in?

- ○ Grade 9
- ○ Grade 10
- ○ Grade 11
- ○ Grade 12

Quebec students only

- ○ Secondary I
- ○ Secondary II
- ○ Secondary III
- ○ Secondary IV
- ○ Secondary V
- ○ Other

2. How old are you today?

- ○ 12 years or younger
- ○ 13 years
- ○ 14 years
- ○ 15 years
- ○ 16 years
- ○ 17 years
- ○ 18 years
- ○ 19 years or older

3. Are you female or male?

- ○ Female
- ○ Male

4. How would you describe yourself? *(Mark all that apply)*

- ○ White
- ○ Black
- ○ Asian
- ○ Aboriginal (First Nations, Métis, Inuit)
- ○ Latin American/Hispanic
- ○ Other

5. About how much money do you usually get <u>each week</u> to spend on yourself or to save?
(Remember to include all money from allowances and jobs like baby-sitting, delivering papers, etc.)

- ○ Zero
- ○ $1 to $5
- ○ $6 to $10
- ○ $11 to $20
- ○ $21 to $40
- ○ $41 to $100
- ○ More than $100
- ○ I do not know how much money I get each week

6. How do you usually travel to and from school? *(If you use two or more modes of travel, choose the one that you spend most time doing)*

To school	From school
○ By car (as a passenger)	○ By car (as a passenger)
○ By car (as a driver)	○ By car (as a driver)
○ By school bus	○ By school bus
○ By public bus, subway, or streetcar	○ By public bus, subway, or streetcar
○ By walking	○ By walking
○ By bicycling	○ By bicycling
○ Other	○ Other

7. Did you attend this school last year?

○ Yes, I attended the same school last year
○ No, I was at another school last year

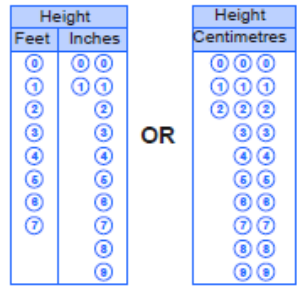
8. How tall are you without your shoes on? (Please write your height in feet and inches **OR** in centimetres, and then fill in the appropriate numbers for your height.)

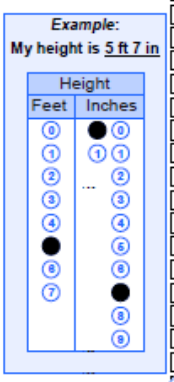
○ I do not know how tall I am

"My height is ____feet, _____inches"

OR

"My height is _____ centimetres"





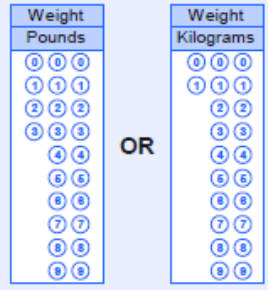
9. How much do you weigh without your shoes on? (Please write your weight in pounds **OR** in kilograms, and then fill in the appropriate numbers for your weight.)

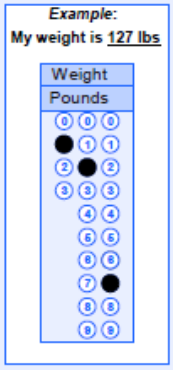
○ I do not know how much I weigh

"My weight is _____ pounds"

OR

"My weight is _____ kilograms"





○○○○○○○○○○○○○○○○○○○○○○○○○○ [serial]

10. How do you describe your weight?

- ○ Very underweight
- ○ Slightly underweight
- ○ About the right weight
- ○ Slightly overweight
- ○ Very overweight

11. Which of the following are you trying to do about your weight?

- ○ **Lose** weight
- ○ **Gain** weight
- ○ **Stay** the same weight
- ○ I am **not trying to do anything** about my weight

12. How much time per day do you *usually* spend doing the following activities?

For example: If you spend about 3 hours watching TV each day, you will need to fill in the 3 hour circle, and the 0 minute circle as shown below:

a) Watching/streaming TV shows or movies — Hours: ● 3 — Minutes: ● 0

	Hours	Minutes
a) Watching/streaming TV shows or movies	0 1 2 3 4 5 6 7 8 9	0 15 30 45
b) Playing video/computer games	0 1 2 3 4 5 6 7 8 9	0 15 30 45
c) Doing homework	0 1 2 3 4 5 6 7 8 9	0 15 30 45
d) Talking on the phone	0 1 2 3 4 5 6 7 8 9	0 15 30 45
e) Surfing the internet	0 1 2 3 4 5 6 7 8 9	0 15 30 45
f) Texting, messaging, emailing (note: 50 texts = 30 minutes)	0 1 2 3 4 5 6 7 8 9	0 15 30 45
g) Sleeping	0 1 2 3 4 5 6 7 8 9	0 15 30 45

13. In the last 30 days, did you gamble online for money?

- ○ Yes
- ○ No

Physical Activity

HARD physical activities include jogging, team sports, fast dancing, jump-rope, and any other physical activities that increase your heart rate and make you breathe hard and sweat.

MODERATE physical activities include lower intensity activities such as walking, biking to school, and recreational swimming.

14. Mark how many minutes of HARD physical activity you did on each of the last 7 days. This includes physical activity during physical education class, lunch, after school, evenings, and spare time.

	Hours					Minutes				
	0	1	2	3	4	0	15	30	45	
Monday	○	○	○	○	○	○	○	○	○	
Tuesday	○	○	○	○	○	○	○	○	○	
Wednesday	○	○	○	○	○	○	○	○	○	
Thursday	○	○	○	○	○	○	○	○	○	
Friday	○	○	○	○	○	○	○	○	○	
Saturday	○	○	○	○	○	○	○	○	○	
Sunday	○	○	○	○	○	○	○	○	○	

For example: If you did 45 minutes of hard physical activity on Monday, you will need to fill in the 0 hour circle and the 45 minute circle, as shown below:

	Hours					Minutes				
	0	1	2	3	4	0	15	30	45	
Monday	●	○	○	○	○	○	○	○	●	

15. Mark how many minutes of MODERATE physical activity you did on each of the last 7 days. This includes physical activity during physical education class, lunch, after school, evenings, and spare time. Do not include time spent doing hard physical activities.

	Hours					Minutes				
	0	1	2	3	4	0	15	30	45	
Monday	○	○	○	○	○	○	○	○	○	
Tuesday	○	○	○	○	○	○	○	○	○	
Wednesday	○	○	○	○	○	○	○	○	○	
Thursday	○	○	○	○	○	○	○	○	○	
Friday	○	○	○	○	○	○	○	○	○	
Saturday	○	○	○	○	○	○	○	○	○	
Sunday	○	○	○	○	○	○	○	○	○	

For example: If you did 1 hour and 30 minutes of moderate physical activity on Monday, you will need to fill in the 1 hour circle and the 30 minute circle, as shown below:

	Hours					Minutes				
	0	1	2	3	4	0	15	30	45	
Monday	○	●	○	○	○	○	○	●	○	

16. Were the last 7 days a typical week in terms of the amount of physical activity that you usually do?

- ○ Yes
- ○ No, I was *more* active in the last 7 days
- ○ No, I was *less* active in the last 7 days

○○○○○○○○○○○○○○○○○○○○○○○○ [serial]

17. Your closest friends are the friends you like to spend the most time with. How many of your closest friends are physically active?

- ○ None
- ○ 1 friend
- ○ 2 friends
- ○ 3 friends
- ○ 4 friends
- ○ 5 or more friends

18. Are you taking a physical education class at school this year?

- ○ **Yes**, I am taking one **this term**
- ○ **Yes**, I will be taking one or have taken one this school year, **but not this term**.
- ○ **No**, I am not taking a physical education class at school this year

19. Do you participate in before-school, noon hour, or after-school physical activities organized by your school? *(e.g., intramurals, non-competitive clubs)*

- ○ Yes
- ○ No
- ○ None offered at my school

20. Do you participate in competitive school sports teams that compete against other schools? *(e.g., junior varsity or varsity sports)*

- ○ Yes
- ○ No
- ○ None offered at my school

21. Do you participate in league or team sports outside of school?

- ○ Yes
- ○ No
- ○ There are none available where I live

22. On how many days in the last 7 days did you do exercises to strengthen or tone your muscles? *(e.g., push-ups, sit-ups, or weight-training)*

- ○ 0 days
- ○ 1 day
- ○ 2 days
- ○ 3 days
- ○ 4 days
- ○ 5 days
- ○ 6 days
- ○ 7 days

Healthy Eating

23. If you do not eat breakfast every day, why do you skip breakfast? *(Mark all that apply)*

- ○ I eat breakfast every day

- ○ I don't have time for breakfast
- ○ The bus comes too early
- ○ I sleep in
- ○ I'm not hungry in the morning
- ○ I feel sick when I eat breakfast
- ○ I'm trying to lose weight
- ○ There is nothing to eat at home
- ○ Other

