SUBSTANCE USE AND MENTAL HEALTH CONCERNS AMONG ADOLESCENTS

CHARACTERIZING THE CO-OCCURRENCE OF SUBSTANCE USE AND MENTAL HEALTH SYMPTOMS AMONG ADOLESCENTS IN GENERAL POPULATION AND CLINICAL SAMPLES

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TITLE: Characterizing the co-occurrence of substance use and mental health symptoms among adolescents in general population and clinical samples

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Lay Abstract

This dissertation deepens our understanding of the patterns of co-occurring substance use and mental health concerns among adolescents. First, a review of all existing studies that explore patterns of multiple substance use among adolescents was conducted. Second, patterns of substance use and mental health symptoms were identified in secondary students and schools across Ontario. Third, the feasibility of assessing substance use and mental health symptoms using standardized approaches on an inpatient adolescent psychiatric unit was evaluated. Overall, this work suggests that substance use and mental health concerns commonly co-occur, and that schools and inpatient psychiatric units are important settings for prevention, assessment, and intervention. This work provides actionable next steps to inform assessment, prevention, and intervention efforts designed to address co-occurring substance use and mental health concerns among adolescents.

Abstract

Background: Despite policy and practice guidelines highlighting the need to identify and treat substance use early and concurrently with other mental health symptoms, efforts remain uncoordinated and guidelines lack specificity. Limited evidence characterizing patterns and correlates of co-occurring substance use and mental health symptoms hinders our ability to effectively address these concerns early during adolescence. This dissertation deepens our understanding of the patterns and correlates of co-occurring substance use and mental health symptoms among adolescents, how to collect relevant data in inpatient settings, and how to rigorously analyze and report findings. **Methods:** The first paper is a systematic review of 70 cluster-based studies examining patterns of multiple substance use among adolescents. The second examines patterns and correlates of co-occurring substance use and mental health symptoms through multilevel latent profile analysis and multilevel multinomial regression using a large, representative sample of secondary students and schools across Ontario. The third paper is a pilot study examining the feasibility, acceptability, and importance of standardized assessments of substance use and mental health symptoms in an adolescent psychiatric inpatient unit. **Results:** The substantive findings of this work include: 1) multiple substance use is common; 2) co-occurrence of substance use and mental health symptoms is common, though not universal; 3) substance use may be related to mental health symptom severity, comorbidity, and hospital service use; 4) school climate, belonging, and safety represent important targets for school-based interventions; and 5) adolescent psychiatric inpatient units may represent important contexts for standardized assessments, though more professional training and standardization in assessments and interventions are needed. Methodological recommendations are also presented to improve the collection, analysis, and reporting of similar work in the field. **Conclusions:** Collectively, this dissertation provides novel, timely, and actionable insight into adolescent substance use patterns, correlates, and potential targets for assessment and intervention efforts.

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List of Abbreviations

ACRA	Adolescent Community Reinforcement Approach
ADHD	Attention Deficit Hyperactivity Disorder
AUDIT	Alcohol Use Disorder Identification Test
BIC	Bayesian Information Criterion
BPG	Best Practice Guideline
CAMP	Cannabis, Alcohol, Mental Health, and Patterns of Service Use
CAN	Cannabis involvement
CCSA	Canadian Centre for Substance use and Addiction
CD	Conduct Disorder
CEDIS	Canadian Emergency Department Information System
CI	Confidence Interval
CIHI	Canadian Institute for Health Information
CLA	Common Liability to Addiction Model
CBPR	Community Based Participatory Research
CYW	Child and Youth Worker
CUDIT-R	Cannabis Use Disorder Identification Test - Revised
DAD	Discharge Abstract Database
DT	Design Thinking
ED	Emergency Department
ESA	East/Southeast/South Asian
FIML	Full Information Maximum Likelihood
GAD	Generalized Anxiety Disorder
HED	Heavy Episodic Drinking
K6	Kessler-6
LCA	Latent Class Analysis
LPA	Latent Profile Analysis
LTA	Latent Transition Analysis
LRT	Likelihood Ratio Test

MBC	Measurement-Based Care
MH	Mental Health
MDE	Major Depressive Episode
MLCA	Multilevel Latent Class Analysis
MLPA	Multilevel Latent Profile Analysis
MMI	Multilevel Multiple Imputation
NACRS	National Ambulatory Care Reporting System
OCHS	Ontario Child Health Study
OCHS-EBS	Ontario Child Health Study – Emotional Behavioural Scales
ODD	Oppositional Defiant Disorder
OR	Odds Ratio
OSDUHS	Ontario Student Drug Use and Health Survey
PHAC	Public Health Agency of Canada
PPV	Positive Predictive Value
PRISMA-P	Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols
RA	Research Assistant
RECORD	Reporting of Studies Conducted Using Observational Routinely-Collected Health Data
RN	Registered Nurses
RoB	Risk of Bias
SES	Socioeconomic Status
SMHS	School Mental Health Surveys
SP	Social Phobia
SPOR	Strategy for Patient Oriented Research
STROBE	Strengthening the Reporting of Observational Studies in Epidemiology
SU	Substance Use
SUD	Substance Use Disorder
TOB	Tobacco smoking

Declaration of Academic Achievement

This is a "sandwich thesis" comprised of 5 chapters. All the work contained herein meets the requirements for inclusion in a Doctor of Philosophy dissertation.

Chapter 1 is unpublished. JH is the sole author.

Chapter 2 is published in *Drug and Alcohol Dependence*. JH conceived of and designed the review. JH led the pre-registration, search, screening, data extraction, and thematic coding. RW and HK were the primary second reviewers in screening, data extraction, and thematic coding. MO, LF, KA, and MK also assisted with screening, data extraction, and verification. CM, JM, MA, and KG provided methodological and substantive support through the manuscript process. JH drafted the first version of the manuscript and was responsible for editing, submitting, and responding to reviewers. All authors approved the final version of the article.

Chapter 3 is under peer review. JH conceived of and designed the secondary analysis. JH led the data cleaning, data analyses, interpretation of results, and writing. JM, CM, MA, and KG provided methodological and substantive support throughout the design, interpretation, and manuscript process. JH drafted the first version of the manuscript and was responsible for editing, submitting, and responding to reviewers. All authors approved the final version of the article.

Chapter 4 is published open access in *Child and Adolescent Mental Health*. JH conceived of and designed the study. JH led work related to approvals (from the Child and Youth Mental Health Research Advisory Committee and the Hamilton Integrated Research Ethics Board) and funding accrual (Hamilton Health Sciences). JH led the data collection, data analysis, and writing of the manuscript. RW assisted with youth and staff primary data collection, data cleaning, and confirming descriptive statistics under the supervision of JH. ZN assisted with chart reviews and descriptive analyse under the supervision of JH. LH, CM, JM, MA, and KG provided methodological and substantive support throughout the study design and manuscript process. JH drafted the first version of the manuscript and was responsible for editing, submitting, and responding to reviewers. All authors approved the final version of the article.

Chapter 5 is unpublished. JH is the sole author.

Chapter 1: Introduction

Prevention and early intervention of substance use and other mental health disorders during mid to late adolescence is imperative to improving overall population health and quality of life. Although most substance use disorders (SUDs) emerge during the mid-twenties, over half of people who use substances in their lifetime initiate use prior to 20 years of age (1) and first symptoms of SUDs appear a median of 9 years earlier than diagnosis (2). Alcohol, cannabis, and tobacco products are the most commonly used substances among adolescents (3, 4) with earlier age of first use being associated with negative psychosocial, mental health, and substance use sequelae (5-7). The co-occurrence of substance use and other mental health symptoms has been related to more severe symptoms, poorer prognosis, and greater likelihood of suicidality (8-18). For decades, governments nationally and internationally have recognized the need to identify substance use problems early in the life course and have called for the development and implementation of integrated substance use and mental health prevention and treatment (19-22). Unfortunately, gaps in integrated efforts persist and there remains uncertainty regarding why, how, when, and for whom substance use and mental health symptoms co-occur.

Characterizing patterns of substance use and mental health symptoms

Substance use and mental health symptoms commonly co-occur (23). For example, individuals with mood and anxiety disorders have been found to be 2 to 4 times more likely to experience a substance use problem than those without these disorders (24). Further, the highest incidence and prevalence of co-occurring problems occurs during late adolescence and emerging adulthood (23). Adolescents are particularly vulnerable to both the initiation and negative effects of substance use – even if not meeting criteria for a SUD – given ongoing brain development (25-27). Among clinical samples of Canadian youth, a large proportion of hospitalizations for substance use (70%) involve concurrent mental health concerns (28) and many adolescents attending outpatient substance use programs (72-83%) present with comorbid elevations in mental

health symptoms (11). This is congruous with findings from an Australian systematic review, which found a majority of individuals (47 to 100%) who attend substance use treatment present with co-occurring mental health symptoms, predominantly related to depression and anxiety (29).

Establishing patterns of co-occurring substance use and mental health symptoms is important for understanding targets for prevention and interventions. First, adolescents may use more than one substance. The types, frequency, and number of substances adolescents use may be related to both etiological and prognostic factors (30, 31). Second, substance use and mental health symptoms overlap, though co-occurrence is not ubiquitous (32). Not all individuals with poor mental health use substances and, at times, presence of mental health symptoms may decrease the likelihood of using substances (33). Similarly, not all individuals who use substances have poor mental health (34, 35). Therefore, focusing on individual substance use or mental health symptoms separately, or on the other hand assuming they consistently co-occur, may result in oversimplification and inaccurate inferences that misguide clinical decisions.

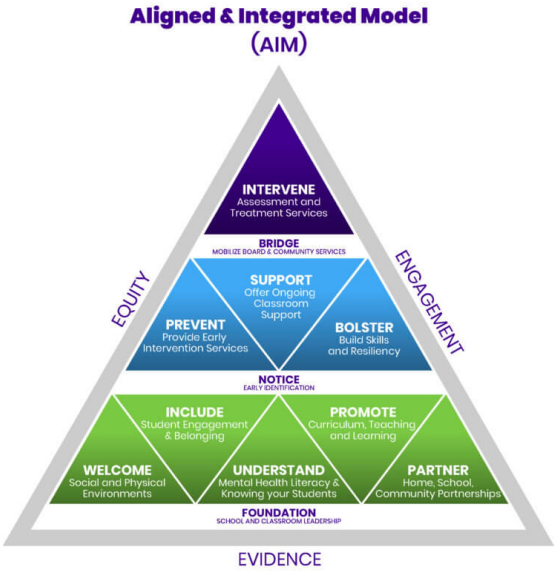
Cluster-based methods are increasingly being used to identify patterns of substance use (36). However, recent systematic reviews have been restricted to summarizing patterns of adolescent multiple substance use (without considering mental health symptoms) (31) or mental health symptoms (without considering substance use) (37). Thus, more work is needed to synthesize existing cluster-based studies related to co-occurring patterns to identify homogenous subgroups that can inform tailored prevention and treatment efforts.

School environments and adolescent substance use

Schools can be sources of risk and resiliency factors related to student health, substance use, and mental health concerns (38). Schools have been found to account for a large amount of the variability in student substance use, with point estimates of up to 20% depending on the substance and frequency pattern being measured (39, 40). Accordingly, the Public Health Agency of Canada (PHAC) recently proposed the Blueprint for Action:

Preventing substance related harms among youth through a comprehensive school health approach (41), suggesting upstream prevention efforts focused on a school's social environment similar to the internationally recognized Icelandic Prevention Model (42). These models focus on schools, which are seen as a hub for youth and their communities, to prevent or delay substance use and improve overall student wellbeing, stating, *"the best prevention measures often have nothing to do with substance use at all"* (pg. 11). In general, mental health and risk behaviours in schools are typically addressed through multi-tiered systems of support addressing promotion and prevention (Tier 1) and intervention (Tiers 2 and 3) where all tiers support, supplement, and build upon one another (see Figure 1) (43). Tier 1 supports are consistent with a public health approach (and PHAC direction) focused on health promotion and prevention by providing universal "whole-school" interventions for all students in a school (44), broadly focused on school organization, culture, integrated curriculum, policies, and general practices and interactions. Historically, interventions across the tiers for youth substance use and mental health symptoms have been explored and implemented separately.

Figure 1. School Mental Health Ontario's continuum of mental health support at school



Understanding the substantive importance of school environments on co-occurring substance use and mental health symptoms is not yet common practice. With the emergence of cluster-based analyses, identification of common student profiles of co-occurrence will enable greater specificity in identifying school-based prevention initiatives applicable to both substance use and mental health symptoms and identifying

specific schools that may require more support. For example, patterns derived from cluster-based analyses of student substance use and mental health can be used: 1) as outcomes of intervention studies and 2) as targets for interventions at the school level by identifying typologies of schools that may require more support. Thus, the contextual factors related to profiles of co-occurrence remains a largely untapped, and potentially powerful, component to understanding and addressing this phenomenon.

Feasibility of standardized substance use assessment during psychiatric hospitalization

For roughly 1 in 3 youth, the hospital is the first point of contact for mental health or substance use related concerns (45). Recently, there has been a disproportionate increase in hospital-related psychiatric service use, relative to outpatient services (46-49). For example, between 2009 and 2017 there was a 58% increase in mental health and substance use related outpatient visits and 136% increase in hospitalizations among Ontario adolescents 14-17 years of age (45). Further, among Ontarians 10-21 years of age there was a >90% increase in emergency department (ED) visits for mental health and substance use concerns (45). Increases in hospital contacts for youth mental health concerns is in part due to repeat visits (50). Canada wide, 39% of youth with a mental health related ED presentation typically have 3 or more related ED visits (51) resulting in repeat presentations accounting for more than 30% of visits (50, 52-54) (55). Further, a recent systematic review found over 10% of youth who experience a psychiatric hospitalization are re-admitted with most returning within 1 year (56).

Information on substance-related predictors of representations and readmissions is limited. In recent reviews, SUDs were unexpectedly related to a lower likelihood of psychiatric readmissions among youth (56) with mixed findings related to re-presentations to ED among youth (57). However, almost all included studies looked at associations between readmission and SUDs, toxicity, or substance-induced mental illnesses with no studies looking at general use of substances. Additionally, few looked at

substances separately (often a global indicator or any use) and those that did came to divergent conclusions for different substances (58).

Collectively, these data signal that there are barriers to accessing outpatient services and follow-up supports post-hospital discharges. Given many youth will engage with psychiatric services prior to substance use treatment (59, 60), youth psychiatric hospitalizations, whether for substance or non-substance related reasons, may be an important context for substance use assessment, early interventions, and referral to or recommendations for community providers. Though multidisciplinary clinical best practice guidelines (BPGs) recommend assessing for substance use prior to diagnosing mental illnesses and treating concurrently if co-presenting (26, 61-63), concurrent disorder recommendations generally lack specificity and consistency, rarely incorporating stakeholder input, and no specific guidelines address the management of youth substance use in emergency or inpatient psychiatric settings (64). Further, there is limited research in adolescent inpatient psychiatric settings regarding patterns of use, clinical correlates, and interventions for substance use. Existing research must often rely on administrative coding of SUDs, which typically do not emerge until later in life. Standardized instruments assessing substance use (not merely disorder) and mental health symptoms could help fill this gap, though they are rarely administered at intake, and less so, at discharge or follow-up (65-68).

Dissertation objectives and program of work

The first step to developing and implementing effective prevention and early interventions for substance use and mental health symptoms among adolescents is to understand **patterns of substance use and mental health co-occurrence in general population and clinical samples of adolescents**. After identifying patterns of co-occurrence, the second step is to identify **correlates of co-occurrence to guide targets for prevention and early intervention efforts**.

This dissertation addresses three overarching objectives: 1) characterizing the patterns of co-occurrence in general population and clinical settings; 2) exploring the

potential importance of schools and psychiatric hospitalizations as critical contexts for assessment and intervention; and 3) identifying possible targets for assessing and addressing substance use and co-occurring mental health symptoms within these contexts (e.g., standardized assessments, universal whole-school approaches). All papers are distinct manuscripts that are either already published (chapters 2 and 4) or under review (chapter 3). The first two chapters utilize methods focused on the application and synthesis of cluster-based designs to understand multiple substance use and co-occurring mental health symptoms, primarily in the general population. The first paper (**chapter 2**) is a systematic review synthesizing all cluster-based studies to date exploring adolescent patterns of multiple substance use, yielding core common patterns of use for future etiological, prognostic, and intervention studies and methodological recommendations for future cluster-based studies. The second paper (**chapter 3**) identifies co-occurring substance use and mental health symptom patterns in a representative sample of secondary students and schools across Ontario, applying and expanding upon results from chapter 2. Patterns are explored at multiple levels and school contextual correlates are examined that may serve as targets for school-based prevention. The third paper (**chapter 4**) focuses on the feasibility of implementing a standardized assessment of substance use and mental health symptoms among adolescents experiencing psychiatric hospitalization, including considerations of the perspectives of frontline providers in this setting.

This work includes multidisciplinary perspectives (e.g., psychiatric epidemiology, population and public health, nursing, psychology, addictions, and health services research) and utilizes various health research methods (e.g., systematic review and meta-syntheses, cluster-based analyses, survey design and evaluation, regression and correlation, content analysis). This work is predominantly grounded in positivist ontology, epistemology, and quantitative methodology. However, chapters 2 and 4 use mixed methods philosophy and methodology to deliberately integrate qualitative and quantitative approaches to gain a more complete picture (i.e., complementarity) and enhanced understanding of the research questions and results (e.g., convergence and explanation) (69). For example, chapter 2 includes a thematic synthesis of cluster results

and chapter 4 includes the collection and analysis of primary qualitative data from frontline provider perspectives. Mixed methods enable practical and pragmatic combinations of deductive (top-down, quantitative/positivistic) and inductive (bottom-up, qualitative/constructivist) reasoning, collection of data in ways "that work," and embracing of both singular and multiple realities (69). Quantitative components are given greater weight across studies, with qualitative components enhancing our understanding and enabling thematic summaries.

Overall, the objectives of this dissertation are to: 1) characterize co-occurrence of substance use and mental health symptoms using advanced analytic methods; 2) identify correlates of those patterns to inform targets for intervention; and 3) establish the feasibility of implementing standardized assessment practices of substance use and mental health symptoms on adolescent psychiatric inpatient units. **Chapter 5** will conclude the dissertation by summarizing key methodological and substantive insights, highlighting the strengths and limitations of this work, and discussing opportunities for future work related to adolescent substance use and co-occurring mental health symptoms.

Chapter 2: Patterns of Substance Use Among Adolescents: A Systematic Review

Halladay, **J.**, Woock, R., El-Khechen, H., Munn, C., MacKillop, J, Amlung, M., Ogrodnik, M., Favotto, L., Aryal, K., Noori, A., Kiflen, M., & Georgiades, K. (2020). Patterns of substance use among adolescents: A systematic review. *Drug and Alcohol Dependence,* 108222. https://doi.org/10.1016/j.drugalcdep.2020.108222

Highlights

- This is a systematic review of 70 studies on patterns of adolescent substance use.
- Typical clusters: low use, single or dual substances, moderate multi- use, high multi-use.
- Alcohol, cannabis, and/or tobacco characterized low, single, dual, and moderate clusters.
- Mental health and substance use co-occurred, but distinct patterns also emerged.
- Clustering methods were heterogenous and poorly reported, limiting comparability.

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Patterns of substance use among adolescents: A systematic review

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ABSTRACT

Purpose: This review characterizes empirically derived patterns of multiple (multi-) substance use among adolescents. A secondary objective was to examine the extent to which mental health symptomatology was included in the empirical analyses examining substance use patterns.

Methods: Eligible studies included those that used cluster-based approaches, included the assessment of at least two different substances, and were based on study samples with mean ages between 11 and 18 years. 4665 records were screened including 461 studies for full-text screening.

Results: 70 studies were included with common clusters being: low use, single or dual substance use, moderate general multi-use, and high multi-use. The most common patterns of single or multi-substance use were: alcohol only, alcohol with cannabis and/or tobacco, and use of alcohol, tobacco, and cannabis with and without other drugs. Lower socioeconomic status, older age, and male gender were consistent predictors of multi-use clusters. Only 37 % of studies compared differences in levels of mental health across clusters with symptoms consistently associated with a greater likelihood of multi-use. Only 29 % of studies included mental health indicators in cluster-based analyses, with over half identifying distinct mental health and substance use clusters. Fit indices in cluster analyses and measurement properties of substance use were heterogeneous and inconsistently reported across studies.

Conclusions: Distinct patterns of substance use were derived but methodological differences prevented direct comparison and reduced capacity to generalize across studies. There is a need to establish standardized methodological approaches to identify robust patterns of substance use to enhance etiological, prognostic, and intervention research.

1. Introduction

Psychoactive substance use during adolescence is both common and concerning due to potential negative impacts on social, emotional, cognitive, physical and academic outcomes (Boak et al., 2016). Early substance use initiation and use of multiple substances are strong predictors of later substance use problems and disorders (Moss et al., 2014). Early interventions have the potential to reduce the severity and persistence of substance use related problems (de Girolamo et al., 2012d), but adolescents rarely seek help (Georgiades et al., 2019; Merikangas et al., 2011; Reavley et al., 2010; Winstanley et al., 2012). Importantly, use of a single substance is rare, while use of multiple substances is common. Patterns of multiple substance use may represent distinct groups of adolescents with unique risk factors and prognostic profiles (Tomczyk et al., 2016). However, most prevention and intervention studies focus on single substances. Identification of the

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consumption patterns among adolescents with single and multiple substance use is fundamental for etiologic and prognostic studies. Previous researchers have indicated a need for tailored interventions, which could be informed by common patterns of use (Connor et al., 2014; Tomczyk et al., 2016).

The most commonly used substances in adolescence are alcohol, cannabis, and tobacco products, followed by other illicit drug use (Boak et al., 2020; Schulenberg et al., 2018). Over half of individuals who use substances in their lifetime initiate use prior to age 20 (Blanco et al., 2018). The average age of substance use initiation in North America has been increasing and is currently between 15–17 years of age (Boak et al., 2020; Richmond-Rakerd et al., 2017). Youth that initiate use during early adolescence (11–14 years) are particularly vulnerable to later substance use related problems (Behrendt et al., 2009; Dawson et al., 2008; Jordan and Andersen, 2017). Early and later adolescents are more likely to both initiate and experience negative effects of substance use than older age groups (Arain et al., 2013; Casey et al., 2008). This increased risk is commonly explained by Casy and Jones' (2010) dual systems model of adolescent risk behaviour, which points to the asynchronous maturation of the emotional limbic regions in the brain (which peaks during adolescence) compared to the regulatory prefrontal cortex (which matures last in young adulthood).

Use of more than one substance, also known as multiple substance or polysubstance use (hereby referred to as multi-use) is common and associated with poor mental health, educational, and social outcomes (Banks et al., 2017; Connor et al., 2014; Yurasek et al., 2017). The Common Liability to Addiction model (CLA) explains the underlying pathways contributing to multi-use (Vanyukov et al., 2012). The CLA model suggests that there are shared underlying latent biobehavioural characteristics that make individuals more "liable" to use multiple substances. This model posits that there are shared factors contributing to the propensity to initiate substance use as well as gradations in the severity of substance use related problems (Vanyukov et al., 2012). Liability is presented on a fluctuating and malleable continuum that goes from resistance to use and problems (i.e., resiliency) to multi-use and severe problems (i.e., affected). Thus, identifying patterns of substance use among adolescents may help to further investigate common liability and resiliency factors to inform prevention and early intervention efforts.

To characterize patterns of multi-use, cluster-based analyses such as Latent Class Analysis (LCA), Latent Profile Analysis (LPA) and related methodologies can be used (Connor et al., 2014). LCA explains patterns in observed responses on "indicator variables," which refer to variables we can observe (i.e., substance use variables). LCA identifies mutually exclusive latent clusters based on the patterns of indicators (Collins and Lanza, 2010). These clusters are meant to be qualitatively distinct, acknowledging that differences may not lie on a single dimension. For example, identified clusters may not be solely indicative of increasing prevalence of substance use, but rather of patterns and types of use (Collins and Lanza, 2010).

The potential impact and applications of latent clustering approaches have led to a dramatic increase in studies pursuing these approaches (Petersen et al., 2019). Additionally, traditional clustering approaches such as hierarchical clustering and k-means are rapidly regaining popularity due to being labelled as "unsupervised machine learning algorithms" for big data. A previous review in 2016 categorized adolescent substance use patterns and found a relatively consistent classification of 3 clusters including: (1) no use or limited use; (2) single substance use (often alcohol only); and (3) polysubstance use (most often defined as multi-use of alcohol, cannabis, and tobacco) (Tomczyk et al., 2016). Numerous studies have been published since this review; thus, an update is needed to enhance our understanding of multi-use patterns in adolescents as well as ongoing methodological limitations in cluster-based research that need to be addressed. Additionally, the previous review focused exclusively on LCAs with substance use indicators, potentially missing other robust methodologies and patterns such as co-occurrence of substance use with mental health concerns.

The co-occurrence of substance use and mental health concerns has demonstrated associations with more severe mental health symptomatology and poor prognosis (Gobbi et al., 2019; Hser et al., 2017; Jacobus et al., 2017; Mammen et al., 2018; Moitra et al., 2016) as well as a greater likelihood of experiencing substance use related problems and progression to a substance use disorder (Chan et al., 2008; Diamond et al., 2006; Hawke et al., 2018). Substance use and mental health concerns are thought to be related because of the potential following mechanisms: (1) similar risk factors or shared biological predispositions (discussed in the CLA model); (2) self-medication hypothesis, whereby individuals use substances to alleviate mental health symptoms; and (3) substance use causing mental illness or worsening symptoms (Bolton et al., 2009; Fergusson et al., 2011; Hathaway, 2003; Leyton and Stewart, 2014). Thus, understanding the co-occurrence of mental health concerns and substance use among adolescents is important.

1.1. Objectives

Given the rapidly expanding empirical literature, the primary objective of this systematic review was to identify, synthesize, and characterize common patterns of substance use among adolescents. A secondary objective was to examine the extent to which mental health symptomatology was included in empirical analyses examining substance use patterns, and to summarize associations found.

2. Methods

This protocol follows procedures outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analysis Protocols (PRISMA-P) statement (see Supplementary Materials). This review was registered on PROSPERO (CRD42018112548).

2.1. Search strategy

The following databases were systematically searched: PsycINFO (1987 to October Week 1 2019), Embase (1996–2019 October 9), OVID MEDLINE Epub Ahead of Print, In-Process & Other Non-indexed Citations, Ovid MEDLINE® Daily and Ovid MEDLINE (R) (1946 to Present), CINAHL (October 9 2019). Abstracts and reference lists of included articles and reviews were checked, and authors were contacted for further information when appropriate. The search strategy combined the exposure (i.e., multiple use of substances), the statistical method (i.e., cluster methods), and the target population (i.e., adolescents). The complete search strategy can be found in the Supplementary Materials. Two review authors screened titles and abstracts of identified studies based on piloted and calibrated screening forms. A total of 4665 records were identified for screening after duplicate removal, with 461 full-text articles selected for further review. All full-text articles were screened in duplicate with disagreements resolved through discussion or consultation with a third reviewer. In total, 70 primary studies reported in 79 publications were included in this review. Primary studies were operationalized as the initial peer-reviewed publication reporting the cluster solution. Some primary studies had multiple publications including follow-up comparative analyses whereby the sample and clusters were the same, but different comparisons were made. Comparisons from all related studies were included in final data extraction. See Fig. 1 for the PRISMA Flow Diagram.

