Phenotyping Risk Profiles of Substance Use and Exploring the Dynamic Transitions in Use Patterns: Machine Learning Models using the COMPASS Data

by

Yang Yang

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EXAMINING COMMITTEE MEMBERSHIP

The following served on the Examining Committee for this thesis. The decision of the Examining Committee is by majority vote.

Supervisor(s): **Helen H. Chen**
Professor of Practice
School of Public Health Sciences
Faculty of Health
Zahid A. Butt
Assistant Professor
School of Public Health Sciences
Faculty of Health

Internal Member(s): **Plinio P. Morita**
Associate Professor
School of Public Health Sciences
Faculty of Health
Scott T. Leatherdale
Professor
School of Public Health Sciences
Faculty of Health

Internal-External Member: **Alexander Wong**
Professor
Systems Design Engineering

External Examiner: **Laura Rosella**
Associate Professor
Dalla Lana School of Public Health
University of Toronto

AUTHOR'S DECLARATION

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

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

Abstract

Background

Polysubstance use is on the rise among Canadian youth. Examining risk profiles and understanding how the transition occurs in use patterns can inform the design and implementation of polysubstance risk reduction intervention. The COMPASS study is longitudinal research examining health-related behaviours among Canadian secondary school students, capturing data from multiple sources. Machine learning (ML) techniques can reveal non-linearity and multivariate couplings associated with population-level longitudinal data to inform public health policies.

Objectives

The overarching goal of this thesis is to identify phenotypes of risk profiles of youth polysubstance use and examine the dynamic transitions of use patterns across time, utilizing both unsupervised ML methods and a latent variable modelling approach. This thesis also aims to understand how ML techniques are best used in modelling transitions and discovering the "hidden" patterns from large complex population-based health survey data, using the COMPASS dataset as a showcase.

Methods

A linked sample (N = 8824) of three annual waves of the COMPASS data collected starting from the school year of 2016-17 was used. Multiple imputations for missing values were performed. Substance use indicators, including cigarette smoking, e-cigarette use, alcohol drinking, and marijuana consumption, were categorized into "never use," "occasional use," and "current use." To examine phenotypes of risk profiles, hierarchical clustering, partitioning around medoids (PAM), and fuzzy clustering algorithms were applied. The Boruta algorithm was used to identify a subset of features for cluster analysis. Both the internal and external indices were employed to evaluate the clustering validity. A multivariate latent Markov model (LMM) was implemented to explore the dynamic transitions of use patterns over time. The least absolute shrinkage and selection operator (LASSO) approach was applied to select the appropriate covariates for entering the LMM. Model selection was based on the Bayesian information criterion (BIC) and the goodness-of-fit test.

Results

The top factors impacting youth polysubstance use included the number of smoking friends, the number of skipped classes, the weekly money to spend/save oneself, and others. Four risk profiles of polysubstance use were identified across the three waves: low, medium-low, medium-high, and high-risk profiles. The heterogeneity in the prevalence and phenotype across these four risk profiles was confirmed. The internal measures of clustering performance measured by average silhouette width ranged from 0.51 to 0.55 across the three waves using different clustering algorithms. The clustering algorithms achieved a relatively high degree of agreement on cluster membership. Comparing the fuzzy (FANNY) clustering with PAM clustering, the adjusted Rand indices were 0.9698, 0.7676, and 0.6452 for the three waves. Four distinct use patterns were identified: no use (S1), occasional single-use of alcohol (S2), dual-use of e-cigarette and alcohol (S3), and current multi-use (S4). The initial probabilities of each subgroup were 0.5887, 0.2156, 0.1487, and 0.0470. The marginal distribution of S1 decreased, while that of S3 and S4 increased over time, indicating a tendency towards increased substance use as the students grew older. Although, generally, most students remained in the same subgroup across time, particularly the individuals in S4 with the highest transition probability (0.8668). Over time, those who transitioned typically moved towards a more severe use pattern group, e.g., S3 → S4. Factors that impact the initial membership of use patterns and the dynamic transitions were multifaceted and complex across the four use patterns across the three waves. Not only do use patterns change with time, but so does the evidence in use patterns.

Conclusion

As the first study of its kind to ascertain risk profiles and dynamics of use patterns in youth polysubstance use, by employing ML approaches to the COMPASS dataset, this thesis provides insights into the opportunities and possibilities ahead for ML in Public Health. Findings from this thesis can be beneficial to practitioners in the field, such as school program managers or policymakers, in their capacity to develop interventions to prevent or remedy polysubstance use among youth.

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Time flies at the speed of light. Four years of my life have been dedicated to pursuing a doctoral degree in a town in the middle of the farmland, accompanied by geese on and off-campus. At the same time, the whole world seems to be advancing much faster around me. My friends even joked about my decision to quit a top management position a few years ago, giving me a heads up about the "bitter" (instead of a "better") life coming back to school as a full-time Ph.D. student. Indeed, pursuing a Ph.D. is a huge commitment. Although I have felt under particular strain from crossing the hurdles throughout the four years of study, I have never regretted this decision. Ultimately, it is part of the learning process; a strong belief that I'm not alone keeps me moving forward without turning back. Following my heart, from afar, here I am, looking back to the past few years as if it was yesterday. Yet, four years are long enough to witness countless ups and downs. Time is merciless but precious. Towards the end of my Ph.D. journey, what remained were recollections of encouragement and spiritual support from great individuals in my life.

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Dedication

I have played numerous roles in my personal life, a daughter, a girlfriend, a wife, a mother. Amongst these roles, being a daughter appears to be the simplest one. Yet, it is the one in which I consistently fail. For my parents, Lianying Hu and Xiancheng Yang, to whom I owe so much, with all my love.

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List of Abbreviations

AI – Artificial Intelligence

AIC – Akaike's Information Criteria

ANCOVA – Analysis of Covariance

ANOVA – Analysis of Variance

ARI – Adjusted Rand Index

BE – Built Environment

BIC – Bayesian Information Criteria

BMI – Body Mass Index

CESD – Center for Epidemiologic Studies Depression 10-Item Scale-Revised

CMRL – CanMap Route Logistics

Co-SEA – COMPASS School Environment Application

CS – Computer Science

CSTADS – Canadian Student Tobacco, Alcohol and Drugs Survey

DERS – Difficulties in Emotion Regulation Scale

DSM-IV – Diagnostic and Statistical Manual of Mental Disorders

EM – Expectation-Maximization

EPOI – Enhanced Points of Interest

FANNY – Fuzzy ANalYsis

FAT – Fairness, Accountability, Transparency

FCM – Fuzzy C-Means

FLOURISH – Diener's Flourishing Scale

GEE – Generalized Estimating Equation

GLM – Generalized Linear Model

GOM – Grade-of-Membership

HMM – Hidden Markov Model

ICC – Intraclass Correlation Coefficient

KL – Kullback-Leibler

LASSO – Least Absolute Shrinkage and Selection Operator

LCA – Latent Class Analysis

LGC – Latent Growth Curve Model

LMM – Latent Markov Model

LOCF – Last Observation Carried Forward

LPA – Latent Profile Analysis

LTA – Latent Transition Analysis

MANOVA – Multivariate ANOVA

MAR – Missing at Random

MCA – Multiple Correspondence Analysis

MI – Multiple Imputation

MICE – Multivariate Imputation via Chained Equations

ML – Machine Learning

MLM – Multilevel Model

MNAR – Missing Not at Random

NLP – Natural Language Processing

NOCB – Next Observation Carried Backward

OR – Odds Ratio

PA – Physical Activity

PAM – Partitioning Around Medoids

PCA – Principal Components Analysis

PMM – Predictive Mean Matching

RF – Random Forest

RM – Repeated Measures

SEM – Structural Equation Modelling

SES – Socioeconomic Status

SHAPES – Canadian Cancer Society's School Health Action Planning and Evaluation System

SPP – School Policies and Practices

SSE – Sum of Squared Errors

SUD – Substance Use Disorder

t-SNE – t-Distributed Stochastic Neighbor Embedding

UPGMA – Unweighted Pair-Group Method using the Average approach

VI – Variation of Information

Chapter 1
Background

1.1 Polysubstance Use Among Youth

Adolescence is a crucial period of development and transition from childhood to adulthood when risky behaviours usually occur. One of the major risky behaviours many adolescents are vulnerable to is substance use, such as alcohol drinking, cigarette smoking, marijuana consumption, and other drug use. Following alcohol drinking and cigarette smoking, marijuana is the third most widely used substance globally. A prior study indicates that Canadian secondary school students have the most significant incidence of using marijuana (1). Data from the most recent 2018-2019 Canadian Student Tobacco, Alcohol and Drugs Survey (CSTADS) demonstrate that 44% of grades 7 to 12 students reported alcohol use, and 18% reported marijuana consumption within the past year. Furthermore, 23% admitted to using tobacco products within the last 30 days of the survey, while 20% reported using e-cigarettes at least once in their lifetime (2).

"Polysubstance use" refers to using multiple addictive substances simultaneously or within a specified period (3). Polysubstance use has numerous negative impacts on health outcomes among youth. The literature reveals that polysubstance users tend to have susceptibility to mental illness such as depression or a combination of depression and anxiety (4–6), heightened risk of contracting sexually transmitted diseases (7), and an increased tendency towards violent behaviours (8,9). The specifics of adverse effects of individual substances follow.

Alcohol intake can lead to serious short- and long-term health issues. For instance, traffic accidents due to drunk driving can end up causing severe injuries and death to persons involved. Automobile accidents are the leading cause of mortality among teenagers, and data suggests that over 50% of fatal injuries were due to drunk driving (1). Smoking cigarettes during adolescence can cause nicotine dependence (10). As one of the main risk factors of early death in adulthood, cigarette smoking leads to various health hazards, including cancer, respiratory, or cardiac diseases (1). Lastly, heavy use of marijuana has been linked to adverse health and psychological outcomes, particularly among youth. Due to regular marijuana consumption, hazards include increased anxiety and panic attacks, cognitive issues, and heightened risk of mental illnesses (11). Additionally, heavy use of marijuana is also

proven to reduce an individual's reaction time, thus adversely impacting their driving abilities (12). The evidence suggests that substance use among youth can result in injuries, traffic accidents, school difficulties, and interpersonal problems, which may have a significant long-term impact on their health and well-being and severe consequences to those around them.

Like many other countries, youth polysubstance use is an ongoing problem in Canada (13,14). Unfortunately, youth polysubstance use surveillance and prevention in North America typically focus on single substance use (15). While monitoring trends is crucial for surveillance purposes, ascertaining the underlying causes of polysubstance use among youth may provide invaluable contextual information in advancing prevention efforts. In combination, surveilling and understanding the factors contributing to polysubstance use patterns among youth may help determine relevant health threats, identify opportunities for intervention, and evaluate the effectiveness of existing policies and practices. The mitigating factors to counteract the growing trend of youth polysubstance use can be multifaceted, from family and peer support to school policies and settings.

1.2 Machine Learning (ML) Models for Analyzing Cross-Sectional Data

Essentially, ML is a learning process that uses mathematics, statistics, logic, and computer programming (16). There are three forms of ML: supervised learning, unsupervised learning, and reinforcement learning. At a high level, for supervised learning, the ML algorithms learn from data with labels. A supervised learning model is trained on data in an iterative procedure using reinforcement rules which adjusts the ML model accordingly (16). Once trained, this ML model can be applied to new data to inform decision-making, including detection, discrimination, and classification (16–18). For unsupervised learning models, the purpose is to discover essential groupings or defining features in the data (16). Unsupervised ML models use unlabelled data to identify hidden patterns or intrinsic structures in the dataset. The unsupervised learning models learn without labels (19,20). For reinforcement learning, the algorithms interact with given environments and take actions to receive penalties or rewards. As a process of learning to control data, reinforcement learning learns by what is referred to as "the best policy," a series of actions that maximize the total rewards after trial and error search (16,20).

The purpose of unsupervised ML models is to discover important clusters or defining features in the data. Unsupervised ML algorithms such as clustering analysis have been used to conduct public

health surveillance and associate patient characteristics with clinical outcomes (16,19,21). Unsupervised learning approaches have been applied to investigate addictive behaviours of substance and non-substance use. Cluster analysis is a class of multivariate techniques for classifying data elements into different groups that are relatively similar (homogeneous) within themselves and dissimilar (heterogeneous) between each other (22). Homogeneity and heterogeneity are measured based on a defined set of variables or characteristics the objects possess (22).

Cluster analysis is commonly used for data exploration, anomaly/outlier detection, data segmentation/partitioning, data mining, and data visualization. Specific applications include similarity searches in patient profiles, medical images in clinical settings, gene categorization in bioinformatics, and many others (23). The primary purpose of cluster analysis is to identify groups within data, i.e., determine the data structure by grouping the most similar observations. As an exploratory technique, cluster analysis is descriptive and non-inferential. Thus, the results from the cluster analysis (a.k.a. subjective segmentation) are not generalizable. Compared to other multivariate methods discussed previously, cluster analysis has no dependent variables but depends on the selected set of independent variables for the similarity measure.

1.3 Methodologies for Analyzing Longitudinal Data

How and when change occurs in an ever-changing world are essential questions in social, behavioural, and health sciences. As research in modelling and predicting data in these fields gains momentum, considerable progress has already been made (24). In general, change can be classified into two mutually exclusive groups, random or stochastic and systematic. Different analytic techniques can be applied to modelling stochastic change (e.g., autoregressive models representing a random process) or systematic change (e.g., transition models that each individual follows a definite track) (24).

Most publications in the health domain tend to rely on longitudinal study design to explore transitions of health conditions, identify risk profiles, or study social phenomena (25,26). In contrast with time-series data, longitudinal data are collected over a relatively few measurement times on a large number of subjects (27). A typical research study on substance use among adolescents tends to rely on health survey data from large samples (usually more than a thousand subjects) collected relatively few times (typically conducted biannually or annually throughout the participants'

adolescence). Evaluating the dynamics of change over time is a common goal when collecting longitudinal data. Diggle *et al.* (2002) identified the top four reasons for applying longitudinal techniques. First, to make progress from assessing "association" towards analyzing "causality"; second, to make prognoses by incorporating historical data using time-varying covariates; third, to study historical information, e.g., transition analysis by applying Markov or autoregressive models; and fourth, to inform policy with subject-specific analysis using random-effects models (28).

In the last few decades, longitudinal data analysis has advanced considerably since the early development of linear models based on analysis of variance (ANOVA). From linear models for continuous response variables to non-Gaussian models for discrete responses, Fitzmaurice and Molenberghs (2009) categorize techniques on longitudinal data analysis as follows: 1) marginal models addressing mean-level change between groups, such as repeated-measures ANOVA and multivariate ANOVA (MANOVA); 2) random-effects models analyzing intra-individual change by modelling within-subject variations related to processes such as growth curve model (GCM), and inter-individual change by modelling between-subject variations related to processes such as structural equation modelling (SEM) framework; and 3) transition models analyzing the effect of explanatory variables on the likelihood of change adjusted by the outcome (29). However, each technique addresses only certain aspects of the data, thus allowing only a few research questions corresponding to transition analysis to be answered with a single modelling technique.

In statistical modelling, linearity is one of the common assumptions to be met before analysis. However, real-world scenarios often violate the linear association between the response and explanatory variable, especially in high-dimensional complex health data (30). Several non-linearity and multivariate couplings make it almost impossible to model the phenomenon using conventional statistical models. The efficiency of statistical modelling over linear and univariate data makes them a misfit for the non-linear and highly complex latent structure problem domain. Thus, there is a rising interest in using ML methods in health research. Public health information has a considerable volume. ML creates the opportunity to systematically analyze vast amounts of population data to assist in data-driven decision-making by examining what causes health change in a population, when it occurs, how it changes, and predict the impact of interventions or solutions (18).

1.4 Motivation

The motivation of this thesis is two-fold. First, we need to understand *how* a transition of behavioural patterns occurs at the population level using the longitudinal design of survey questionnaires. Second, ML techniques, particularly various clustering methods, can be utilized in population research. Monitoring and understanding risk profiles of youth polysubstance use may help determine their overall health threats, identify their most need for intervention, and evaluate the effectiveness of existing policies and practices in their school environment. Discovering the nature of the hierarchical high-dimensional data structure will better understand longitudinal data analysis in real-world practice.

1.5 Thesis Structure

This thesis is organized as follows. Chapter 1 briefly introduces the background of this thesis. Chapter 2 provides a comprehensive review of the existing literature related to youth polysubstance use and methodologies for modelling cross-sectional and longitudinal data in addiction and health research. The rationale, the overarching goal, specific objectives, and research questions for this study are presented in Chapter 3. Chapter 4 describes the research methodologies, introducing the dataset and the variables of interest. Chapter 5 presents the study results, including data preprocessing, descriptive statistics, cluster analysis, risk profiles of youth polysubstance use, and the modelling results of use patterns and dynamic transitions. Chapter 6 discusses the key findings of this thesis surrounding the research questions and perceptions from ML methodological perspectives. The contributions to practice in public health and research communities in literature, the strengths and limitations of this thesis, and future works are also discussed in this chapter. Finally, Chapter 7 concludes this thesis by summarizing the principal findings and highlighting the contributions to bridging the ML and Public Health research communities.

Chapter 2
Literature Review

This chapter provides an overview of youth polysubstance use, methodologies for modelling cross-sectional data in addiction research, and the current methods in transition modelling in the health domain. The review focuses on the descriptions of the methods used, their applications, and comparisons drawn by various studies in the published literature. This chapter summarizes the existing evidence on both the ML and statistical methods used in pattern discovery and transition analysis, including main applications employed using health data through a literature search, and identifies current research gaps and potentials for future research. In this chapter, the basic features of the clustering techniques and transition modelling are described. Additionally, a comprehensive literature review regarding the methodology, the nature of the research questions they can address, and the quality of the answer provided in real-life examples are summarized.

2.1 Youth Polysubstance Use

2.1.1 Prevalence of Risk Behaviours and Use Patterns

Youth substance use is one of the persistent public health issues in Canada and many other countries. The Health Behaviour in School-aged Children (HBSC) study is the most prominent ongoing youth surveillance research across Canada that collects data from school-aged children between 11 to 15 years old (grades 6 through 10) every four years (31). The HBSC study aims to obtain insights into youth health behaviours, well-being, and social determinants. The HBSC survey on youth substance use examines daily cigarette smoking, e-cigarettes use, binge drinking, marijuana consumption, and illegal drugs and medication use. According to the most recent national report by the HBSC survey in 2018, among grades 6 to 10 students, boys who smoke cigarettes daily in the last 30 days range from 0.1% to 2%, and 0.5% to 1.8% for girls. The proportion of boys who use e-cigarettes in the last 30 days ranges from 7% to 28%, 4% to 24% for girls. Twenty-nine percent of grade 10 female students (vs. 1% in grade 6) and 26% of grade 10 males (vs. 1% in grade 6) get drunk on two or more occasions in their lifetime. 17% of grade 9 and 10 male students reported marijuana consumption in the past year, the proportion declined by 20% from the 2002 HBSC survey. The same proportion of 17% female students in 2018 used marijuana in the last 12 months, declined by 14% from 2002. A

continued decline in marijuana use and low percentages of daily cigarette smoking and illegal drug use was reported in the 2018 survey cycle compared to the previous survey in 2014. Although encouraging, the 4-year data collection cycle has a significant gap in examining health behaviours among adolescents, mainly after non-medical cannabis was legalized in 2018.

There is increasing evidence about youth polysubstance use in Canada. Recent work from the COMPASS study, a large prospective cohort study of a convenience sample of Canadian students, found that in the 2017-18 school year, 18% of high school students reported dual-use or multi-use of substances, 16% reported single-use (one substance), and 61% reported no substance use in the past 30 days (14). Studies of these trends for the past five years indicate that approximately 60% of high school students have not used substances. Although the number of non-user has remained stable, the multi-use of substances cohort is on the rise, possibly due to the emerging trend of e-cigarette use (13).

The majority of polysubstance use literature has identified three or four use patterns among youth (32). Common use patterns include no or low use, alcohol use (i.e., alcohol only or predominantly alcohol use), and multi-use (32). Most of these studies focus primarily on tobacco, alcohol, and marijuana consumption due to their high prevalence of use among youth. For example, a study of Canadian adolescents aged 12-18 in Victoria, BC, examined the past year substance use and identified three use patterns: low/no use (63%), dual-use of marijuana and alcohol (23%), and multi-use of cigarettes, alcohol, marijuana, and other illicit drugs (11%) (33). E-cigarettes have not been considered in many of these studies due to their novelty. However, their popularity has surged among youth in recent years and may be contributing to a rise in youth polysubstance use (13,14,34). Recent research identifies classes of use that involve dual and multi-use e-cigarettes with other substances, indicating the importance of considering these devices when examining multiple substance use (14).

2.1.2 Adverse Effects and Perceived Impact

As opposed to a single substance, using multiple substances is associated with further risky behaviours and adverse health outcomes (35,36). First of all, adolescent polysubstance users tend to continue using numerous substances as they transition from adolescence to adulthood. They are more likely to increase the number of substances currently used instead of reducing them over time (37). This cohort is at higher risk of substance use disorder (SUD), with fewer chances of ceasing multi-substances (37,38). Secondly, polysubstance users among youth tend to perform poorly academically

(6), with lower marks and less likely to complete their secondary education (39). In addition, polysubstance users tend to engage in other risky behaviours, including risky sexual behaviour (6) and participation in violence (8,9). The culminating evidence has shown that this cohort tends to have poorer overall health outcomes, including being more susceptible to mental illnesses than their peers (6).

2.1.3 Current Evidence on Risk Factors

2.1.3.1 Individual-Level Risk Factors

Age, sex, and ethnicity are the primary individual-level risk factors impacting adolescent polysubstance users in the literature. With age, the older the students, the higher their risk of using multiple substances (13,14). Additionally, early use of the substance is a risk factor for becoming polysubstance users in the future (40). While evidence concerning age as a risk factor is apparent, sex and ethnicity on youth polysubstance use are inconsistent. Although most studies show that male students tend to be in a higher use subgroup than their female peers (13,14,40,41), there are some studies among Australian (42) and Brazilian adolescents (42,43) that found no difference. A few studies among US youth reveal that female students are at higher risk of using multiple substances, including non-medical and medical use for prescription drugs (44,45).

Regarding the relationship between ethnicity and polysubstance use, Indigenous students in Canada (13,14) and the US (46) are more likely to engage in multiple substances. In contrast, studies of Asian, Hispanic, and other ethnical students consistently are shown to be at lower risk of using more than three substances (14,41). Other studies have also found that black students are less likely to use multiple substances than their white peers (47,48).

Substance use was found associated with depression and anxiety among youth. However, most of this research has only focused on the effects of single substance use on mental illness (49,50). Other individual-level factors that may influence the risk of youth substance use have also been explored, including eating habits, sedentary lifestyle, social connectedness, and family and peer influence. Lesjak and Stanojević-Jerković (2015) revealed that sedentary behaviour is a risk factor associated with dual-use of alcohol and tobacco among youths, while leisure-time physical activity (PA) is a determinant for daily cigarette smoking (51). Substance use is associated with adolescents' attitudes and behaviours towards health, including eating habits (52). Concerning the correlation between

youth polysubstance use behaviour and attitudes towards nutrition, Isralowitz & Trostler (1996) found that substance users were more likely to be at higher risk of unhealthy eating habits. These habits include skipping breakfast or not eating three meals daily (52).

Other individual-level risk factors for multiple substance use among youth include low social connectedness (53). In contrast, youth disapproval of substance use is related to a lower possibility of belonging to a higher use class (54). School connectedness or engagement are also identified as being associated with substance use among youths. Adolescents' sense of connectedness has been found to have mixed results on multi-use. Some studies have shown no effect of school connectedness or engagement (54,55), whereas others have found lower school connectedness associated with increased multi-use (14,42).

2.1.3.2 Population-Level Risk Factors

Population-level (or environmental) factors such as living in a non-urban setting are associated with multi-use involving predominantly tobacco use (44). Family, peer, and school factors also influence youth polysubstance use. Parental drinking and peer effect have both been identified to correlate with multi-use positively (32,56). Not all studies have assessed socioeconomic status (SES), an environmental factor that contributes to youth polysubstance use, and among those that have considered SES, their results are inconsistent. Some studies have identified no effect (42,44,57), while others have determined that students in higher use classes are more likely to have higher family affluence or access to spending money (14,43). One study, in contrast, has found lower SES to be associated with increased multi-use (58).

2.1.4 Research on Canadian Youth Substance Use on COMPASS Data

2.1.4.1 The COMPASS System

The COMPASS system is a longitudinal data system initiated in 2012-2013 examining health-related behaviours among Canadian secondary school students. Specifically, COMPASS is a prospective cohort study based on school settings, collecting hierarchical (student-level and school-level) health data via anonymous COMPASS Questionnaires (hereinafter “Cq”). The COMPASS system facilitates collecting, translating, and exchanging data from secondary school students and their participating schools that are convenience samples across several provinces in Canada each school year (59,60). In

the COMPASS study, student participants are asked about various health behaviours, including healthy eating, PA, smoking, alcohol and drug use, school connectivity, and mental health (59). Participating schools use a different questionnaire surrounding the school policies and practices (SPP) concerning their students' health behaviours. Furthermore, school SES, urbanity, and built environment (BE) are collected as supplementary community-level information. A copy of Cq (2017-18) is available in Appendix A.

The primary objective of the COMPASS study is to improve youth prevention research and practice (60). Adapted from the Canadian Cancer Society's School Health Action Planning and Evaluation System (SHAPES) framework, the COMPASS study was developed to address knowledge gaps in school-based prevention research and provide a knowledge exchange system for comprehensive research and evaluation (59). Contextually relevant information is crucial for developing meaningful interventions that target modifiable risk factors for chronic diseases and health behaviours. Context-specific adaptation activities are supported by COMPASS research and generate additional practice-based evidence that can be reapplied to similar settings (61). With the COMPASS data, youth health interventions are better informed and can be optimized by adopting programs or policies based on recognized capacities and needs.

Data collection is an integral aspect of the COMPASS system and is the foundation of subsequent processes (e.g., knowledge translation, intervention activities, system improvement). Strict protocols have been developed to ensure data collection is consistent across participating schools to preserve data integrity. COMPASS researchers make use of multiple data collection tools that have been specifically designed to capture actionable, context-specific data (62). Student-level data, which forms the bulk of the COMPASS dataset, is gathered using the paper-based Cq (63). The 12-page questionnaire is completed anonymously and consists mainly of multiple-choice questions about physical characteristics, health behaviours, and academic performance (59). The data generated through completion of the Cq are essentially categorical; however, some continuous values are reported for select variables such as weight, height, and the amount of PA in hours and minutes.

Participating schools are first evaluated based on their existing health policies and programs. Subsequently, they undergo a facility evaluation (conducted by COMPASS researchers) that examines health influencing characteristics of their internal and external environment (59). For schools that participate in COMPASS research across multiple years, Cq is conducted annually. The

questionnaire has been adapted several times throughout the study in response to participant feedback. It better reflects emerging COMPASS research priorities (e.g., cannabis use among youth in the wake of legalization) (62). The characteristics of the schools participating in COMPASS research are evaluated using three data collection tools. Details regarding existing SPP are typically reported by having a knowledgeable school administrator complete the SPP Questionnaire (59). The SPP is completed annually (at the same time as the Cq and provides researchers with an overview of each schools' policy environment (59).

Alternatively, the COMPASS School Environment Application (Co-SEA) is used to measure aspects of a school's internal BE related to youth health and youth health behaviour (59). Co-SEA is a software application used by COMPASS researchers as a direct observation tool when auditing participating schools for the presence of healthy or unhealthy physical features (e.g., vending machines, exercise facilities, and drinking fountains) (59). The contextual data captured by Co-SEA may exist as photographs, free-text, or categorical ratings. Data is obtained annually from the CanMap Route Logistics (CMRL) database with spatial information and the Enhanced Points of Interest (EPOI) data resource to assess the external school environment for health influencing factors (59). COMPASS researchers can remotely evaluate the physical environment surrounding participating schools in terms of impact on student health. This was achieved by combining land-use and street network data from CMRL with opportunity structure location data from EPOI (e.g., presence of fast food outlets, tobacco retailers, parks, recreation facilities etc.) (59).

2.1.4.2 Substance Use Among Canadian Youth

Recent focus has been given to substance use among Canadian secondary school students, such as exploring the two-way relationship between e-cigarette and tobacco smoking (63), examining the impact of a potential mediator facilitating the transition from one substance use to another (64), identifying alcohol drinking patterns (65), psychological and behavioural correlates of cannabis use (66), trends of polysubstance use (13), and many others. Over half of the 120 plus journal publications under the COMPASS study conducted research surrounding the topic of substance use, and the majority focused on one or dual substances and their correlation with other health behaviours, academic outcomes, and mental health.

2.2 Methodologies for Analyzing Cross-Sectional Evidence in Addiction Research

Table 1 highlights the advantages and disadvantages of the various modelling techniques that have been discussed in this section.

Table 1. Advantages and disadvantages of various clustering analysis techniques

Method	Type	Advantages	Disadvantages
Latent Class Analysis (LCA)	Statistical	• Model-based approach: probabilistic models (finite mixture models) to describe the distribution of the data	• Local vs. global maximum • Estimated probability zero/one yield extensive negative/positive logit parameters
K-Means Clustering	Unsupervised	• Simple, easy to understand • Objects are automatically assigned to clusters • Works effectively for small datasets - low time complexity	• Sensitive to outliers • *A priori* knowledge of cluster # before analysis • All objects forced to a group • Unsuitable for non-convex groups • It does not scale well for large datasets - high time complexity
Hierarchical Clustering	Unsupervised	• *A priori* about the # of clusters not required • Easy visualization with a dendrogram • Provide hierarchical relations between clusters • Able to capture concentric clusters	• Once a decision is made, cannot undo • Sensitive to outliers • Difficult to model clusters with varying sizes and convex shapes • Difficult to identify the optimal number of groups • High time complexity

2.2.1 Statistical Methods

Depending on the research questions, statistical methods for analyzing youth polysubstance use vary in the literature. A recent systematic review by Halladay *et al.* (2020) examined the substance use patterns among youth. Of the 70 included articles, the majority (50 out of 70) studies applied latent

class analysis (LCA) for the categorical outcome variable. In contrast, three studies used latent profile analysis (LPA) for the continuous outcome (67).

Measuring polysubstance use, which can be estimated by adding the total amount of substances used in a certain period, presents some statistical challenges (13,14,42). When considering the use of multiple substances, the number of substances consumed and any potential use combinations must be considered (14). A contingency table of all possible groupings may result in low cell counts that limit statistical power. To additionally consider the frequency of use only intensifies this problem. LCA is a solution that uses responses to two or more categorical variables to identify homogeneous subgroups in mutually exclusive data (68). LCA is the most common method to measure the use of multiple substances (32,33,44,56).

2.2.2 ML Approaches

2.2.2.1 Supervised Learning

In a recent systematic review on existing applications of ML in addiction studies, Mak, Lee, & Park (2019) revealed that most of the included articles applied supervised learning (13 out of 17). Among these studies, six used regression, five used ensemble learning approaches or comparing multiple algorithms, and two used classification. The results show that ML, mainly supervised learning methods, is increasingly used to assist in decision-making in addiction psychiatry (69). Jing *et al.* (2020) used the random forest (RF) classifier to predict individuals at high risk of developing SUD. The authors identified 30 predictors, including poor health behaviours in late childhood, psychological dysregulation, irregular social interactions in mid to late adolescence, among others that strongly predict SUD (70). The RF algorithm can optimally detect SUD individuals between 10 and 22 years old, compared with other ML algorithms. The RF algorithm outperforms other ML classifiers by increasing the prediction accuracy from 74% for 10–12-year-old youths to 86% for 22-year-old young adults (70).

2.2.2.2 Unsupervised Learning

The unsupervised learning method can be further divided into cluster analysis and dimensionality reduction. Clustering approaches include data-based, distance-based, similarity-based, kernel-based, information-theoretic-based, and graph-theory-based clustering. There are various types of clustering; some common ones are stochastic and non-stochastic, fuzzy and crisp clustering, hierarchical and

non-hierarchical clustering, and exact and approximate algorithms. According to Halladay *et al.* (2020), 13 out of the 70 included articles in their systematic review applied cluster analysis methods to examine the patterns of youth substance use. Among these studies, K-means and hierarchical clustering were the dominant clustering methods (67).

2.2.2.2.1 K-Means Clustering

Partition-based (or centroid-based) clustering algorithms group data elements into clusters based on their similarity. It considers the center of objects in each group as the cluster representative. K-means, one of the classical partition-based clustering algorithms, divides the total data points into k clusters. This approach is computationally efficient but is sensitive to the number of k clusters and outliers. In a cross-sectional survey study, Gray *et al.* (2015) examined subgroups of gamblers on two sites, implementing k-means clustering with gap statistics and elbow method. The first site is a casino with 217 employees, and the second one is an online gambling company with 178 operators (71). The clustering results yield four subgroups and two subgroups on the first and second sites(71). For model evaluation, the authors performed ANOVA with post hoc tests.

2.2.2.2.2 Hierarchical Clustering

Hierarchical (or connectivity-based) clustering methods measure multivariate on each subject. Clusters are constructed by merging from bottom-up (agglomerative) or splitting (divisive) previously built clusters from top-down, represented with a dendrogram, a tree-like diagram. Hierarchical clustering algorithms are suitable for datasets with arbitrary shapes of clusters. Unlike partitional clustering, hierarchical clustering takes several partitions instead of grouping the data objects into a specific number of clusters at one step. Hierarchical clustering produces a set of nested clusters presented as a hierarchical tree. A dendrogram records the order of splitting or merging. Agglomerative and divisive clustering are the two major types of hierarchical clustering. The former approach starts with the data objects as individual clusters and merges the closest pair of clusters from the bottom up until only one cluster, or k clusters, are left. The latter takes the opposite top-down approach by separating the data objects successively into more delicate clusters.

The standard agglomerative methods include single linkage, complete linkage, group average linkage, weighted average, median, centroid linkage, and Ward's method (22). For example, single linkage (a.k.a. nearest neighbour) defines the minimum distance between clusters, whereas complete

linkage (a.k.a. furthest neighbour) represents the maximum distance between clusters. Single linkage and complete linkage do not consider the cluster structure. Group average linkage (a.k.a. unweighted pair-group method using the average approach, UPGMA) is an intermediate method between single and complete linkage, considering the cluster structure. Like the average linkage, the weighted average linkage weighs the distance between clusters based on the inverse of the number of data elements in each cluster. It is considered a practical approach for a dataset with unbalanced cluster sizes. Details of these methods are summarized in Appendix B.

Hierarchical clustering has been widely used in health-related data. For example, Ashok *et al.* (2019) applied the agglomerative clustering technique to analyze Twitter data and disease surveillance. In this comparative study, the agglomerative clustering algorithm outperforms the other two clustering methods, namely k-means and spectral clustering (72). Elliott *et al.* (2019) applied cluster-type analyses, using dendrogram to visualize the relationships between substance types. The results show significant distinctions in the use patterns of substances and polysubstance between States in the U.S. Common combinations such as cannabis/MDMA and heroin/cocaine can be clustered well. In contrast, cathinone and synthetic cannabinoids do not cluster well with other substances. Interventions to address clinical challenges of multi-use of substances are essential for individuals who engage in concurrent use of other substances with binge drinking (73).

A cross-sectional family-based genetic study recruited 5390 subjects in the US to identify inherited patterns of opioid use. Computer-assisted interviews and Semi-Structured Assessment for Drug Dependence and Alcoholism were applied to diagnose SUD defined by the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) (74). The authors employed multiple correspondence analysis (MCA) for feature selection (74). Implementing hierarchical and k-medoids clustering algorithms, Sun *et al.* (2012) identified five homogenous inherited patterns of opioid use, varying by use levels, onset time, and comorbidity.

In summary, the existing evidence on methodologies for modelling cross-sectional data in addiction research, LCA, K-means, and hierarchical clustering are commonly used techniques. LCA is a model-based approach for clustering, using probabilistic models (finite mixture models) to describe the data distribution (22). As a statistical modelling technique, LCA is based on the assumption of conditional independence; that is, the categorical variables in each subgroup are

independent of each other (22). Whereas K-means and hierarchical clustering are unsupervised ML methods, applying distance-based clustering algorithms to group objects into heterogeneous clusters.

2.2.3 Comparison Between ML and Statistical Modelling

There is often confusion between ML and statistical terminology and methods. ML is a practice that uses algorithms to analyze data, learn from data, and predict with new data. “Learning from data” is the primary focus of ML. As its name implies, with ML, the machine is trained using a large volume of data and algorithms to perform a task without explicit instructions. As a newer field of study than statistics, ML can result in more detailed information than statistical modelling. ML is a sub-field of Computer Science (CS) and AI and contributes to building systems that can learn from data without explicit programming. ML emphasizes predictions and tends to evaluate prediction performance. Due to better accuracy from the predictive models, ML relies on fewer assumptions than statistical modelling.

On the contrary, as a sub-field of Mathematics, statistical modelling uses mathematical equations to identify associations between predictors and outcomes. It handles small amounts of data with fewer predictors. Statistical modelling requires practitioners to understand the relationship and realization of variables on the equation to best estimate the output of the function or make inferences about specific errors. In comparison, ML requires minimal human effort, as the workload involved in computing is placed squarely on the machine. Furthermore, ML has strong predictive power, as the machine itself is fit and trained to find patterns within the data. Although ML models have the advantages of automating high throughput computational tasks, meaningful interpretation of the modelling results is of utmost importance in adopting ML techniques.

The scenario of “the data is a sample from a larger population” is often not applicable to ML approaches, nor is it required to consider through statistical assumptions. There is much concern over performance and robustness, unlike traditional statistical analysis, which focuses on population inference. One of the main distinctions that make ML helpful is that it also works well with large datasets, such as population-level health data. In contrast, statistical modelling has difficulty performing the tasks. Overfitting is a common issue for ML with tremendous solutions to it. Generalizability from a classical statistical test is given by the connection of the data to a population-level model. That theoretical construct provides generalizability. However, it is challenging to achieve generalizability in ML, which is usually obtained through the algorithm's performance on

novel datasets. ML works well for a particular dataset and does not generalize when applied to other datasets in conjunction with overfitting. The general approach of ML is from a data-driven, purely practical sense, which makes ML a very data-oriented discipline. That is why ML appeals to data scientists because they like to rely on the data as much as possible and a little bit less so on conceptual and statistical models.

The rise of ML in decision-making has moved in tandem with big data, computational resources, and advanced information and computer technology (9). Big data can be viewed as the data source for ML. On the other hand, big data creates more dimensions (with more relationships between predictors and the outcome variable) and more complexity (landscape overlay of those relationships). As a learning process, ML applies mathematics, statistics, logic, and computer programming. Supervised learning employs reinforcement rules to train an ML model iteratively. These rules will adjust the ML model accordingly. After training, the model can be applied to new data to provide decision-making, such as classification, discrimination, and detection. The previous Section 2.2.2.1 provides an example of using the RF classifier to predict individuals at high risk of developing SUD. For unsupervised learning models, the purpose is to discover important clusters or defining features in the data. For example, k-means and hierarchical clustering are the two commonly used unsupervised learning methods in identifying the patterns of youth substance use.

2.2.4 Gaps Identified

Based on the literature review conducted, out of the 70 studies included in the systematic review by Mak, Lee, & Park (2019), only 13 studies applied ML techniques (69). The evidence shows that ML approaches have not been widely used in addiction research, particularly for unsupervised learning methods compared to supervised learning approaches. According to Wang *et al.* (2015), current obstacles that prevent unsupervised algorithms from getting accurate clustering results from large datasets include (75):

- Leverage of existing knowledge: it is hard to use human knowledge during the identification step without deploying rule-based algorithms
- Deriving distinct phenotypes: some algorithms may result in overlapping phenotypes
- Missing and noisy data: robust algorithm required to deal with the missing data

- Scalability: when developing algorithms, it is necessary to pay more attention to scalability as health data has an exponential growth rate

Unsupervised ML methods, particularly a variety of clustering algorithms, were applied in this thesis to ascertain meaningful phenotyping results in risk profiles of youth polysubstance use. The clustering algorithms that were implemented in this thesis are elaborated in Chapter 4 Methods, Section 4.4.4.

2.3 Methodologies for Analyzing Longitudinal Evidence in Health Research

Table 2 summarizes the advantages and disadvantages of the various modelling techniques that have been discussed in this section.

Table 2. Advantages and disadvantages of various latent variable modelling techniques

Method	**Type**	**Advantages**	**Disadvantages**
Latent Markov Model (LMM)	Statistical/ ML	• Formulated based on strong statistical foundation • Efficient learning algorithms can be learned directly from the original sequence data • Can handle variable-length inputs • Widely applied in many fields, such as data mining and classification, pattern discovery, structural analysis, etc.	• Many unstructured parameters • Limitation on first-order Markov property: unable to capture higher-order correlation • Cannot express dependencies between latent states • A reasonably constrained LMM can only represent a small part of the distribution in the possible sequence space
Latent Transition Analysis (LTA)	Statistical	• Some development can be represented as movement through discrete categories or stages • Heterogeneity may be unobserved	• Not suitable for small samples • No consensus on the best approach for model selection • There may be errors associated with the measurement of the discrete categories
Latent Growth Curve Models	Statistical	• Individual intercepts and slopes can be different • Allow predictors error	• Cannot easily accommodate multilevel nesting • Data preprocessing: needs

(LGC)		• Handle predictor errors, correlated errors and heterogeneity • Latent variables can have multiple indicators • The pattern of changes can be checked from multiple dimensions • Estimate direct and indirect effects	time-structured data • No. of estimated parameters can increase rapidly • Fewer functions to test the interaction or adjust the effect

2.3.1 Overview of Longitudinal Data Analysis

Depending on the data structure of the response variable and research interest, longitudinal data can be divided into two main types, i.e., time-to-event data and repeated measures (RM) data (76). The best modelling tool for analyzing time-to-event data is survival analysis, with a particular research interest focusing on whether and when an event occurs. For example, Koenig, Haber, & Jacob (2020) examined the transitions in alcohol intake across time, assessing the determinants of the three transitions of onset, remission, and relapse, using survival analyses (77). Survival analysis is a special technique for modelling time-to-even data, which is out of the scope of this thesis.

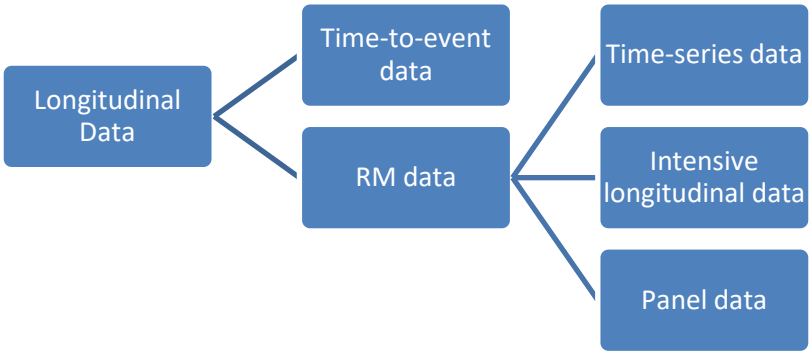

Figure 1. Types of longitudinal data

RM data can be further classified into time-series, intensive longitudinal, and panel data, based on the number of subjects and the time occasions available. As a particular type of pooled data, panel data derives from individual surveys. A panel is a cohort of the same cross-sectional unit being surveyed repeatedly across time (78). Panel data is longitudinal, allowing for the study of dynamic processes (79). In addiction research, observed data are often collected through a relatively small number of time occasions (e.g., annual surveys) from a relatively large number of subjects, as the

COMPASS data used in this thesis. By "relatively," it is compared to time-series data, typically collected from a single sample unit with a long sequence of measurements (78). Figure 1 shows the common types of longitudinal data (76).

In addition to the COMPASS dataset, the HBSC study also collects data from school-aged children in grades 6 to 10 every four years through a standard student questionnaire (31). Individual and societal resources, health behaviours and outcomes are the core data elements in the HBSC study (31). Another source of longitudinal data related to addiction research is the National Survey on Drug Use and Health (NSDUH), a household survey on substance use, SUD, mental health, and the receipt of treatment services for these disorders in the US. The data sample includes all 50 states and DC, with approximately 67500 participants are interviewed annually. The study population of NSDUH is the general public aged 12 and older, with data collected all year long, from January to December (80).

Panel data analysis can be further divided into the marginal model and random effect growth model. The former focuses on modelling the mean change, while the latter focuses on the individual or within-subject variations (76). Marginal models allow for making inferences to the entire population based on the drawn sample. To further differentiate random effect models, assumptions about within-subject variation can be divided into continuums or categories. The multilevel, latent curve and mixed-effects models are the appropriate modelling tools for continuum differentiations. Semi-parametric groups-based approach and latent class growth analysis can be applied to qualitative differences between subgroups (76). Table 3 summarizes modelling techniques that are widely utilized in panel data analysis, adopted from Bauer & Curran (76).

Table 3. Panel data analysis by research focus

Research Focus	Modelling Technique
Mean differences across ≥ two waves	RM-ANOVA Analysis of Covariance (ANCOVA) Generalized Estimating Equations (GEE)

Within-subject variation across ≥ three waves	Quantitative variations: multilevel model, latent curve model, mixed-effects model Qualitative variations: general growth mixture model Qualitative + Quantitative variations: semiparametric group-based approach, latent class growth analysis
Change in one process related to another	Trajectories: multivariate growth model Pairs of time points: latent change score model
Bidirectional effects over time	Auto-regressive (AR) cross lag
Change + bidirectional	Latent curve model with structured residuals
Progression through stages/sequence	Latent transition analysis (LTA)

2.3.2 Statistical Methods

LTA, a longitudinal extension to LCA, analyzes longitudinal data to determine a transition between latent classes across time. Suppose a change occurs, how that transition is characterized (68). In LTA, latent classes are called latent states to convey the potentially temporary nature of the grouping (68). In addiction research, LTA is a commonly used analytic technique that helps researchers identify hidden subgroups of individuals within a population. In LCA, the classes (latent states) are static, but in LTA, the classes are dynamic, such that individuals can transition from one class to another across time. In LTA, researchers are interested in understanding how subjects transition over time between subgroups that are identified using LCA. Different individuals may take different pathways over time, which is what researchers are primarily interested in examining.

For example, given that social networks are complex and multidimensional, Bray and colleagues used LTA to understand why smokers become more socially isolated when they try to quit. In this work, LTA was first used to describe subgroups of individuals post-quit with different social networks and then examine the dynamic transition of social network types over time (81). The study used data from the Wisconsin Smokers' Health Study, a long-term smoking cessation trial in Wisconsin (81). This analysis looked at 691 smokers who completed assessments at baseline and then

at one, two, and three years post-quit (81). The research focused on transitions of former smokers' social network statuses across that three-year post-quit date. In addition to understanding how people transition, the authors also examined how these different transitions were associated with abstinence over time. Modelling multiple features of social networks simultaneously allows researchers to explore how various sources of smoking exposure work together holistically (81). The authors also linked transitions of class membership to other outcomes. This study underscores the need for interventions that address situations in which subjects had partners who smoke and suggest new interventions to target broader social networks as people attempt to quit smoking (81).

2.3.3 A Brief Introduction to Transition Models

Transition models are statistical methods used to analyze longitudinal data to study change across time with natural, historical data. Transition models focus on modelling the response variable y_{it} for subject i at time occasion t, conditional on the subject's history, denoted as H_{it},

$$H_{it} = \{y_{ik}, k = 1,2, \dots, t-1\} \quad (1)$$

Such methods are often modelled as a n-order Markov chain, where the conditional distribution of y_{it} depends only on the most previous n responses for subject i,$\{y_{it-1}, y_{it-2}, \dots, y_{it-n}\}$. A Markov process is a chain of memoryless events, assuming that the next event will depend only on what is happening now and not what happened previously.

The LMM is a generative model for analyzing panel data (82). As one practical class of probabilistic template models, the LMM contains two probabilistic components, the transition model and the observation model. The former reveals the change from one hidden state to another across time, and the latter indicates how likely different observations can be seen in a given state. Interestingly, the LMMs often have an internal structure that manifests most notably in the transition model but sometimes in the observation model. Although LMMs can be viewed as a subclass of dynamic Bayesian networks, they have a unique structure that makes them particularly useful for many successful applications. The architecture of LMMs is very similar to that of hidden Markov models (HMM), assuming to follow a Markov chain, typically of first order (27). Both HMM and LMM approaches rely on a latent process with conditionally independent response variables (27). HMMs are well-known for time-series and stochastic processes with various applications such as robot localization, speech recognition, activity recognition, machine translation, time series prediction, biological sequence analysis, and others (83–85). The HMMs and LMMs rely on a solid

statistical foundation. However, the literature also refers to such probability template models as ML models. Therefore, the LMM lies at the intersection between statistical modelling and ML modelling. To emphasize the analysis of longitudinal data, the LMM is the term used throughout this thesis.

2.3.4 Latent Markov Models (LMM)

The LMM was initially developed in multiple directions with applications in sociology, psychology, and medicine (86). The first development involves using covariates, which may be included either in the latent or measurement model. A multivariate LMM was developed by Bartolucci and Farcomeni (2009), in which the conditional response probabilities of a given latent process were parameterized by multivariate logistic transformation. Using both time-invariant and time-varying covariates, Vermunt *et al.* (1999) modelled the initial probability and transition probability of the LMM process with multinomial logit regression models. Further extending this method, Bartolucci *et al.* (2007) applied more than one response variable, estimating transition probabilities based on lagging response variables (87). The LMM methodology allows various models to be estimated, and the best model can be selected from a latent class model to a heterogeneous model with subgroups.

The two fundamental problems that an LMM can address are predicting the probability of a sequence and predicting the most likely order of latent states based on observed data. Bartolucci, Farcomeni, & Pennoni (2012) stated two main applications of LMM, decoding and forecasting. Decoding uses the observed data of a sample unit to predict the order of its latent states (27). Decoding is further classified into local decoding and global decoding. The former refers to identifying the most likely latent state for each time occasion, while the latter identifies the most likely order of latent states. Another application of LMM is to forecast a latent state for future time occasions or a future response, given the observed historical data (27).

LMMs have been utilized in recently published health-related research. Some examples include examining the tendency of substance use (88), evaluating the performance of different nursing homes (89), assessing the dynamic association between expenditures and health conditions in the ageing population (90), and modelling the determinants of health care utilization (91). To examine whether age is associated with an increasing tendency of marijuana consumption, Bartolucci (2006) applied a univariate LMM (with no covariates) to the “National Youth Survey” data with five annual waves of marijuana consumption. The analysis was based on three latent states (not inclined to use cannabis, incidental use of cannabis, and inclined to use cannabis), with homogenous transition probabilities

and a parametric measurement model with simplicity provided global logits. The author tested different hypotheses of the latent process on the transition matrix. A tridiagonal structure was identified for the transition matrix. It has been proven that the LMM can handle distribution assumptions, such as excessive dispersion of polynomial distribution flexibly, considering the measurement error (88).

Mitchell *et al.* (2008) examined the drinking patterns of American Indian adolescents, the predictive factors and developmental outcomes that co-occurred (92). The authors applied an LMM to 6 bi-annual data collected from American Indian high school students to study dynamics in latent statuses of youth alcohol drinking in the past six months (92). The three latent statuses identified to describe alcohol drinking patterns across the three years were: abstainers, inconsistent drinkers, and consistent drinkers (92). The modelling results provide valuable insights into distinguishing youth who should be considered inconsistent drinkers (92). This study also indicates that extensive interventions for youth may not be the most important measures to minimize adverse health outcomes. Given limited resources, future interventions for alcohol intake and the use of other drugs may be more strategic (92).

The dynamic LMM has also been used to model the determinants of health care utilization leading to policy implications. Gil, Donni, & Zucchelli (2019) applied a bivariate LMM to model healthcare usage trends, dynamic unobserved heterogeneity, transitions between latent states, and the endogeneity of uncontrolled diabetes (91). The authors estimated the impact of uncontrolled diabetes on primary and secondary health care use on longitudinal administrative data, using biomarkers to measure uncontrolled diabetes (91). An LMM was applied to the longitudinal health survey and registration data on health care expenditures to examine the dynamic association between expenditures and health status in the ageing population (90).

Rijmen, Vansteelandt, & De Boeck proposed a hierarchical structure of the LMM to examine the emotional change process of patients with anorexia based on the ecological transient assessment research (93). Four latent states were selected for the analysis, including “positive mood,” “neutral to moderately positive mood,” “low intensity for all emotions except tension,” and “negative mood” (93). To illustrate that data from different day levels are dependent, Rijmen *et al.* (2008) fitted a hierarchical LMM by incorporating latent variables at the day level. Assuming a first-order Markov chain that is time-homogeneous, the author modelled the dynamics between the latent statuses at

signal- and day levels. It is estimated that there will be more positive sentiment trends in the initial probability and conditional probability of the chain over signal and day (93).

Bartolucci, Lupparelli, & Montanari proposed an LMM for assessing the performance of different nursing homes regarding the level of care provided for their patients in one region of Italy (89). This study is about the evolution of psycho-physic conditions of a sample of elderly individuals hosted in certain Italian nursing homes. Assuming a latent Markov chain exists for the transition of patients' health conditions, the LMM is used to analyze the repeated administration of questionnaires. With a manageable number of nursing homes (11) in this study, the authors utilized the multilevel structure of this longitudinal dataset. Instead of using random effects, fixed effects were applied to capture the impact of each institution on their patients' health conditions. The advantage of this method is that it explicitly considers the transition of health conditions, which is the metric used to evaluate the nursing homes' performance. However, this application may need a multilevel approach based on random effects with many clusters.

The LMM approach has also been applied in psychological and educational research (94), labour market and marketing-related fields (95), criminological research (87), and many others.

2.3.5 Multilevel Model (MLM) Framework

The MLM framework is a hierarchical modelling approach that allows for nested data structure and provides clear and structured semantic descriptions of growth pathways. There are other terms in the literature, such as hierarchical linear model, general linear mixed model, GCM, and random coefficient model (96,97). Although these models are not identical, their analytic approach is similar. They contain variables defined at different levels of the structured population with hierarchy; thus, these terms can be used interchangeably in practice.

LMMs can be extended to multilevel data, where individual samples are collected into subgroups. The fact that the samples are hierarchical is sufficient. Significant intraclass correlation coefficients (ICC) between levels are not required. Based on fixed effects, Bartolucci *et al.* (2009) employed a method to represent the common factors of all samples in the same subgroup. Based on random parameters with discrete distribution, Bartolucci *et al.* (2011) proposed a method related to mixed LMMs and LMM with random effects. These formulations for multilevel data are related to the extended LMM, allowing parameters to be changed in different latent subgroups. This method is known as the foundation of LTA (98).