24. In a *usual* school week *(Monday to Friday)*, on how many days do you do the following?

	None	1 day	2 days	3 days	4 days	5 days
a) Eat breakfast	○	○	○	○	○	○
b) Eat breakfast provided to you **as part of a school program**	○	○	○	○	○	○
c) Eat lunch at school - lunch packed and brought from home	○	○	○	○	○	○
d) Eat lunch at school - lunch purchased in the cafeteria	○	○	○	○	○	○
e) Eat lunch purchased at a fast food place or restaurant	○	○	○	○	○	○
f) Eat snacks purchased from a vending machine **in your school**	○	○	○	○	○	○
g) Eat snacks purchased from a vending machine, corner store, snack bar, or canteen **off school property**	○	○	○	○	○	○
h) Drink sugar-sweetened beverages (soda pop, Kool-Aid, Gatorade, etc.) Do not include diet/sugar-free drinks	○	○	○	○	○	○
i) Drink high-energy drinks (Red Bull, Monster, Rock Star, etc.)	○	○	○	○	○	○
j) Drink coffee or tea **with sugar** (include cappuccino, frappuccino, iced-tea, iced-coffees, etc.)	○	○	○	○	○	○
k) Drink coffee or tea **without sugar**	○	○	○	○	○	○

25. On a *usual* weekend *(Saturday and Sunday)*, on how many days do you do the following?

	None	1 day	2 days
a) Eat breakfast	○	○	○
b) Eat lunch	○	○	○
c) Eat foods purchased at a fast food place or restaurant	○	○	○
d) Eat snacks purchased from a vending machine, corner store, snack bar, or canteen	○	○	○
e) Drink sugar-sweetened beverages (soda pop, Kool-Aid, Gatorade, etc.) Do not include diet/sugar-free drinks	○	○	○
f) Drink high energy drinks (Red Bull, Monster, Rock Star, etc.)	○	○	○
g) Drink coffee or tea **with sugar** (include cappuccino, frappuccino, iced-tea, iced-coffees, etc.)	○	○	○
h) Drink coffee or tea **without sugar**	○	○	○

○○○○○○○○○○○○○○○○○○○○○○○○○ [serial]

63 62 61 60 59 58 57 56 55 54 53 52 51 50

26. YESTERDAY, *from the time you woke up until the time you went to bed*, how many servings of meats and alternatives did you have? *One 'Food Guide' serving of meat and alternatives includes cooked fish, chicken, beef, pork, or game meat, eggs, nuts or seeds, peanut butter or nut butters, legumes (beans), and tofu.*

- ○ None
- ○ 1 serving
- ○ 2 servings
- ○ 3 servings
- ○ 4 servings
- ○ 5 or more servings

Canada's Food Guide **Serving Sizes of Meats and Alternatives**

49 48 47 46 45 44 43 42 41 40 39 38 37 36 35 34 33

27. YESTERDAY, *from the time you woke up until the time you went to bed*, how many servings of vegetables and fruits did you have? *One 'Food Guide' serving of vegetables and fruit includes pieces of fresh vegetable or fruit, salad or raw leafy greens, cooked leafy green vegetables, dried or canned or frozen fruit, and 100% fruit or vegetable juice.*

- ○ None
- ○ 1 serving
- ○ 2 servings
- ○ 3 servings
- ○ 4 servings
- ○ 5 servings
- ○ 6 servings
- ○ 7 servings
- ○ 8 servings
- ○ 9 or more servings

Canada's Food Guide **Serving Sizes of Vegetables and Fruits**

32 31 30 29 28 27 26 25 24 23 22 21 20 19 18

28. YESTERDAY, *from the time you woke up until the time you went to bed*, how many servings of milk and alternatives did you have? *One 'Food Guide' serving of milk or milk alternatives includes milk, fortified soy beverage, reconstituted powdered milk, canned (evaporated) milk, yogurt or kefir (another type of cultured milk product), and cheese.*

- ○ None
- ○ 1 serving
- ○ 2 servings
- ○ 3 servings
- ○ 4 servings
- ○ 5 servings
- ○ 6 or more servings

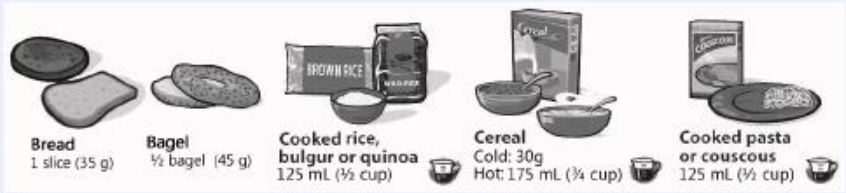
Canada's Food Guide **Serving Sizes of Milk and Alternatives**

17 16 15 14 13 12 11 10 9 8 7 6 5 4 3 2 1

29. YESTERDAY, *from the time you woke up until the time you went to bed*, how many servings of grain products did you have? *One 'Food Guide' serving of grain products includes bread, bagels, flatbread such as tortilla, pita, cooked rice or pasta, and cold cereal.*

- ○ None
- ○ 1 serving
- ○ 2 servings
- ○ 3 servings
- ○ 4 servings
- ○ 5 servings
- ○ 6 servings
- ○ 7 servings
- ○ 8 servings
- ○ 9 or more servings

Canada's Food Guide **Serving Sizes of Grain Products**



Your Experience with Smoking

30. Have you ever tried cigarette smoking, even just a few puffs?

- ○ Yes
- ○ No

31. Do you think in the future you might try smoking cigarettes?

- ○ Definitely yes
- ○ Probably yes
- ○ Probably not
- ○ Definitely not

32. If one of your best friends were to offer you a cigarette, would you smoke it?

- ○ Definitely yes
- ○ Probably yes
- ○ Probably not
- ○ Definitely not

33. At any time during the next year do you think you will smoke a cigarette?

- ○ Definitely yes
- ○ Probably yes
- ○ Probably not
- ○ Definitely not

34. Have you ever smoked 100 or more whole cigarettes in your life?

- ○ Yes
- ○ No

35. On how many of the last 30 days did you smoke one or more cigarettes?

- ○ None
- ○ 1 day
- ○ 2 to 3 days
- ○ 4 to 5 days
- ○ 6 to 10 days
- ○ 11 to 20 days
- ○ 21 to 29 days
- ○ 30 days *(every day)*

36. Your closest friends are the friends you like to spend the most time with. How many of your closest friends smoke cigarettes?

- ○ None
- ○ 1 friend
- ○ 2 friends
- ○ 3 friends
- ○ 4 friends
- ○ 5 or more friends

37. Have you ever tried to quit smoking cigarettes?

- ○ I have never smoked
- ○ I have only smoked a few times
- ○ I have never tried to quit
- ○ I have tried to quit once
- ○ I have tried to quit 2 or 3 times
- ○ I have tried to quit 4 or 5 times
- ○ I have tried to quit 6 or more times

38. Have you ever tried an electronic cigarette, also known as an e-cigarette?

- ○ Yes
- ○ No

39. Have you used e-cigarettes for any of the following reasons? *(Mark all that apply)*

- ○ I have not used e-cigarettes
- ○ Curiosity / to try something new
- ○ I can use e-cigarettes in places where smoking is not allowed
- ○ To smoke fewer cigarettes
- ○ To help me quit smoking cigarettes
- ○ I have used e-cigarettes for some other reason

40. In the last 30 days, did you use any of the following? *(Mark all that apply)*

- ○ Pipe tobacco
- ○ Cigarillos or little cigars (*plain or flavoured*)
- ○ Cigars (not including cigarillos or little cigars, *plain or flavoured*)
- ○ Roll-your-own cigarettes (tobacco only)
- ○ Loose tobacco mixed with marijuana
- ○ E-cigarettes (electronic cigarettes that look like cigarettes/cigars, but produce vapour instead of smoke)
- ○ Smokeless tobacco (chewing tobacco, pinch, snuff, or snus)
- ○ Nicotine patches, nicotine gum, nicotine lozenges, or nicotine inhalers
- ○ Hookah (water-pipe) to smoke tobacco
- ○ Hookah (water-pipe) to smoke herbal sheesha/shisha
- ○ Blunt wraps (a sheet or tube made of tobacco used to roll cigarette tobacco)
- ○ I have not used any of these things in the last 30 days

41. On how many of the last 30 days did you use an e-cigarette?

- ○ None
- ○ 1 day
- ○ 2 to 3 days
- ○ 4 to 5 days
- ○ 6 to 10 days
- ○ 11 to 20 days
- ○ 21 to 29 days
- ○ 30 days *(every day)*

○○○○○○○○○○○○○○○○○○○○○○○○ [serial]

Alcohol and Drug Use

*Please remember that we will keep your answers **completely confidential**.*

A **DRINK** means: 1 regular sized bottle, can, or draft of beer; 1 glass of wine; 1 bottle of cooler; 1 shot of liquor (rum, whisky, etc); or 1 mixed drink (1 shot of liquor with pop, juice, energy drink).