2.2. Eligibility criteria

Studies were included that met the following criteria:

1 Population: Samples of adolescents with mean ages between 11 and

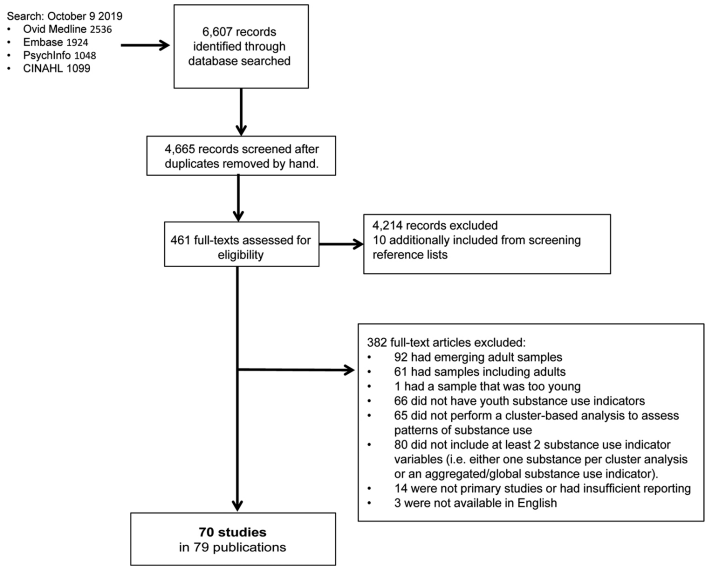

Fig. 1. A flow diagram following the PRISMA template of included studies.

18 (minimum age of 11 and maximum of 22). Study samples that included individuals over 19 years of age were eligible, only if they were school-based with the oldest enrolled in grades 12/13. Grade 6 was the youngest grade. This range was selected based on age of initiation of substance use over the past two decades, recent prevalence estimates, prior search strategies, and sampling frames of popular population surveys.

2 Substance use: More than one substance was assessed (i.e., multiple substance indicator variables), operationalized as prevalence or frequency of use within a defined time period or substance use disorder; including alcohol, tobacco, cannabis, other illicit drug use, and/or prescription drug misuse. Studies were excluded if analyses were conducted separately for different substances or combined substances into one global indicator.

3 Types of studies and methodologies: All quantitative study designs were included that used a statistical approach to identify clusters of substance use patterns. Methods included cluster analysis (i.e., hierarchical cluster analysis, k-means), LCA or LPA, and finite mixture modelling. Studies that used latent trajectory/transition analysis (LTA) were included if they reported cluster results at one time point. Given the consistencies in statistical approaches and reporting, the term "LCA" will hereby refer to LCAs, LPAs, and LTAs.

4 Publication status: Studies that were published in peer-reviewed journals.

5 Language: Restricted to English.

6 Sampling Frame: All studies were included regardless of sampling context (i.e., school, community, hospital, clinic, etc.).

7 Outcomes: Studies had to report the number and nature of substance use clusters among adolescents.

2.3. Data extraction and synthesis

Two review authors independently extracted data including: study ID, design, demographics, risk of bias (RoB), statistical techniques, indicator variables, outcomes/clusters, correlations between clusters and extrinsic variables, an overall summary of author's findings, and other comments (See Supplementary Materials for more details). Calibration exercises and resolution of discrepancies mirrored screening methods. Data were combined and presented narratively regarding: the types of indicators; the number and nature of clusters; correlates and clusters related to mental health symptomatology; and sociodemographic correlates.

Cluster solutions are partly based on theoretical (as opposed to quantitative) decisions, and heterogeneity in the measurement and methodological decisions across studies made direct objective comparisons difficult. Accordingly, narrative summaries informed by content analytical techniques were used to identify common themes within and across cluster solutions (Elo and Kyngäs, 2008). The individual clusters were used as the unit of analysis and narrative data was extracted for coding purposes. Researchers reviewed all identified clusters and engaged in open coding, then iteratively established a higher order thematic coding scheme, ending with abstraction of final themes (Elo and Kyngäs, 2008). To enhance credibility and confirmability, all data extractors approved of final overarching cluster themes. Comparisons were made to existing evidence and theoretical understandings of substance use and mental health comorbidity among adolescents. This approach was used to present a meta-synthesis of identified substance use cluster solutions across studies.

2.4. Risk of Bias (RoB) and quality assessment

RoB tools for cross-sectional designs endorsed by Evidence Partners were used and adapted to assess RoB (CLARITY Group at McMaster University, 2019). Domains included: (a) representativeness of the source population; (b) adequacy of response rate (> 60 %); (c) amount of missing data ($<= 20$ %); (4) reliability and validity of measurement tools. The quality of reporting cluster-analytic approaches was evaluated based on recommendations from Connor et al. (2014) and Collins and Lanza (2010) . Where LCAs were used, studies were evaluated regarding reporting and assessment of: fit indices, local independence,

and transparency in model selection. For other cluster techniques, methods were examined for reporting of fit indices, competing models, sensitivity analyses, and cross-replication.

3. Results

70 primary studies published up to October 2019 were included. Data in these studies was collected between 1980 and 2017. Of note, 26 % of these studies were also included in the previous review (which went up to June 2015), with the remaining studies published from 2015 onwards and/or not included in the previous review. Across all included studies, the average age was 15 years, with males constituting 47 %, and 49 % were white/Caucasian. A majority (k = 48, 69 %) were general population studies, in which the sample did not have specific inclusion/exclusion criteria and recruitment occurred in schools or communities (non-general population studies are labelled "targeted" populations). Most studies were US-based (k = 52, 74 %). Additionally, most studies included the full sample in their analyses and did not conduct subgroup analyses by age. About 44 % of studies included grade 6–12 students (~11 to 18 years) and 24 % included grade 9–12 students (~14 to 18 years). Please refer to Table 1 for a summary of included studies and participant characteristics.

3.1. Identification and characterization of substance use patterns

3.1.1. Substance use indicators

The number and nature of indicator variables directly impacts cluster solutions. The most common substance use indicators included in the cluster-based analyses were alcohol (99 %), tobacco (81 %), and cannabis (79 %). Most substance indicators were measured as general use (59 % alcohol; 66 % tobacco; 90 % cannabis), with few including specific products or methods of use apart from heavy episodic drinking [HED] (27 %). Across these common substance use indicators, scales of measurement varied with 62 % using dichotomous indicators (typically ever/never use), 22 % using categorical indicators reflecting frequency of use, and 13 % using continuous indicators (e.g., counts, such as number of days). The time period of reporting was lifetime (23 %), past year (25 %), or past month (43 %). Other illicit drugs (60 %) and prescription drugs (30 %) were also included; most often as a combined global indicator of any use (62 %) measured dichotomous (79 %) either using a lifetime (38 %) or past year (42 %) timeframe. Of note, the operationalization of indicator variables was not always consistent in one study – i.e., alcohol, tobacco, and cannabis may have been included categorically or continuously with shorter timelines than illicit or prescription drug misuse.

A large proportion of studies included alcohol, tobacco, and cannabis (63 %). About a third also included other illicit drugs (36 %), a fifth also included misuse of prescription drugs (21 %), and about a fifth included all (19 %). The majority of studies only included substance use indicators (63 %) in the cluster-based analyses, with few including a combination of substance use and mental health indicators (16 %), and the remaining including other additional non-substance or mental health indicators (21 %). These non-substance and mental health indicators were usually related to sexual behaviours or general health behaviours (e.g., exercise, nutrition, sleep). See the left portion of Table 2 for a summary of indicators across studies. See Supplementary Material for a thorough summary of indicator characteristics.

3.1.2. Characterization of substance use clusters

In 70 studies (k), there were 89 cluster solutions. After removing one outlier cluster solution[1], solutions had an average of 4 clusters after model enumeration (minimum 2 and maximum 6). Cluster themes were predominantly defined by the number and type of substances used. Consistent themes found across studies included: (1) **low use**; (2) **single or dual substance use**; (3) **moderate general multi-use**; and (4) **high multi-use.** Moderate and high multi-use typically included use of alcohol, cannabis, and tobacco with or without other substances. Within the 'single or dual substance' cluster, the most common themes in descending order were: (1) alcohol; (2) cannabis with alcohol; (3) tobacco with alcohol; (4) tobacco. Each cluster was classified into a mutually exclusive overarching theme. See the right side of Table 2 for themes identified across individual studies, Table 3 for more detailed thematic descriptions, and Fig. 3 for a visual depiction of themes.

Overall, most cluster solutions fit into these overarching themes and were found in both general and targeted population studies, with some exceptions. General population studies had more alcohol focused clusters (k = 20, 43 % general vs. k = 4, 18 % targeted). Targeted population studies had larger proportions of adolescents categorized as high multi-use (~10 % general versus ~16 % targeted) and targeted identified more "higher" multi-use clusters (k = 2, 4 % general vs. k = 6, 27 % targeted). In several situations, clusters were difficult to fit within identified themes typically occurring when: (a) multiple time points and/or age of initiation was included, making the pattern more reflective of trajectories; (b) indicators were included as interactions with one another; and (c) when there were a large number of indicators using a k-means or hierarchical cluster analysis. There were also times when cluster solutions "relatively" fit the identified themes. Relative fit occurred in targeted population studies whereby the sample was selected based on use of a particular substance – and therefore, all youth were at an elevated risk, but clusters were found relative to this inclusion criteria. Of note, when targeted populations were not selected based on particular substance use or mental health risk factors or behaviours, patterns fit identified overarching themes similarly to general population studies.

3.2. Identification and characterization of mental health considerations

3.2.1. Mental health indicators

In total, 20 studies (29 %) included one or more mental health indicator variables. Four studies included internalizing symptoms (e.g., mood and anxiety disorders), typically using a sum of several symptom items that align with a particular diagnosis. 18 studies included externalizing behaviours, often included as single items that reflected one specific behaviour (e.g., delinquency, fighting, truancy). Less common mental health indicators were suicidal thoughts and behaviours, general distress, and eating disorders. Studies with mental health indicators are specified in Table 2 and more details are provided in Supplementary Materials.

3.2.2. Cluster solutions with mental health indicators

Almost universally, each cluster solution that included mental health indicator(s) identified a lower and higher co-occurring cluster related to both substance use and mental health symptomatology (Quadrants 1 and 4 respectively in Fig. 4). Over 50 % of studies with mental health indicators found distinct substance use and mental health symptom clusters (Quadrant 2 and 3) in addition to general positive correlations between substance use and mental health (Quadrant 4). There were several studies that identified clusters of high mental health symptomatology but low to no substance use (Quadrant 2), high mental health symptomatology and moderate substance use (Qaudrant 2), and high multi-substance use and low mental health symptomatology (Quadrant 3). Therefore, although co-occurrence was common, it was not the only emerging pattern.

3.2.3. Mental health predictors of cluster membership

Only 37 % (k = 26) of studies compared substance-use clusters based on mental health symptomatology. Of these studies, 96 % found at least one significant difference between substance use clusters based

[1] One study had 15/16 clusters using the k-mean approach and was not included in the summary (Hallfors, 2004; Waller; 2006 supp).

Table 1
Summary of included studies.

Study	Sampling Characteristics	Participant Characteristics	Methods
	Country, Collection Year Population, Sampling (specifics)	sample size, age mean (SD if reported), min to max age, % males, ethnicity	Method (#indicators)
Ansary and Luthar (2009)	USA, 1996 General, City	n = 256 age = 16.1 (0.5), all gr10s 46.5% males 78.7% Caucasian	K-means (7)
Assanangkornchai, Li, McNeil, and Saingam (2018)	Thailand, 2009 General, National	n = 25566 age = 13 (42%), 12 to 15 years of age 46% males NR Ethnicity	LCA (20)
Baggio, Spilka, Studer, Iglesias, and Gmel (2016)	France, 2011 General, National (exception had to use substances ~6% excluded)	n = 23882 age = all 17 49.7% males NR Ethnicity	LCA (14)
Bartlett et al. (2005)	USA, 1994-1995 & 1996 General, National	n = 12617 age = 15.8 (1.6), 11.6 to 21.2 (gr7-12, +1 year after gr12) 48% males 69% Caucasian 22% Black	Cluster Analysis (14)
Bohnert et al. (2014)	USA, 2007-2009 Targeted, Cities (Low SES clinics)	n = 1416 age = 15.2 (2), 12 to 18 37.2% males 63.6% Black	LCA (7)
Charak, Koot, Dvorak, Elklit, and Elhai (2015)	USA, 1995 Targeted, National (youth who have been assaulted)	n = 918 age = 14.9 (1.6), 12 to 17 50.4% males 68.6% Caucasian	LCA (8)
Chen et al. (2015)	USA, 2006-2011 Targeted, National (youth endorsing ADHD stimulant use)	n = 2203 age groups = 12-13 (11%), 14-15 (20%), 16-17 (59%) 48.71% males 76.3% White 23.7% Minorities	LCA (8)
Childs and Ray (2017)	USA, 1995-1996 General, National (black and white youth only)	n = 8963 age = 15.5 (1.2), 13 to 17 48% males 74.65% Caucasian 25.35 Black	LCA (9)
Choi, Lu, Schulte, and Temple (2018)	USA, 2011-2013 General, State (public schools only)	n = 990; 886; 782 age = 15.1 (0.8), 16 to 18 44% males 30% Caucasian 29% Black	LCA (5)
Chung and Elias (1996)	USA, NR General, City	n = NR age = NR, gr9 to gr12 49.3% males NR Caucasian 5% Black and Latino	Cluster Analysis (7)
Chung, Kim, Hipwell, and Stepp (2013)	USA, 2005-2012 Targeted, City (black and white females only in low-income neighbourhoods)	n = 1076 age = NR, all gr12s 0% males 43.2% Caucasian 56.8 Black	LTA (3)
Cleveland, Collins, Lanza, Greenberg, and Feinberg (2010)	USA, 2005 General, State	n = 8879 age = all gr12s 47% males 90.1% Caucasian	LCA (5)
Connell, Gilreath, Aklin, and Brex (2010)	USA, 2000-2003 General, State	n = 1236 age = 14.6 (0.7), gr9 to gr10 47% males 89% Caucasian 1% Black	LCA (6)
Connell, Gilreath, and Hansen (2009)	USA, 2005 General, National	n = 13953 age = ~16, gr9 to gr12 50.5% males 62% Caucasian 15% Black	LCA (7)
Conway et al. (2013)	USA, 2010 General, National	n = 2524 age = all gr10s 45.6% males 57.9% Caucasian 17.5% Black	LCA (6)
Coulter, Ware, Fish, and Plankey (2019)	USA, 2015 General, National	n = 124519 age = 16, gr9 to gr12	LCA & Multinomial Logistic Regression (5)

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Table 1 (*continued*)

Study	Sampling Characteristics	Participant Characteristics	Methods
	Country, Collection Year Population, Sampling (specifics)	sample size, age mean (SD if reported), min to max age, % males, ethnicity	Method (#indicators)
		56.1%males 41.0-48.2% Caucasian 10.2-18.0% Black 27.5-30.2% Hispanic	
Cranford et al. (2013)	USA, NR General, State	n = 2744 age = 14.8 (1.9), gr7 to gr12 49.6% males 64.1% Caucasian 30.6% Black	LCA (6)
Davila and Tubman (2019)	USA NR	n = 371 age = 16.3 (1.2), 12 to 18 71.1% males 44.9% Caucasian 9.1% Black 20.6% Hispanic	K-means (6)
Delk et al. (2019)	USA, 2015-2016 General, State	n = 2733 age 7th grade = 12.3 age 9th grade = 14.3 age 11th grade = 16.0 51% males 27.2-33.0% Caucasian 13.2-18.0% Black 52.8-55.7% Hispanic	LCA (9)
Dermody et al. (2016)	USA, 2011 General, City	n = 2064 age = 17.2 (1.3), 15 to 19 0% males 39% Caucasian 55% Black	MM (4)
Dermody (2018)	USA, 2015 General, National	n = 15607 age = NR, gr9 to gr12 49.59% males 43.85% Caucasian	LCA (7)
Dierker, Vesel, Sledjeski, Costello, and Perrine (2007)	USA, 1995-1996 General, National	n = 4707 age = NR, gr7 to gr12 47.6% males 67.7% Caucasian 23.7% Black	LCA (6)
Espelage, Davis, Basile, Rostad, and Leemis (2018)	USA, 2012-2013 General, State	n = 1875 age = 15.8 (1), 14 to 18 49.2% males 29.1% Caucasian 44.3% Black	LCA (4)
Essau and de la Torre-Luque (2019)	USA, 2001-2004 General, National	n = 10123 mean age = 15.2 (1.5), 13 to 18 48.93% males 55.66% Caucasian 19.29% Black	LCA (26)
Finch and Pierson (2011)	USA, 2009 Generaiol, National	n = 16410 age = 16 (1.2), gr9 to gr12 52.2% males 58.7% Caucasian	MM (14)
Fraga, Severo, Costa, Lopes, and Ramos (2011)	Portugal, 2003-2004 General, City	n = 1612 age = all 13 45.7% 100% Portuguese	Hierarchical Cluster (6)
Gilreath et al. (2014)	USA, 2005-2007 General, State	n = 418702 age = gr9, gr7 to gr11 47.5% males 33.1% Caucasian 8.1% Black 58.8% Latino	LCA (3)
Graham, Collins, Wugalter, Chung, and Hansen (1991)	USA, 1987-1988 General, City	n = 2009 age Time 1 = 7th grade age Time 2 = 8th grade NR males 47% Caucasian 2.5% Black 28% Latino	LTA (3)
Green et al. (2013)	Scotland, 1987 General, City	n = 1383 age Time 1 = 15.7 age Time 2 = 17.1 age Time 3 = 18.6	LCA (9)

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Table 1 (*continued*)

Study	Sampling Characteristics	Participant Characteristics	Methods
	Country, Collection Year Population, Sampling (specifics)	sample size, age mean (SD if reported), min to max age, % males, ethnicity	Method (#indicators)
		time 1: 48.6% males time 2: 46.5% males time 3: 47.5% males 100% Scottish	
Hallfors et al. (2004)	USA, 1994 General, National	n = 18924 median age = 16.3, 11.6 to 21.4 (gr7 to gr12) 50.92% males 76.13% Caucasian 16.66% Black	K-means (9)
Hedden, Whitaker, Von Thomsen, Severtson, and Latimer (2010)	USA, NR Targeted, City (African American youth with signs of risk behaviours)	n = 212 age = NR, 11 to 14 50.94% males NR Ethnicity	LCA (5)
Jordão et al. (2018)	Brazil, 2012 General, National	n = 105164 age = 13-15 (86%), all year 9 11% < 13 and 13% > = 16 47.8% males 36.8% Caucasian 13.4% Black 42.2% "Brown"	Hierarchical Agglomerative Cluster Analysis (17)
Karlsson et al. (2019)	Sweden, 2012-2015 Targeted, National (youth who have used illicit drugs)	n = 3374 age = 11th grade (67.9%), gr9 to gr11 56.1% males NR Caucasian	LCA (10)
Kelly, Chan, Mason, and Williams (2015)	Australia, NR General, State	n = 9966 age = 14.5 (0.6), gr7 to gr11 49.34% males NR Ethnicity	LCA (4)
Kemppainen et al. (2007)	Russia, Finland, 2005 General, Town	n = 2318 age = ~15, all gr9s NR males NR Ethnicity	K-means and Hierarchical Cluster Analysis (8)
Kliewer, Wan, Parham, and Ring (2019)	Myanmar/Burma, NR General, Town	n = 1918 age = 15.4 (1.1), 14 to 18 44.3% males 61.3% Kachin 22.3% Myanmar	LCA (5)
Lamont, Woodlief, and Malone (2014)	USA, 1997 General, National	n = 1550 age = 17 to 18 51.7% males 52.7% Caucasian 24.6% Black	LCA (7)
Lazzeri et al. (2016)	Italy, 2010 General, National	n = 3291 age = ~13, 11 to 15 NR males 100% Italian	K-means and Hierarchical Cluster Analysis (8)
Mazur, Tabak, Dzielska, Wąż, and Oblacińska (2016)	Poland, 2013-14 General, National	n = 1202 age = 15.6 (0.3), 11 to 15 46.1% males NR Ethnicity	K-means (3)
Merrin, Thompson, and Leadbeater (2018)	Canada, 2003-2013 General, City	n = 662 age = 15.5 (1.9), 12 to 18 48% males NR Ethnicity	LCA (4)
Mitchell and Plunkett (2000)	USA, 1993 Targeted, State ("American Indians")	n = 2012 age: NR, ~15 to 18 (all high school) NR males 100% American Indian	LCA (5)
Morean et al. (2016)	USA, 2013 General, State	n = 2241 age = 15.6 (1.2), gr9 to gr12 45.6% males 65.1% Caucasian 9.1% Black 14.3% Latino	LCA (8)
Okumu et al. (2019)	USA, 2017 General, National	n = 14765 age = 16 (29.1%), 15 to 18+ (all gr9 to gr12) 48.6% males 43.4% Caucasian 19.4% Black 20.3% "Multiracial"	LCA (7)
Oshri et al. (2011)	USA, NR Targeted, City (youth receiving outpatient	n = 394 age = 16.3 (1.2), 12 to 18 71.1% males	LPA (5)

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Table 1 (*continued*)

Study	Sampling Characteristics	Participant Characteristics	Methods
	Country, Collection Year Population, Sampling (specifics)	sample size, age mean (SD if reported), min to max age, % males, ethnicity	Method (#indicators)
	substance use services with sexual activity in past 6 months)	25.4% Caucasian 20.6% Black 44.9% Latino	
Park and Kim (2018)	Korea, 2013 General, National	n = 72435 age = grade 11/12 (34.1%) , gr7 to gr12 52% males 100% Korean	LCA (7)
Parker and Bradshaw (2015)	USA, 2013 General, State	n = 18680 age = 15.9 (1.3), 12 to 21 (all gr9 to gr12) 50.2% males 50.5% Caucasian 31.9% Black	LCA (6)
Picoito, Santos, Loureiro, Aguiar, and Nunes (2019)	Portugal, 2010 General, National	n = 1551 age: all 15 43.8% males NR Ethnicity	LCA (7)
Pilatti, Godoy, Brussino, and Pautassi (2013)	Argentina, NR General, City	n = 583 age = 15 (1.5), 13 to 16.5 40.5% males 100% Argentinian	LCA (5)
Potter and Jenson (2003)	USA, 1999 Targeted, City (youth in juvenile detention centres with mental health or substance use concerns)	n = 155 age = 15.6 (1.4), range NR 79% males 69% Caucasian	K-means (14)
Ranney et al. (2018)	USA, 2013-2014 Targeted, National (youth presenting to US ERs with non-life threatening conditions)	n = 5001 age = 14.5 (1.7), 12 to 17 45.4% males 54.2% Caucasian 31.8% Black	LCA (7)
Ray, Thornton, Frick, Steinberg, and Cauffman (2016)	USA, 2011 Targeted, States (males in juvenile justice system)	n = 1216 age = 15.3 (1.3), 13 to 17 100% males 14.8% Caucasian 36.9% Black	LCA (4)
Riehman, Stephens, and Schurig (2009)	USA, 1997-2000 Targeted, National (youth with a mental health concern attending services in a US funded system of care community)	n = 1228 age = 14.6 (1.6), 11 to 18 60.6% males 58.2% Caucasian 19.1% Black	LCA (10)
Rivera et al. (2018)	USA, 2007-2016 Targeted, City (general population of females in US but selected to compare maltreatment)	n = 504 age = 18.2 (1.1), 14 to 17 0% males 49.2% Caucasians for non-maltreated; 40.3 % Caucasians for maltreated	LCA (8)
Rose, Evans, Smokowski, Howard, and Stalker (2018)	USA, 2014 Targeted, City (rural population)	n = 4822 age = 14.8, gr6 to gr12 48.2% males 29% Caucasian 26% Black	LCA (5)
Salas-Wright et al. (2016)	USA, 2002-2012 Targeted, National (pregnant teens)	n = 810 age = 15-17 (89%), 12 to 17 0% males 39.4% Caucasian 23.9% Black 27.6% Latino	LCA (18)
Schmiege and Bryan (2016)	USA, NR Targeted, City (sexually active youth in juvenile probation offices)	n = 596 age = 15.7, 14 to 18 66.6% 15.7% Caucasian 24.5% Black 40.9% Latino	LPA (5)
Shin, Hong, and Hazen (2010)	USA, 1996-1997 Targeted, City (youth involved in publicly funded service systems)	n = 1019 age = 15.9, 13 to 18 66% males 31% Caucasian 21% Black 32% Latino	LCA (6)
Shook et al. (2013)	USA, 2006-2010 Targeted, National (youth who had sold drugs in the past year)	n = 3080 age = 15.7 (1.2), 12 to 17 70.1% males 60.2% Caucasian 18% Black	LPA (17)

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Table 1 (*continued*)

Study	Sampling Characteristics	Participant Characteristics	Methods
	Country, Collection Year Population, Sampling (specifics)	sample size, age mean (SD if reported), min to max age, % males, ethnicity	Method (#indicators)
Silveira, Green, Iannaccone, Kimmel, & Conway (2019)	USA, 2013-2014 General, National	n = 6127 age = NR, 15 to 17 NR males NR ethnicity	LCA (17)
Snyder, Gwaltney, and Landeck (2015)	USA, 2008-2009 Targeted, National (representative of child welfare in US)	n = 890 age = 13.6, 11 to 17 59.82% males 45.97% Caucasian 18.33% Black 26.76% Latino	LCA (6)
Stanley and Swaim (2018)	USA, 2009- 2013 Targeted, National (American youth on or near reserve)	n = 4964 age = American Indian (grade 7-8) = 13.3; American Indian (grade 9-12) = 15.9; white (grade 7-8) = 13.3; white (grade9-12) = 15.9 50.56% males 30% Caucasian 70% American Indian	LCA (6)
Su, Supple, and Kuo (2018)	USA, 2009 General, City	n = 9155 age = 15.6 (1.1), 13 to 17 49% males 84% Caucasian 7% Black	LCA (13)
Sullivan, Childs, and O'Connell (2010)	USA, NR General, State	n = 2549 age = 16 (1.2), gr9 to gr12 50% males 59% Caucasian 31% Black	LCA (12)
Tomczyk, Hanewinkel, and Isensee (2015)	Germany, 2013 General, State	n = 2490 age = 13.3 (0.6), gr7s 51% males NR Ethnicity	LCA (6)
Valente, Cogo-Moreira, and Sanchez (2017)	Brazil, NR General, City	n = 6391 age = 12.6, 11 to 15 48.79% males NR Ethnicity	LCA (5)
Vaughn et al. (2012)	USA, 2008 Targeted, National (non-prescription opioid users)	n = 1783 age = NR, 12 to 17 44.7% males 66% Caucasian 11.9% Black	LCA (16)
Weden and Zabin (2005)	USA, 1997-2000 General, National	n = 3183 age = ~18 50.5% males 64.8% Caucasian 34.9% Black	LCA (6)
White et al. (2013)	Australia, 2007 General, National	n = 1402 age = 14.6, 12 to 17 48.5% males NR Ethnicity	LCA (10)
Zapert et al. (2002)	USA, 1980-1982 General, City	n = 764 age = NR, gr6 to gr11 42% males 87% Caucasian	Cluster Analysis (12)
Zweig et al. (2001)	USA, 1994-1995 General, National	n = 12955 age males = 16.5, gr9 to gr12 age females = 16.3, gr9 to gr12 48.85% males 66% males 66% Caucasian 16% Black	Cluster Analysis (8)

on mental health symptomatology, although these were often based on univariate analyses. 34 % (k = 24) of studies compared groups based on internalizing symptoms, most commonly based on symptoms of depression, anxiety, or general psychological distress. Levels of internalizing symptoms were significantly higher in most multi-use clusters (83 %), compared to other clusters. 21 % (k = 15) of studies compared groups based on externalizing symptoms, most commonly including general externalizing symptoms. Externalizing symptoms were almost universally (93 %) higher in the substance use and multi-use clusters, compared to the other clusters. These associations were found in both general and targeted population studies, including those targeting higher risk adolescents engaged in publicly funded services, substance use treatment, or the justice system.