This particular modelling technique has been applied in healthcare services, such as assessing the nursing homes' performances (99) and school services. For example, Bartolucci and colleagues (100) evaluated school performance, and Williford and Zinn identified bullying experiences with classroom-level mixtures taking advantage of nested structures of peer children in the classroom and school environments (101). These studies provide insights into individualized interventions corresponding to different latent states and transitions. This multilevel approach allows us to fit and further extend the LMMs by applying that same concept but at the level of repeated measures.

Koukounari *et al.* (2013) used a nonparametric multilevel LMM approach to study two trachoma-endemic communities in Gambia and Tanzania (102). This approach allows for nested data structure and addresses the computational difficulties of the multilevel longitudinal mixed model. Simultaneously, this study assesses three diagnostic and variance tests without a gold standard, based on data collected from a large-scale drug management intervention (102). The Multilevel LMM was used to assess the impact of interventions on infection and disease prevalence. Level 1 and level 2 were the within-household model and the between-household model, respectively.

2.4 ML in Public Health

The two most common public health topics where ML is currently employed are chronic diseases and associated risk factors and infectious, parasitic, and communicable diseases (20). The most common ML algorithms used in the literature were classification algorithms, including decision trees, random forest, logistic regression, and support vector machines (20). It is likely driven by the number of use cases where text mining and sentiment analysis were used to classify the concerns of individuals towards public health problems. This analysis was most commonly completed using free/open-source tools like R and Python. Common datasets that were used for this analysis included census data, social media data (e.g., Twitter), and specialized databases such as vaccine or risk databases (20).

Most ML techniques have been applied for descriptive and predictive purposes by mapping inputs to outputs in a data-driven manner. The objective includes public health surveillance, disease diagnosis, disease incidence, and individual-level and population-level prediction (19). ML offers health researchers new tools to tackle problems for which classical statistical methods may encounter limitations. ML is well-equipped to analyze vast amounts of health, environmental and other geo-special data to explore associations, identify disease patterns, and predict health outcomes in a

population, when it occurs, how it changes, and predict the impact of interventions or solutions (18). ML techniques may also generate hypotheses from large datasets and could be used to inform health research (19). ML can help public health researchers explore causality in some studies, although these methods do not necessarily change our conceptual understanding of the causal paradigm (17).

ML provides tremendous opportunities for improving public health. In a presentation of ML for public health hosted by Public Health Ontario, Rosella, Fisher, and Song (2019) summarized the rationale behind the rapidly growing interest in AI, including quickly evolving data environment, increasing computational capacity, improvements in data ingestion and processing, and greater demand for data-driven decisions (17). All these elements nurture our developing data science ecosystem in the public health sector. Population health focuses on the health outcomes of a group of people and the distribution of their results. Public health information has a considerable volume and can be viewed as the data source for ML, paving the way for precision public health (21). This term has recently been used in the public health literature, referring to "providing the right intervention to the right population at the right time (103)."

In the early days of designing this thesis, we conducted some preliminary searches for the topic of "ML for Public Health" on a variety of bibliographic databases, including PubMed, Scopus, IEEE, Web of Science, ACM, and ProQuest. From this preliminary search, ML applications in public health are primarily focused on infectious disease epidemics, lifestyle diseases, and predicting demographic information. Major themes have emerged in the field of public health through the application of ML methods, including disease screening/prediction/detection/outbreak/surveillance, non-communicable diseases, communicable/infectious diseases, risk factors/behaviours, mental health, maternal and child health, accidents/injuries/disability, and respiratory diseases and allergic disorders (104).

Some key enablers to facilitate the use of ML to understand and tackle public and population health problems have been identified (105). These enablers include understanding the governance context of big data in public health, modernizing data and analytic infrastructure, applying ML best practices, nurturing educated staffing, and establishing strategic collaborative partnerships between ML researchers and public health professionals. The significant hurdles of ML in public health include data acquisition (access and sharing), informed consent, security and privacy concerns, and making decisions under uncertainty (16,19). Overfitting is also a concern, which requires careful model evaluation before deployment. The potential ethics and bias-related issues related to ML-based

systems must also be considered. For example, biased data can lead to faulty algorithms, intensifying public health issues at the community level. How do we ensure that the data we are training and validating these automation tools do not contain inherent bias? Ethical issues such as who is accountable in the event of an error. Security and privacy of patient health data will be an ongoing concern (106). Achieving fairness, accountability and transparency (FAT) is the goal of explainable ML in the public health sector, with an interdisciplinary research focus. However, it is at an early stage of adopting ML in public health, and the level of sophistication is deficient.

In summary, this chapter provided a literature review on youth polysubstance use, approaches for modelling cross-sectional data in addiction research, advanced methods in transition modelling, and ML in public health. The review explained the methodologies utilized, their applications, and comparisons drawn by diverse research in the published literature. The research gap was identified that ML approaches had not been widely applied in addiction research. The study rationale and specific objectives follow in the next chapter.

Chapter 3
Study Rationale and Objectives

This chapter presents the rationale for this study and summarizes the aims, specific objectives, and research questions for this thesis.

3.1 Study Rationale

Although it is known that healthy habits during adolescence tend to persist into adulthood, the amount of research focusing on social correlates of youth health behaviours (e.g., peer relations, parental support, school programs) has been inadequate (107). The COMPASS longitudinal study addresses this gap by collecting multifaceted information pertaining to youth health behaviours from multiple sources to examine the relationship between school environmental characteristics and youth health behaviours in Canada. The COMPASS dataset is diverse, including Cq, BE assessments and policy evaluations. It has been utilized in many health-related disciplines. The COMPASS research has produced over a hundred academic publications ranging from environmental health and health promotion to preventative medicine (108). Early COMPASS publications revealed the substantial variability across Canadian jurisdictions regarding youth PA levels, substance use, mental well-being, and healthy school environments and policies (59). The COMPASS data have been continuously used to assess how school environments, policies, and practices affect multiple youth health behaviours and outcomes (59).

From a methodological perspective, the existing literature using the COMPASS data primarily applied LCA or LPA to identify single substance use patterns. For example, Lee *et al.* (2021) examined stage-sequential alcohol drinking patterns using multilevel latent class profile analysis (109). Gohari *et al.* (2020) applied a multilevel LCA to discover alcohol consumption patterns among youths from Canadian secondary schools (65). Hammami *et al.* (2019) studied risk behaviours associated with BMI on chronic diseases using the sex-stratified multilevel LCA approach (110). In addition, using LCA, Laxer *et al.* (2017) examined modifiable behaviours and their impact on obesity and overweight among adolescents (111).

However, none of the studies that used COMPASS data examined the ***transition*** of polysubstance use patterns among youth across time or explored ***risk profiling*** based on student characteristics and

school environment perspectives. Furthermore, current studies using the COMPASS data predominately select features for modelling based on *a priori* knowledge from existing literature in the appropriate research domain. By discriminatingly selecting only a few variables from the dataset that the researchers deem relevant to their study, they may inadvertently overlook meaningful relationships, hidden patterns, or underlying trends that could have been captured with the omitted variables. This could result in missed opportunities in identifying critical information to revise policies and interventions concerning youth health behaviours in school settings. Additionally, selectively overlooking variables provides an opportunity for implicit biases that can then be further imparted into the data analysis.

ML algorithms have unique advantages for revealing "hidden" patterns and unexpected associations in large and complex datasets, discovering relevant patterns in such high-dimensional data that are structural and/or temporal. Unless otherwise well-established, these patterns ("knowledge") are often unobservable, and human experts cannot directly access them. Yet, we may need these patterns to assist in better decision support. Most population-level health data are non-standardized and are often weakly structured, with a high dimension >3 (112). Although human experts are good at $\leqslant$3-dimensional pattern recognition, any higher-dimensional datasets make manual analysis difficult and impossible (112). We are unsure about the hidden knowledge, and ML approaches hold a promise to quickly identify hidden patterns on a vast volume of health data. However, thus far, none of the published studies using the COMPASS data have applied ML methods. This thesis employed ML techniques to the COMPASS dataset to enhance data exploration capabilities and identify complex associations between variables. On the one hand, the COMPASS dataset is explicitly concerned with youth health behaviours and corresponding school policies and practices. On the other hand, the multifaceted characteristics of this large-scale survey data, including the complexity of influence/behaviour models, modifiable risk factors, and disease progression and intervention, make it the optimal candidate for ML approaches in population-based health research.

3.2 Objectives

ML in public health is a new field, and its applications are underutilized. This thesis is designed to realize the huge potential of ML applications in the public health domain, engaging ML practitioners to move towards research in this field and bridging these two communities. The overarching goal of this thesis is to further the understanding of the appropriate way of fitting transition models and

exploring the “hidden” patterns generated from large complex population-based health survey data. The research objectives are achieved by implementing appropriate ML models to the COMPASS data.

First, this thesis aims to apply an LMM technique on longitudinal data to explore the dynamic transitions of polysubstance use patterns from one state to another across time, showcasing the ability of this type of modelling technique to examine inter-individual differences in transition analysis. Second, unsupervised ML algorithms have the unique advantages of revealing “hidden” patterns and unexpected associations in a large and complex dataset. The secondary aim of this thesis is to explore and obtain a better understanding of the structure of the COMPASS data in the context of risk profiling of polysubstance use among youth, which is primarily achieved through the application of cluster analysis.

More specifically, the objectives of this thesis are to:

- Estimate the transition probabilities of dynamic membership of use patterns over time using the COMPASS data.
- Experiment and apply a variety of clustering algorithms to analyze the COMPASS data that are explainable.
- Identify the most significant features or actionable insights for polysubstance use prevention derived from an ML model.

3.3 Research Questions

This thesis investigates how the various ML models can be applied to the longitudinal data for analyzing polysubstance use among adolescents using the COMPASS dataset. According to the literature on youth polysubstance use, it is anticipated to identify several latent states (subgroups) of individuals differing in their use patterns and transition over time. More specifically, this thesis is set to address the deficiency in understanding the dynamic transitions of use patterns using the COMPASS data.

3.3.1 Primary Research Questions

The primary research questions are:

- **RQ1:** What are the risk profiles of polysubstance use among Canadian secondary school students?
- **RQ2:** What are the patterns of polysubstance use among Canadian secondary school students?
- **RQ3:** How do transition behaviours change over time in use patterns?

3.3.2 Secondary Research Questions

The secondary research questions include:

- **RQ4:** What factors are associated with patterns of polysubstance use among Canadian adolescents?
- **RQ5:** What factors are associated with dynamic transitions of use patterns?
- **RQ6:** What are the advantages and limitations of the ML methods appropriate to modelling risk profiles and dynamic transitions using the COMPASS data?

In summary, this chapter provided the study rationale and summarized the specific objectives and research questions for this thesis. The research methodologies throughout this thesis follow in the next chapter.

Chapter 4
Methods

This thesis applied various research methodologies to achieve the aims and objectives outlined in the previous chapter. This chapter describes all these methods, ranging from data preprocessing, missing data analysis, feature selection, and various model fitting and validation approaches. The different research communities, i.e., ML and public health, use different terminologies in the same context. Table 4 summarizes the key terms/concepts used throughout this thesis, making it easy to understand by public health professionals and researchers.

Table 4. Glossary of terms/concepts for public health practitioners

Term	**Relevant Public Health Concept/Term with Interpretation**
Cluster	A.k.a "class" or "state" refers to a subgroup or a cohort of subjects with similar characteristics.
Feature	A.k.a "predictor variable" or "covariate" refers to an independent variable (or explanatory variable) in statistical modelling
Overfitting	A common issue in ML models with poor performance, referring to the model that fits the training data very well (i.e., very low training error, "too good to be true") but fits the test data poorly (high test error). This phenomenon is often caused by too many complex predictors than necessary in the model and can be addressed with multiple solutions (see Section 6.1. 4.3).
Phenotype	Originated from genetics, meaning a set of observed characteristics of an organism. In the context of this thesis, it represents the characteristics of youth polysubstance use collected through the COMPASS host study. "Phenotyping risk profiles" refers to the process of identifying subgroups of individuals with different characteristics related to polysubstance use.
Unsupervised learning	A type of ML algorithm. Unlike supervised learning algorithms that use labelled data for prediction (discrimination, classification), unsupervised learning algorithms explore the data and draw inferences from unlabeled data (i.e., no pre-

	defined outcome variable) to uncover inherent structure or hidden patterns. As one type of unsupervised learning, cluster analysis has been extensively investigated and applied to partition data into homogenous clusters (see Section 2.2.2.2).

4.1 Study Design and Participants

This study is a retrospective cohort study, taking the secondary analysis approach of an ongoing longitudinal study, i.e., the COMPASS study. The COMPASS data are a de-identified health survey at the population level. As introduced in Section 2.1.4.1, the COMPASS study collects student- and school-level information from a convenience sample of secondary schools across several provinces in Canada each school year (59,60). Substantial efforts have also been made to streamline data collection methods to minimize interruptions to class time and reduce the burden of work on participating schools (113). Eligible students at participating secondary institutions complete the questionnaire during class time on a prearranged "data collection day" (114).

Since COMPASS research involves youth under 18 years old, parental/guardian consent is required for participation. The University of Waterloo Office of Research Ethics has approved the active-information passive-consent protocols, which help achieve high participation rates and reduce sampling bias while preserving student confidentiality (113). The protocol provides parents with pamphlets that detail important COMPASS research and contact information, including contact information of the recruitment coordinator if parents would like to withdraw their child(ren) from the study. Eligible students whose parents do not contact the recruitment coordinator within the two-week time frame provided are considered participants who are allowed to complete the Cq (113). Additionally, students are permitted to withdraw participation during the consent process or data collection period (59).

In this thesis, the three-year linked sample of the COMPASS data collected includes Wave I (the school year 2016-2017, Y5), Wave II (the school year 2017-2018, Y6), and Wave III (the school year 2018-2019, Y7). The COMPASS study has received ethics clearance from the University of Waterloo Office of Research Ethics (ORE 30118).

4.2 Dataset and Data Preprocessing

4.2.1 Dataset

The longitudinal dataset being analyzed in this study is the three-year linked sample of the COMPASS data collected from Wave I, Wave II, and Wave III. Each linked dataset contains over 200 variables collected from 9307 Canadian students from grades 7 to 12 (secondary I through V in Quebec) at the initial measurement occasion (Wave I). The participating students were from 76 secondary schools located in Ontario, Quebec, British Columbia, and Alberta. Of the 9307 linked samples, the present analyses are restricted to the 8824 students with regular patterns on their grade levels. “Regular patterns” refer to the advancement of students from one grade to another at each school year. The COMPASS host study uses grade to be relevant to school planners who make plans based on grade, not age. Thus, the students’ grade level is a proxy of their age throughout this thesis. The Cq data contains demographic and personal information, such as grade, sex, ethnicity, primary language spoken, height and weight. Additionally, it includes student responses to multiple-choice questions regarding their behaviour and perspectives on health and wellness topics. The supplementary community-level data, i.e., school-level socioeconomic status, urbanity, and BE, are linked to each participating school. The survey is conducted annually, with three consecutive waves available for each subject within the same cohort.

As previously discussed, the COMPASS data is collected using annual student questionnaires Cq, school program/policy questionnaires (SPP, completed by a school administrator), and internal/external school environmental assessments (Co-SEA) (59). Students complete the cover page of the Cq to generate a unique code that allows COMPASS researchers to link data collected from the same student across multiple years of participation (59). The use of self-generated identification codes for anonymizing questionnaire data collected in longitudinal studies has been well documented and strikes a favourable balance between privacy and research methodology (115). Anonymization using unique self-generated codes is perhaps the principal strategy for ensuring COMPASS data remains confidential throughout the remainder of its life cycle.

Although the SPP data provides a wealth of information regarding policies and programs, they are not commonly used as student-level data, possibly due to the qualitative nature of many open-ended text responses. Since the research focus of this thesis is not directly related to the content from SPP

data, it was excluded in this thesis. Of note, the initial three waves COMPASS data contains 46862, 66434, and 74501 subjects at Y5, Y6, and Y7, respectively. To distinguish the initial three waves data and the linked samples, Wave I, Wave II, and Wave III are used throughout this thesis, representing linked samples at Y5, Y6, and Y7, respectively.

4.2.2 Data Preprocessing

Several data preprocessing steps were taken to prepare the data for analyses, including data cleaning, linking, merging, and missing data analysis. Figure 2 illustrates the flowchart of the steps taken from full samples down to final linked samples.

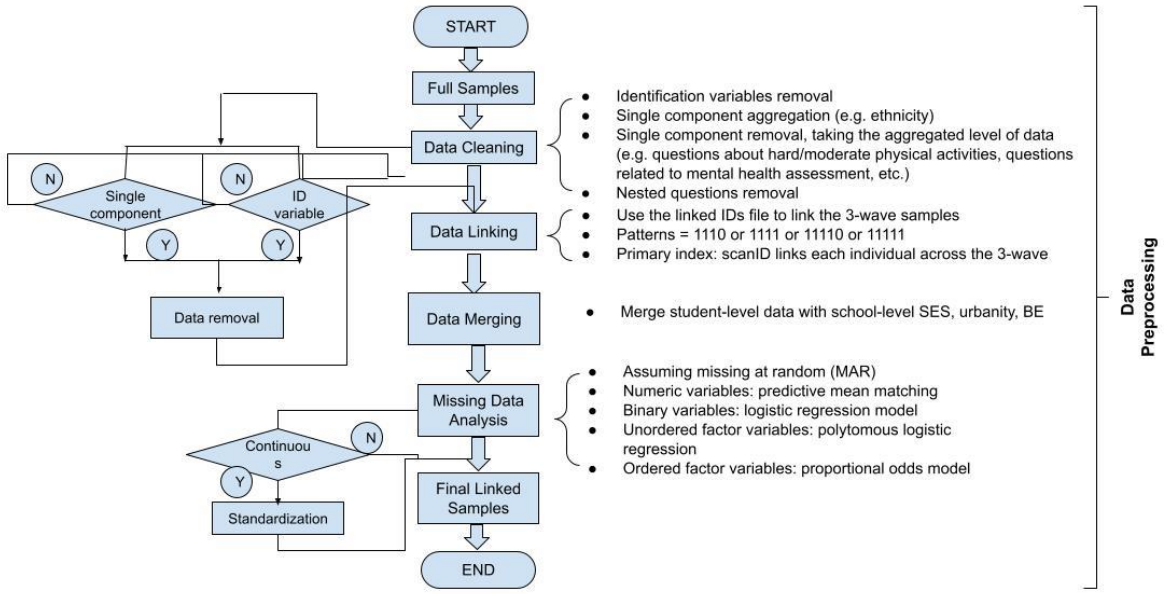

Figure 2. Flowchart of data preprocessing

4.2.2.1 Step 1: Data Cleaning

Redundant variables, such as nested questions which tend to have redundant information, and irrelevant variables, such as information inconsequential for analyses, were removed. For example, the subsequent question, “In the last 12 months, how often did you use marijuana or cannabis? (a joint, pot, weed, hash)” is, “If you have used marijuana or cannabis in the last 12 months, how did you use it?” Since the response to the nested question assumes an affirmative response to the parent question, such questions were considered redundant and thus were removed from the analyses. Redundant and irrelevant variables were identified by individually reviewing each nested question.

The process of cleaning irrelevant data included removing original data while retaining the data derived from them. For instance, body mass index (BMI) is derived from weight and height; thus, the calculated BMI data is included while the original data, namely, weight and height, were discarded. Likewise, hours and minutes of PA from Monday to Sunday were aggregated to total PA, mental health-related measures such as FLOURISH (Diener's Flourishing Scale), GAD7 (Generalized Anxiety Disorder 7-item Scale), CESD (Center for Epidemiologic Studies Depression 10-Item Scale-Revised), and DERS (Difficulties in Emotion Regulation Scale) were derived from relative scale items. The original data they are derived from were discarded. Data cleaning aims to keep intact relevant and necessary data for analysis while removing irrelevant and redundant ones.

4.2.2.2 Step 2: Data Linking

In addition to the complete cross-sectional student datasets, a separate linked IDs file was available for connecting the samples across waves. The updated linked IDs file covers the last five years. The new linked sample is updated each year based on further information about students. There is a pattern variable within the linked IDs file as a flag, indicating if a student participated in a year (denoted by 1) or not (denoted by 0). The years go from 2015-16 to 2019-20. Although the link is available in 5-year cycles, most students only attend secondary school for four years, so a 4-year worth of data tends to be used when performing any analysis. This thesis only included students who participated across all three consecutive years from 2016-17 to 2018-19. Therefore, patterns 1110, 1111, 11110, and 11111 were used to link the samples across these three waves. Table 5 demonstrates the identification of linking patterns across the three waves data. The scanID within each cross-sectional student dataset was a primary index linking each individual across the three waves.

Table 5. Identification of linking patterns across the three waves

2015-16	2016-17 (Wave I)	2017-18 (Wave II)	2018-19 (Wave III)	2019-20
0	1	1	1	0
0	1	1	1	1
1	1	1	1	0
1	1	1	1	1

4.2.2.3 Step 3: Data Merging

The supplementary school-level data, including household income level and urbanity, were merged into the student-level dataset using the corresponding school ID as the primary index. For the school-level BE, although 1500 meters is closer to the 1-mile buffer often used in US studies (116), the radial distance for points of interest, such as drug and liquor stores, were selected to be within1000 meters of the school zone. This distance of 1000 meters has commonly been used in tobacco retailer density literature for examining the relationship between school environments and youth smoking behaviours since it is relatively close to the school (117,118). The radial distance of 1000 meters approximates the furthest commuting distance for students from home to school, approximately 15-20 minutes walking distance. The school-level BE variables that were utilized in this thesis include total points of interest, such as the number of locations that sell alcohol, drugs, and tobacco products, within a 1000 meters radius of a school.

4.2.2.4 Step 4: Missing Data Analysis

Missing data were analyzed by identifying the missing patterns. Multiple imputations (MI) for missing values were performed by implementing the MICE (Multivariate Imputation via Chained Equations) package, generating five imputed datasets, with 50 iterations for each imputed dataset. It is assumed that the missing values are Missing at Random (MAR) using the MICE package. Missing data were imputed by specifying an imputation model for each variable with missing values one by one. For numeric variables, such as total points of interest within the school BE, sedentary time in minutes, total scores related to mental health assessment like CESD, predictive mean matching (PMM) was selected as the method for MI. A logistic regression model was specified for binary variables, responses with only two levels/options, e.g., gamble online for money (Yes/No). In contrast, for unordered factor variables with more than two levels, e.g., ethnicity (“White/Black/Asian/Indigenous/Latin American/Other”), a polytomous logistic regression was specified for imputing missing values. Lastly, for ordered factor variables with greater than two levels, e.g., evaluating the level of school support available for students to help quit drugs and/or alcohol (“Very supportive/Supportive/Unsupportive/Very unsupportive”), a proportional odds model was specified. After performing MI, statistical tests on each imputed dataset were conducted to pool the results for summary estimates. The optimal imputed dataset was identified by obtaining the best pooling statistical tests on most covariates.

Of note, the mental health-related items (FLOURISH, GAD7, CESD, and DERS) and the online gamble question were not asked in the Year 5 survey questionnaire. Those items were collected from Year 6 onwards. Since these variables are completely missing and the missing value imputation was not applicable for this type of missingness, these variables were imputed based on "Next Observation Carried Backward (NOCB)." NOCB is a reverse approach to the well-known "Last Observation Carried Forward (LOCF)" method by taking the first available value after the missingness and moving it backward (119). In addition to these missing values, BMI has been top missingness across the three waves data. Since BMI data are usually missing not at random (MNAR), multiple imputations may not be appropriate for this specific variable. In some papers, what researchers have done instead is coded missing as its category. Instead of the initial four classification categories, i.e., underweight, healthy weight, overweight, and obese, one more category was added, representing "not stated." In this thesis, we follow the same strategy of imputing the BMI missing data.

4.3 Substance Use Indicators

Substance use indicators, including cigarette smoking, e-cigarette use, alcohol drinking, and marijuana consumption, were assessed using the COMPASS Cq. Given that there is so much variability in the initial responses to the use frequency of the four substances (ranging from 1 to 8 or 1 to 9 for each substance), it generates a relatively large contingency table with 8 x 8 x 9 x 9 = 5184 cells. Each cell of the contingency table corresponds to the combination of response patterns of substance use. As this thesis focuses on risk profiles and use patterns rather than frequencies, the ordinal responses were collapsed into three-category indicators to avoid the sparseness of the observed frequency table. Following the most common categorization for determining the patterns of youth polysubstance use, the initial responses were categorized into "0," "1," and "2," representing "never use," "occasional use," and "current use," respectively. Further information on the Cq questions and their categorization follows.

Cq posed two questions for cigarette smoking and e-cigarette use to determine the incidence and frequency of these substances. The questions and the categorization of the initial responses can be seen in Figures 3-4. While for alcohol drinking and marijuana consumption, only a single measure was used on Cq. Figures 5-6 demonstrate the questions and the categorization of the initial responses for these two substances.

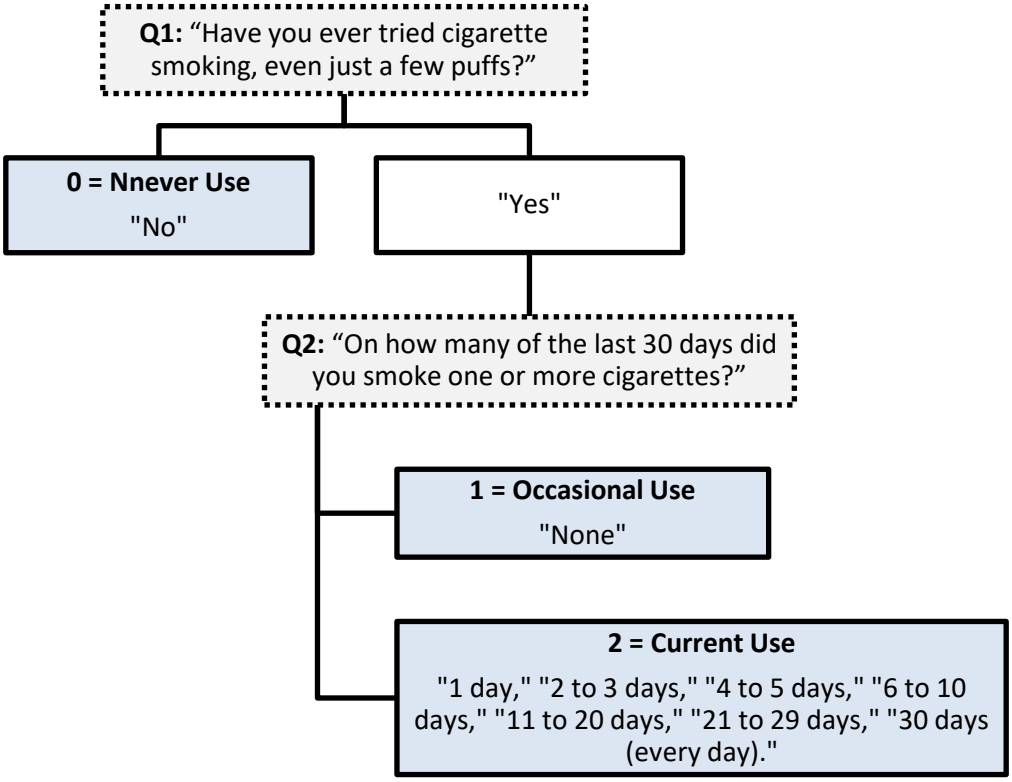

Figure 3. Measurement of cigarette smoking

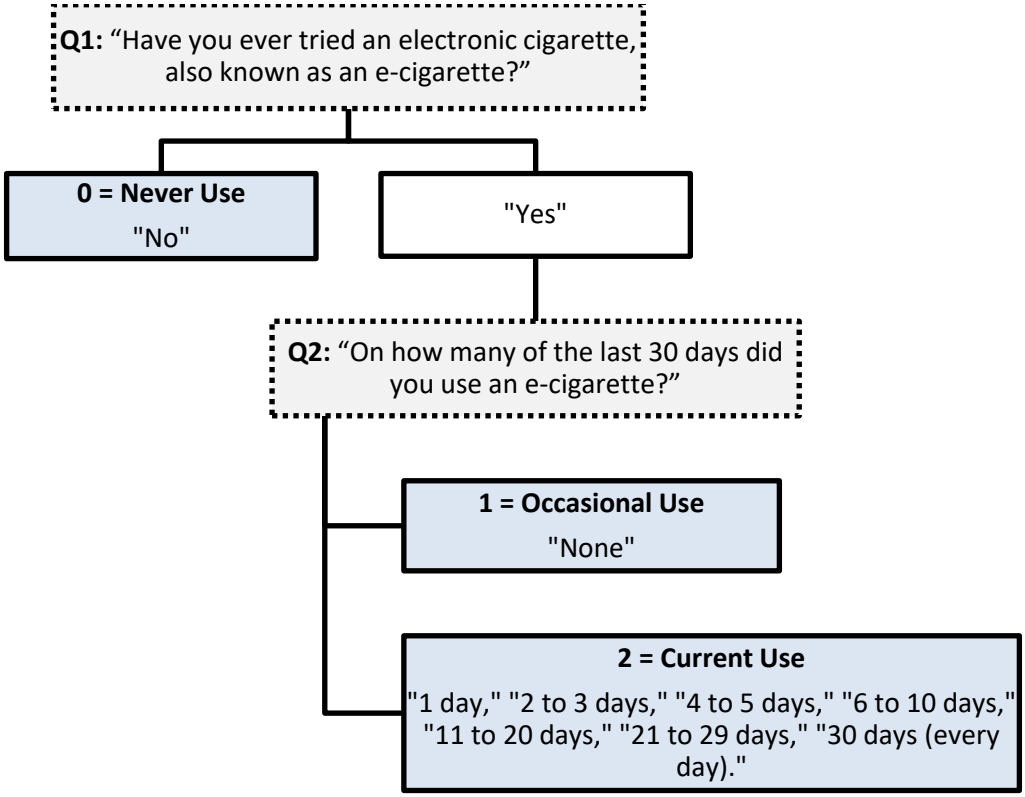

Figure 4. Measurement of e-cigarette use

Alcohol Drinking

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

0 = Never Use	1 = Occasional Use	2 = Current Use
• “I have never drunk alcohol” • "I have only had a sip of alcohol"	• “I did not drink alcohol 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"

Figure 5. Measurement of alcohol drinking

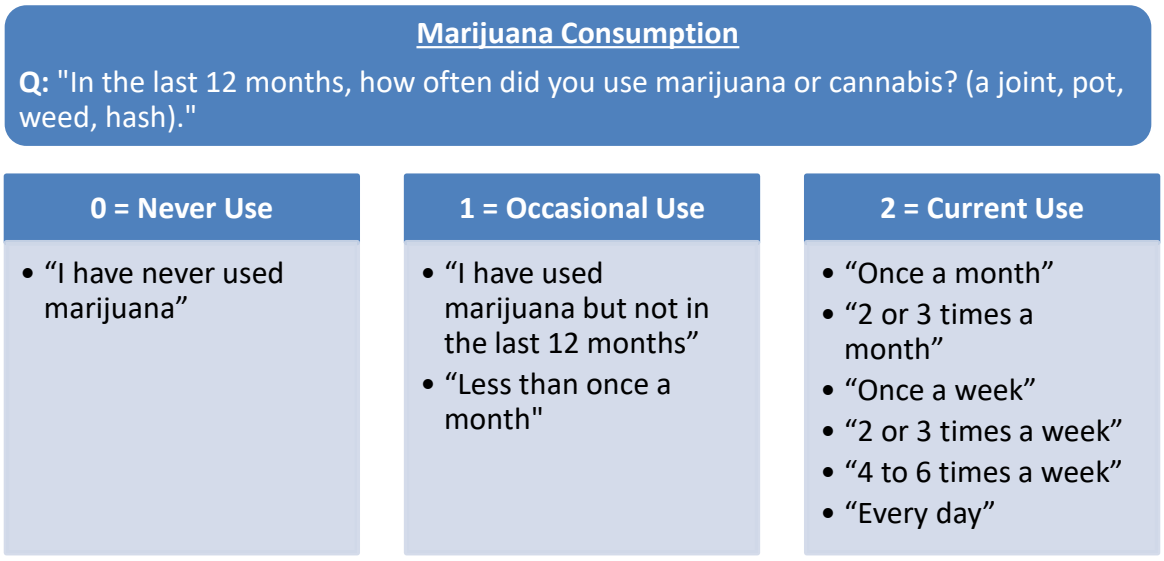

Figure 6. Measurement of marijuana consumption

4.4 Cluster Analysis

4.4.1 Feature Selection

Feature selection and feature extraction are the two main methods of dimensionality reduction, which is crucial in modelling, especially when the dataset contains redundant or unnecessary variables for model fitting. To better preserve the interpretability of ML results, the feature selection approach was employed instead of feature extraction algorithms. Feature selection refers to selecting a subset of the original features, whereas feature extraction constructs derived features from the initial ones to achieve good modelling performance. In this thesis, a commonly used feature selection algorithm, Boruta, was applied to obtain the most representative subset of features for clustering. Boruta works as a random forest-based feature selection algorithm, an ensemble of decision trees. See Appendix E for a detailed description of the Boruta algorithm.

The same procedure of feature selection was repeated for each wave. The most notable subset of features was identified for the cluster analysis. For each feature, the score of variable importance was summed up across the three waves. The total score was sorted from largest to smallest. At the experimental stage, we selected from the top one up to all the features into modelling clusters. Preliminary results demonstrated that the number of features around 10 led to more meaningful clustering solutions. Since the top 8 features covered as many risk aspects as the top 10, the former

was selected for parsimonious model fitting and a more straightforward interpretation. Including the four substance use indicators, all the variables specified in the cluster analysis were standardized to ensure equal weighting before clustering.

4.4.2 Data Visualization

t-Distributed Stochastic Neighbor Embedding (t-SNE) was employed in this thesis to visually present both the local and global structure of high-dimensional COMPASS data in one map. t-SNE is a non-linear ML algorithm used for reducing dimensionality and visualizing high-dimensional data. That is, it takes a high-dimensional dataset and projects it onto a lower-dimensional (two-dimensional or 2D in this thesis) space for visualization. Van der Maaten & Hinton (2008) developed the t-SNE algorithm, which has since been well adopted by various research communities, such as genomics, natural language processing (NLP), speech recognition, and many other fields (120). t-SNE tends to preserve both local and global structures as much as possible simultaneously. Principal components analysis (PCA) or multi-dimensional scaling are other dimensionality reduction methods that can preserve the global structure while losing the local structure.

An essential step to use the t-SNE algorithm effectively is to tune hyperparameters, such as perplexity and the number of iterations. As a smooth measure of the adequate number of neighbours, Van der Maaten suggests setting the typical range of perplexity values between 5 and 50 to achieve a fairly robust performance of t-SNE (120). For a larger or denser dataset, the rule of thumb is to select a larger value of perplexity (121). Oskolkov proposed the optimal perplexity approximates $\sqrt[2]{N}$, which is analytically derived from the power law, given that t-SNE is based on the minimization of Kullback-Leibler (KL) divergence (121). In this thesis, a range of perplexity, from 5 to 100, was experimented with. Perplexity = 100, which approximates $\sqrt[2]{N}$, is the optimal value for the linked three waves COMPASS datasets. A detailed description of the t-SNE algorithm can be seen in Appendix F.

4.4.3 Determining the Optimal Number of Clusters

One of the most challenging decisions to make in cluster analysis is determining the optimal number of clusters. When plotting the number of clusters, the optimal number can be found by observing the number of clusters with inflection points, peaks or declining points in the evaluation measures. Some commonly used approaches include the elbow method, silhouette analysis, the sum of squares

method, the GAP statistic, the D index, the Hubert index, among many others (22). For example, both the Hubert and D index are graphical methods. They seek the significant peak that corresponds to a substantial increase in the value of the measure. The silhouette analysis can help determine the optimal number of clusters via visualization. The average silhouette method calculates the silhouette coefficient of different k observations, where k is the number of clusters that maximizes the average silhouette coefficient over a selected range of values. The sum of squares method picks the best number of clusters by minimizing the sum of squares within-cluster and maximizing the sum of squares between-cluster. Within-cluster is a measure of how tight each cluster is, and between-cluster measures how separated each cluster is from the others.

Although each method helps identify the best clustering numbers, different criteria often suggest different numbers of clusters. This is mainly due to each stopping criterion being in favour of one particular validation method. Shi and Zeng (2013) presented a biased result of using the silhouette analysis alone without considering the sum of squared errors (SSE) for each k value. Therefore, they proposed a combination of SSE and silhouette coefficient in determining the best clustering numbers (122). A voting scheme by implementing 26 available indices was applied in this thesis. The optimal clustering analysis was proposed from the results obtained from all cluster combinations, distance measures, and clustering algorithms. Based on the majority voting among all indices, the optimal number of clusters was obtained for each of the three waves datasets. Although the computational complexity is much higher than a single index, this method provides an unbiased approach to selecting the most appropriate clusters for the COMPASS data.

4.4.4 Clustering Algorithms

This thesis implemented various clustering algorithms to explore and identify the most appropriate method for the COMPASS data, including hierarchical clustering, partitioning around medoid (PAM), and fuzzy clustering.

4.4.4.1 Hierarchical Clustering

Hierarchical clustering is one of the commonly used clustering algorithms to identify use patterns in addiction research (see Chapter 2 Literature Review, Section 2.2.2.2.2). We applied the agglomerative clustering algorithm with all the available linkage methods on the linked three waves of the COMPASS data. A detailed description of all the linkage methods can be seen in Appendix B.

4.4.4.2 PAM

As its name implies, PAM is a type of partitional clustering method. The average dissimilarity between data elements of the cluster and all the data elements in the cluster is minimal, that is, the center point in the cluster. Compared with the classic k-means algorithm, k-medoids selects the data point as the center (a.k.a. medoids or exemplars). The PAM algorithm is the most common implementation of k-medoids. It initializes and randomly selects *k* of the *n* data points as the medoids. Then it associates each object to the closest medoid. For each medoid *m* and each non-medoid object *o*, the PAM algorithm swaps *m* and *o* and computes the total cost associated with the configuration. The lowest cost of the configuration is selected. The PAM algorithm repeats the above-described steps until the medoid does not change. See Appendix C for a detailed description of the PAM algorithm with diagrams to illustrate each step.

4.4.4.3 Fuzzy Clustering

In fuzzy clustering, data objects are not grouped into one specific cluster. On the contrary, a membership function assigns each object the membership of all or some clusters. In the previously discussed clustering algorithms, the membership value is either one or zero. These clustering techniques are often referred to as hard clustering or crisp methods. Fuzzy clustering is different from other hard clustering techniques by estimating membership probabilities for each observation in each cluster.

In contrast to hard clustering techniques, fuzzy clustering is a type of soft clustering with two significant advantages. First, cluster memberships can combine other information. Second, the cluster membership for any given object may exist as a “second best” subgroup, often unavailable with different clustering algorithms (22). Given the multifaceted and intricate nature of risk profiling in substance use data, which can be illustrated through the data visualization, this thesis mainly focuses on applying fuzzy clustering methodology. This thesis applied two fuzzy clustering algorithms, Fuzzy C-Means (FCM) and FANNY (Fuzzy ANalYsis). See Appendix D for a detailed description of these two fuzzy clustering algorithms.

The clustering results were compared. Only the best clustering results were reported in Chapter 5 Results.

4.4.5 Clustering Validation

Two types of validity indices, i.e., external and internal measures for clustering validation, can be used to objectively and quantitatively assess clustering results. External measures are used where the clustering structure is known (123). External indices use the adjusted Rand index (ARI) or Meila's variation index VI to measure the consistency between the partition clusters and the external reference. Although the Rand index ranges between 0 and 1, the value of ARI can be negative, indicating the index is less than expected. Thus, the range of ARI is between -1 and 1, representing no agreement to perfect agreement (123). External measures can be applied to choose the appropriate clustering method for a given dataset by comparing the identified clusters to an external reference. In this analysis, the ARI was implemented for selecting the proper clustering algorithms for the COMPASS data.

Given that knowing the clustering structure is not the typical case in a real-world scenario, an internal index uses inherent quantities and features in the dataset to measure an unknown clustering structure (124). There are tens of internal indices, among which the silhouette coefficient is the most common measure for evaluating clustering results. The silhouette coefficient assesses the applicability of assigning a subject to one cluster rather than another, considering cluster compactness and separation (125). Silhouette values close to 1 indicate the data element is strongly matched to its cluster and weakly matched to other clusters. Silhouette values close to 0 indicate observations between two clusters. Any inaccurate clustering assignment will get a negative silhouette value (125). In addition to the total silhouette value, the silhouette coefficient for each cluster was also calculated by taking the average of the total silhouette values for the objects within that cluster.

For consistency and robustness, results from each applied clustering method were compared with the indices discussed in this section.

4.5 Latent Markov Model (LMM)

The LMM was employed in this thesis to test hypotheses that subgroups of youths tend to differ in their patterns of polysubstance use behaviours over time. Derived from latent variable models, an LMM consists of two components: the structural and measurement models (27). Structural models include latent (or unobserved) endogenous factors, such as the substance use indicators in this thesis, to model the conditional probabilities of the response variables. While measurement models only

have manifested (or observed) endogenous factors, conditional on the latent status of substance use patterns.

4.5.1 Selection of the Covariates

It is essential to select the appropriate covariates for model fitting. Each covariate is considered to have a strong correlation with substance use. This thesis employed the least absolute shrinkage and selection operator (LASSO) method to select a subset of covariates for fitting LMMs. LASSO regression is a feature selection technique used to filter out irrelevant or redundant features from a large number of variables by shrinking coefficients towards zero. This is achieved by imposing a LASSO regression penalty. See Appendix H for a detailed description of the LASSO regression.

In this thesis, the response variable for substance use is ordinal (see Section 4.3). An adaptive approach to LASSO regression was applied by implementing the coordinate descent fitting algorithm with an ordinal response (126). A penalized regularization model was fitted by extracting all estimated coefficients and non-zero coefficient estimates. Lambda, the tuning parameter, regulates the penalty strength. That is, the smaller the lambda value, the less penalty it applies to all regression parameters. The LASSO regression essentially leads to the least squares estimates. Therefore, shrinkage of coefficient occurs as lambda increases. The optimal value of lambda was determined using the k-fold cross-validation during the selection process. We repeated the same procedure of adaptive LASSO regression for each wave. Only variables with non-zero coefficients after shrinking were selected and fitted in the follow-up LMMs for further analysis.

4.5.2 A General LMM Framework

For a general LMM framework, response variables are denoted as Y_{it}, where $i = 1, \dots, n$ and $t = 1, \dots, T$ representing the number of observed time occasions. For each time point, Y_{it} are collected in the random vector $Y_t, t = 1, \dots, T$. The overall vector of response variables in a vector $n \times T$ can be denoted by $\hat{Y}$. Corresponding to Y_t, a vector of covariates is denoted by X_t. Similarly, the vector of all the covariates, obtained by stacking $X_1, \dots, X_T$, can be denoted as $\hat{X}$ (127). The LMM framework assumes that there exists a latent process, $U = (U_1, \dots, U_T)$, which follows a first-order Markov chain with k number of latent states. Assuming local independence, the random vectors $Y_1, \dots, Y_T$ are conditionally independent given U. Based on this assumption, the LMM can be simplified and

relaxed. Another assumption is that the distribution of each response vector Y_t only depends on the covariates $\hat{X}$ and the latent process U (127).

Based on a set of measure time points in classical Markov models, transition probabilities are estimated to describe whether a subject stays in the same subgroup (representing *stability*) over time or transitions to another subgroup (representing *change*). LMMs are transition models developed for panel data where subjects can transition between classes (27). In LMMs, transition probabilities represent how the transition occurs from time $t-1$ to t between subgroups. Besides observed data, LMMs include a latent process (sequence of latent variables) for each subject, which follows a finite state of the Markov chain. Applied to substance use measures, the LMM estimates the overall probability of being in a particular use pattern (latent state) given the use pattern at the previous time occasion. A detailed description of the LMM framework with covariates and multivariate extension to the basic LMM and decoding can be seen in Appendix I.

4.5.3 Model Selection

The final model was selected based on one of the most common model fit criteria, Bayesian information criteria (BIC). Although Akaike's information criteria (AIC) is also commonly used, due to a less severe penalization, AIC tends to select a larger number of latent states than BIC, especially with large sample sizes (27). Several studies in the literature of latent variable modelling have demonstrated that AIC often yields to a larger number of latent classes than necessary. In contrast, BIC is a more reliable model selection criterion to identify the optimal number of latent states. In addition to BIC and AIC, there are other criteria, such as the likelihood ratio approach. However, this method is not encouraged due to the need for a bootstrap resampling procedure (27).

The goodness-of-fit was measured to evaluate the quality of the fitted models, using the index

$$R^2 = 1 - \exp\left(\frac{2(lk_1 - lk_\theta)}{nJ}\right) \quad (2)$$

where lk_1 is the maximum likelihood of basic version of LMM, corresponding to M_1 with k = 1 and the number of parameters J. R^2 can be explained as average improvement of the new model in predicting each observed response sequence, as compared to the baseline model M_1 (89,128). Similar to other indicators of model goodness-of-fit, R^2 is a relative index with a value between 0 and 1. The

higher the value of R^2, the better the fit of the model. In this thesis, we estimated R^2 as an additional measure to the BIC index for model selection.

4.6 Software Packages and Computing Environment

In this thesis, the data analysis was performed primarily using the R language, open-source software to compute statistics and perform graphics. In particular, the following key packages were employed.

- FactoMineR, missMDA, and naniar packages for missing data analysis and visualization
- MICE package for missing data imputation
- Boruta, a wrapper Algorithm for all relevant feature selection
- glmnetcr package for LASSO (L1 regularization) for ordinal response
- NbClust, cluster, ppclust, factoextra, clvalid, fpc, and Rtsne packages for cluster analysis and visualization
- LMest for generalized LMMs

RStudio Server 1.4 was set up on Ubuntu 18.04 with a 64 GiB RAM virtual machine running on Microsoft Azure.

In summary, this chapter described all the methods applied in this thesis, including missing data analysis, feature selection, clustering analysis, transition modelling, and various model fitting and validation approaches (see Figure 7). The results of this thesis will be presented in the next chapter.

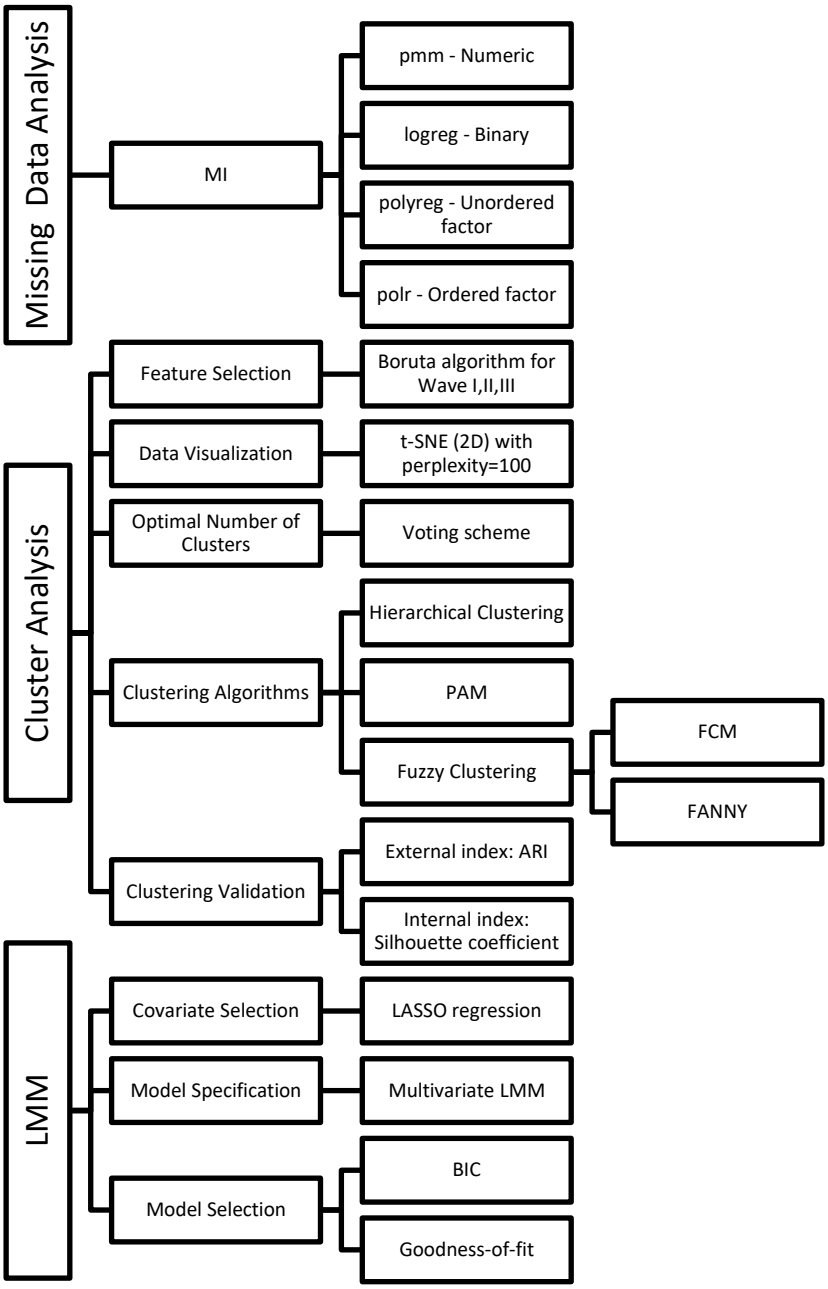

Figure 7. Summary of the methods applied in this thesis

Chapter 5
Results

This chapter presents the results of this thesis in the following seven sections. Section 5.1 reports the results of data preprocessing, followed by descriptive statistics of the linked three waves data presented in Section 5.2. Sections 5.3 and 5.4 report the clustering and LMM modelling results. Sections 5.5 through 5.7 present the risk profiles of youth polysubstance use, the patterns of polysubstance use among Canadian secondary school students, and the dynamic transitions of these use patterns across time.

5.1 Data Preprocessing

5.1.1 Missing Data Analysis

The overall percentage of missing values for the three waves linked data were 14.5%, 2.3%, and 2.1% for Wave I, Wave II, and Wave III, respectively. The much higher missingness for Wave I data was because questions regarding mental health-related (FLOURISH, GAD7, CESD, and DERS) and online gambling were not asked in the Year 5 survey questionnaire. Aside from these, BMI and SupportQuitDrugAlcohol variables accounted for 27.1% and 4.2% of total missingness for Wave I. BMI, CESD, and GAD7 were identified as the top 3 missingness for Wave II and Wave III datasets, with 22.6%, 11.6%, and 5.8% of total missingness for Wave II, and 18.2%, 10.1%, and 5.4% of total missingness for Wave III data, respectively.

Fortunately, the missingness of substance use indicators was much less than those of the other features in all three wave datasets. For example, there were only 237, 122, and 136 missing responses to the substance use variables at Wave I, Wave II, and Wave III, accounting for 2.5%, 1.3%, and 1.5% of total missingness, respectively. The missing values were omitted during cluster analysis due to the low missingness of these variables of interest. Since LMMs can facilitate multivariate responses by treating the missingness as MAR. Thus, missing values for these response variables were not imputed prior to fitting the LMMs. This approach can maximize the use of linked data with missing responses at the time occasions of measurement. See Appendix J for a detailed illustration of the amount of missing data and the missing patterns (i.e., the combinations of missingness across

observations) for each wave. The plots of the missing patterns of substance use indicators can be seen in Appendix J as well.

Figures 8-10 demonstrate the distribution of imputed data for each wave. It is observed that the five imputed datasets (as represented in **red** lines) had a reasonably consistent distribution as the original dataset with no missing values (as described in a **blue** line) for each feature.