42. In the last 12 months, how often did you have a drink of alcohol that was more than just a sip?

- ○ I have never drunk alcohol
- ○ I did not drink alcohol in the last 12 months
- ○ I have only had a sip of alcohol
- ○ Less than once a month
- ○ Once a month
- ○ 2 or 3 times a month
- ○ Once a week
- ○ 2 or 3 times a week
- ○ 4 to 6 times a week
- ○ Every day

43. How old were you when you first had a drink of alcohol that was more than just a sip?

- ○ I have never drunk alcohol
- ○ I have only had a sip of alcohol
- ○ I do not know

- ○ 8 years or younger
- ○ 9 years
- ○ 10 years
- ○ 11 years
- ○ 12 years
- ○ 13 years
- ○ 14 years
- ○ 15 years
- ○ 16 years
- ○ 17 years
- ○ 18 years or older

44. In the last 12 months, how often did you have 5 drinks of alcohol or more on one occasion?

- ○ I have never done this
- ○ I did not have 5 or more drinks on one occasion in the last 12 months
- ○ Less than once a month
- ○ Once a month
- ○ 2 to 3 times a month
- ○ Once a week
- ○ 2 to 5 times a week
- ○ Daily or almost daily

45. In the last 12 months, have you had alcohol mixed or pre-mixed with an energy drink (such as Red Bull, Rock Star, Monster, or another brand)?

- ○ I have never done this
- ○ I did not do this in the last 12 months
- ○ Yes
- ○ I do not know

46. In the last 12 months, how often did you use marijuana or cannabis? (a joint, pot, weed, hash)

- ○ I have never used marijuana
- ○ I have used marijuana but not in the last 12 months
- ○ Less than once a month
- ○ Once a month
- ○ 2 or 3 times a month
- ○ Once a week
- ○ 2 or 3 times a week
- ○ 4 to 6 times a week
- ○ Every day

47. If you have used marijuana or cannabis in the last 12 months, how did you use it? *(Mark all that apply)*

- ○ I have used it by smoking it (e.g., in a joint, a pipe, a bong)
- ○ I have used it by vaping it
- ○ I have used it by eating or drinking it (e.g., in brownies, cookies, candies, tea)
- ○ I have not used marijuana or cannabis in the last 12 months

48. How old were you when you first used marijuana or cannabis?

- ○ I have never used marijuana
- ○ I do not know

- ○ 8 years or younger
- ○ 9 years
- ○ 10 years
- ○ 11 years
- ○ 12 years
- ○ 13 years
- ○ 14 years
- ○ 15 years
- ○ 16 years
- ○ 17 years
- ○ 18 years or older

49. Do you think it would be difficult or easy for you to get marijuana if you wanted some?

- ○ Difficult
- ○ Easy
- ○ I do not know

50. Have you used or tried any of the following medications TO GET HIGH?

	No, I have never done this	Yes, I have done this in the last 12 months	Yes, I have done this, but NOT in the last 12 months
a) Oxycodone (oxy, OC, APO, OxyContin®, percs, roxies, OxyNEO®)	○	○	○
b) Fentanyl (china white, synthetic heroin, china girl)	○	○	○
c) Other prescription pain relievers (codeine, morphine, Tylenol 3)	○	○	○

51. Do you think it would be difficult or easy to get pain relievers (Oxycodone, Fentanyl, codeine, etc.) if you wanted some?

- ○ Difficult
- ○ Easy
- ○ I do not know

○○○○○○○○○○○○○○○○○○○○○○○○ [serial]

Mental Health

52. How much do you agree or disagree with the following statements?

	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
a) I have a happy home life	○	○	○	○	○
b) My parents/guardians expect too much of me	○	○	○	○	○
c) I can talk about my problems with my family	○	○	○	○	○
d) I can talk about my problems with my friends	○	○	○	○	○

53. How much do you agree or disagree with the following statements?

	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
a) I lead a purposeful and meaningful life	○	○	○	○	○
b) My social relationships are supportive and rewarding	○	○	○	○	○
c) I am engaged and interested in my daily activities	○	○	○	○	○
d) I actively contribute to the happiness and well-being of others	○	○	○	○	○
e) I am competent and capable in the activities that are important to me	○	○	○	○	○
f) I am a good person and live a good life	○	○	○	○	○
g) I am optimistic about my future	○	○	○	○	○
h) People respect me	○	○	○	○	○
i) I generally recover from setbacks quickly	○	○	○	○	○

54. Choose the answer that best describes how you feel.

	True	Mostly true	Sometimes true, sometimes false	Mostly false	False
a) In general, I like the way I am	○	○	○	○	○
b) Overall, I have a lot to be proud of	○	○	○	○	○
c) A lot of things about me are good	○	○	○	○	○
d) When I do something, I do it well	○	○	○	○	○
e) I like the way I look	○	○	○	○	○

55. If you had concerns regarding your mental health, are there any reasons why you would not talk to an adult at school (e.g., a school social worker, child and youth worker, counsellor, psychologist, nurse, teacher, or other staff person)? *(Mark all that apply)*

- ○ I would have no problem talking to an adult at school about my mental health

- ○ Worried about what others would think of me (e.g., I'd be too embarrassed)
- ○ Lack of trust in these people - word would get out
- ○ Prefer to handle problems myself
- ○ Do not think these people would be able to help
- ○ Would not know who to approach
- ○ There is no one I feel comfortable talking to

56. Over the last 2 weeks, how often have you been bothered by the following problems?

	Not at all	Several days	Over half the days	Nearly every day
a) Feeling nervous, anxious, or on edge	○	○	○	○
b) Not being able to stop or control worrying	○	○	○	○
c) Worrying too much about different things	○	○	○	○
d) Trouble relaxing	○	○	○	○
e) Being so restless that it is hard to sit still	○	○	○	○
f) Becoming easily annoyed or irritable	○	○	○	○
g) Feeling afraid as if something awful might happen	○	○	○	○

57. Please indicate how often the following statements apply to you:

	Almost never	Sometimes	About half the time	Most of the time	Almost always
a) I have difficulty making sense out of my feelings	○	○	○	○	○
b) I pay attention to how I feel	○	○	○	○	○
c) When I'm upset, I have difficulty concentrating	○	○	○	○	○
d) When I'm upset, I believe there is nothing I can do to make myself feel better	○	○	○	○	○
e) When I'm upset, I lose control over my behaviour	○	○	○	○	○
f) When I'm upset, I feel ashamed for feeling that way	○	○	○	○	○

58. On how many of the last 7 days did you feel the following ways?

	None or less than 1 day	1-2 days	3-4 days	5-7 days
a) I was bothered by things that usually don't bother me	○	○	○	○
b) I had trouble keeping my mind on what I was doing	○	○	○	○
c) I felt depressed	○	○	○	○
d) I felt that everything I did was an effort	○	○	○	○
e) I felt hopeful about the future	○	○	○	○
f) I felt fearful	○	○	○	○
g) My sleep was restless	○	○	○	○
h) I was happy	○	○	○	○
i) I felt lonely	○	○	○	○
j) I could not get "going"	○	○	○	○

59. In general, how would you rate your mental health?

- ○ Excellent
- ○ Very good
- ○ Good
- ○ Fair
- ○ Poor

If you are a young person in Canada who needs support, you can reach out to Kids Help Phone's professional counsellors by calling 1-800-668-6868 or visiting kidshelpphone.ca. Their service is free, anonymous, confidential, and available 24/7/365.

Kids Help Phone

1-800-668-6868

○○○○○○○○○○○○○○○○○○○○○○○○○ [serial]

Your School and You

60. How strongly do you agree or disagree with each of the following statements?

	Strongly agree	Agree	Disagree	Strongly disagree
a) I feel close to people at my school	○	○	○	○
b) I feel I am part of my school	○	○	○	○
c) I am happy to be at my school	○	○	○	○
d) I feel the teachers at my school treat me fairly	○	○	○	○
e) I feel safe in my school	○	○	○	○
f) Getting good grades is important to me	○	○	○	○

61. In the last 30 days, in what ways were you bullied by other students? *(Mark all that apply)*

- ○ I have not been bullied in the last 30 days
- ○ Physical attacks (e.g., getting beaten up, pushed, or kicked)
- ○ Verbal attacks (e.g., getting teased, threatened, or having rumours spread about you)
- ○ Cyber-attacks (e.g., being sent mean text messages or having rumours spread about you on the internet)
- ○ Had someone steal from you or damage your things

62. In the last 30 days, how often have you been bullied by other students?

- ○ I have not been bullied by other students in the last 30 days
- ○ Less than once a week
- ○ About once a week
- ○ 2 or 3 times a week
- ○ Daily or almost daily

63. In the last 30 days, in what ways did you bully other students? *(Mark all that apply)*

- ○ I did not bully other students in the last 30 days
- ○ Physical attacks (e.g., beat up, pushed, or kicked them)
- ○ Verbal attacks (e.g., teased, threatened, or spread rumours about them)
- ○ Cyber-attacks (e.g., sent mean text messages or spread rumours about them on the internet)
- ○ Stole from them or damaged their things