Table 2
Summary of indicators and thematic patterns across included studies.

	Indicators								Pattern themes							
Study	Alc	HED	Tob	Can	Pres	Ill	MH	Oth	Low	Mod	Alc	C/A	Tob	High	MH	Oth
Ansary, 2009	■		■	■			■		L	A/T/C			T/A	A/T/C	MH	
Assanangkornchai, 2018	■	■	■	■	■	■	■	■	L		A			A/T/C/O		
Baggio, 2016	■		■	■		■			A	A/T/C/O			T/A	A/T/C/O (2)	N/A	
Bartlett, 2005	■			■			■	■	A	A/C			N/A	A/C		
Bohnert, 2014 (T)	■	■	■	■	■	■			L					A/T/C/O	N/A	C
Charak, 2015 (T)	■	■	■		■	■			L	A/T/O		N/A		A/T/O	N/A	
Chen 2015 (T)	■			■	■	■			A(r)	A/C(r)			N/A	A/C/O (2)	N/A	
Childs, 2017	■	■	■	■			■	■	L(2*)				T	A/T/C	MH(r)	
Choi, 2018	■		■	■	■	■			A			C/A		A/T/C/O	N/A	
Chung, 1996	■		■			■	■		L	A/T	A	N/A		A/T/O		
Chung, 2013 (T)	■		■	■					L		A			A/T/C	N/A	
Cleveland, 2010	■	■	■	■					L	A/T/C	A (2)		T	A/T/C	N/A	
Connell, 2010	■		■	■	■	■			L	A/T/C	A			A/T/C/O	N/A	
Connell, 2009	■	■	■	■		■			L	A/T/C	A			A/T/C/O	N/A	
Conway, 2013	■	■	■	■	■	■			L	A/T/C				A/T/C/O	N/A	C
Coulter, 2019	■	■	■	■					A	A/T/C (2)		C/A	T/A	A/T/C	N/A	
Cranford, 2013	■		■	■	■				L	A/T/C				A/T/C/O (2)	N/A	
Davila, 2019 (T)	■					■	■	■	L(r)	A/O (r)		N/A	N/A	A/O	MH(r)	
Delk, 2019	■	■	■	■				■	L	A/T/C (2)				A/T/C	N/A	
Dermody, 2016	■	■	■	■					L		A	C/A	T/A	A/T/C	N/A	
Dermody, 2018	■	■	■	■					L	A/T/C	A			A/T/C	N/A	C/T
Dierker, 2007	■	■	■	■					L		A	C/A	T	A/T/C	N/A	
Espelage, 2018	■	■			■				L		A	N/A	N/A	A/O	N/A	
Essau, 2019	■		■				■		L			N/A		A/T/O	MH	
Finch, 2011	■		■	■	■	■		■	L		A		T/A	A/T/O	N/A	
Fraga, 2011	■		■					■	L	A/T		N/A		A/T	N/A	
Gilreath, 2014	■		■	■					L	A/T/C (2)				A/T/C	N/A	
Graham, 1991	■	■	■						L	A/T (2)	A	N/A	T	A/T	N/A	
Green, 2013	■		■				■		L	A/T (2)	A	N/A			MH	
Hallfors, 2004	■	■	■	■		■		■	Did not fit directly into patterns due to outlying cluster solution (k-means, c=15/16)							
Hedden, 2010 (T)	■		■	■			■	■	L					A/T/C		
Kelly, 2015	■		■	■		■			L		A			A/T/C/O	N/A	
Jordao, 2018	■	■	■			■	■	■	L*			N/A		A/T/O*		
Karlsson, 2019 (T)				■		■			L(r)	A/T/C(r)			N/A	A/T/C/O (2)	N/A	
Kemppainen, 2007	■	■	■					■	L	A/T (2)		N/A		A/T	N/A	
Kliewer, 2019	■		■		■	■			A/O	A/T/O (m)		N/A		A/T/O	N/A	1 (f)
Lamont, 2014	■	■	■	■		■			L				T/A	A/T/C/O	N/A	C/T
Lazzeri , 2018	■		■				■	■	L	A/T (3)		N/A	T		MH	
Mazur, 2016	■		■	■					L			C/A	T/A	A/T/C	N/A	
Merrin, 2018	■	■	■	■		■			A			C/A		A/T/C/O	N/A	
Mitchell, 2000 (T)	■			■		■			L	A/C			N/A	A/C/O (2)	N/A	
Morean, 2016	■		■	■					L			C/A	T/A	A/T/C	N/A	
Okumu , 2019	■	■		■		■	■		A	A/C			N/A	A/C/O	MH(r)	
Oshri, 2011 (T)	■					■	■		L(r)			N/A	N/A	A/O	MH(r)	
Park, 2018	■		■						L	A/T	A	N/A		A/T	N/A	
Parker, 2015	■	■	■	■	■				L	A/T/C (2)	A			A/T/C/O	N/A	
Picoito, 2019	■	■	■	■					L	A/T/C (m)	A		T/A (f)	A/T/C	N/A	
Pilatti, 2013	■	■	■			■			L	A/T	A (2)	N/A		A/T/O	N/A	

(*continued on next page*)

Table 2 (*continued*)

Potter, 2003 (T)									L(r)*				N/A	A/T/O (2)*		
Ranney, 2018 (T)									L	A/T/C				A/T/C/O		
Ray, 2015 (T)									L	A/T/C				A/T/C/O	N/A	
Riehman, 2009 (T)										A/T/C		C/A	T	A/T/C/O	*all	
Rivera, 2017 (T)									L		A	C/A		A/T/C (2)	N/A	C/T
Rose, 2018 (T)									L	A/T/C	A			A/T/C/O	N/A	
Salas-Wright, 2016 (T)									L	A/C	A		N/A	A/C/O	N/A	
Schmiege, 2016 (T)													N/A			3
Shin, 2010 (T)									L	A/C			N/A	A/C/O(2f, 1m)	N/A	
Shook , 2013 (T)									L(r)	A/T/C(r)				A/T/C/O		
Silveira, 2019									L	A/T/C (2)*		C/A*		A/T/C/O	N/A	
Snyder, 2015 (T)									A	A/C			N/A	A/C/O	N/A	
Stanley, 2018 (T)									L	A/T/C				A/T/C/O	N/A	C/T
Su, 2017									L	A/T/C	A			A/T/C/O	N/A	
Sullivan , 2010									L	A/T/C (2)				A/T/C		
Tomczyk, 2015									L	A/T		N/A		A/T	N/A	
Valente, 2017									L		A			A/T/C/O	N/A	
Vaughn , 2012 (T)									L(r)	A/T/C(r)				A/T/C/O	MH	
Weden, 2005									L	A/T/C				A/T/C	MH	
White, 2013									A	A/T/C				A/T/C/O	N/A	
Zapert, 2002									L	A/T/C/O (3*)	A			A/T/C/O*	N/A	
Zweig , 2001									L	A/T/C				A/T/C/O	MH (f)	C/T/O (m)
TOTAL (k = 70)	**69**	**29**	**57**	**55**	**20**	**42**	**20**	**19**	**67**	**47**	**24**	**10**	**15**	**66**	**11**	
T=targeted samples	grey = measured/included								L=No/low use; L(r)= relatively low use in a high risk sample; A=Alcohol; T=Tobacco/Smoking; C=Cannabis; O=Other prescription or illicit drugs; MH=Mental Health; MH(r)=high/highest mental health symptomatology alongside moderate general substance multi-use; (#)=when there is more than 1 of these types of clusters included; (m/f)=when the cluster only applies to males or females when stratified; *=fit general pattern with some exceptions/distinctions						

3.3. Patterns of sociodemographic characteristics

The majority of studies compared substance use clusters based on sociodemographic characteristics. 86 % of studies compared clusters based on sex or gender, 75 % of which found significant differences. There were consistent, but not universal, associations between sex and/or gender and substance use cluster solutions. Males were typically more likely to be in high multi-use clusters and experience more externalizing symptoms. Females were more likely to be in the low use clusters, experience more internalizing symptoms, and be in clusters with high mental health symptomatology and low substance use. Although males were often more likely to use substances than females, several studies found that females who did use substances were more likely to be in the high multi-use clusters rather than moderate general multi-use, to use more heavily, misuse prescription drugs, and experience co-occurring mental health concerns.

The second most common comparison was age, with 71 % of studies comparing clusters based on age, 88 % of which found significant differences demonstrating higher multi-use groups among older age groups. Of note, five studies stratified their cluster solutions by age with three finding similar cluster solutions across age groups but with different distributions (i.e., higher prevalence of multi-use clusters in older age strata). The remaining two identified fewer and more limited range cluster solutions in the middle school strata (i.e., grade 6–8) compared to the secondary school strata (i.e., grade 9 – 12).

Race/ethnicity was compared in 53 % of the studies, of which 92 % found significant differences with inconsistent findings. The most common pattern was white youth being more likely to be in higher multi-use clusters and black youth being more likely to be in low use clusters or alcohol-focused clusters. 33 % of studies compared groups based on socioeconomic status (SES), with 65 % finding significant differences. Most studies found lower SES was related to higher likelihood of multi-use, with two exceptions (Picoito et al., 2019; Salas-Wright et al., 2016).

3.4. Quality of included studies

An overview of the RoB of included studies is presented in Fig. 2 with more details found in Supplementary Materials. In summary, 50 % were deemed low risk of sampling bias with higher RoB due to sample exclusions or restrictions (including geography) limiting representativeness, not reporting sampling frames, self-selection, and discrepancies in reporting. Most studies had initial response rates greater than 60 % (74 %) and less than 20 % missing data (64 %), however 21 % and 30 % did not report enough information to determine response rates and missingness, respectively. 37 % of studies did not report how they dealt with missing data, 27 % used complete cases only, 29 % used Full information maximum likelihood (FIML), and 7 % used other missing data strategies. Most studies relied on self-reports of substance use and mental health symptoms using single or multi–item scales.

Overall, quality of cluster reporting was inconsistent and poor. Of the included articles, 81 % (k = 57) performed LCAs. Of note, the type of cluster analysis was significantly related to cluster solution findings whereby studies using LCAs identified more single and dual clusters than other cluster methods. Most studies using LCA provided some type of fit statistic(s) for determining the final number of clusters although several did not report Likelihood Ratio Test (LRT; k = 22); entropy or Positive Predictive Value (PPV; k = 15); or Bayesian Information Criterion (BIC; k = 9). Only 28 % selected a final solution that was mostly or fully consistent with reported fit indices. When discrepancies exist across fit statistics, it is recommended to use BIC for model enumeration (Nylund et al., 2007). Often BIC was the primary index used for model selection – either denoted by the lowest BIC or accelerated flattening - although this was not universal. Regarding the model

Table 3
Substance Use Pattern Themes.

Theme	Brief Descriptions	Sub-themes	Proportion reported as median (min to max)
Low Use	The lowest *relative* levels and probabilities of use in the sample, usually reflective of the largest proportion of adolescents.	No/low use Some alcohol use	53 % (8%–91%)
Moderate general multi-use	Typically, adolescents in these clusters endorsed more than 2 substances, most commonly alcohol, cannabis and tobacco. Use of other illicit or misuse of prescription substance use was either absent or low. When the scale of measurement of the indicator variables reflected a continuum of frequency of use, occasional levels of use of alcohol, cannabis, and tobacco were most common, alongside infrequent or rare use of other drugs.	Alcohol, Tobacco, and/or Cannabis Alcohol, Tobacco, and/or Cannabis + some experimental use of other substances	22 % (4%–52%)
Single or dual substance use	These clusters indicate moderate to high levels of a single substance or dual substances, exclusively pertaining to the use of Alcohol, Cannabis, and Tobacco. Of note, in order to be classified into a dual Tobacco & Alcohol or Cannabis & Alcohol focused group, we required all three common substances to be included as indicators. If all three substances were not included, those clusters were classified into general multi-use clusters given inability to determine difference between dual versus multi-use.	Alcohol focused. This cluster theme is distinct from low use class in that it reflects notably higher levels of just alcohol use, and in some instances had a similar or larger prevalence than the low use cluster. Cannabis & Alcohol Focused. Note: tobacco had to be included as an indicator variable Tobacco focused (with and without co-alcohol). Note: cannabis had to be included as an indicator variable.	25 % (8%–45%) 19 % (5%–44%) 13 % (4%–31%)
High multi-use	Adolescents in these clusters endorsed use of all included substances. When the scale of measurement of the indicator variables reflected a continuum of frequency of use, high multi-use clusters reflected regular or frequent levels of use of alcohol, cannabis, and tobacco alongside other illicit or prescription drug use (when included). At times "high" and "higher" multi-use clusters emerged, differentiated by the frequency and type of other illicit or prescription substance misuse in addition to the Alcohol, Tobacco, and/or Cannabis. This cluster usually represented the smallest proportion of adolescents within study samples.	Highest levels of Alcohol, Tobacco, and/or Cannabis Highest levels of Alcohol, Tobacco, and/or Cannabis + other substances Highest levels of Alcohol, Tobacco, and/or Cannabis + advanced other substances	12 % (0.03%–53%)

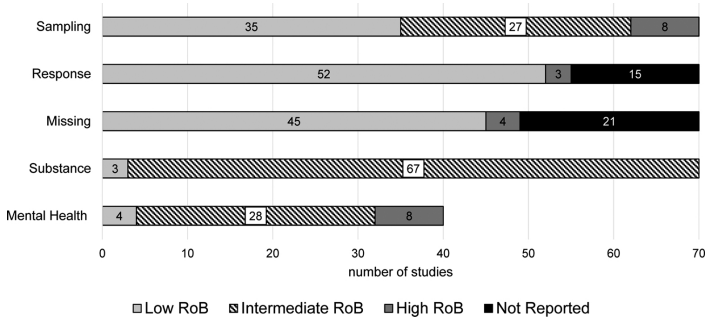

Fig. 2. Risk of Bias Summary.

assumption of local independence, only 12 % mentioned local independence. Of studies that did not mention this assumption. 28 % may have been in violation given inclusion of indicators that were dependent on one another (e.g., HED indicator is dependent upon any alcohol use indicator). Lastly, 46 % stated there were competing models that made final model selection difficult, with 25 % indicating using theoretical rationale to guide final decision-making. Other methodologies that were not model-based similarly did not typically report fit indices, competing models, sensitivity analyses, or cross- replication. Most commonly, these studies stated they selected the number of clusters that maximized the squared Euclidean distances but did not report specific details.

4. Discussion

Seventy studies were identified which investigated substance use patterns among adolescents with over half published in the last five years, demonstrating that this is a rapidly emerging field. The following distinct patterns of substance use were derived: low use, single or dual substance use (i.e., alcohol only, cannabis with alcohol, and tobacco with and without alcohol), moderate general multi-use, and high multi-use. Our review presents extensive evidence that latent subgroups of adolescent substance use exist. The patterns identified in this review provide a robust foundation for evaluating etiological and prognostic models as well as prevention and intervention studies. If we see consistent and distinct risk factors and treatment responses based on common multi-substance patterns, novel tailored interventions will be needed.

Our review provides a critical update on the state of the literature on multi- substance use patterns, with some replication from the previous review (Tomczyk et al., 2016). The patterns replicated include: (a) the highest proportion of adolescents typically falling into a low use

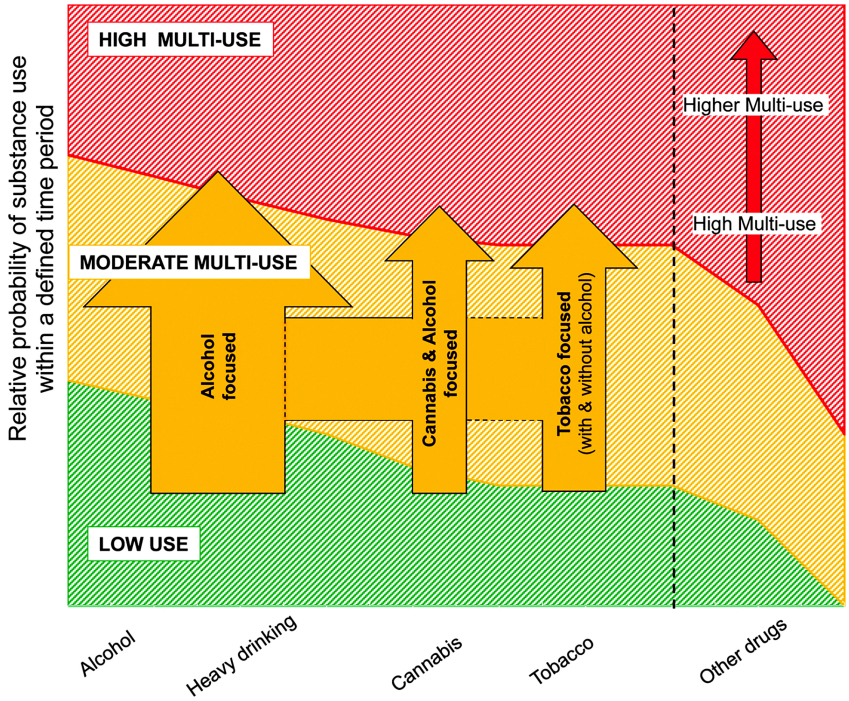

Fig. 3. Visual representation of substance use patterns.

Caption Fig. 3. This figure visually depicts substance use themes found across studies within this review. The y-axis represents the relative probability of endorsement of each substance (within a defined time period and/or frequency of use) and the x-axis depicts commonly included substance use indicators. The black dotted line indicates that other illicit drugs and prescription drug misuse are less likely to be included as indicators in cluster generation. The green shading reflects relative endorsement for *low use*, whereby there is low to no use across all substances (although at times, alcohol may be slightly more elevated). The yellow shading reflects relative endorsement in *moderate general multi-use clusters*, where adolescents in these clusters typically have higher relative levels of alcohol, cannabis, and tobacco use with low to no use of other illicit drugs and prescription drug misuse. The yellow arrows represent *single and dual substance focused* clusters that typically fall into moderate to high probabilities of endorsement on specific substances. The *alcohol focused cluster* is the largest of the three arrows as it was most commonly found and typically represented a large proportion of adolescents. The *cannabis* arrow is directly connected to the alcohol arrow as predominant cannabis use often co-occurred alongside reported alcohol use (as a dual substance cluster), more-so than cannabis on its' own. For the *tobacco* arrow, the connection with alcohol is represented by a dotted line since there was a relatively large proportion of single substance tobacco focused clusters although a majority were still dual-substance alongside alcohol. The red shading reflects relative endorsement in *high multi-use* clusters, where adolescents typically endorse the highest levels across all included substance use indicators. The red arrow represents the distinction between *high and higher multi-use* clusters, which were typically reflective of differences in the prevalence and frequency of use of other illicit drugs and prescription drug misuse.

group, which at times includes experimental or low levels of alcohol; (b) the next most common pattern being predominant alcohol use; (c) higher multi-use groups typically identified as small and most often comprised of the highest relative levels of alcohol, tobacco, and cannabis use; and (d) that low SES and older age are related to higher multi-use (Tomczyk et al., 2016). The replication of these key patterns strengthens their importance and validity. Additionally, our review refined and disaggregated previously identified single-substance patterns, multi-use, and extended sociodemographic and mental health correlates (Tomczyk et al., 2016). Specifically, our review found that: (1) cannabis and tobacco have distinct patterns of use that are separate from general multi-use across all substances; (2) mental health is important to consider when generating and characterizing clusters; and (3) gender/sex differences are important.

First, substance use patterns should be considered in prevention, identification, and treatment strategies. The National Institute on Drug Abuse (NIDA, 2014) suggests that for adolescent substance use, it is critical to identify and intervene early even when youth do not meet criteria for a substance use disorder. Guidelines recommend asking about substance use during annual primary care visits (starting around age 11) and in mental health settings (Burkstein, 2020; Pan and Brent, 2018; National Institute on Drug Abuse (NIDA, 2014; Swinson, 2017). Common brief screeners include Brief Screener for Tobacco, Alcohol, and other drugs (BSTAD) and the Screening to Brief Intervention (S2BI), both of which provide steps for asking about all types of substances that can help identify patterns. Once assessed, recent research has focused on the use of brief motivational interventions, although these are typically single-substance specific (Carney et al., 2016; Halladay et al., 2019a, 2019b; O'Connor et al., 2018; Towns et al., 2017). Our review suggests that although stand-alone interventions for alcohol and tobacco may still be warranted, there seems to be a particular need for interventions focusing on dual use of cannabis and alcohol as well as different levels of multi-use (i.e., separating those using alcohol, cannabis, and tobacco occasionally from those using more frequently with

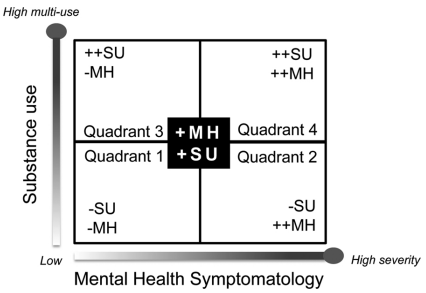

Fig. 4. Visual representation of mental health and substance use patterns.
Caption Fig. 4. This figure visually depicts the relationship between the clustering of substance use and mental health symptomatology. This figure was adapted from the four-quadrant model of concurrent disorders. The y-axis represents the level of endorsement of substance use and multi-use and the x-axis represents the level of endorsement of mental health symptomatology. Quadrant 1 represents low substance use (-SU) and low mental health symptomatology (-MH), Quadrant 2 represents high mental health symptomatology (+ +MH) but low substance use, the Quadrant 3 represents high multi-substance use (+ +SU) and low mental health symptomatology, and the Quadrant 4 depicts high co-occurring substance use and mental health symptomatology. Within included studies that considered mental health symptomatology, clusters reflective of all quadrants were identified.

and without other drug use). Given the sensitivity of the adolescent brain to rewards and the opportunity to address potential common liability factors, there is also interest in the use of alternative activities and drug free reinforcement strategies (McKay, 2017) as well as school climate and social skills interventions (Das et al., 2016).

Secondly, our review highlights the co-occurrence of mental health and substance use concerns among adolescents. When mental health was considered, almost all studies found significant differences, suggesting that mental health symptomatology is associated with higher multi-use clusters. This is consistent with positive correlations between substance use and mental health symptomatology found in general population samples of youth (Cheung et al., 2019) and high prevalence of co-occurring substance use among clinical samples of youth. For example, studies have found that the majority of youth who present to hospital or outpatient clinics for substance use concerns experience co-occurring mental health concerns, and this co-occurrence is related to greater severity of problems (Chan et al., 2008; Diamond et al., 2006; Hawke et al., 2018). Additionally, it has been found that youth who present to the hospital for mental health concerns commonly use substances (Blevins et al., 2019), and that co-occurring substance use is related to poorer mental health treatment outcomes (Gobbi et al., 2019; Hser et al., 2017; Jacobus et al., 2017; Mammen et al., 2018; Moitra et al., 2016). For many years, it has been suggested that, "co-occurring disorders are an expectation, not an exception" (pg. iv, SAMHSA, 2002) and our review reinforces the need to examine and address them concurrently (Addiction and Mental Health Collaborative Project Steering Committee, 2014).

Although co-occurrence was common, our review also demonstrated distinct subgroups of adolescents with substance use and mental health concerns (i.e., Quadrants 2 and 3). This suggests that not all adolescents using substances experience mental health concerns (and vice versa). The four-quadrant model of concurrent disorders (adapted in Fig. 4) illustrates that individuals can present in various ways with substance use concerns only, mental health concerns only, or with co-occurring problems (Sacks et al., 2005). The model points to the need to assess and treat both mental health and substance use concerns in a stepped, integrated, and coordinated manner (see the following for a review of integrated care: Evidence Exchnage Network for Mental Health and Addictions (EEnet, 2016). Our review found different cross-sectional patterns consistent with all four quadrants among adolescents in general and targeted populations. This suggests that in addition to continuing to promote concurrent assessment and treatment in primary care and specialized mental health and substance use settings (see the following for summaries of concurrent treatment: CSAT, 2007; Drake et al., 2008; Kelly et al., 2012), it may also be helpful to extend this concurrent lens to the development of health prevention, promotion, and early identification protocols. Future research should consider patterns of mental health and substance use in order to develop distinct referral and care pathways in various settings, including schools.

Third, our review suggests gender and sex are associated with different patterns of substance use among adolescents. Other studies have similarly found that females may be particularly vulnerable to the effects of substances, may be more likely to progress to higher risk use and to experience problems from their use (McHugh et al., 2018), including co-occurring mental health concerns (Halladay et al., 2019a). In line with international recommendations, future research should consider findings related to both sex and gender independently from one another in order to further refine our understanding of the nature of these associations (Heidari et al., 2016).

4.1. Strengths and limitations

We undertook a comprehensive search strategy resulting in the inclusion of many studies, which were extensively described and analyzed. We used content analytical techniques (due to limitations of existing meta-analytical software) to iteratively identify consistent themes across studies, leading to a meta-synthesis. Our review focused on cross-sectional cluster analyses and did not include longitudinal analyses; thus, it is focused on cross-sectional cluster identification and not on general etiology and prognosis of specific patterns. Greater inclusivity led to increased heterogeneity of studies in terms of sampling design, participant characteristics, methods, and indicators, although was focused exclusively on studies written in English. Therefore, overarching themes were consistent but this heterogeneity may have resulted in missed nuances in cultural, ethnic, or targeted population differences.

Although the review process itself was methodologically rigorous, there were a number of limitations in individual studies that restrict generalizability and direct comparison. Regarding population and contextual characteristics, 3/4 of included studies were conducted in the US and – although studies were published recently – data itself was at least 3 years old and often older. This limits our ability to know if patterns are similar globally and if they have persisted or changed due to the recent opioid crisis and changes in cannabis legislation. There may also be other contextual factors including regional differences in drug availability, cultural practices, local drug policy, and cost. Additionally, most included studies did not stratify the analyses based on age or developmental period, although age was typically included as a covariate, precluding our ability to examine developmental differences in patterns of substance use. Similarly, few studies empirically evaluated differences across sex/gender and ethnicity/race. Most sociodemographic and mental health correlates were assessed univariately, thus conclusions regarding associations are threatened by unmeasured confounding. There were also a number of methodological shortcomings including moderate to high RoB, poor reporting of cluster-methodological decisions, and heterogeneity/inconsistency in measurement of indicator variables. Given cluster-methods are person-centred and most solutions are sample- and indicator-dependent, patterns were captured relatively and, as such, there were large variations in "low" "moderate" and "high." Thus, there is a critical need for greater consistency, clarity, and standardization of methods for future cluster studies. Further, more research is needed to understand if patterns differ or persist across global, political, contextual, and demographic factors.