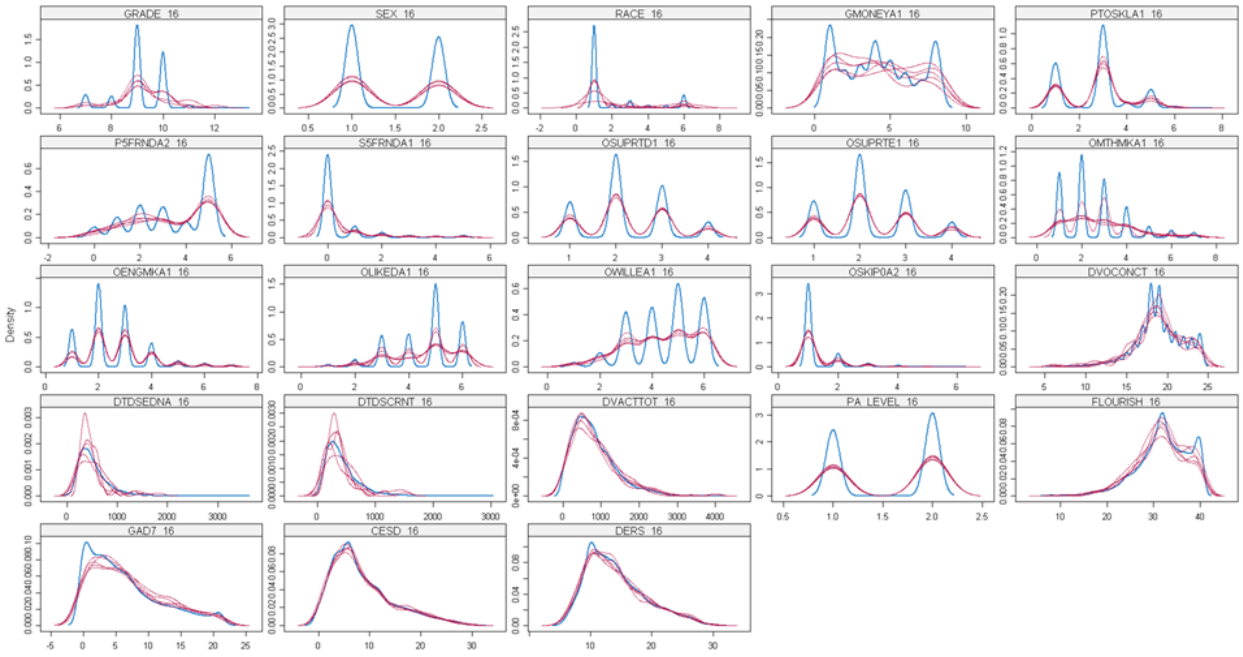

Figure 8. Density plot of imputed data by feature (Wave I, 2016-17)

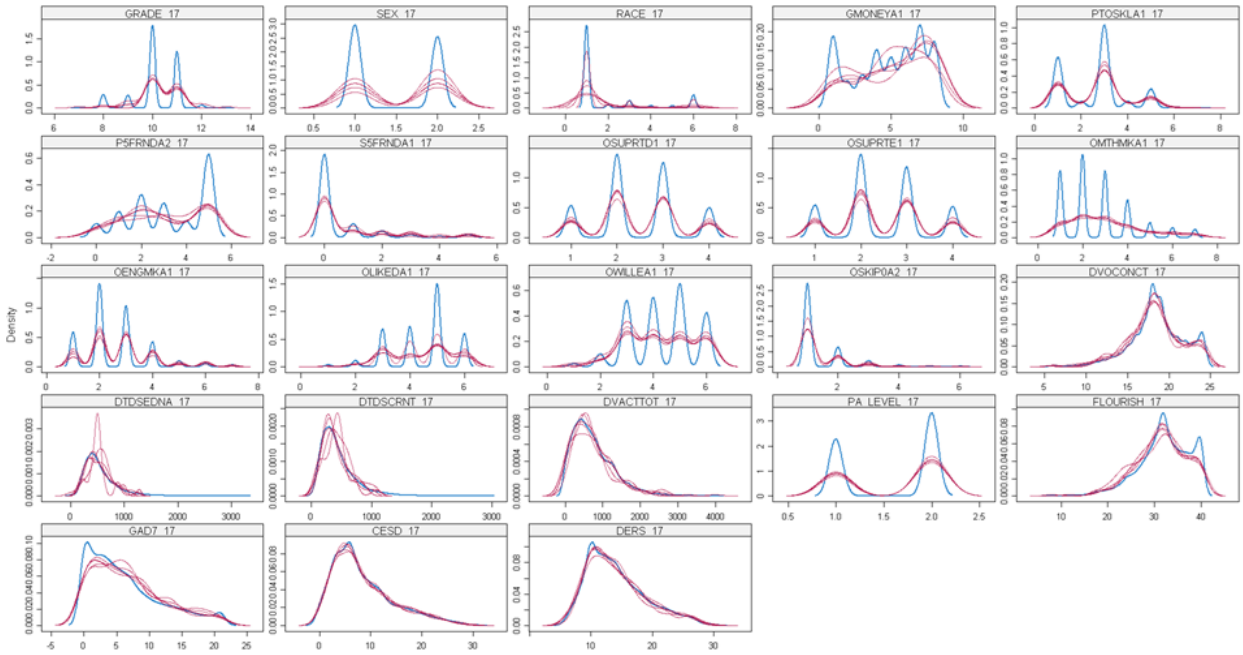

Figure 9. Density plot of imputed data by feature (Wave II, 2017-18)

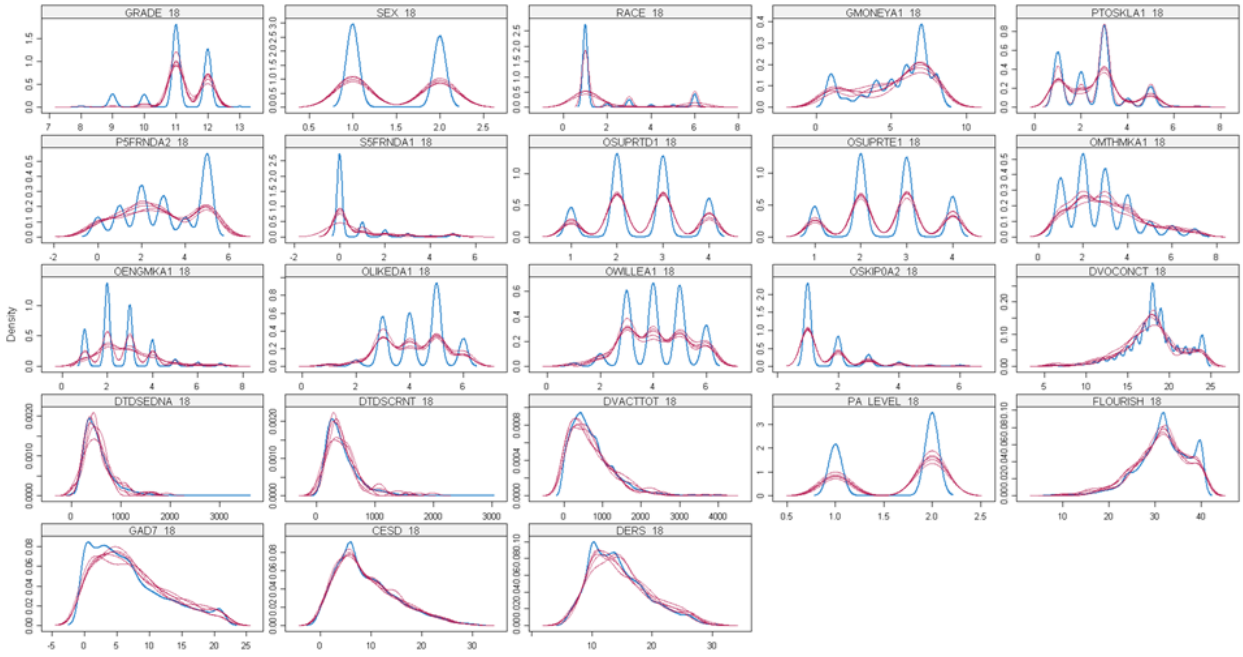

Figure 10. Density plot of imputed data by feature (Wave III, 2018-19)

5.2 Descriptive Statistics

Of the 8824 linked samples collected from the COMPASS study of grades 7 to 10 Canadian secondary school students at Wave I, 54.6% were females while 45.4% were males, and 74.2% were white. Grades 9 and 10 students accounted for 50.9% and 34.2% of the total linked sample size, respectively. 67.5% of the students were from Ontario, and 54.3% live in large urban areas. In terms of cigarette smoking in the last 30 days, 90% responded as having never smoked, while 6.6% admitted to smoking occasionally, and 2.8% identified as current smokers. 82% of the students admitted that they have never used an e-cigarette, while those who acknowledged themselves as occasional and current users of e-cigarette accounted for 10.1% and 6.5%, respectively. 61.2% of the students indicated that they never had drunk alcohol in the past year, while those admitted to occasional use and current alcohol use accounted for 20.4% and 17.2%, respectively. Lastly, 88.7% of the students said they never used marijuana in the past year, while admittance to occasional use and current use of marijuana accounted for 5.9% and 4.0%, respectively. These frequencies make sense compared to surveillance data from representative samples. Thus, we are confident that our linked samples are similar to the youth population in general. Tables 6-7 demonstrate the characteristics of this linked sample (N = 8824) and the prevalence of each substance used by type and by wave, respectively.

Table 6. Characteristics of the linked samples

		TOTAL	
TOTAL		**N = 8824**	**100 (%)**
Sex	Female	4814	54.6
	Male	4010	45.4
Grade	7	691	7.8
	8	628	7.1
	9	4487	50.9
	10	3018	34.2

		TOTAL	
TOTAL		**N = 8824**	**100 (%)**
Ethnicity	White	6545	74.2
	Black	255	2.9
	Asian	610	6.9
	Aboriginal	192	2.2
	Latin American	186	2.1
	Other	1036	11.7
Province	AB	428	4.9
	BC	420	4.8
	ON	5960	67.5
	QC	2016	22.8
Urbanity	Rural	26	0.3
	Small urban	2726	30.9
	Medium urban	1280	14.5
	Large urban	4792	54.3
Household Income	$25K - $50K	1381	15.6
	$50K - $75K	4109	46.6
	$75K - $100K	2935	33.3
	> $100K	399	4.5

Table 7. Prevalence of each substance used by type and by wave

Substance Use Indicator	Label	Wave I (2016-17) Frequency (%)	Wave II (2017-18) Frequency (%)	Wave III (2018-19) Frequency (%)
Cigarette	Never use	7944 (90.0)	7310 (82.8)	6728 (76.2)
	Occasional use	580 (6.6)	974 (11.0)	1437 (16.3)
	Current use	250 (2.8)	508 (5.8)	615 (7.0)
	Missing	50 (0.6)	32 (0.4)	44 (0.5)
E-Cigarette	Never use	7238 (82.0)	5982 (67.8)	4403 (49.9)
	Occasional use	889 (10.1)	1195 (13.5)	1525 (17.3)
	Current use	577 (6.5)	1589 (18.0)	2834 (32.1)
	Missing	120 (1.4)	58 (0.7)	62 (0.7)
Alcohol	Never use	5400 (61.2)	3710 (42.0)	2573 (29.2)
	Occasional use	1799 (20.4)	2490 (28.2)	2684 (30.4)
	Current use	1515 (17.2)	2565 (29.1)	3501 (39.7)
	Missing	110 (1.2)	59 (0.7)	66 (0.7)
Marijuana	Never use	7831 (88.7)	6784 (76.9)	5569 (63.1)
	Occasional use	521 (5.9)	1162 (13.2)	1784 (20.2)
	Current use	357 (4.0)	820 (9.3)	1401 (15.9)
	Missing	115 (1.3)	58 (0.7)	70 (0.8)

Figures 11-14 are 3D graphs of substance use prevalence by type and wave for cigarettes, e-cigarette, alcohol, and marijuana use. The overall trend shows that, in general, the prevalence of "never use" had been decreasing over time, while the prevalence of "occasional use" and "current use" had been increasing for all substances across the three waves. In particular, as demonstrated in Figures 12 and 14, respectively, the prevalence of current use for e-cigarette and marijuana consumption had increased significantly. E-cigarette use increased by 4.94 times from 6.5% in 2016

to 32.1% in 2018, while marijuana consumption had increased by 3.98 times from 4.0% in 2016 to 15.9% in 2018. Regarding alcohol drinking, the increase in the prevalence of occasional or current use was not as significant as that of e-cigarette and marijuana consumption. However, the much lower prevalence of never use at Wave I and the considerable decrease of never use over time (from 61.2% in 2016 to 29.2% in 2018) raise as much concern as the other substances.

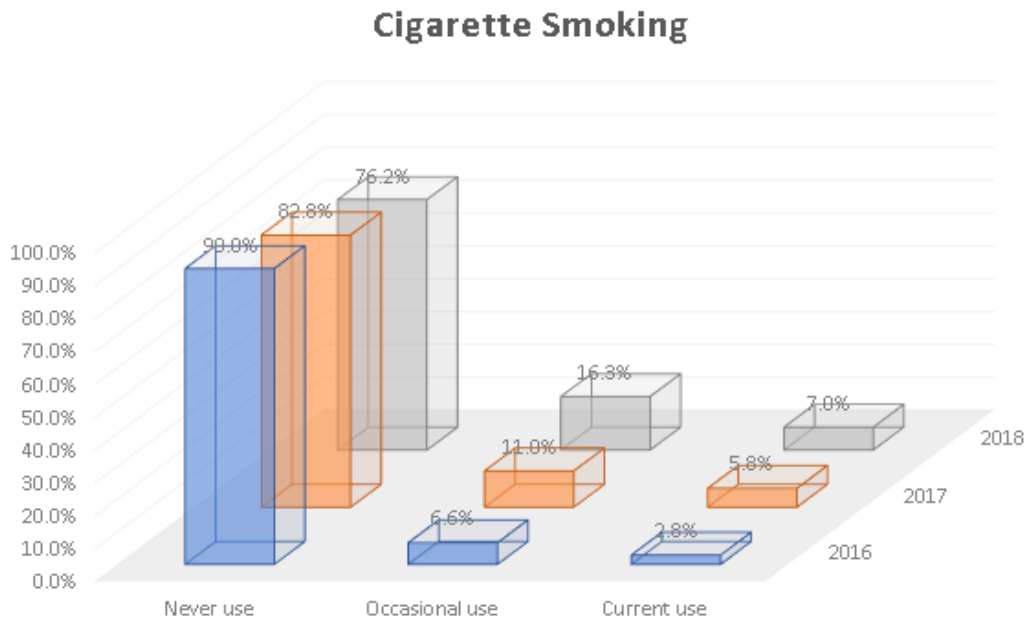

Figure 11. Prevalence of cigarette smoking by type and wave

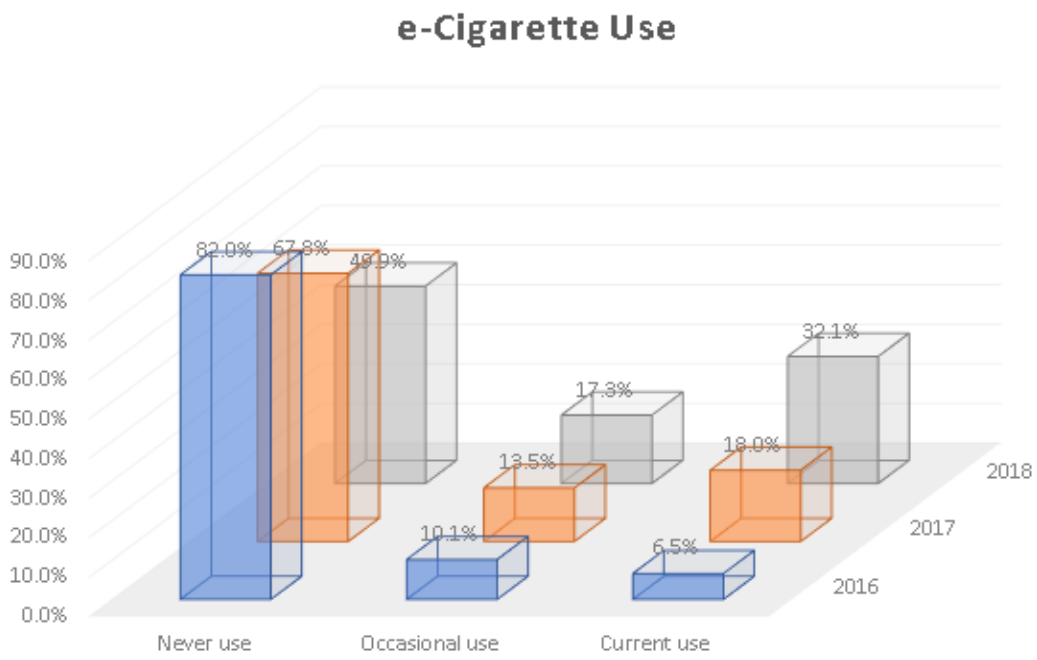

Figure 12. Prevalence of e-cigarette use by type and wave

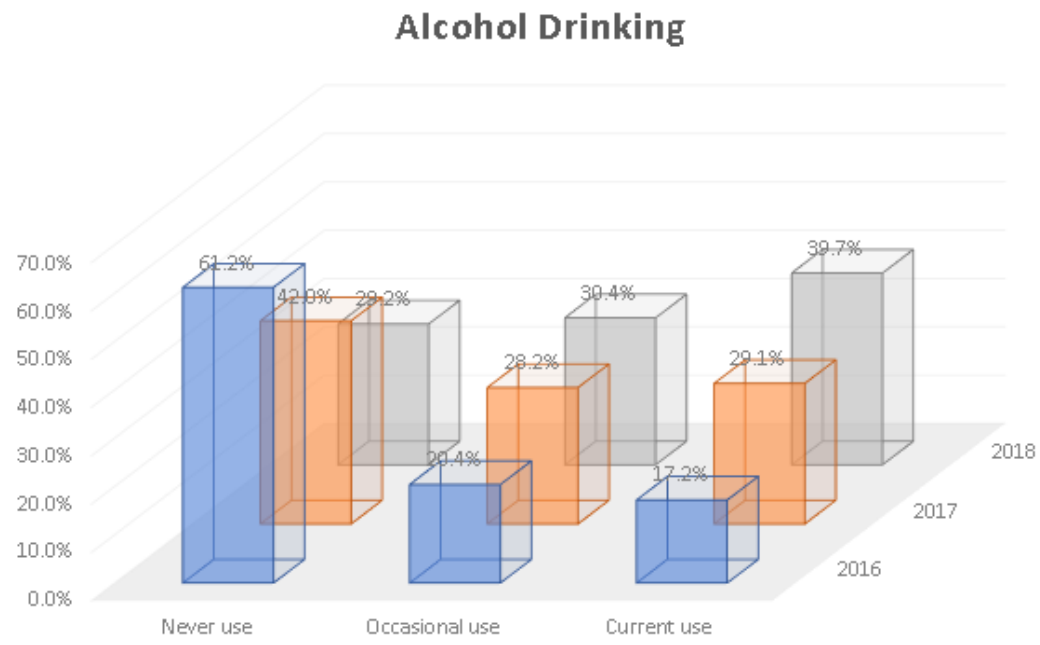

Figure 13. Prevalence of alcohol drinking by type and wave

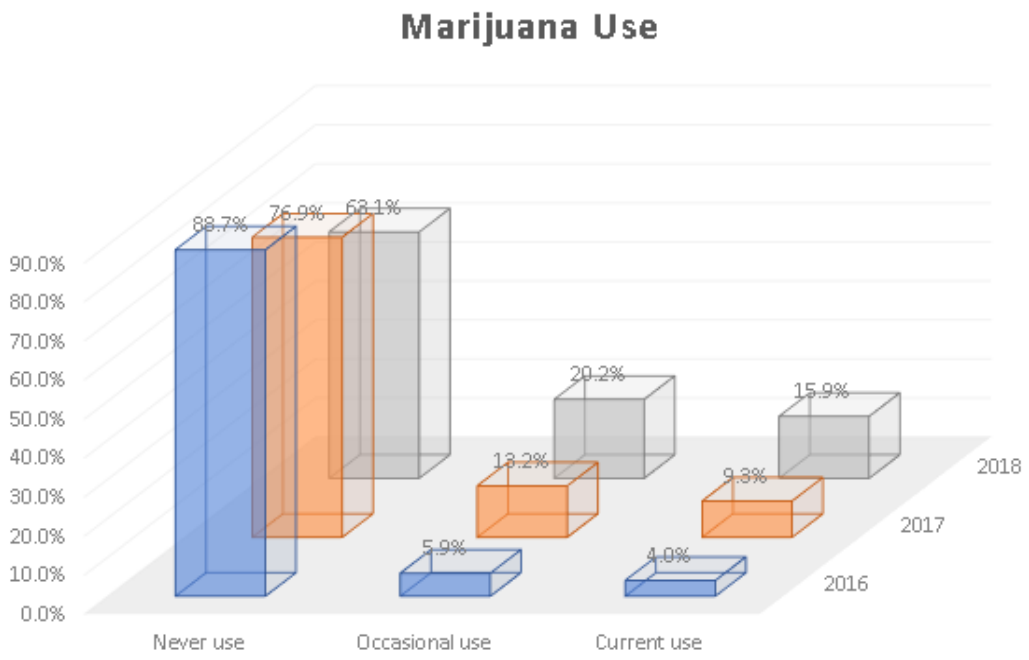

Figure 14. Prevalence of marijuana consumption by type and wave

5.3 Cluster Analysis

5.3.1 The Optimal Number of Clusters

The indices of clustering validity inconsistently voted for different numbers of clusters across the three waves. For Wave II and Wave III, 9 and 10 indices proposed that the best number of clusters is 4, respectively. While for Wave I, seven indices each proposed, the best number of clusters is either 2 or 6, and the second-best number of clusters is 4 with four indices voted. The optimal number of 4 clusters was selected across the three waves for further clustering analysis to make the results consistent and easier to interpret. Figures 15-17 illustrate the voting results for the optimal number of clusters for the three waves datasets.

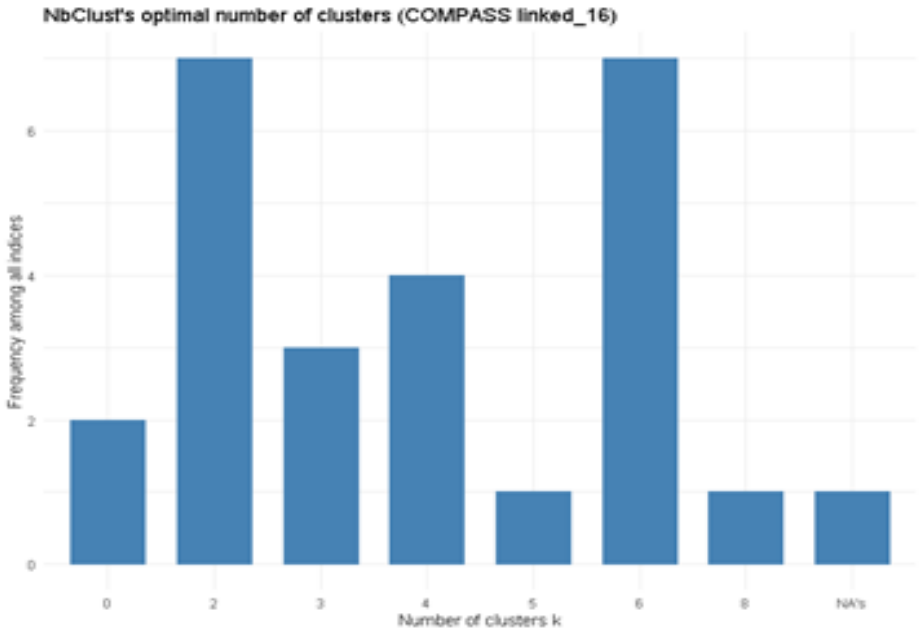

Figure 15. Voting results for the optimal number of clusters (Wave I, 2016-17)

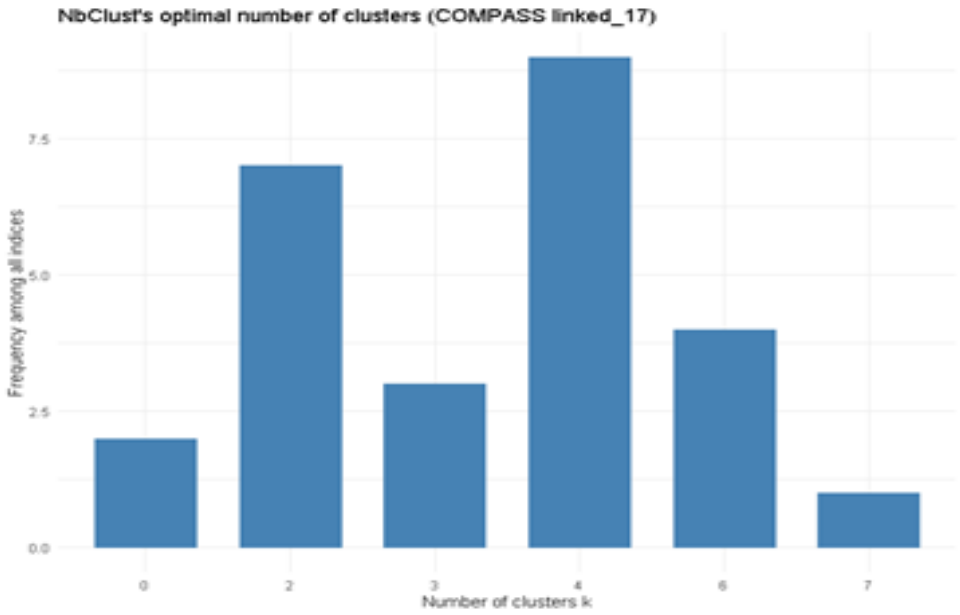

Figure 16. Voting results for the optimal number of clusters (Wave II, 2017-18)

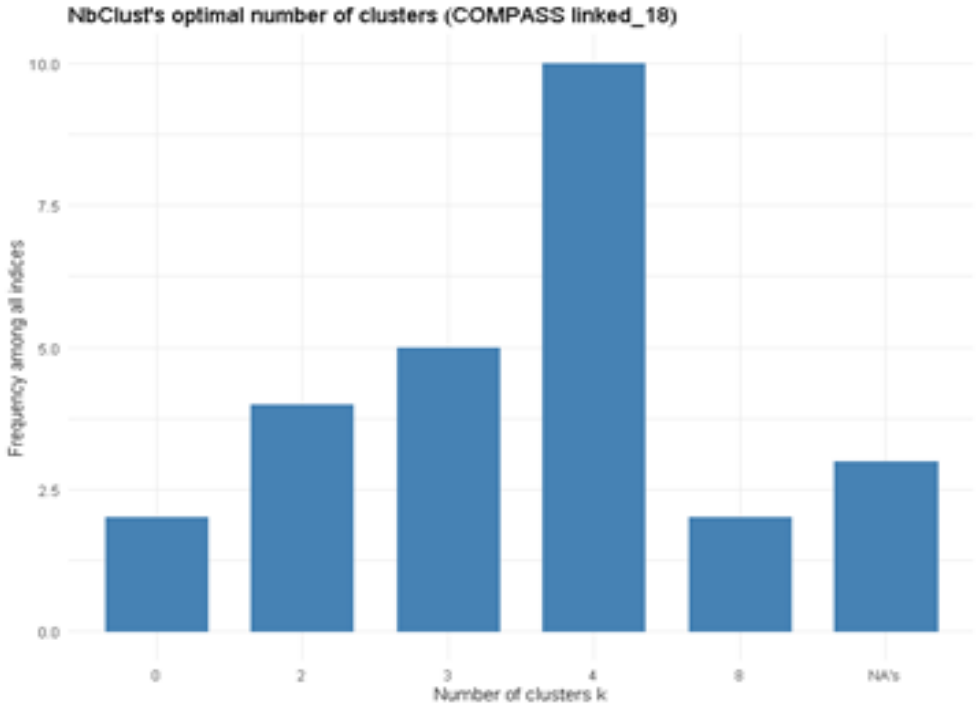

Figure 17. Voting results for the optimal number of clusters (Wave III, 2018-19)

5.3.2 Clustering Results

5.3.2.1 Fuzzy (FANNY) Clustering

The left panels of Figures 18-20 demonstrate the 2D representation of the student data with coloured cluster membership based on the fuzzy (FANNY) clustering. The cluster subgroups ranged from 986 to 2799 students at Wave I, 684 to 3082 at Wave II, and 686 to 3385 at Wave III. It is observed that except for the minority group with the lowest silhouette value, the average silhouette width for all clusters was positive. The average silhouette widths were 0.52, 0.53, and 0.53 at Wave I, Wave II, and Wave III, respectively. The silhouette values for each cluster ranged from 0.31 to 0.57 at Wave I, 0.35 to 0.58 at Wave II, and 0.30 to 0.56 at Wave III. Kaufman *et al.* (2009) proposed that the silhouette values between 0.71 and 1 indicate a strong structure for that particular cluster (129). Reasonable and weak structures are shown by the silhouette values between 0.51 and 0.70 and below 0.50, respectively. The two clusters with the second-largest and largest sample size had reasonable structures, whereas the other two with the smallest and the second smallest sample size had weak structures at Wave I and II. As for Wave III, three clusters had reasonable structures, and only one cluster with the smallest sample size had a weak structure. The right panels of Figures 18-20 demonstrate the average silhouette widths for all clusters. These clustering results support the applicability of phenotyping risk profiles of youth polysubstance use.

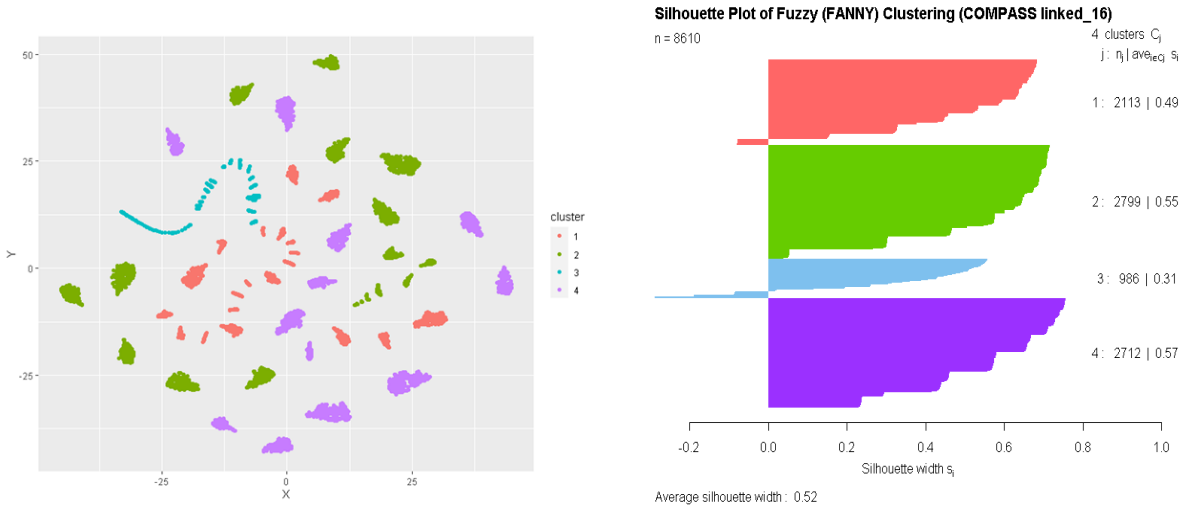

Figure 18. Fuzzy (FANNY) Clustering, left-panel: 2D representation; right-panel: silhouette plot (Wave I, 2016-17)

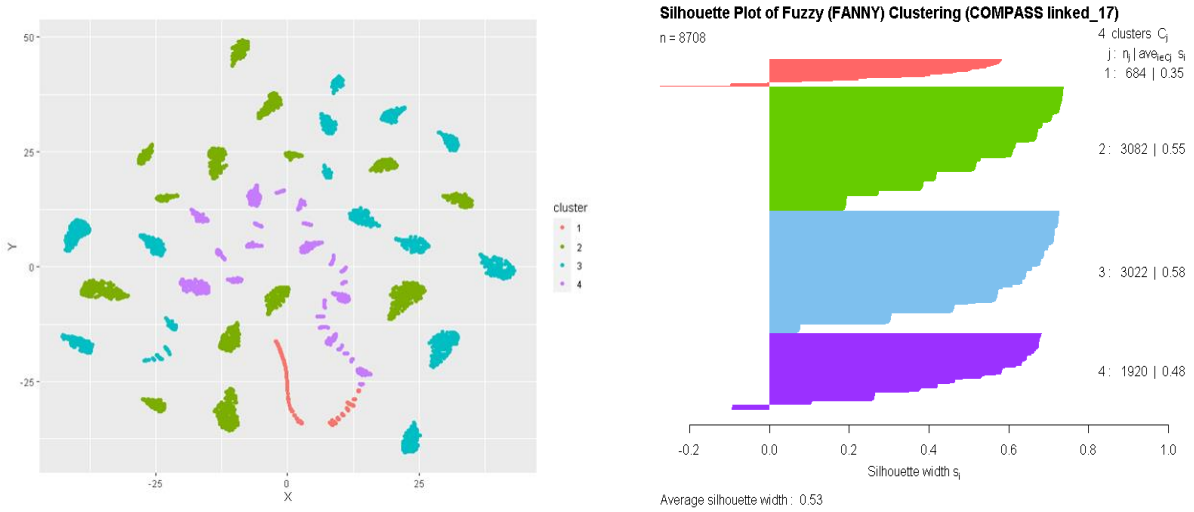

Figure 19. Fuzzy (FANNY) Clustering, left-panel: 2D representation; right-panel: silhouette plot (Wave II, 2017-18)

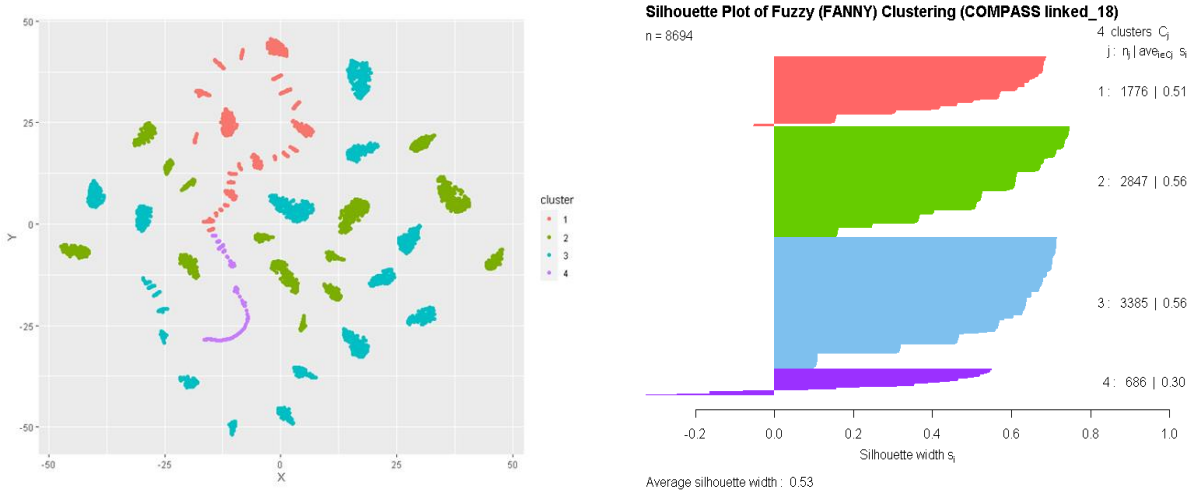

Figure 20. Fuzzy (FANNY) Clustering, left-panel: 2D representation; right-panel: silhouette plot (Wave III, 2018-19)

5.3.2.2 FCM Clustering

The cluster subgroups ranged from 1042 to 3312 students at Wave I, 994 to 3390 at Wave II, and 863 to 3607 at Wave III. Similar to the FANNY algorithm of fuzzy clustering, the average silhouette widths for all clusters were positive. The average silhouette widths were 0.51 across the three waves.

The silhouette values for each cluster ranged from 0.26 to 0.58 at Wave I, 0.21 to 0.56 at Wave II, and 0.23 to 0.60 at Wave III. It is observed across the three waves that three clusters had reasonable structures while only one cluster with the smallest sample size had a weak structure. The 2D representation of the student data with coloured cluster membership and the average silhouette widths for all clusters based on the FCM clustering can be seen in Appendix K.

5.3.2.3 PAM Clustering

The cluster subgroups ranged from 1138 to 2799 students at Wave I, 1018 to 2879 at Wave II, and 841 to 2925 at Wave III. The average silhouette widths for all clusters were positive. Same as the FCM clustering, the average silhouette widths were 0.51 at all three waves. The silhouette values for each cluster ranged from 0.27 to 0.56 at Wave I, 0.26 to 0.57 at Wave II, and 0.29 to 0.57 at Wave III. Three clusters had reasonable structures for Wave I and Wave II, and only one cluster with the smallest sample size had a weak structure. For Wave I, the two clusters with the second-largest and largest sample size had reasonable structures, and the other two clusters with the smallest and the second smallest sample size had weak structures. The 2D representation of the student data with coloured cluster membership and the average silhouette widths for all clusters based on the PAM clustering can be seen in Appendix L.

5.3.2.4 Hierarchical Clustering

The cluster subgroups ranged from 383 to 4975 students at Wave I, 131 to 3627 at Wave II, and 175 to 4037 at Wave III. The average silhouette widths for all clusters were positive, being 0.55, 0.53, 0.53 at Wave I, Wave II, and Wave III, respectively. The silhouette values for each cluster ranged from 0.35 to 0.64 at Wave I, 0.43 to 0.66 at Wave II, and 0.38 to 0.68 at Wave III. Three clusters had reasonable structures for Wave I, and only one cluster with the smallest sample size had a weak structure. For Wave II, clusters #3 and #4, the two clusters with the smallest and the second-largest sample size had reasonable structures, while the other two clusters with the largest and the second smallest sample size (cluster #1, #2) had weak structures. For Wave III, the two clusters with the second-largest and the second-smallest sample size had reasonable structures, while the other two clusters with the smallest and the largest sample size had weak structures. The dendrogram based on hierarchical clustering for each wave, the 2D representation of the student data with coloured cluster membership, and the average silhouette widths for all clusters can be seen in Appendix M.

5.3.3 Clustering Validity

The internal measures of clustering performance measured by average silhouette width ranged from 0.51 to 0.55 across the three waves with different clustering algorithms. Both the partitioning and hierarchical clustering algorithms achieved a relatively high degree of agreement on cluster membership. Comparing the fuzzy clustering (FANNY) and PAM clustering, the ARIs were 0.9698, 0.7676, and 0.6452. The variation of information (VI) indices was 0.1154, 0.6023 0.7621 for Wave I, Wave II, and Wave III, respectively. Nevertheless, the results of the two fuzzy clustering algorithms achieved a high degree of the membership agreement. Considering the overlapping nature of risk profiles related to polysubstance use, we decided to use fuzzy clustering (FANNY) to analyze further and report risk profiles. Table 8 shows the comparison of clustering validity for each pair of the clustering algorithms.

Table 8. Comparison of clustering validity for each pair of clustering algorithms

Clustering Algorithm	**Index**	**Wave I (2016-17)**	**Wave II (2017-18)**	**Wave III (2018-19)**
FCM vs FANNY	ARI	0.7447	0.8221	0.8603
	VI	0.5696	0.4315	0.4096
FANNY vs PAM	ARI	0.9698	0.7676	0.6452
	VI	0.1154	0.6023	0.7621
FCM vs PAM	ARI	0.7394	0.7046	0.6366
	VI	0.5942	0.6179	0.7024
PAM vs Hierarchical	ARI	0.4905	0.5093	0.4898
	VI	0.8621	0.9181	0.9315
FANNY vs Hierarchical	ARI	0.4736	0.5449	0.6651
	VI	0.9241	0.9106	0.7029
FCM vs Hierarchical	ARI	0.4903	0.6839	0.7483
	VI	0.9305	0.6761	0.4786

5.4 LMM

5.4.1 Selection of Covariates

As stated in Section 4.5.1, the lambda value in the LASSO regression controls the penalty of the regression parameters. The smaller the lambda value, the less penalty it applies to all coefficients of the predictors. It results in having more predictors in the model. In this thesis, the optimal value of lambda was determined using the 10-fold cross-validation during the selection process. The best lambda for the LASSO regression was set as 0.1, 0.0794, and 0.0794 for Wave I, Wave II, and Wave III, respectively. Table 9 demonstrates the selected covariates by waves, sorted by alphabet. See Appendix N for the detailed report and plots of final coefficients from the LASSO regression by waves.

Table 9. LASSO selected covariates by wave

	Wave I (2016-17)	**Wave II (2017-18)**	**Wave III (2018-19)**
Selected Covariates[1]	BMI_CATEGORY_16 EatingBreakfast_16 EnglishMarks_16 GetMoney_16 Grade_16 SchoolConnectedness_16 SedentaryTime_16 SkipClass_16 SmokingFriends_16 SupportQuitDrugAlcohol_16 Urbanity_16 WillingEdu_16	BMI_CATEGORY_17 CESD_17 DERS_17 EatingBreakfast_17 EnglishMarks_17 GambleOnline_17 GetMoney_17 Grade_17 PAfriends_17 Race_17 SchoolConnectedness_17 SedentaryTime_17 SkipClass_17 SmokingFriends_17 SupportQuitDrugAlcohol_17 Urbanity_17 WillingEdu_17	BMI_CATEGORY_18 CESD_18 DERS_18 DrugStores_18 EatingBreakfast_18 EnglishMarks_18 GAD7_18 GambleOnline_18 GetMoney_18 Grade_18 PAfriends_18 PA_LEVEL_18 Race_18 SchoolConnectedness_18 SedentaryTime_18 SkipClass_18 SmokingFriends_18 SupportQuitDrugAlcohol_18 Urbanity_18 WillingEdu_18

The number of coefficients being shrunk to zero varies across the three waves. 12, 17, and 20 features were selected from Wave I, Wave II, and Wave III, respectively. We chose the 20 features

[1] The last three characters of each feature name indicate the school year of the survey, i.e., "_16," "_17," and "_18" represents the school year of 2016-17, 2017-18, and 2018-19, respectively.

from the LASSO regression on Wave III to model the initial probabilities of the latent process. Note that these 20 features are nested within confirmed features derived from the Boruta algorithm in clustering analysis. The same 20 covariates and time between occasions (T = 3) were used to model the transition probabilities, assuming time is heterogeneous, i.e., the dynamics are different across the three waves. Table 10 summarizes the final selected covariates by level and time-varying status, sorted by alphabet.

Table 10. Final selected covariates for LMM

	Student-Level	**School-Level**
Time-Invariant	Race/Ethnicity	DrugStores Urbanity
Time-Varying	BMI_CATEGORY CESD DERS EatingBreakfast EnglishMarks GAD7 GambleOnline GetMoney Grade PAfriends PA_LEVEL SchoolConnectedness SedentaryTime SkipClass SmokingFriends WillingEdu	SupportQuitDrugAlcohol

A description of the features follows.

BMI_CATEGORY – This is a derived variable representing BMI categories, including 0 = "Not Stated," 1 = "Underweight," 2 = "Healthy Weight," 3 = "Overweight," and 4 = "Obese."

CESD – This is a derived variable, scoring from 0 to 30. In the COMPASS study, depressive symptoms were assessed using CESD-R-10, the Center for Epidemiologic Studies Depression 10-Item Scale-Revised. For example, one of the ten scale items was, "On how many of the last 7 days did you feel the following ways? I was bothered by things that usually don't bother me." The other nine items were "I had trouble keeping my mind on what I was doing," "I felt depressed," "I felt that

everything I did was an effort," "I felt hopeful about the future," "I felt fearful," "My sleep was restless." "I was happy," "I felt lonely," and "I could not get "going." The response options were "None or less than 1 day," "1-2 days," "3-4 days," and "5-7 days." The response to each of the 10-items was reverse-scored from 0 to 3 and then summed. The higher the score is, the more significant depressive symptoms are.

DERS – This is a derived variable, scoring from 6 to 30. In the COMPASS study, difficulties in regulating emotion were assessed using the Difficulties in Emotion Regulation Scale (DERS). For example, one of the ten scale items was, "Please indicate how often the following statements apply to you: I have difficulty making sense out of my feelings." The response options were "Almost never," "Sometimes," "About half the time," "Most of the time," and "Almost always." The other five items were "I pay attention to how I feel," "When I'm upset, I have difficulty concentrating," "When I'm upset, I believe there is nothing I can do to make myself feel better," "When I'm upset, I lose control over my behaviour," "When I'm upset, I feel ashamed for feeling that way," and "Feeling afraid as if something awful might happen." The response to each of the 6- items was reverse-scored from 1 to 5 and then summed. The higher the score is, the more complicated an individual is in regulating emotion.

DrugStores – BE data, the number of drug stores & proprietary stores within 1000 meters of schools.

EatingBreakfast – Binary indicator variable, 0 = "No" and 1 = "Yes."

EnglishMarks – Students were asked, "In your current or most recent French/English course, what is your approximate overall mark? (Think about last year if you have not taken English this year)." The response options were 1 = "90% - 100%," 2 = "80% - 89%," 3 = "70% - 79%," 4 = "60% - 69%," 5 = "55% - 59%," 6 = "50% - 54%," and 7 = "Less than 50%."

GAD7 – This is a derived variable, scoring from 0 to 21. In the COMPASS study, generalized anxiety symptoms were assessed using GAD7, the Generalized Anxiety Disorder 7-item Scale. For example, one of the seven scale items was, "Over the last 2 weeks, how often have you been bothered by the following problems? Feeling nervous, anxious, or on edge." The response options were "Not at all," "Several days," "Over half the days," and "Nearly every day." The other six items were "Not being able to stop or control worrying," "Worrying too much about different things," "Trouble

relaxing," "Being so restless that it's hard to sit still," "Becoming easily annoyed or irritable," and "Feeling afraid as if something awful might happen." The response to each of the 7- items was scored from 0 to 3 and then summed. The higher the score is, the more severe level of anxiety is per the GAD-7 scaling.

GambleOnline – Students were asked, "In the last 30 gays, did you gamble online for money?" The response options are 1 = "Yes" and 2 = "No."

GetMoney – Students were asked, "About how much money do you usually get each week to spend on yourself or to save? (Remember to include all money from allowances and jobs like babysitting, delivering papers, etc.)." The initial responses were categorized into 0 = "I do not know how much money I get each week," 1 = "Zero," 2 = "$1-$20," 3 = "$21-$100," and 4 = "$100+."

Grade – Students were asked, "What grade are you in?" The responses include grades 9-12 and students in Quebec in secondary 1 and 2 (equivalent to Ontario grades 7 and 8). This variable is a proxy of students' age.

PAfriends – Students were asked, "Your closest friends are the friends you like to spend the most time with. How many of your closest friends are physically active?" The response options are 0 = "None," 1 = "1 friend," 2 = "2 friends," 3 = "3 friends," 4 = "4 friends," and 5 = "5 friends or more."

PA_LEVEL – This is a derived variable, indicating whether respondents meet the guidelines for at least 60 minutes of PA per day. Binary variable, 0 = "No" and 1 = "Yes."

Race/Ethnicity – Students were asked, "How would you describe yourself?" The response options are 1 = "White," 2 = "Black," 3 = "Asian," 4 = "Aboriginal (First Nations, Métis, Inuit)," 5 = "Latin American/Hispanic," and 6 = "Other."

SchoolConnectedness – This is a derived variable, scoring from 6 to 24. Higher scores indicate higher connectedness.

SedentaryTime - This is a derived variable representing "Total daily sedentary activity, with homework excluded," ranging from 0 to 2925 in minutes.

SkipClass – Students were asked, "In the last 4 weeks, how many classes did you skip when you were not supposed to?" The response options are 1 = "0 classes," 2 = "1 or 2 classes," 3 = "3 to 5 classes," 4 = "6 to 10 classes," 5 = "11 to 20 classes," and 6 = "More than 20 classes."

SmokingFriends – Students were asked, “Your closest friends are the friends you like to spend the most time with. How many of your closest friends smoke cigarettes?” The response options are 0 = “None,” 1 = “1 friend,” 2 = “2 friends,” 3 = “3 friends,” 4 = “4 friends,” and 5 = “5 or more friends.”

SupportQuitDrugAlcohol – Students were asked, “How supportive is your school of the following? Giving students the support they need to resist or quit tobacco.” The response options are 1 = “Very supportive,” 2 = “Supportive,” 3 = “Unsupportive,” and 4 = “Very unsupportive.”

Urbanity – In which the school resides, including “rural,” “small urban,” “medium urban,” and “large urban.” The urban/rural classification is defined according to the number of populations and population density per square kilometre (126). The detailed definition of the four categories used in the COMPASS study is listed in Appendix O.

WillingEdu – Students were asked, “What is the highest level of education you think you will get?” The response options are 0 = “I don’t know,” 1 = “Some high school or less,” 2 = “High school diploma or graduation equivalency,” 3 = “College/trade/vocational certificate,” 4 = “University Bachelor's degree,” and 5 = “University Master’s/PhD/law school/medical school/teachers’ college degree.”

5.4.2 Selection of the Number of Latent States

Determining the number of latent states was an essential step of the analysis. An increasing number of latent statuses between 1 and 6 was fitted to a multivariate LMM, assuming that: i) the conditional response probabilities are time homogenous and are independent of the included covariates, ii) the probability of using a substance is constrained to 0 for the first latent state; iii) the initial probabilities are distinct for any categories of the included covariates, and iv) the transition probabilities are time heterogeneous and distinct for any categories of the included covariates.

The information criteria provided slightly different results of which model best balances model fit and parsimony. The BIC value indicated that the model with four latent statuses is preferred, whereas the AIC value pointed to a preferable six latent states. Since BIC is a more reliable criterion (27) and considers parsimony, conceptual appeal, and more straightforward interpretation, the 4-latent-status model was selected for further analysis. Figure 21 shows the BIC and AIC criteria for the multivariate LMM.

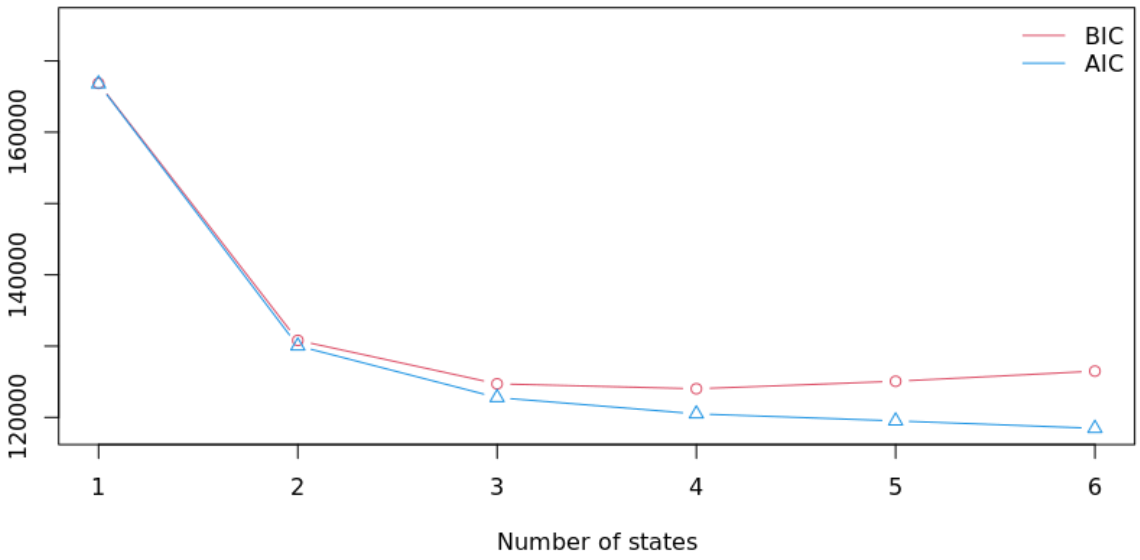

Figure 21. BIC and AIC criteria for selecting the number of latent states

5.4.3 Model Selection and Evaluation

Table 11 displays the number of parameters (n), the maximum log-likelihood (lk), the BIC values of the initial LMM (denoted as M_1) for several latent states (k) between 1 and 6, as well as the value of R^2 for assessing the goodness-of-fit. The lowest BIC value corresponding to M_1 was obtained when $k = 4$, where the model showed a fair value of R^2.

We found that a few covariates, including EnglishMarks, WillingEdu, PA_LEVEL, DrugStores, CESD, GAD7, and DERS were not consistently significant from the preliminary model fitting results in their effects on both the initial and transition probabilities between latent states. To fine-tune the initial model (denoted as M_1) and obtain the best-fitted model, we considered several models nested in M_1 with four latent states. For example, M_2 was based on removing PA_LEVEL effects on both the initial and transition probability formulas. From the model fitting results in Table 11, under the same number of latent states ($k = 4$), the BIC value of M_2 was smaller than that of M1 (122825.8 < 122935.5), and the number of parameters of M_2 was smaller than that of M_1 (332 < 347). Thus, M_2 was preferable over M_1 with the same number of latent states. The covariate PA_LEVEL was therefore removed from the model.

Similarly, the other covariates EnglishMarks, WillingEdu, and SedentaryTime, were removed from model fitting one by one and by pairs. That is how the models $M_2 \sim M_{18}$ were fitted, assuming that certain covariate(s) do not affect the initial and the transition probabilities of the latent process. Comparing these models with M_1, it is concluded that EnglishMarks, WillingEdu, PA_ LEVEL, DrugStores, CESD, GAD7, and DERS did not significantly affect these probabilities. The model was formulated by removing these covariates, denoted by M_{16}.

Although sex was not identified as an important predictor by the LASSO regression, the literature review on the risk factors of youth polysubstance use indicates its inconsistent effects from various studies; it was determined as a factor worth investigating as a predictor. Therefore, we decided to include the covariate sex into LMMs as one of the time-invariant covariates (M_{17} and M_{18}). In the COMPASS dataset, sex was dummy coded as 1 = "Female" and 2 = "Male" across all waves. Since further simplification significantly increased the BIC value, M_{18} was selected as the final model. Among all the fitted models, M_{18} had the lowest BIC, which equals 122349.6. Under this model, the maximum log-likelihood equals -60007.4 with 257 parameters, and a fair value of the index R^2 was obtained. Table 11 summarizes the preliminary fitting of the LMMs with different values of k and various constraints discussed in this section.

Table 11. Preliminary fitting of various LMMs

Model	**k**	**n**	**lk**	**BIC**	**R^2**
M_1	1	8	-83391.2	166855.1	
	2	79	-64967.2	130652	0.4067
	3	192	-61218.2	124180.8	0.4664
	4	**347**	**-59891.5**	**122935.5**	**0.4861**
	5	544	-59168.5	123279.3	0.4966
	6	783	-58391.4	123896.5	0.5075
M_2: M_1 – PA_LEVEL	4	332	-59904.8	122825.8	0.4859
M_3: M_1 – GAD7	4	332	-59908	122832.4	0.4859

Model	k	n	lk	BIC	R^2
M_4: M_1 – CESD	4	332	-59903.1	122822.5	0.4860
M_5: M_1 – DERS	4	332	-59914.7	122845.6	0.4858
M_6: M_1 – EnglishMarks	4	332	-59928.8	122873.8	0.4856
M_7: M_1 – WillingEdu	4	332	-59932.8	122881.9	0.4855
M_8: M_7 – EnglishMarks	4	317	-59977.1	122834.3	0.4849
M_9: M_7 – PA_LEVEL	4	317	-59943.1	122766.2	0.4854
M_{10}: M_9 – CESD	4	302	-59952.8	122649.4	0.4852
M_{11}: M_8 – PA_LEVEL	4	317	-59946.8	122773.6	0.4853
M_{12}: M_{11} – CESD	4	302	-59960.3	122664.3	0.4851
M_{13}: M_1 – CESD – GAD7 – DERS	4	302	-59963.1	122669.9	0.4851
M_{14}: M_{13} – EnglishMarks – PA_LEVEL	4	272	-60021.6	122514.3	0.4842
M_{15}: M_{13} – WillingEdu – PA_LEVEL	4	272	-60005	122481.2	0.4845
M_{16}: M_{14} – WillingEdu	4	257	-60053.3	122441.5	0.4838
M_{17}: M_{16} + Sex	4	272	-59994.1	122459.3	0.4846
M_{18}: M_{17} – DrugStores	**4**	**257**	**-60007.4**	**122349.6**	**0.4844**

5.5 Phenotyping Risk Profiles of Youth Polysubstance Use

5.5.1 Factors Associated with Polysubstance Use Among Canadian Adolescents

The first primary research question (RQ1) investigated was, "What are the prominent risk profiles of polysubstance use among Canadian secondary school students?" Before answering this question, we need to identify factors associated with youth polysubstance use. Table 12 lists the top 8 factors for each of the three waves, with the importance scores in brackets. The number of smoking friends, the number of skipped classes, and weekly money to spend/save oneself were the top 3 factors

consistently appearing across the three waves. Other correlates ranked differently by waves. The total importance scores for each factor can be seen in the last column of Table 12.