64. In the last 30 days, how often have you taken part in bullying other students?

- ○ I did not bully other students in the last 30 days
- ○ Less than once a week
- ○ About once a week
- ○ 2 or 3 times a week
- ○ Daily or almost daily

65. How supportive is your school of the following?

	Very supportive	Supportive	Unsupportive	Very unsupportive
a) Making sure there are opportunities for students to be physically active	○	○	○	○
b) Making sure students have access to healthy foods and drinks	○	○	○	○
c) Making sure no one is bullied at school	○	○	○	○
d) Giving students the support they need to resist or quit tobacco	○	○	○	○
e) Giving students the support they need to resist or quit drugs and/or alcohol	○	○	○	○

Appendix B

Supplementary Materials for Chapter 5

This appendix includes supplementary material from the first manuscript in this dissertation: *Substance use classes and symptoms of anxiety and depression among Canadian secondary school students.*

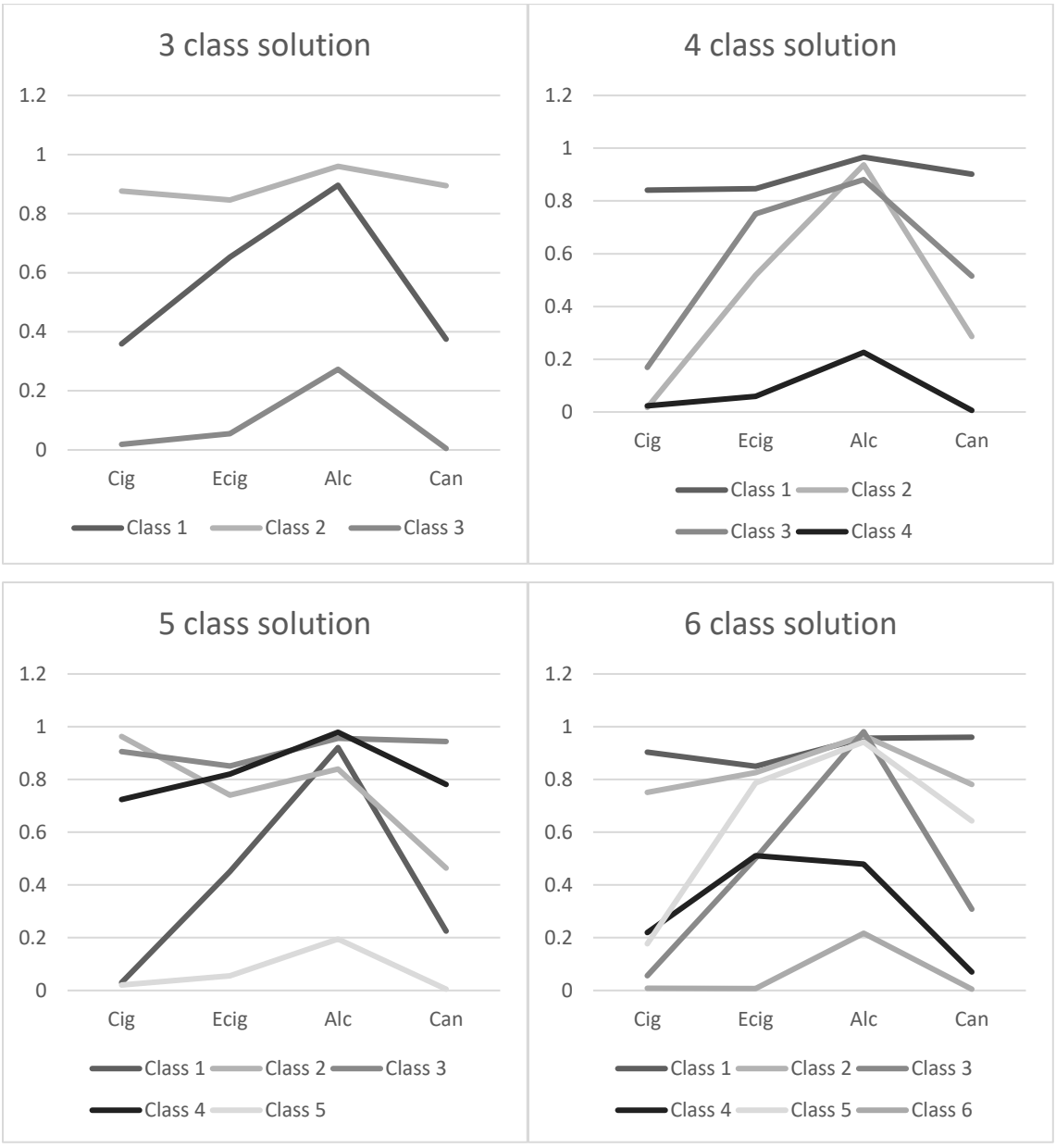
Supplementary Table 1 provides a test for measurement invariance comparing models where classes are allowed to differ by gender versus a model where classes are constrained by gender. Chi square, AIC, and BIC results indicate that a model that is allowed to differ by gender is most appropriate.

Supplementary Table 1. Chi-square test for measurement invariance comparing a model where classes are allowed to differ by gender versus a model where classes are constrained by gender

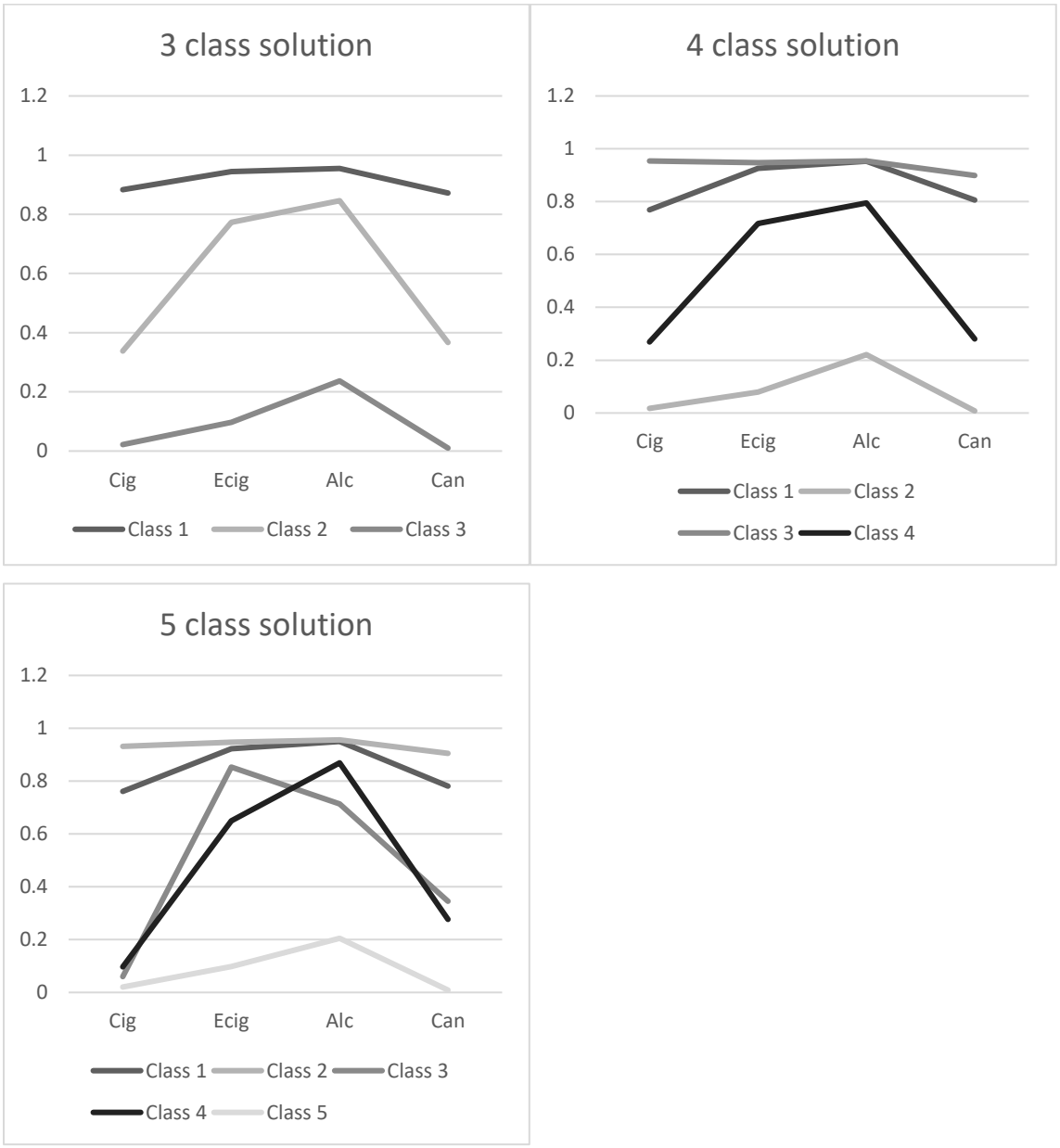
	Log-likelihood	DF	AIC	BIC	entropy	G^2	P-value:
Differ by gender	-212722	1146	425646.1	426540.4	0.856	2855.057	
Constrained by gender	-213421	1194	426947.6	427416.9	0.858	3135.247	
Test for measurement invariance	1397.46	48				280.19	0.0000

DF=Degrees of freedom; AIC = Akaike information criterion; BIC = Bayesian information criterion; G^2= goodness-of-fit statistic

Supplementary Figure 1 compares item response probabilities for ever—use of the 4 substances for the 3-class to the 6-class latent class models among female students. Supplementary Figure 2 does the same for the 3-class to the 5-class latent class models among male students. Based on the interpretability of the classes, the three-class solution was chosen for both females and males.