4.2. Methodological recommendations

Our review suggests a need for more consistent and clear reporting of response rates, missingness, and cluster-based methodological decisions including statistical fit indices, evaluation of the assumptions of local independence, and presentation of competing models. Focusing on LCA studies, there was poor reporting of cluster solutions and inconsistencies in model enumeration strategies. Poor reporting and inconsistencies in model enumeration have been echoed in previous reviews related to youth mental health and substance use (Petersen et al., 2019; Tomczyk et al., 2016) and reflect larger cluster-based methodological concerns that span across fields (van Smeden et al., 2014v). To our knowledge, there are no current reporting guidelines for LCAs, however, there are reporting guidelines for observational research (STROBE Guidelines; Von Elm et al., 2014), latent trajectory models (van de Schoot et al., 2017v), and other papers that discuss how to appropriately report LCAs (Petersen et al., 2019; Schreiber, 2017). At minimum, LCA-type studies should include: (a) statistical fit indices across all three domains (absolute, relative, predictive probabilities) for selected and competing models; (b) evaluations for the assumption of local independence; and (c) a transparent discussion regarding final model selection and competing models (including presenting patterns for competing models).

The heterogeneity in the selection and measurement of indicator variables alongside cluster-analytical methodological decisions preclude direct comparisons. Previous researchers have similarly expressed concerns regarding the ability to replicate and compare clusters across studies due to differences in the number, nature, and types of indicators (Nylund-Gibson and Choi, 2018; Petersen et al., 2019; Tomczyk et al., 2016). Our review highlights that:

1 Separate indicators for alcohol, cannabis, and tobacco should be included when examining patterns of substance use among adolescents. These are the most common substances used globally, and without including all indicators, substance-specific patterns carrying distinct risks cannot emerge;
2 Using continuous indicators, as opposed to dichotomous or categorical, is recommended as it increases sample variability and also allows for identification of clusters based on frequency and higher risk use versus any use;
3 Indicators related to mental health symptomatology should be included, as different and important patterns and shared liability factors may be revealed which warrant further exploration;
4 Maximizing consistency and comparability across studies is crucial. First, a set of standardized substance use measures and operationalization of use would greatly advance the field. Secondly, future studies should consider cross-replication using different clustering techniques such as comparing model-based approaches to machine-learning approaches;
5 There is a need for novel advanced meta-analytical software or strategies to pool study-level cluster solutions while accounting for heterogeneity across sampling and methodological decisions.

5. Conclusion

There is a large and multifarious empirical literature identifying patterns of multiple substance use in adolescents. Patterns of adolescent substance use typically included low use, single and dual substance use, moderate general multi-use, and high multi-use. A minority of studies considered mental health symptomatology, but those that did suggest important correlations as well as concurrent and distinct patterns. Further exploration of the role of mental health in patterns of substance use is warranted. More broadly, there is a need to identify robust substance use patterns using standardized methodological approaches and to conduct etiologic, prognostic, and intervention research using these patterns that is rigorous and comparable. The benefits of cluster methods, in that they are person-centred approaches that reduce complex patterns into homogenous sub-groups, may currently be outweighed by heterogeneity across studies which limits direct comparisons and syntheses of results across studies and samples. Future cluster-based research needs to balance the desire for person-centred exploration with the need for consistency and comparability.

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Contributors

JH conceived of and designed the review. JH lead the screening, data extraction, data analysis, and writing of the review. RW and HK were the primary second reviewers in screening, data extraction, and thematic coding. MO, LF, KA, MK also helped with screening, data extraction, and verification. CM, JM, MA, and KG provided methodological and substantive support throughout the manuscript process. All authors have reviewed and approve of the final submission.

Declaration of Competing Interest

No conflicts declared for all authors other than JM, who is a principal in BEAM Diagnostics, Inc.

Appendix A. Supplementary data

Supplementary material related to this article can be found, in the online version, at doi:https://doi.org/10.1016/j.drugalcdep.2020.108222.

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Chapter 2: Select Supplementary Materials

All supplementary files available here: https://doi.org/10.1016/j.drugalcdep.2020.108222

Supplemental Materials File 1

1. PRISMA Checklist

doi:10.1371/journal.pmed1000097

2. Search Strategy

STEP 1. Database search strategy

(1) Met with McMaster Health Sciences librarian to review search strategy and refine. (2) Reviewed with Dr. Kathy Georgiades. (3) Reviewed with colleagues in HEI. (4) Reviewed key terms in target studies and search terms in related systematic reviews

Mapped in EMBASE		
EXPOSURE, *and…*	**METHOD,** *and…*	**POPULATION**
Cannabis addiction/ "Cannabis use" Cannabis/ Cannabis smoking/ Cannabis* Exp drug abuse/ Exp drug abuse pattern/ Exp alcoholism/ Exp alcohol abuse/ Exp alcohol consumption/ Alcohol.mp Binge drinking.mp Illicit drug*.mp Substance abuse.mp ***ANY OF THE ABOVE***	Exp latent class analysis/ (also captures latent structure analysis) Cluster analysis/ Latent profile analysis.mp Latent cluster*.mp Cluster analysis.mp Latent class analysis.mp Profile analysis.mp. LCA.mp LPA.mp Mixture model*.mp factor analysis/ factor analysis.mp FMM.mp Factor mixture*.mp group-based trajectory model*.mp group-based model*.mp trajectory model*.mp group membership.mp discriminant function analysis.mp ***ANY OF THE ABOVE***	Young adult.mp Exp young adult/ Emerging adult.mp Exp juvenile/ Youth.mp Adolescen*.mp Exp student/ Student.mp Teen*.mp ***ANY OF THE ABOVE***

STEP 2a. Title & Abstract Screening

Criteria 1. Population: Is the sample or population youth (i.e., elementary, high school, post-secondary age)? Exclude: mean age <11 or >25; lower limit of age range below 6 and upper limit above 30. *Decision*: If clear yes or unsure, go to exposure. If clear no, exclude.
Criteria 2. Exposure: Is there some mention of more than one type of substance use? i.e., ever/never use, frequency of use, or patterns of use of multiple substances. *Decision*: If clear yes or unsure, go to method. If clear no, exclude.
Criteria 3. Method: 1) Is the study identifying groups/patterns/clusters/profiles or make reference to any of the following methods: cluster analysis**,** latent class analysis (e.g., LCA)**,** profile analysis (e.g., LPA)**,** mixture modeling (e.g., FMM)**,** factor analysis, group-based trajectory modeling, discriminant function analysis; and 2) use of more than one substance appears in more than one cluster/grouping. Notes: 1) These methods must be used for the purpose of identifying patterns of substance use (i.e., frequency, ever/never). Substance use must be an indictor variable – not the external/auxiliary variable. Patterns of "Healthy behaviours" or "risky behaviours" that include substance use are to be included. 2) Be cautious as "cluster" sometimes refers to sampling methods not the analysis. Exclude: • Measures of substance use such as motives or expectancies or other substance-related variables *besides* frequency/ever-never use. • Studies performing psychometric testing of measures or questionnaires. • Studies only using regression. *Decision*: If clear yes or unsure, include for full text screening. If clear no, exclude.

STEP 2b. Full Text Screening

Is the population <u>only</u> adolescents?	**Was more than one substance use variable used as <u>indicator variables</u>?**	**Did they do a <u>cluster/grouping</u> based analysis?**	**Please <u>specify</u> the type of analysis.**	**Reason for exclusion**
1= Yes <18 or high school. Youngest age >=11 or grade 6. 2= No, emerging adults >18 or postsecondary 3=No, a combination of adolescents and emerging adults 0=No, all adults	1=yes 2=only 1 substance 0=no. <u>NOTE:</u> a. The cluster analysis must be used for the purpose of identifying patterns of substance use (i.e. frequency, ever/never, substance use disorder). Substance use must be an *indictor variable* – <u>not</u> the external/auxiliary variable. b. in some instances, more than one substance is measured but they then combine all the substance use measures together into a summative or aggregated global or overall substance use variable. Although they technically measured multiple substances, they included substance use in the model as a single variable. This type of analysis would merit exclusion (coding 2) c. in some instances, they have measured multiple substances but in separate models. This is most common in the longitudinal studies (i.e. growth models, trajectory models). In this case, although they measured two separate substances, they did not do so in the same model. Therefore, this type of analysis would merit exclusion (coding 2) <u>Exclude:</u> • Including only measures of substance use such as motives or expectancies or other substance-related variables besides frequency/ever-never use/disorder. • Studies only looking at patterns of use of one substance. • Studies only using regression.	1=yes 0=no NOTE: 1. Regressions /correlations are excluded 2. Be cautious as "cluster" sometimes refers to sampling methods not the analysis.	This **will mainly** include any of the following methods: • Cluster analysis • Latent Class analysis (e.g. LCA) • Profile analysis (e.g. LPA) This **might (but rarely)** include: • Mixture Modeling (usually this type of model only uses one type of indicator variable - i.e. an aggregate substance use score or a single type of substance) • Factor analysis (usually this type of model refers to clustering of **variable or items** for a test of psychometric properties and we are interested in clustering of **people**). • Group-based trajectory modeling (usually this type of model only uses one type of indicator variable - i.e. an aggregate substance use score or a single type of substance) • Discriminant function analysis Or other, and specify.	1=emerging adult/university student 2=included adults 3=no substance use indicators 4=only 1 substance use indicator or aggregate score 5=not a cluster-based analysis 6=other, please specify

3. Non-English Studies

Laaser, U., & Allhoff, P. (1982). [Prevention during adolescence: cardiovascular risk profile in juveniles of Cologne]. Monatsschrift Kinderheilkunde. Organ der Deutschen Gesellschaft fur Kinderheilkunde, 130(10), 760-766.

Reis, O., Fegert, J. M., & Hassler, F. (2006). Patterns of multiple substance use among adolescents in low-threshold care. [German]. [Muster polyvalenten drogengebrauchs bei niedrigschwellig betreuten jugendlichen.]. Sucht, 52(5), 305-316.

Selecka, L., Vaclavikova, I., Blatny, M., & Hrdlicka, M. (2017). Typology of antisocial behaviour: Specific manifestations of adolescent boys and girls in the relation to risky sexual behaviour. Ceska a Slovenska Psychiatrie, 113(6), 258-267.

4. Data Extraction Content

Study and Sample Characteristics
First author name, year of publication, Country, type of study (1=longitudinal comparisons made, 2=cross-sectional, 3=longitudinal study but analysis from only 1 cross-sectional wave; 4=other (specify)), year data was collected, population setting (1=school, 2=general community, 3=street youth, 4=youth in primary care (specify), 5= youth in mental health or substance use care (specify), 6=other (please specify)), specifics including title/name of study data comes from, type of sampling (1=random, 2=all youths available in setting of interest during recruitment, 3=volunteer, 4=other please specify), target sample size/sample size included/response rate, mean age with minimum and maximum, if parental consent was required, inclusion and exclusion criteria (other than consent or general sampling frame), % males, racial profile (specifics for race/ethnicity >=20% of the sample), any other comments.
Analysis Details
Type of cluster analysis, specifics (i.e. multilevel, covariances, standardization, centering, stratification, equivalency tests, inclusion of covariates, missing data strategies), statistics and theoretical model fit indices, substance use indicator variables

including alcohol, tobacco/nicotine, cannabis, prescription drug misuse, other illicit drug use (all included presence/absence, type of use, coding in analysis, time period for reporting, and measurement tool specifics), mental health indicator variables including internalizing, externalizing, and combined concerns (all of which included presence/absence and how they were measured), list of any other indicator variables, list of covariates.

Results

- **Clusters:** Subgroups (if results stratified), # of clusters/profiles, name of clusters, n of clusters and % of total sample, brief description re: indicator variables only. Note: If there were more than 8 clusters, specifics were not extracted.
- **Comparisons:** Specific to sex/gender, age, race/ethnicity, SES, other demographic characteristics (all measured yes/no, significant differences yes/no, specifics). Specific to mental health concerns including internalizing mental health concerns, externalizing mental health concerns, combined (all: measured yes/no, how was it measured, significant differences yes/no, specific findings). Specific to service use (measured yes/no, how were they measured, and findings). A list of other outcomes/comparisons and general overview.

Risk of Bias

RISK OF BIAS #1A: Is the source population (sampling frame) representative of the general population? Answer options:

- Low risk of bias (definitely yes): selection of the target population is from a representative population roster such as a registry or random sampling of students within school's representative of the population.
- Intermediate risk of bias (probably yes/ probably no): exclusions limiting representativeness, lack of reporting of sampling frame, limited geographical spread.
- High risk of bias (definitely no): self-selection, convenience sampling, very limited geographical spread, studies where the source population cannot be defined.

RISK OF BIAS #1B: What is your rationale/reason for your judgment?

RISK OF BIAS #2: Is the assessment of the substance use accurate? Answer options:

- Low risk of bias (definitely yes): biological measure (e.g., urinalysis), Timeline Follow-back, Diagnostic Interview
- Intermediate risk of bias (probably yes/ probably no): structured validated item(s)
- High risk of bias (definitely no): single non-validated item or no details

RISK OF BIAS #2B: What is your rationale/reason for your judgment?

IF APPLICABLE - RISK OF BIAS #3A: Is the assessment of the mental health accurate? Answer options:

- Low risk of Bias (definitely yes): structured interview or administrative data diagnosis
- Intermediate risk of bias (probably yes): structured validated scale
- Intermediate risk of bias (probably no): structured validated single item
- High risk of bias (definitely no): self-reported non-validated item or no details.

More details: https://www.evidencepartners.com/wp-content/uploads/2017/09/Tool-to-Assess-Risk-of-Bias-Longitudinal-Symptom-Research-Studies-Aimed-at-the-General-Population.pdf

RISK OF BIAS #3B: What is your rationale/reason for your judgment?

Conclusions

General study conclusions.

5. Risk of Bias (RoB) of Individual Studies

RoB tools for cross-sectional designs created by the CLARITY group at McMaster University and endorsed by Evidence Partners were used and adapted to assess RoB (CLARITY Group at McMaster University, 2019). Domains included: (a) representativeness of the source population; (b) adequacy of response rate (>60%); (c) amount of missing data (<=20%); (4) reliability and validity of measurement tools. For the assessment of substance use, Time-Line Follow-Back [TLFB] (Robinson, Sobell, Sobell, & Leo, 2014) or structured, diagnostic interviews were judged as lowest RoB and items based on measures from large epidemiological studies that have undergone cognitive and psychometric testing were judged as intermediate RoB (Brener, Collins, Kann, Warren, & Williams, 1995; Currie et al., 2010; Substance Abuse and Mental Health Services Administration, 2010). For the assessment of mental health symptoms, structured, diagnostic interviews were judged as lowest RoB, while pre-validated clinical questionnaires were judged as intermediate RoB and single item questions with no psychometric evaluation were judged as high RoB (CLARITY Group at McMaster University, 2019).

First author last name	year	Nat/State/City	General or Targeted Population	Sampling RoB	Response Rate RoB	Missingness RoB	Substance Use Measure RoB	Mental Health Measure RoB
Assanangkornchai	2018	National	General	L	>60	<20	I	H
Bartlett	2005	National	General	L	>60	<20	I	I
Connell	2009	National	General	L	>60	NR	I	N/A
Conway	2012	National	General	L	>60	NR	I	I
Coulter	2019	National	General	L	>60	<20	I	N/A
Dermody	2018	National	General	L	>60	<20	I	N/A
Dierker	2007	National	General	L	>60	<20	I	I
Essau	2019	National	General	L	>60	<20	L	L
Finch	2011	National	General	L	>60	<20	I	N/A
Hallfors	2004	National	General	L	>60	<20	I	I
Jordao	2018	National	General	L	>60	<20	I	H
Karlsson	2019	National	Targeted	I (prob yes)	NR	<20	I	N/A
Lamont	2014	National	General	L	>60	<20	I	N/A
Lazzeri	2016	National	General	L	>60	<20	I	I
Mazur	2016	National	General	L	>60	<20	I	N/A
Okumu	2019	National	General	L	>60	<20	I	H
Park	2018	National	General	L	>60	<20	I	I
Picoito	2019	National	General	L	>60	<20	I	I
Silveira	2019	National	General	L	>60	<20	I	I
Weden	2005	National	General	L	>60	<20	I	H
White	2013	National	General	L	>60	<20	I	I
Zweig	2001	National	General	L	>60	<20	I	H
Baggio	2016	National	General	I (prob yes)	>60	<20	I	N/A
Childs	2017	National	General	I (prob yes)	>60	<20	I	I
Charak	2015	National	Targeted	L	NR	NR	I	N/A

Chen	2015	National	Targeted	L	>60	NR	I	I
Riehman	2009	National	Targeted	L	NR	NR	I	L
Salas Wright	2016	National	Targeted	L	NR	NR	I	N/A
Shook	2013	National	Targeted	L	>60	NR	I	H
Snyder	2015	National	Targeted	L	>60	<20	I	I
Stanley	2018	National	Targeted	L	>60	NR	I	N/A
Ranney	2018	National	Targeted	I (prob yes)	NR	NR	I	I
Vaughn	2012	National	Targeted	L	>60	NR	I	H
Cleveland	2010	State	General	L	<60	NR	I	N/A
Gilreath	2014	State	General	L	>60	<20	I	N/A
Kelly	2015	State	General	L	>60	<20	I	I
Sullivan	2010	State	General	L	>60	<20	I	H
Tomczyk	2015	State	General	L	<60	>=20	I	N/A
Parker	2015	State	General	I (prob yes)	NR	<20	I	N/A
Choi	2018	State	General	I (prob no)	>60	NR	I	N/A
Connell	2010	State	General	I (prob no)	NR	NR	I	I
Cranford	2013	State	General	I (prob no)	>60	NR	I	I
Espelage	2018	State	General	I (prob no)	>60	<20	I	N/A
Morean	2016	State	General	H	>60	<20	I	N/A
Ray	2015	State	Targeted	L	>60	NR	I	I
Mitchell	2000	State	Targeted	I (prob no)	>60	<20	I	N/A
Delk	2019	State	General	I (prob no)	>60 student, <60 school	<20	I	N/A
Davila	2018	State	Targeted	H	NR	<20	L	L
Fraga	2011	City	General	I (prob no)	>60	>=20%	I	N/A
Green	2013	City	General	I (prob no)	>60	<20	I	I
Kemppainen	2007	City	General	I (prob no)	>60	<20	I	I
Kliewer	2019	City	General	H	>60	NR	I	N/A

Merrin	2018	City	General	I (prob no)	>60	<20	I	N/A
Su	2017	City	General	I (prob no)	>60	NR	I	N/A
Valente	2017	City	General	I (prob no)	>60	>=20	I	N/A
Zapert	2002	City	General	I (prob no)	>60	<20	I	N/A
Ansary	2009	City	General	H	>60	<20	I	I
Chung	1996	City	General	H	NR	<20	I	I
Graham	1991	City	General	H	>60	>=20	I	N/A
Pilatti	2013	City	General	H	NR	NR	I	N/A
Bohnert	2014	City	Targeted	I (prob no)	>60	<20	I	I
Chung	2013	City	Targeted	I (prob no)	>60	<20	I	I
Dermody	2016	City	General	I (prob no)	>60	<20	I	I
Hedden	2011	City	Targeted	I (prob no)	NR	<20	I	I
Oshri	2011	City	Targeted	I (prob no)	NR	<20	L	L
Potter	2003	City	Targeted	I (prob no)	>60	<20	I	I
Rivera	2018	City	Targeted	I (prob no)	NR	NR	I	N/A
Schmiege	2016	City	Targeted	I (prob no)	NR	NR	I	I
Shin	2010	City	Targeted	I (prob no)	NR	NR	I	I
Rose	2018	City	Targeted	H	>60	<20	I	N/A

Where L=low risk of bias, I=Intermediate risk of bias (split into probably yes and probably no), H=high risk of bias, NR=not reported.

6. Summary of Indicator Characteristics

	General Population	Targeted Population	Total
Alcohol Use	47	22	69
Type of Use			
Any/general use	47	20	67
Heavy episodic drinking	25	6	31
Other	10	5	15
Coding in Analysis			
Dichotomous	47	22	69
Continuous	13	2	15
Categorical	18	7	25
Other; not reported	4	0	0;4
Timeline of Recall			
Lifetime	23	11	34
Past year	20	14	34
Past month	35	2	37
Other; not reported	11	5	10;6
Smoking/Tobacco Use	44	13	57
Type of Use			
Smoking	48	14	62
Snuff, dip, chew	7	1	8
Vaping, e-cigarette, Hookah	10	0	10
Cigars	6	0	6
Other	7	1	8
Coding in Analysis			
Dichotomous	50	12	62
Continuous	11	1	12
Categorical	16	3	19
Other; not reported	1	0	0;1
Timeline of Recall			
Lifetime	18	5	23
Past year	21	6	27
Past month	35	3	38
Other	7	2	9
Not reported	2	0	2
Cannabis Use	34	21	55
Type of Use			
Any/general use	35	20	55
Other; not reported	1	5	6
Coding in Analysis			
Dichotomous	18	18	36
Continuous	6	3	9
Categorical	10	4	14
Other; not reported	2	0	0;2

Timeline of Recall			
Lifetime	11	8	19
Past year	9	11	20
Past month	20	2	22
Other	0	4	4
Not reported	2	0	2
Prescription Drug Use	12	8	20
Measurement			
Combined prescription drugs	11	6	17
Separate prescription drugs	2	2	4
Coding in Analysis			
Dichotomous	13	7	20
Continuous	0	1	1
Timeline of Recall			
Lifetime	5	4	9
Past year	7	2	9
Other	1	2	3
Other Illegal Drug Use	23	19	42
Measurement			
Individual drug	4	2	6
Combined “all other drugs”	16	9	25
Combined separate drugs	5	11	16
Coding in Analysis			
Dichotomous	18	17	35
Continuous	4	4	8
Categorical	2	1	3
Not reported	1	0	1
Timeline of Recall			
Lifetime	11	8	19
Past year	10	9	19
Past month	2	3	5
Other	1	3	4
Not reported	1	0	1
Mental Health	13	7	20
Measurement			
Any internalizing mental health problems	3	1	4
Any externalizing mental health problems	11	7	18
Any suicide-related indicator	3	1	4
Any general psychological distress	2	1	3
Other (e.g., eating disorders)	1	0	1
Other	14	5	19
Sexual behaviours	7	2	9
Health-related behaviours	2	0	2
Drug-related behaviours	3	2	5
Combined other behaviours	2	1	3

7. Summary of Studies with Mental Health Patterns

Quadrant 3: High Substance Use, Low Mental Health	**Quadrant 4:** High Substance Use, High Mental Health
1. Ansary (2009) doi:10.1017/s0954579409000182 2. Lazzeri (2016) doi:10.1093/pubmed/fdw134 3. Okumu (2019) doi:10.1007/s12529-019-09783-6 4. Shook (2013) doi:10.1016/j.jcrimjus.2013.07.008 5. Vaughn (2012) doi:10.1016/j.addbeh.2012.03.015	1. Ansary (2009) doi:10.1017/s0954579409000182 2. Bartlett (2005) doi:10.1002/nur.20078 3. Childs (2017) doi: 10.1177/0306624X15599401 4. Chung (1996) https://doi.org/10.1007/BF02511034 5. Green (2013) https://doi.org/10.1016/j.jadohealth.2013.02.023 6. Lazzeri (2016) doi:10.1093/pubmed/fdw134 7. Sullivan (2010) doi: 10.1007/s10964-009-9445-5 8. Zweig (2001) https://doi.org/10.1023/A:1012281628792 9. Assanangkornchai (2018) doi:10.1186/s12889-018-6205-z 10. Essau (2019) doi:10.1016/j.psychres.2019.06.007 11. Weden (2005) https://doi.org/10.1080/13557850500115744 12. Hedden (2010) https://doi.org/10.1080/1067828X.2011.534358 13. Oshri (2011) doi: 10.1007/s10461-011-9890-5 14. Potter (2003) https://doi.org/10.1177/0093854802251007 15. Ranney (2018) doi:10.1016/j.acap.2018.02.016 16. Shook (2013) doi:10.1016/j.jcrimjus.2013.07.008 17. Vaughn (2012) doi:10.1016/j.addbeh.2012.03.015 18. Davila (2019) https://doi.org/10.1007/s10560-019-00637-4

Quadrant 1: Low Substance Use, Low Mental Health	**Quadrant 2:** Low Substance Use, High Mental Health
1. Ansary (2009) doi:10.1017/s0954579409000182 2. Bartlett (2005) doi:10.1002/nur.20078 3. Childs (2017) doi: 10.1177/0306624X15599401 4. Chung (1996) https://doi.org/10.1007/BF02511034 5. Green (2013) https://doi.org/10.1016/j.jadohealth.2013.02.023 6. Lazzeri (2016) doi:10.1093/pubmed/fdw134 7. Sullivan (2010) doi: 10.1007/s10964-009-9445-5 8. Zweig (2001) https://doi.org/10.1023/A:1012281628792 9. Assanangkornchai (2018) doi:10.1186/s12889-018-6205-z 10. Weden (2005) https://doi.org/10.1080/13557850500115744 11. Essau (2019) doi:10.1016/j.psychres.2019.06.007 12. Okumu (2019) doi:10.1007/s12529-019-09783-6 13. Hedden (2010) https://doi.org/10.1080/1067828X.2011.534358 14. Oshri (2011) doi: 10.1007/s10461-011-9890-5 15. Potter (2003) https://doi.org/10.1177/009385480225100707 16. Ranney (2018) doi:10.1016/j.acap.2018.02.016 17. Shook (2013) doi:10.1016/j.jcrimjus.2013.07.008 18. Vaughn (2012) doi:10.1016/j.addbeh.2012.03.015 19. Davila (2019) https://doi.org/10.1007/s10560-019-00637-4	1. Ansary (2009) doi:10.1017/s0954579409000182 2. Essau (2019) doi:10.1016/j.psychres.2019.06.007 3. Green (2013) https://doi.org/10.1016/j.jadohealth.2013.02.023 4. Lazzeri (2016) doi:10.1093/pubmed/fdw134 5. Vaughn (2012) doi:10.1016/j.addbeh.2012.03.015 6. Weden (2005) https://doi.org/10.1080/13557850500115744 7. Zweig (2001; female) https://doi.org/10.1023/A:1012281628792 Relative (High mental health, Moderate substance) 8. Childs (2017; Black youth) doi: 10.1177/0306624X15599401 9. Okumu (2019) doi:10.1007/s12529-019-09783-6 10. Oshri (2011) doi: 10.1007/s10461-011-9890-5 11. Davila (2019) https://doi.org/10.1007/s10560-019-00637-4

8. Predictors of Substance Use Patterns

	Sex/gender	Age	Race/ethnicity	SES
# studies that made comparisons (% of total)	60 (86%)	50 (71%)	37 (53%)	23 (33%)
# found significant differences (% of those that compared)	45 (75%)	44 (88%)	34 (92%)	15 (65%)

	Any Mental Health	Internalizing problems	Externalizing Problems	Help Seeking
# studies that made comparisons (% of total)	26 (37%)	24 (34%)	15 (21%)	1 (1%)
# found significant differences (% of those that compared)	25 (96%)	20 (83%)	14 (93%)	1 (100%)

Chapter 3: Patterns of Student Substance Use and Mental Health Symptoms: A Multilevel Latent Profile Analysis

Halladay, J., MacKillop, J., Munn, C., Amlung, M., Georgiades, K. Patterns of student substance use and mental health symptoms: A multilevel latent profile analysis. (*Under Review at Drug and Alcohol Dependence*)

Highlights

- 5 substance use and mental health symptom profiles were identified among adolescents reflecting comorbidity
- 3 types of schools were found, including schools with low, moderate, and high levels of adolescent substance use and comorbidity with disproportionate representation of rural schools in higher risk types
- School climate, belonging, and safety appeared protective
- Substance use and mental health concerns should be considered concurrently
- Schools are important contexts for addressing student substance use and comorbid mental health symptoms

Abstract

Background: While substance use and mental health symptoms commonly co-occur among adolescents, few population-level studies have examined profiles of co-occurrence to inform tailored prevention and early intervention efforts.