Table 12. Top 8 factors associated with polysubstance use by wave

Ranking	Wave I (2016-17)	Wave II (2017-18)	Wave III (2018-19)	Voting (Total Score)
1	SmokingFriends_16 (47.92)	SmokingFriends_17 (60.05)	SmokingFriends_18 (56.90)	SmokingFriends (164.87)
2	SkipClass_16 (38.01)	SkipClass_17 (43.76)	SkipClass_18 (54.12)	SkipClass (135.89)
3	GetMoney_16 (17.48)	GetMoney_17 (31.07)	GetMoney_18 (37.66)	GetMoney (86.21)
4	SchoolConnectedness_16 (16.65)	SedentaryTime_17 (20.12)	SedentaryTime_18 (20.26)	SedentaryTime (53.14)
5	Grade_16 (15.58)	CESD_17 (15.87)	EatingBreakfast_18 (19.03)	CESD (42.74)
6	CESD_16 (14.19)	SchoolConnectedness_17 (14.29)	PAfriends_18 (17.41)	SchoolConnectedness (42.51)
7	Province_16 (13.38)	Urbanity_17 (13.95)	EnglishMarks_18 (15.16)	EatingBreakfast (38.29)
8	SedentaryTime_16 (12.76)	EatingBreakfast_17 (13.32)	Urbanity_18 (14.95)	Grade/Age (38.05)

Figures 22-24 illustrate variable importance by waves. X-axis and Y-axis represent variables and importance, respectively. The higher value of Y, the more important the corresponding variable was.

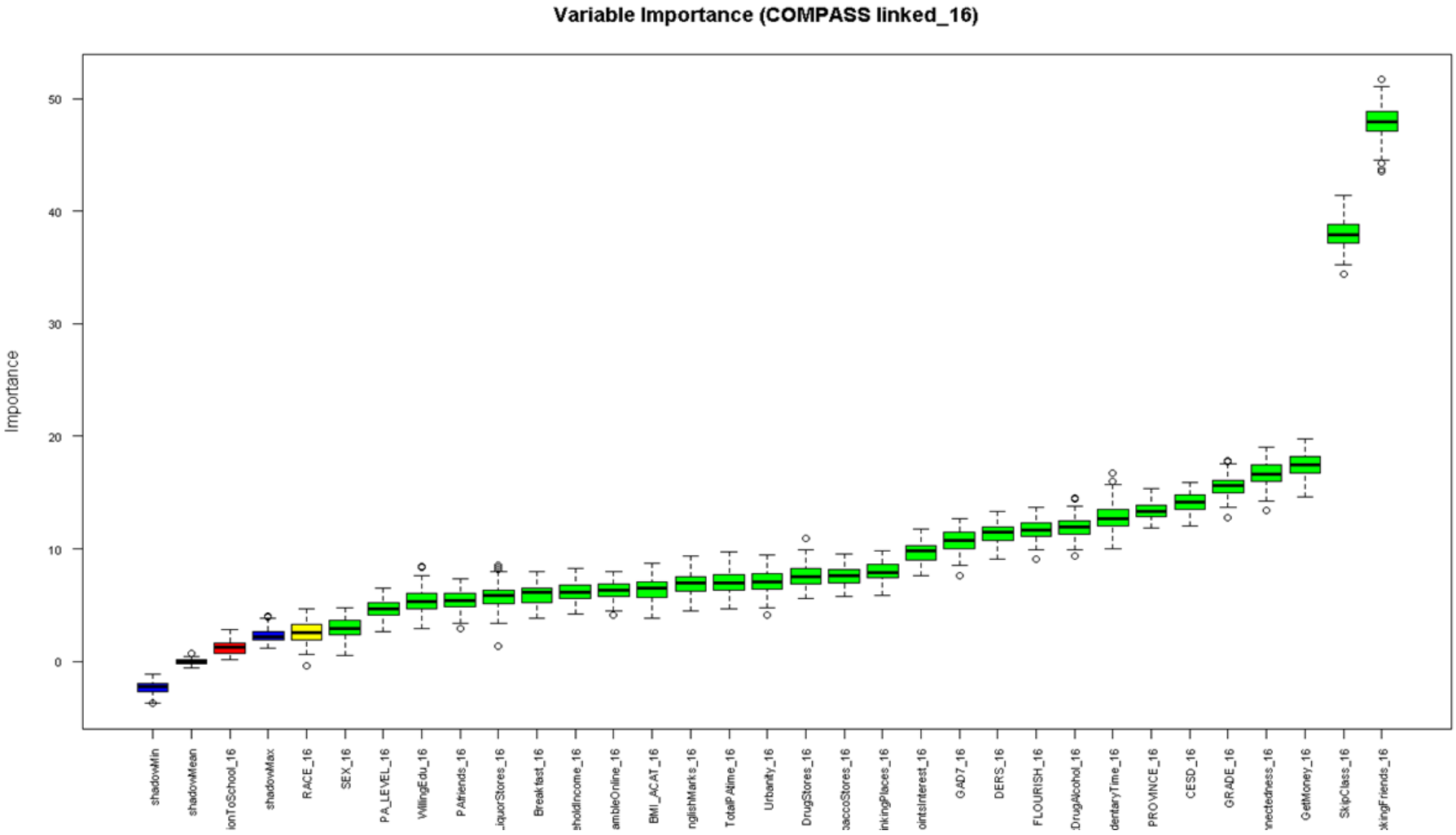
Variable Importance (COMPASS linked_16)
Importance
50
40
30
20
10
0
shadowMin
shadowMean
ionToSchool_16
shadowMax
RACE_16
SEX_16
PA_LEVEL_16
WillingEdu_16
PAfriends_16
iquorStores_16
Breakfast_16
sholdIncome_16
ambleOnline_16
BMI_ACAT_16
nglishMarks_16
TotalPAtime_16
Urbanity_16
DrugStores_16
baccoStores_16
inkingPlaces_16
ointsInterest_16
GAD7_16
DERS_16
FLOURISH_16
DrugAlcohol_16
dentaryTime_16
PROVINCE_16
CESD_16
GRADE_16
nnectedness_16
GetMoney_16
SkipClass_16
kingFriends_16

Figure 22. Variable importance (Wave I, 2016-17)

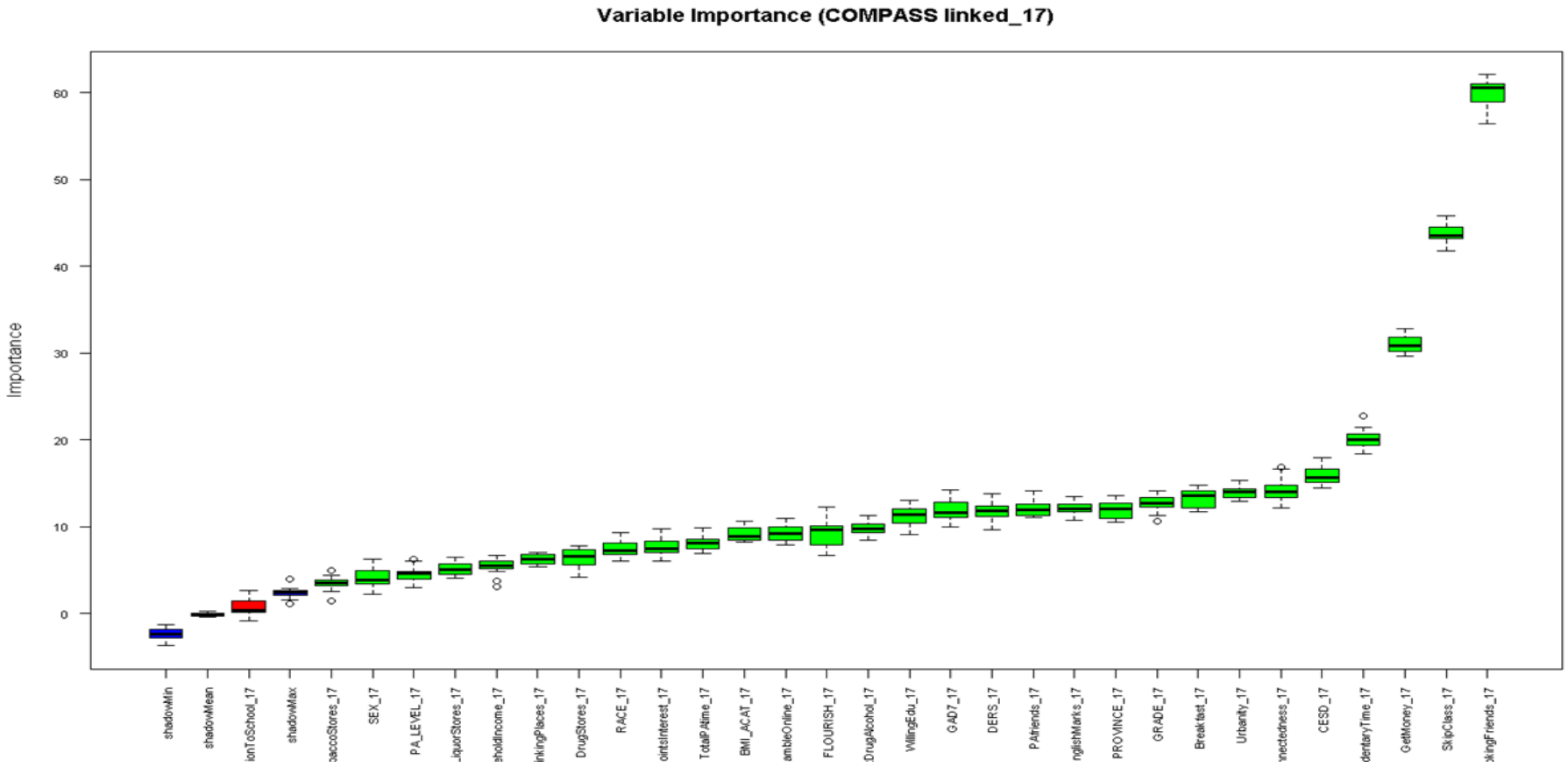

Figure 23. Variable importance (Wave II, 2017-18)

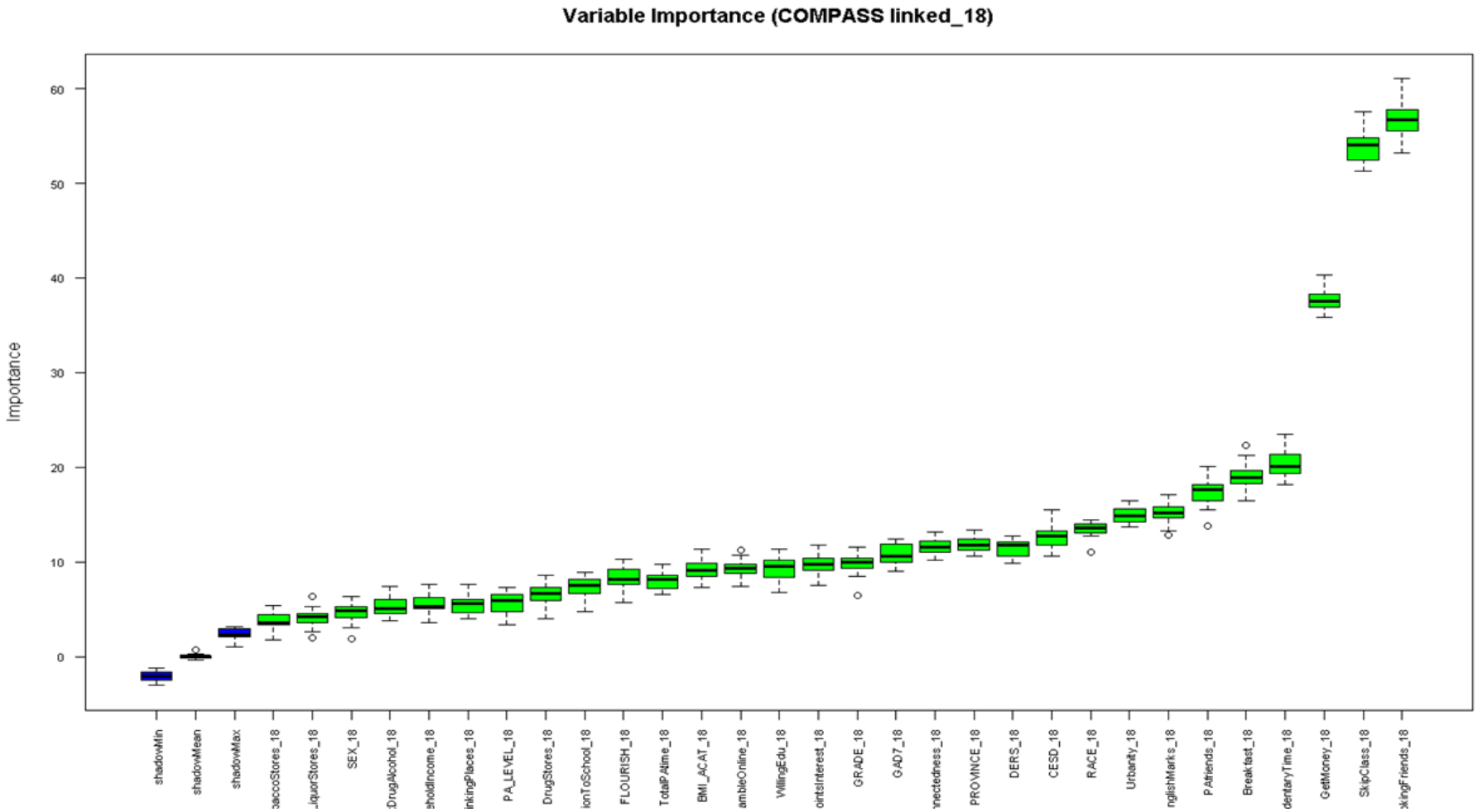

Figure 24. Variable importance (Wave III, 2018-19)

5.5.2 Risk Profiles of Polysubstance Use Among Canadian Secondary School Students

Four risk profiles of polysubstance use were identified across the three waves, i.e., low risk (L1), medium-low risk (L2), medium-high risk (L3), and high risk (L4). This was determined by the average group score of substance use indicators and the included risk factors. In general, students with the lowest mean values (scores) of each substance use, CESD and sedentary time, fewest smoking friends, fewest skipped classes, highest mean scores of school connectedness, and the majority eating breakfast were in the low-risk group. On the contrary, those majority who reported not eating breakfast, with the lowest mean scores of school connectedness, highest mean values (scores) of each substance use, CESD and sedentary time, a larger number of smoking friends, and a higher number of skipped classes were in the high-risk group. Two intermediate risk profiles were identified in-between, i.e., medium-low risk and medium-high risk groups. The average group scores of substance use indicators and risk factors ranged between L1 and L4. Tables 13-15 list the group mean scores with standard deviation (SD in bracket) of substance use indicators and all risk factors of these four risk profiles by waves based on fuzzy (FANNY) clustering.

Each of the four substance use indicators was categorized as 0 = "never use," 1 = "occasional use," and 2 = "current use." These values were treated as continuous scores to fit the Euclidean distance calculation. That is, the higher scores are indicative of more frequent use of the corresponding substance. In general, the lower the risk profile, the lower the score of the substance use indicator that the risk group had. At Wave I, on average, the low-risk (L1) group had the lowest score of indicators 0.06 ± 0.29 (mean ± SD, cigarette smoking), 0.14 ± 0.44 (e-cigarette use), 0.39 ± 0.68 (alcohol drinking), and 0.06 ± 0.30 (marijuana consumption). Whereas the high-risk (L4) group had the highest scores of 0.25 ± 0.56 (cigarette smoking), 0.35 ± 0.65 (e-cigarette use), 0.71 ± 0.82 (alcohol drinking), and 0.29 ± 0.63 (marijuana consumption). The magnitudes comparing L4 vs. L1 are 4.17 (cigarette smoking), 2.5 (e-cigarette use), 1.82 (alcohol drinking), and 4.83 (marijuana consumption) times at Wave I.

By observing the top risk factor, "the number of smoking friends," students in the high-risk group (L4) had the highest score being 0.64 ± 1.21 at Wave I. In contrast, students in the low-risk group (L1) had the lowest score of 0.19 ± 0.65, significantly differentiating between risk groups. Students at medium-high (L3) and medium-low (L2) risk groups scored between 0.46 ± 1.03 and 0.31 ± 0.81.

The initial values of this variable are categorical, coded as 0 = “None”, 1 = “1 friend”, 2 = “2 friends”, 3 = “3 friends”, 4 = “4 friends”, and 5 = “5 or more friends”. These values were treated as continuous scores; the higher the score is, the more smoking friends it represents. The magnitudes of these scores across the four risk groups (Wave III vs. Wave I) are close to each other, ranging from 1.41 times (L3) to 1.68 times (L1) over time.

The difference between students who were at low risk (L1) having, on average, the smallest sedentary time (170 ± 61.3 minutes) compared to their peers at high risk (L4, 1021 ± 269 minutes) was by a magnitude of **6.01** times. The sedentary time significantly increased with the increasing risk profiles, 345 ± 50.7 and 563 ± 83.3 minutes for L2 and L3, respectively. In Wave I data, students in the L4 group have a CESD score of 10.8 ± 6.70, whereas those in the low-risk group (L1) have the smallest CESD score of 7.08 ± 5.39, with significant differences between risk groups. The medium-low (L2) and medium-high (L3) risk groups have moderate CESD scores of 8.34 ± 5.89 and 9.30 ± 6.04, respectively. The same trend is observed in Wave II and III datasets.

The risk profiling reveals that students in the high-risk group (L4) of polysubstance use have the lowest school connectedness score, 18.0 ± 3.35 at Wave I. In contrast, students in the low-risk group (L1) have the highest score of 19.8 ± 2.78, significantly different between risk groups. In between, students in the medium-low (L2) and medium-high risk group (L3) have the scores of school connectedness being 19.1 ± 2.66 and 18.6 ± 2.81, respectively.

At Wave I, the majority (65.4%) of the participants who ate breakfast were in the low-risk group (L1), while the majority (68.1%) of the participants in the high-risk group (L4) did not eat breakfast. The prevalence of eating breakfast decreases while the risk level rises from low-risk (65.4%), medium-low (51.6%), medium-high (42.4%), to high-risk (31.9%). A similar pattern can be seen throughout the three waves. The longitudinal evidence suggests that the prevalence of the students eating breakfast decreased across the three waves in the low-risk group, being 61.7% and 55.5% at Wave II and Wave III. In this cohort, the percentage of students eating breakfast at Wave III (55.5%) was 0.85 times less than that of Wave I (65.4%), indicating a decrease over time. The same trend was observed among the other three risk profile groups (L2 to L4). Comparing the other three risk profiles (Wave III vs. Wave I), the differences were similar to that of L1, being 0.81 times (L2), 0.79 times (L3), and 0.78 times (L4).

This study identified that age is one of the top factors associated with youth polysubstance use, using students' grade level to proxy their age. Among the four risk profiles of polysubstance use, the high-risk group comprises mostly older students, while the majority in the low-risk group are their younger peers. For example, within the low-risk group (L1) at Wave I, 23.9% of students in grades 7 and 8 and 26.9% in grade 10. Whereas in the high-risk group (L4) at the same wave, only 7.8% of students are in grades 7 and 8, and 42.9% in grade 10.

It is observed that similar trends of risk profiling appear throughout the three waves, showing consistent risk profiles over time, including the four substance use indicators and the top factors associated with youth polysubstance use.

Table 13. Group mean scores of substance use indicators and all risk factors of the four risk profiles (Wave I, 2016-17)

	L1 (Low)	**L2 (Medium-low)**	**L3 (Medium-high)**	**L4 (High)**
	N=2799 (32.5%)	*N=2712 (31.5%)*	*N=2113 (24.5%)*	*N=986 (11.5%)*
Cigarette_16	0.06 (0.29)	0.11 (0.38)	0.17 (0.47)	0.25 (0.56)
eCigarette_16	0.14 (0.44)	0.22 (0.55)	0.31 (0.63)	0.35 (0.65)
Alcohol_16	0.39 (0.68)	0.57 (0.77)	0.65 (0.82)	0.71 (0.82)
Marijuana_16	0.06 (0.30)	0.12 (0.40)	0.21 (0.54)	0.29 (0.63)
SmokingFriends_16	0.19 (0.65)	0.31 (0.81)	0.46 (1.03)	0.64 (1.21)
SkipClass_16	1.20 (0.58)	1.23 (0.59)	1.31 (0.70)	1.38 (0.81)
GetMoney_16	1.70 (1.14)	1.81 (1.11)	1.82 (1.13)	1.90 (1.15)
SedentaryTime_16	170 (61.3)	345 (50.7)	563 (83.3)	1012 (269)
CESD_16	7.08 (5.39)	8.34 (5.89)	9.30 (6.04)	10.8 (6.70)
SchoolConnectedness_16	19.8 (2.78)	19.1 (2.66)	18.6 (2.81)	18.0 (3.35)
EatingBreakfast_16	1831 (65.4%)	1400 (51.6%)	896 (42.4%)	315 (31.9%)
Grade_16				
7	370 (13.2%)	170 (6.27%)	107 (5.06%)	33 (3.35%)
8	299 (10.7%)	176 (6.49%)	100 (4.73%)	44 (4.46%)
9	1377 (49.2%)	1430 (52.7%)	1088 (51.5%)	486 (49.3%)
10	753 (26.9%)	936 (34.5%)	818 (38.7%)	423 (42.9%)

Table 14. Group mean scores of substance use indicators and all risk factors of the four risk profiles (Wave II, 2017-18)

	L1 (Low) *N=3022 (34.7%)*	L2 (Medium-low) *N=3082 (35.4%)*	L3 (Medium-high) *N=1920 (22.0%)*	L4 (High) *N=684 (7.9%)*
Cigarette_17	0.14 (0.43)	0.22 (0.52)	0.29 (0.60)	0.45 (0.72)
eCigarette_17	0.35 (0.68)	0.52 (0.80)	0.61 (0.83)	0.67 (0.85)
Alcohol_17	0.73 (0.80)	0.91 (0.84)	0.96 (0.84)	1.05 (0.86)
Marijuana_17	0.17 (0.48)	0.33 (0.64)	0.43 (0.72)	0.57 (0.78)
SmokingFriends_17	0.28 (0.79)	0.44 (1.01)	0.64 (1.21)	0.94 (1.47)
SkipClass_17	1.28 (0.65)	1.37 (0.76)	1.40 (0.75)	1.62 (1.06)
GetMoney_17	2.06 (1.31)	2.17 (1.32)	2.24 (1.28)	2.24 (1.31)
SedentaryTime_17	193 (64.2)	385 (60.0)	647 (101)	1176 (308)
CESD_17	7.31 (5.54)	8.33 (5.80)	9.37 (5.96)	11.5 (7.07)
SchoolConnectedness_17	19.4 (2.97)	18.7 (3.01)	18.0 (3.15)	17.3 (3.54)
EatingBreakfast_17	1865 (61.7%)	1443 (46.8%)	718 (37.4%)	201 (29.4%)
Grade_17				
8	336 (11.1%)	231 (7.50%)	93 (4.84%)	25 (3.65%)
9	302 (9.99%)	207 (6.72%)	87 (4.53%)	24 (3.51%)
10	1415 (46.8%)	1578 (51.2%)	1035 (53.9%)	390 (57.0%)
11	969 (32.1%)	1066 (34.6%)	705 (36.7%)	245 (35.8%)

Table 15. Group mean scores of substance use indicators and all risk factors of the four risk profiles (Wave III, 2018-19)

	L1 (Low) *N=3385 (38.9%)*	L2 (Medium-low) *N=2847 (32.7%)*	L3 (Medium-high) *N=1776 (20.4%)*	L4 (High) *N=686 (7.9%)*
Cigarette_18	0.21 (0.50)	0.30 (0.59)	0.40 (0.66)	0.53 (0.74)
eCigarette_18	0.66 (0.84)	0.87 (0.90)	0.95 (0.91)	1.05 (0.90)
Alcohol_18	1.03 (0.83)	1.14 (0.82)	1.16 (0.82)	1.19 (0.82)
Marijuana_18	0.37 (0.66)	0.53 (0.75)	0.68 (0.82)	0.83 (0.87)
SmokingFriends_18	0.32 (0.86)	0.46 (0.99)	0.65 (1.19)	0.94 (1.50)
SkipClass_18	1.47 (0.83)	1.56 (0.88)	1.69 (1.03)	1.87 (1.21)
GetMoney_18	2.47 (1.38)	2.57 (1.36)	2.58 (1.33)	2.50 (1.32)
SedentaryTime_18	209 (68.0)	403 (58.2)	653 (94.2)	1191 (347)
CESD_18	8.02 (5.57)	9.16 (5.95)	10.0 (6.15)	12.2 (6.87)
SchoolConnectedness_18	18.9 (3.08)	18.4 (3.04)	17.7 (3.32)	17.0 (3.81)
EatingBreakfast_18	1878 (55.5%)	1195 (42.0%)	593 (33.4%)	170 (24.8%)
Grade_18				
9	363 (10.7%)	202 (7.10%)	99 (5.57%)	20 (2.92%)
10	346 (10.2%)	179 (6.29%)	75 (4.22%)	22 (3.21%)
11	1611 (47.6%)	1441 (50.6%)	976 (55.0%)	392 (57.1%)
12	1065 (31.5%)	1025 (36.0%)	626 (35.2%)	252 (36.7%)

5.6 Patterns of Polysubstance Use Among Canadian Secondary School Students

5.6.1 What are the Polysubstance Use Patterns?

In this thesis, another primary research question (RQ2) investigated was, "What are the patterns of polysubstance use among Canadian secondary school students?" Overall, four distinct polysubstance use patterns were identified and summarized as follows: subgroup 1 (S1) represented no use of any substances; subgroup 2 (S2) was the cohort with occasional single-use of alcohol; individuals in subgroup 3 (S3) had dual-use of e-cigarette and alcohol; and subgroup 4 (S4) represented current multi-use group, respectively.

Table 16 summarizes the estimates of the conditional response probabilities of each substance use under the selected model with four latent statuses, denoted as states 1 to 4. Category 0, 1, and 2

correspond to the "never use," "occasional use," and "current use," respectively. Predominant conditional response probabilities with larger values are highlighted in bold font to help with interpretation. Overall, the conditional response probabilities were well separated, demonstrating good heterogeneity between subgroups.

Table 16. Conditional response probabilities

Cigarette				
	Subgroup			
Category	**S1**	**S2**	**S3**	**S4**
0 (Never)	**0.9910**	0.9976	0.7653	0.1494
1 (Occasional)	0.0087	0.0024	0.2114	**0.4736**
2 (Current)	0.0002	0.0000	0.0232	**0.3770**
E-Cigarette				
	Subgroup			
Category	**S1**	**S2**	**S3**	**S4**
0 (Never)	**0.9637**	0.8545	0.2946	0.1115
1 (Occasional)	0.0327	0.1218	**0.3249**	0.1438
2 (Current)	0.0036	0.0237	**0.3805**	**0.7448**
Alcohol				
	Subgroup			
Category	**S1**	**S2**	**S3**	**S4**
0 (Never)	**0.9472**	0.1048	0.1412	0.0296
1 (Occasional)	0.0528	**0.6066**	**0.3441**	0.1755
2 (Current)	0.0000	0.2887	**0.5147**	**0.7949**
Marijuana				
	Subgroup			
Category	**S1**	**S2**	**S3**	**S4**
0 (Never)	**0.9979**	0.9803	0.5453	0.0653
1 (Occasional)	0.0016	0.0196	0.3553	0.3337
2 (Current)	0.0005	0.0001	0.0994	**0.6010**

Figure 25 illustrates conditional response probabilities involving multivariate response categories. Each subgroup was determined by the predominant conditional response probabilities of the substance use(s). The latent status can be explained based on the corresponding distribution of the response variables in the parameter estimation.

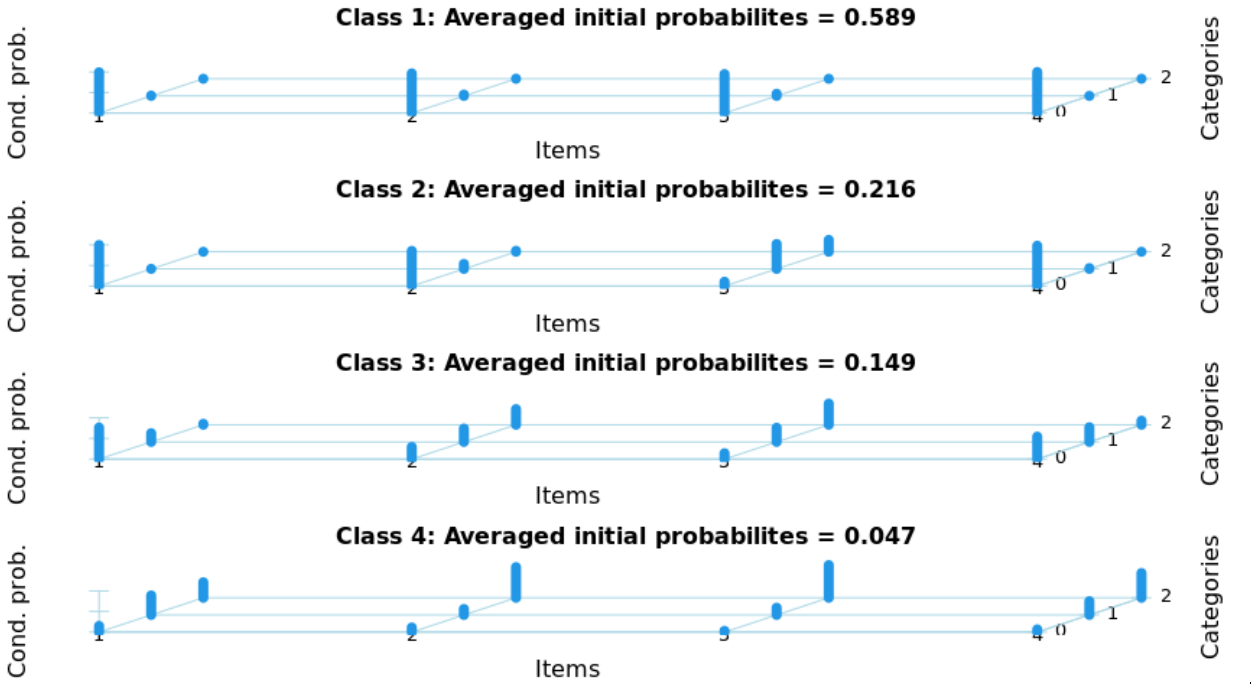

Figure 25. Conditional response probabilities

It is observed that Class 1 (S1) corresponds to students with no use of any substances, where the probability of the first category (never use) was greater than 94.7% for any substance. Class 2 (S2) was composed of individuals who typically used alcohol on an occasional basis. This is due to a more significant probability of occasional alcohol drinking (60.7%), whereas over 85.5% of probabilities never used the other three substances in this subgroup. Individuals in Class 3 (S3) had larger probabilities of occasional and current use of e-cigarette and alcohol, being 70.5% and 85.9%, respectively. The probabilities of using other substances in this subgroup were not prominent, although there were 21.1% and 35.5% of probabilities of smoking cigarettes and consuming marijuana, respectively. Individuals in Class 4 (S4) differed from those in S3 by having a greater probability of using multiple substances concurrently. For instance, the conditional response

probabilities of current e-cigarette use, alcohol drinking, and marijuana consumption were 74.5%, 79.5%, and 60.1%, respectively. Thus, S4 corresponds to the heavy multi-user group.

At the beginning of the observation period, the initial probabilities of each use pattern were 0.5887, 0.2156, 0.1487, and 0.0470, representing the chance of being in the no-use (S1), occasional single-use of alcohol (S2), dual-use of e-cigarette and alcohol (S3), and multi-use (S4) subgroup, respectively. The sizes of each use pattern are summarized in Table 17. In particular, S1 was the largest subgroup, containing 5320 students, accounting for 60.3% of the total sample size (N = 8824) at Wave I, followed by S2 (21.1%) and S3 (14.1%). Lastly, S4, the highest risk group, comprising current multi-use of substance users, consisted of 399 students, accounting for 4.5% of the total sample size at Wave I.

Table 17. Size of each pattern at Wave I (2016-17)

	Count	**%**
Wave I (2016-17)		
S1: No-use	5320	60.3
S2: Occasional single-use (A)	1859	21.1
S3: Dual-use (E+A)	1246	14.1
S4: Multi-use	399	4.5
Grand Total	**8824**	**100.0**

5.6.2 What Factors are Associated with Patterns of Polysubstance Use?

Associated with the primary research question RQ2, a secondary research question (RQ4) examined was, “What factors are associated with patterns of polysubstance use among Canadian adolescents?” We estimated the covariates' effects on their initial probabilities to investigate the factors associated with the diverse use patterns of substances among youth. Table 18 lists the coefficients of all predictors with corresponding odds ratios (OR) affecting the initial probabilities for each use pattern membership under the selected model. To evaluate the significance of predictors on the effect of subgroup membership for the initial probabilities, Wald test statistics (t-test) was performed based on

the parameter estimates and standard errors. Corresponding *p*-values were obtained, as shown in Table 18 below.

Table 18. Predictors of subgroup membership for the initial probabilities at Wave I (Ref: S1)

	Subgroup		
	S2	**S3**	**S4**
intercept			
β (beta coefficient)	-0.84	-0.54	-0.44
Odds Ratios	0.43***	0.58***	0.65***
Urbanity			
β (beta coefficient)	-0.20	-0.27	-0.42
Odds Ratios	0.82***	0.77***	0.66***
Grade/Age			
β (beta coefficient)	0.28	0.23	0.41
Odds Ratios	1.32***	1.26***	1.51***
Race/Ethnicity			
β (beta coefficient)	-0.08	-0.06	-0.04
Odds Ratios	0.92**	0.94*	0.96^{+++}
GetMoney			
β (beta coefficient)	0.13	0.25	0.29
Odds Ratios	1.14***	1.29***	1.34***
PAfriends			
β (beta coefficient)	0.19	0.17	0.10
Odds Ratios	1.21***	1.18***	1.10*
EatingBreakfast			
β (beta coefficient)	-0.22	-0.45	-0.59
Odds Ratios	0.80*	0.64***	0.56**
SmokingFriends			
β (beta coefficient)	0.30	0.59	1.01
Odds Ratios	1.35***	1.81***	**2.75*****

	Subgroup		
	S2	**S3**	**S4**
SupportQuitDrugAlcohol			
β (beta coefficient)	0.22	0.26	0.36
Odds Ratios	1.25***	1.30***	1.43***
Sex			
β (beta coefficient)	-0.30	0.29	-0.22
Odds Ratios	0.74**	1.34**	0.80^{+++}
SkipClass			
β (beta coefficient)	0.51	0.65	1.03
Odds Ratios	1.67***	1.92***	**2.79*** **
BMI_CATEGORY			
β (beta coefficient)	0.20	0.18	0.25
Odds Ratios	1.22***	1.20***	1.28**
SchoolConnectedness			
β (beta coefficient)	-0.05	-0.09	-0.20
Odds Ratios	0.95**	0.91***	0.82***
SedentaryTime			
β (beta coefficient)	0.00	0.00	0.00
Odds Ratios	1.00*	1.00***	1.00***
GambleOnline			
β (beta coefficient)	-1.55	-1.98	-2.54
Odds Ratios	0.22***	0.14***	**0.08*** **

Note: *** $p < .00001$; ** $p < .001$; * $p < .05$; $^{+++}$The result is *not* significant at $p < .05$.

This table demonstrates that most of the predictors had statistically significant effects on the subgroup membership across all groups, relative to S1. A couple of predictors did not have consistent results showing significant effects of the initial probability across subgroups. For example, although ethnicity and sex had significant effects on the membership of S2 and S3 for the initial probability, they were not significant on the initial membership of S4.

The following sections summarize the variable impact based on their positive, negative, or mixed effects.

5.6.2.1 Positive Effects

Overall, urbanity, race/ethnicity, eating breakfast, school connectedness, and (not) gambling online consistently had positive effects on the initial membership in the S2 through S4 subgroups, relative to S1. In other words, the odds of starting in any of the S2 to S4 patterns, relative to S1, were consistently lower for students who reported, for example, living in large urban (vs. medium urban[2]), being Black (vs. White[3]), eating breakfast (vs. not eating breakfast), having a higher score of school connectedness (vs. one-score lower), or not gambling online (vs. gambling online).

Taking the covariate "GambleOnline" as an example (see Figure 26), at Wave I, students who reported not gambling online for money for the last 30 days were less than 0.08 times likely to start in the current multi-use (S4) subgroup, relative to the no-use (S1) subgroup than were those who reported gambling online, assuming that all the other variables were held constant. Similar interpretations apply to other positive-effect covariates, referring to Table 18.

GambleOnline	S1 (REF)	S2	S3	S4
•Yes (REF)	•REF	•REF	•REF	•REF
•No	•REF	•OR = 0.22***	•OR = 0.14***	•**OR = 0.08*****

Figure 26. Example of positive effects on the initial membership

5.6.2.2 Negative Effects

On the contrary, eight covariates, namely: grade/age, weekly money to spend/save oneself, the number of physically active friends, the number of smoking friends, school support for quitting drugs and alcohol, the number of skipped classes, BMI category, and sedentary time consistently had negative effects on the initial membership in the S2 through S4 subgroups, relative to S1. That is, the odds of starting in any of the S2 to S4 patterns, relative to S1, were consistently higher for students who reported, for example, in a higher grade (vs. one-grade lower), having greater than $100 weekly

[2] Large urban vs. medium urban vs. small urban vs. rural
[3] Other vs. Latin American/Hispanic vs. First Nations vs. Asian vs. Black vs. White

money (vs. $21-$100[4]), five or more physically active friends (vs. 4[5]), five or more smoking friends (vs. 4[6]), residing in a school very unsupportive (vs. unsupportive[7]), having more than 20 classes skipped (vs. 11 to 20 classes[8]), being obese (vs. overweight[9]), or having longer sedentary time (vs. one-minute shorter).

Taking the covariate "SkipClass" as an example (see Figure 27), at Wave I, an individual who reported skipping 1 or 2 classes was more than 2.79 times likely to start in the current multi-use (S4) subgroup relative to the no-use (S1) subgroup than was an individual who reported zero skipped classes, assuming that all the other variables were held constant. The same OR applies to comparing all the categories, i.e., "zero" vs. "1 or 2 classes" vs. "3 to 5 classes" vs. "6 to 10 classes" vs. "11 to 20 classes" vs. "More than 20 classes." Similar interpretations hold for other negative-effect covariates, referring to Table 18.

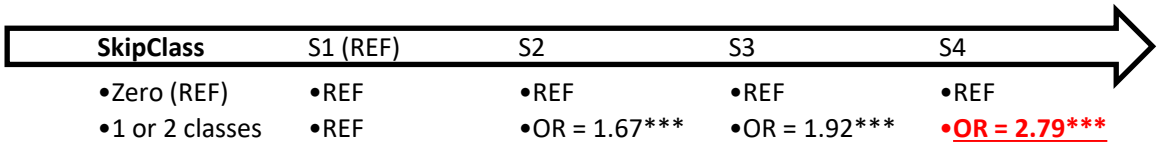

Figure 27. Example of negative effects on the initial membership

5.6.2.3 Mixed Effects

The covariate sex had mixed negative and positive effects on the initial membership in the S2 through S4 subgroups relative to S1. The interpretation of this finding can be summarized as follows. Assuming that all the other variables were held constant, at Wave I, a male student was less than 0.74 times as likely to be in the occasional single-use of alcohol (S2) subgroup relative to the no-use (S1) subgroup and was less than 0.80 times as likely to be in the current multi-use (S4) subgroup relative to non-users (S1) subgroup than a female student. Whereas at Wave I, a male student was more than 1.34 times as likely to be in the dual-use of e-cigarette and alcohol (S3) subgroup relative to the no-use (S1) subgroup than a female student, with all the other variables held constant. Figure 28

[4] Greater than $100 vs. $21-$100 vs. $1-$20 vs. zero
[5] 5 or more friends vs. 4 friends vs. 3 friends vs. 2 friends vs. 1 friend vs. none
[6] 5 or more friends vs. 4 friends vs. 3 friends vs. 2 friends vs. 1 friend vs. zero
[7] Very unsupportive vs. unsupportive vs. supportive vs. very supportive
[8] More than 20 classes vs. 11 to 20 classes vs. 6 to 10 classes vs. 3 to 5 classes vs. 1 or 2 classes vs. zero
[9] Obese vs. overweight vs. healthy weight vs. underweight vs. not stated

illustrates the mixed effects of sex on the initial membership of use patterns, with a positive effect highlighted in **green** and a negative effect in **red**.

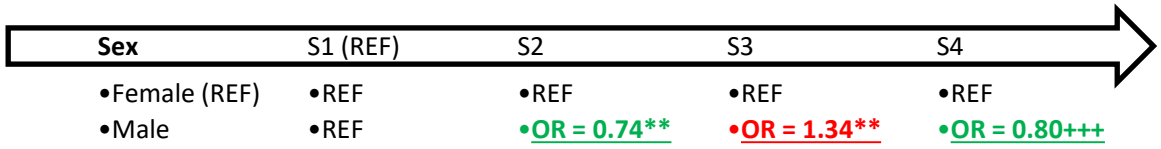

Figure 28. Example of mixed effects on the initial membership

5.6.3 Initial Probabilities of Different Subgroup Membership by Demographics

To further investigate initial probabilities of different subgroup membership by various demographic cohorts, e.g., sex, grade, etc., Table 19 summarizes the initial probabilities of diverse subgroup membership by additional demographic information, with significant information highlighted in bold font.

Table 19. Initial probabilities of different subgroup membership by a demographic cohort at Wave I (2016-17)

Characteristics		**Subgroup**			
		S1	**S2**	**S3**	**S4**
Sex	Female	0.5896	0.2350	0.1245	0.0509
	Male	0.5877	0.1923	0.1778	0.0422
Grade	7	0.7578	0.1354	0.0895	0.0173
	8	0.6743	0.1852	0.1139	0.0266
	9	0.6125	0.2077	0.1392	0.0405
	10	**0.4967**	**0.2520**	**0.1836**	**0.0676**
Province	**AB**	**0.4505**	0.2594	**0.2024**	**0.0878**
	BC	0.5876	0.2135	0.1494	0.0495
	ON	0.5691	0.2240	0.1568	0.0501
	QC	0.6762	0.1820	0.1133	0.0285

Characteristics		**Subgroup**			
		S1	**S2**	**S3**	**S4**
Urbanity	**Rural**	**0.2977**	0.2734	**0.2539**	**0.1751**
	Small urban	0.5155	0.2370	0.1811	0.0664
	Medium urban	0.5435	0.2335	0.1682	0.0548
	Large urban	0.6440	0.1983	0.1245	0.0332
Ethnicity	White	0.5828	0.2264	0.1483	0.0426
	Black	0.5668	0.2094	0.1698	0.0540
	Asian	0.6375	0.1882	0.1327	0.0416
	Aboriginal	**0.4354**	0.1935	**0.2253**	**0.1457**
	Latin American	0.6129	0.1735	0.1533	0.0603
	Other	0.6269	0.1771	0.1406	0.0555
Household Income	$25K - $50K	0.6845	0.1831	0.1062	0.0262
	$50K - $75K	0.5723	0.2184	0.1579	0.0514
	$75K - $100K	0.5711	0.2260	0.1536	0.0492
	>$100K	0.5548	0.2233	0.1650	0.0568
BMI	Not stated	0.6684	0.1651	0.1248	0.0418
	Underweight	0.6598	0.1850	0.1214	0.0338
	Healthy weight	0.5778	0.2303	0.1481	0.0438
	Overweight	0.5030	0.2493	0.1836	0.0641
	Obese	**0.4540**	0.2577	**0.2128**	0.0755

5.7 Exploring Dynamic Transitions of Youth Polysubstance Use Patterns

5.7.1 How Do Transition Behaviours Change Over Time?

The last primary research question (RQ3) investigated was, “How do transition behaviours change over time in use patterns?” Transition probabilities were calculated with the LMM modelling to address this research question. Tables 20-21 show the averaged transition probability matrix across

the three waves and the transition probabilities from Wave I to Wave II (upper portion) and Wave II to Wave III (lower part), with the diagonal in bold font to assist interpretation. Figures 29-31 illustrate the averaged transition probabilities and transition probabilities between subgroups (Wave I → Wave II and Wave II → Wave III). Although the subgroup prevalence at different time occasions was similar, and the transition probability matrix revealed that an individual's use pattern membership at any time occasion was likely to be the same as the previous time occasion, there was nevertheless change between subgroups. Except for the diagonal, the largest transition probabilities under each subgroup were marked with an underscore, showing the most significant chance of change between subgroups. For instance, those in the S1 subgroup at Wave I had a 25.1% chance of being in the S2 at Wave II. Those in the S2 subgroup had a 43.8% chance of transitioning to the S3 subgroup at Wave II. Those in the S4 subgroup had a 9.4% chance of moving to the S1 subgroup and a 6.4% chance of moving to the S3 subgroup at Wave II.

Table 20. Averaged transition probability matrix across the three waves

Subgroup	**S1**	**S2**	**S3**	**S4**
S1	**0.5740**	0.2510	0.1528	0.0223
S2	0.0061	**0.5210**	0.4447	0.0283
S3	0.0098	0.0007	**0.7092**	0.2804
S4	0.0754	0.0051	0.0528	**0.8668**

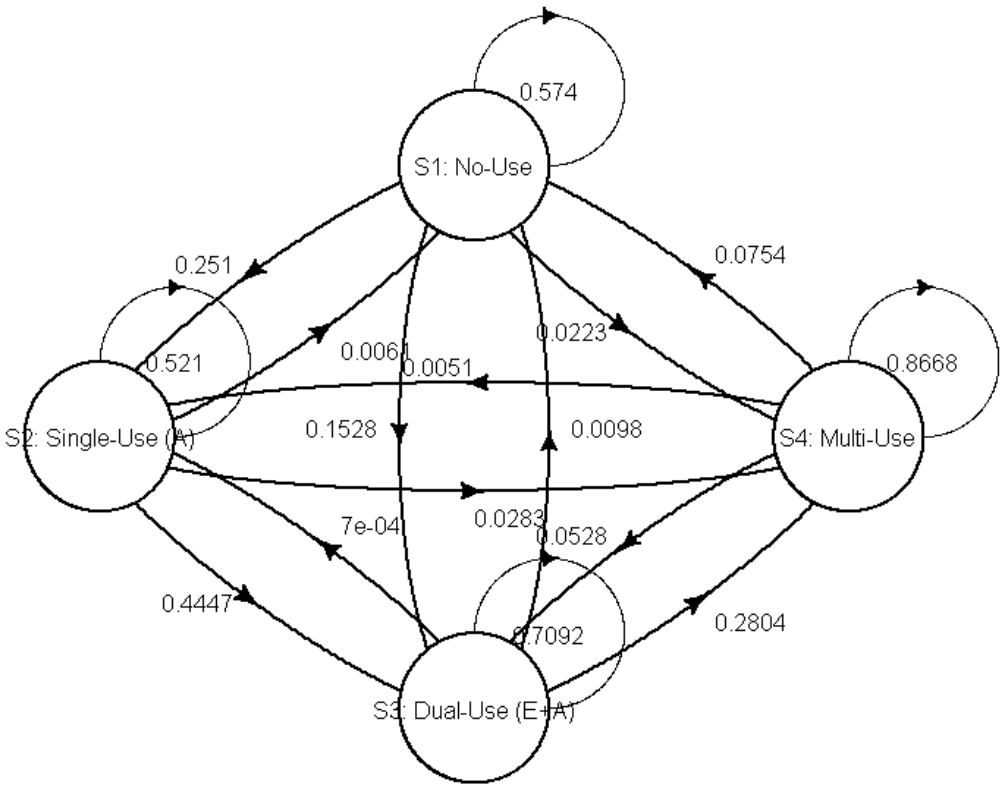

Figure 29. Diagram of averaged transition probabilities across the three waves

Table 21. Transition probabilities by waves (upper portion: Wave I → Wave II; lower portion: Wave II → Wave III)

Wave	Subgroup	S1	S2	S3	S4
II	**S1**	**0.5845**	0.2512	0.1433	0.0209
(2017-18)	**S2**	0.0066	**0.5271**	0.4375	0.0288
	S3	0.0127	0.0007	**0.7176**	0.2690
	S4	0.0943	0.0061	0.0635	**0.8361**
III	**S1**	**0.5635**	0.2507	0.1622	0.0236
(2018-19)	**S2**	0.0055	**0.5149**	0.4519	0.0277
	S3	0.0068	0.0007	**0.7007**	0.2918
	S4	0.0565	0.0040	0.0420	**0.8975**

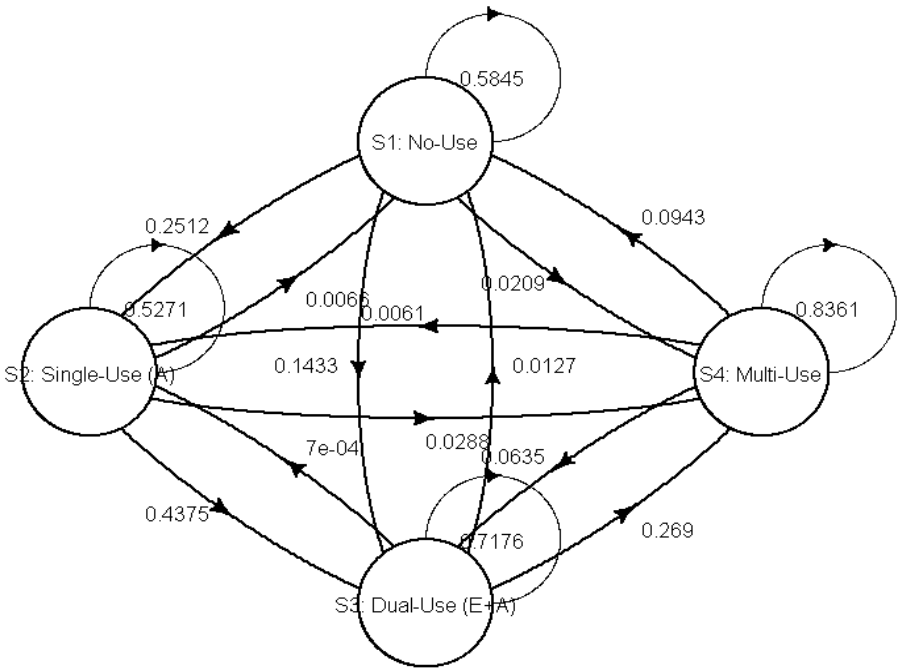

Figure 30. Diagram of transition probabilities (Wave I → Wave II)

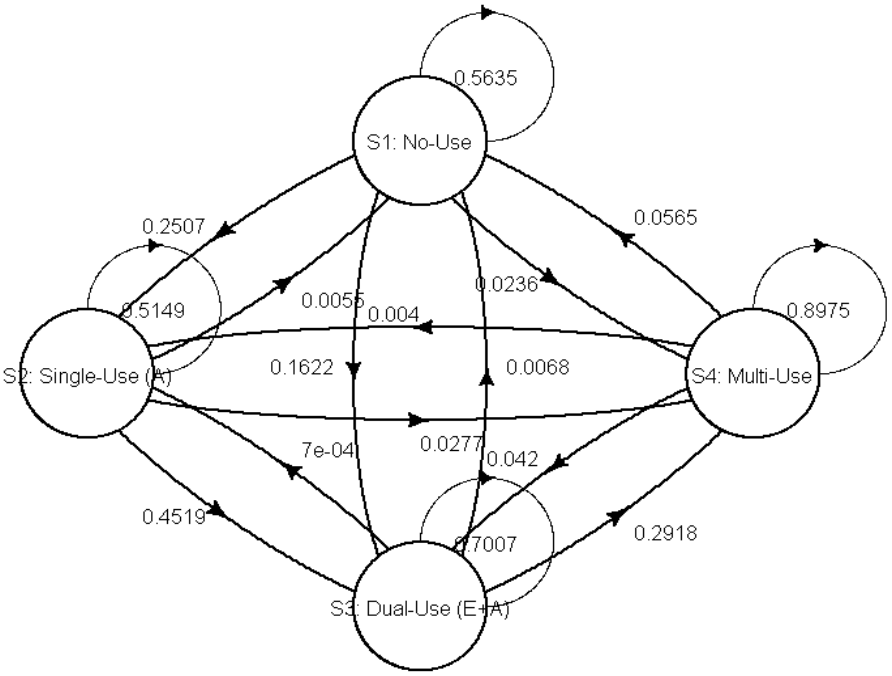

Figure 31. Diagram of transition probabilities (Wave II → Wave III)

Table 22 demonstrates the estimated marginal distribution of the four patterns of polysubstance use (S1 through S4) for each wave.

Table 22. Estimated marginal distribution of the four use patterns (S1-S4)

Wave	**Subgroup**			
	S1	**S2**	**S3**	**S4**
I (2016-17)	0.5887	0.2156	0.1487	0.0470
II (2017-18)	0.3742	0.2504	0.2652	0.1101
III (2018-19)	0.2368	0.2201	0.3408	0.2022

It shows that the probability of S1 constantly decreased across the three waves (0.5887 → 0.3742 → 0.2368); the probability of S2 increased from Wave I to Wave II (0.2156 → 0.2504) and then decreased from Wave II to Wave III (0.2504 → 0.2201). The marginal distribution of S3 (0.1487 → 0.2652 → 0.3408) and S4 (0.0470 → 0.1101 → 0.2022) steadily increased over time, indicating a general tendency towards increasing use in dual and multiple substances. It is observed that the growth rate of S3 (Δ = +0.1156) was greater than that of S4 (Δ = +0.0631) from Wave I to Wave II, and the growth rate for S3 (Δ = +0.0756) and S4 (Δ = +0.0921) was similar from Wave II to Wave III. Figure 32 illustrates the marginal distribution of all the four use patterns over time.