Supplementary Figure 1. Substance ever-use item probabilities for 3-class to 6-class latent class models among female students



Supplementary Figure 2. Substance ever-use item probabilities for 3-class to 5-class latent class models among male students

Supplementary Tables 2 and 3 present the full regression results that were presented in part in Table 4 of the main manuscript.

Supplementary Table 2. Regression results latent class membership on mental health symptoms and covariates among female students

Variable	Class 1 (poly-use) vs Class 3 (non-use)	Class 2 (dual use) vs Class 3 (non-use)
Grade		
9 (Ref)	-	-
10	1.441 (1.205-1.723)	1.544 (1.385-1.721)
11	1.860 (1.517- 2.281)	1.962 (1.770-2.175)
12	1.980 (1.569-2.498)	2.032 (1.747-2.364)
Other	0.717 (0.563-0.912)	0.578 (0.468-0.715)
Ethnicity		
White (Ref)	-	-
Other	0.496 (0.392-0.628)	0.452 (0.389-0.526)
Weekly Spending Money		
Zero (Ref)	-	-
$1-$20	1.343 (1.161-1.554)	1.585 (1.411-1.781)
$21-$100	2.599 (2.236-3.022)	2.750 (2.420-3.125)
$100+	5.017 (4.258-5.911)	4.012 (3.464-4.646)
Don't Know	1.214 (1.003-1.470)	1.508 (1.310-1.734)
Family support		
No (Ref)	-	-
Yes	0.537 (0.487-0.591)	0.637 (0.588-0.690)
Friend support		
No (Ref)	-	-
Yes	1.542 (1.391-1.709)	1.639 (1.484-1.810)
Skipping school		
No (Ref)	-	-
Yes	9.414 (8.202-10.805)	3.103 (2.792-3.448)
Anxiety and depression symptoms		
None (Ref)	-	-
Anxiety only	1.482 (1.199-1.832)	1.325 (1.161-1.513)
Depression only	2.645 (2.305-3.035)	1.480 (1.336-1.639)
Both	4.088 (3.593-4.653)	1.812 (1.651-1.988)

Supplementary Table 3. Regression results latent class membership on mental health symptoms and covariates among male students

Variable	Class 1 (poly-use) vs Class 3 (non-use)	Class 2 (dual use) vs Class 3 (non-use)
Grade		
9 (Ref)	-	-
10	1.704 (1.471-1.974)	1.513 (1.341-1.707)
11	2.032 (1.698-2.431)	1.844 (1.616-2.105)
12	2.226 (1.823-2.717)	2.226 (1.823-2.717)
Other	0.532 (0.421-0.671)	0.532 (0.421-0.671)
Ethnicity		
White (Ref)	-	-
Other	0.526 (0.426-0.648)	0.475 (0.407-0.554)
Weekly Spending Money		
Zero (Ref)	-	-
$1-$20	1.738 (1.472-2.051)	1.536 (1.366-1.727)
$21-$100	3.455 (2.910-4.101)	2.401 (2.139-2.695)
$100+	7.990 (6.710-9.514)	3.697 (3.192-4.283)
Don't Know	1.853 (1.538-2.232)	1.463 (1.278-1.674)
Family support		
No (Ref)	-	-
Yes	0.584 (0.530-0.642)	0.636 (0.591-0.685)
Friend support		
No (Ref)	-	-
Yes	2.068 (1.843-2.320)	1.834 (1.696-1.984)
Skipping school		
No (Ref)	-	-
Yes	8.514 (7.590-9.550)	2.947 (2.675-3.245)
Anxiety and depression symptoms		
None (Ref)	-	-
Anxiety only	1.408 (1.142-1.734)	1.134 (0.940-1.368)
Depression only	1.688 (1.522-1.873)	1.214 (1.102-1.337)
Both	2.475 (2.191- 2.795)	1.178 (1.054-1.318)

Finally, Supplementary Table 4 presents a comparison of the complete case sample and students who were removed due to missing data. There were no significant differences in chi-square tests comparing those included and excluded based on missing outcome data.

Supplementary Table 4. Comparison of the complete case sample (N=51,767) and students who were removed due to missing data (N=14,667) in Year 6 (2017-18) of the COMPASS study

Variable	Total sample (N=66,434)		Complete case (N=51,767)		Removed (N=14,667)		Chi square			Cramer's V
	n	%	n	%	n	%	df	Value	p-value	
Gender										
Female	32986	50.1	26308	50.8	6678	47.3	1	53.5455	<.0001	-0.0285
Male	32886	49.9	25459	49.2	7427	52.7				
Missing	562									
Grade										
9	15937	24.18	12197	23.6	3740	26.4	4	295.5482	<.0001	0.0670
10	16086	24.40	12767	24.7	3319	23.5				
11	15271	23.17	12406	24.0	2865	20.2				
12	10100	15.32	8168	15.8	1932	13.7				
Other	8527	12.94	6229	12.0	2298	16.2				
Missing	513									
Ethnicity										
White	43506	65.92	34890	67.4	8616	60.6	1	233.1346	<.0001	-0.0594
Non-White	22491	34.08	16877	32.6	5614	39.5				
Missing	437									
Weekly Spending Money										
Zero	10605	16.15	8318	16.1	2287	16.5	4	49.8110	<.0001	0.0275
$1-$20	16618	25.31	13029	25.2	3589	25.8				
$21-$100	15546	23.67	12433	24.0	3113	22.4				
$100+	12272	18.69	9819	19.0	2453	17.7				
Don't Know	10626	16.18	8168	15.8	2458	17.7				
Missing	767									
Past year alcohol use										
None	31690	48.49	24537	47.6	7153	51.9	3	179.9821	<.0001	0.0525
<1x/month	12897	19.73	10532	20.4	2365	17.2				
1-3x/month	14727	22.53	11930	23.1	2797	20.3				
>=1x/week	6045	9.25	4568	8.9	1477	10.7				
Missing	1075									
Past year cannabis use										
None	50145	76.70	39808	77.1	10337	75.3	3	183.7927	<.0001	0.0530
<1x/month	6047	9.25	4959	9.6	1088	7.9				
1-3x/month	3939	6.02	3088	6.0	851	6.2				

>=1x/week	5248	8.03	3790	7.3	1458	10.6				
Missing	1055									
Cigarette use										
None	50209	76.29	39820	77.0	10389	73.8	3	131.1575	<.0001	0.0446
Ever use	9014	13.70	7049	13.6	1965	14.0				
1-5 days	3677	5.59	2790	5.4	887	6.3				
6+ days	2910	4.42	2067	4.0	843	6.0				
Missing	624									
E-cigarette use										
None	41169	63.10	32616	63.4	8553	62.1	3	39.0149	<.0001	0.0245
Ever use	9461	14.50	7522	14.6	1939	14.1				
1-5 days	8683	13.31	6844	13.3	1839	13.4				
6+ days	5929	9.09	4494	8.7	1435	10.4				
Missing	1192									
Family support										
No	26566	41.25	21245	41.0	5321	42.1	1	5.0093	0.0252	0.0088
Yes	37830	58.75	30522	59.0	7308	57.9				
Missing	2038									
Friend support										
No	16200	25.01	12684	24.5	3516	27.0	1	35.6869	<.0001	0.0235
Yes	48570	74.99	39083	75.5	9487	73.0				
Missing	1664									
Skipping school										
No	42327	66.54	34648	66.9	7679	64.9	1	18.6227	<.0001	-0.0171
Yes	21280	33.46	17119	33.1	4161	35.1				
Missing	2827									
Anxiety and depression symptoms										
None	32786	60.6	31335	60.5	1451	61.3	3	0.8854	0.8290	0.0040
Anxiety only	2312	4.3	2209	4.3	103	4.4				
Depression only	8104	15.0	7764	15.0	340	14.4				
Both	10934	20.2	10459	20.2	475	20.1				
Missing	12298									

Appendix C
Supplementary Materials for Chapter 6

This appendix includes supplementary material from the second manuscript in this dissertation: *Exploring the bi-directional associations between poly-substance use and symptoms of anxiety and depression among a large sample of Canadian adolescents.*

In my thesis proposal, Manuscript 2 was designed to answer the following research questions:

1. Do grade 9 and 10 students in the COMPASS study transition to substance use profiles that include an increased number of substances from Y6 (2017/18) to Y7 (2018/19) of the COMPASS study?
2. If yes, is that transition associated with depression (CESD) and anxiety (GAD-7) scores in Y7 (2018/19)?