Methods: A multilevel latent profile analysis was conducted on a representative sample of 11,994 students in 68 secondary schools to: 1) identify distinct profiles of co-occurring substance use and mental health symptoms; 2) identify types of schools based on student substance use and mental health patterns; and 3) explore school correlates of student profiles and school types, including school climate, belonging, and safety.

Results: Five student profiles and three school types were identified. Among students, 57.6% were in a low substance use and mental health profile, 22.5% were in a high mental health but low substance use profile, 9.7% were in a heavy drinking and cannabis profile, 3.7% were in a heavy drinking and smoking profile, and 6.5% were in a high substance use and mental health profile. Positive school climate, belonging, and safety increased the odds of students being in the low profile, with belonging yielding larger effects among females. Among schools, 28% had low, 57% had moderate, and 15% had high levels of student substance use and comorbid mental health symptoms. Rural schools were disproportionately represented in higher risk school types.

Conclusions: The identified student substance use and mental health symptom profiles can serve as targets for tailored prevention and early interventions. Results support examining school-based interventions targeting school climate, belonging, and safety with potential benefits to both substance use and mental health.

Background

Substance use and mental health concerns are the leading cause of morbidity worldwide (World Health Organization, 2018), with half of lifetime mental disorders beginning during adolescence (Solmi et al., 2021). Substance use is a particular concern in adolescence due to its' impact on neurodevelopment (Casey et al., 2008), making any substance use during this time important to understand and address, even when not at the level of a substance use disorder.

Adolescents often use more than one substance, making it important to consider patterns of use (Halladay et al., 2020). To characterize these patterns, cluster-based analyses, such as latent profile analysis (LPA), can be used to identify distinct subpopulations based on unique patterns of substance use. A recent review of a large number of cluster-based studies on adolescent substance use (Halladay et al., 2020) found common patterns including: 1) low or no use; 2) single or dual substance use, such as alcohol only, cannabis and alcohol, and tobacco with or without alcohol; 3) moderate multiple use; and 4) high multiple use. When mental health symptoms were included as correlates (37% of studies), almost all studies found significant associations between higher substance use and poorer mental health. When mental health was incorporated directly into the cluster models (29% of studies), distinct profiles of adolescent substance use with and without comorbidity emerged, mapping on to the four-quadrant model of concurrent disorders (i.e., low in both substance use and mental health concerns, high in one domain but not the other, high in both). However, few studies incorporated mental health symptoms, and indicators were often limited to one type of mental health problem (e.g., a single item regarding behavioural problems).

Differentiating and characterizing adolescents with and without co-occurring substance use and mental health concerns will assist in selecting and creating tailored and integrated prevention and early intervention programs. Prior research has shown that adolescent substance use differs by age, sex, and gender (Boak, 2020); race, ethnicity, and immigrant status (Hamilton et al., 2018; Keyes et al., 2015); and indicators of socioeconomic disadvantage including family socioeconomic status (Lee et al., 2018) and

family structure (Hoffmann, 2017). Adolescent mental health symptoms are also known to differ across these demographic characteristics (Georgiades et al., 2019). For example, patterns often differ by gender whereby, most consistently, females are more likely to be in low substance use profiles and experience more emotional symptoms (Halladay et al., 2020). Also, females who use substances may progress to higher risk use and experience more co-occurring problems from use such as depression, anxiety, and distress (Halladay et al., 2019; McHugh et al., 2018). Sex is a biologically driven variable, impacting the neurobiological and physiological effects of substances, while gender is a sociocultural variable, impacting the context and reasons for substance use and related consequences (Greaves & Hemsing, 2020). To date, most research has not distinguished between sex and gender, typically providing binary response options, limiting our ability to understand the causal mechanisms for differences observed.

School Effects

Substance use is heavily influenced by social environments and peer networks (Henneberger et al., 2021), including schools. Up to 20% of the variability in adolescent substance use may be attributed to between-school differences (Hale et al., 2014; Shackleton et al., 2016). A school's social environment is often considered along a number of dimensions that are malleable to targeted interventions, including: 1) *school climate*, often defined by community and interpersonal relationships, fairness and clarity of rules, and academic support and values; 2) *school belonging,* defined by how connected students feel to their school; and 3) *school safety*, including how safe students feel at and around school (Aldridge & McChesney, 2018; Daily et al., 2020; Marraccini et al., 2020). These dimensions of a school's social environment, and interventions designed to improve them, have been associated with higher levels of student wellbeing, and lower mental health problems and substance use (Daily et al., 2020; Durlak et al., 2011; Faggiano et al., 2014; Faulkner et al., 2009; Fletcher et al., 2008; Ford et al., 2021; Taylor et al., 2017; Thapa et al., 2013).

Multilevel LPA (MLPA) models can account for and identify variability in student profiles between schools; answering the question, *do student profiles vary significantly across schools?* (i.e., parametric MLPA (Henry & Muthén, 2010)). MLPA can also be employed to identify school-level classes that reflect qualitatively different environments relative to the frequency and distribution of student profiles within schools; answering the question, *can school types be classified based on the proportions of students in various profiles within schools?* (i.e., nonparametric MLPA (Henry & Muthén, 2010)). Two studies have recently applied multilevel latent class analysis (MLCA) to examine both student-level patterns of alcohol use and school-level classes, without considering mental health symptoms (Gohari et al., 2020; Lee et al., 2021). Two types of schools were found, characterized by low or high student alcohol use. They examined contextual correlates of these classes, namely alcohol outlet density and median family income, though neither found significant associations. The authors indicated a paucity of related literature and given the known importance of school context and identification of unique school classes, the need for further exploration of other school characteristics that differentiate substance use patterns to better inform school-based prevention and intervention efforts (Gohari et al., 2020; Lee et al., 2021). To date, no studies have incorporated common dimensions of school environments within a multilevel cluster-based analysis of both substance use and mental health.

Objectives

To address these existing limitations, the current study used a large, representative sample of secondary (grades 9-12) students, including school-based data, to address three objectives: 1) identify distinct profiles of co-occurring substance use and mental health symptoms; 2) identify types of schools based on student substance use and mental health patterns; and 3) explore school correlates of student profiles and school types, including school climate, belonging, and safety.

Methods

Sample

All reporting follows the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines (See Supplementary Information S7). Data for analyses come from grade 9-12 students in secondary schools included in the cross-sectional 2014-2015 School Mental Health Surveys (SMHS). The SMHS was designed to examine associations between school contexts and student mental health. All study procedures, including consent and confidentiality requirements, were approved by the Hamilton Integrated Research Ethics Board at McMaster University and the Research Ethics Committees of the School Boards involved in the study. The selection of schools was based on the sampling design of a companion study– the 2014 Ontario Child Health Study (OCHS) (Boyle et al., 2019), resulting in a representative sample of schools in Ontario (excluding schools on First Nations reserves). In total, 359 elementary and secondary schools were selected to participate and 248 agreed (69% response rate), with no notable differences between participating versus non-participating schools on key school variables (data available from the author). This analysis focused on secondary schools. Within selected secondary schools, anonymous surveys were administered to a random sample of three classrooms per grade. In total, survey data was collected from 11,994 secondary school students (response rate=60.5%) within 68 schools.

Measures

See S2 and S3 for more item details.

Substance Use and Mental Health

Frequency of Heavy Episodic Drinking (HED) was measured along a frequency continuum of having 5 or more drinks on the same occasion over the previous month, from never to 5 or more times (0-5). Cannabis Involvement (CAN) was measured along a continuum including: never, tried once or twice, previous weekly use but not past month, less than weekly, and at least once a week (0-4). Tobacco Smoking (TOB) was measured

along a continuum including: never, once or twice, previous daily use but not past month, sometimes but not every day, and daily (0-4). Sensitivity analyses were done where previous regular cannabis and smoking were removed and treated as missing (recoded 0-3).

Mental health symptomatology was assessed using a modified subset of the OCHS Emotional and Behavioural Scales (Duncan et al., 2018) to measure frequency of symptoms over the preceding 6 months on a scale from never/not true to often/very true (0-2) for: Generalized Anxiety Disorder (GAD; 4 items), Major Depressive Episode (MDE; 5 items), Oppositional Defiant Disorder (ODD; 5 items), and Attention Deficit Hyperactivity Disorder (ADHD; 4 items). A series of confirmatory factor analyses suggested a 4-factor model where all subdomains were included separately (invariant across gender; see S2). Items were summed where higher scores reflect more symptoms.

School Climate, Belonging, and Safety

School climate was measured by summing the following subdomains: 1) Student-Student Relationships (4 items); 2) Teacher-Student Relationships and Fairness (6 items), 3) Academic Pressure and Expectations (3 items), and 4) Positive Behavioural Support and Social and Emotional Learning (7 items) (Bear et al., 2014). Response options were scored from disagree a lot to agree a lot (0-3) for a total score from 0-60. School belonging was measured by summing 3-items rated from strongly disagree to strongly agree (0-4): 1) *I feel close to people at this school*, 2) *I feel like I belong at this school*, and 3) *I am happy to be at this school* (total scores 0-12) (Harris & Udry, 2001). School safety was measured by summing 5 items rated from not safe to very safe (0-3), asking about safety in and around the school (total scores 0-15) (Consortium on Chicago School Research, 2009).

Student Covariates

Gender. Students were asked, *"Are you…. Female? Male?"* The question stem did not specify whether the question was referring to sex (which is typically associated

with the terms female, intersex, or male) or gender (which is typically associated with the terms girl/women, boy/man, or transgender or gender diverse). In this paper, this variable has been labeled as gender given students self-identified and no reference to biology of sex at birth was made. Given only binary response options were provided, and there was no explicit reference to sex or gender, some students were likely misclassified.

Age. Students were asked to indicate their age based on response options ranging from 9 to 22 years of age.

Family Assets. Items were adapted from the Health Behaviour in School Aged Children Survey (6). Students self-reported their family's assets, including how many vehicles, computers, cellphones, or electronic tablets their family owns. A standardized factor score (Z-score) was derived using Principal Component Analysis of the 4 items where higher scores indicate greater assets. A single factor emerged and accounted for 46.3% of the variance in secondary students.

Race. Students were asked to select the category that best described their "race or cultural group" with the following response options: White, East Asian (Chinese, Japanese, Korean), Southeast Asian (Vietnamese, Filipino, Cambodian, Malaysian, Laotian), South Asian (East Indian Pakistani, Sri Lankan, Afghan, Bangladeshi), West Asian or Arab (Iraqi, Syrian, Lebanese, Egyptian), Black, Latin, Aboriginal, and/or "other" race or cultural group. Though "race and culture" were included in the question stem, the variable is labelled as race as response options are more reflective of race (i.e., perceived differences based on physical appearance) than ethnicity (i.e., multidimensional construct related to cultural group membership). Response categories were combined based on frequencies in crosstabs, whereby groups with <20 individuals in any student-level profiles were combined. This resulted in the following coding: White (reference); East Asian/Southeast Asian/South Asian (ESA); Black; or Other (including options: West Asian or Arab, Latin, Aboriginal, Other), and Multiracial (~80% White + another racial group[s], ~20% non-white racial groups). White was used as the reference as it represented the largest group of adolescents.

Immigrant Background. Students were asked to indicate if they were born in Canada and whether 1 or both of their parents were born in Canada. Students were coded as either first generation immigrant (1st gen), second generation immigrant (2nd gen), or non-immigrant (reference).

Family Structure. Students were asked who lives with them in their home. Responses were collapsed into two-parents (1; 2 Parents) compared to 1 or no parents (0).

Parental Education. Students were asked about the highest level of education one of their parents had completed. Responses were collapsed into post-secondary education including graduate from college or university (1; Parent PS) compared to high school or less (0).

School Covariates

Median Family Income. School SES was determined through a combination of student postal codes and median family income in the neighbourhoods of attending students using the National Household Survey 2011 data (7). Median family income was converted into increments of $10,000.

School Enrolment. School size was based on 2014/2015 school enrolment data from the Ontario Ministry of Education. Enrolment was analyzed in increments of 200 students.

Rural or Urban Designation. Each school was assigned to be either rural (1) or urban (0) through linking the school postal code with Statistics Canada's Postal Code Conversion File.

Statistical Methods

Regarding missingness, mean substitution was used within summative scale variables for those with <=30% missingness. Overall, 80.8% were complete on all variables with 98.3% and 97.7% having complete mental health and substance use data, respectively. Missingness was addressed using Full Information Maximum Likelihood (FIML) in cluster analyses. Given 17.3% of the sample had at least one socio-

demographic variable missing, Multilevel Multiple Imputation (MMI) using BLIMP (Keller & Enders, 2017) was applied to address missingness for regression models using Latent Fully Conditional Specification imputation with the Gibbs sampler (20 imputations). See S1 for more details.

Student-level substance use and mental health symptom profiles were identified through LPA using Mplus (version 7), with all indicators treated continuously. Random split halves were generated for sample cross-validation, with final models re-estimated in the full sample. Models were estimated for 1-k profiles when the model no longer converged or when Bayesian Information Criterion (BIC) began to increase (Collins & Lanza, 2009; Masyn, 2013). Solutions were compared based on class enumeration and separation diagnostics, indicator specific class homogeneity and separation statistics, and theoretical clinical relevance of profiles (specifics in S4). Measurement invariance across gender was examined by stratifying the sample and using the multi-group function to compare the fit of models with constrained versus freed parameters (Collins & Lanza, 2009; Masyn, 2013).

Subsequently, multilevel latent profile analysis (MLPA) was conducted to estimate the distribution and structure of student profiles at the school-level following methods provided by Mäkikangas et al. (2018) and Henry and Muthén (2010). First, a parametric MLPA was conducted allowing the student profile probabilities to vary across schools. Second, non-parametric MLPA was conducted whereby school-level classes were identified based on the relative frequency of student profiles. Models were compared based on similar diagnostics as the student-level, with BIC being the primary model selection criterion. The posterior probabilities and most likely class memberships from the final MLPA for both student profiles and school classes were used for subsequent modeling.

All subsequent analyses were conducted in SAS ® Enterprise Guide 7.1. First, descriptive statistics were estimated across all student profiles and school classes pooled across imputations. Next, a series of multilevel (students within schools) multinomial regression models were conducted to predict most likely student-level profile

membership. Random intercept generalized linear mixed models were estimated using PROC GLIMMIX with the residual pseudo-likelihood (RSPL) method and applying the Satterthwaite adjustment. Regressions were estimated by imputation, pooling estimates and standard errors for final results utilizing Rubin's rules. Models were run separately for school climate, belonging, and safety and all models were adjusted for socio-demographics. Differential gender effects were explored through interaction terms followed by stratified models where indicated. A conservative p-value of <0.005 was used to denote statistical significance.

Results

Student-Level Profiles

A 5-profile model was selected. The final model estimated in the full sample had an entropy of 0.92 with average posterior probabilities all >0.9. The profiles identified included: low substance use (SU) and low mental health symptoms (MH) (n=6,855, 57.6%, 'Low-SU/MH'), high substance use and high mental health symptoms (n=772, 6.5%, 'High-SU/MH'), low substance use with high emotional and moderate behavioural symptoms (n=2,672, 22.5%, 'Low-SU/High-MH'), high heavy episodic drinking and cannabis use with moderate mental health symptoms (n=1,160, 9.7%, 'HEDCAN/Moderate-MH'), and high heavy episodic drinking and tobacco use with moderate mental health symptoms (n=443, 3.7%, 'HEDTOB/Moderate-MH'). See Figure 1. Final models were deemed invariant across genders. Sensitivity analyses converged on a similar 5-profile solution. See S4 for detailed results.

[Figure 1]

School-Level Classes

Adding random effects via the parametric MLPA approach improved model fit compared to the student-level only (i.e., fixed effects) model, maintained entropy, and yielded significant variances in the probability of student profiles at the school-level

(BIC= 287715, Entropy= 0.916). This indicated that, depending on the school, the probability distributions of the 5 student-level profiles were different. Next, the non-parametric MLPA identified distinct school types, with a 3-class model fitting best; this model also improved model fit compared to the fixed-effects model (BIC=287791, Entropy=0.915). The 3-classes included a Type 1 School with low levels of student substance use and comorbid mental health symptoms (n=19 schools, 28%), Type 2 School with moderate levels of student substance use and comorbidity (n=39 schools, 57%), and a Type 3 School with high levels of student substance use and comorbidity (n=10 schools, 15%). All classes had average posterior probabilities >0.85 (See Figure 3). Compared to Type 1 Schools (low), for students in Type 2 (moderate) and Type 3 (high) schools respectively, the odds of being assigned to the: HEDCAN/Moderate-MH profile was 2.4 and 2.8 times greater; HEDTOB/Moderate-MH was 2.1 and 7.0 times greater; and High-SU/MH profile was 2.8 and 8.2 times greater. There were no significant school-type differences for students in the Low-SU/High-MH profile and thus school differences were mainly driven by the prevalence of student substance use with varying levels of comorbid mental health symptoms. See S5 for detailed results.

[Figure 2]

Characterizing and Predicting Student Profiles

See Table 1 for descriptives and Table 2 for regression results. In the adjusted demographic only model, all student-level covariates were significantly related to student substance use and mental health profile membership. Older students, compared to younger students, had greater odds of being in all profiles with elevated substance use and mental health symptoms. Females were more likely than males to be in the Low-SU/High-MH profile compared to the Low-SU/MH profile. No school-level socio-demographics were significantly related to student profile membership in adjusted models.

Students reporting higher school climate, belonging, and safety had greater odds of being in the Low-SU/MH profile compared to all other profiles. Several differential gender effects emerged, most consistently where belonging had more pronounced protective effects among female students. When analyses were stratified, females endorsing higher school belonging had lower odds compared to males of being in the HEDCAN/Moderate-MH (OR_{fem}=0.78[0.76-0.81]; OR_{male}=0.87[0.84-0.9]), HEDTOB/Moderate-MH (OR_{fem}=0.73[0.70-0.77]; OR_{male}=0.87[0.83-0.92]), and High-SU/MH (OR_{fem}=0.71[0.68-0.74]; OR_{male}=0.76[0.73-0.79]; $p_{fem*belong}$=0.006) profiles compared to the Low-SU/MH profile. There was also a significant gender interaction for safety, though only apparent for the HEDTOB/Moderate-MH profile ($OR_{fem*safe}$=.91[0.86-0.96]; p=0.001).

[Table 1 and Table 2]

Predictors of School Types

School size, rural neighbourhoods, and average student endorsements of school climate were correlated with school classes. Type 2 and 3 schools were smaller in size, more often in rural neighbourhoods, and had lower climate scores than Type 1 schools (See Table 3). Median family income and average student endorsements of safety and belonging were not significantly different across types. Notably, 0% of Type 1 (low) schools were rural while 50% (5/10) of Type 3 (high) schools were rural.

[Table 3]

Discussion

In a representative sample of 11,994 secondary students and 68 schools, five substance use and mental health student profiles and three school substance use types were identified. These findings reflect the largest epidemiological MLPA to date that provides a population-level characterization of the overlap and separation of common

substance use and mental health symptoms among adolescents and across schools. Specifically, 4 in 10 adolescents exhibited elevations in substance use or mental health symptoms, of which half demonstrated high levels of mental health symptoms (predominantly anxiety and depression) with low substance use and the other half had comorbid elevations in both substance use and mental health symptoms. Perceptions of positive school climate, belonging, and safety increased the odds of students being in the low substance use and mental health symptom profile, with school belonging yielding larger protective effects for females. At the school-level, mean levels of students' perceptions of school climate were higher in schools with low substance use and comorbid mental health symptoms (28% of schools) compared to schools with moderate (57%) and high (15%) proportions of comorbidity. Thus, school climate, belonging, and safety may provide promising targets for future universal school-based prevention and interventions to address both substance use and mental health concerns simultaneously.

Across student substance use and mental health profiles, symptom overlap was a common theme with no profile principally defined by a single indicator. Regarding substance use, we found profiles similar to the prior review (Halladay et al., 2020) including: 1) a low substance use group, 2) dual substance use groups (e.g., alcohol/cannabis, alcohol/tobacco), and 3) a high multiple use group. These profiles all had concurrent elevations in mental health symptoms, though differed in severity based on the patterns of substance use, which mapped onto the fourth quadrant of the concurrent disorders model (Substance Abuse and Mental Health Services Administration, 2020). Thus, we did not find a high substance use and low mental health profile (third quadrant). We also found a high mental health only profile, similar to the second quadrant, where there were elevations across all mental health symptoms – high levels of depression and anxiety symptoms and moderate levels of ADHD and ODD symptoms. Overall, these patterns suggest that combined approaches are critical for preventing and addressing substance use and mental health symptoms among adolescents.

Substantial variability was present in student profiles across schools, predominantly regarding substance use profiles with varying levels of comorbidity. This

is consistent with prior research demonstrating that schools explain a small proportion of the variability in student mental health while explaining larger proportions of substance use (Hale et al., 2014; Shackleton et al., 2016). These findings indicate that patterns of substance use and comorbid mental health concerns are, in part, context specific. Select schools, such as those with elevated substance use and comorbid mental health symptoms, may benefit from more intensive, targeted prevention and early intervention efforts. Similar to the prior school MLCAs (Gohari et al., 2020; Lee et al., 2021), we did not find significant school differences based on median family income. Our study examined a broader range of school characteristics and found that school size, rurality, and school climate were significantly related to school types. Notably, rural schools were disproportionately represented in the types of schools with the highest prevalence of student substance use and comorbidity. This is consistent with national reports indicating higher rates of substance use among rural youth (McInnis et al., 2015). Although perceived need for mental health care has increased among rural Ontarian youth (Comeau et al., 2019), higher rates of stigma, greater socioeconomic issues, and disparities in access to care in rural settings persist (Friesen, 2019). School social environmental factors have the potential to buffer some of these risks (Nguyen et al., 2021). This highlights the critical need to support schools with higher risk students, particularly rural schools, to develop, implement, and sustain substance use prevention and intervention efforts. Special considerations are needed when designing interventions for rural settings (McInnis et al., 2015).

Improving school climate, belonging, and safety may help schools improve student substance use and mental health outcomes concurrently. We found that as positive student perceptions of climate, belonging, and safety increased, students were more likely to be in the low profile compared to all other profiles. School belonging conferred larger protective effects for females, compared to males. Our findings are consistent with prior research indicating these aspects of a school's social environment are associated with lower psychiatric symptoms (Durlak et al., 2011; Ford et al., 2021; Taylor et al., 2017; Thapa et al., 2013), lower substance use (Daily et al., 2020; Faggiano et al., 2014;

Faulkner et al., 2009; Fletcher et al., 2008; Taylor et al., 2017), and may provide more robust protective effects among females (Faulkner et al., 2009; Langille et al., 2015). Further, these findings support recent recommendations for a comprehensive school health approach (e.g., (Public Health Agency of Canada, 2021), which promotes strategies to improve interpersonal relationships and help build social and emotional skills, increase student feelings of school belonging, and design spaces to promote safety.

Strengths of this study include a large, representative sample and both individual- and school-based data, but a number of considerations apply. The data are cross-sectional in nature, and thus temporal directionality or causality cannot be inferred. Although we did control for known student and school-level confounders, it is possible that not all confounders were incorporated. All measures were self-reported and, though mental health measures yielded good psychometric properties, there are no clinical cut-points for these measures and should be interpreted as clinical indicators but not diagnoses. The LPA model was selected through a rigorous global review of objective fit and theoretical considerations, though fit indices did not unanimously converge on one solution, a common circumstance in cluster-based studies (Halladay et al., 2020). The questions related to gender did not explicitly ask about gender or sex, and only included binary response options. Thus, some students were likely misclassified and there is a risk that sex and gender were conflated. Similarly, race and culture were combined into a single question, and thus unable to differentiate the potential pathways giving rise to between group differences. Lastly, the sample was limited to students attending school in Ontario, Canada (Canada's most populous province), though representative and likely applicable to other provinces and contexts. Future studies should consider oversampling schools in rural areas given known disparities.

Conclusion

Using a comprehensive multilevel latent profile approach, this study identified five unique substance use and mental health profiles in a large representative sample of secondary students, and subsequently identified three types of schools based on the

distributions of these student profiles within them. These results support interventions for overlapping patterns of substance use and mental health, and pursuing school interventions targeting school climate, belonging, and safety, particularly in rural areas. Collectively, this study identified: 1) adolescent substance use and mental health symptom profiles that can serve as ***targets*** for prevention and early intervention efforts; and 2) school settings as important ***contexts*** for these interventions, and suggests that improving school climate, belonging, and safety may represent key mechanisms of change in future prevention and interventions programs.