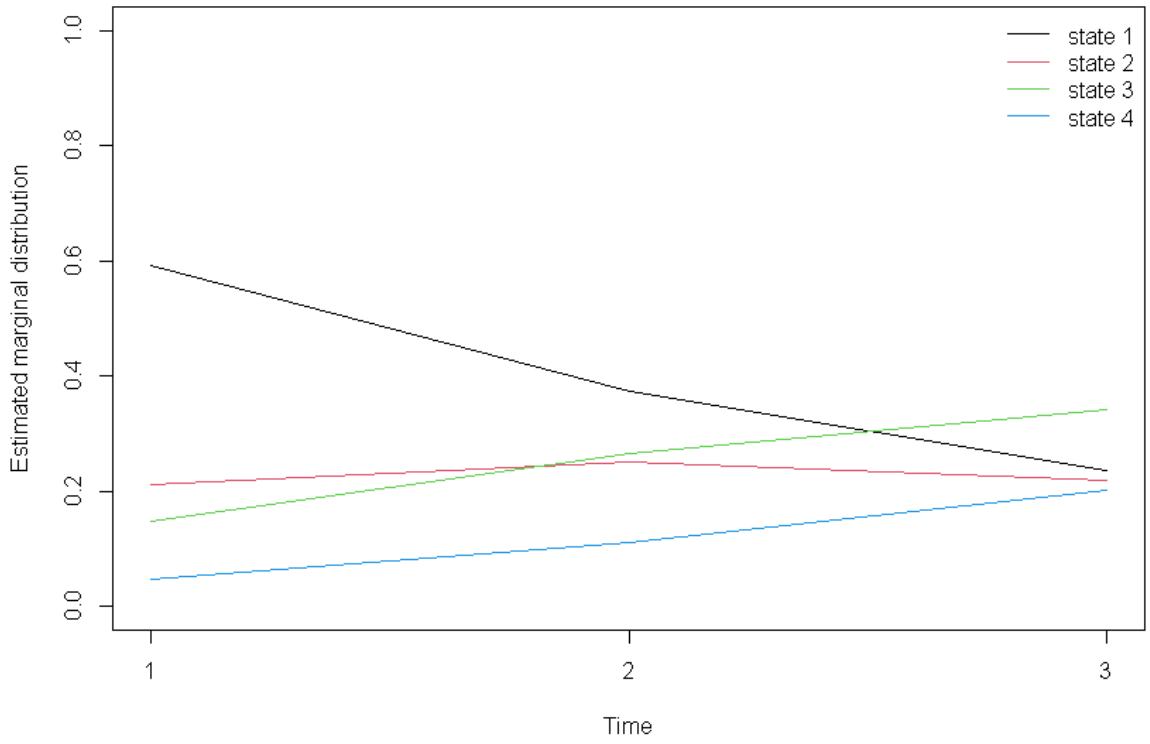

Figure 32. Estimated marginal distribution of the four subgroups (S1-S4)

By examining the incremental change (Δ) in transition probabilities from Wave II to Wave III vs. Wave I to Wave II, we found that the probability of staying in S4 increased (Δ_{S4} = +0.0614) across time. In contrast, the probability of staying in any of the lower use pattern subgroups S1 to S3 decreased over time (Δ_{S1} = -0.0210, Δ_{S2} = -0.0122, and Δ_{S3} = -0.0169). In terms of *change*, the following transition probabilities increased across time: S1 → S3 ($\Delta_{S1\rightarrow S3}$ = +0.0189), S1 → S4 ($\Delta_{S1\rightarrow S4}$ = +0.0027), S2 → S3 ($\Delta_{S2\rightarrow S3}$ = +0.0144), and S3 → S4 ($\Delta_{S3\rightarrow S4}$ = +0.0228). On the contrary, the decreased transition probabilities included S1 → S2 ($\Delta_{S1\rightarrow S2}$ = -0.0005), S2 → S1 ($\Delta_{S2\rightarrow S1}$ = -0.0011), S2 → S4 ($\Delta_{S2\rightarrow S4}$ = -0.0011), S3 → S1 ($\Delta_{S3\rightarrow S1}$ = -0.0059), S4 → S1 ($\Delta_{S4\rightarrow S1}$ = -0.0378), S4 → S2 ($\Delta_{S4\rightarrow S2}$ = -0.0021), and S4 → S3 ($\Delta_{S4\rightarrow S3}$ = -0.0215). The transition probability of S3 → S2 across the three waves was unchanged ($\Delta_{S3\rightarrow S2}$ = 0). Table 23 summarizes these incremental changes of the initial membership probabilities over time.

Table 23. Incremental change in transition probabilities across the three waves

$\Delta = P_{WII \circledcirc WIII} - P_{WI \circledcirc WII}$	S1	S2	S3	S4
S1	**-0.0210**	-0.0005	0.0189	0.0027
S2	-0.0011	**-0.0122**	0.0144	-0.0011
S3	-0.0059	0	**-0.0169**	0.0228
S4	-0.0378	-0.0021	-0.0215	**0.0614**

Local decoding is based on the maximum posterior probability. Table 24 presents the prediction of each subgroup membership at different time occasions. It is noted that the prevalence of S1 through S4 gradually decreased at Wave II as well, being 38.8%, 24.8%, 24.7%, and 11.7%. A similar trend was observed in Wave III data, 24.9%, 22.6%, 32.4%, and 20.1%, with the obvious exception in S3, with the highest prevalence of 32.4%, instead of S1 found with the other two waves. The longitudinal evidence of use patterns showed that although the no-use (S1) subgroup at Wave I was prominent, its prevalence decreased over time (Wave I → Wave II: Δ_{S1} = -21.5%; Wave II → Wave III: Δ_{S1} = -13.9%). In contrast, the prevalence of the other three use patterns (S2 to S4) increased (Wave I → Wave II: Δ_{S2} = +3.7%, Δ_{S3} = +10.6%, Δ_{S4} = +7.2%; Wave II → Wave III: Δ_{S2} = -2.2%, Δ_{S3} = +7.7%, Δ_{S4} = +8.4%), except for S2 decreased by 2.2% from Wave II to Wave III. By Wave III, S3 became the prominent use pattern. Although S4 had been the minor use pattern across the three waves, it is alarming that the prevalence increased by 4.5 times from Wave I to Wave III, and by Wave III, its prevalence became very close to S2 and S1. The estimated marginal distribution plot and transition patterns (Figures 32-33 in Chapter 5 Results, Section 5.7.1) depict this trend.

Table 24. Prediction of subgroup membership at different time occasions

	Count	**%**
T1 (Wave I, 2016-17)		
S1: No-use	5320	60.3
S2: Occasional single-use (A)	1859	21.1
S3: Dual-use (E+A)	1246	14.1
S4: Multi-use	399	4.5
T2 (Wave II, 2017-18)		
S1: No-use	3425	38.8
S2: Occasional single-use (A)	2191	24.8
S3: Dual-use (E+A)	2178	24.7
S4: Multi-use	1030	11.7
T3 (Wave III, 2018-19)		
S1: No-use	2197	24.9
S2: Occasional single-use (A)	1992	22.6
S3: Dual-use (E+A)	2861	32.4
S4: Multi-use	1774	20.1
Grand Total	**8824**	**100.0**

Figure 33 illustrates each individual's transition curves (left panel) and transition patterns (right panel) across the three waves.

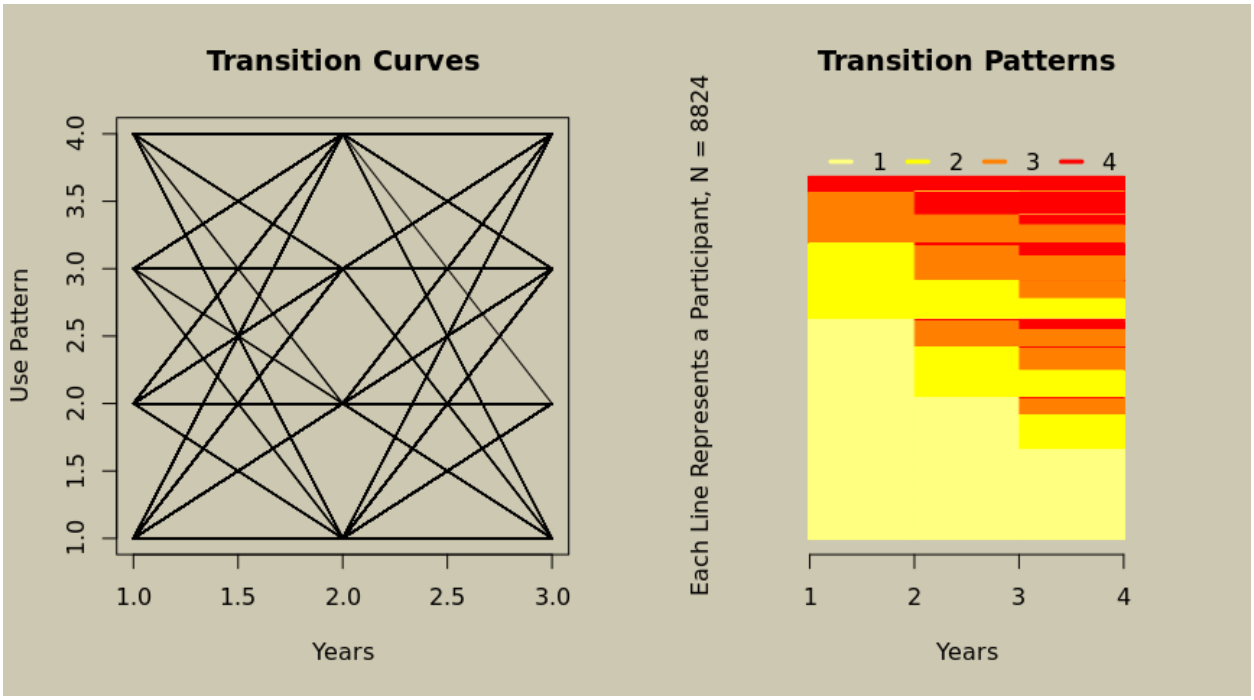

Figure 33. Transition curves (left panel) and transition patterns (right panel)

5.7.2 What Factors are Associated with Dynamic Transitions of Use Patterns?

One of the secondary research questions (RQ5), in association with the primary research question RQ3, examined, “What factors are associated with dynamic transitions of use patterns?” Given that the parameter estimation is cumbersome and the interpretation may be difficult, the ORs for all covariates of transition between different use patterns are presented in Table 25. This table demonstrates the average effect of each covariate on the transition probability to the different subgroups, conditional on the subgroup at Wave I. See Appendix P for detailed covariates' effects on the transition probabilities with coefficients.

Table 25. Odds ratios for all predictors of transition between use patterns (N = 8824)

Characteristics/Subgroup	S1	S2	S3	S4
Urbanity				
S1	REF	0.87**	0.87*	0.74^{+++}
S2	5.19***	REF	0.93^{+++}	1.20^{+++}
S3	0.83^{+++}	0.62***	REF	0.86*
S4	51.62***	3.25***	0.03***	REF
Grade/Age				
S1	REF	0.93*	0.90*	0.77*
S2	0.68*	REF	0.93^{+++}	0.66*
S3	0.97^{+++}	1.28*	REF	0.95^{+++}
S4	0.41***	0.69*	0.75^{+++}	REF
Race/Ethnicity				
S1	REF	0.90***	0.99^{+++}	0.54*
S2	1.76*	REF	0.97^{+++}	0.94^{+++}
S3	1.25^{+++}	0.56***	REF	0.82***
S4	1.29^{+++}	0.85^{+++}	1.86*	REF
GetMoney				
S1	REF	1.20***	1.38***	1.59*
S2	0.59^{+++}	REF	1.19***	1.30^{+++}
S3	0.59*	0.71*	REF	1.18*
S4	0.72^{+++}	0.87^{+++}	0.21***	REF
PAfriends				
S1	REF	1.25***	1.25***	1.34*
S2	0.33***	REF	1.23***	0.94^{+++}
S3	0.67^{+++}	1.03^{+++}	REF	1.10*

Characteristics/Subgroup	S1	S2	S3	S4
S4	0.18***	0.30***	175.92***	REF
EatingBreakfast				
S1	REF	0.81*	0.56***	0.42*
S2	1.55***	REF	0.69**	0.96^{+++}
S3	1.16**	1.15**	REF	0.60**
S4	59.03***	0.03***	135.32***	REF
SmokingFriends				
S1	REF	1.14*	1.60***	2.98***
S2	0.51***	REF	1.39**	2.95***
S3	0.46***	7.18***	REF	2.29***
S4	0.00***	0.96^{+++}	0.00***	REF
SupportQuitDrugAlcohol				
S1	REF	1.25***	1.22**	1.97**
S2	5.67***	REF	1.14*	1.55*
S3	0.13***	1.82**	REF	1.03^{+++}
S4	0.14***	0.96^{+++}	0.02***	REF
Sex				
S1	REF	1.28***	1.72***	2.53***
S2	0.63***	REF	1.38***	2.43***
S3	0.36***	0.53***	REF	1.50***
S4	0.00***	0.96^{+++}	0.06***	REF
SkipClass				
S1	REF	1.17***	1.16**	0.95^{+++}
S2	0.27**	REF	1.00^{+++}	1.16^{+++}
S3	0.29***	0.27***	REF	1.06^{+++}

Characteristics/Subgroup	S1	S2	S3	S4
S4	0.71*	0.02***	98.97***	REF
BMI_CATEGORY				
S1	REF	1.02*	0.94**	0.94^{+++}
S2	0.68*	REF	1.00^{+++}	0.88*
S3	1.44**	0.73*	REF	0.95*
S4	1.15^{+++}	1.35*	1.03^{+++}	REF
SchoolConnectedness				
S1	REF	0.65***	1.31*	2.29*
S2	2.26***	REF	1.10^{+++}	0.18***
S3	1.65***	1.30***	REF	1.82***
S4	300.22***	0.05***	0.46***	REF
SedentaryTime				
S1	REF	1.00^{+++}	1.00***	1.00*
S2	0.99*	REF	1.00**	1.00*
S3	1.00^{+++}	0.99^{+++}	REF	1.00**
S4	1.00*	1.00^{+++}	1.01***	REF
GambleOnline				
S1	REF	1.37^{+++}	0.91^{+++}	0.17***
S2	1.44***	REF	1.32^{+++}	3.34***
S3	0.72***	0.70***	REF	1.38^{+++}
S4	0.68***	1.02^{+++}	0.00***	REF

Note: *** $p < .00001$; ** $p < .001$; * $p < .05$; $^{+++}$The result is *not* significant at $p < .05$.

Similar to the interpretation of the covariates' effects on initial probabilities, we summarize the covariates' effects on the transition probabilities based on their positive, negative, or mixed effects. This was determined by examining the upper and lower triangular matrices of each covariate in Table 25. Suppose the odds ratios on the upper-triangular matrix were greater than one. In that case, it

indicates a higher OR (>1) of transitioning to a higher use pattern, conditional on the reference group at Wave I. In other words, these factors are more likely to contribute to the dynamic transition to a higher subgroup. Suppose the odds ratios on the upper-triangular matrix were less than 1. In that case, it indicates a lower OR (<1) of transitioning to a higher use pattern, conditional on the reference group at Wave I, suggesting a positive effect on the transition probability to a higher subgroup. Suppose the ORs on the upper-triangular matrix were mixed with values greater than one and less than one. In that case, it indicates mixed effects on transition probability to a higher use pattern, conditional on the reference group at Wave I.

5.7.2.1 Moving From a Lower Use Pattern to a Higher One

5.7.2.1.1 Positive Effects

Overall, grade/age, race/ethnicity, and eating breakfast consistently had positive effects on the transition probabilities from a lower use pattern to a higher use group over time. Taking the covariate EatingBreakfast as an example (see Figure 34), among students who started in the no-use subgroup (S1) at Wave I, those who reported eating breakfast were less than 0.42 times likely to move to the current multi-use subgroup (S4) relative to S1 at Wave II than were those who reported not eating breakfast, with all the other variables held constant.

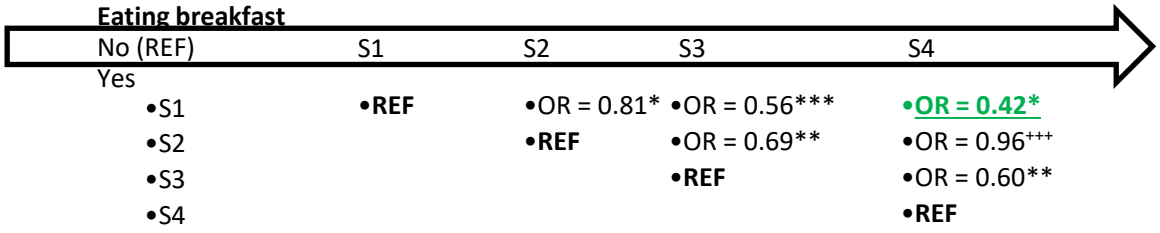

Figure 34. Example of positive effects on the dynamic transitions from a lower use pattern to a higher one

5.7.2.1.2 Negative Effects

Generally, five covariates, including weekly money to spend/save oneself, the number of smoking friends, school support for quitting drugs and alcohol, sex (being males), and sedentary time had consistently negative effects on the dynamic transitions from a lower use pattern to a higher one. For instance, for the covariate "the number of smoking friends" (see Figure 35), with all the other

variables held constant, among students who started in the no-use subgroup (S1) at Wave I, those who reported having one smoking friend were more than 2.98 times likely to transition to the current multi-use subgroup (S4) in relation to S1 at Wave II than were those who reported zero friends who smoke. The same OR applies to "None" vs. "1 friend" vs. "2 friends" vs. "3 friends" vs. "4 friends" vs. "5 or more friends."

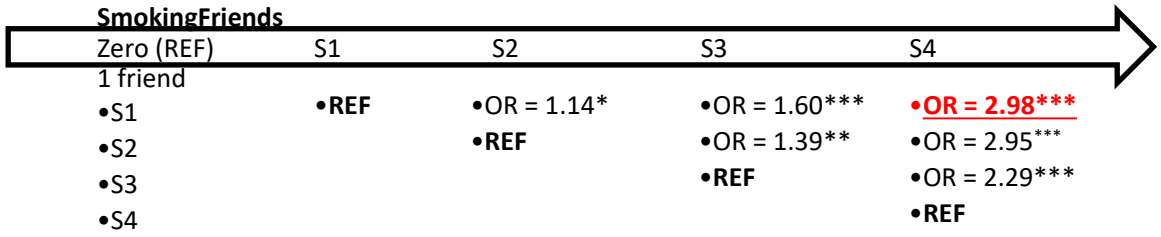

Figure 35. Example of negative effects on the dynamic transitions from a lower use pattern to a higher one

5.7.2.1.3 Mixed Effects

More covariates had mixed effects on transition probabilities than on initial probabilities. The variables with inconsistent effects on the transition probabilities from a lower use pattern to a higher one include urbanity, the number of physically active friends, the number of skipped classes, BMI category, school connectedness, and gamble online. Taking the GambleOnline effect as an example, with all the other variables held constant, among students who started in the single-use of alcohol subgroup (S2) at Wave I, those who reported not gambling online for money for the last 30 days were more than 3.34 times likely to move to the multi-use subgroup (S4) in relation to S2 at Wave II than were those who reported gambling online. Whereas among students who started in the no-use subgroup (S1) at Wave I, those who reported not gambling online for money for the last 30 days were less than 0.17 times likely to transition to the current multi-use subgroup (S4) in relation to S1 at Wave II than were those who reported gamble online. Figure 36 demonstrates the mixed effects of GambleOnline on the dynamic transitions from a lower use pattern to a higher one, with a positive effect highlighted in **green** and a negative effect in **red**.

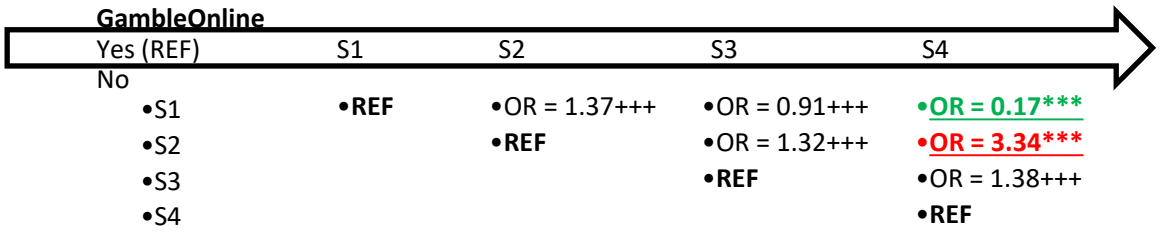

Figure 36. Example of mixed effects on the dynamic transitions from a lower use pattern to a higher one

5.7.2.2 Moving from a Higher Use Pattern to a Lower One

Likewise, the odds ratios on the lower-triangular matrix indicate the effects on transition probability from a higher use pattern to a lower one, conditional on the reference group at Wave I. A summary of the variables and their effects follows, based on the lower-triangular matrix presented in Table 25.

5.7.2.2.1 Negative Effects

Only two covariates, weekly money to spend/save oneself and sex, consistently affected the transition probabilities from a higher use pattern to a lower one in a negative way. Being males or having more weekly money was associated with an increased risk of dynamic transitioning from a higher use pattern to a lower one over time. For instance, among students who started in the dual-use of e-cigarette and alcohol subgroup (S3) at Wave I, male students were less than 0.36 times as likely to transition to the no-use subgroup (S1) in relation to S3 at Wave II than were female students, with all the other variables held constant. Figure 37 demonstrates the negative effects of gender on the dynamic transitions from a higher use pattern to a lower one.

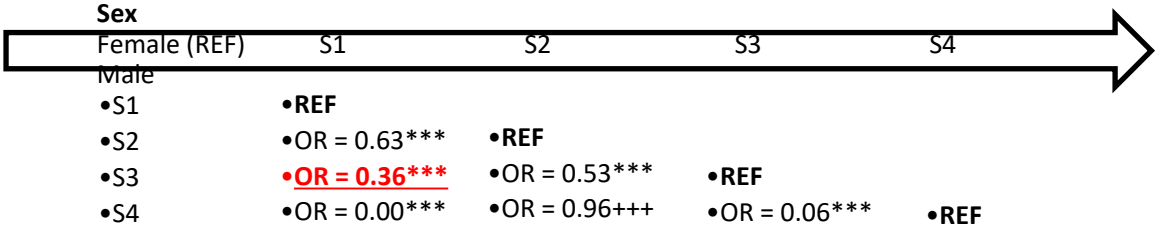

Figure 37. Example of negative effects on the dynamic transitions from a higher use pattern to a lower one

5.7.2.2.2 Mixed Effects

More covariates had inconsistent effects on the transition probabilities from a higher use pattern to a lower one. These variables are urbanity, grade/age, race/ethnicity, the number of physically active friends, eating breakfast, the number of smoking friends, school support for quitting drugs and alcohol, the number of skipped classes, BMI category, school connectedness, sedentary time, and gamble online. For example, with all the other variables held constant, among students who started in the single-use of alcohol subgroup (S2) at Wave I, those who reported not gambling online were more than 1.44 times as likely to transition to the no-use subgroup (S1) in relation to S2 at Wave II than were those who reported gamble online. However, among students who started in the current multi-use subgroup (S4) at Wave I, those who reported not gambling online were less than 0.68 times as likely to transition to the no-use subgroup (S1) in relation to S4 at Wave II than were those who reported gamble online. Figure 38 shows the mixed effects of GambleOnline on the dynamic transitions from a higher use pattern to a lower one, with a positive effect highlighted in **green** and a negative effect in **red**.

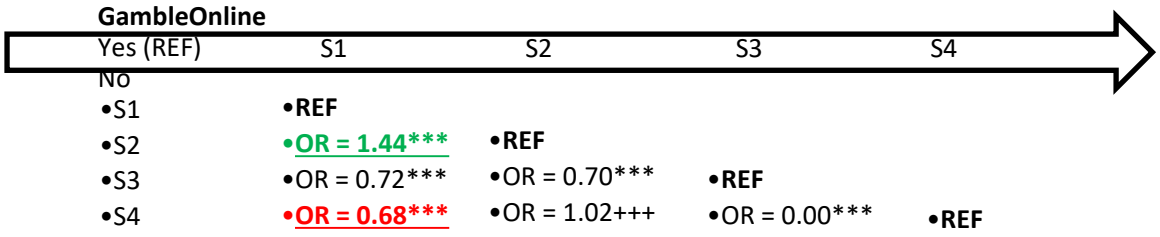

Figure 38. Example of mixed effects on the dynamic transitions from a higher use pattern to a lower one

In summary, this chapter reported the study results, starting from MI for missing values, descriptive statistics, factors associated with youth polysubstance use, risk profiles phenotypes, and the dynamic transitions of polysubstance use patterns among youth. The next chapter will discuss the key findings from public health and ML methodological perspectives, the contributions to the practice and the literature, strengths and limitations of this thesis, and future research directions.

Chapter 6
Discussion

This chapter discusses the key findings of this thesis, including the main results of risk profiling, patterns of polysubstance use among youths, and the dynamic transitions of these use patterns over time. The perceptions from a methodological perspective, particularly the selection and appropriate application of ML methods modelling risk profiles and dynamic transitions using the COMPASS data, ML interpretability and fairness, and data infrastructure and capacity that enables ML, are also discussed. Finally, the contributions of this thesis to public health practitioners and the research communities, the strengths and limitations, and future works are presented in this chapter.

6.1 Key Findings

6.1.1 Phenotyping Risk Profiles of Youth Polysubstance Use

6.1.1.1 Overview of the Risk Profiles and Associated Factors

One of the primary research questions (RQ1) of this thesis was, "What are the risk profiles of polysubstance use among Canadian secondary school students?" Before examining the risk profiles, we first identified the top eight factors associated with youth polysubstance use. Ranked by the variable importance, these factors include the number of smoking friends, the number of skipped classes, weekly money to spend/save oneself, sedentary time, CESD, school connectedness, eating breakfast, and grade (as a proxy of age). These factors are consistent with the findings in the literature. Some of the risk factors that correlate with polysubstance use among youth included age, sex, ethnicity, eating habits, PA and sedentary behaviour, social connectedness, and family and peer influence (see Chapter 2 Literature Review, Section 2.1.3). Although some studies reported that sex and race/ethnicity play an important role in youth polysubstance use (13,14,40,41), these two were not ranked as top features in the COMPASS data. Therefore, we did not include them for phenotyping risk profiles.

The four risk profiles of polysubstance use among Canadian youth identified in this thesis were low risk (L1), medium-low risk (L2), medium-high risk (L3), and high risk (L4), based on the three annual waves of the linked samples from the COMPASS datasets analyzed. This was achieved by

utilizing the top eight factors correlated with polysubstance use and the four substance use indicators, i.e., cigarette smoking, e-cigarette use, alcohol drinking, and marijuana consumption. Numerous studies in addiction research have examined the risk factors associated with polysubstance use among youth or have identified use patterns. To our knowledge, no literature thus far has ever taken such a holistic approach to explore ***risk profiles*** among youth. Although no direct comparisons between our results and other studies can be performed, this thesis sheds light on the phenotyping risk profiles of youth polysubstance use with cross-sectional and longitudinal evidence. The four profiles identified in this thesis provide a more comprehensive overview of the prominent characteristics for each of the different risk levels of engaging in polysubstance use among this cohort.

The following section discusses the heterogeneity in the prevalence and phenotype across these four risk profiles. The numbers presented in the next section represent the group average across the risk profiles unless otherwise stated.

6.1.1.2 Heterogeneity in Risk Profile Phenotypes

Overall, at Wave I, the majority of students (32.5%) were at low risk (L1), closely followed by L2 (31.5%) and then L3 (24.5%). Only about a tenth of students belonged to the high-risk (L4) profile for Wave 1, accounting for 11.5% of the total sample size (N = 8610), which equates to approximately one-third of the low-risk population for all three waves. This trend is observed across all three waves, except for Wave II, where a slightly higher percentage (35.4%) of students were at medium-low risk (L2) than those at low risk (L1, 34.7%) (see Tables 13-15 in Chapter 5 Results, Section 5.5.2). By examining the longitudinal prevalence across the three waves, we found that over time, the number of students at low risk (L1) increased (from Wave I to Wave III: 32.5% → 34.7% → 38.9%). In contrast, the number of students decreased at both the medium-high risk (L3, from Wave I to Wave III: 24.5% → 22.0% → 20.4%) and the high-risk group (L4, from Wave I to Wave III: 11.5% → 7.9% → 7.9%), over time. Interestingly, the prevalence of students at medium-low risk (L2) increased from Wave I to Wave II (31.5% → 35.4%) and decreased from Wave II to Wave III (35.4% → 32.7%).

In general, our findings reveal that students who belonged to the low-risk (L1) profile group, on average, had the lowest mean values (scores) for substance use, CESD, and sedentary time. They also had, on average, fewest smoking friends, fewest skipped classes, highest mean scores of school connectedness, and reported eating breakfast. On the contrary, those who belonged to the high-risk

group (L4), on average, had the highest mean values (scores) for substance use, CESD, and sedentary time. And in contrast to L1, they tended to have the highest number of smoking friends, the highest number of skipped classes, the lowest mean scores of school connectedness, and on average, reported not eating breakfast. Additionally, two intermediate risk profiles were identified between L1 and L4: the medium-low risk (L2) and the medium-high risk (L3) group. It is observed that similar trends of risk profiling appear throughout the three waves, showing consistent risk profiles over time, including the four substance use indicators and the top factors associated with youth polysubstance use.

It is observed that alcohol was the most prevalent substance used by Canadian youth, followed by e-cigarettes. Cigarette and marijuana shared a similar prevalence at Wave I across the four risk profiles. However, the prevalence of marijuana consumption increased more rapidly than that of cigarette smoking over time.

Based on the Boruta algorithm of variable importance ranking, the top 3 features that affect youth polysubstance use are unrelated to demographic information like age or sex. Instead, "the number of smoking friends," "the number of skipped classes," and "weekly money to spend/save oneself" ranked top 3 across the three waves. The first two features reflect peer influence and risky behaviour. The risk profiling indicates that peer influence has more impact on polysubstance use among youth than any other identified risk factors.

By investigating the cross-sectional evidence on other included factors, this thesis reveals that a sedentary lifestyle was associated with high risk of polysubstance use. Our finding agrees with West *et al.* (2020) that sedentary behaviour was positively related to adolescent drinking and marijuana consumption (130). Existing research indicates that sedentary behaviour might be a determinant for adolescent alcohol and marijuana consumption (130). The same trend was observed for Wave II and Wave III. Comparing L4 vs. L1 for the last two waves, the sedentary time differences were similar to Wave I, 6.09 times (1176/193) for Wave II and 5.70 times (1191/209) for Wave III. Similar to the top 3 factors, the magnitudes of sedentary time across the four risk groups (Wave III vs. Wave I) range from 1.16 times (L3) to 1.23 times (L1) over time.

Students in the high-risk group (L4) had a lower mental health status, which was indicated by the largest CESD scores. That is, the higher the CESD scores, the more significant the depressive symptoms that were reported. According to Radloff (1977), a CESD score $\geqslant 10$ indicates clinically relevant depressive symptoms (131). In Wave I data, students in the L4 group had a CESD score of

10.8 ± 6.70, indicating that, on average, this group of individuals already experienced clinically relevant depressive symptoms. In contrast, those in the low-risk group (L1) had the smallest CESD score of 7.08 ± 5.39. Subsequently, the medium-low (L2) and medium-high (L3) risk groups had average CESD scores of 8.34 ± 5.89 and 9.30 ± 6.04, respectively, with significant differences between each risk group. The same trend was observed in Wave II and III data. This agrees with Halladay *et al.* (2020), which also found an association between substance use and mental health. Many studies have found that individuals in the multi-use group report higher psychiatric symptoms, including depression and anxiety, than the single-use group (49,50). In a systematic review by Cairns *et al.* (2014), the authors identified polysubstance use as a modifiable risk factor for depression among youth (132).

Comparing across the four risk profiles L1 through L4 (Wave III vs. Wave I), the magnitudes of the CESD score were similar, 1.13 times (L1), 1.10 times (L2), 1.08 times (L3), and 1.13 times (L4), implying that the incremental rates for the CESD score were consistent across the four risk patterns over time. As previously discussed, students in the high-risk group (L4) already experienced clinically relevant depressive symptoms at Wave I and throughout Wave III due to the increasing CESD scores over time. It was noted that, on average, individuals in the L3 risk group started to have clinically relevant depressive symptoms at Wave III.

In addition, this thesis identified good nutritional habits, such as eating breakfast, were associated with the low risk of polysubstance use among Canadian youth. For example, at Wave I, the majority (65.4%) of the students in the low-risk group (L1) ate breakfast, while only 31.9% of the students in the high-risk group (L4) ate breakfast. The prevalence of eating breakfast decreased while the risk level increased from low-risk (65.4%), medium-low (51.6%), medium-high (42.4%), to high-risk (31.9%). This similar pattern can be seen throughout the three waves, as shown in Tables 13-15. Our finding is consistent with the literature about youth polysubstance use and the correlation of nutrition-related attitudes. For example, Isralowitz and Trostler (1996) reported that substance users were more likely to be at greater risk of poor eating habits, including not eating breakfast or not eating three meals daily (52).

The longitudinal evidence of the risk profiles concerning the four substance use indicators showed that, in general, the scores of these indicators increased across the three waves, indicating that with time, students engaged to higher use of each substance across the risk profiles (L1 through L4). Note

that the incremental rate of marijuana consumption in the low risk (L1) group from Wave I to Wave III was the largest (6.17) among the four substances, followed by e-cigarette use (4.71), cigarette smoking (3.5), and alcohol drinking (1.64). Comparing the incremental rates of the score of substance use indicators across the four risk profiles, the low-risk group had the most significant increase, followed by L2, L3, and L4, subsequently.

Lastly, using students' grade level as a proxy of their age, this thesis identified that age was one of the top factors associated with youth polysubstance use. Among the four risk profiles identified, the high-risk group comprises mainly older students, while most low-risk groups were their younger peers. For example, within the low-risk group (L1) at Wave I, 23.9% of students were in grades 7/8 and 26.9% in grade 10. In the high-risk group (L4) at the same wave, only 7.8% of students were in grades 7/ 8, and 42.9% were in grade 10. A similar pattern was observed at Wave II and III (see Tables 13-15 in Chapter 5 Results, Section 5.5.2). This finding concurs with published literature that the age of adolescents directly correlates with increased risk of using substances (13,32,41,44,46,133,134), i.e., the older the youth, the higher the likelihood of using substances.

6.1.2 Patterns of Polysubstance Use Among Canadian Secondary School Students

6.1.2.1 What are the Polysubstance Use Patterns?

Another primary research question (RQ2) investigated in this thesis was, "What are the patterns of polysubstance use among Canadian secondary school students?" We identified four distinctive polysubstance use patterns among youth, which were no-use (S1), occasional single-use of alcohol (S2), dual-use of e-cigarette and alcohol (S3), and current multi-use (S4). Each use pattern represents a mutually exclusive overarching theme. The patterns identified suggest an increasing tendency and frequency of polysubstance use with decreasing membership size with higher risk groups, and each use pattern has considerably different sizes.

Most studies on polysubstance use among youth focus primarily on tobacco, alcohol, and marijuana use due to the high prevalence of use in this cohort (67). E-cigarettes have not been considered in many of these studies due to their novelty. However, the popularity of e-cigarette use has surged among youth in recent years; it may now be a significant contributing factor to the rise in youth polysubstance use (13,14). Morean *et al.* (2016) examined the co-use of multiple substances such as tobacco products, e-cigarettes, alcohol, and marijuana among high school students in

Connecticut, US (133). They identified four classes of use: abstainers (82% of the sample), alcohol and e-cigarette users (5%), cannabis and alcohol users (7%), and users of all products (7%) (133). Recent research identifies use patterns that involve dual- and multi-use of e-cigarettes with other substances, indicating the importance of considering these devices when examining multiple substance use (133).

In the existing literature on youth polysubstance use utilizing LCA, most studies have identified three or four patterns of polysubstance use (32). Typical patterns include no or low use, alcohol use (i.e., alcohol only or predominantly alcohol use), and polysubstance use (32). In a systematic review of substance use patterns among youth, Halladay *et al.* (2020) highlighted an average of four use patterns, including low use, one- or dual-use, moderate multi-use, and high multi-use (67). Their results have been drawn from 70 individual studies and 89 cluster solutions. Before model enumeration, the minimum and maximum users are two and six, respectively (67). Our research has identified four use patterns, which align with the findings by Halladay *et al.* (2020).

6.1.2.2 What Factors are Associated with Patterns of Polysubstance Use?

One of the secondary research questions (RQ4) examined in this thesis was, "What factors are associated with patterns of polysubstance use among Canadian adolescents?" Existing evidence suggests that the factors impacting youth polysubstance use patterns include gender, race, early onset of alcohol drinking, academic achievements in secondary school, and friendship goals (135). According to Lanza, Patrick & Maggs (2010), examining alcohol, cigarette, and marijuana use, males were 4.5 times more likely to be in the highest use group ("bingers with marijuana use") than their female counterparts, in comparison to non-users (135). However, with non-users being the reference, in contrast, females were more prone to smoking cigarettes (OR = 1/0.6) or binge drinking (OR = 1/0.9) than their male counterparts (135). Their findings were consistent with the results of this thesis concerning the mixed effects of gender on polysubstance use membership among youth. Yet, the gender difference between the study results by Lanza, Patrick & Maggs (2010) and ours was inconsistent.

In this thesis, the gender of the cohort had mixed effects on the initial probabilities for different use patterns. In particular, we found that males were 1.34 times more likely to start in the dual-use of e-cigarette and alcohol subgroup (S3) than females, relative to the no-use subgroup (S1). In contrast, at Wave I, females were 1.35 times more likely to engage in occasional single-use of alcohol (S2) and

1.25 times more likely to experience current multi-use (S4), the highest use group in this thesis than their male peers, relative to S1. Except for the implication that female students tend to be more likely to engage in alcohol intake than their male counterparts, the disparity in gender differences between our findings and those by Lanza, Patrick & Maggs (2010) could be due to the differences between substance use indicators and the corresponding measurements assigned. For instance, this thesis included e-cigarette as an emerging substance, whereas Lanza, Patrick & Maggs (2010) did not. Additionally, this thesis did not differentiate between regular drinking and binge drinking for alcohol use, as was it done by Lanza, Patrick & Maggs (2010). Some other differences include the method of data collection and the age of the population. Lanza, Patrick & Maggs (2010) used data collected at baseline and 14-days follow-ups in Fall 2007 and Spring 2008 among first-year college students (135). In comparison, our three waves data were collected from 2016-2017 among secondary school students. As such, a difference in nearly a decade in data collection and a study population age and level of education difference between the two studies cannot be neglected as contributing to the difference in findings.

There is inadequate literature about factors that impact the initial membership of polysubstance use patterns among youth. Regarding race/ethnicity contributing to polysubstance use membership among youth, Lanza, Patrick & Maggs (2010) identified that Hispanic Americans were 1.5 times more likely to be cigarette smokers or "bingers with marijuana use" than European Americans, relative to non-users. African Americans and Asian Americans were less likely to engage in substance use than European Americans relative to non-users (135). Our results showed that Black students were 0.92 times less likely to engage in the single-use subgroup (S2) than their White peers, relative to non-users (S1). Concerning the no-use subgroup (S1), the odds ratios to start in the dual-use (S3) and current multi-use pattern (S4) for Black vs. White were 0.94 and 0.96, respectively. The study results indicate that Black students were less likely to engage in a higher use group than their White peers, same as Black vs. Asian, Asian vs. First Nations, First Nations vs. Latin American/Hispanic, and Latin American/Hispanic vs. Other. However, the effect was not statistically significant for S4 vs. S1.

In addition to the gender difference and race/ethnicity, what brings new insights into the literature on the patterns of youth polysubstance use in this thesis is the multifaceted covariates and their effects that we examined. Within the limited evidence, no other studies included all the variables investigated in this thesis to evaluate the impact on the initial membership of use patterns, summarized based on

their positive, negative, or mixed effects. One should be cautious about interpreting the BMI effect on the initial membership. The missing values were coded as one category instead of performing multiple imputations as other missing data. However, the results show that the BMI category did impact the initial probabilities of the use pattern membership. Generally, the higher the BMI (i.e., not stated vs. underweight vs. healthy weight vs. overweight vs. obese), the more likely the individual started in a higher use pattern at Wave I.

It is observed that students who reported, for example, at lower grade levels (e.g., grades 7 or 8), residing in Quebec, living in large urban settings in Canada, from a household income level between $25K and $50K, or being underweight according to their BMI, tended to belong to the no-use (S1) subgroup. Additionally, students with these characteristics generally had a lower chance of being at the other three higher use groups (S2 to S4) than non-users (S1) at Wave I. In contrast, at Wave I, students with the highest grade (grade 10), residing in Alberta, from rural areas across Canada, self-identified as Indigenous, or being obese according to their BMI had a higher chance of belonging to one of the higher use groups (S2 to S4) and a lower chance of being in the no-use (S1) subgroup.

6.1.3 Exploring Dynamic Transitions of Youth Polysubstance Use Patterns

6.1.3.1 How Do Transition Behaviours Change Over Time?

One of the primary research questions (RQ3) explored in this thesis was, "How do transition behaviours change over time according to use patterns analysis?" The LMM applied for this thesis allowed us to investigate the dynamics of polysubstance use patterns among youth. In general, the resulting transition probabilities provide us with two aspects of the dynamics across time, i.e., *stability* (a subject stays in the same subgroup) and *change* (transitions to another subgroup). This section discusses our findings surrounding these two perspectives.

6.1.3.1.1 Stability

Our results revealed that generally, students remained in the same use pattern subgroup across time. On average, across the three waves, the probabilities for students staying in the no-use (S1), single-use (S2), dual-use (S3), and multi-use (S4) subgroup were 0.5740, 0.5210, 0.7092, and 0.8668, respectively. The current multi-use (S4) was the most stable use pattern, followed by the dual-use (S3) and the no-use (S1) pattern. Among these four patterns, occasional single-use of alcohol (S2)

was the least stable pattern, with the probability of remaining in this subgroup across time was the lowest (0.5210). When they transitioned, it was typically to a higher use pattern adjacent to their current subgroup (i.e., S1 → S2, S2 → S3, or S3 → S4), rather than to a lower one, except for the highest use group S4. This finding is consistent with current literature that examines adolescent polysubstance use with LTA. The evidence suggests that youth are most likely to remain in the same subgroup of use pattern or transition to a higher use group as they grow older (134,136).

A similar trend was observed by investigating the longitudinal evidence of the transition patterns, i.e., Wave I → Wave II and Wave II → Wave III. In particular, from Wave I to Wave II, probabilities for students staying in the no-use (S1), single-use (S2), dual-use (S3), and multi-use (S4) subgroup were 0.5845, 0.5271, 0.7176, and 0.8361, respectively. From Wave II to Wave III, the probabilities were 0.5635, 0.5149, 0.7007, and 0.8975 for remaining in the S1, S2, S3, and S4 subgroup. It is observed that the chance of staying in S4 from Wave II to Wave III was higher (Δ = +0.0614) than that of from Wave I to Wave II, meaning that with time, current multi-users were more likely than the last time occasion to stay in this highest use pattern subgroup. While for the other three use patterns (S1 through S3), the stability decreased over time (Δ_{S1} = -0.0210; Δ_{S2} = -0.0122; and Δ_{S3} = -0.0169). The decreased stability implies that students starting at any of these use patterns had an increased chance of transitioning to other use patterns across time.

6.1.3.1.2 Change

Table 20 highlights the changing pattern, with underscores indicating the largest transition probabilities within each subgroup. For example, on average of the two transitions (i.e., Wave I → Wave II and Wave II → Wave III), for students in the S2 subgroup, the chance of moving to S3 was 0.4447, the largest probability representing the change of use patterns across the three waves. The second-largest transition probability was S3 → S4 (0.2804), followed by S1 → S2 (0.2510). In contrast, students in the S3 subgroup were least likely to transition to S2, with the slimmest chance of 0.0007. Similarly, students in the S4 subgroup were unlikely to move to S2 across time, with the transition probability being 0.0051. In addition, those in S2 or S3 subgroups were less likely to transition to the S1 subgroup, with small transition probabilities for S2 → S1 (0.0061) and S3 → S1 (0.0098).

Similar to the longitudinal observation of the transition probabilities for stability, we examined the incremental change in transition probabilities, comparing Wave II → Wave III vs. Wave I → Wave

II. Concerning *change*, in general, the chances of transitioning from a lower use pattern to a higher one increased over time. This was determined by the increased transition probabilities across time (positive Δ in Table 23 in Chapter 5 Results, Section 5.7.1). On the contrary, the decreased transition probabilities (negative Δ in Table 23) indicate slimmer chances of moving from a higher use pattern to a lower one with time. There were two exceptions, moving from S1 to S2 and S2 to S4, with decreased probabilities of 0.0005 and 0.0011, respectively.

Note that the measurement interval of cigarette and e-cigarette smoking was the last 30 days, whereas the measurement interval of alcohol and marijuana use was past year. Many transitions may have occurred between when student participants were asked about cigarette or e-cigarette smoking in the last 30 days at Wave I and when they were asked again one year later. It is impossible to estimate how much movement between subgroups has occurred between these measurement windows for these two specific substances. In this case, the upper bound of the diagonal elements and the lower bound of the off-diagonal elements of the transition matrix were used to explain the transition probabilities (68). Although the lower bound of the off-diagonal elements tends to underestimate transition over time, the general transition pattern is consistent, as previously discussed.

It is worth noting that not only do use patterns change with time but so does the evidence in use patterns. For example, with the emerging trend of e-cigarette use among youth, adding e-cigarette as new evidence while examining use patterns would be more meaningful than ever. Unfortunately, no prior research examined the dynamic transitions of polysubstance use patterns among youth include the e-cigarette as a substance use indicator. It contributes to one of the novelties to this thesis. In the meantime, it makes the direct comparison between our findings and others impossible.

6.1.3.2 What Factors are Associated with Dynamic Transitions of Use Patterns?

One of the secondary research questions (RQ5) explored was, "What factors are associated with dynamic transitions of use patterns?" Choi *et al.* (2018) reported that males were more likely to transition from using legal to more illicit substances than females, while female polysubstance users were more likely to transition to a less use pattern than males (131,135). Although we did not examine licit vs. illicit substances in this thesis, the finding is consistent with our results. Our finding of the gender difference on the dynamic transition of use patterns indicates that male students were more likely to transition to a higher use group and were less likely to transition to a lower one than their female peers over time. For example, among students who started in the no-use subgroup (S1) at

Wave I, males were 2.53 times more likely to transition to the current multi-use subgroup (S4) at Wave II than were female students. Whereas transitioning from a higher use pattern to a lower one, among students who started in the current multi-use subgroup (S4), females were 16.67 times more likely to move to the dual-use subgroup (S3) relative to S4 at Wave II than were males.

Except for the gender difference, there is inadequate literature about what other variables lead to the dynamic transitions of membership. Thanks to the rich longitudinal evidence available in the COMPASS data, we examined multifaceted covariates to determine if they were significant in predicting the subgroup membership at baseline (Wave I) as discussed in Section 6.1.2.2 or predicting the dynamic transitions of use patterns over time. These covariates range from demographic information to health behaviours, from individual-level to population-level (environmental). Ultimately, our study results provide new insights into what characteristics lead to the dynamic transitions of youth polysubstance use patterns, summarizing in two directions, i.e., moving from a lower use pattern to a higher one or the other way around.

On the bright side, students in a higher grade (grade 10 vs. grade 9 vs. grade 8 vs. grade 7), being Black (vs. White[10]), or eating breakfast were less likely to transition from a lower use pattern to a higher one. Among these covariates, eating breakfast had a statistically significant effect on the dynamic transition of use pattern membership except for moving from S2 to S4. Except for transitioning from S2 to S3 and S3 to S4, grade/age significantly affected the dynamic transition of use pattern membership. Race/Ethnicity demonstrated statistical significance in the dynamic change of membership, i.e., S1 → S2, S1 → S4, and S3 → S4. On the other hand, having more weekly money, having more smoking friends, attending schools with less support for quitting drugs and alcohol, being male, or experiencing larger sedentary time were more likely to transition from a lower use pattern to a higher one. In particular, having more weekly money or being male was less likely to experience a positive change, i.e., transition from a higher use pattern to a lower one over time.

The other covariates, including urbanity, the number of physically active friends, the number of skipped classes, BMI category, school connectedness, and tendency to gamble online, had mixed effects on the transition probabilities from a lower use pattern to a higher one. Among these covariates, school connectedness had statistically significant effects on the transition probabilities of

[10] The same OR applies to the comparison of other ethnicity categories, i.e., Other vs. Latin American/Hispanic vs. First Nation vs. Asian vs. Black vs. White

use patterns for individuals who started in the S1, S3, and S4 subgroups. The number of physically active friends significantly affected the transition probabilities for students who began in subgroups S1 and S4. Urbanity, the number of skipped classes, and BMI category significantly affected the dynamic transition of use pattern membership in S3 and S4. The covariate GambleOnline demonstrated non-significance on the dynamic change of membership for any subgroup.

We found that more covariates had mixed effects by investigating the transition probabilities from a higher use pattern to a lower one. These additional covariates included grade/age, race/ethnicity, eating breakfast, the number of smoking friends, school support for quitting drugs and alcohol, and sedentary time. It is observed that many covariates had significant effects on the transition probabilities among some use pattern subgroups. However, none of the covariates was consistently significant for the dynamic transitions between all use pattern membership (see Table 25 in Chapter 5 Results, Section 5.7.2).

In summary, our findings indicate that the factors leading to the dynamic transitions of use patterns are multifaceted. Their effects are more complex than those on the initial membership of use patterns. Some factors, such as grade/age, race/ethnicity, are non-modifiable. Public health practitioners should pay more attention to those modifiable factors, including individual health behaviours (e.g., eating habits, PA and sedentary lifestyle), peer influence (e.g., friends who smoke), and environmental impact factors (e.g., school support initiatives). On that note, more discussion follows in Section 6.2.1.

6.1.4 Learnings from ML Methodological Perspectives

One of the secondary research questions (RQ6) asked, “What are the advantages and limitations of the ML methods appropriate to modelling risk profiles and dynamic transitions using the COMPASS data?” This section addresses RQ6, discussing the two feature selection methods applied in this thesis, unsupervised ML methods for phenotyping risk profiles and an LMM approach for exploring the dynamic transitions of use patterns. Then we discuss perceptions from ML interpretability and fairness to data infrastructure and capacity that enables ML in public health.

6.1.4.1 Feature Selection

While working with high-dimensional datasets, mainly where the number of features is much larger than the sample size, raises the problem called “the curse of dimensionality.” As the number of

features increases, the number of samples needed to train the model increases proportionally. Although this issue is not prominent in our study, redundant or unnecessary variables exist for model fitting on the COMPASS dataset. Therefore, performing dimensionality reduction and selecting the most appropriate features for model fitting is an essential step in our analysis. As previously discussed in Chapter 4 Methods, Section 4.4.1, we prefer feature selection approaches over feature extraction due to better interpretation of the model.

In an unsupervised learning paradigm, the class label is unknown, which increases complexity and uncertainty. Unsupervised feature selection methods tend to address this issue. For example, Laplacian Score is one of the unsupervised feature selection algorithms. However, the idea behind Laplacian Score is to employ the k-means clustering method to select the top k features. Unfortunately, the disadvantages of the k-means clustering algorithm significantly affect the feature selection result, increasing the complexity of the Laplacian Score. For example, some of the disadvantages of the k-means clustering algorithm include: 1) it requires *a priori* knowledge of the optimal value of k, 2) it is sensitive to noise and outliers, and 3) it is sensitive to an initial assignment of the centroid (i.e., different initial partitions can lead to different clustering results). As a result, the preliminary results applying the Laplacian Score for feature selection are highly inconsistent across the three waves datasets, with less meaningful interpretation. Therefore, we did not implement an unsupervised feature selection method for further analysis.

Moreover, preliminary feature selection results for clustering analysis indicated that including all features tends to cause overfitting. In addition to learning from the data and identifying authentic patterns, the clustering algorithms also learn from stochastic noises in the dataset and thus identify "patterns" that are not representative of the COMPASS data. On the contrary, too few features in this research, such as less than 5, also impact clustering results based on the internal validation criterion. Therefore, different subsets of features have been experimented with to leverage the model performance and a more meaningful clustering solution. Eventually, a subset of features (top 8) that contributes to the risk profile phenotypes was identified.

In this thesis, we explored two commonly used embedded feature selection approaches. In particular, Boruta uses a random forest-based algorithm to select the top features for clustering analysis. For the selection of covariates fitting the LMM, regression-based LASSO (or L1 regularization) was applied. Each method has its advantages and limitations. For example, as an

approach to model fitting and variable selection, LASSO can be used for different regression types. Regularization adds additional constraints or penalties to a model for preventing overfitting and improving generalization. Each non-zero coefficient will increase the penalty in LASSO regression and force the coefficient of weak features to zero. Therefore, LASSO regression produces sparse solutions, meaning that few features are used in the prediction model. When the number of non-zero parameters is small enough, practitioners can interpret whether the variables corresponding to these parameters are meaningful or not. LASSO has proven to be a better method than other automatic variable selection approaches in statistical modellings, such as forward selection, backward elimination, and stepwise selection. However, LASSO tends to ignore non-significant features that may be important to the response variables during the penalization procedure. To overcome this drawback, we purposely selected the largest subset of features from the results of LASSO regression on the three waves data.

6.1.4.2 Phenotyping Using Unsupervised Learning Methods

To our knowledge, none of the studies in the current literature on youth polysubstance use ever took such an approach of phenotyping risk profiles. Instead, individual risk factors associated with substance use among youth have been identified, and the statistical power of each factor has been investigated. Applying statistical models, such as LCA for static class membership analysis and LTA for the dynamic membership transition, polysubstance use patterns among youth have been examined. Clustering algorithms, primarily k-means and hierarchical clustering, have been employed for identifying use patterns. However, none of these studies assessed risk profiling of youth polysubstance use, involving the indicators of substance use and their multifaceted impact factors.

Unsupervised learning methods, particularly the various clustering algorithms implemented in this thesis, showcase their capability of revealing the hidden patterns in the COMPASS dataset. We implemented different similarity and dissimilarity measures, including Euclidean distance and Gower distance specific to categorical data. The preliminary results indicate that using the Euclidean distance matrix achieved better clustering results with a higher silhouette index than Gower distance. Furthermore, for hierarchical clustering, among the different linkage methods discussed in Chapter 2 Literature Review, Section 2.2.2.2.2, average linkage outperforms other linkage methods.

Cluster analysis has advantages and potential limitations; for example, the various clustering algorithms usually provide very different results due to the different criteria for merging clusters.

Although cluster analyses have unique advantages for revealing “hidden” patterns and unexpected associations in variables, no backward option can be made in earlier steps due to the hierarchical nature of the analysis. Therefore, to mitigate these limitations, we implemented various clustering algorithms, including partitioning-based, hierarchical-based, and fuzzy clustering. The first two types of cluster methods are hard clustering algorithms that assign data elements to one cluster. Unlike hard clustering, fuzzy clustering algorithms are soft-clustering methods, assigning membership coefficients of objects to all clusters.

Particular focus was given to fuzzy clustering algorithms, considering the overlapping nature of risk profiling observed on the linked sample of COMPASS data. Both the FCM and FANNY algorithms were implemented in this thesis. The optimal number of clusters was determined by implementing multiple validation indices available in the NbClust package. In addition, an automatic voting scheme was applied to avoid bias towards a specific criterion, such as the silhouette index alone. The majority of indices proposed 4 clusters as the optimal number for the linked COMPASS data.