To accomplish this, 28,199 students in grades 9-11 and grade "other" were linked from Y6 (2017/18) to Y7 (2018/19). After removing students with missing data 19,983 were kept in the final sample.

First, latent class analyses (LCA) were conducted at each time point to determine the best latent class solution at each time point. Results are shown in Supplementary Table 5.

Supplementary Table 5. Results of LCA at each time point from 1- to 6-class solution among students linked from Y6 (2017/18) to Y7 (2018/19) of the COMPASS study.

	FP	Loglikelihood	AIC	BIC	aBIC	DF	Entropy
Female							
Time 1							
2-solution	25	-28847.077	57744.155	57926.381	57846.934	229	0.818
3-solution	38	-28416.186	56908.372	57185.357	57064.598	215	0.765
4-solution	51	-28349.772	56801.544	**57173.286**	57011.215	203	0.821
5-solution	64	-28294.950	56717.900	57184.400	**56981.016**	189	0.811
6-solution	77	-28277.973	**56709.946**	57271.203	57026.507	177	0.779
Time 2							
2-solution	25	-37695.322	75440.645	75622.871	75543.425	229	0.792
3-solution	38	-36941.752	73959.503	74236.487	74115.728	217	0.739
4-solution	51	-36865.627	73833.253	**74204.995**	74042.924	204	0.715
5-solution	64	-36806.477	73740.954	74207.453	**74004.070**	191	0.727
6-solution	77	-36783.191	**73720.383**	74281.640	74036.944	178	0.712
Male							
Time 1							
2-solution	25	-25587.801	51225.602	51403.678	51324.232	227	0.835
3-solution	38	-25137.685	50351.369	**50622.045**	**50501.287**	215	0.777
4-solution	51	-25103.545	50309.089	50672.364	50510.295	202	0.794
5-solution	64	-25074.014	50276.028	50731.902	50528.521	189	0.805
6-solution	77	-25057.679	**50269.357**	50817.831	50573.138	176	0.812
Time 2							
2-solution	25	-32449.551	64949.103	65127.179	65047.733	230	0.833
3-solution	38	-31699.065	63474.131	63744.806	63624.048	217	0.752
4-solution	51	-31613.358	63328.716	**63691.991**	**63529.922**	204	0.726
5-solution	64	-31574.784	63277.568	63733.442	63530.061	191	0.801
6-solution	77	-31552.307	**63258.615**	63807.089	63562.395	178	0.774

FP=Free parameters, AIC= Akaike Information Criterion, BIC= Bayesian Information Criterion, aBIC=adjusted Bayesian Information Criterion, DF=degrees of freedom
Bold indicates best value for each measure

Next, longitudinal measurement invariance was tested to determine if latent classes were the same over time. The number of classes were selected based on the most favourable BIC scores in the table above (Supplementary Table 5). Results in Supplementary Table 6 indicated that measurement invariance did not hold and therefore latent classes were statistically different over time.

Supplementary Table 6. Testing longitudinal measurement invariance of substance use classes from Y6 (2017/18) to Y7 (2018/19) of the COMPASS study

	MI	G^2	AIC	BIC	DF	Diff G^2	Diff DF	P-value
Female								
4-solution	Yes	15883.28	122583.5	123042.7	65218			
	No	15328.79	**121586.2**	**122395.3**	65203	554.483	15	<0.001
5-solution	Yes	15184.72	121404.6	122016.8	65220			
	No	14431.95	**120499.2**	**121548.8**	65183	752.762	37	<0.001
Male								
3-solution	Yes	13375.38	107976.1	108289.5	65244			
	No	12468.32	**106978.8**	**107548.7**	65200	907.061	44	<0.001
4-solution	Yes	12678.01	106648.9	107097.7	65217			
	No	11805.43	**105795.3**	**106586**	65171	872.579	46	<0.001

The same methods were attempted using a variety of different approaches to attempt to find a situation where latent classes were the same over time, so that Latent Transition Analyses could be successfully implemented. First, substance use variables were categorized as binary based on past 30-day use. Next, grade 9 only samples and Ontario only samples were tested. Finally, partial measurement invariance was tested. None of these scenarios resulted in similar substance use classes over time.

Therefore, Manuscript 2 was updated to examine the following objectives:

1. What are the bi-directional associations between the number of substances used and anxiety and depression scores?
2. What are the bi-directional associations between single versus poly-substance use and anxiety and depression scores?

Manuscript 2 was then able to inform the direction of effect examined in Manuscript 3.
The following tables provide supplementary information for Manuscript 2:

Supplementary Table 7. Comparison of 3-year (Wave 1: 2017/18 to Wave 3: 2019/20) unlinked (ref) vs linked students at Wave 1 in the COMPASS study

Wave 1 variables	Unlinked (n=4180)		Linked (n=2904)		Chi-square or t-test p-value	Cramer's V
	n	%	n	%		
Grade						
9	1903	45.53	1597	54.99	<.0001	-0.0931
10	2277	54.47	1307	45.01		
Sex						
Female	1872	45.26	1582	54.59	<.0001	-0.0918
Male	2264	54.74	1316	45.41		
Missing	44		6			
Ethnicity						
White	2452	59.14	1933	66.77	<.0001	-0.0774
Non-White	1694	40.86	962	33.23		
Missing	34		9			
Weekly spending money						
Zero	799	19.11	651	22.42	<.0001	0.0817
$1-$20	1335	31.94	1025	35.30		
$21-$100	928	22.20	527	18.15		
$100+	463	11.08	228	7.85		
Don't know/missing	655	15.67	473	16.29		
Past 30-day alcohol use						
No	2956	72.49	2425	84.14	<.0001	-0.1371
Yes	1122	27.51	457	15.86		
Missing	102		22			
Past 30-day cannabis use						
No	3454	84.74	2733	94.83	<.0001	-0.1583
Yes	622	15.26	149	5.17		
Missing	104		22			
Past 30-day cigarette use						
No	3623	87.77	2786	96.17	<.0001	-0.1462
Yes	505	12.23	111	3.83		
Missing	52		7			
Past 30-day e-cigarette use						

No	3160	77.47	2487	86.75	<.0001	-0.1171
Yes	919	22.53	380	13.25		
Missing	101		37			
Past 30-day number of substances used						
0	2458	61.40	2189	76.94	<.0001	0.1826
1	687	17.16	382	13.43		
2	400	9.99	163	5.73		
3	247	6.17	74	2.60		
4	211	5.27	37	1.30		
Missing	177		59			
Family support						
No	1780	44.67	1097	38.53	<.0001	0.0613
Yes	2205	55.33	1750	61.47		
Missing	195		57			
Friend support						
No	1098	27.34	788	27.53	0.8599	-0.0021
Yes	2918	72.66	2074	72.47		
Missing	164		42			
Skipping school						
No	2814	70.88	2374	84.60	<.0001	-0.1596
Yes	1156	29.12	432	15.40		
Missing	210		98			
Anxiety score (GAD-7; mean, SD)	6.56	6.09	6.02	5.49	0.0002	
Missing	390		208			
Depression score (CESD; mean, SD)	9.27	6.22	8.30	5.70	<.0001	
Missing	801		448			

Note: Missing values without corresponding percentages were not included in chi-square tests.

Supplementary Table 8. Comparison of Wave 1 characteristics of students with complete data versus students who were removed due to incomplete data in a 3-year (Wave 1: 2017/18 to Wave 3: 2019/20) linked sample of grade 9 and 10 students in the COMAPSS study

	Complete (n=2179)		**Incomplete (n=725)**		**Chi-square or t-test p-value**	**Cramer's V**
Wave 1 variables	**n**	**%**	**n**	**%**		
Grade						
9	1183	54.29	414	57.10	0.1873	0.0245
10	996	45.71	311	42.90		
Sex						
Female	1187	54.47	395	54.94	0.8289	0.0040
Male	992	45.53	324	45.06		
Missing			6			
Ethnicity						
White	1482	68.01	451	62.99	0.0133	-0.0460
Non-White	697	31.99	265	37.01		
Missing			9			
Weekly spending money						
Zero	498	22.85	153	21.10	0.3073	0.0407
$1-$20	757	34.74	268	36.97		
$21-$100	403	18.49	124	17.10		
$100+	178	8.17	50	6.90		
Don't know/missing	343	15.74	130	17.93		
Past 30-day alcohol use						
No	1836	84.26	589	83.78	0.7643	-0.0056
Yes	343	15.74	114	16.22		
Missing			22			
Past 30-day cannabis use						
No	2072	95.09	661	94.03	0.2680	-0.0206
Yes	107	4.91	42	5.97		
Missing			22			
Past 30-day cigarette use						
No	2100	96.37	686	95.54	0.3142	-0.0187
Yes	79	3.63	32	4.46		
Missing			7			

Past 30-day e-cigarette use						
No	1896	87.01	591	85.90	0.4536	-0.0140
Yes	283	12.99	97	14.10		
Missing			37			
Past 30-day number of substances used						
0	1681	77.15	508	76.28	0.6044	0.0310
1	296	13.58	86	12.91		
2	117	5.37	46	6.91		
3	58	2.66	16	2.40		
4	27	1.24	10	1.50		
Missing			59			
Family support						
No	808	37.37	289	42.19	0.0240	0.0423
Yes	1354	62.63	396	57.81		
Missing	17		40			
Friend support						
No	596	27.43	192	27.87	0.8222	0.0042
Yes	1577	72.57	497	72.13		
Missing	6		36			
Skipping school						
No	1829	85.11	545	82.95	0.1801	-0.0253
Yes	320	14.89	112	17.05		
Missing	30		68			
Anxiety score (GAD-7; mean, SD)	6.00	5.42	6.12	5.75	0.6313	
Missing			208			
Depression score (CESD; mean, SD)	8.17	5.65	9.29	5.94	0.0020	
Missing			448			

Note: Missing values without corresponding percentages were not included in chi-square tests.