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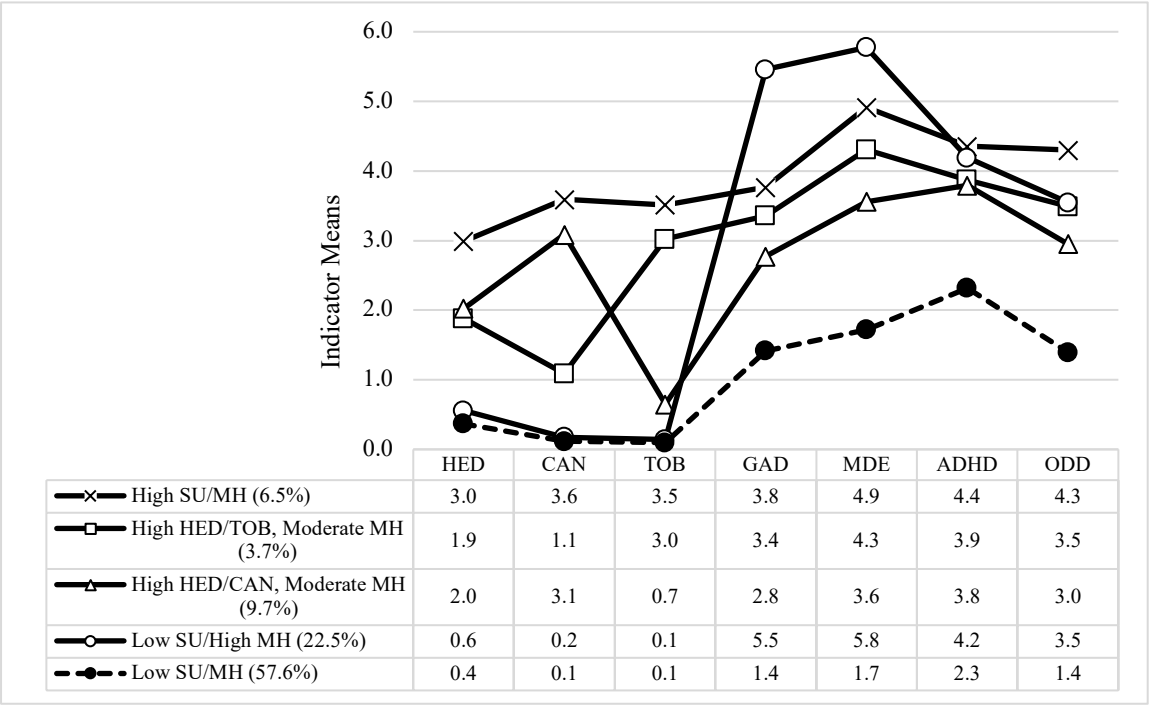
Figure 1

Student-Level 5 Profile Model (Single Level)

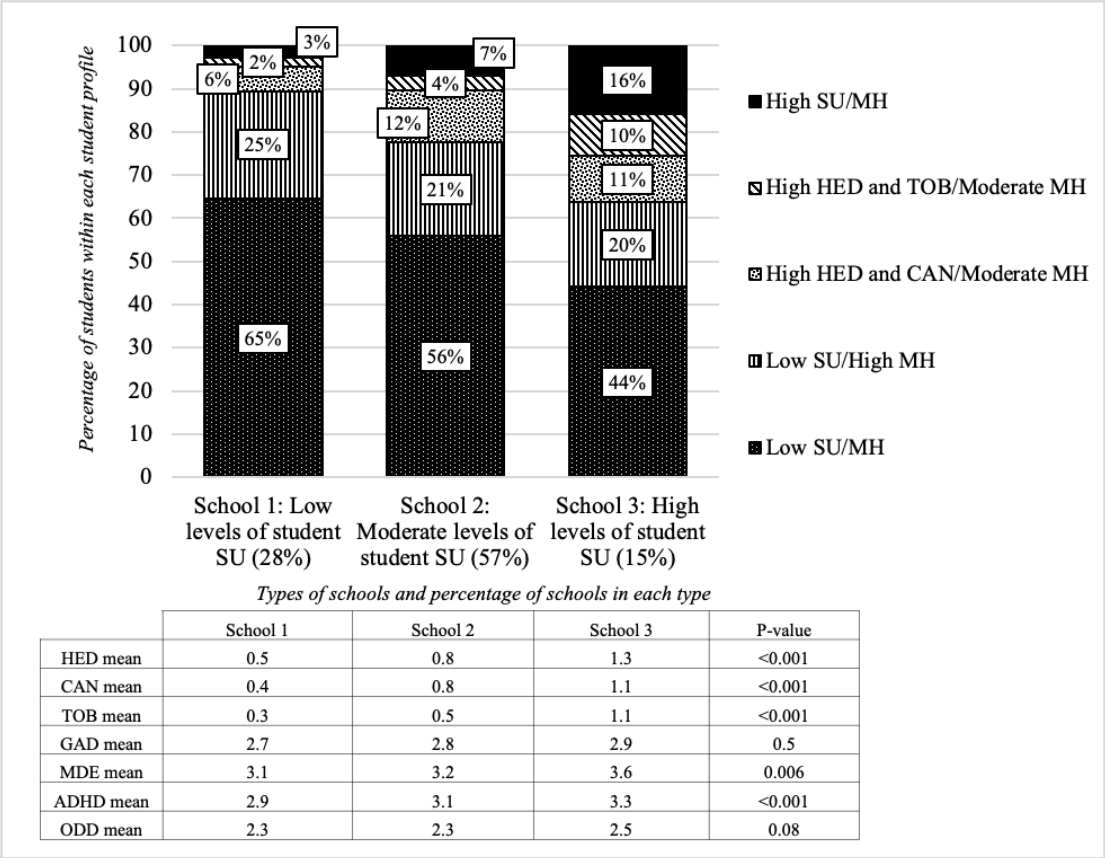


	HED	CAN	TOB	GAD	MDE	ADHD	ODD
High SU/MH (6.5%)	3.0	3.6	3.5	3.8	4.9	4.4	4.3
High HED/TOB, Moderate MH (3.7%)	1.9	1.1	3.0	3.4	4.3	3.9	3.5
High HED/CAN, Moderate MH (9.7%)	2.0	3.1	0.7	2.8	3.6	3.8	3.0
Low SU/High MH (22.5%)	0.6	0.2	0.1	5.5	5.8	4.2	3.5
Low SU/MH (57.6%)	0.4	0.1	0.1	1.4	1.7	2.3	1.4

Note: The mean (range; 40%/80% percentiles) for the indicators in the full sample for the LPA were: HED 0.8(0-5;1/2), CAN 0.7(0-4;0/1), TOB 0.5(0-4;0/1), GAD 2.7(0-8;1/5), MDE 3.1(0-10;2/5), ADHD 3.1(0-8;2/5), ODD 2.3(0-10;1/4).

Figure 2

School-Level 3-Class Model (Multilevel)



	School 1	School 2	School 3	P-value
HED mean	0.5	0.8	1.3	<0.001
CAN mean	0.4	0.8	1.1	<0.001
TOB mean	0.3	0.5	1.1	<0.001
GAD mean	2.7	2.8	2.9	0.5
MDE mean	3.1	3.2	3.6	0.006
ADHD mean	2.9	3.1	3.3	<0.001
ODD mean	2.3	2.3	2.5	0.08

Note: The within-school means(SD) of the student-level indicators in the full sample were: HED 0.8 (0.4), CAN 0.7(0.3), TOB 0.5(0.3), GAD 2.8(0.3), MDE 3.2(0.4), ADHD 3.1(0.3), ODD 2.3(0.3). P-values are based on univariable pooled ANOVA's.

Table 1

Student-Level Descriptives

	Total	Student Profiles				
		Low-SU/MH (57.6%)	Low-SU/High-MH (22.5%)	HEDCAN/ Moderate-MH (9.7%)	HEDTOB/ Moderate-MH (3.7%)	High-SU/MH (6.5%)
Female	51.4%	48.1%	65.1%	45.0%	48.8%	44.9%
Age	15.6 (1.5)	15.4 (1.4)	15.5 (1.4)	16.2 (1.3)	16.2 (1.4)	16.2 (1.6)
Assets	0.07 (1.0)	0.11 (0.9)	0.05 (1.0)	0.10 (1.0)	-0.05 (1.2)	-0.22 (1.4)
1st gen	16.3%	18.0%	17.5%	10.0%	12.1%	9.2%
2nd gen	28.3%	30.2%	29.2%	26.5%	18.1%	17.2%
2 parents	77.2%	81.5%	75.8%	68.9%	65.5%	63.7%
Parents PS	80.2%	83.6%	79.2%	75.1%	73.0%	65.0%
White	60.1%	58.3%	57.9%	66.2%	69.8%	68.6%
ESA	16.0%	18.9%	18.2%	6.1%	5.0%	5.1%
Black	6.2%	6.8%	4.8%	7.0%	4.6%	4.8%
Other	8.9%	8.3%	9.1%	10.7%	9.3%	11.0%
Multiracial	8.8%	7.7%	10.0%	10.1%	11.3%	10.5%
Climate	37.0 (7.9)	39.0 (7.1)	35.2 (7.4)	34.3 (7.1)	34.6 (7.8)	30.6 (10.1)
Belonging	7.7 (2.8)	8.4 (2.4)	6.7 (2.9)	7.1 (3.0)	6.7 (3.1)	6.0 (3.4)
Safety	11.3 (3.3)	11.7 (2.9)	10.3 (3.3)	11.7 (3.4)	10.7 (3.7)	10.3 (4.4)

Table 2

Multilevel Multinomial Regressions Predicting Student Profile Membership

Reference: Low SU/MH	Low-SU/High-MH	HEDCAN/ Moderate-MH	HEDTOB/ Moderate-MH	High-SU/MH
		School Climate Model		
Climate	0.93(0.92-0.93);<.0001[a]	0.92 (0.91-0.93);<.0001[a]	0.93 (0.91-0.94);<.0001[a]	0.88 (0.87-0.89);<.0001[a]
		School Belonging Model		
Belonging	0.79 (0.76-0.81);<.0001**	0.87 (0.84-0.9);<.0001**	0.87 (0.83-0.91);<.0001**	0.76 (0.73-0.79);<.0001**
Female*Belonging	0.99 (0.95-1.03);0.5664	0.9 (0.86-0.95);<.0001**	0.84 (0.78-0.9);<.0001**	0.93 (0.88-0.98);0.0064*
		School Safety Model		
Safety	0.86 (0.85-0.88);<.0001**	0.97 (0.95-0.99);0.002**	0.89 (0.86-0.91);<.0001**	0.86 (0.84-0.88);<.0001**
		Demographic Only Model		
Female	1.99 (1.81-2.19);<.0001**	0.87 (0.77-1);0.0445	1.04 (0.85-1.27);0.7026	0.88 (0.75-1.03);0.1051
Age	1.1 (1.06-1.14);<.0001**	1.56 (1.49-1.64);<.0001**	1.52 (1.41-1.63);<.0001**	1.45 (1.37-1.54);<.0001**
Family Assets	0.95 (0.9-1);0.0609	1.04 (0.97-1.12);0.2484	0.93 (0.84-1.04);0.1956	0.82 (0.76-0.89);<.0001**
1[st] gen	0.92 (0.78-1.08);0.3019	0.49 (0.38-0.64);<.0001**	0.78 (0.53-1.14);0.1987	0.45 (0.32-0.63);<.0001**
2[nd] gen	0.91 (0.8-1.04);0.1699	0.78 (0.66-0.94);0.0069*	0.63 (0.47-0.85);0.0025**	0.48 (0.38-0.61);<.0001**

2 parents	0.73 (0.65-0.82);<.0001**	0.52 (0.44-0.6);<.0001**	0.49 (0.39-0.62);<.0001**	0.5 (0.42-0.6);<.0001**
Parents PS	0.81 (0.71-0.91);0.0008**	0.63 (0.53-0.74);<.0001**	0.65 (0.51-0.84);0.0008**	0.43 (0.35-0.52);<.0001**
ESA	0.99 (0.84-1.18);0.9529	0.4 (0.3-0.54);<.0001**	0.3 (0.17-0.5);<.0001**	0.51 (0.34-0.78);0.0015**
Black	0.71 (0.56-0.9);0.0041**	1.14 (0.85-1.54);0.3769	0.64 (0.37-1.1);0.1047	0.96 (0.64-1.44);0.8369
Other	1.15 (0.96-1.38);0.134	1.43 (1.12-1.81);0.0035**	1.18 (0.81-1.74);0.3858	1.84 (1.39-2.45);<.0001**
Multiracial	1.31 (1.11-1.56);0.0016**	1.34 (1.06-1.7);0.0141	1.47 (1.04-2.07);0.0284	1.59 (1.21-2.08);0.0009**
School Size (increments of 200)	0.98 (0.94-1.02);0.2879	1.03 (0.96-1.11);0.446	0.91 (0.82-0.99);0.0388	0.93 (0.84-1.02);0.1041
Median Income (increments of $10,000)	1.02 (0.99-1.05);0.1343	1.05 (0.99-1.11);0.1153	0.93 (0.86-1);0.0662	1.04 (0.96-1.12);0.3314
Rural	0.98 (0.83-1.15);0.7895	1.01 (0.74-1.39);0.9288	1.41 (0.98-2.03);0.0605	1.5 (1.04-2.17);0.0305

**Significant p<0.005

*Near significant p<0.01

Note. Reported as pooled Odds Ratios (95% Confidence Interval); p-value. All models are adjusted for all socio-demographics. Only significant interaction effects were retained/reported in this table. Detailed results in S6.

Table 3

School-Level Descriptives

	Total	LOW (n=19)	MOD (n=39)	HIGH (n=10)	P-value[a]
		mean(SD) or n(%)			
School Size	980 (320)	1,140 (340)	1,000 (280)	640 (200)	0.0002
Median	\$86,000 (\$19,00)	\$91,000 (\$22,00)	\$88,000 (\$18,000)	\$73,000 (\$13,000)	0.04
Rural	10 (14.7%)	0	5 (12.8%)	5 (50%)	0.002
Climate (mean)	37.0 (1.6)	37.9 (0.9)	36.8 (1.5)	35.7 (1.9)	0.0007
Belonging (mean)	7.7 (0.6)	7.9 (0.5)	7.8 (0.6)	7.4 (0.4)	0.07
Safety (mean)	11.4 (0.7)	11.2 (0.8)	11.5 (0.7)	11.3 (0.6)	0.3

[a]P-values based on pooled ANOVA or Fisher's Exact tests.

Chapter 3: Supplementary Material

S1. Missingness

Prior to examining missingness, mean substitution was used within summative scale variables for those with <=30% missingness. There were 178 missing data patterns where about 80.8% were complete cases (See table 1.1 for detailed results). Specifically, 98.3% had complete mental health related data and 97.7% had complete substance use responses. Missingness was addressed using Full Information Maximum Likelihood (FIML) in cluster analyses. However, 17.3% of the sample had at least one demographic variable missing, with the highest missing on parental education (12.1%) followed by family assets (3.2%), family structure (2.3%), school size (1.7%), then race (1.5%). Notably, no other variables were missing >=1% with no missing for median family income.

To explore missingness, a series of logistic regressions were performed to evaluate predictors of missingness for any variable. Any missing was coded as a 1 and those with complete data were coded as 0. Missingness was significantly more likely among students who were male, younger, Black, 'other' racial minority, non-immigrants (compared to 2nd generation), and came from families with lower family assets, <2 parents, and parents without post-secondary education (other demographics not significant). Regarding main variables of interest, tobacco use, higher ADHD symptoms, higher ODD symptoms, and lower school climate, belongingness, and safety were related to missingness. Further, clustering in schools accounted for about 22% of the variability in missing. See Table 1.2 for detailed results.

Table 1.1 Proportion of Item Missingess.

Variables	**N (%)**
GAD	186 (1.55%)
MDE	166 (1.38%)
ADHD	143 (1.19%)
ODD	158 (1.32%)
HED	181 (1.51%)
CAN	217 (1.81%)
TOB	212 (1.77%)
Female	89 (0.74%)
Age	46 (0.38%)
Assets	387 (3.23%)
Immigrant Status	89 (0.74%)
Family Structure	273 (2.28%)
Parental Education	1456 (12.14%)
Race	185 (1.54%)
School Size	203 (1.69%)
Median Family Income	0
Rural/Urban Status	0*
School Climate	85 (0.71%)
School Belonging	81 (0.68%)
School Safety	63 (0.53%)
Any missing	**2307 (19.23%)**
Any SU missing	**275 (2.29%)**
Any MH missing	**202 (1.68%)**
Any DEMO missing	**2078 (17.33%)**

*1 missing (as postal code did not have a Statistics Canada designation) but imputed with the Probability Sampling Unit Designation

Table 1.2 Logistic Regressions Predicting Missingness for Multinomial Regression

Any substance or mental health missing	Missing OR (95% CI) p-value
Female	0.71 (0.64-0.78); <.0001
Age	0.86 (0.83-0.89); <.0001
Family Assets	0.8 (0.76-0.84); <.0001
1st gen	0.92 (0.79-1.08); 0.3255
2nd gen	0.82 (0.72-0.94); 0.0033
2 parents	0.65 (0.58-0.73); <.0001
Parents PS	0.7 (0.57-0.86); 0.0006
ESA	1.14 (0.95-1.36); 0.1589
Black	1.78 (1.47-2.16); <.0001
Other	1.35 (1.13-1.6); 0.0007
Multiracial	1.13 (0.93-1.36); 0.2127
School Size	1 (1-1); 0.0697
Median Family Income	1 (1-1); 0.1199
Rural	0.87 (0.47-1.61); 0.6598
Climate	0.99 (0.98-0.99); <.0001
Belonging	0.93 (0.92-0.95); <.0001
Safety	0.92 (0.91-0.94); <.0001
HED	1.03 (0.99-1.07); 0.1368
CAN	1.03 (0.99-1.07); 0.1993
TOB	1.1 (1.04-1.15); 0.0002
GAD	1 (0.98-1.02); 0.8378
MDE	1.02 (1-1.03); 0.1215
ADHD	1.08 (1.06-1.11); <.0001
ODD	1.1 (1.07-1.12); <.0001

S2. Detailed CFA Results

A psychometric evaluation of the SMHS OCHS:EBS item subset was tested for use across the full SMHS sample, including both elementary and secondary students (measurement invariance was confirmed). Note, the SMHS Conduct Disorder (CD) items have minimal overlap with the complete OCHS (i.e., less than 40% of SMHS CD items included in the OCHS, with all other subscales having >75% coverage) and the sum score was heavily skewed (4.4) and kurtotic (23.3). Thus, CD was not included.

Summary: The 4-factor mental health structure consistently produced the best model fit estimates when compared to the 2- and 3-factor models (See Table 2.1). The 4-factor model was the only CFA to surpass all *a priori* model thresholds including CFI>0.95 and RMSEA <0.06 and had the lowest WRMR. Using standardized effects coded loadings, all indicators loaded >0.6 on their respective pre-specified factors including GAD (0.85 to 0.92), MDE (0.71 to 0.88), ADHD (0.66 to 0.83), ODD (0.63 to 0.91) (See Table 2.2). Mental health latent variables were moderately-strongly positively correlated (r=0.5 to 0.8; stronger within than between domain correlations) and all AVE's were above 0.5, demonstrating convergent validity. Discriminant validity was established for 5/6 comparisons whereby the square root of AVE was larger than inter-factor correlations. Discriminant validity 'failures' occurred for MDE(GAD); however, this was expected due to high comorbidity of these disorders (See Table 2.3). Measurement invariance across gender and school level for each factor separately and the full 4-factor mental health measurement model was established (See Table 2.4).

Table 2.1 Model fit

Model	X^2 (df)	CFI	TLI	RMSEA (90% CI)	WRMR
2 Factor (INT, EXT)	36746 (134)	0.924	0.913	0.095 (0.094, 0.095)	12.78
3 Factor (INT, ODD, ADHD)	26113 (132)	0.946	0.938	0.080 (0.079, 0.081)	10.06
4 Factor (GAD, MDE, ADHD, ODD)	12755 (129)	0.974	0.969	0.057 (0.056, 0.057)	6.7
4 Factor (2-level)	13425 (276)	0.933	0.926	0.039	n/a

Table 2.2 Single Level Standardized Factor Loadings Using the Fixed Factor Method

Variable name	Question	Standardized loading	School ICC
Generalized Anxiety Disorder (GAD); Cronbach's alpha 0.882			
SD515	I am too fearful or anxious	0.905	2.1%
SD516	I find it hard to stop worrying	0.848	2.1%
SD517	I am anxious or on edge	**0.924**	2.3%
SD518	I am nervous or tense	0.876	1.3%
Major Depressive Episode (MDE); Cronbach's alpha 0.826			
SD510	I am unhappy, sad or depressed	0.851	1.8%
SD511	I am moody or irritable	0.820	3.0%
SD512	I get no pleasure from usual activities	0.722	1.9%
SD513	I feel overtired or lack energy	0.709	6.5%
SD514	I feel worthless or inferior	**0.876**	1.8%
ADHD; Cronbach's alpha 0.76			
SD51	I have trouble concentrating or paying attention	**0.834**	3.5%
SD52	I am easily distracted, have difficulty sticking to any activity	0.815	2.5%
SD53	I have trouble sitting still	0.658	2.9%
SD54	I fail to finish things I start	0.756	1.9%
Oppositional Defiant Disorder (ODD); Cronbach's alpha 0.802			
SD55	I lose my temper	0.790	2.0%
SD56	I argue a lot with adults	0.765	1.6%
SD57	I am defiant and talk back to people	0.763	2.1%
SD58	I am angry and resentful	**0.910**	1.7%
SD59	I get back at people	0.628	1.6% (factor loading negative at school level)

**bolded/strongest factor used as marker for invariance testing*

Table 2.3 Single Level Latent Correlations and Internal Convergent and Discriminant Validity

Domain	AVE(√AVE)	Interfactor Correlations			
		GAD	MDE	ADHD	ODD
GAD	0.790 (0.889)	1			
MDE	0.638 (0.798)	**0.833**	1		
ADHD	0.591 (0.769)	0.465	0.593	1	
ODD	0.635 (0.776)	0.477	0.668	0.630	1

Note: Although there was a discriminant validity failure between GAD and MDE, given differential associations between substance use and anxiety versus depression exist and the overall model fit pointed towards a 4-factor model, subscales were kept separate in subsequent models

Table 2.4 Measurement invariance for the 4-factor model across gender and school level.

Model	X^2 (df)	CFI	RMSEA (90% CI)	WRMR	Model Comp	Δ X^2	ΔCFI	ΔRMSEA	ΔWRMR	Decision
Gender (n=30362; fem=15805; male=14557)										
M1: Configural	12225 (258)	0.974	0.055 (0.054, 0.056)	6.5	none					
M2: Metric	14015 (272)	0.970	0.058 (0.057, 0.059)	6.9	M1	1891 (14) p<0.0001	-0.004	0.003	0.1	passed
M3: Scalar	13950 (286)	0.971	0.056 (0.055, 0.057)	7.1	M2	363 (14) p<0.0001	0.001	-0.002	0.2	passed
School Level (n=30536; elem=18665; sec=11871)										
M1: Configural	13000 (258)	0.973	0.057 (0.056, 0.058)	6.8	none					
M2: Metric	14084 (272)	0.971	0.058 (0.057, 0.058)	7.1	M1	1156 (14) p<0.0001	-0.002	0.001	0.3	passed
M3: Scalar	14375 (286)	0.970	0.057 (0.056, 0.058)	7.3	M2	590 (14) p<0.0001	-0.001	-0.001	0.2	passed

S3. Detailed List of Variables

3.1 Substance Use

All substance use items came from the National Longitudinal Survey of Children and Youth (1).

Frequency of Heavy Episodic Drinking (HED). Students were identified as having engaged in past month HED if they reported having 5 or more drinks of alcohol on the same occasion at any point within the past 4 weeks. Response options regarding frequency of HED over the previous month went from never (0) to 5 or more times (5).

Level of Cannabis Involvement (CAN). Cannabis was measured along a continuum of current involvement including: I have never tried marijuana (0); I have tried marijuana, but only once or twice (1; experimental); I used to smoke marijuana once a week, but have not done so in the last month (2; previous regular); I smoke sometimes, but not every week (3; occasional); and I usually smoke marijuana at least once a week (4; regular). Responses represent a stepped increase in use, except for previous regular use; therefore, a sensitivity analysis was performed removing and treating the previous regular option as missing and recoding the continuum from 0 to 3.

Tobacco Smoking (TOB). Smoking was measured along a continuum of current involvement including: I have never tried smoking, not even a few puffs (0); I have tried smoking, but only once or twice (1; experimental); I used to smoke every day, but have not smoked a cigarette in the last month (2; previous regular); I smoke sometimes, but not every day (3; occasional); and I usually smoke at least 1 cigarette a day (4; regular). Similar to cannabis, a sensitivity analysis was done where previous regular smoking was removed and treated as missing.

3.2 Mental Health Symptomatology

Mental health symptomatology was assessed using a modified subset of the 2014 OCHS-EBS (2) to measure frequency of symptoms over the preceding 6 months on a 3-point adjectival scale from no or not true (0) to often or very true (2). Scores are summed

where higher scores reflect more symptoms. The OCHS:EBS has undergone psychometric testing (2) demonstrating good internal consistency and test-retest reliability, and internal and external convergent and discriminant validity (2). This study included a modified subset of the OCHS:EBS scales for Generalized Anxiety Disorder (GAD; 4 items), Major Depressive Episode (MDE; 5 items), Oppositional Defiant Disorder (ODD; 5 items), and Attention Deficit Hyperactivity Disorder (ADHD; 4 items). We included MDE, GAD, ODD, and ADHD as separate indicators due to results from the Confirmatory Factor Analyses (CFA; See Supplementary Materials Section 2).

3.3 School Environment and Experience

School Climate. All school climate items came from the Delaware School Survey (3). Our school climate score is derived from summing the following subdomains: 1) *Student to Student Relationships ,* including 4 items asking if students in the school are friendly, care about each other, respectful, and get along; 2) *Teacher Student Relationships and Fairness ,* including 6 items asking if teachers treat students with respect, care about their students, listen to students when they have problems and whether adults treat students fairly, school rules are fair, and consequences of breaking rules are fair; 3) *Academic Pressure and Expectations ,* including 3 items asking whether teachers expect students to work hard, require students to work hard to get good grades, and expect students to do their best at all times; and 4) *Positive Behavioural Support and Social and Emotional Learning*, including 5 items specifically related to SEL strategies implemented within their schools (e.g., whether students are taught to feel responsible for how they act, understand how others think and feel, that they can control their own behaviour, solve conflicts with others, and that they should care about how others feel) and 2 items related to the PBS concept of clarity of rules (e.g., whether students know how they are expected to act and know what the rules are). All items are worded to reflect student perceptions of how the student body feels (i.e., “students feel…” vs. “I feel…”) and had response options scored from disagree a lot (1) to agree a lot (4).

School Belonging. This measure came from the Longitudinal Study of Adolescent Health Wave 1 In-School Survey (4). Participants rated 3-items items from strongly disagree (0) to strongly agree (4): 1) *I feel close to people at this school*, 2) *I feel like I belong at this school*, and 3) *I am happy to be at this school*.'

***School Safety*.** This measure includes 5 items adapted from the Chicago Public Schools Survey (5) asking about safety in the school hallways or stairwells, bathrooms or change rooms, classes as well as safety outside or around your school and on your way to school. Items were scored from not safe (0) to very safe (3).

S4. Detailed Student LPA Results

Detailed Methods

Substance use and mental health profiles were identified through LPA using Mplus (version 7). Random split halves were generated to perform sample cross-validation. All substance use and mental health indicators were treated continuously, and different variance-covariance matrices were estimated (8). Using the first split half, models were estimated for 1 profile up until k profiles when the model no longer converged with up to 500 random starts or when Bayesian Information Criterion (BIC) began to increase (8-10). The following class enumeration diagnostics were compared across models: convergence, BIC and Corrected Akaike's Information Criterion (CAIC), Approximate Weight of Evidence Criterion (AWE), Lo-Mendell-Rubin adjusted likelihood ratio test (LMR-LRT), bootstrapped likelihood ratio test (BLRT), and Relative Improvement (RI) (8). Models were also compared quantitatively and qualitatively based on clinical relevance of latent class separation, with quantitative class separation diagnostics including: posterior class probability (p), modal class assignment proportion (mcaP), average posterior probability (AvePP >0.9), odds of correct classification (OCC>5), and overall entropy (>0.9) for the k-profile model (8). Models containing only substance use indicators were also explored and compared with the best fitting combined models to visualize whether any meaningful independent substance use profiles were lost when combining mental health and substance use indicators into one model. Lastly, indicator specific class homogeneity and separation were also explored. Class homogeneity was examined by comparing within class indicator variance to the overall sample variance whereby ratios of >0.9 indicate low homogeneity and <0.6 indicate high homogeneity. Class indicator separation was examined using standardized mean differences (SMDs) whereby SMDs >2 indicated high separation and <0.85 reflect low separation. Using the second split half, the best model was replicated by fixing parameter estimates based on the first split half estimates (8). The same k-class models, but now with freed parameters, were also estimated and compared using the same diagnostics as above. Subsequently, all models examined within split half one were re-estimated in split

half two to see if all model estimates converged on the same final model selection. The best fitting model was re-estimated in the full sample. Measurement invariance across gender was then examined by: 1) stratifying the sample into males and females and re-estimating best fitting models, and 2) using multi-group functioning where groups were i) constrained to have equal parameter estimates versus ii) freed parameter estimates (8, 10). Models were compared based on BIC and CAIC, AWE. Models were also compared quantitatively and qualitatively based on clinical relevance of latent class separation.