Moreover, one hyperparameter to determine the distribution of membership values was tuned with variation between 1 and 2 to evaluate the appropriate value of the fuzziness. The fuzziness parameter (a.k.a. fuzzifier) is a weighting exponent; closing to 1 indicates hard clustering. The larger value of the fuzzifier, the better the FCM handles noise and outliers. In this thesis, we set the fuzzifier to equals 2. Except for the silhouette index, an internal index, external indices like ARI and VI were assessed for each pair of clustering algorithms. Compared to FCM clustering, the FANNY algorithm slightly outperforms FCM on both the internal and external validities across the three waves data, achieving good agreement on clustering membership.

6.1.4.3 Exploring Dynamic Transitions with an LMM Approach

As longitudinal data becomes more available in many fields, researchers rely on specific statistical models tailored to their applications. This thesis applied an LMM modelling technique on a linked sample of the COMPASS dataset, with three annual waves available for analysis. LMMs can provide three types of analysis, including i) identifying subgroups of units and examining how the transition occurs between these subgroups, ii) transition analysis with measurement errors, and iii) unobserved heterogeneity analysis (27). When we estimate the LMM with a function lmest available in the LMest

package in R, we estimate the covariates' effects on the initial probabilities of various use patterns and the transition probabilities of the use pattern membership.

Started with the basic version of the LMM without covariates, the preliminary results yield a relatively large number of latent statuses ($k = 10$) with the lowest $BIC = 121524.6$. Then we tried model fitting with 29 covariates selected from the Boruta algorithm, the number of latent statuses reduced to $k = 4$. However, the corresponding $BIC = 124018.1$, and the number of parameters for estimation increased to 497. The evidence showed that the more covariates added in the LMMs, the more complex the model is. It implies potential overfitting.

Eventually, we added the covariates selected from the LASSO regularization into the basic version of the LMM. During fine-tuning of the models, it is observed that fewer covariates lead to a larger value of k, which increases the difficulty of interpretation. There is a trade-off between the appropriate number of latent statuses (k) and the BIC value. The model selection was performed based on adding covariates derived from the LASSO regression with certain constraints, as discussed in Chapter 5 Results, Section 5.4.3. The best model was selected considering both the lowest $BIC = 122349.6$ and the parsimony of the selected model with 257 parameters for estimation, compared to other fitted models.

To evaluate the goodness-of-fit for the selected LMMs, we used the index R^2. The main difference between BIC and R^2 is that the latter is suitable for measuring overall fit instead of comparison between models because model complexity is not included in the index R^2. In this thesis, the values of R^2 where $k = 4$ were very similar, ranging from 0.4838 (M_{16}) to 0.4861(M_1), indicating the overall fit amongst the fitted models is good. This confirms the adequacy of the proposed LMM modelling using the COMPASS data at hand.

In terms of computational complexity, the EM algorithm converged much faster on the basic version of the LMM without covariates than the subsequent models with various constraints. It is observed that the EM algorithm rapidly increases the log-likelihood, but the run-time becomes much slower when it is close to convergence.

This thesis has demonstrated that LMMs can be used to evaluate how the polysubstance use patterns among youth transition over time using the multivariate COMPASS dataset with selected covariates. It is generally recommended that the LMM methodology considers transition profiling of

latent processes corresponding to health behaviours without standard measurement protocols. To analyze longitudinal data with repeated observations, LMMs take advantage of the additional information, detecting other latent states compared to using the LCA method at each point in time. This provides the LMM methodology with greater statistical power than LCA. Moreover, LMM is particularly suitable for evaluation intervention monitoring and evaluation studies because it can model dynamics in latent states transition and hypothesis test the measurement invariance across time (27).

6.1.4.4 ML Interpretability and Fairness

Along with the rising opportunities, there also exist challenges to adopting ML approaches in public health. For instance, although ML models are recognized for their predictive powers, how they function and achieve this end remains obscure. As a result, some ML models, particularly those using deep learning techniques, are considered a "black box." This thesis challenges this assumption and provides practitioners with the appropriate tools to explain the ML model. The most fundamental reason is a lack of explainability/interpretability in outcomes that creates hesitation in adopting and implementing policies driven by ML. Interpretability is the degree to which a human can understand how a decision is made (19). Interpretability of model output and models themselves has been noted as a concern for ML has been applied to public health and clinical medicine (19). Early clinical applications of ML were criticized for "black-box" decision-making processes, but this issue can now be mitigated using interpretable models and model-agnostic methods (19). For reasons of interpretability and knowledge creation, parsimony is a crucial attribute of classical statistical methods. ML also emphasizes parsimony, with the simplest possible explanation of the data still fits the model reasonably well. For example, in this thesis, we selected the final LMM based on the BIC criterion with fewer latent states than the AIC value indicating a larger number of latent states.

Interpretability can be helpful in model validation, model debugging, knowledge discovery, and social acceptance. We investigate fairness and trust through model validation, i.e., whether the ML model has employed valid evidence instead of biases. Debugging and analyzing the misbehaviour of models can assist in accountability and transparency of the modelling results. Obtaining new insights from the decision-making process of the ML model can achieve knowledge discovery. Health researchers are currently investigating if ML algorithms would have better success in end-user acceptance if they can provide rationale/justification for its prediction. With increased efforts towards

achieving interpretability, we expect (are hopeful) that ML decision-making systems will become more acceptable, and in turn, play a more conducive role in human decision processes.

Working towards fairness and justice goals, ML models that are FAT-driven can mitigate the effects of unwarranted bias or discrimination on people in the ML applications. Fairness is inherently a social and ethical concept, representing a growing area of interdisciplinary research. The primary focus is on algorithmic formalisms of fairness and developing solutions for these formalisms. In this thesis, we attempted to address issues of fairness and bias in the following ways. Firstly, instead of handpicking important variables based on substance use research available in the literature, we applied feature selection algorithms as previously discussed. These algorithms are robust and highly interpretable among ML algorithms for automatically selecting a subset of features important to youth polysubstance use applicable to the COMPASS dataset. Secondly, having unbiased approaches in mind, we applied a voting scheme to determine the optimal number of clusters from all available indices to avoid biases towards a specific criterion. Although issues of fairness are out of the scope of this thesis, as ML practitioners, we could examine further by conducting subgroup analysis based on students' demographic differences to achieve a fairer interpretation of the modelling results.

Note that the definition of bias differs from statistics (such as the bias-variance trade-off) or social science. Instead, algorithmic bias has a wide range of social and political influences, and in these scientific fields, the exact meaning of bias may become blurred. Even the dataset itself can reflect human biases since humans sometimes label data. The dataset may also exclude specific populations or not be representative. Biases beyond statistical contexts are our focus when discussing this issue. According to Danks & London (2017), different algorithmic biases co-exist in autonomous systems, including biases deriving from training data, algorithmic focus or processing, transfer context, and interpretation (137).

Various strategies can be employed at different developmental stages to create a fair ML system, i.e., preprocessing, training, and post-processing. For example, eliminating sensitive features from the dataset is a naïve approach for unbiased ML models at the preprocessing stage, which can be achieved by applying dimensionality reduction techniques. At the training stage, the adversarial debiasing method can be utilized by training two models simultaneously (138). While at the post-processing stage, the decision threshold for different subgroups can be shifted towards meeting the fairness goals. For predictive models, calibration can be performed to ensure that the matching ratio

of actual labels reflects the probability output. A well-calibrated model will have similar error rates across different values of sensitive features (137).

6.1.4.5 Data Infrastructure and Capacity Enabling ML

Rosella, Fisher, and Song (2019) identified the opportunities for adopting ML solutions in public health, including more quickly identification of emerging threats, more detailed and up-to-date understanding of population disease and risk factor distributions such as online disease surveillance tools, forecasting of disease incidence of population health planning, improved targeting of health promotion activities such as sentiment analysis, and many more related to population health management. In the meantime, there exist challenges from explainability, bias, security and privacy concerns, data access and sharing, outdated data and analytic infrastructure, and lack of ML education and skills within public health.

Availability of high quality and adequate quantity of data is essential to enable ML systems. First of all, ML algorithms rely on a good quality large volume of training data. Although ML is known for making predictions and focusing less on variables, understanding the data is essential. This includes data elements, variable characteristics, data collection and data quality procedures, such as who collects data, how often data is collected, self-reported survey questionnaires, unmoderated or in-person moderated, and so on. From a data science perspective, both the quantity and quality of training data contribute to the successful adoption of ML systems. Taking a prescriptive approach, collecting, organizing, analyzing, and infusing data are deemed a four-step AI ladder as part of data management (139).

Data infrastructure enables data-driven decision-making (e.g., analytic techniques) and drives AI-powered solutions, including information systems with ML-enabled intelligence. The data infrastructure ranges from the pipes that carry data to storage solutions such as cloud-based storage analytics that house data, ML models that analyze data, dashboards that make data easy to understand and interpret ML models, and much more. From ML libraries to automated data pipelines, to data catalogues, depending on the goal of scaling up or scaling down, ML-enabled intelligent infrastructure varies. Data infrastructure requirements can be distilled down to the following key areas: compute integration, data persistence and access, scaling and tiering, software-defined storage, deployment agility and flexibility (140).

The capacity that enables ML (or AI ecosystem) includes technical aspects (e.g., computational power, data environment, data interoperability, legacy system migration), organizational or management capacity/incentives, and environmental or societal capacity fostering ML applications. When organizations are ready to scale their ML applications, they face a wide range of challenges. From data preparation to model development to runtime environments to training, deploying, and managing ML models, the requirements for the underlying infrastructure defy the old models of general-purpose hardware. Investments in an infrastructure designed for data-intensive workloads, superior performance, scaling, data access and integration, and blend into a hybrid cloud environment provide long-term value and service quality. Organizations will need to make decisions about replacing or supplementing existing general-purpose storage platforms with storage systems that are geared towards ML-specific processing tasks.

Adequate talent is a vital capacity to ensure the successful adoption and scale-up of ML systems. Bridging and accelerating joint research with ML techniques applied in public health require more interdisciplinary training and a research environment. Thus, addressing the shortage of ML education and skills within public health is a mandate. ML certificate programs and online courses provide a good opportunity for data science practitioners to obtain the necessary education and skills to adopt ML. Increasing numbers of ML certification courses are available, such as ML Stanford Online, eCornell ML Certificate, Harvard University ML, to name a few (141). Similar certificate programs are offered by prestigious universities, such as Applied AI for Health Care by Harvard University, AI in Healthcare by Stanford, AI in Health by the University of Toronto, etc. However, professional training on ML in public health seems lacking. Designing and delivering ML courses customized for students at schools of public health can facilitate the best preparation of existing and new students with appropriate education and skills working in the public health sector after graduation. All of this will serve as the foundation for developing and running cutting-edge ML solutions.

6.2 Contributions

6.2.1 Contribution to Practice in Public Health

The practice perspective brings insights from multifaceted COMPASS data to phenotyping risk profiles of youth polysubstance use and examining how the use patterns transition from one type to another across time. Youth is a crucial period of development and transition when risky behaviours

usually occur, such as polysubstance use. Taking advantage of an ongoing health survey from a sample of Canadian secondary school students and their attending institutions, it provides a holistic view of the longitudinal COMPASS data. The study results offer stakeholders evidence-based best practices to guide the implementation of the school environment, policies and procedures for improving youth health behaviours.

The complexity of student characteristics, modifiable individual-level risk factors, school environment and community-level status can lead to the transition of risk profiles. Taking the natural multilevel structure within the multiple sources of the COMPASS data brings new insights into strengthening the longitudinal evidence of risk profiling and polysubstance use patterns. There are distinct patterns in the associations between risk factors and polysubstance use among youth. The dynamic process of use patterns can inform clinicians and intervention experts how to deal with these behaviours at this developmental stage and throughout the process.

The thesis results have implications from public health and health policy perspectives. First, the study results suggest that the correlates of youth polysubstance use are multifaceted, concerning individual-level factors, peer influence, and population-level (environmental) effects. In the context of our research, age, sedentary behaviour, eating habits, depression status, truancy, weekly money to spend/save oneself, and school connectedness are individual-level factors. Peer influence includes the number of smoking friends and the number of physically active friends. Province and urbanity are population-level effects. The diverse associations between polysubstance use and multifaceted health-related behaviours should be considered for decision-makers who want to invest in interventions targeting multiple youth behaviours.

A good understanding of the risk profiles will help school program managers or policymakers identify and characterize valuable measures to evaluate control interventions. For instance, designing and implementing any quit smoking/alcohol/drugs programs should not be a stand-alone practice. Instead, the school policies should integrate such a program with other approaches like fostering PA, healthy eating, anti-depression, etc. Counselling programs such as peer mentoring or group therapy for high-risk students can help this cohort learn coping strategies, improve health behaviours, and prevent more costly substance abuse treatment later in their lives.

Furthermore, province and urbanity differences have been shown to impact the initial membership of polysubstance use patterns among Canadian youth at Wave I (see Table 19 in Chapter 5 Results,

Section 5.6.3). Therefore, provincial and federal jurisdictions should collaborate to establish more specialized preventive programmes tailored to the requirements of the youths. For example, our study results revealed that students from Alberta or living in rural areas had a higher chance of starting at a higher substance use pattern than those from other provinces or living in other urban areas (see Table 19). Particular programs should be considered in these jurisdictions to be more specific to these problematic areas.

The overall trend of substance use is increasing, and the four use patterns of substances identified in this thesis indicate an increase of severity by each subgroup. For example, our results revealed that students residing in the intermediate use pattern groups, particularly starting in the occasional single-use of alcohol (S2) subgroup at Wave I, were most likely to transition to a higher level use group. An early detection-prevention approach should be initiated across all jurisdictional school boards. It is observed that use patterns generally remain in the same subgroup across time. However, transitions do occur, typically to the adjacent severe use pattern rather than mild. Except for the multi-use subgroup (S4), the most significant change is transitioning to the no-use (S1) subgroup over time. Although this highest level of polysubstance use is the most stable subgroup, with an averaged probability of 86.7% staying in the same use pattern over time, there is still a 7.5% chance that these heavy users would transition to the no-use subgroup over time. Prevention programs should target their particular needs for making such a good switch.

The complexity of risk profiles, modifiable individual-level risk factors, family/friends/school environment and community-level status can lead to the transition of use patterns. Due to the multifaceted determinants associated with youth polysubstance use, there is a need to initiate prevention programs that are more comprehensive to tackle the wide range of risk factors. The study results will provide stakeholders with evidence-based best practices to guide the implementation of the school environment, policies and procedures for improving youth health behaviours.

6.2.2 Contribution to Research Communities in Literature

This thesis is the first study that takes advantage of data-driven approaches using advanced ML techniques on the COMPASS data. It contributes to ML in public health by investigating a complex public health challenge, i.e., youth polysubstance use as a case study using a range of machine learning techniques. Both unsupervised ML methods and a multivariate LM modelling approach are employed in this thesis. The applied methodologies are on population-level health surveys to enhance

data exploration capabilities and further discover hidden patterns. ML methods can quickly identify hidden patterns from such high-dimensional population-level data. When applied holistically, the result is quick detection of phenotypes acquired. The study results are consistent with other research that have taken statistical modelling approaches.

Firstly, we applied the methodologies on population-level health surveys to enhance data exploration capabilities and further discover hidden patterns and the transition of patterns over time. From the population level, differences between risk profiling may have essential effects on subjective youth behavioural and mental health. This can be further conceptualized by having different preventive capabilities against addictive behaviours in school settings.

Secondly, the multidimensional impact factors are highly representative of how ML approaches can be used to process large amounts of survey data in health research. Instead of hand-picking a few variables from the dataset relevant to the research questions, the feature selection algorithms, as previously discussed, are a superior approach to identifying the correlates to the outcome variable. The algorithms calculate the variable importance (the Boruta algorithm) or shrink the coefficients of unimportant variables into zeros (the LASSO regression). Implementing these algorithms was within a few minutes based on the linked samples of the COMPASS data with high computational capacity, as highlighted in Chapter 4 Methods, Section 4.6. The resulting impact factors are highly interpretable with visualized graphs demonstrating the importance scores (the Boruta algorithm) or variable coefficients (the LASSO regression).

Furthermore, although statistical modelling is the dominating approach in quantitative health research, our study demonstrated that ML techniques are more than adequate for identifying inherent structures like hidden patterns of high-dimensional data. Unsupervised ML approaches automatically explore the data for pattern discovery without referring to an outcome variable. The LMM modelling takes advantage of a latent Markov chain to investigate the transition of youth polysubstance use patterns, revealing the dynamics of use patterns across time. Lying at the intersection between statistical modelling and ML approaches, the LMMs seem easier to adopt than any other advanced ML algorithms residing in a black box. This is particularly true for researchers from the public health realm.

In the ML paradigm, the trade-off is a standard agreement, such as interpretability and accuracy. Although this thesis does not involve measuring accuracy as predictive models do, we applied a few

strategies to improve the interpretability of the various ML models in this thesis. Our interpretable techniques include feature selection over feature extraction method and feature importance plots to inform us how important the feature is in predicting polysubstance use. Furthermore, we performed data visualization via the t-SNE algorithm to project high-dimensional data to lower-dimensional space. In addition, silhouette plots demonstrate the internal index of clustering validation, and different risk levels with associated characteristics represent risk profiling. In terms of the modelling results of LMM and parameter estimation with odds ratios that are easier to interpret for public health practitioners, various plots were generated. Plots such as initial probabilities by item, estimated marginal distribution, transition probabilities, transition curves, and transition patterns present an excellent visualization method, conveying our findings to the audience outside the ML field. We are highly confident that the results of our ML models in this thesis are explainable.

In addition, the ML pipeline developed in this thesis can be used in real-world decision support. The terminology "pipeline" is derived from bioinformatics, representing a sequence of tools applied to a dataset, making it from raw data towards the final analysis results interpretable to the stakeholders (19). In this thesis, the ML pipeline includes data preprocessing (Section 4.2.2), feature selections (Section 4.4.1 using Boruta algorithm and Section 4.5.1 using LASSO regression), data visualization (Section 4.4.2), cluster analysis and validation (Sections 4.4.4 and 4.4.5), and LMM modelling (Sections 4.5.2 and 4.5.3), using a variety of R packages summarized in Section 4.6.

6.3 Strengths and Limitations

This section outlines the strengths and limitations of this thesis. We first detail the significant strengths, identify the limitations, and discuss methods for mitigating these limitations with future research.

The strengths of this thesis lie in the COMPASS dataset and the methodologies we applied. One of the strengths of the COMPASS data derives from the large sample size with reliable data quality, using national surveillance instruments-based measurements (142). The Cq uses the active-information passive-consent protocols, which help achieve high participation rates and reduce sampling bias while preserving student confidentiality (113). This protocol is of utmost importance in research related to youth health behaviours, such as polysubstance use, encouraging honest responses. In general, the COMPASS study had a high percentage of participation each school year, with a

reasonable participation rate of 78%, 82%, and 84% for all student participants across the three waves. The COMPASS host study collects multifaceted information annually in Canada as longitudinal evidence. The complexity of data structure provides real-world evidence pertaining to youth health behaviours from multiple sources to examine the relationship between school environmental characteristics and youth health outcomes.

Another strength of this thesis is that we undertook a comprehensive data preprocessing process, and some of the work that we did may be useful to future COMPASS researchers. One of the most challenging aspects of this thesis was cleaning up the raw data, including missing pattern analysis and MI for handling missing data. We applied a variety of imputation techniques to impute missing values based on different types of missingness. MI assumes that the data are at least MAR, which means that the MI procedures can also be applied on data that are MCAR and work best when data are MCAR. For data were MNAR, e.g., BMI category, we treated differently than MAR or MCAR mechanisms. That is, instead of performing MI procedures, we coded missing BMI as its category "not stated." Ultimately, by having this clean and imputed linked dataset, the hope is that COMPASS researchers can spend less time processing raw data and more time analyzing it. We also plan to provide all necessary code to COMPASS researchers to learn how the ML models were implemented, and perhaps they can customize them for their individual research needs. The same goes for all of the visualizations presented in this thesis, which were designed to make it flexible across different research scenarios.

Finally, we applied comprehensive modelling strategies for addressing different research questions. For example, considering the overlapping nature of youth polysubstance use risk profiles, advanced ML methods such as fuzzy clustering were implemented to identify risk profiles among Canadian adolescents. It helps discover hidden patterns or intrinsic structures within the COMPASS dataset. Furthermore, applying a dynamic modelling approach on the three annual waves of linked data showcasing the ability of this type of model to evaluate individual differences in transition behaviours across time. These diverse modelling strategies help public health practitioners gain insights into the COMPASS data with a holistic approach.

This thesis has certain limitations. The ability of this research to provide multi-level granularity for modelling transitions in youth polysubstance use patterns is hindered by the limited number of waves available for analysis. It would be ideal to have all waves available from the beginning of the

COMPASS data collection up to the latest school year of 2019-2020 (Y8). However, there was a fundamental change in 2016, and the SPP has been changed significantly throughout the COMPASS study. Therefore, a decision was made to use student-level, and supplementary community-level (school SES, urbanity, and BE) linked data from 2016-2017 onward.

As an extension to the classical Markov model and the LMM, the multilevel LMM is a structured stochastic process, generalizing LMM with a bottom-up hierarchical control structure. The multilevel LMM structures have the following properties: i) a vector of response variables (multivariate) is in discrete state-space, ranging from 0 to 2, ii) covariates are stochastic, and iii) transition of use patterns (sequences) are correlated in time (27). The model selection can be performed without covariates, and once the best model is selected, covariates are added at both levels and estimate the model jointly, not separately. However, the currently available function in the LMest package for MLMM modelling does not allow covariates. When completing this thesis, the LMest package developers are still working on adding this function. As one limitation, the data analyses in this thesis could not benefit from the multilevel modelling approach.

As for the model validation, we were hoping to obtain Wave IV (the school year 2019-2020, Y8) data to serve as a test set for validating the models. However, this school year's COMPASS data collection cycle was challenging due to the COVID-19 pandemic. Given the impact of COVID-19 on school closures in March 2020, half of the school sample completed a pre-COVID paper-based questionnaire, and another half completed an online questionnaire in May-June. The online questionnaire included many new questions specific to COVID-19 and removed many of the questions used in the paper-based version. The sample size for the paper-based questionnaire is ~30,000 students from 51 participating schools, while the sample size for the online questionnaire is ~9,500 students from 51 schools. The participation rate for the online questionnaire was much lower than the paper-based (~30% vs. ~80%) due to the school closures and lack of set class time for data collections. Although linked longitudinal data are available for both questionnaire types, connecting to the previous three waves (i.e., Wave I, Wave II, and Wave III in the current study) significantly reduces the sample size from ~9,000 to ~1,000. It is preferable to have external validation data. However, we stick to the current study design with the three waves data due to the constraints above.

Lastly, many participating schools in the COMPASS study are purposefully sampled (i.e., a non-random convenience sample). As a result, the COMPASS data is not extensible for use in population-

level statistics (59). Therefore, one must be cautious when interpreting and generalizing results since the sample of schools may not be genuinely representative and external validity cannot be guaranteed. As with any large-scale health survey, response bias is inevitable; mainly, non-responses introduce missing values. This research applied multiple imputation techniques to impute missing values. Regardless, the consensus among stakeholders remains that COMPASS methodologies are sufficiently robust given the delicate balance of data accuracy and participant anonymity in longitudinal studies that concern youth health behaviours (143).

6.4 Future Works

Although the results of this thesis are meaningful, more work is guaranteed to analyze school programs and policies, hierarchical BE effects, and dynamic social characteristics on youth polysubstance use. For example, immediate effort should be given to the multilevel LMM framework to examine geographical distribution and variation further. This approach uses SPP measures to account for school policy perspectives and contextual features surrounding polysubstance use among youth. In addition to the students' health behaviours, adding data from multi-sources like SPP would undoubtedly leverage the strengths of ML modelling strategies.

Another future work is to conduct external validation. This can be achieved by obtaining a validation dataset from external sources to ensure our final models fit the new data well. Alternatively, using any data collected from the COMPASS study in the future years can also validate our models generated from this thesis internally. Given the particularity of the school year 2019-2020 due to the COVID-19 pandemic situation, it would be insightful to evaluate the impact of overwhelming social events such as lockdown during the pandemic. Analyses like comparing the commonality and dissimilarity of polysubstance use patterns in the same cohort and any change of their characteristics would make future research appealing.

After model development, more work can be done to transform the modelling results into tools/apps in a real-world scenario. After all, there is a significant difference between building an ML model and preparing it for end-users to use in their organizations. For example, more careful model evaluation before deployment is required. One of the most challenging aspects of adopting ML systems is deploying and maintaining an accurate model, which requires constant access to new data to update and validate the model and improve its accuracy (144). In addition, beyond building ML

models, turning the ML solutions into a genuine product is an interdisciplinary effort involving not only technical but organizational strategic planning (145).

One of the objectives of this thesis was to identify the most significant features associated with risk profiles or use patterns of youth polysubstance use with an ML modelling approach, which is a typical association analysis. As previously discussed, most ML methods are being used for descriptive and predictive purposes, such as association studies, public health surveillance, disease diagnosis and incidence, individual- vs. population-level prediction, data-driven mapping of inputs to outputs, and so on. Although ML models are good at uncovering subtle patterns in large high-dimensional datasets, they have struggled to make causal inferences. Causal inference approaches are well-known methods in statistics, with many practical applications in numerous industries, such as healthcare (145). Pearl (2019) highlighted that causal inference is restricted and governed by a three-level causal hierarchy, i.e., association, intervention and counterfactual (146). From association towards causality, intervention modelling is in the causal pathway. Prosperi *et al.* (2020) argued that health practitioners need to apply causal approaches with causal structures when pursuing intervention modelling (147). Researchers can use the same tools for causal purposes to reveal mechanisms of causality, going beyond association to investigate causation and building this into our models. Once a causal model is available, focusing on particular exposures, whether through a learning process or subject matter experts' knowledge, causal inference allows conclusions to be drawn on the impact of interventions, counterfactuals, and potential outcomes (148). A more causal approach can be achieved by removing confounders. In intervention studies, double-blinded randomized controlled trials (RCT) are considered gold-standard to control confounding. For observational studies, we can take a mathematical approach to conduct causal analysis by stratifying on confounders or via propensity score matching (149).

In this thesis, both the ML models and statistics provide numeric information about phenotypes of risk profiles and dynamic transitions of polysubstance use patterns among youth. In addition to these quantitative methodologies, we may obtain qualitative evidence to supplement the statistical evidence. Qualitative research can provide a more comprehensive understanding of students' risk behaviours, their perceptions towards polysubstance use, and the pros and cons of school practices and policies to tackle this public health issue. Furthermore, a more comprehensive profile of participants' health behaviours may offer a deeper understanding of ***WHY*** these behaviours affect the

dynamic transition of polysubstance use patterns in this cohort. For example, future research can integrate the SPP data with open- and closed-ended questions, drawing on all possibilities from multiple forms of the COMPASS host study. It may lead to a mixed-methods study, an emerging method in social health sciences, combining both the statistical trends of what occurs and the phenomenon of why it happens.

In summary, this chapter discussed the key findings of this thesis surrounding the risk profiles of youth polysubstance use, the patterns and the dynamics among Canadian youth, followed by reviewing the advantages and limitations of the ML methods appropriate to modelling risk profiles and dynamic transition using the COMPASS data. Finally, the contributions, strengths and limitations, and future works were discussed. The next chapter will review the principal findings of this thesis, highlighting the contributions to the ML and Public Health research communities and concluding with some final remarks.

Chapter 7
Summary of the Key Points

7.1 What We Know from this Research

Phenotyping risk profiles of youth polysubstance use among Canadian youth

- The four risk profiles of polysubstance use among Canadian youth identified in this research were low risk, medium-low risk, medium-high risk, and high risk, demonstrating the heterogeneity in the prevalence and phenotype across these four risk profiles.

Patterns of polysubstance use among Canadian secondary school students

- The four distinctive polysubstance use patterns among Canadian adolescents were no-use, occasional single-use of alcohol, dual-use of e-cigarette and alcohol, and current multi-use.
- Although the no-use subgroup was prominent at Wave I, its prevalence decreased over time. The prevalence of the other three use patterns increased across time, except for the occasional single-use of alcohol subgroup.
- The current multi-use subgroup was the most stable use pattern, followed by the dual-use and the no-use subgroups. Among these four patterns, occasional single-use of alcohol was the least stable pattern.

Exploring dynamic transitions of youth polysubstance use patterns

- As they grow older, youth were most likely to remain in the same subgroup of use pattern across time or transition to a higher use pattern instead of a lower one.
- Factors that impact the initial membership of polysubstance use patterns and the dynamics were multifaceted and complex across the four use patterns across the three waves.
- Not only do use patterns change with time, but so does the evidence in use patterns.

The appropriateness of ML methods to modelling risk profiles and dynamic transitions using the COMPASS data

- The application of cluster analysis determined risk profiles of youth polysubstance use. LMMs identified polysubstance use patterns and examined the dynamic transitions of these

use patterns over time. It is recommended that these advanced ML methods be applied in settings with high-dimensional population-level longitudinal data.

- However, not all studies have all those same variables, neither have we in the COMPASS dataset. This dilemma makes the study results difficult to compare or consolidate.

7.2 What this Dissertation Contributes to the Research Communities

To the COMPASS Host Study

- The first application of ML models on the COMPASS dataset
- First research applying dynamic models (LMM) to examine the transition of polysubstance use patterns over time
- First research phenotyping risk profiles taking a holistic approach

To the Public Health Community

- Identification of risk profiles of polysubstance use among Canadian secondary school students, providing a more comprehensive overview of the prominent characteristics for each of the different risk levels
- Examination of factors (and estimates) that impact the initial membership of use patterns at baseline (Wave I)
- Examination of factors (and estimates) that lead to the dynamic transitions of use patterns over time
- Inclusion of e-cigarette as an emerging substance for modelling the dynamics of use patterns

To the ML Community

- Showcasing the application of various ML models (both unsupervised and supervised learning) using real-world longitudinal health survey data
- Bridging the ML and Public Health communities

7.3 What We Still Need to Know and How We Can Get there

- How well do our models perform?
    - Internal validation: e.g., cross-replication, comparing statistical model-based methods (e.g., LCA) vs. clustering algorithms, LTA vs. LMM
    - External validation: using external data, e.g., newer waves
- What are the characteristic differences in the dynamic transition of use patterns among youth? This will be achieved by conducting a stratified analysis with the LMM framework, e.g., sex, race, age, urbanity, etc.
- How do the school programs and policies impact youth behaviours on polysubstance use? This will be performed by adding the SPP data into a multilevel LMM framework upon the availability of the software package.
- What are the risk profiles at the school level reflecting youth polysubstance use? This will be examined using aggregated student-level data and hierarchical BE and other environmental data available in the COMPASS study.
- Given the impact of COVID-19 on school closures and lockdown throughout the school year of 2020-2021, it would be worthwhile to examine any rare patterns or emerging trends of polysubstance use among Canadian secondary school students. Comparing the use patterns and the dynamic transitions between this school year and other years would be meaningful to public health practitioners.

7.4 Final Thoughts

This thesis epitomizes the emergence of a new and exciting field at the intersection of two research communities, ML and Public Health. As this is also the first study of its kind to ascertain risk profiles and dynamics of use patterns in youth polysubstance use, by employing ML approaches to the COMPASS dataset, this research provides insights into the opportunities and possibilities ahead for ML in Public Health. By using complex and high-dimensional longitudinal health survey data, this thesis demonstrates the application of LMMs to evaluate the transition of youth substance use

patterns over time. Furthermore, this thesis describes the application of cluster analysis, one type of unsupervised ML approach in determining the risk profiles of polysubstance use in this cohort. Findings from studies like this can be beneficial to practitioners in the field, such as school program managers or policymakers, in their capacity to develop interventions to prevent or remedy polysubstance use among youth.

This thesis exemplifies one specific application of ML in public health, namely, identifying behavioural patterns affecting health. By tackling prevalent population health issues, such as youth substance uses investigated herein, this research contributes to advancing public health research and practices. One of humanity's collective responsibilities is to ensure the welfare of our youth, as they are the future generation. Unfortunately, the current trend in polysubstance use among adolescents is becoming a growing challenge facing many countries with severe consequences both for the individual and our society. Thus, an aspiration behind this thesis is to provide a means to accelerate the research that can provide insights to design and implement programs and interventions for those directly affected by the detrimental effects of youth polysubstance use.

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Appendix A

The COMPASS Questionnaire (2017-18)

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) © COMPASS 2017

○○○○○○○○○○○○○○○○○○○○○○○○ [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

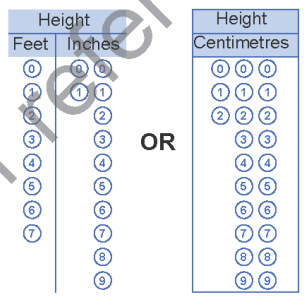
8. How tall are you without your shoes on? (Please write your height in feet and inches **OR** in centimetres, and then fill in the appropriate numbers for your height.)

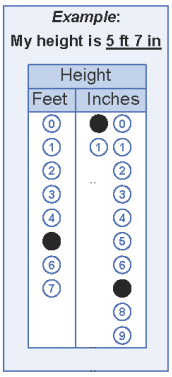
○ **I do not know how tall I am**

"My height is ____feet, _____inches"

OR

"My height is _____ centimetres"





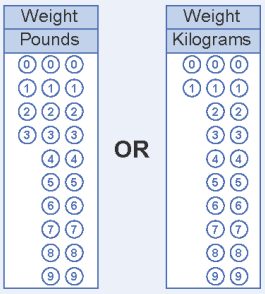
9. How much do you weigh without your shoes on? (Please write your weight in pounds **OR** in kilograms, and then fill in the appropriate numbers for your weight.)

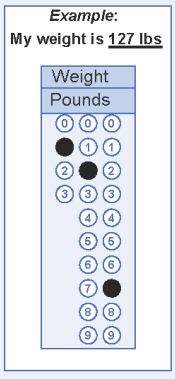
○ **I do not know how much I weigh**

"My weight is _____ pounds"

OR

"My weight is _____ kilograms"





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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

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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**	○	○	○

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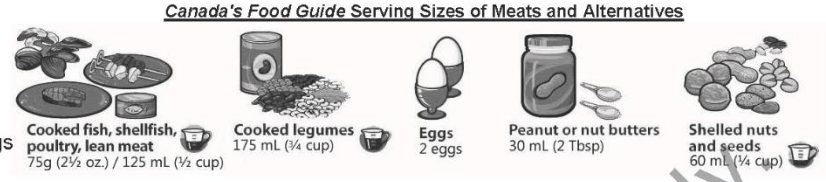
26. YESTERDAY, *from the time you woke up until the time you went to bed*, how many servings of meats and alternatives did you have? *One 'Food Guide' serving of meat and alternatives includes cooked fish, chicken, beef, pork, or game meat, eggs, nuts or seeds, peanut butter or nut butters, legumes (beans),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



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.*

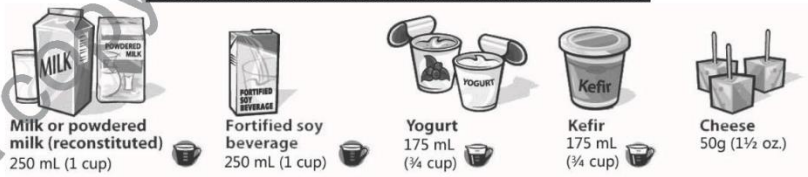
- ○ None
- ○ 1 serving
- ○ 2 servings
- ○ 3 servings
- ○ 4 servings
- ○ 5 servings
- ○ 6 servings
- ○ 7 servings
- ○ 8 servings
- ○ 9 or more servings

Canada's Food Guide Serving Sizes of Vegetables and Fruits

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

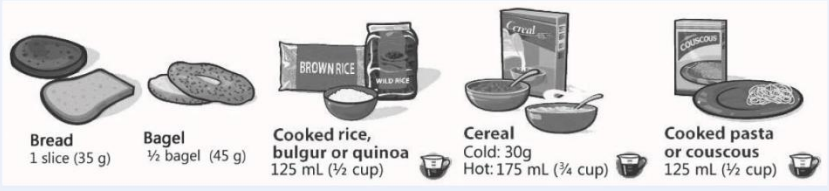
Canada's Food Guide Serving Sizes of Milk and Alternatives



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)*

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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

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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	○	○	○	○

66. In your current or most recent Math course, what is your approximate overall mark?
(Think about last year if you have not taken math this year)

- ○ 90% - 100%
- ○ 80% - 89%
- ○ 70% - 79%
- ○ 60% - 69%
- ○ 55% - 59%
- ○ 50% - 54%
- ○ Less than 50%

67. In your current or most recent English course, what is your approximate overall mark?
(Think about last year if you have not taken English this year)

- ○ 90% - 100%
- ○ 80% - 89%
- ○ 70% - 79%
- ○ 60% - 69%
- ○ 55% - 59%
- ○ 50% - 54%
- ○ Less than 50%

68. What is the highest level of education you would like to get? *(Choose only one)*

- ○ Some high school or less
- ○ High school diploma or graduation equivalency
- ○ College/trade/vocational certificate
- ○ University Bachelor's degree
- ○ University Master's / PhD / law school / medical school / teachers' college degree
- ○ I don't know

69. What is the highest level of education you think you will get? *(Choose only one)*

- ○ Some high school or less
- ○ High school diploma or graduation equivalency
- ○ College/trade/vocational certificate
- ○ University Bachelor's degree
- ○ University Master's / PhD / law school / medical school / teachers' college degree
- ○ I don't know

70. In the last 4 weeks, how many days of school did you miss because of your health?

- ○ 0 days
- ○ 1 or 2 days
- ○ 3 to 5 days
- ○ 6 to 10 days
- ○ 11 or more days

71. In the last 4 weeks, how many classes did you skip when you were not supposed to?

- ○ 0 classes
- ○ 1 or 2 classes
- ○ 3 to 5 classes
- ○ 6 to 10 classes
- ○ 11 to 20 classes
- ○ More than 20 classes

72. How often do you go to class without your homework complete?

- ○ Never
- ○ Seldom
- ○ Often
- ○ Usually

○○○○○○○○○○○○○○○○○○○○○○○○ [serial]

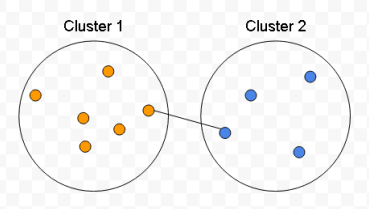
Appendix B

Agglomerative Clustering Linkage Methods (Dissimilarity Measures)

Single Linkage (Nearest Neighbor)

Minimum distance or dissimilarity between nearest data points in clusters

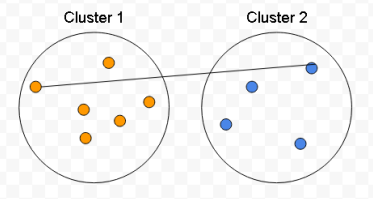
$$D(k_1, k_2) = \min D(x_1, x_2) \tag{3}$$



Complete Linkage (Furthest Neighbor)

Maximum distance or dissimilarity between furthest data points in clusters

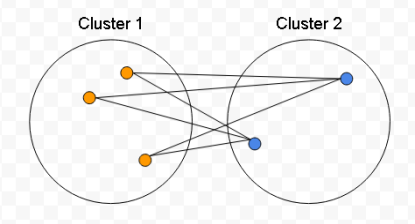
$$D(k_1, k_2) = \max D(x_1, x_2) \tag{4}$$



Average Linkage (UPGMA)

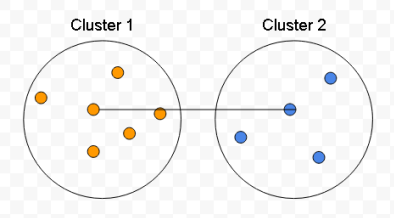
The average distance of all pairs of data points between clusters

$$D(k_1, k_2) = \frac{1}{|k_1|}\frac{1}{|k_2|}\sum D(x_1, x_2) \tag{5}$$



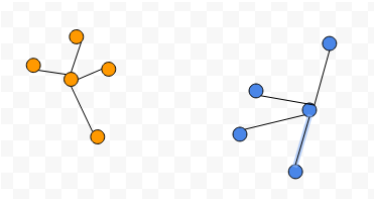
Centroid Method (UPGMC)

Squared Euclidean distance between centroids of clusters, combining clusters with minimum distance between centroids of the two clusters



Ward's Method (Minimum Sum of Squares)

It aims to minimize the total within-cluster variance, combining clusters where an increase in within-cluster variance to the minimal degree.

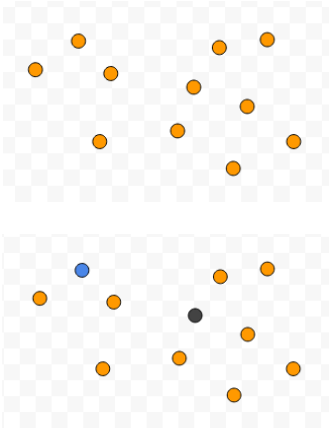


Appendix C

PAM Clustering Algorithm

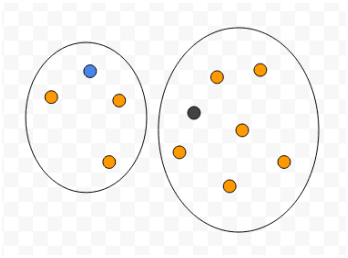
Step 1

Arbitrarily choose k object as initial medoids (e.g., $k = 2$)



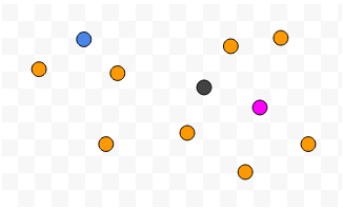
Step 2

Assign each remaining object to the nearest medoids, compute the initial cost (C_1)



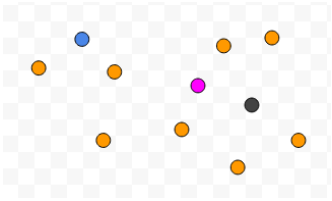
Step 3

Randomly select a non-medoid object o_{random}



Step 4

Swap medoid m and non-medoid object o_{random}, compute the total cost of swapping (C_2), evaluate if cost function decreases ($C_2 < C_1$)



Step 5

Repeat Steps 2-4 until the total cost of swapping is not improving anymore

Appendix D
Fuzzy Clustering Algorithms

Fuzzy C-Means (FCM)

The FCM algorithm applies a weighted sum-of-squares criterion for continuous data. The FCM clustering algorithm calculates the optimal membership degree by minimizing the Euclidean distance between the data element and the cluster centre (22), expressed as

$$\sum_{v=1}^{k}\sum_{i=1}^{n} \mathrm{u(i,v)}^{\mathrm{t}}\, d^2(\mathrm{x}_i, m_v) \tag{6}$$

where n is the sample size, k is the number of clusters, t is the fuzzifier, $\mathrm{u(i,v)}^{\mathrm{t}}$ is the membership, and $d^2(\mathrm{x}_i, m_v)$ is the Euclidean distance between subject i and the cluster center m_v. The fuzzifier t affects the distribution of the final membership; $t = 1$ leads to the hard clustering (i.e., crisp solution), and a default setting of $t = 2$ for soft clustering (fuzzy clustering). The applications of the FCM algorithm in the health domain have been published in the literature. For instance, Kettenring (2009) implemented it in the immediate valuation of patient portfolio assets with cluster analysis (150). A fuzzy version of density-based spatial clustering was applied by Nasibov and Ulutagay (2010) for comparison with fuzzy k-means (151).

Like any fuzzy clustering, data elements can belong to any cluster with a certain degree of membership. It provides a more detailed description of the objects in the cluster. In addition, the time complexity is low. The FCM algorithm also has some disadvantages: 1) it is sensitive to outliers and initial centroid; 2) different initialization may lead to different clustering results; 3) the FCM algorithm can become trapped into local maxima resulting in the final clustering being in a local optimum instead of global maxima.

FANNY (Fuzzy ANalYsis)

Another well-known fuzzy algorithm, FANNY, minimizes the objective function

$$\sum_{v=1}^{k}\sum_{i,j=1}^{n} \frac{\mathrm{u(i,v)}^{\mathrm{r}}\, \mathrm{u(j,v)}^{\mathrm{r}}\, \mathrm{d(i,j)})}{(2\ \sum_j \mathrm{u(j,v)}^{\mathrm{r}})} \tag{7}$$

where n is the sample size, k is the number of clusters, r is the membership exponent, and $d(i,j)$ is the dissimilarity between subjects i and j. Increasingly crisper clustering can be achieved when r is

close to 1 and complete fuzziness when r approaches infinity (129). Further note that even the default value, r = 2, will lead to complete fuzziness, that is, the degree of membership $u(i, v) = \frac{1}{k}$. FANNY is more robust to non-spherical clusters than other fuzzy clustering algorithms, accepting a proximity matrix $d(i, j)$ instead of estimating central values, i.e., Euclidean distances as in the FCM algorithm (22).

Given the mixed type of COMPASS data, with most of the data being categorical, different dissimilarity matrices have experimented, and the clustering results were compared. Firstly, as part of the clustering process, grade-of-membership (GOM) analysis assigns two or more latent subgroups for each object based on probabilities of their cluster membership. One specific distance metric, the Gower distance, was implemented in this study. Gower distance is calculated as the average of partial dissimilarities between data elements, depending on the evaluated variable types (152). Each feature has a specific standardization applied, and the distance between two individuals is the average of the particular distances of all. Each partial dissimilarity (i.e., the Gower distance) ranges between 0 and 1. Secondly, the ordinal data were treated as continuous, so the most commonly used Euclidean distance measure can be implemented. The Euclidean distance measure is appealing because the distance between two objects can be interpreted as physical distance obtained from multivariate used for clustering.

Appendix E
Boruta Algorithm

The Boruta algorithm is an RF-based feature selection algorithm utilizing an ensemble of decision trees. With tree-based models, a sequence of decisions (or splits) is calculated at training time. A stopping criterion can be specified by not splitting nodes once the decision cannot bring a specific minimum benefit to control the overfitting of the decision trees. Reduction in Gini impurity is often defined as a benefit within this context. Corresponding to the Gini coefficient, Gini impurity indicates the effectiveness of the classifier for a given subset of data. Non-parametric is one property of Gini impurity, which works with any numerical data containing a large sample size for choosing input features. The feature ranking mechanism extends the decision tree mechanism as the impurity decreased from each feature is averaged over all the trees. The term impurity represents either the Gini impurity or entropy for classification and the variance for regression trees. These impurity measures are used to select the feature that best splits the dataset.

The Boruta algorithm can be described as follows (153).

Step 1: For each feature X_j, randomly permute it to generate a "shadow feature" (random feature) $X_j^{(s)}$.

Step 2: Fit a random forest classifier to the original features $\{X_1, \dots, X_p\}$ and the shadow features $\{X_1^{(s)}, \dots, X_p^{(s)}\}$.

Step 3: Calculate feature importance on the original features $\{H_1, \dots, H_p\}$ and the shadow features $\{H_1^{(s)}, \dots, H_p^{(s)}\}$.

Step 4: The feature is important for a single run if its importance is higher than the maximum importance of all shadow features, i.e., $H_1 > E(H)$.

Step 5: Eliminate all features whose importance across all runs is low enough. Keep all features whose importance across all runs are high enough.

Step 6: Repeat Steps 1-5 with all tentative features for a pre-defined number of iterations until all features have been identified as important or rejected.

The pseudo-code of the Boruta algorithm (153) can be written as follows.

Input: $originalData$ (input dataset); $RFruns$ (# of iterations of RF)

Output: $featureSet$

$confirmedSet = \emptyset$

$rejectedSet = \emptyset$

for $each\ RFruns$ **do**

$originalPredictors\ <-\ originalData(predictors)$

$shadowFeatures\ <-\ permute(originalPredictors)$

$extendedPredictors\ <-\ cbind(originalPredictors, shadowFeatures)$

$extendedData\ <-\ cbind(extendedPredictors, originalData(decisions))$

$zScoreSet\ <-\ randomForest(extendedData)$

$maxzScoreshadowFeatures\ <-\ max(zScoreSet(shadowFeatures))$

for $each\ x \in originalPredictors$ **do**

if $zScoreSet(x)\ >\ maxzScoreshadowFeatures$ **then**

$H(x) + +$

for $each\ x \in originalPredictors$ **do**

$significance(x) < -twoSidedSignificanceTest(x)$

if $significance(x) \gg maxzScoreshadowFeatures$ **then**

$confirmedSet < -featureSet \cup x$

else if $significance(x) \ll maxzScoreshadowFeatures$ **then**

$rejectedSet < -rejectedSet \cup x$

return $featureSet\ <-\ confirmedSet \cup rejectedSet$

Appendix F
t-SNE Algorithm

A precursor method of t-SNE, Stochastic Neighbor Embedding (SNE), aims to match distributions of distances between data elements in high- and low-dimensional space via conditional probabilities. SNE assumes that the distances in both high- and low-dimensional space are Gaussian distributed. SNE is performed by defining the similarities and a cost function, obtaining the gradient for the cost function and minimizing it to get the low-dimensional map. SNE has two main drawbacks. The first one is that it is challenging to optimize the cost function. The second one is related to the "crowding problem," representing the phenomenon that SNE clumps data elements nearby and moderately far apart to make them crowded.

t-SNE with novel features represented to cost function overcome these two drawbacks. The first improvement of t-SNE is that its cost function is symmetrized version of that in SNE, i.e.,$p_{i|j} = p_{j|i}$ and $q_{i|j} = q_{j|i}$. The main feature in symmetric SNE is that $p_{ij} = p_{ji}$ and $p_{ii} = q_{ii} = 0$ for all i,j. The low-dimensional representation is

$$q_{ij} = \frac{\exp\left(-||y_i - y_j||^2\right)}{\sum_{k \neq l} \exp\left(-||y_k - y_l||^2\right)} \tag{8}$$

The high-dimensional representation is

$$p_{ij} = \frac{\exp\left(-\left|\left|x_i - x_j\right|\right|^2 / 2\sigma^2\right)}{\sum_{k \neq l} \exp\left(-||x_k - x_l||^2 / 2\sigma^2\right)} \tag{9}$$

The gradient of the cost function is

$$\frac{\delta C}{\delta y_i} = 4 \sum_j (p_{ji} - q_{ji})(y_i - y_j) \tag{10}$$

The second improvement in t-SNE is that t-SNE uses Student t-distribution instead of the normal distribution to compute the similarities between data elements in a low-dimensional map. In t-SNE, a Student t-distribution with one degree of freedom, Cauchy distribution, represents the low-dimensional map.

$$q_{ij} = \frac{(1 + ||y_i - y_j||^2)^{-1}}{\sum_{k \neq l} (1 + ||y_k - y_l||^2)^{-1}} \tag{11}$$

It is observed that this representation has no exponent and looks similar to the kernel of a t-distribution. The main reason for using t-distribution is that it is robust to outliers. Unlike the Gaussian distribution, it has no exponent, making it faster to evaluate. In Gaussian distribution, there is an exponent in the kernel, making the calculation more computationally expensive. Thus, choosing a certain t-distribution is much faster.

The gradient of the cost function via the KL divergence can be expressed as follows.

$$\frac{\delta C}{\delta y_i} = 4\sum_j (p_{ji} - q_{ji})(y_i - y_j)\,(1 + ||y_i - y_j||^2)^{-1} \tag{12}$$

The general idea of the t-SNE algorithm is that for a high-dimensional dataset χ with data elements $x_1, x_2, \ldots x_n$, each data element has high dimensions. The cost function parameter, perplexity, is associated with variance σ in the cost function. The optimization parameters include the number of iterations T, learning rate φ, and momentum $\alpha(t)$. All these components are utilized to obtain the low-dimensional representation Y.

Essentially, the t-SNE algorithm starts with pairwise affinities $p_{j|i}$ in the high-dimensional map with a given perplexity. Then set $p_{ij} = \frac{p_{i|j} + p_{j|i}}{2n}$, where n is the number of data elements. Then sample the initial solution for Y at the 0^{th} iteration for $y_1, y_2, \ldots y_n$ from a normal distribution with the mean 0 and variance 10^{-4} $N(0, 10^{-4}I)$, where I represents the identity matrix. Then start with the iteration for $t = 1$ to T, which is the maximum number of iteration, first compute the lower-dimensional affinities q_{ij}, and then compute the gradient $\frac{\delta C}{\delta y}$ through the KL divergence. Then use the gradient descent formula to get the solution at the t^{th} solution, set

$$y^{(t)} = y^{(t-1)} + \varphi\frac{\delta C}{\delta y} + \alpha(t)(y^{(t-1)} - y^{(t-2)}) \tag{13}$$

Iterate through all these processes until the maximum iteration is reached or until it converges to the asymptotic point of the solution.

Beyond the basic t-SNE algorithm, there are modifications to reduce complexity using Barnes-Hut-SNE approximation, a sophisticated methodology with a tree-based algorithm.

t-SNE is a popular method, which has been implemented in various software packages and languages. The research community has widely adopted t-SNE, but there are also some criticisms

against it. Wattenberg, Viegas, & Johnson (2016) list some of the drawbacks of t-SNE with some interactive visualization tools. The first drawback is that the different perplexity can lead to entirely different clusters (154). The perplexity measure is loosely interpreted as several neighbours of a certain point. Wattenberg, Viegas, & Johnson (2016) suggested that a perplexity between 5 and 50 is optimal and robust within that range (154). If a perplexity is too small, then the local variations are dominant. On the other hand, a too large perplexity leads to a dominating global change (154).

Another disadvantage of t-SNE is that cluster size does not have any meaning to it. In PCA, the X-axis has a reasonable interpretation, and the Y-axis is the direction with the highest variance explained. However, t-SNE does not have that intrinsic interpretation. It also tends to expand dense clusters and contrast sparse clusters. Therefore, a dense cluster does not mean that cluster points have minimal variance. A huge cluster does not necessarily imply those data elements have enormous within-cluster variance.

Another criticism is that the distance between clusters might not have a clear interpretation. For example, if two clusters are close to each other, two clusters are far apart. The inter-cluster distance does not mean those clusters are far apart are very different from each other, or close enough clusters are very similar.

Finally, if random noise is provided in the data, t-SNE can lead to a false positive structure in the projection, where in reality, no structure in this random noise. Researchers need to be careful about using t-SNE, tuning the hyperparameters, and interpreting the results. In summary, t-SNE is a valuable tool for clustering and data visualization. It provides a better structure for high-dimensional data. Its high flexibility leads to other drawbacks such as a lack of interpretability, not being intuitive for parameter tuning, including perplexity, iterations, tolerance or convergence, etc.