Supplementary Table 9. Number of substances used and mean depression and anxiety scores across 3 waves (2017/18-2019/20) of the COMPASS study (n=2179)

	Wave 1 (2017/18)		**Wave 2 (2018/19)**		**Wave 3 (2019/20)**		**Wilcoxon signed-rank / paired t-test**
Female (n=1187)							
Number of substances used	n	%	n	%	n	%	
0	941	79.3	737	62.5	618	52.3	W2 vs W1*
1	145	12.2	219	18.6	241	20.4	W3 vs W2*
2	64	5.4	136	11.5	181	15.3	W3 vs W1*
3	29	2.4	54	4.6	105	8.9	
4	8	0.7	34	2.9	36	3.0	
Missing			7		6		
Anxiety (mean, SD)	7.5	5.7	8.4	5.7	8.8	5.9	W2 vs W1* W3 vs W2*
Missing			42		28		W3 vs W1*
Depression (mean, SD)	9.3	6.1	10.6	6.3	10.8	6.3	W2 vs W1* W3 vs W2
Missing			92		63		W3 vs W1*
Male (n=992)							
Number of substances used							
0	740	74.6	602	61.4	520	52.8	W2 vs W1*
1	151	15.2	183	18.7	184	18.7	W3 vs W2*
2	53	5.3	115	11.7	145	14.7	W3 vs W1*
3	29	2.9	55	5.6	89	9.0	
4	19	1.9	25	2.6	47	4.8	
Missing			12		7		
Anxiety (mean, SD)	4.2	4.4	4.9	5.2	5.3	5.1	W2 vs W1* W3 vs W2*
Missing			28		27		W3 vs W1*
Depression (mean, SD)	6.8	4.7	7.8	5.5	8.2	5.6	W2 vs W1* W3 vs W2*
Missing			81		72		W3 vs W1*

Note: variables with missing were included in models as dependent variables and were not included in Wilcoxon signed-rank or paired t-tests.
*$p<0.01$

Supplementary Table 10. Patterns of substance use across 3 waves (2017/18-2019/20) of the COMPASS study (n=2179)

Pattern of substance use	Wave 1 (2017/18)		Wave 2 (2018/19)		Wave 3 (2019/20)	
	n	%	n	%	n	%
No substances	1681	77.1	1339	62.0	1138	52.5
1 substance						
Alcohol only	162	7.4	212	9.8	257	11.9
Cannabis only	21	1.0	24	1.1	23	1.1
Cigarettes only	7	0.3	6	0.3	2	0.1
E-cigarettes only	106	4.9	160	7.4	143	6.6
2 substances						
Alcohol and cannabis	7	0.3	24	1.1	39	1.8
Alcohol and cigarettes	13	0.6	2	0.1	4	0.2
Alcohol and e-cigarettes	85	3.9	178	8.2	235	10.8
Cannabis and cigarettes	3	0.1	6	0.3	3	0.1
Cannabis and e-cigarettes	5	0.2	30	1.4	37	1.7
Cigarettes and e-cigarettes	4	0.2	11	0.5	8	0.4
3 substances						
Alcohol, cannabis, and cigarettes	2	0.1	4	0.2	5	0.2
Alcohol, cannabis, and e-cigarettes	33	1.5	74	3.4	131	6.0
Alcohol, cigarettes, and e-cigarettes	14	0.6	25	1.2	41	1.9
Cannabis, cigarettes, and e-cigarettes	9	0.4	6	0.3	17	0.8
4 substances						
Alcohol, cannabis, cigarettes, and e-cigarettes	27	1.2	59	2.7	83	3.8
Missing			19		13	

Supplementary Table 11. Characteristics at Wave 1 (2017/18) by sex, among high school students who used substances each year linked across 3 waves (2017/18-2019/20) of the COMPASS study (n=401)

Wave 1 variables	Female (n=195)		Male (n=206)		Chi-square / t-test p-value	Cramer's V
	n	%	n	%		
Grade						
9	88	45.1	80	38.8	0.4340	0.0334
10	107	54.9	126	61.2		
Ethnicity						
White	153	78.5	159	77.2	0.4951	0.0291
Non-White	42	21.5	47	22.8		
Weekly spending money						
Zero	29	14.9	34	16.5	0.6164	0.0695
$1-$20	60	30.8	57	27.7		
$21-$100	41	21.0	62	30.1		
$100+	38	19.5	36	17.5		
Don't know/missing	27	13.8	17	8.3		
Poly-substance use						
Single substance use	103	52.8	117	56.8	0.5184	-0.0282
Poly-substance use	92	47.8	89	43.2		
Family support						
No	102	52.6	83	40.7	0.0178	0.1024
Yes	92	47.4	121	59.3		
Missing	1		2			
Friend support						
No	46	23.6	49	23.9	0.6426	-0.0200
Yes	149	76.4	156	76.1		
Missing			1			
Skipping school						
No	122	63.2	133	65.8	0.6455	-0.0201
Yes	71	36.8	69	34.2		
Missing	2					
Anxiety score	8.9	6.0	5.2	4.9	<.0001	

(GAD-7; mean, SD)						
Depression score (CESD; mean, SD)	11.3	6.8	8.3	5.6	<.0001	

Note: Variables with missing values were included in models only in Waves 2 and 3 and missing values at those time points were removed.

Supplementary Table 12. Poly-substance use and mean anxiety and depression scores across 3 waves (2017/18-2019/20) of the COMPASS study (n=401)

	Wave 1 (2017/18)		**Wave 2 (2018/19)**		**Wave 3 (2019/20)**		**McNemar / paired t-test**
Female (n=195)							
Poly-substance use	**n**	**%**	**n**	**%**	**n**	**%**	
Single substance	103	52.8	49	25.3	47	24.4	W2 vs W1*
Poly-substance	92	47.2	145	74.7	146	75.6	W3 vs W2
Missing			1		2		W3 vs W1*
Anxiety (mean, SD)	8.9	6.0	9.8	5.8	10.1	6.1	W2 vs W1 W3 vs W2
Missing			5		6		W3 vs W1*
Depression (mean, SD)	11.3	6.8	12.0	6.2	11.5	6.4	W2 vs W1 W3 vs W2
Missing			18		10		W3 vs W1
Male (n=206)							
Poly-substance use							
Single substance	117	56.8	68	33.2	46	22.4	W2 vs W1*
Poly-substance	89	43.2	137	66.8	159	77.6	W3 vs W2*
Missing			1		1		W3 vs W1*
Anxiety (mean, SD)	5.2	4.9	5.5	5.7	6.2	5.5	W2 vs W1 W3 vs W2
Missing			4		3		W3 vs W1
Depression (mean, SD)	8.3	5.6	8.4	6.1	9.5	6.3	W2 vs W1 W3 vs W2
Missing			16		16		W3 vs W1*

Note: variables with missing were included in models as dependent variables and were not included in McNemar of paired t-tests.
*$p<0.01$

Supplementary Table 13. Cross-lag relationships between number of substances used and anxiety and depression among students participating in all three waves of the study (n = 2179)