Detailed Results

Table 4.1 Model enumeration fit statistics

Table 4.2 Class diagnostics

Table 4.3 Class homogeneity statistics

Table 4.4 Class separation statistics

Figure 4.1 Plots of model fit indices

Figure 4.2 Plots of competing models

Figure 4.3 Plots of models testing for gender invariance

In the first random split half, the 4 and 5 class invariant diagonal models fit best based on a combination of convergence, relative model fit indices (e.g., lowest BIC and significant LRTs), class diagnostics, and indicator specific homogeneity. The 4 and 5 profile models shared 4 qualitatively and quantitatively similar profiles – low across all, high across all, low substance but high internalizing, and high alcohol and cannabis and moderate mental health. The 5-profile model had a small additional distinct profile characterized by high alcohol and tobacco smoking and moderate mental health (3.6%). When examining substance use indicators alone (without mental health symptoms), a 4-profile model suggested high across all, low across all, high alcohol and cannabis only, and alcohol and tobacco smoking only. Thus, the 5-profile combined substance use and mental health model was retained as the additional profile (alcohol and tobacco smoking) was qualitatively distinct and important in the context of adolescent substance use

patterns. A 5-profile model was then fit to the second split half sample and both freed and fixed models yielded good model fit and similar class diagnostics. When re-estimating all models in split half 2, model fit, class homogeneity, and separation statistics were similar to split half 1. Thus, a 5-profile model was selected and re-estimated in the full sample to be used in subsequent school level profile estimation and regression modelling.

The final 5-profile substance use and mental health model in the full sample had an entropy of 0.92 identifying a low substance use and mental health profile (n=6,855, 57.6%, 'LOW'), a high substance use and mental health profile (n=772, 6.5%, 'HIGH'), a low substance use with high internalizing and moderate externalizing mental health symptom profile (n=2,672, 22.5%, 'HIGH MH'), a heavy episodic drinking and cannabis use with moderate mental health symptoms profile (n=1,160, 9.7%, 'HED/CAN'), and a heavy episodic drinking and tobacco use with moderate mental health symptoms profile (n=443, 3.7%, 'HED/TOB'). Average posterior probabilities were all >=0.9, OCCs all >5, and all mcaP were contained in the 90% CI for the model-estimated class proportion. Profile homogeneity was high for CAN, TOB, GAD, and MDE and moderate for HED, ADHD, and ODD. In general, there was high substance indicator separation between profiles in expected directions and mental health indicators were consistently moderately to highly separated between low and both high groups (i.e., HIGH and HIGH MH). See Figure 1 for a visual representation of the profiles. Sensitivity analyses revealed similar profiles and converged on a similar 5-profile solution.

Regarding gender invariance, although the free model had a lower BIC, CAIC, and AWE, both the fixed and freed models had high entropy (0.942 vs 0.943) and high posterior probabilities (all >0.88). Upon visual inspection (See Figure 4.3), males had slightly higher means of substance use whereas females had higher means of anxiety and depression scores – the differences in internalizing symptoms explained most of the difference in model fit as identified by a partially constrained model. Since the general qualitative pattern of profiles were similar, subsequent models and analyses were not stratified by gender to favour parsimony, interpretability, and chance of conversion in upper level.

Table 4.1 Model enumeration fit statistics (class-invariant diagonal)

k-classes	LL	Npar	BIC	CAIC	AWE	LMR-LRT p-value	BLRT p-value	Relative Improvement
Secondary Split Half 1 (n=5908)								
1	-82650.21	14	165421.99	165367.21	165374.21	n/a	n/a	n/a
2	-76641.62	22	153474.28	153388.204	153399.204	0.0000	0.0000	n/a
3	-74744.72	30	149749.97	149632.591	149647.591	0.0000	0.0000	0.315697
4	-72521.52	38	145373.04	145224.359	145243.359	0.0000	0.0000	0.370004
5	-71206.14	46	142811.75	142631.768	142654.768	0.0000	0.0000	0.218917
6	-70282.07	54	141033.49	140821.804	140848.804	0.0000	not replicated	0.153791
7	-69764.98	62	140068.38	139825.793	139856.793	0.6764	1.0000	0.086059
Secondary Split Half 2 (n=5994)								
1	-83977.969	14	168077.717	168022.826	168029.826	n/a	n/a	n/a
2	-77985.165	22	156161.695	156075.44	156086.44	0.0000	0.0000	n/a
3	-75761.599	30	151784.197	151666.53	151681.53	0.0000	0.0000	0.37103933
4	-74019.498	38	148369.54	148220.549	148239.549	0.0000	0.0000	0.29069881
5 - freed	-72619.174	46	145638.48	145458.123	145481.123	0.0000	0.0000	0.62976498
5 - fixed	-72683.593	4	145401.979	145386.2969	145388.297	0.0000	0.0000	n/a
6	-71665.746	54	143082.11	143589.489	143616.489	0.0000	0.0000	0.15909548
7	-71038.314	62	142615.936	142372.846	142403.846	0.0000	0.0000	0.10469757
8	Not replicated							
Secondary Full Sample (n=11902)								
5	-143857.68	46	288147.053	287948.847	287971.847	0.0000	0.0000	n/a
Gender Invariance Testing (n=11817)								
5 - fixed	-150738.34	51	301954.928	301735.384	301760.884			
5 - free	-149742.15	86	300290.753	299920.542	299963.542			
5 - partial	-149916.31	61	300404.631	300142.039	300172.539			
M - 1	-79932.609	14	159986.347	159931.824	159938.824			
M - 2	-74275.737	22	148741.82	148656.14	148667.14	0.0000	0.0000	
M - 3	-72390.526	30	145040.613	144923.778	144938.778	0.0000	0.0000	0.33326032
M - 4	-70373.891	38	141076.561	140928.569	140947.569	0.0000	0.0000	0.35649295

M - 5	-69057.728	46	138513.451	138334.303	138357.303	0.0000	0.0000	0.0000	0.23266622
M - 6	-68151.217	54	136769.646	136559.342	136586.342	0.0005	0.0006	0.0006	0.16024952
M - 7	-67441.396	62	135419.221	135177.76	135208.76	0.0046	0.0049	0.0049	0.12547942
M - 8	-66957.855	70	134298.355	134248.738	134283.738	0.6935	0.6941	0.6941	0.08547851
F - 1	-84272.621	14	168667.255	168612.232	168619.232				
F - 2	-77996.294	22	156184.323	156097.857	156108.857	0.0000	0.0000	0.0000	
F - 3	-75869.172	30	151999.8	151881.893	151896.893	0.0000	0.0000	0.0000	0.33891191
F - 4	-73777.55	38	147886.279	147736.929	147755.929	0.0000	0.0000	0.0000	0.33325574
F - 5	-72373.875	46	145148.651	144967.859	144990.859	0.0000	0.0000	0.0000	0.22364593
F - 6	not replicated								
Sensitivity Analysis (n=11902)									
1	-158614.63	14	317360.64	317300.317	317307.317				
2	-147627	22	295462.455	295365.66	295376.66	0.0000	0.0000		
3	-143845.14	30	287971.82	287842.555	287857.555	0.0000	0.0000	0.0000	0.34419203
4	-140985.01	38	282326.624	282162.888	282181.888	0.0000	0.0000	0.0000	0.26030506
5	-137977.07	46	276385.827	276187.621	276210.621	0.0008	0.0009	0.0009	0.27375655
6	not replicated								

Figures 4.1 Elbow plots of model fit indices

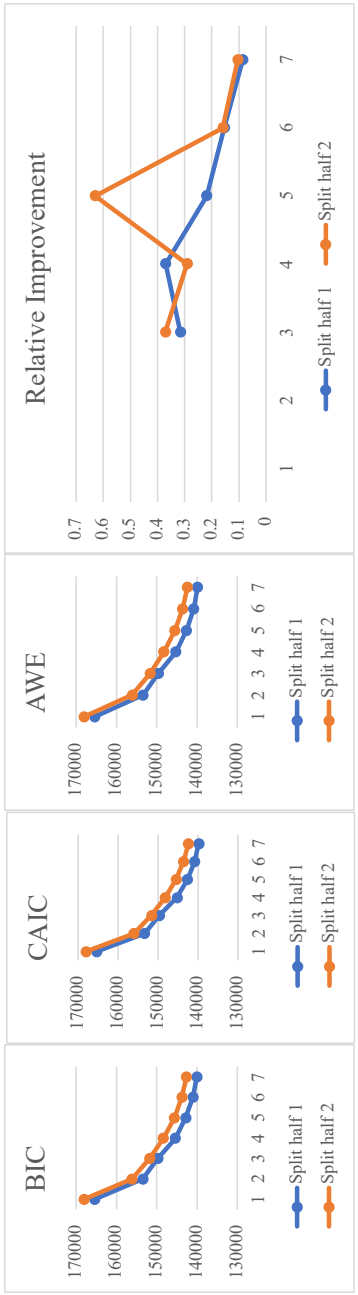


Table 4.2 Class diagnostics (class-invariant diagonal)

	n assigned	Posterior class probability (90% CI*)	mcaPK	$AvePP_K$	OCC_K	Entropy
Split half 1						
4 profile model						
1	3419	0.574 (0.564, 0.585)	0.579	0.952	14.7	
2	585	0.099 (0.093, 0.106)	0.099	0.966	257.3	
3	1381	0.237 (0.228, 0.246)	0.234	0.896	27.8	
4	523	0.090 (0.083, 0.096)	0.089	0.993	1443.0	0.902
5 profile model						
1	206	0.034 (0.031, 0.038)	0.035	0.964	751.4	
2	1353	0.233 (0.224, 0.242)	0.229	0.899	29.3	
3	3400	0.571 (0.560, 0.582)	0.575	0.952	14.9	
4	374	0.064 (0.059, 0.069)	0.063	0.987	1110.9	
5	575	0.098 (0.091, 0.104)	0.097	0.983	534.3	0.919
6 profile model						
1	3069	0.517 (0.506, 0.528)	0.519	0.95	17.7	
2	1091	0.189 (0.181, 0.198)	0.185	0.885	32.9	
3	723	0.120 (0.113, 0.127)	0.122	0.957	163.5	
4	453	0.077 (0.071, 0.083)	0.077	0.992	1486.6	
5	205	0.034 (0.030, 0.038)	0.035	0.975	1097.7	
6	367	0.063 (0.057, 0.068)	0.062	0.992	1858.7	0.926
Split half 2						
4 profile model						
1	569	0.096 (0.089, 0.102)	0.095	0.959	221.0	
2	1357	0.232 (0.223, 0.241)	0.226	0.894	28.0	
3	598	0.100 (0.094, 0.107)	0.100	0.983	518.2	
4	3470	0.572 (0.562, 0.583)	0.579	0.947	13.4	0.897
5 profile model (freed)						
1	236	0.038 (0.034, 0.042)	0.039	0.954	520.2	
2	584	0.097 (0.091, 0.104)	0.097	0.977	393.9	
3	3443	0.569 (0.558, 0.579_	0.574	0.949	14.1	
4	401	0.068 (0.062, 0.073)	0.067	0.984	845.7	
5	1330	0.228 (0.219, 0.237)	0.222	0.894	28.6	0.914
6 profile model						
1	716	0.116 (0.109, 0.123)	0.119	0.950	144.4	
2	1160	0.201 (0.192, 0.209)	0.194	0.888	31.6	
3	3035	0.502 (0.491, 0.513)	0.506	0.946	17.4	
4	464	0.078 (0.072, 0.083)	0.077	0.985	781.3	
5	224	0.037 (0.033, 0.041)	0.037	0.978	1143.2	
6	395	0.066 (0.061, 0.071)	0.066	0.986	995.1	0.922
5 profile model (fixed)						
1	233	0.038 (0.034, 0.043)	0.039	0.966	709.9	
2	1321	0.225 (0.216, 0.234)	0.220	0.893	28.7	
3	3460	0.572 (0.561, 0.582)	0.577	0.95	14.2	
4	396	0.067 (0.062, 0.072)	0.066	0.986	981.1	
5	584	0.098 (0.091, 0.104)	0.097	0.979	431.1	0.916
Full Sample						
5 profile model						
1	443	0.036 (0.032, 0.040)	0.037	0.957	590.2	
2	1160	0.098 (0.091, 0.104)	0.097	0.979	431.1	
3	6855	0.570 (0.559,0.581)	0.576	0.95	14.3	
4	772	0.066 (0.061, 0.071)	0.065	0.987	1075.5	0.916

5	2672	0.230 (0.221, 0.239)	0.225	0.897	29.1	
Gender fixed						
Male – 5 profile model						
1	842	0.074 (0.068, 0.079)	0.071	0.880	91.9	
2	221	0.018 (0.015, 0.021)	0.019	0.950	1026.7	
3	630	0.054 (0.049, 0.058)	0.053	0.980	866.9	
4	3608	0.302 (0.293, 0.312)	0.305	0.962	58.4	
5	421	0.036 (0.032, 0.040)	0.036	0.988	2184.6	0.942
Female – 5 profile model						
1	1860	0.160 (0.152, 0.167)	0.157	0.908	52.0	
2	216	0.018 (0.015, 0.021)	0.018	0.969	1691.9	
3	519	0.044 (0.039, 0.048)	0.044	0.978	969.6	
4	3157	0.265 (0.256, 0.274)	0.267	0.939	42.7	
5	343	0.029 (0.026, 0.033)	0.029	0.983	1917.7	
Gender Freed						
Male – 5 profile model						
1	222	0.019 (0.016, 0.021)	0.019	0.970	1706.0	
2	3400	0.285 (0.275, 0.295)	0.288	0.956	54.5	
3	1054	0.092 (0.086, 0.098)	0.089	0.891	80.7	
4	422	0.036 (0.032, 0.040)	0.036	0.986	1885.9	
5	624	0.053 (0.048, 0.058)	0.053	0.981	926.4	0.943
Female – 5 profile model						
1	3367	0.283 (0.274, 0.293)	0.285	0.947	45.2	
2	529	0.045 (0.040, 0.049)	0.045	0.981	1100.1	
3	1642	0.141 (0.133, 0.148)	0.139	0.903	56.9	
4	210	0.017 (0.014, 0.020)	0.018	0.950	1085.7	
5	347	0.030 (0.026, 0.034)	0.029	0.986	2283.5	
Gender partially constrained (all but internalizing)						
Male – 5 profile model						
1	3303	0.275 (0.266, 0.285)	0.280	0.948	48.0	
2	428	0.037 (0.033, 0.041)	0.036	0.984	1617.9	
3	218	0.018 (0.015, 0.021)	0.018	0.956	1176.0	
4	625	0.053 (0.048, 0.058)	0.053	0.982	974.6	
5	1148	0.101 (0.095, 0.108)	0.097	0.894	74.9	0.941
Female – 5 profile model						
1	3497	0.295 (0.285, 0.305)	0.296	0.953	48.5	
2	337	0.029 (0.025, 0.033)	0.029	0.988	2761.7	
3	219	0.018 (0.015, 0.021)	0.019	0.966	1531.8	
4	530	0.044 (0.040, 0.049)	0.045	0.977	912.7	
5	1512	0.129 (0.122, 0.137)	0.128	0.899	59.9	

*90% confidence interval based on calculations for proportions.

Table 4.3 Class homogeneity comparing within class variance for each indicator to the overall sample variance, where >0.9 indicates low homogeneity and <0.6 indicates high homogeneity.

	HED		**CAN**		**TOB**		**GAD**		**MDE**		**ADHD**		**ODD**	
	Var	**Ratio**	**Var**	**Ratio**	**Var**	**Ratio**	**Var**	**Ratio**	**Var**	**Ratio**	**Var**	**Ratio**	**Var**	**Ratio**
Random Split Half 1														
Comparison (Full)	*2.04*	*n/a*	*1.55*	*n/a*	*1.09*	*n/a*	*6.89*	*n/a*	*7.15*	*n/a*	*4.29*	*n/a*	*5.70*	*n/a*
4 LPA	1.41	0.69	0.33	0.21	0.16	0.14	4.00	0.58	4.06	0.57	3.50	0.82	4.54	0.80
5 LPA	1.41	0.69	0.19	0.12	0.15	0.14	4.03	0.59	4.09	0.57	3.50	0.82	4.52	0.79
6 LPA	1.35	0.66	0.08	0.05	0.14	0.13	4.49	0.65	4.44	0.62	3.52	0.82	4.58	0.80
Random Split Half 2														
Comparison (Full)	*2.03*	*n/a*	*1.54*	*n/a*	*0.50*	*n/a*	*6.79*	*n/a*	*7.06*	*n/a*	*4.44*	*n/a*	*5.71*	*n/a*
4 LPA	1.40	0.69	0.34	0.22	0.16	0.33	4.00	0.59	4.00	0.57	3.63	0.82	4.54	0.79
5 LPA	1.41	0.70	0.18	0.12	0.16	0.31	4.07	0.60	4.06	0.58	3.64	0.82	4.54	0.80
6 LPA	1.34	0.66	0.08	0.05	0.15	0.29	4.38	0.65	4.31	0.61	3.63	0.82	4.57	0.80
Full sample														
Comparison (Full)	*2.04*	*n/a*	*1.55*	*n/a*	*1.10*	*n/a*	*6.84*	*n/a*	*7.10*	*n/a*	*4.37*	*n/a*	*5.71*	*n/a*
5 LPA final	1.41	0.69	0.18	0.12	0.15	0.14	4.06	0.59	4.08	0.57	3.57	0.82	4.53	0.79

Figure 4.2 Plots of competing models and substance-use only models (random split half 1) where 1=HED, 2=CAN, 3=TOB, 4=GAD, 5=MDE, 6=ADHD, 7=ODD.

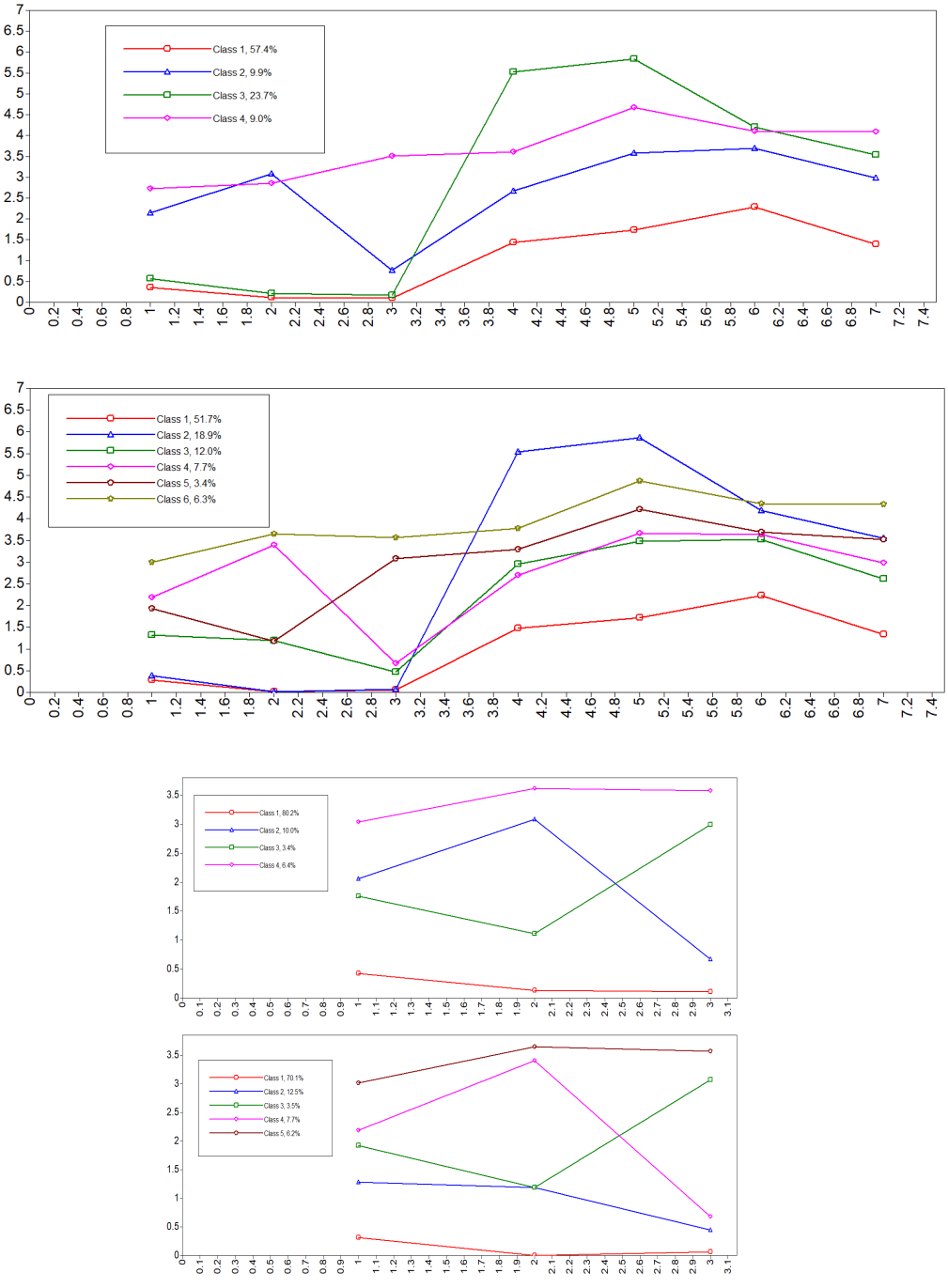
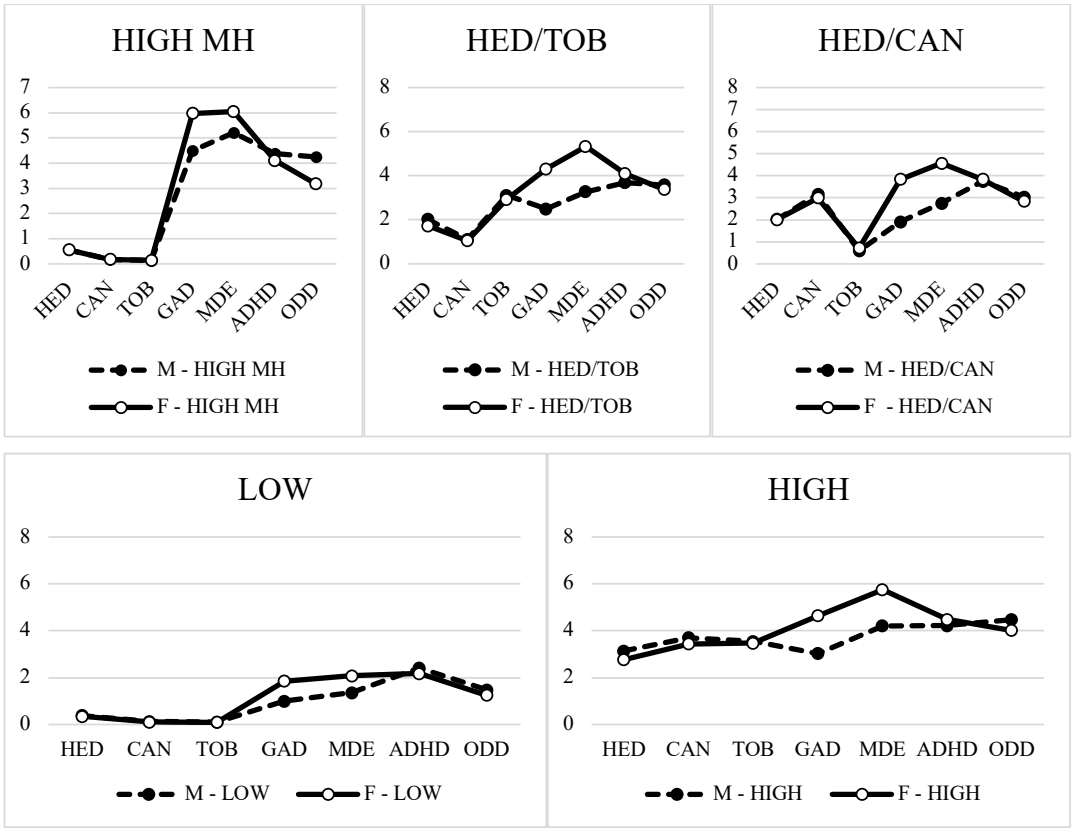


Table 4.4 Class separation, comparing standardized mean differences (via cohen's d) between classes where d<0.85 is a low degree of class separation and d>2 is high in the final 5-LPA.

HED Summary: • HED&TOB and HED&CAN are poorly separated • HIGH MH is poorly separated from LOW and both HIGH MH and LOW are highly separated from HIGH					
	HED/TOB	HED/CAN	Low	High	Low SU, High MH
HED/TOB (3.7%)	0	-0.12	1.27	-0.93	1.11
HED/CAN (9.7%)	0.12	0.00	1.39	-0.81	1.23
Low (57.6%)	-1.27	-1.39	0.00	-2.20	-0.16
High (6.5%)	0.93	0.81	2.20	0.00	2.05
Low SU, High MH (22.5%)	-1.11	-1.23	0.16	-2.05	0.00
CAN Summary: • Cannabis use is highly separated between the classes with the exception of the low separation between LOW and HIGH MH and moderate separation between HIGH and HED/CAN					
	HED/TOB	HED/CAN	Low	High	Low SU, High MH
HED/TOB (3.7%)	0	-4.66	2.27	-5.84	2.13
HED/CAN (9.7%)	4.66	0.00	6.92	-1.18	6.78
Low (57.6%)	-2.27	-6.92	0.00	-8.10	-0.14
High (6.5%)	5.84	1.18	8.10	0.00	7.96
Low SU, High MH (22.5%)	-2.13	-6.78	0.14	-7.96	0.00
TOB Summary: • Smoking is highly separated between the classes with the exception of the low separation between LOW and HIGH MH and moderate separation between LOW and HED/CAN and HIGH and HED/TOB					
	HED/TOB	HED/CAN	Low	High	Low SU, High MH
HED/TOB (3.7%)	0	6.10	7.52	-1.27	7.40
HED/CAN (9.7%)	-6.10	0.00	1.42	-7.36	1.31
Low (57.6%)	-7.52	-1.42	0.00	-8.79	-0.12
High (6.5%)	1.27	7.36	8.79	0.00	8.67
Low SU, High MH (22.5%)	-7.40	-1.31	0.12	-8.67	0.00
GAD Summary: • High separation between the LOW and HIGH MH group • Low separation between HED/TOB, HED/CAN, and HIGH as well as LOW and HED/CAN • Moderate separation between LOW with HED/TOB and HIGH as well as HIGH MH with HED/TOB and HED/CAN					
	HED/TOB	HED/CAN	Low	High	Low SU, High MH
HED/TOB (3.7%)	0	0.29	0.96	-0.20	-1.04
HED/CAN (9.7%)	-0.29	0.00	0.67	-0.49	-1.33
Low (57.6%)	-0.96	-0.67	0.00	-1.17	-2.01
High (6.5%)	0.20	0.49	1.17	0.00	-0.84

Low SU, High MH (22.5%)	1.04	1.33	2.01	0.84	0.00
MDE Summary: • High separation between the LOW and HIGH MH group • Low separation between HED/TOB, HED/CAN, and HIGH • Moderate separation between LOW all substance use profiles. And HIGH MH with HED/CAN					
	HED/TOB	HED/CAN	Low	High	Low SU, High MH
HED/TOB (3.7%)	0	0.37	1.28	-0.30	-0.73
HED/CAN (9.7%)	-0.37	0.00	0.91	-0.67	-1.10
Low (57.6%)	-1.28	-0.91	0.00	-1.58	-2.01
High (6.5%)	0.30	0.67	1.58	0.00	-0.43
Low SU, High MH (22.5%)	0.73	1.10	2.01	0.43	0.00
ADHD Summary: • Low separation between most classes – of note, high variance in the sample • Moderate separation between LOW with HIGH and HIGH MH					
	HED/TOB	HED/CAN	Low	High	Low SU, High MH
HED/TOB (3.7%)	0	0.04	0.82	-0.25	-0.17
HED/CAN (9.7%)	-0.04	0.00	0.78	-0.30	-0.21
Low (57.6%)	-0.82	-0.78	0.00	-1.08	-0.99
High (6.5%)	0.25	0.30	1.08	0.00	0.09
Low SU, High MH (22.5%)	0.17	0.21	0.99	-0.09	0.00
ODD Summary: • Low separation between most classes – of note, high variance in the sample • Moderate separation between LOW with HIGH and HIGH MH					
	HED/TOB	HED/CAN	Low	High	Low SU, High MH
HED/TOB (3.7%)	0	0.25	0.98	-0.38	-0.03
HED/CAN (9.7%)	-0.25	0.00	0.73	-0.63	-0.28
Low (57.6%)	-0.98	-0.73	0.00	-1.36	-1.01
High (6.5%)	0.38	0.63	1.36	0.00	0.36
Low SU, High MH (22.5%)	0.03	0.28	1.01	-0.36	0.00

Figure 4.3 Plots of models testing for gender invariance (5-profile model)



S5. Detailed school MLPA results

Models were compared based on AIC, BIC, LRT-LMR, BLRT, statistical convergence, and theoretical interpretation; BIC was the primary criterion for model selection. Student profiles were then regressed on school classes using multinomial regression to determine if there were statistically significant differences between student latent profile proportions for school latent classes. Once a final model was selected, the posterior probabilities and most likely class memberships for both student level profiles and school level classes from the MLPA were used for subsequent modeling.