Appendix G
Clustering Procedures

In a nutshell, clustering procedures include the following major steps (22).

1. Identify Objects to Cluster

Ideally, objects should be randomly sampled and representative of the cluster structure. However, since cluster analysis is a non-inferential tool, if generalization to a larger population is not required, it may be acceptable for over-sampling small populations.

2. Select Variables (Features)

Feature selection or extraction is one of the key steps for cluster analysis, particularly with high-dimensional data. Feature selection refers to choosing a subset of original features from the dataset. In contrast, feature extraction applies transformation methods to the original features to generate new ones that are useful for analysis. Ideally, a good choice of features should distinguish various patterns belonging to different clusters, be insensitive to outliers, and be easy to interpret. Feature extraction is often used for dimensionality reduction and data visualization, where interpretability is not mandatory. Considerations will also be given to data standardization and addressing multicollinearity issues among features (155).

3. Measure Proximity

Proximity is a general term used to quantitatively measure how close (*similarity*) objects are to each other or how far apart (*dissimilarity* or *distance*) they are. There exists a large number of similarity or dissimilarity coefficients. The choice between coefficients is given by the nature of the data, i.e., continuous or categorical.

3.1 Distance or Dissimilarity Measures

The most commonly used dissimilarity measure is *Euclidean distance*, which is written as

$$d(a,b) = \sqrt{[\sum_{n=1}^{k}(x_{an} - x_{bn})^2]} \quad (14)$$

where x_{an} and x_{bn} represent for object a and b, respectively, the value of n^{th} variable of the p-dimensional observations. $d(a,b)$ represents physical distances between two p-dimensional observations $x_a = (x_{a1}, \dots, x_{ap})$ and $x_b = (x_{b1}, \dots, x_{bp})$ in Euclidean space (22). A variety of dissimilarity measures has been developed to accommodate different weighting of multivariate. For example, the well-known Manhattan distance (156) is the city block distance that measures distances on a rectilinear configuration, similar to travelling in street configuration. The correlation coefficients, e.g., Pearson correlation, can be transformed into dissimilarities within the interval [0,1].

3.2 Similarity Measures

Similarity measures are often used for categorical data, in which the measurements are scaled within the interval [0,1]. A similarity coefficient $s(a,b)$ describes how close the two objects a and b to each other. The value of $s(a,b)$ equals one represents the two objects a and b differ minimally for all variables. A dissimilarity coefficient $d(a,b)$ takes a simple manner to convert its similarity coefficient $s(a,b)$ by taking $1 - s(a,b)$. The commonly used similarity measures for binary variables include the matching coefficient, Jaccard coefficient, and Gower and Legendre (157).

4. Choose Clustering Algorithm

Appropriate clustering algorithms should be a good fit for the dataset, discovering the underlying structure of the clusters and insensitive to errors (22). In addition, a model-based algorithm is recommended to accommodate data-generating processes. An ML pipeline was built to implement various clustering algorithms in this research, as discussed in Section 4.4.4.

5. Evaluate and Interpret Clustering Results

As an exploratory analysis, one of the most challenging aspects of cluster analysis is evaluating the results. Some classical validity indices, including external and internal measures, were introduced in Section 4.4.5. As part of the interpretation of clustering results, descriptive statistics and cluster visualization are often appropriate for clustering analysis. The commonly used techniques include PCA, correspondence analysis (158), silhouette plot, neighbourhood plot, and stripes and shadow plot (159).

Appendix H
LASSO Regression

The LASSO regression is similar to Ridge regression, which minimizes the sum of the squared residuals plus lambda times the squared slope. Ridge regression is least squares plus the ridge regression penalty. Ridge regression has more bias than least squares. In turn, for that small amount of bias, the ridge regression has a significant drop in the variance. The main idea is that ridge regression provides better long-term predictions by starting with a slightly worse fit. The ridge regression penalty uses the slope squared, while the lasso regression takes the absolute value of the regressors instead of squaring it. The value of lambda is determined by cross-validation. Similar to ridge regression, a lambda can go from zero to positive infinity. When lambda equals zero, then the LASSO regression will be the same as the least squares. As lambda increases in value, the slope gets smaller until the slope equals zero. Likewise, LASSO regression leads to a small amount of bias but less variance than least squares. Both ridge and LASSO regression can be applied to complicated models that combine different types of data.

The significant difference between ridge and LASSO regression is that the former can only shrink the slope asymptotically close to zero. In contrast, the latter can shrink the slope to zero. The greater the value of lambda, the greater the shrinkage rate is. Generally, a moderate lambda value will cause the solution to shrinking towards zero, and some coefficients may end up precisely zero. Since LASSO regression can exclude unimportant variables from the equation, it is better than ridge regression to reduce the variance in models containing many irrelevant features, making the final equation simpler and easier to interpret. As an alternative to a model or subset of feature selection, LASSO often gives sparse solutions due to the $L1$ penalty (160).

Consider a simple least squares regression model

$$Y = \beta_0 + \beta_1 x_1 + \cdots + \beta_p x_p + \varepsilon, \tag{15}$$

where $x_1, \ldots, x_p$ are predictor variables, Y is the response variable, and ε is the residual error term. The LASSO regression corresponds to the penalization, shown as the second component in the following expression

$$\sum_{i=1}^{n}(y_i - \beta_0 - \sum_{j=1}^{p}\beta_j x_{ij})^2 + \lambda \sum_{j=1}^{p}|\beta_j| \quad (16)$$

Instead of penalizing the sum of the beta squares as in Ridge regression, the penalization term of LASSO regression is the sum of the absolute of the regression parameters.

Appendix I

Latent Markov Model (LMM)

Latent Variable Models in General

Latent variable models are a type of statistical model, including latent variables which are not directly observable. The purposes of including latent variables in the statistical models are i) to account for the unobserved heterogeneity among objects, ii) to account for measurement errors, and iii) to summarize different measurements of the same unobservable characteristics (127). Essentially a latent variable model formulates assumptions on:

- **Measurement Model:** $f(y|u,x)$ implies the conditional distribution of a set of response variables denoted as Y given latent variables denoted by U and possible covariates denoted by X.
- **Structural Model:** $f(u|x)$ formulates the assumption of latent variable U distribution given covariates X.

By marginalizing out the latent variables, the manifest distribution $f(y|x)$ will be obtained; by the Bayes theorem, the posterior distribution of the latent variable given the observable variables $f(u|x,y)$ will be obtained.

A common assumption of latent variable models is *local independence*, meaning the response variables are conditionally independent given the latent variables and covariates (161). In this research, a particular focus was given to LMM for panel data.

The Basic Version of LMM

Let X denotes a categorical latent variable with K categories (latent states), T denotes equidistant time occasions, subject i can be in a different latent states $k = 1,2,\dots,K$ at different time occasions $t = 0,1,\dots,T$

$x\_\{t\}$ = latent state variable at time t.

$$P(y_i) = \sum_{x_0=1}^{K} \sum_{x_1=1}^{K} \dots \sum_{x_T=1}^{K} P(x_0, x_1, \dots x_T) P(y_i|x_0, x_1, \dots x_T) \quad (17)$$

LMM parameters: each latent state u $(u = 1,\dots,k)$ corresponds to a class of subjects in the population and consists of the following probability parameters

- **Initial State Probability (b_0)**

$$P(X_0 = k) \tag{18}$$

Logit model may include covariates X (e.g., sex, ethnicity in this study)

$$log\frac{P(x_0 = k)}{P(x_0 = 1)} = \alpha_{0k} \tag{19}$$

- **Transition Probabilities (b_t)**

$$P(X_t = r|X_{t-1} = k) \tag{20}$$

$$log\frac{P(x_t = r|x_{t-1} = k)}{P(x_t = 1|x_{t-1} = k)} = \gamma_{0r} + \gamma_{1rk} + \gamma_{2rt} + \gamma_{3rkt} \tag{21}$$

Logit model may include fixed and time-varying predictors.

To combine the initial latent state and transition sub-models,

$$P(x_0, x_1, \dots x_T) = P(x_0)\prod_{t=1}^{T} P(x_t|x_{t-1}) \tag{22}$$

The transition matrix $\prod$ of size $k \times k$ represents transition probabilities.

- **Measurement Probabilities**

Measurement equivalence, distribution of the response variables with categorical responses

$$P(y_t = j|X_t = k) \tag{23}$$

One or more response variables Y can accommodate different scale types (e.g., continuous, categorical, count, nominal). For a single categorical response variable,

$$log\frac{P(y_{it} = l|x_t = k)}{P(y_{it} = 1|x_t = k)} = \beta_{0l} + \beta_{1lk} \tag{24}$$

$$P(y_i|x_0, x_1, \dots x_T) = \prod_{t=0}^{T} P(y_{it}|x_t) = \prod_{t=0}^{T} \prod_{j=1}^{J} P(y_{itj}|x_i) \tag{25}$$

The particular set of latent states (k_0, k_1, k_2) defines a changing pattern for subject i. Given the unconditional distribution (no predictor) of a basic version of LMM, extension to multiple indicators is immediate (162).

Manifest distribution: local independence indicates that the conditional distribution of Y_i given X_i is

$$p(y_i|x_i) = p(Y_i = y_i|X_i = x_i)\prod_{t=1}^{T} \emptyset y_{it}|x_{it} \tag{26}$$

Distribution of X_i is:

$$p(x_i) = p(X_i = x_i) = \pi x_{i1} \prod_{t>1} \pi x_{it} | x_{i,t-1} \quad (27)$$

Manifest distribution of Y_i is:

$$p(y_i) = p(X_i = x_i) = \sum_x p(y_i|x)p(x) \quad (28)$$

Maximum likelihood estimation of the basic LMM

Model log-likelihood can be expressed as

$$l(\theta) = \sum_{i=1}^{n} \log p(y_i) = \sum_y n(y) \log p(y) \quad (29)$$

where θ is the vector of all model parameters π_u, $\pi_{v|u}$, $\emptyset_{y|u}$ for categorical data. $n(y)$ is the frequency of the response variable y. The Expectation-Maximization (EM) algorithm can be applied to maximize $l(\theta)$ (163,164).

The EM algorithms iterate the following two steps until convergence.

- **E-Step** computes the posterior distribution of the latent states given the current value of observed data and parameters.
- **M-Step** maximizes the posterior expected value of the log-likelihood of complete data concerning the model parameters.

Suitable recursions must compute the $l(\theta)$ and perform the E-Step (163). Being $l(\theta)$ multimodal, different initializations (deterministic and random) of the algorithm are necessary to increase the chance to get its global maximum. Extended models, such as multivariate, with covariates, and mixed are still fitted by the EM algorithm in which the main adjustments are in the M-Step. If necessary, the selection of k may be based on suitable statistical criteria (165):

- $AIC = -2l(\hat{\theta}) + 2k$ (k: number of estimated parameters in the model)
- $BIC = -2l(\hat{\theta}) + \log(n)\, k$ (n: sample size; k: number of estimated parameters in the model)

Inclusion of Covariates in the Basic LMM

Two possible choices to include individual covariates collected in $X_i = x_{i1}, \dots, x_{iT}$

- The first is random intercepts in the measurement model; for binary variables, it is assumed

$$\lambda_{itu} = p(Y_{it} = 1 | U_i = u, X_i) \quad (30)$$

$$\log \frac{\lambda_{itu}}{1 - \lambda_{itu}} = \alpha_u + x'_{it}\beta \rightarrow (i = 1, \dots, n; t = 1, \dots, T; u = 1, \dots, k) \quad (31)$$

- The second is in the structural model, governing the distribution of the latent variables via a multinomial logit parametrization.

Initial Probabilities:

$$\pi_{iu} = p(U_{i1} = u|x_{i1}) \tag{32}$$

$$\log\frac{\pi_{iu}}{\pi_{i1}} = x'_{i1}\beta_u \rightarrow (u = 2, \dots, k) \tag{33}$$

Transition Probabilities:

$$\pi_{itv|u} = p(U_{it} = v|U_{i,t-1} = u, x_{it}) \tag{34}$$

$$\log\frac{\pi_{itv|u}}{\pi_{itu|u}} = x'_{it}\gamma_{uv} \rightarrow (u, v = 1, \dots, k, u \neq v) \tag{35}$$

Multivariate Extension to the Basic LMM

A vector of J response variables $Y_{it} = (Y_{i|t}, \dots, Y_{iJt})'$ is considered for subject i at time occasion $t, i = 1, \dots, n; t = 1, \dots, T$. With categorical responses, it is assumed that the components of y_{it} are conditionally independent given X_{it} (local independence), so that

$$p(y_{it}|x_{it}) = p(Y_{it} = y_{it}|X_{it} = x_{it}) = \prod_{j=1}^{J} \emptyset_{jy_{ijt}|x_{it}} \tag{36}$$

$$\emptyset_{jy|x} = p(Y_{ijt} = y|x_{it} = x) \tag{37}$$

Another assumption is that the latent variables $X_{i1}, \dots, X_{iT}$ follow a first-order Markov chain, possibly non-homogeneous.

Model Specification with Multivariate Extension

In this thesis, we started with fitting an unrestricted LMM, the basic version of an LMM, denoted by M_1. For the i^{th} individual at time t on Q observed substance use indicators ($Q = 4$), a response pattern can be expressed as $Y_i^{(t)} = (y_{i1}^{(t)}, \dots, y_{iQ}^{(t)})$. In this thesis, each of the observed substance use indicators has three categories, being 0, 1, and 2, indicating "never use," "occasional use," and "current use," respectively. It is assumed that for each subject, the actual underlying substance use pattern at each time occasion t (where $t = 1, \dots, T$, and $T = 3$ representing Wave I, Wave II, and Wave III) is explained by a vector of covariates with K latent states of substance use patterns. It is assumed that the responses to the (Q x T) y indicators are conditionally independent given the substance use patterns.

Given that the response variables have more than two categories with ordinal in nature, Colombi and Forcina (2001) suggest that local logits, global logits, or continuation logits can be applied as the specific function (166). In particular, the global logit function, related to cumulative logits for ordinal response variables, is the counterpart of the logit link function for binary response variables (27). The vector of global logits can be expressed as

$$\eta_{y|u}^{(t)} = \log \frac{\emptyset_{y|u}^{(t)} + \cdots + \emptyset_{c-1|u}^{(t)}}{\emptyset_{0|u}^{(t)} + \cdots + \emptyset_{y-1|u}^{(t)}} \qquad (t = 1, \dots, T;\ u = 1, \dots, k;\ y = 0, \dots, c-1) \qquad (38)$$

where c is the number of categories ($c = 3$) of the response variables, u is the latent state, and $\eta_{y|u}^{(t)}$ is the y^{th} global logit given u^{th} latent state for the t^{th} time occasion (27).

To further extend the LMM with multivariate responses, local independence is the key assumption for the response variables and the corresponding latent variable. In the case of restrictions on the measurement model, the same principles apply. Let $\emptyset_{q|u}^{(t)}$ be the vector with elements $\emptyset_{qy|u}^{(t)}$, $(y = 0, \dots, c_q - 1)$. As an extension to the univariate response formulation, $\emptyset_{q|u}^{(t)} = \emptyset_{q|u}, (q = 1, \dots r; u = 1, \dots, k; t = 1, \dots, T)$, where $\emptyset_{q|u}$ is the vector of conditional response probabilities with elements $\emptyset_{qy|u}, (y = 0, \dots, c_q - 1)$. The conditional distribution of each response variable can be parameterized using generalized linear models (GLM). The corresponding link function can be simplified as $\eta_{q|u}^{(t)} = W_{q|u}^{(t)}\beta = g_q(\emptyset_{q|u}^{(t)})$, where $g_q(*)$ is a type of link function discussed previously.

The Expectation-Maximization (EM) algorithm was implemented in this thesis to estimate the maximum likelihood of LMM parameters. Given the existing values of the parameters and the observed data, the E-step computes the frequency of subjects belonging to latent states (*conditional response probabilities*), the frequency of subjects in latent state u at time point t (*initial probabilities*), and the number of transitions from one latent state to another at time point t (*transition probabilities*). The expected values of these three components may be maximized separately via M-step. Applying the EM algorithm on multivariate response variables, the complete data log-likelihood is expressed as

$$l^*(\theta) = \sum_{y=0}^{c_q-1} \sum_{u=1}^{k} \sum_{t=1}^{T} \sum_{q=1}^{r} a_{quy}^{(t)} \log \emptyset_{qy|u} + \sum_{u=1}^{k} b_u^{(1)} \log \pi_u + \sum_{u=1}^{k} \sum_{\hat{u}=1}^{k} \sum_{t=2}^{T} b_{\hat{u}u}^{(t)} \log \pi_{u|\hat{u}}^{(t)} \quad (39)$$

where $a_{quy}^{(t)}$ represents the frequency of subjects with outcome y in latent state u for the q^{th} response variable at time occasion t (27). In general, the EM algorithm has the same structure as outlined above. An alternative method to the EM algorithm, Bayesian estimation of LMM, can also estimate maximum likelihood. However, the existing software package only supports the EM algorithm; this thesis did not implement Bayesian inference.

Decoding

As introduced in Section 2.3.4, decoding refers to a process of dynamic pattern recognition, predicting the order of the latent states with observed data for a subject (27). The two types of decoding, local and global decoding, each has its purposes. Local decoding aims to identify the most likely latent state for each time occasion. Global decoding finds the most likely order of latent states, requiring specific algorithms, such as an iterative algorithm developed by Viterbi (83,167).

In local decoding, the estimated posterior probabilities $p(u_t|y_i) = p(U_{it} = u_t|Y_i = y_i)$ maybe used to assign subject i to a latent state at a given time occasion t: $\hat{u}_{it}: p(\hat{u}_{it}|y_i) = \max_{u_t} p(u_t|y_i)$, derived from the EM algorithm. Whereas in global decoding, the problem of path detection is more complex, i.e., identifying the most likely order $\tilde{u}_i = (\tilde{u}_{i1}, \dots, \tilde{u}_{iT})'$ for subject i: $\tilde{u}_i: p(U_{i1} = \tilde{u}_{i1}, \dots, U_{iT} = \tilde{u}_{iT}|y_i) = \max_{u} p(u|y_i)$.

Mixed LMM

Additional random effects/latent variables may be included in an LMM to account for other sources of unobserved heterogeneity (168). Among the mixed LMMs, a particular focus is based on initial and transition probabilities of the individual latent processes defined conditional on a discrete latent variable $V_i (i = 1, \dots, n)$ The model assumes that individuals are divided into latent clusters, with individuals in the same cluster following the same LMM, while the measurement model is common to all individuals. Mixed LMMs may also be used for multilevel longitudinal data collected in observable groups (100).

Appendix J
Missing Data Analysis

Figures 39-41 illustrate missing data distribution, missing patterns, and missing patterns on response variables for Wave I (2016-17).

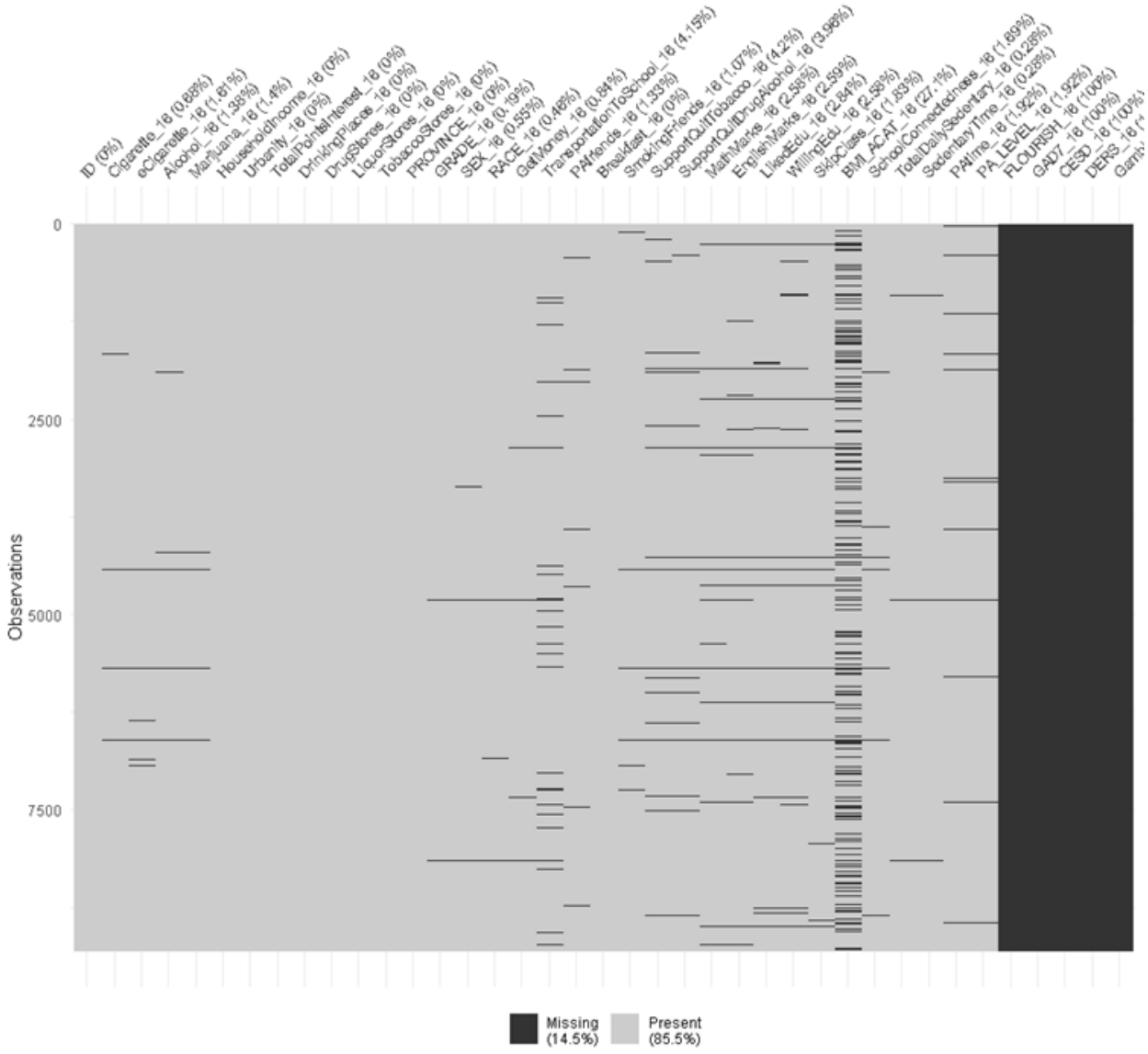


Figure 39. Missing data distribution (Wave I, 2016-17)

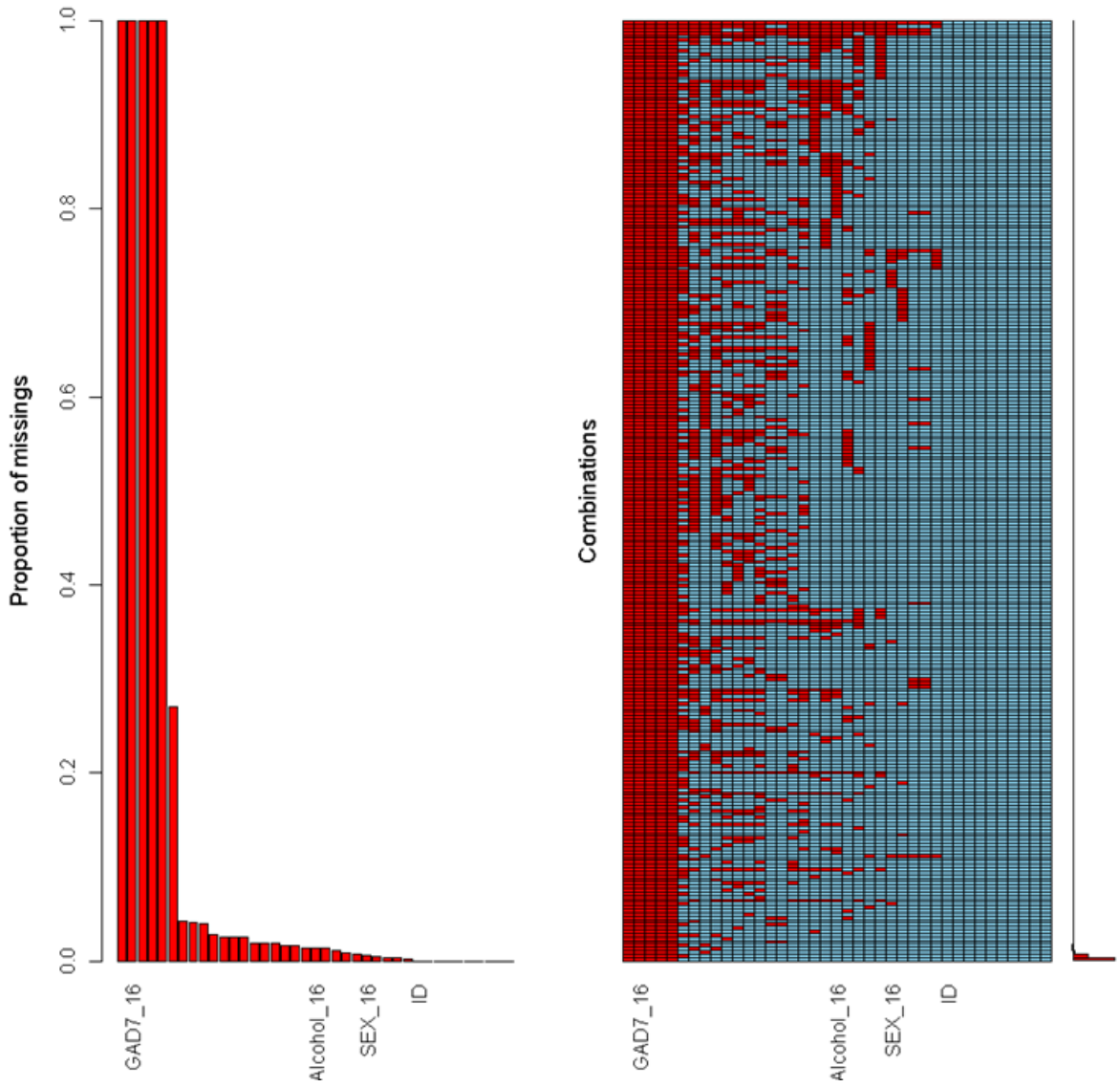


Figure 40. Missing patterns (Wave I, 2016-17)

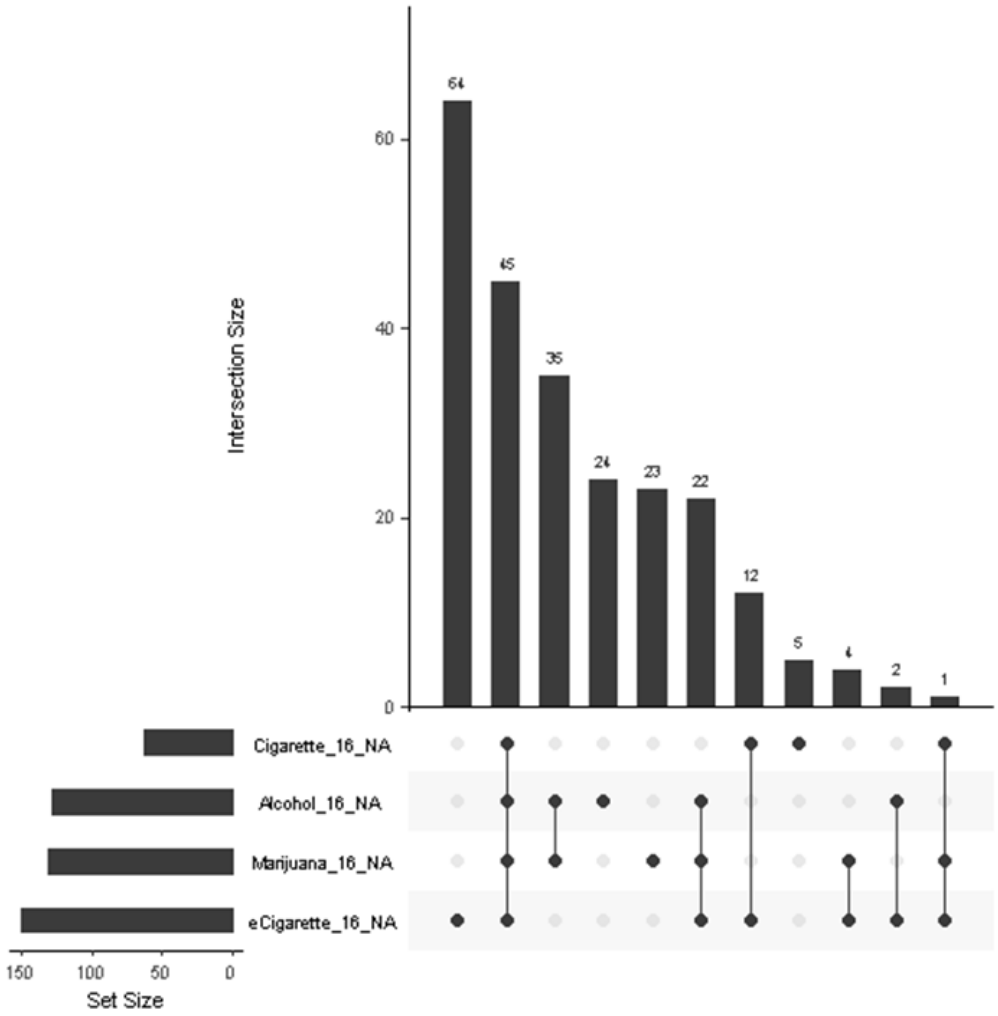


Figure 41. Missing patterns on response variables (Wave I, 2016-17)

Figures 42-44 illustrate missing data distribution, missing patterns, and missing patterns on response variables for Wave II (2017-18).

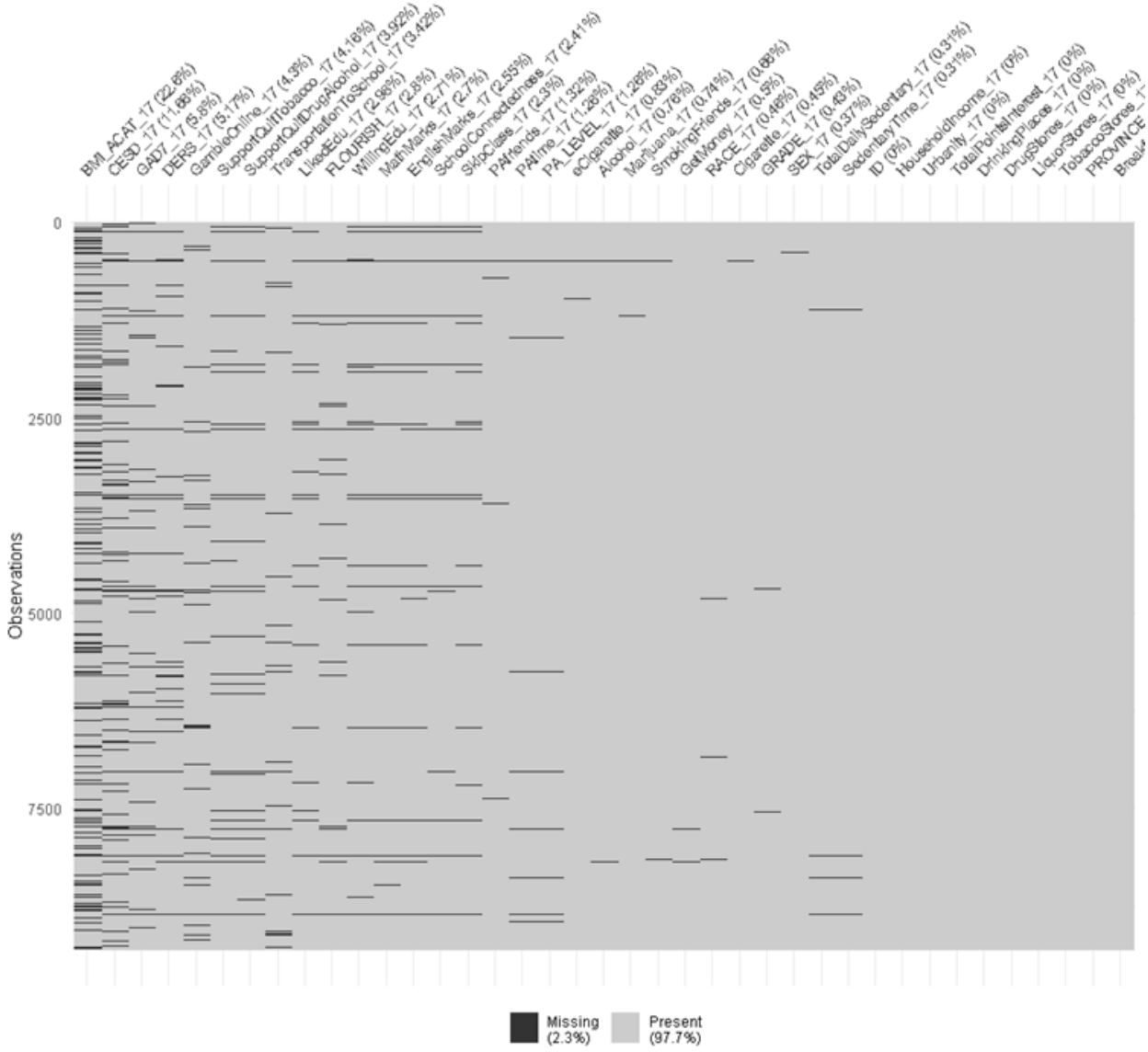


Figure 42. Missing data distribution (Wave II, 2017-18)

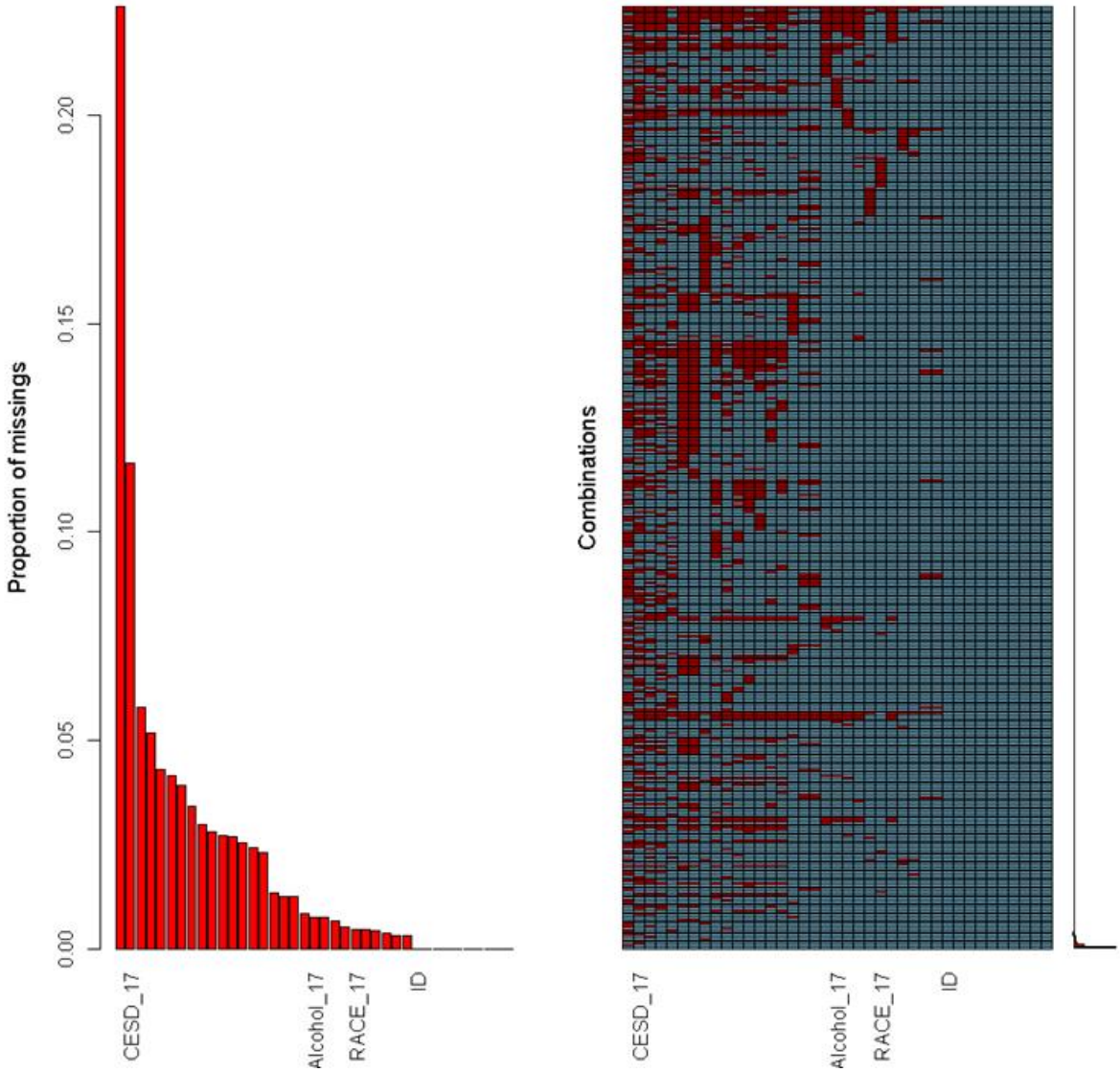


Figure 43. Missing patterns (Wave II, 2017-18)

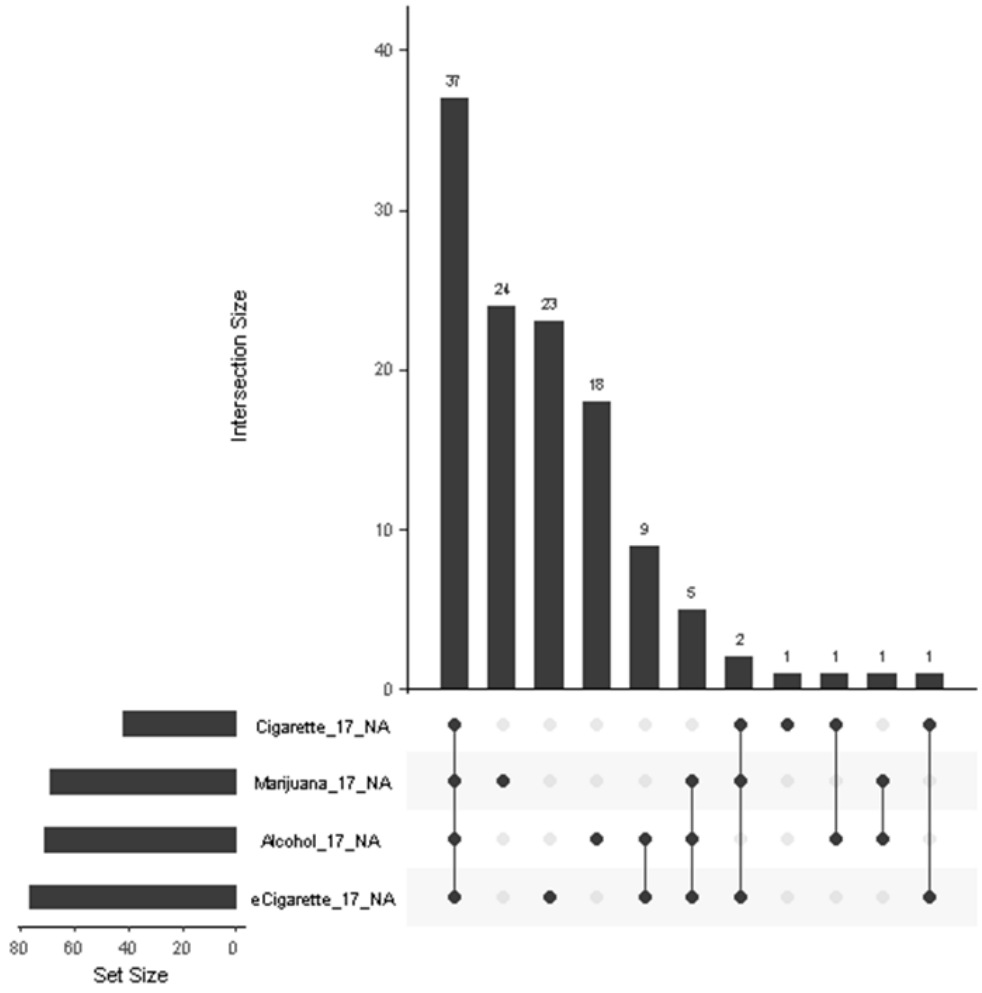


Figure 44. Missing patterns on response variables (Wave II, 2017-18)

Figures 45-47 illustrate missing data distribution, missing patterns, and missing patterns on response variables for Wave III (2018-19).

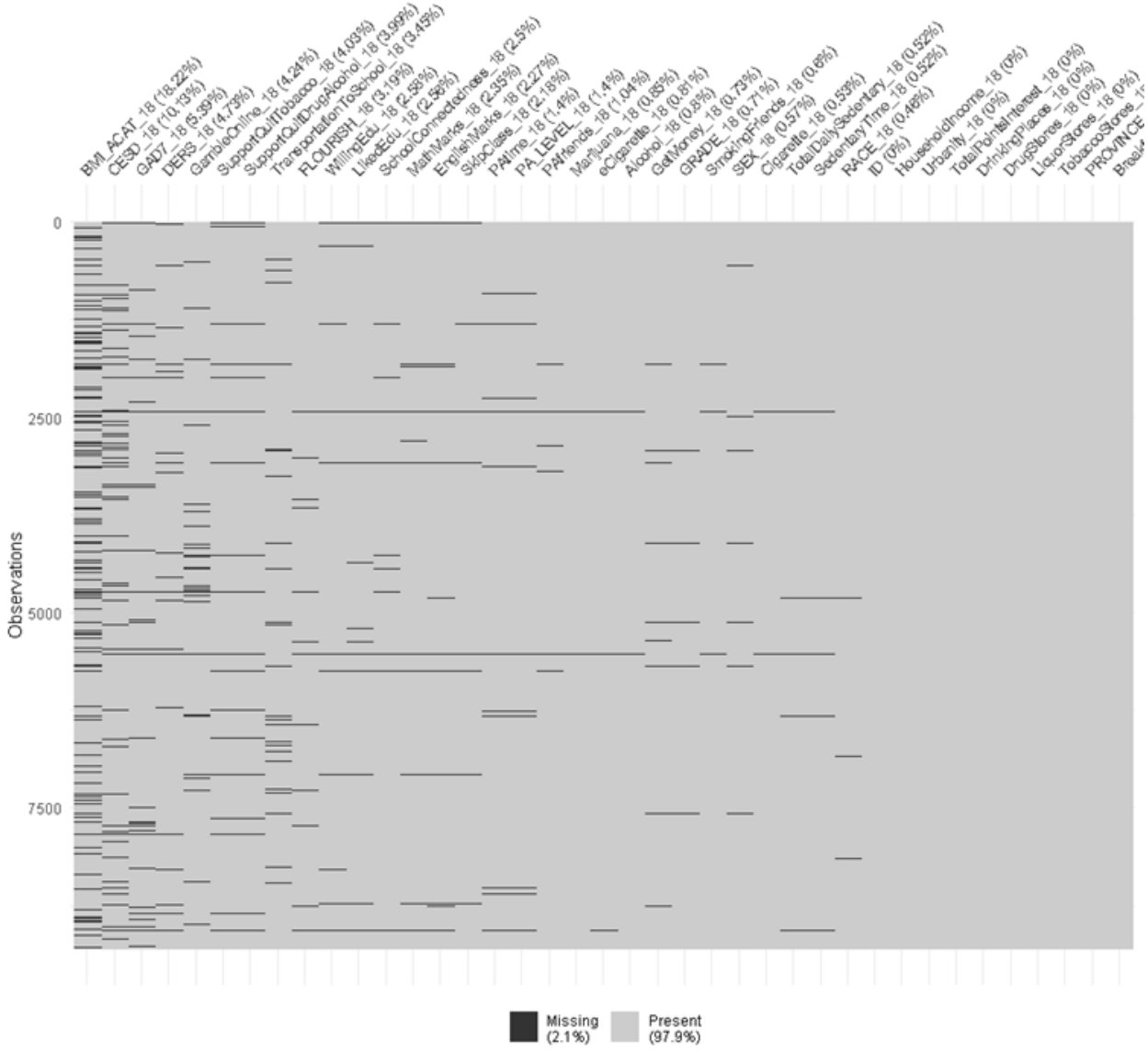


Figure 45. Missing data distribution (Wave III, 2018-19)

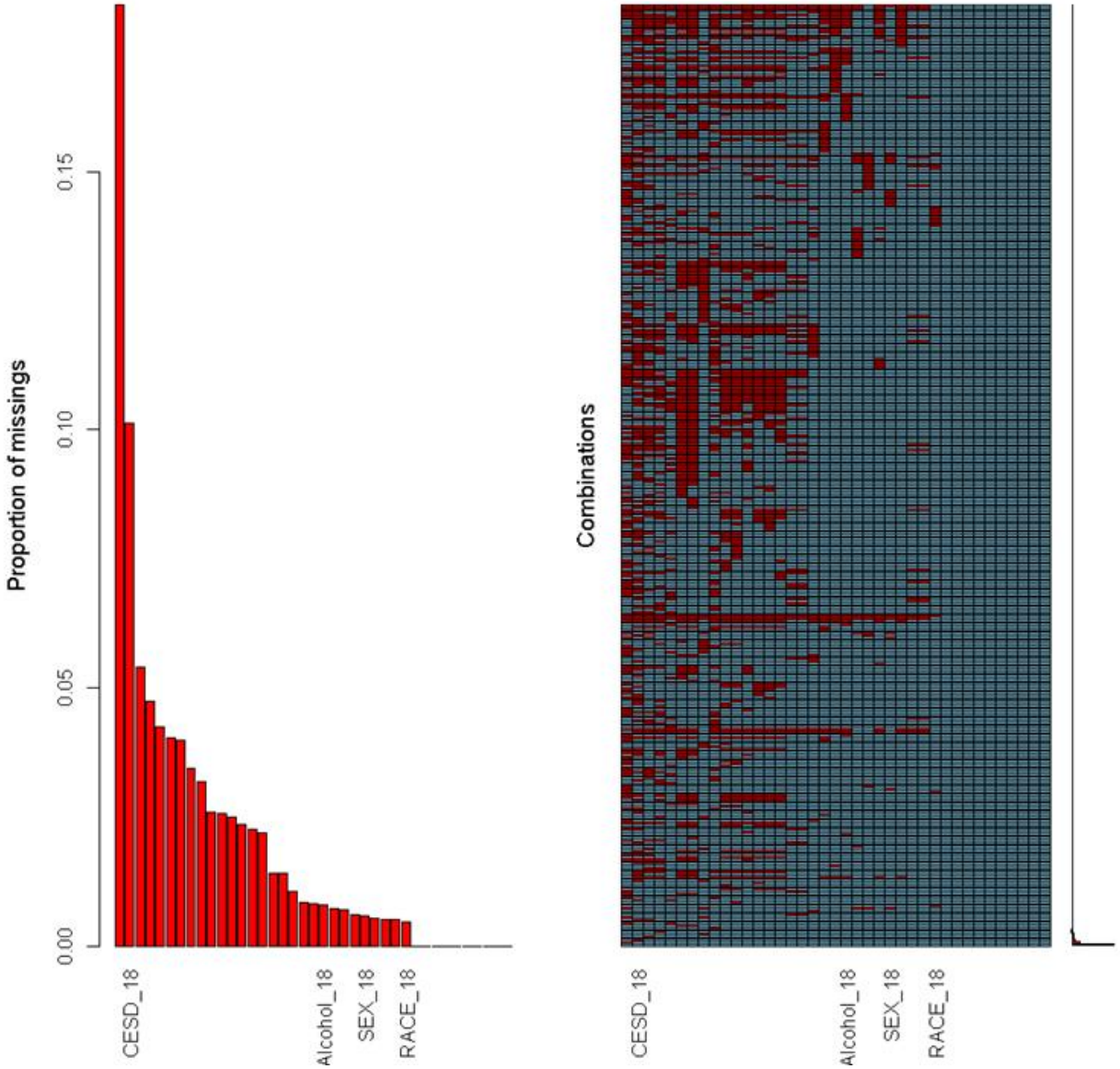


Figure 46. Missing patterns (Wave III, 2018-19)

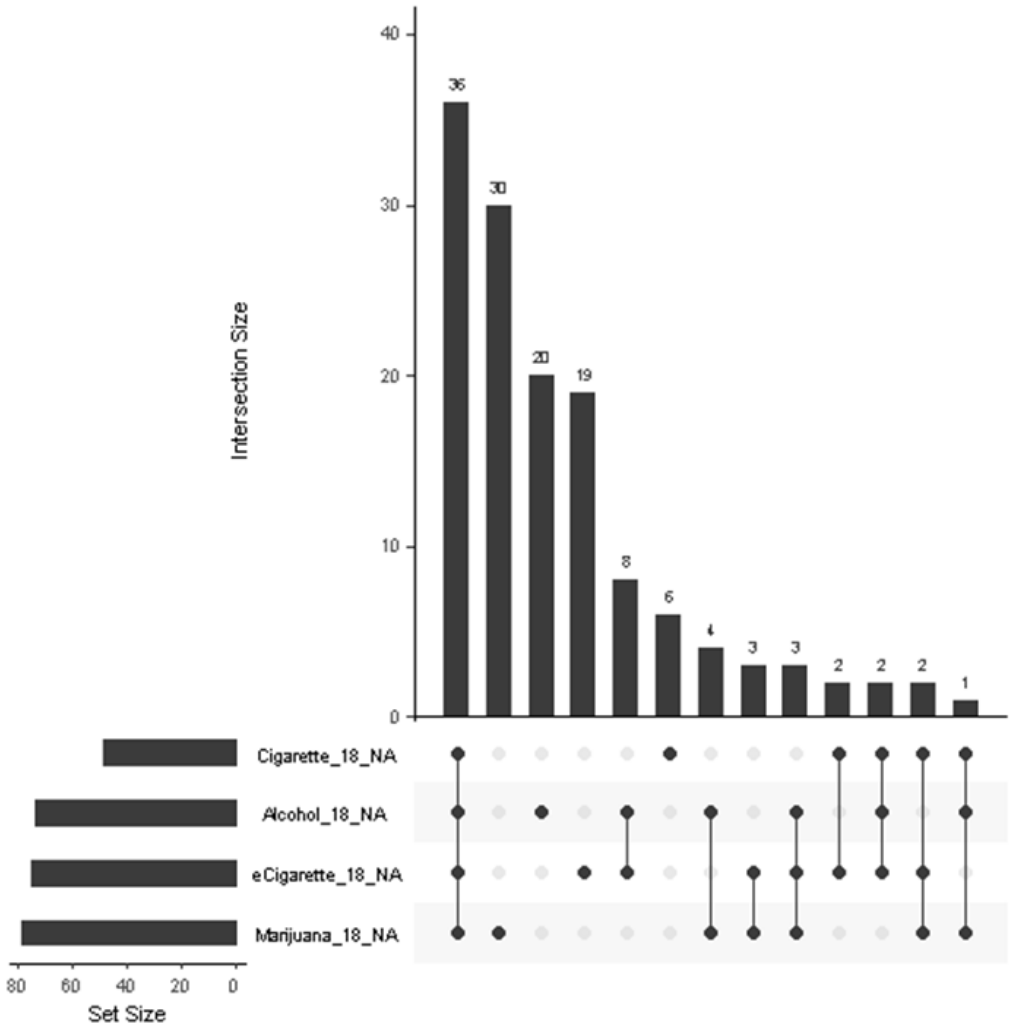


Figure 47. Missing patterns on response variables (Wave III, 2018-19)

Appendix K

Clustering Results – FCM Clustering

Figures 48-50 illustrate the two-dimensional (2D) representation and the silhouette plot of FCM clustering on the linked COMPASS data by waves.