	Female (n=1187)			Male (n= 992)		
Regression	Estimate	SE	p-value	Estimate	SE	p-value
Poly_y7 on						
• Poly_y6	**0.764**	**0.037**	**0.000**	**0.707**	**0.032**	**0.000**
• Cesd_y6	0.003	0.007	0.673	0.009	0.008	0.272
• Gad7_y6	0.002	0.007	0.741	-0.002	0.008	0.807
Gad7_y7 on						
• Poly_y6	-0.093	0.192	0.630	**-0.388**	**0.173**	**0.025**
• Cesd_y6	**0.148**	**0.041**	**0.000**	**0.128**	**0.057**	**0.025**
• Gad7_y6	**0.460**	**0.039**	**0.000**	**0.498**	**0.059**	**0.000**
Cesd_y7 on						
• Poly_y6	-0.027	0.185	0.886	-0.368	0.226	0.104
• Cesd_y6	**0.428**	**0.046**	**0.000**	**0.363**	**0.053**	**0.000**
• Gad7_y6	**0.203**	**0.046**	**0.000**	**0.26**	**0.063**	**0.000**
Poly_y8 on						
• Poly_y7	**0.700**	**0.025**	**0.000**	**0.708**	**0.043**	**0.000**
• Cesd_y7	0.006	0.006	0.298	-0.002	0.009	0.846
• Gad7_y7	-0.002	0.006	0.684	0.003	0.007	0.719
Gad7_y8 on						
• Poly_y7	0.059	0.141	0.676	0.097	0.156	0.533
• Cesd_y7	0.023	0.032	0.473	**0.116**	**0.041**	**0.004**
• Gad7_y7	**0.589**	**0.032**	**0.000**	**0.43**	**0.051**	**0.000**
Cesd_y8 on						
• Poly_y7	-0.045	0.161	0.781	0.162	0.169	0.336
• Cesd_y7	**0.346**	**0.038**	**0.000**	**0.395**	**0.044**	**0.000**
• Gad7_y7	**0.276**	**0.035**	**0.000**	**0.194**	**0.046**	**0.000**

Adjusted for grade, ethnicity, weekly spending money, having friend and family support, and skipping school.

Supplementary Table 14. Cross-lag relationships between poly-substance use (2+ substances vs 1 substance only) and anxiety and depression among students who used substances in all three waves of the study (n = 401)

	Female (n=195)			Male (n= 206)		
Regression	Estimate	SE	p-value	Estimate	SE	p-value
Poly_y7 on						
• Poly_y6	**1.574**	**0.212**	**0.000**	**0.825**	**0.203**	**0.000**
• Cesd_y6	-0.005	0.019	0.811	0.037	0.029	0.192
• Gad7_y6	0.046	0.029	0.11	0.031	0.032	0.330
Gad7_y7 on						
• Poly_y6	0.008	0.799	0.992	-0.786	0.568	0.167
• Cesd_y6	**0.165**	**0.081**	**0.042**	0.089	0.094	0.345
• Gad7_y6	**0.48**	**0.076**	**0.000**	**0.629**	**0.082**	**0.000**
Cesd_y7 on						
• Poly_y6	0.34	0.772	0.659	-1.149	0.697	0.099
• Cesd_y6	**0.453**	**0.09**	**0.000**	**0.254**	**0.098**	**0.010**
• Gad7_y6	0.115	0.101	0.253	**0.577**	**0.128**	**0.000**
Poly_y8 on						
• Poly_y7	**0.34**	**0.089**	**0.000**	**0.731**	**0.073**	**0.000**
• Cesd_y7	-0.054	0.038	0.159	-0.015	0.041	0.723
• Gad7_y7	0.003	0.047	0.951	-0.032	0.04	0.42
Gad7_y8 on						
• Poly_y7	**0.735**	**0.326**	**0.024**	**0.82**	**0.303**	**0.007**
• Cesd_y7	-0.258	0.145	0.075	0.163	0.127	0.198
• Gad7_y7	**0.779**	**0.187**	**0.000**	**0.329**	**0.141**	**0.020**
Cesd_y8 on						
• Poly_y7	0.407	0.337	0.226	**1.079**	**0.295**	**0.000**
• Cesd_y7	**0.304**	**0.149**	**0.040**	**0.541**	**0.123**	**0.000**
• Gad7_y7	0.223	0.158	0.158	0.052	0.144	0.720

Adjusted for grade, ethnicity, weekly spending money, having friend and family support, and skipping school.

Appendix D
Supplementary Materials for Chapter 7

The following tables were included as supplementary information in the publication of Manuscript 3: *Associations between Longitudinal Patterns of Substance Use and Anxiety and Depression Symptoms among a Sample of Canadian Secondary School Students*

Supplementary Table 15. Comparison of 3-year (Wave 1: 2017/18 to Wave 3: 2019/20) unlinked (ref) vs linked students at Wave 1 in the COMPASS study

Wave 1 variables	Unlinked (n=4180)		Linked (n=2904)		Chi-square or t-test p-value	Cramer's V
	n	%	n	%		
Grade						
9	1903	45.53	1597	54.99	<.0001	-0.0931
10	2277	54.47	1307	45.01		
Sex						
Female	1872	45.26	1582	54.59	<.0001	-0.0918
Male	2264	54.74	1316	45.41		
Missing	44		6			
Ethnicity						
White	2452	59.14	1933	66.77	<.0001	-0.0774
Non-White	1694	40.86	962	33.23		
Missing	34		9			
Weekly spending money						
Zero	799	19.11	651	22.42	<.0001	0.0817
$1-$20	1335	31.94	1025	35.30		
$21-$100	928	22.20	527	18.15		
$100+	463	11.08	228	7.85		
Don't know/missing	655	15.67	473	16.29		
Past 12-month alcohol use						
No use	2299	56.38	1969	68.32	<.0001	0.1475
Ever/less than monthly	657	16.11	456	15.82		
Monthly	811	19.89	370	12.84		
Weekly	311	7.63	87	3.02		
Missing	102		22			
Past 12-month cannabis use						
No use	3178	77.97	2602	90.28	<.0001	0.1763
Ever/less than monthly	276	6.77	131	4.55		
Monthly	209	5.13	83	2.88		
Weekly	413	10.13	66	2.29		

Missing	104		22			
Ever/Past 30-day cigarette use						
No use	3097	75.02	2588	89.33	<.0001	0.1899
Ever/less than monthly	526	12.74	198	6.83		
Monthly	240	5.81	82	2.83		
Weekly	265	6.42	29	1.00		
Missing	52		7			
Ever/Past 30-day e-cigarette use						
No use	2623	64.30	2225	77.61	<.0001	0.1523
Ever/less than monthly	537	13.16	262	9.14		
Monthly	578	14.17	288	10.05		
Weekly	341	8.36	92	3.21		
Missing	101		37			
Anxiety score (GAD-7; mean, SD)	6.56	6.09	6.02	5.49	0.0002	
Missing	390		208			
Depression score (CESD; mean, SD)	9.27	6.22	8.30	5.70	<.0001	
Missing	801		448			

Note: Missing values without corresponding percentages were not included in chi-square tests.

Supplementary Table 16. Comparison of Wave 1 characteristics of students with complete data versus students who were removed due to incomplete data in a 3-year (Wave 1: 2017/18 to Wave 3: 2019/20) linked sample of grade 9 and 10 students in the COMAPSS study

	Incomplete (n=1052)		**Complete (n=1852)**		**Chi-square or t-test p-value**	**Cramer's V**
Wave 1 variables	**n**	**%**	**n**	**%**		
Grade						
9	599	56.94	998	53.89	0.1121	0.0295
10	453	43.06	854	46.11		
Sex						
Female	565	54.02	1017	54.91	0.6409	-0.0087
Male	481	45.98	835	45.09		
Missing	6					
Ethnicity						
White	704	67.50	1229	66.36	0.5330	0.0116
Non-White	339	32.50	623	33.64		
Missing	9					
Weekly spending money						
Zero	238	22.62	413	22.30	0.1241	0.0499
$1-$20	395	37.55	630	34.02		
$21-$100	169	16.06	358	19.33		
$100+	76	7.22	152	8.21		
Don't know/missing	174	16.54	299	16.14		
Past 30-day alcohol use						
No use	716	69.05	1253	67.91	0.5702	0.0264
Ever/less than monthly	157	15.14	299	16.21		
Monthly	128	12.34	242	13.12		
Weekly	36	3.47	51	2.76		
Missing	15		7			
Past 30-day cannabis use						
No use	920	89.23	1682	90.87	0.3936	0.0322
Ever/less than monthly	48	4.66	83	4.48		
Monthly	35	3.39	48	2.59		
Weekly	28	2.72	38	2.05		
Missing	21		1			

Past 30-day cigarette use						
No use	920	88.04	1668	90.06	0.1131	0.0454
Ever/less than monthly	82	7.85	116	6.26		
Monthly	28	2.68	54	2.92		
Weekly	15	1.44	14	0.76		
Missing	7					
Past 30-day e-cigarette use						
No use	786	76.53	1439	78.21	0.7814	0.0194
Ever/less than monthly	99	9.64	163	8.86		
Monthly	108	10.52	180	9.78		
Weekly	34	3.31	58	3.15		
Missing	25		12			
Anxiety score (GAD-7; mean, SD)	5.93	5.49	6.06	5.48	0.5622	
Missing	208					
Depression score (CESD; mean, SD)	8.64	5.83	8.18	5.65	0.0860	
Missing	448					

Note: Missing values without corresponding percentages were not included in chi-square tests.