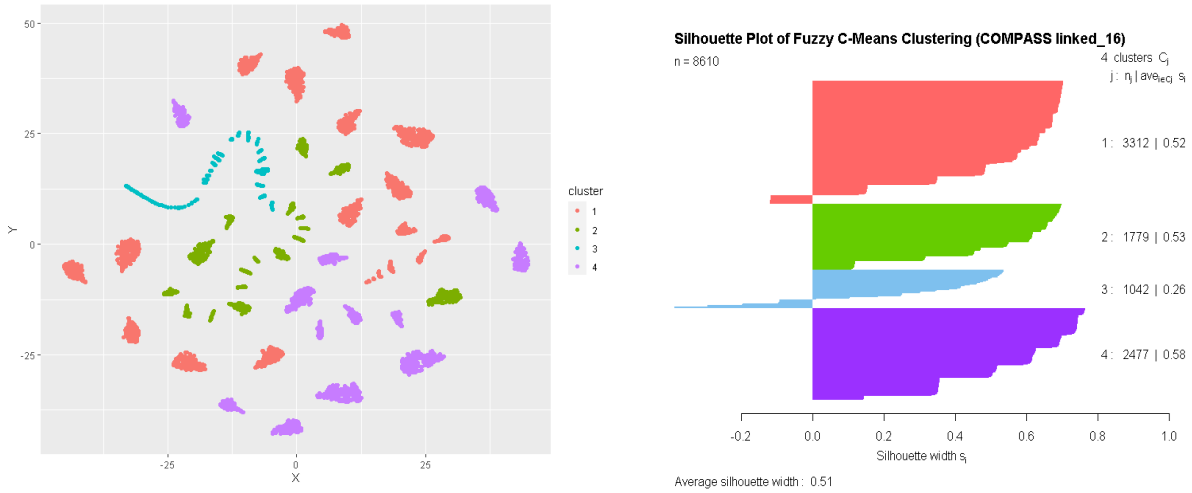
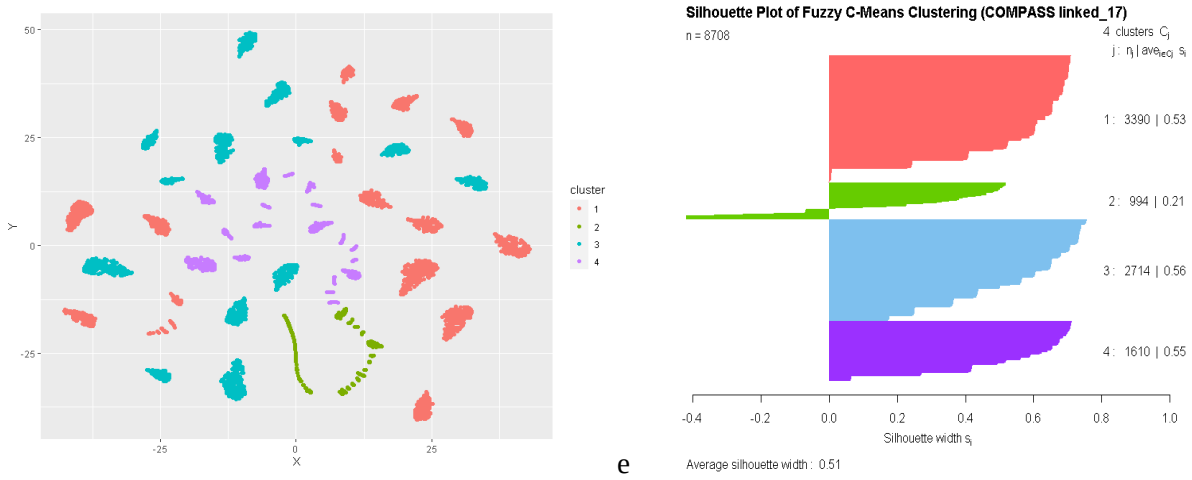


Figure 48. FCM Clustering, left-panel: 2D representation; right-panel: silhouette plot (Wave I, 2016-17)



e

Figure 49. FCM Clustering, left-panel: 2D representation; right-panel: silhouette plot (Wave II, 2017-18)

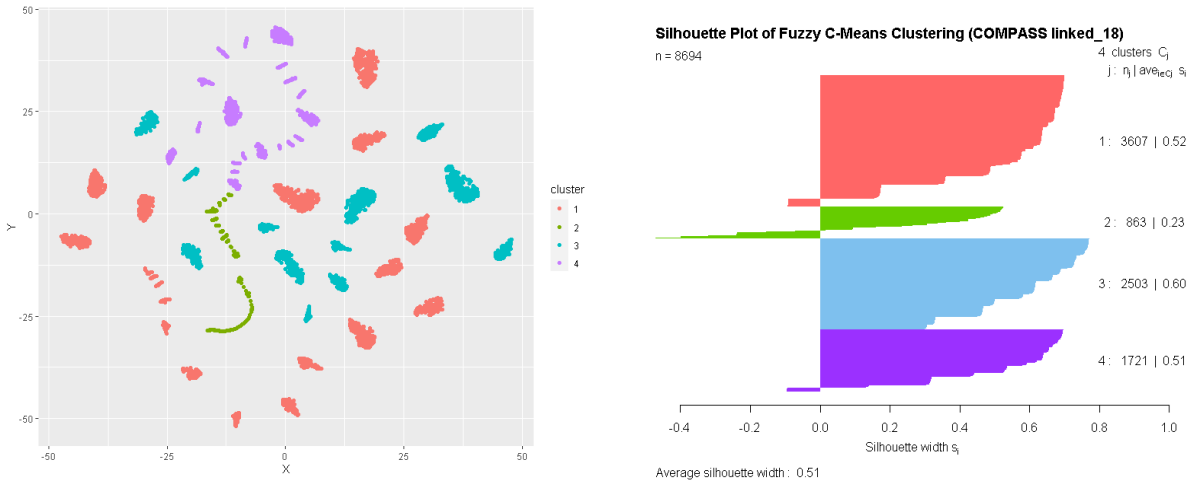


Figure 50. FCM Clustering, left-panel: 2D representation; right-panel: silhouette plot (Wave III, 2018-19)

Appendix L

Clustering Results – PAM Clustering

Figures 51-53 illustrate the two-dimensional (2D) representation and the silhouette plot of PAM clustering on the linked COMPASS data by waves.

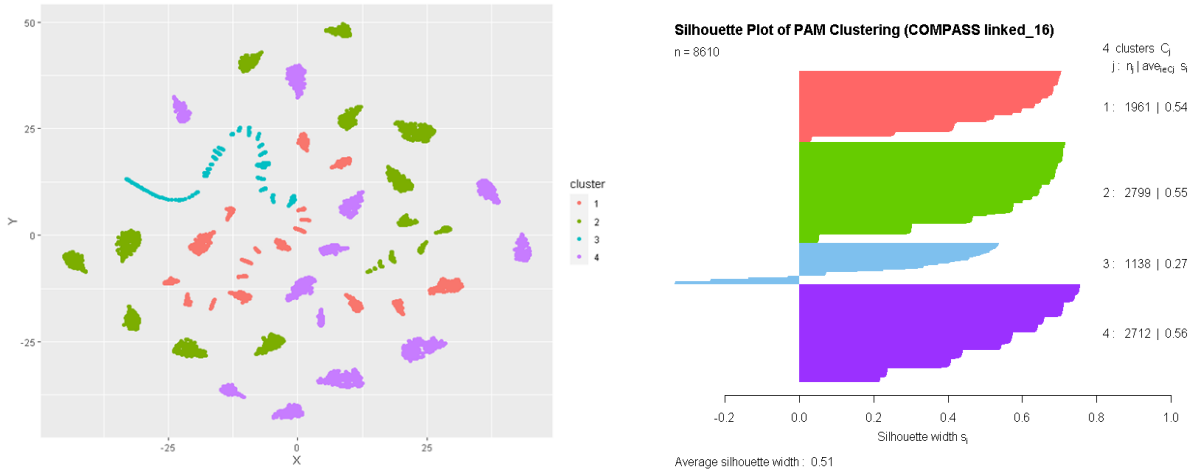


Figure 51. PAM Clustering, left-panel: 2D representation; right-panel: silhouette plot (Wave I, 2016-17)

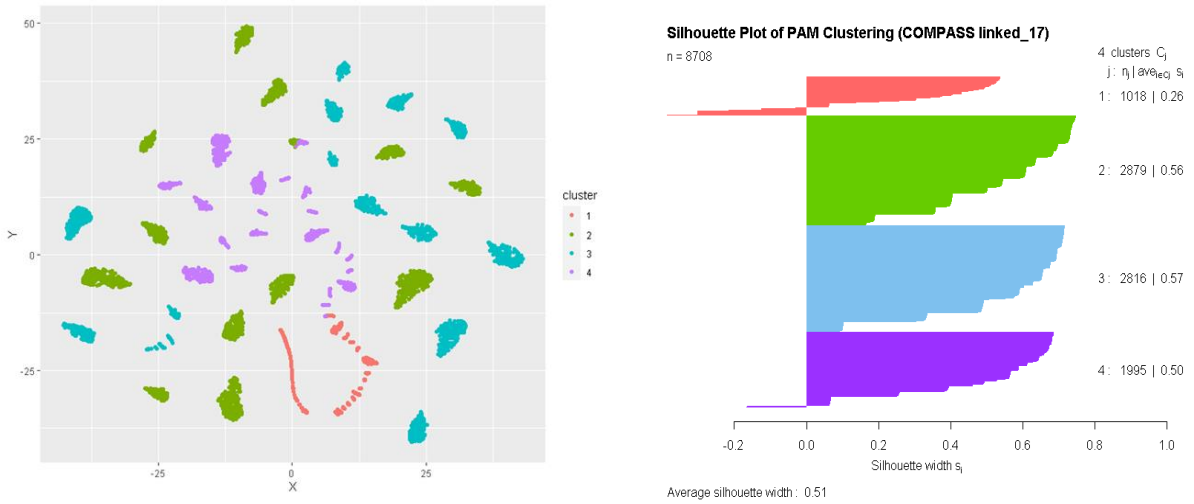


Figure 52. PAM Clustering, left-panel: 2D representation; right-panel: silhouette plot (Wave II, 2017-18)

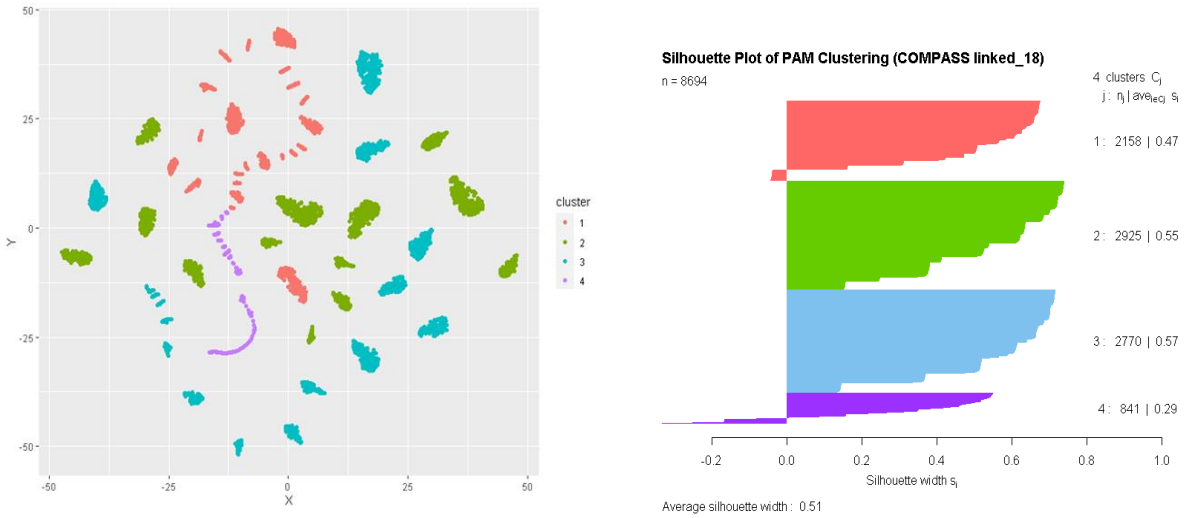


Figure 53. PAM Clustering, left-panel: 2D representation; right-panel: silhouette plot (Wave III, 2018-19)

Appendix M

Clustering Results – Hierarchical Clustering

Figures 54, 56, & 58 demonstrate the dendrogram of hierarchical clustering on the linked COMPASS data by waves. Figures 55, 57, & 59 illustrate the two-dimensional (2D) representation and the silhouette plot of hierarchical clustering on the linked COMPASS data by waves.

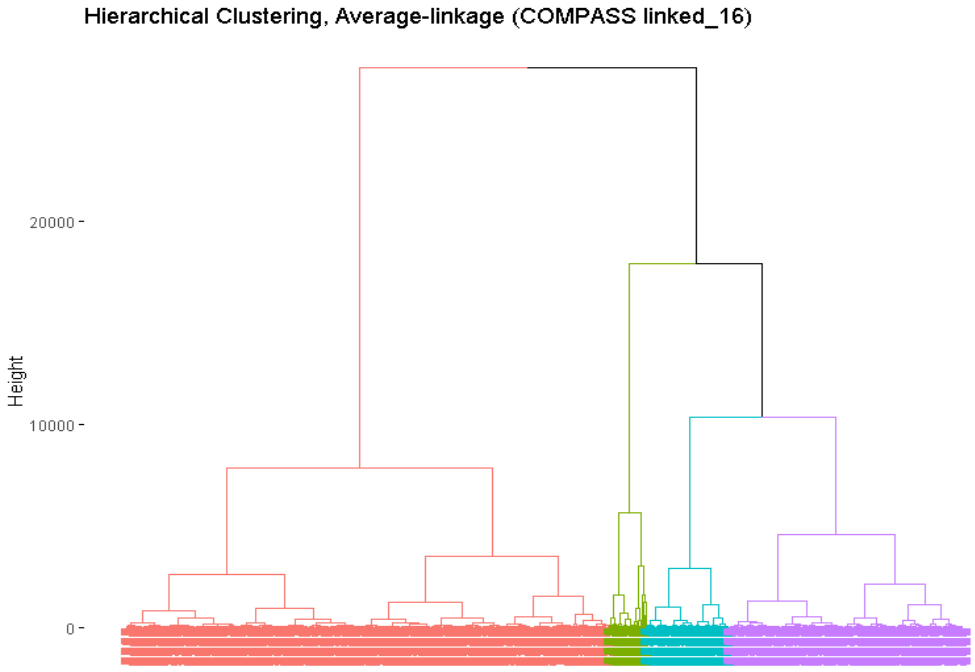


Figure 54. Hierarchical Clustering, Dendrogram (Wave I, 2016-17)

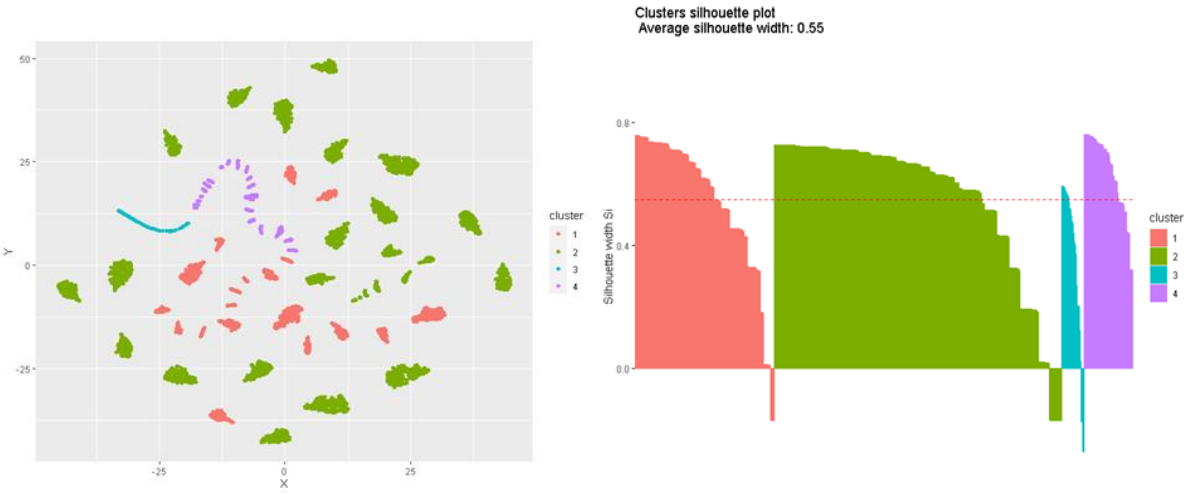


Figure 55. Hierarchical Clustering, left-panel: 2D representation; right-panel: silhouette plot (Wave I, 2016-17)

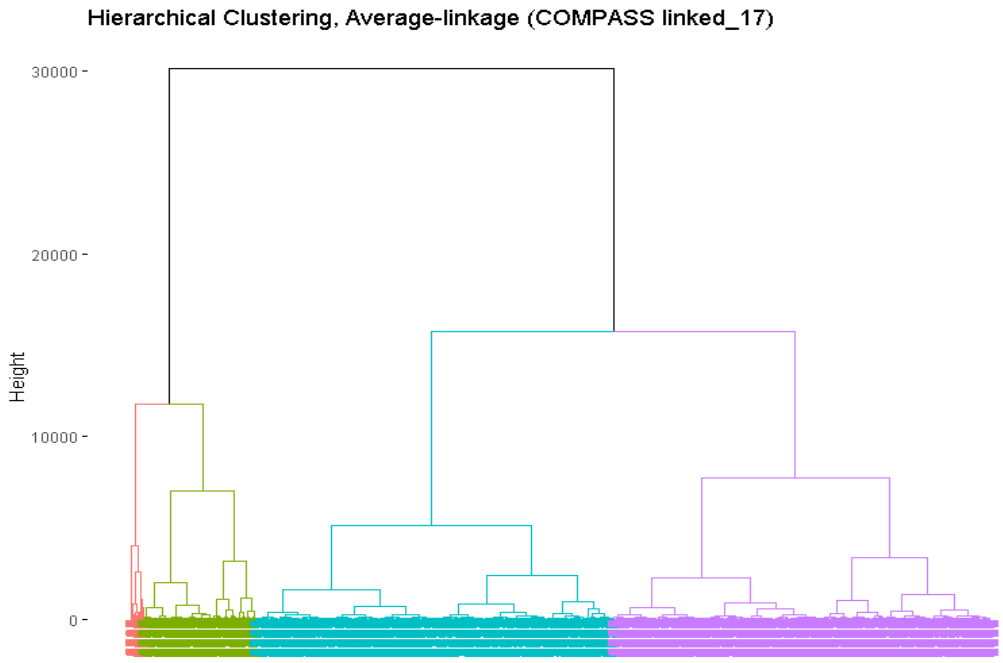


Figure 56. Hierarchical Clustering, Dendrogram (Wave II, 2017-18)

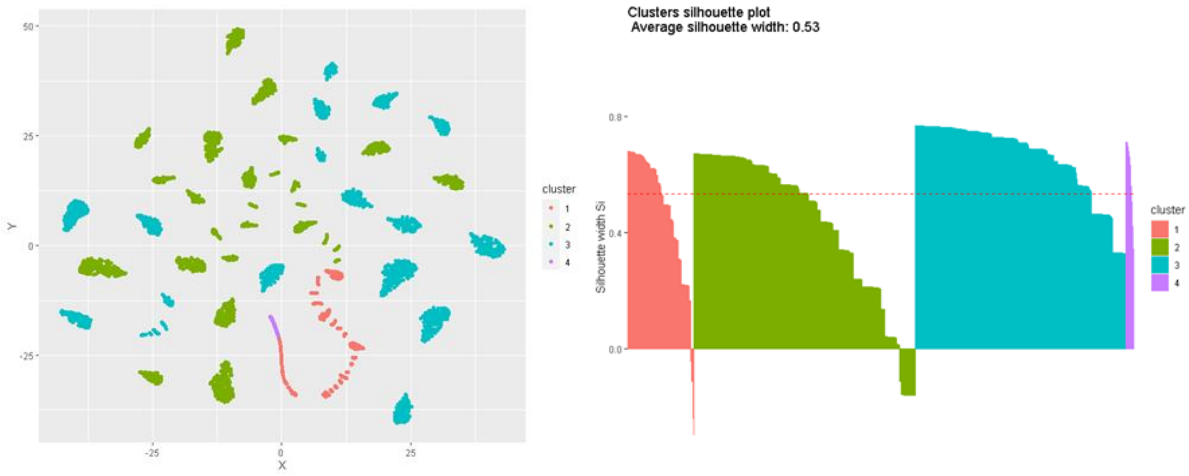


Figure 57. Hierarchical Clustering, left-panel: 2D representation; right-panel: silhouette plot (Wave II, 2017-18)

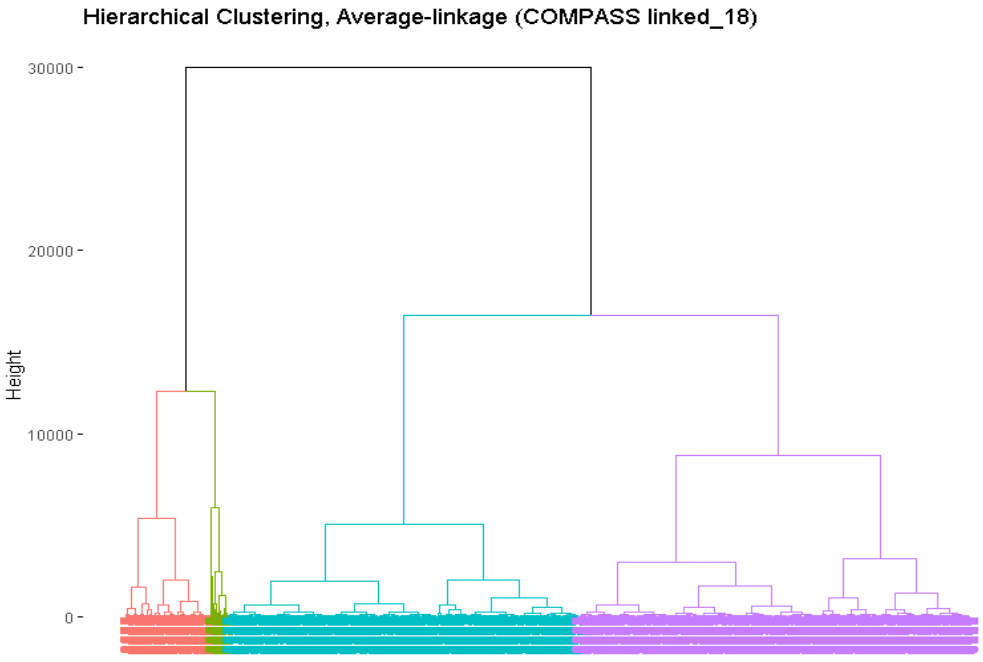


Figure 58. Hierarchical Clustering, Dendrogram (Wave III, 2018-19)

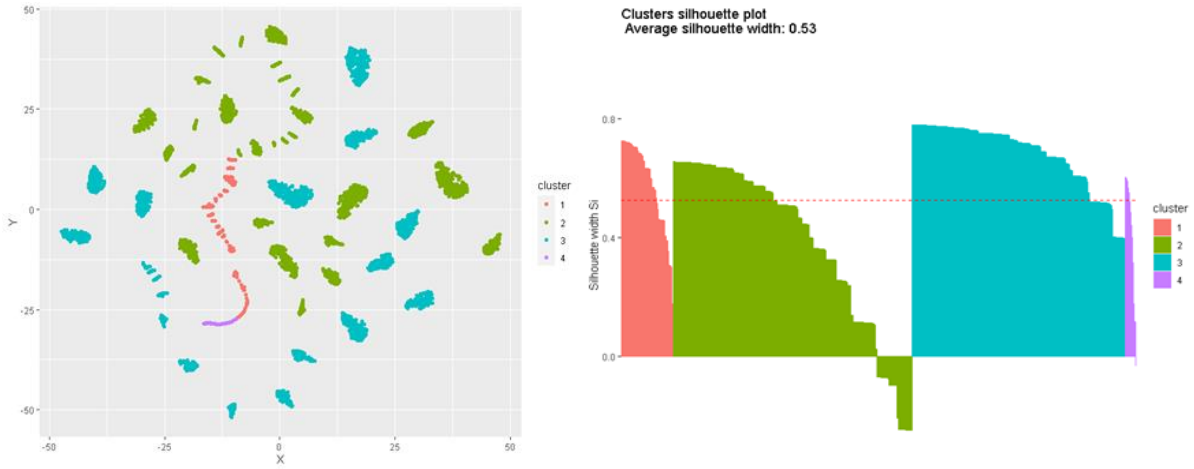


Figure 59. Hierarchical Clustering, left-panel: 2D representation; right-panel: silhouette plot (Wave III, 2018-19)

Appendix N

Selection of the Covariates Using LASSO Regression

Tables 26-28 summarize LASSO regression coefficients for all features by waves. Coefficients that were not shrunk to zero are highlighted in bold font, which was selected for further modelling. Figures 60-62 illustrate the LASSO coefficients for all features by waves.

Table 26. LASSO coefficients (Wave I, 2016-17)

Number	Feature*	Coefficient
1	(Intercept)	0.0000
2	HouseholdIncome_16	0.0000
3	**Urbanity_16 [a]**	**-0.0126**
4	TotalPointsInterest_16	0.0000
5	DrinkingPlaces_16	0.0000
6	DrugStores_16	0.0000
7	LiquorStores_16	0.0000
8	TobaccoStores_16	0.0000
9	Province_16 [a]	0.0000
10	**Grade_16 [a]**	**0.1000**
11	Sex_16	0.0000
12	Race_16 [a]	0.0000
13	**GetMoney_16 [a]**	**0.0780**
14	TransportationToSchool_16	0.0000
15	PAfriends_16 [a]	0.0000
16	**EatingBreakfast_16 [a]**	**-0.0650**
17	**SmokingFriends_16 [a]**	**0.4925**
18	**SupportQuitDrugAlcohol_16 [a]**	**0.1088**
19	**EnglishMarks_16 [a]**	**0.0194**
20	**WillingEdu_16 [a]**	**-0.0269**
21	**SkipClass_16 [a]**	**0.3878**

Number	Feature*	Coefficient
22	**BMI_CATEGORY_16 [a]**	**0.0161**
23	**SchoolConnectedness_16 [a]**	**-0.0180**
24	**SedentaryTime_16 [a]**	**0.0003**
25	TotalPAtime_16	0.0000
26	PA_LEVEL_16[a]	0.0000
27	FLOURISH_16	0.0000
28	GAD7_16 [a]	0.0000
29	CESD_16 [a]	0.0000
31	DERS_16 [a]	0.0000
31	GambleOnline_16 [a]	0.0000

*The last three char "_16" indicates the school year of 2016-17; [a] see Section 5.4.1 for descriptions

DrinkingPlaces – BE data, counts of drinking places within 1000 meters of schools. Establishments primarily engaged in the retail sale of alcoholic drinks, such as beer, ale, wine, and liquor, for consumption on the premises. The sale of food frequently accounts for a substantial portion of the receipts of these establishments.

FLOURISH – This is a derived variable, scoring from 8 to 40. The higher the score is, the more psychological resources and strengths are, based on the Flourishing Scale.

HouseholdIncome – SES data, the median total income of households in 2015 ($), categorized into "25001-50000," "50001-75000," "75001-100000," and ">100000," dummy coded from 1 to 4, respectively.

LiquorStores – BE data, counts of liquor stores within 1000 meters of schools. Establishments primarily engaged in retailing packaged alcoholic beverages, such as ale, beer, wine, and liquor, for consumption off the premises. Stores selling prepared drinks for consumption on the premises are classified in Industry 5813.

TobaccoStores – BE data, counts of tobacco stores & stands within 1000 meters of schools. Establishments primarily engaged in the retail sale of cigarettes, cigars, tobacco, and smokers' supplies.

TotalPAtime - This is a derived variable, representing total combined HARD and MODERATE physical activity in minutes, ranging from 0 to 3990.

TotalPointsInterest – BE data, counts of EPOI total points of interest within 1000 meters of schools.
TransportationToSchool – Students were asked, "How do you usually travel to and from school? (If you use two or more modes or travel, choose the one that you spend most time doing) To school" The response options are: "By car (as a passenger)," "By car (as a driver)," "By school bus," "By public bus, subway, or streetcar," "By walking," "By bicycling," and "Other," dummy coded from 1 to 7, respectively.

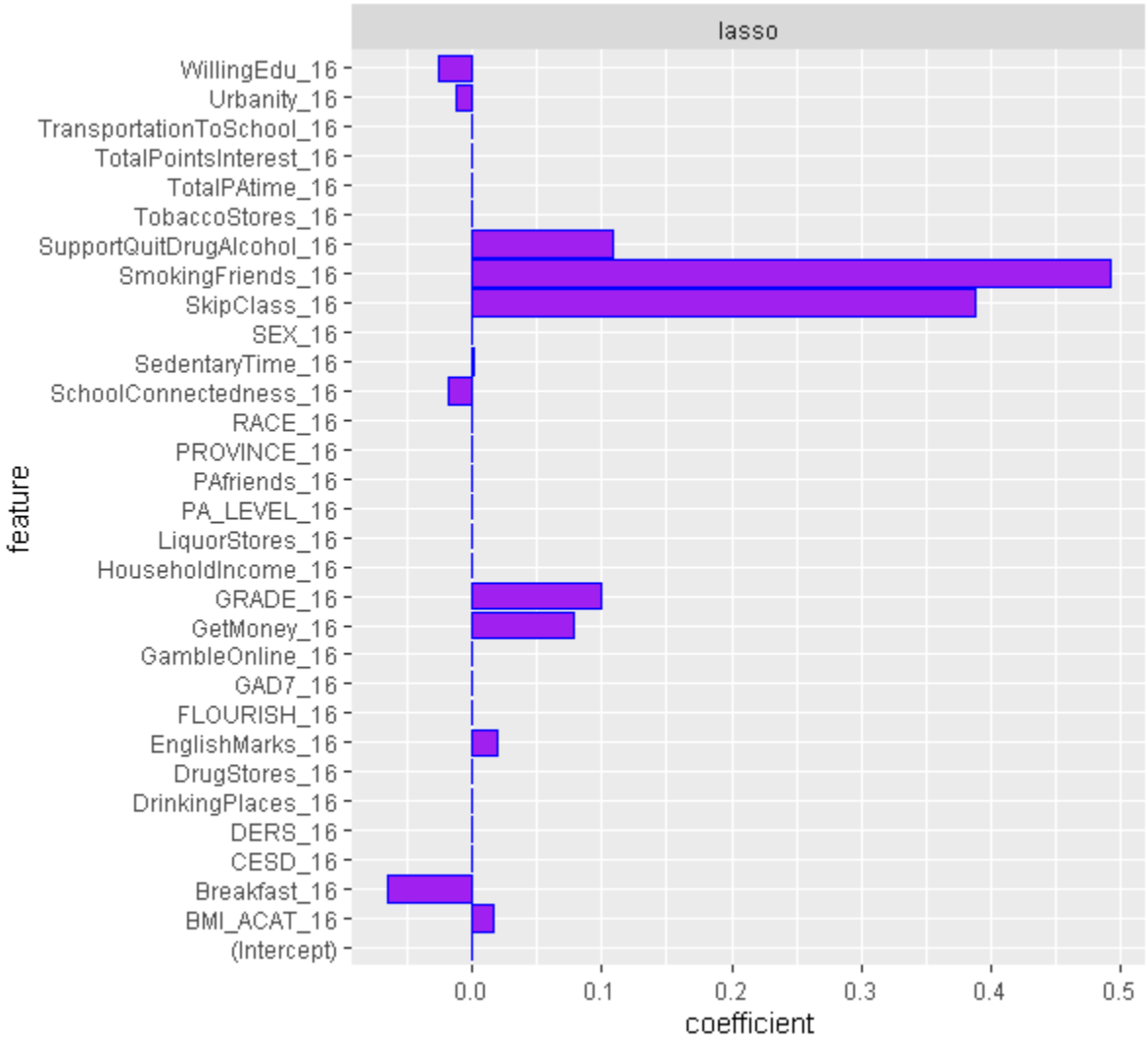


Figure 60. LASSO coefficients (Wave I, 2016-17)

Table 27. LASSO coefficients (Wave II, 2017-18)

Number	Feature*	Coefficient
1	(Intercept)	0.0000
2	HouseholdIncome_17	0.0000
3	**Urbanity_17 [a]**	**-0.1336**
4	TotalPointsInterest_17	0.0000
5	DrinkingPlaces_17	0.0000
6	DrugStores_17	0.0000
7	LiquorStores_17	0.0000
8	TobaccoStores_17	0.0000
9	Province_17 [a]	0.0000
10	**Grade_17 [a]**	**0.0705**
11	Sex_17	0.0000
12	**Race_17 [a]**	**-0.0090**
13	**GetMoney_17 [a]**	**0.2031**
14	TransportationToSchool_17	0.0000
15	**PAfriends_17 [a]**	**0.0750**
16	**EatingBreakfast_17 [a]**	**-0.2294**
17	**SmokingFriends_17 [a]**	**0.5538**
18	**SupportQuitDrugAlcohol_17 [a]**	**0.1280**
19	**EnglishMarks_17 [a]**	**0.0974**
20	**WillingEdu_17 [a]**	**-0.0593**
21	**SkipClass_17 [a]**	**0.4602**
22	**BMI_CATEGORY_17 [a]**	**0.0671**
23	**SchoolConnectedness_17 [a]**	**-0.0122**
24	**SedentaryTime_17 [a]**	**0.0003**
25	TotalPAtime_17	0.0000
26	PA_LEVEL_17 [a]	0.0000
27	FLOURISH_17	0.0000

Number	Feature*	Coefficient
28	GAD7_17 [a]	0.0000
29	**CESD_17 [a]**	**0.0071**
31	**DERS_17 [a]**	**0.0047**
31	**GambleOnline_17 [a]**	**-0.2051**

*The last three char "_17" indicates the school year of 2017-18; [a] see Section 5.4.1 for descriptions

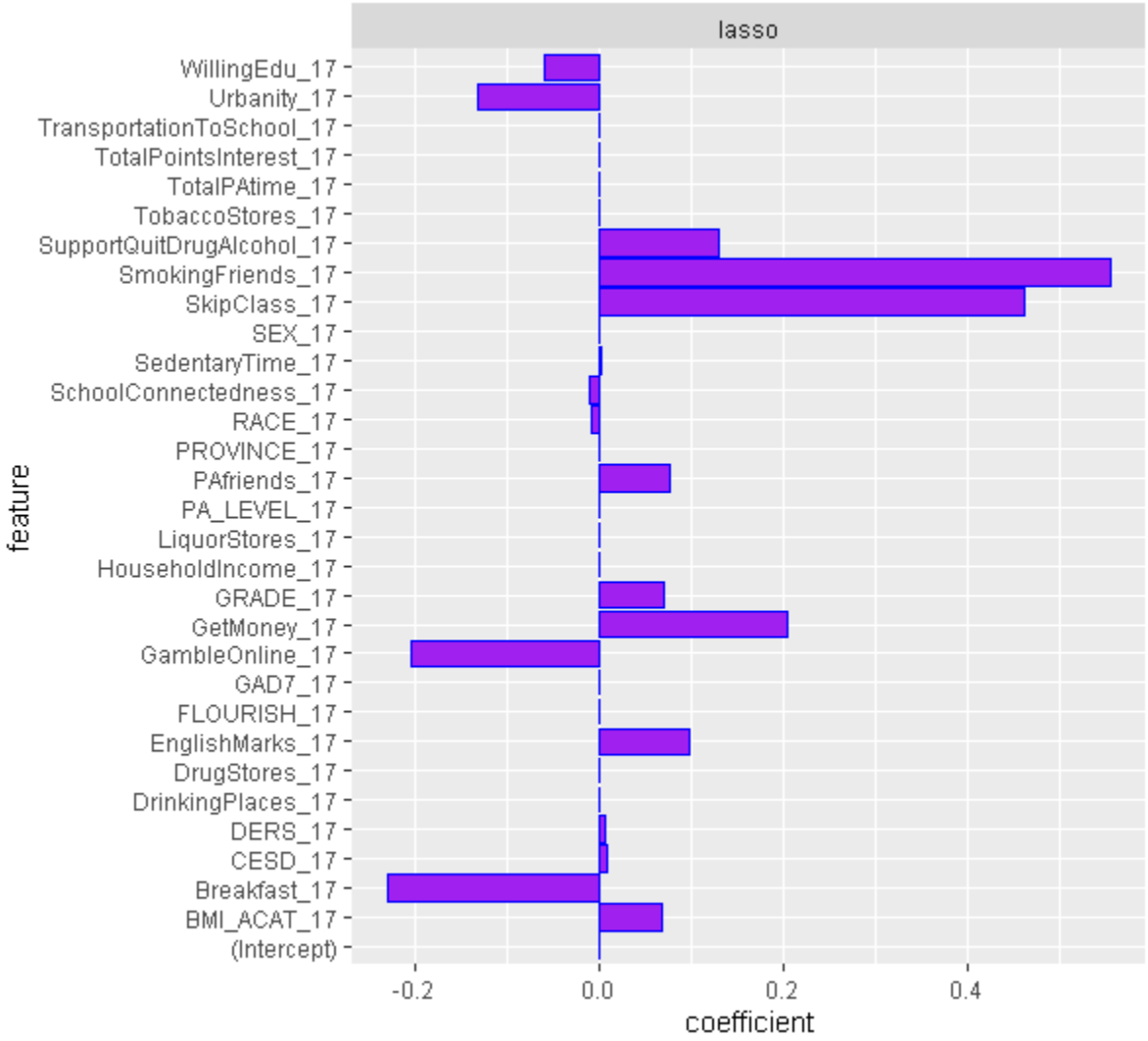


Figure 61. LASSO coefficients (Wave II, 2017-18)

Table 28. LASSO coefficients (Wave III, 2018-19)

Number	Feature*	Coefficient
1	(Intercept)	0.0000
2	HouseholdIncome_18	0.0000
3	**Urbanity_18** [a]	**-0.1697**
4	TotalPointsInterest_18	0.0000
5	DrinkingPlaces_18	0.0000
6	**DrugStores_18**	**-0.0026**
7	LiquorStores_18	0.0000
8	TobaccoStores_18	0.0000
9	Province_18 [a]	0.0000
10	**Grade_18** [a]	**0.0238**
11	Sex_18	0.0000
12	**Race_18** [a]	**-0.0387**
13	**GetMoney_18** [a]	**0.2642**
14	TransportationToSchool_18	0.0000
15	**PAfriends_18** [a]	**0.1221**
16	**EatingBreakfast_18** [a]	**-0.4282**
17	**SmokingFriends_18** [a]	**0.5113**
18	**SupportQuitDrugAlcohol_18** [a]	**0.0569**
19	**EnglishMarks_18** [a]	**0.1049**
20	**WillingEdu_18** [a]	**-0.0461**
21	**SkipClass_18** [a]	**0.4876**
22	**BMI_CATEGORY_18** [a]	**0.0696**
23	**SchoolConnectedness_18** [a]	**-0.0007**
24	**SedentaryTime_18** [a]	**0.0004**
25	TotalPAtime_18	0.0000
26	**PA_LEVEL_18** [a]	**-0.0240**
27	FLOURISH_18	0.0000

Number	Feature*	Coefficient
28	**GAD7_18 [a]**	**0.0036**
29	**CESD_18 [a]**	**0.0051**
31	**DERS_18 [a]**	**0.0073**
31	**GambleOnline_18 [a]**	**-0.1580**

*The last three char "_18" indicates the school year of 2018-19; [a] see Section 5.4.1 for descriptions

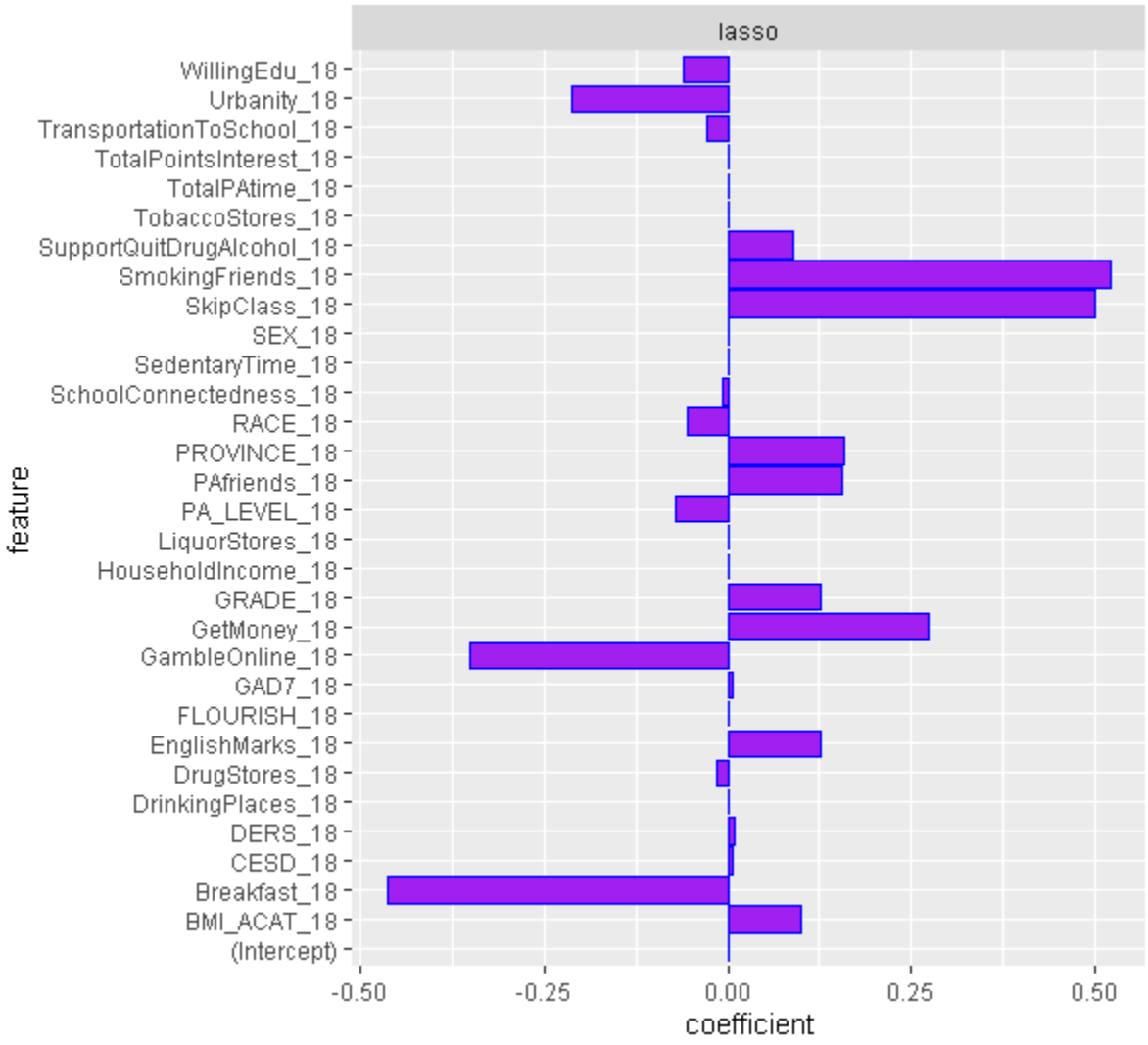


Figure 62. LASSO coefficients (Wave III, 2018-19)

Appendix O

Definition of urban/rural classification[11]

Large Urban	Populations from ≥100,000 and a population density of at least 400 per square kilometre
Medium Urban	Populations between 30,000 to 99,999 and a population density of at least 400 per square kilometre
Small Urban	Populations between 1,000 to 29,999 and a population density of at least 400 per square kilometre
Rural	Population less than 1,000 or population density less than 400 per square kilometre

[11] Source: Dictionary, Census of Population, 2016, Population Centre (POPCTR)
https://www12.statcan.gc.ca/census-recensement/2016/ref/dict/geo049a-eng.cfm

Appendix P

Variables Lead to the Dynamic Transition of Use Patterns

The covariates' effects on the transition probabilities were estimated, as shown in Tables 29-32.

Table 29. Estimated effects on the transition probabilities (Ref: S1)

	Subgroup		
	S2	**S3**	**S4**
intercept			
β (beta coefficient)	-2.2200	-2.4323	-2.6834
Odds Ratios	0.11***	0.09***	0.07***
Urbanity			
β (beta coefficient)	-0.1372	-0.1388	-0.2968
Odds Ratios	0.87**	0.87*	0.74^{+++}
Grade			
β (beta coefficient)	-0.0762	-0.1052	-0.2646
Odds Ratios	0.93*	0.90*	0.77*
Race/Ethnicity			
β (beta coefficient)	-0.1001	-0.0063	-0.6236
Odds Ratios	0.90***	0.99^{+++}	0.54*
GetMoney			
β (beta coefficient)	0.1817	0.3237	0.4645
Odds Ratios	1.20***	1.38***	1.59*
PA_Friends			
β (beta coefficient)	0.2255	0.2246	0.2913
Odds Ratios	1.25***	1.25***	1.34*
EatingBreakfast			
β (beta coefficient)	-0.2147	-0.5852	-0.8587
Odds Ratios	0.81*	0.56***	0.42*

	Subgroup		
	S2	**S3**	**S4**
SmokingFriends			
β (beta coefficient)	0.1268	0.4672	1.0920
Odds Ratios	1.14*	1.60***	2.98***
SupportQuitDrugAlcohol			
β (beta coefficient)	0.2249	0.2011	0.6768
Odds Ratios	1.25***	1.22**	1.97**
Sex			
β (beta coefficient)	0.2451	0.5443	0.9265
Odds Ratios	1.28***	1.72***	2.53***
SkipClass			
β (beta coefficient)	0.1563	0.1515	-0.0565
Odds Ratios	1.17***	1.16**	0.95^{+++}
BMI_CATEGORY			
β (beta coefficient)	0.0235	-0.0622	-0.0672
Odds Ratios	1.02*	0.94**	0.94^{+++}
SchoolConnectedness			
β (beta coefficient)	-0.4251	0.2683	0.8271
Odds Ratios	0.65***	1.31*	2.29*
SedentaryTime			
β (beta coefficient)	0.0002	0.0009	0.0014
Odds Ratios	1.00^{+++}	1.00***	1.00*
GambleOnline			
β (beta coefficient)	0.3140	-0.0981	-1.7807
Odds Ratios	1.37^{+++}	0.91^{+++}	0.17***

Note: *** $p < .00001$; ** $p < .001$; * $p < .05$; $^{+++}$The result is *not* significant at $p < .05$.

Table 30. Estimated effects on the transition probabilities (Ref: S2)

	Subgroup		
	S1	**S3**	**S4**
intercept			
β (beta coefficient)	-2.1540	-2.0710	-2.1830
Odds Ratios	0.12***	0.13***	0.11***
Urbanity			
β (beta coefficient)	1.6465	-0.0724	0.1817
Odds Ratios	**5.19*** **	0.93^{+++}	1.20^{+++}
Grade			
β (beta coefficient)	-0.3805	-0.0682	-0.4207
Odds Ratios	0.68*	0.93^{+++}	0.66*
Race/Ethnicity			
β (beta coefficient)	0.5650	-0.0325	-0.0636
Odds Ratios	1.76*	0.97^{+++}	0.94^{+++}
GetMoney			
β (beta coefficient)	-0.5312	0.1749	0.2594
Odds Ratios	0.59^{+++}	1.19***	1.30^{+++}
PA_Friends			
β (beta coefficient)	-1.1226	0.2104	-0.0643
Odds Ratios	0.33***	1.23***	0.94^{+++}
EatingBreakfast			
β (beta coefficient)	0.4412	-0.3779	-0.0386
Odds Ratios	1.55***	0.69**	0.96^{+++}
SmokingFriends			
β (beta coefficient)	-0.6685	0.3290	1.0821
Odds Ratios	0.51***	1.39**	2.95***
SupportQuitDrugAlcohol			
β (beta coefficient)	1.7343	0.1345	0.4364
Odds Ratios	**5.67*** **	1.14*	1.55*

	Subgroup		
	S1	**S3**	**S4**
Sex			
β (beta coefficient)	-0.4571	0.3200	0.8886
Odds Ratios	0.63***	1.38***	2.43***
SkipClass			
β (beta coefficient)	-1.2956	-0.0010	0.1493
Odds Ratios	0.27**	1.00^{+++}	1.16^{+++}
BMI_CATEGORY			
β (beta coefficient)	-0.3804	0.0027	-0.1336
Odds Ratios	0.68*	1.00^{+++}	0.88*
SchoolConnectedness			
β (beta coefficient)	0.8150	0.0996	-1.7318
Odds Ratios	2.26***	1.10^{+++}	0.18***
SedentaryTime			
β (beta coefficient)	-0.0070	0.0008	0.0014
Odds Ratios	0.99*	1.00**	1.00*
GambleOnline			
β (beta coefficient)	0.3639	0.2774	1.2055
Odds Ratios	1.44***	1.32^{+++}	3.34***

Note: *** $p < .00001$; ** $p < .001$; * $p < .05$; $^{+++}$The result is *not* significant at $p < .05$.

Table 31. Estimated effects on the transition probabilities (Ref: S3)

	Subgroup		
	S1	**S2**	**S4**
intercept			
β (beta coefficient)	-2.4023	-2.3339	-2.2921
Odds Ratios	0.09***	0.10***	0.10***
Urbanity			
β (beta coefficient)	-0.1822	-0.4733	-0.1478
Odds Ratios	0.83^{+++}	0.62***	0.86*
Grade			
β (beta coefficient)	-0.0294	0.2473	-0.0504
Odds Ratios	0.97^{+++}	1.28*	0.95^{+++}
Race/Ethnicity			
β (beta coefficient)	0.2227	-0.5857	-0.1943
Odds Ratios	1.25^{+++}	0.56***	0.82***
GetMoney			
β (beta coefficient)	-0.5358	-0.3363	0.1615
Odds Ratios	0.59*	0.71*	1.18*
PA_Friends			
β (beta coefficient)	-0.3957	0.0263	0.0917
Odds Ratios	0.67^{+++}	1.03^{+++}	1.10*
EatingBreakfast			
β (beta coefficient)	0.1441	0.1383	-0.5118
Odds Ratios	1.16**	1.15**	0.60**
SmokingFriends			
β (beta coefficient)	-0.7769	1.9719	0.8264
Odds Ratios	0.46***	**7.18*** **	2.29***
SupportQuitDrugAlcohol			
β (beta coefficient)	-2.0587	0.5995	0.0252
Odds Ratios	0.13***	1.82**	1.03^{+++}

	Subgroup		
	S1	**S2**	**S4**
Sex			
β (beta coefficient)	-1.0160	-0.6422	0.4037
Odds Ratios	0.36***	0.53***	1.50***
SkipClass			
β (beta coefficient)	-1.2329	-1.3169	0.0608
Odds Ratios	0.29***	0.27***	1.06^{+++}
BMI_CATEGORY			
β (beta coefficient)	0.3661	-0.3142	-0.0467
Odds Ratios	1.44**	0.73*	0.95*
SchoolConnectedness			
β (beta coefficient)	0.5030	0.2629	0.5969
Odds Ratios	1.65***	1.30***	1.82***
SedentaryTime			
β (beta coefficient)	-0.0027	-0.0069	0.0008
Odds Ratios	1.00^{+++}	0.99^{+++}	1.00**
GambleOnline			
β (beta coefficient)	-0.3335	-0.3544	0.3193
Odds Ratios	0.72***	0.70***	1.38^{+++}

Note: *** $p < .00001$; ** $p < .001$; * $p < .05$; $^{+++}$The result is *not* significant at $p < .05$.

Table 32. Estimated effects on the transition probabilities (Ref: S4)

	Subgroup		
	S1	**S2**	**S3**
intercept			
β (beta coefficient)	-2.6126	-2.1970	-2.1976
Odds Ratios	0.07***	0.11***	0.11***
Urbanity			
β (beta coefficient)	3.9439	1.1785	-3.5171
Odds Ratios	**51.62*** **	3.25***	0.03***
Grade			
β (beta coefficient)	-0.8983	-0.3643	-0.2941
Odds Ratios	0.41***	0.69*	0.75^{+++}
Race/Ethnicity			
β (beta coefficient)	0.2548	-0.1680	0.6228
Odds Ratios	1.29^{+++}	0.85^{+++}	1.86*
GetMoney			
β (beta coefficient)	-0.3315	-0.1367	-1.5793
Odds Ratios	0.72^{+++}	0.87^{+++}	0.21***
PA_Friends			
β (beta coefficient)	-1.7282	-1.1891	5.1700
Odds Ratios	0.18***	0.30***	**175.92*** **
EatingBreakfast			
β (beta coefficient)	4.0780	-3.6413	4.9077
Odds Ratios	**59.03*** **	0.03***	**135.33*** **
SmokingFriends			
β (beta coefficient)	-6.0500	-0.0407	-8.7344
Odds Ratios	0.00***	0.96^{+++}	0.00***
SupportQuitDrugAlcohol			
β (beta coefficient)	-1.9738	-0.0413	-3.8081
Odds Ratios	0.14***	0.96^{+++}	0.02***

	Subgroup		
	S1	**S2**	**S3**
Sex			
β (beta coefficient)	-7.2141	-0.0427	-2.8812
Odds Ratios	0.00***	0.96^{+++}	0.06***
SkipClass			
β (beta coefficient)	-0.3462	-3.9090	4.5949
Odds Ratios	0.71*	0.02***	**98.97*** **
BMI_CATEGORY			
β (beta coefficient)	0.1361	0.2995	0.0328
Odds Ratios	1.15^{+++}	1.35*	1.03^{+++}
SchoolConnectedness			
β (beta coefficient)	5.7045	-3.0077	-0.7665
Odds Ratios	**300.22*** **	0.05***	0.46***
SedentaryTime			
β (beta coefficient)	-0.0048	-0.0001	0.0058
Odds Ratios	1.00*	1.00^{+++}	1.01***
GambleOnline			
β (beta coefficient)	-0.3883	0.0197	-6.7661
Odds Ratios	0.68***	1.02^{+++}	0.00***

Note: *** $p < .00001$; ** $p < .001$; * $p < .05$; $^{+++}$The result is *not* significant at $p < .05$.

Glossary

Term	Definition
Bayesian information criterion (BIC)	A criterion based on the likelihood function for model selection in statistics (closely associated with the Akaike information criterion, AIC criterion)
Boruta	A random forest-based feature selection algorithm
Cluster	A.k.a "class" or "state" refers to a subgroup or a cohort of subjects with similar characteristics
Conditional probability	The probability of one event occurring given the condition of another event occurs
Dimensionality reduction	A method to convert high-dimensional data to a low-dimensional space retains relevant characteristics of the original data as close as possible to its intrinsic dimension
Elbow method	A heuristic technique used in cluster analysis to determine the number of clusters in a given dataset
FANNY	A type of fuzzy clustering algorithm
Feature	A.k.a "predictor variable" or "covariate" refers to an independent variable (or explanatory variable) in statistical modelling
Fuzzy clustering	A type of soft clustering where each object can belong to more than one cluster
Fuzzy C-Means	A type of fuzzy clustering algorithm
GAP statistic	A method for estimating the number of clusters in a given dataset, using the output of any clustering algorithm to compare the variation in within-cluster dispersion with that predicted under an acceptable reference null distribution
Goodness-of-Fit	A statistical test to evaluate how well a model fits a set of observed data
Hierarchical clustering	A type of clustering method produces nested clusters that can be visually represented as a tree-like diagram (a.k.a, dendrogram)
Interpretability	The degree to which a human can understand how a decision is made

Latent Markov model (LMM)	A type of latent variable model, similar to the hidden Markov model (HMM) for modelling the probability of a sequence, assuming a Markov process with hidden states
Latent variable model	A type of statistical model, modelling a collection of observable variables to hidden variables
Least absolute shrinkage and selection operator (LASSO)	A regression analysis technique for variable selection and regularization
Marginal distribution	The probability distribution of an event occurring regardless of the values of the other variables
Multiple imputation (MI)	Imputation in statistics is the process of substituting values for missing data. MI is a method to generate multiple different imputed datasets that are plausible to account for uncertainty about missing data
Multivariate analysis	A type of statistical analysis, including the simultaneous observation and analysis of multiple outcome variables
Non-linearity	A statistical concept describes a scenario in which an independent variable and a dependent variable do not have a linear (straight-line) relationship. In other words, changes in the output are not proportional to changes in any of the inputs in a nonlinear relationship
Partitioning around medoids (PAM)	A type of partitional clustering belonging to the family of the k-medoids algorithm, selecting real data points as centres (medoids or exemplars), allowing for higher interpretability of cluster centres than k-means
Polysubstance use	Use of multiple addictive substances simultaneously or within a specified time
Rand index	A similarity measure between two data clusterings. Adjusted Rand index (ARI) is a form of the Rand index adjusting for the chance grouping of elements.
Silhouette index	One of the internal validity indices evaluates clustering results. It measures the consistency within-cluster of data compared to other clusters. This method visually represents how well each data element is clustered.
Spectral clustering	A type of clustering algorithm rooted in graph theory to identify communities of nodes in a graph based on the edges connecting them

t-Distributed Stochastic Neighbor Embedding (t-SNE)	A non-linear machine learning algorithm for reducing dimensionality and visually presenting high-dimensional data