Table 5.1 Model enumeration fit statistics (n=11902)

k-classes	LL	Npar	BIC	CAIC	AWE	Entropy
School random effects only	-143595	56	287715	287474	287502	0.916
school 1	-143858	46	288147	287949	287972	0.916
school 2	-143694	51	287866	287646	287672	0.903
school 3	-143633	56	287791	287550	287578	0.915
school 4*	-143603	61	287779	287516	287546	0.905

*had to fix parameters to estimate resulting in invalid/untrustworthy SEs due to model nonidentification

Table 5.2 Class diagnostics

	n assigned	Posterior class probability (90% CI*)	mcaPK	$AvePP_K$	OCC_K	Entropy
2-School class model						
School 1: LOWER SUBSTANCE SCHOOL						
HIGH MH	1382 (24.0%)	0.113 (0.106, 0.120)	0.116	0.875	54.980	
LOW	3661 (63.6%)	0.312 (0.302, 0.322)	0.308	0.929	28.901	
HED/TOB	126 (2.2%)	0.011 (0.009, 0.013)	0.011	0.923	1094.847	
HED/CAN	384 (6.7%)	0.034 (0.030, 0.038)	0.032	0.949	525.004	
HIGH	204 (3.5%)	0.018 (0.015, 0.021)	0.017	0.956	1171.423	0.903
School 2: HIGH SUBSTANCE USE SCHOOL						
HIGH MH	1300 (21.2%)	0.107 (0.101, 0.114)	0.109	0.850	47.199	
LOW	3185 (51.8%)	0.258 (0.249, 0.268)	0.268	0.904	27.030	
HED/TOB	317 (5.2%)	0.025 (0.022, 0.029)	0.027	0.931	515.842	
HED/CAN	773 (12.6%)	0.063 (0.058, 0.069)	0.065	0.938	223.725	
HIGH	570 (5.7%)	0.048 (0.043, 0.052)	0.048	0.959	466.458	
3-School class model						
School 1: LOWER SUBSTANCE SCHOOL						
LOW	2650 (64.5%)	0.226 (0.217, 0.235)	0.223	0.916	37.349	
HIGH	117 (2.8%)	0.011 (0.008, 0.013)	0.010	0.949	1722.070	
HED/TOB	82 (2.0%)	0.007 (0.005, 0.009)	0.007	0.887	1126.480	
HIGH MH	1023 (24.9%)	0.091 (0.084, 0.097)	0.086	0.86	61.652	
HED/CAN	236 (5.7%)	0.021 (0.018, 0.024)	0.020	0.923	569.907	0.915
School 2: HIGH SUBSTANCE USE SCHOOL						
LOW	593 (44.1%)	0.049 (0.045, 0.054)	0.050	0.929	253.023	
HIGH	215 (16.0%)	0.018 (0.015, 0.021)	0.018	0.964	1460.877	
HED/TOB	128 (9.5%)	0.010 (0.009, 0.013)	0.011	0.952	1878.093	
HIGH MH	264 (19.6%)	0.022 (0.019, 0.025)	0.022	0.873	304.308	
HED/CAN	146 (10.8%)	0.012 (0.010, 0.014)	0.012	0.947	1471.126	
School 3: MODERATE SUBSTANCE USE SCHOOL						
LOW	3611 (56.0%)	0.295 (0.285, 0.305)	0.303	0.908	23.598	
HIGH	445 (6.9%)	0.037 (0.033, 0.041)	0.037	0.951	501.197	
HED/TOB	232 (3.6%)	0.019 (0.016, 0.022)	0.019	0.913	546.230	
HIGH MH	1385 (21.5%)	0.117 (0.11, 0.0124)	0.116	0.854	43.953	
HED/CAN	775 (12.0%)	0.065 (0.060, 0.070)	0.065	0.954	298.275	

*90% confidence interval based on calculations for proportions.

Figure 5.1 Visual representation of competing model

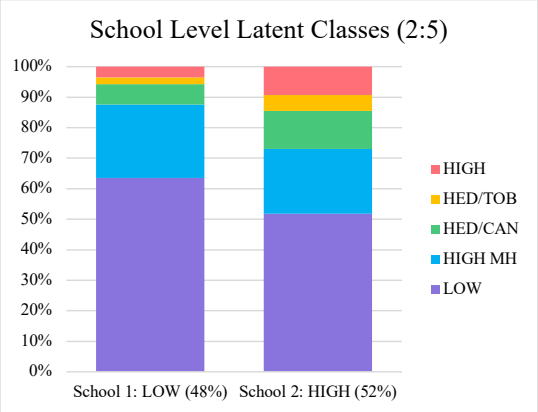


Table 5.3 Multilevel multinomial logistic regression using School Classes to predict individual Student Profile Membership, using the low school and low student profile as the references (n=11902). Results presented as ORs (95% CIs); p-values.

	LOW	HIGH MH	HED/CAN	HED/TOB	HIGH
Low-Use School	reference	reference	reference	reference	reference
Moderate-Use School	reference	1.15 (0.98 to 1.36); 0.0845	2.41 (2.07 to 2.81); <.0001	2.08 (1.61 to 2.68); <.0001	2.79 (2.26 to 3.44); <.0001
High-Use School	reference	0.99 (0.9 to 1.09); 0.894	2.76 (2.21 to 3.46); <.0001	6.98 (5.21 to 9.33); <.0001	8.21 (6.45 to 10.46); <.0001

Table 5.4 Multilevel linear regression using School Classes to predict individual student indicator mean, using the low school as the references (n=11835). Results presented as ORs (95% CIs); p-values.

	HED	CAN	TOB	GAD	MDE	ADHD	ODD
Low-Use School	reference						
Moderate-Use School	1.44 (1.27-1.64); <.0001	1.49 (1.36-1.62); <.0001	1.27 (1.19-1.36); <.0001	1.05 (0.89-1.25); 0.5538	1.03 (0.85-1.26); 0.7392	1.25 (1.1-1.41); 0.0006	0.96 (0.83-1.12); 0.6137
High-Use School	2.38 (1.98-2.87); <.0001	2.05 (1.81-2.32); <.0001	2.27 (2.06-2.5); <.0001	1.17 (0.91-1.51); 0.2217	1.61 (1.2-2.14); 0.0017*	1.55 (1.29-1.86); <.0001	1.33 (1.07-1.66); 0.0115

*when reference group changed to moderate, no significant difference in MDE between high and moderate schools

Table 5.5 Pooled aggregate descriptive statistics for student substance use and mental health symptomatology across school types across imputations All estimates at the school level.

	Total	LOW (n=19)	MOD (n=39)	HIGH (n=10)	P-value*
HED mean	0.8 (0.4)	0.5 (0.2)	0.8 (0.2)	1.3 (0.4)	<0.001
CAN mean	0.7 (0.3)	0.4 (0.1)	0.8 (0.2)	1.1 (0.2)	<0.001
TOB mean	0.5 (0.3)	0.3 (0.1)	0.5 (0.1)	1.1 (0.2)	<0.001
GAD mean	2.8 (0.3)	2.7 (0.3)	2.8 (0.4)	2.9 (0.3)	0.5
MDE mean	3.2 (0.4)	3.1 (0.3)	3.2 (0.4)	3.6 (0.5)	0.006
ADHD mean	3.1 (0.3)	2.9 (0.2)	3.1 (0.2)	3.3 (0.2)	<0.001
ODD mean	2.3 (0.3)	2.3 (0.2)	2.3 (0.3)	2.5 (0.4)	0.08

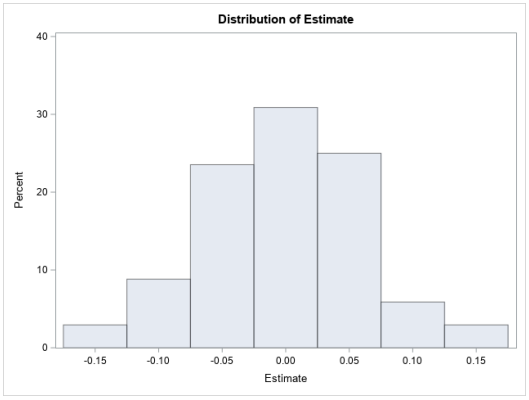
***** from univariable pooled ANOVA or Fisher's Exact

S6. Detailed Model Fit and Multinomial Regression Results

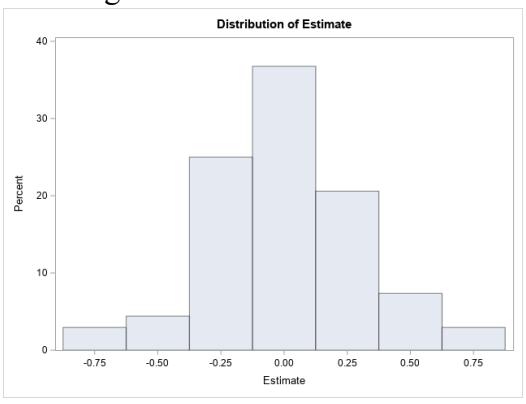
Model Fit: Given the parametric random effects MLPA fit well (with a slightly lower/better BIC and entropy than the nonparametric approach), a random intercept model was appropriate for controlling for school clustering in regression analysis of student level profiles. The appropriateness of this approach was confirmed by examining the distribution of random intercepts, ensuring a normal distribution across models (See figures below). To note, the variance inflation factor was <2 for all models.

Figure 6.1 Random intercept distributions (example, belonging fully adjusted model using imputation 1, reference group=LOW)

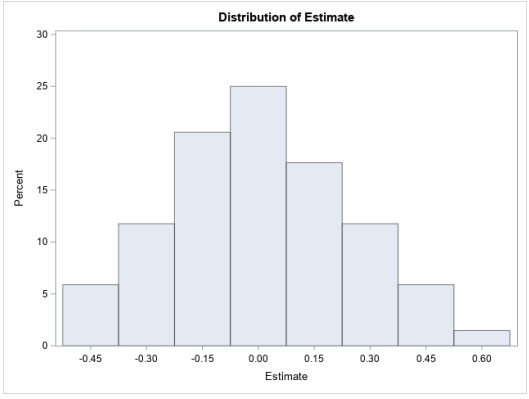
6.1.1 Low SU/High MH



6.1.2 High HED and CAN/Moderate MH



6.1.3 High HED and TOB/Moderate MH



6.1.4 High SU/MH

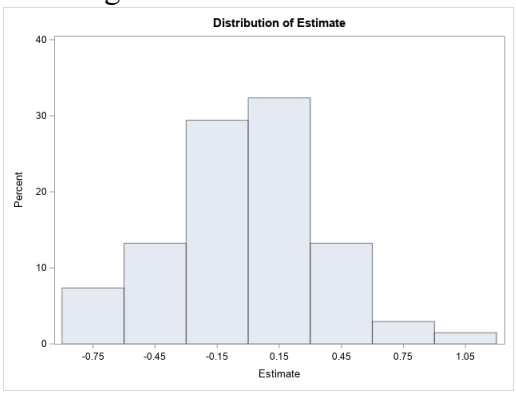
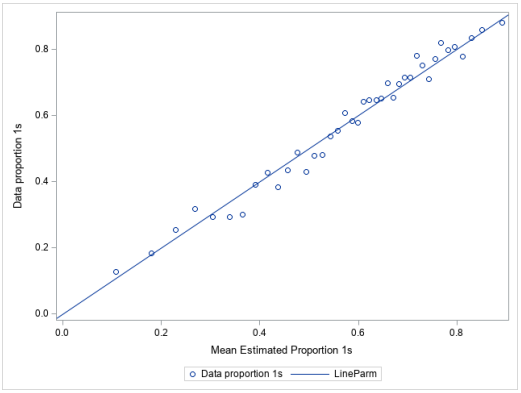
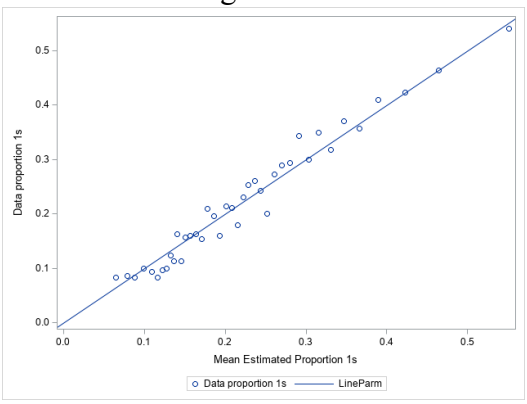


Figure 5.2 Predicted probabilities versus observed profile membership (example, belonging fully adjusted model using imputation 1, reference group = LOW). Note, observations ordered based on predicted probability and then grouped into 40 ~equal group to be able to visualize.

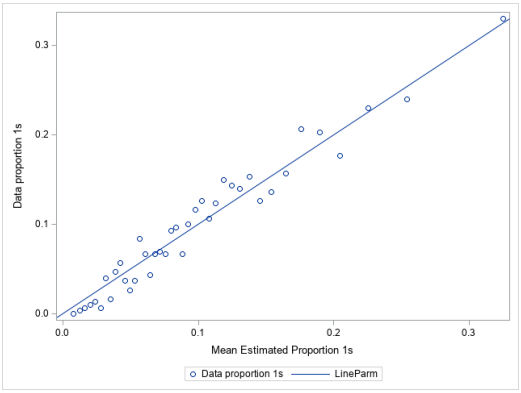
6.2.1 Low SU/MH



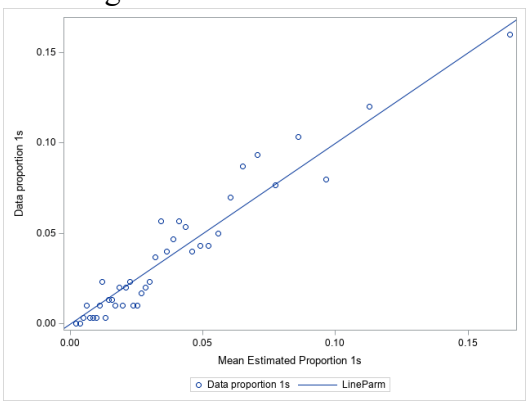
6.2.2 Low SU/High MH



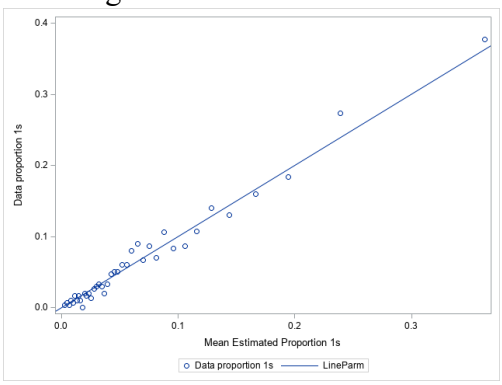
6.2.3 High HED and CAN/Moderate MH



6.2.4 High HED and TOB/Moderate MH



6.2.5 High SU/MH



Full Multinomial Regression Results.

Table 6.1A School Climate Model (reference=Low SU/MH). Reported as Odds Ratios (95% Confidence Interval); p-value.

Reference Group: Low SU/MH	Low SU/High MH	High HEDCAN/ Moderate MH	High HEDTOB/ Moderate MH	High SU/MH
Climate	0.93 (0.92-0.93); <.0001	0.92 (0.91-0.93); <.0001	0.93 (0.91-0.94); <.0001	0.88 (0.87-0.89); <.0001
Female	2.13 (1.93-2.34); <.0001	0.93 (0.81-1.06); 0.2791	1.1 (0.9-1.35); 0.3537	1.02 (0.86-1.2); 0.8536
Age	1.09 (1.05-1.13); <.0001	1.55 (1.48-1.63); <.0001	1.51 (1.4-1.63); <.0001	1.46 (1.37-1.55); <.0001
Family Assets	0.95 (0.91-1.01); 0.0861	1.04 (0.97-1.12); 0.2437	0.94 (0.84-1.04); 0.2021	0.86 (0.79-0.93); 0.0001
1st gen	0.99 (0.84-1.17); 0.9257	0.54 (0.41-0.69); <.0001	0.84 (0.57-1.24); 0.374	0.48 (0.34-0.67); <.0001
2nd gen	0.94 (0.82-1.07); 0.3548	0.81 (0.68-0.97); 0.0241	0.66 (0.49-0.88); 0.0054	0.52 (0.41-0.67); <.0001
2 parents	0.76 (0.68-0.86); <.0001	0.54 (0.46-0.63); <.0001	0.51 (0.41-0.64); <.0001	0.54 (0.45-0.65); <.0001
Parents PS	0.83 (0.73-0.95); 0.0059	0.65 (0.55-0.77); <.0001	0.67 (0.52-0.87); 0.0022	0.47 (0.38-0.57); <.0001
ESA	1.04 (0.87-1.23); 0.6719	0.41 (0.3-0.56); <.0001	0.31 (0.18-0.53); <.0001	0.54 (0.36-0.82); 0.0038
Black	0.62 (0.49-0.79); 0.0001	1 (0.74-1.35); 0.9984	0.58 (0.33-1); 0.0488	0.65 (0.42-1.02); 0.0589
Other	1.05 (0.88-1.27); 0.5728	1.31 (1.03-1.67); 0.0266	1.09 (0.74-1.6); 0.661	1.57 (1.17-2.1); 0.0029
Multiracial	1.26 (1.06-1.5); 0.0084	1.28 (1.01-1.63); 0.0414	1.41 (1-2); 0.0488	1.39 (1.05-1.85); 0.0231
School Size (increments of 200)	0.99 (0.95-1.02); 0.4949	1.04 (0.96-1.12); 0.3288	0.91 (0.83-1); 0.0584	0.94 (0.86-1.04); 0.2243
Median Income (increments of $10,000)	1.03 (1-1.06); 0.0628	1.05 (0.99-1.12); 0.1012	0.93 (0.86-1.01); 0.0906	1.04 (0.96-1.12); 0.3067
Rural	0.94 (0.8-1.1); 0.4522	0.97 (0.71-1.33); 0.8546	1.36 (0.94-1.96); 0.1025	1.42 (0.98-2.06); 0.0659

Table 6.1B School Climate Model (reference=Low SU/High MH). Reported as Odds Ratios (95% Confidence Interval); p-value.

Reference Group: Low SU/High MH	Low SU/ MH	High HEDCAN/ Moderate MH	High HEDTOB/ Moderate MH	High SU/MH
Climate	1.08 (1.07-1.09); <.0001	0.99 (0.98-1); 0.1448	1 (0.99-1.01); 0.9347	0.95 (0.94-0.96); <.0001
Female	0.47 (0.43-0.52); <.0001	0.44 (0.38-0.51); <.0001	0.52 (0.42-0.64); <.0001	0.48 (0.4-0.57); <.0001
Age	0.92 (0.89-0.95); <.0001	1.43 (1.35-1.51); <.0001	1.39 (1.29-1.5); <.0001	1.34 (1.26-1.42); <.0001
Family Assets	1.05 (0.99-1.1); 0.0829	1.09 (1.01-1.18); 0.0224	0.98 (0.88-1.09); 0.7229	0.9 (0.83-0.97); 0.009
1st gen	1 (0.85-1.19); 0.9688	0.54 (0.41-0.71); <.0001	0.84 (0.56-1.25); 0.3874	0.48 (0.33-0.68); <.0001
2nd gen	1.06 (0.93-1.21); 0.3912	0.86 (0.71-1.05); 0.1427	0.7 (0.51-0.95); 0.0212	0.56 (0.43-0.72); <.0001
2 parents	1.31 (1.16-1.48); <.0001	0.71 (0.6-0.84); <.0001	0.67 (0.53-0.85); 0.0011	0.71 (0.58-0.86); 0.0005
Parents PS	1.2 (1.06-1.37); 0.0049	0.78 (0.65-0.94); 0.0078	0.81 (0.62-1.05); 0.1112	0.56 (0.46-0.69); <.0001
ESA	0.94 (0.79-1.12); 0.4909	0.39 (0.28-0.54); <.0001	0.29 (0.17-0.5); <.0001	0.51 (0.33-0.78); 0.0019
Black	1.59 (1.25-2.02); 0.0002	1.59 (1.13-2.24); 0.0081	0.92 (0.52-1.63); 0.7658	1.04 (0.65-1.65); 0.8688
Other	0.94 (0.78-1.14); 0.5441	1.24 (0.95-1.62); 0.11	1.03 (0.69-1.53); 0.8952	1.48 (1.08-2.02); 0.0141
Multiracial	0.79 (0.66-0.94); 0.008	1.01 (0.79-1.31); 0.9182	1.12 (0.78-1.59); 0.5439	1.1 (0.82-1.47); 0.5358
School Size (increments of 200)	1.02 (0.98-1.05); 0.3985	1.05 (0.98-1.14); 0.1826	0.93 (0.84-1.02); 0.1152	0.96 (0.87-1.05); 0.3722
Median Income (increments of $10,000)	0.97 (0.94-1); 0.0612	1.02 (0.96-1.09); 0.4948	0.91 (0.84-0.98); 0.0152	1.01 (0.94-1.09); 0.7815
Rural	1.06 (0.9-1.25); 0.5016	1.03 (0.74-1.42); 0.8749	1.43 (0.99-2.07); 0.0561	1.5 (1.03-2.18); 0.0344

Table 6.1C School Climate Gender Interaction Model. Reported as Odds Ratios (95% Confidence Interval); p-value.

Reference: Low	Low SU/High MH	HEDCAN/Moderate MH	HEDTOB/Moderate MH	High SU/MH
Climate	0.93 (0.92-0.94); <.0001	0.92 (0.91-0.93); <.0001	0.94 (0.92-0.96); <.0001	0.88 (0.87-0.89); <.0001
Female	2.03 (1.23-3.34); 0.0053	1.02 (0.52-2); 0.9507	3.22 (1.23-8.43); 0.0173	1.61 (0.78-3.29); 0.1956
Climate*Female	1 (0.99-1.02); 0.824	1 (0.98-1.02); 0.7962	0.97 (0.94-1); 0.025	0.99 (0.97-1.01); 0.1998
Age	1.09 (1.05-1.13); <.0001	1.55 (1.48-1.63); <.0001	1.51 (1.4-1.63); <.0001	1.46 (1.37-1.54); <.0001
Family Assets	0.95 (0.91-1.01); 0.086	1.04 (0.97-1.12); 0.2461	0.94 (0.84-1.04); 0.2037	0.86 (0.79-0.93); 0.0001
1st gen	0.99 (0.84-1.17); 0.9341	0.53 (0.41-0.69); <.0001	0.84 (0.57-1.24); 0.3745	0.48 (0.34-0.67); <.0001
2nd gen	0.94 (0.82-1.07); 0.3578	0.81 (0.68-0.97); 0.024	0.65 (0.49-0.88); 0.0052	0.52 (0.41-0.67); <.0001
2 parents	0.76 (0.68-0.86); <.0001	0.54 (0.46-0.64); <.0001	0.51 (0.41-0.64); <.0001	0.54 (0.45-0.65); <.0001
Parents PS	0.83 (0.73-0.95); 0.0058	0.65 (0.55-0.77); <.0001	0.67 (0.52-0.87); 0.0022	0.47 (0.38-0.57); <.0001
ESA	1.04 (0.87-1.23); 0.6815	0.41 (0.3-0.56); <.0001	0.31 (0.19-0.53); <.0001	0.55 (0.36-0.83); 0.0044
Black	0.62 (0.49-0.79); 0.0001	1 (0.74-1.35); 0.9984	0.57 (0.33-0.99); 0.0468	0.65 (0.42-1.02); 0.0591
Other	1.05 (0.88-1.27); 0.5738	1.31 (1.03-1.67); 0.0265	1.09 (0.74-1.6); 0.6643	1.56 (1.17-2.1); 0.0029
Multiracial	1.26 (1.06-1.5); 0.0085	1.28 (1.01-1.63); 0.0422	1.42 (1.01-2.01); 0.0454	1.39 (1.05-1.85); 0.0224
School Size	0.99 (0.95-1.02); 0.4941	1.04 (0.96-1.12); 0.3292	0.91 (0.83-1); 0.0576	0.94 (0.86-1.04); 0.2222
Median Income	1.03 (1-1.06); 0.0628	1.05 (0.99-1.12); 0.1005	0.94 (0.87-1.01); 0.0952	1.04 (0.96-1.12); 0.3041
Rural	0.94 (0.8-1.1); 0.4469	0.97 (0.71-1.33); 0.8541	1.37 (0.95-1.98); 0.0947	1.42 (0.98-2.07); 0.0636

Table 6.2A School Belonging Model (reference=Low SU/MH). Reported as Odds Ratios (95% Confidence Interval); p-value.

Reference Group: Low SU/MH	Low SU/High MH	High HEDCAN/ Moderate MH	High HEDTOB/ Moderate MH	High SU/MH
Belonging	0.78 (0.77-0.8); <.0001	0.83 (0.81-0.85); <.0001	0.8 (0.77-0.82); <.0001	0.74 (0.72-0.76); <.0001
Female	1.84 (1.67-2.03); <.0001	0.81 (0.71-0.92); 0.0016	0.94 (0.77-1.16); 0.5806	0.76 (0.64-0.89); 0.0008
Age	1.09 (1.05-1.12); <.0001	1.55 (1.47-1.62); <.0001	1.5 (1.39-1.61); <.0001	1.43 (1.34-1.51); <.0001
Family Assets	0.98 (0.93-1.03); 0.4126	1.07 (0.99-1.15); 0.0863	0.96 (0.87-1.06); 0.4467	0.86 (0.8-0.93); 0.0002
1st gen	0.87 (0.73-1.03); 0.1031	0.47 (0.36-0.61); <.0001	0.72 (0.49-1.07); 0.1038	0.41 (0.3-0.58); <.0001
2nd gen	0.92 (0.8-1.05); 0.2032	0.79 (0.66-0.94); 0.0083	0.64 (0.47-0.86); 0.0031	0.5 (0.39-0.63); <.0001
2 parents	0.82 (0.72-0.92); 0.0011	0.56 (0.48-0.65); <.0001	0.54 (0.43-0.68); <.0001	0.56 (0.47-0.68); <.0001
Parents PS	0.88 (0.77-1); 0.045	0.67 (0.56-0.79); <.0001	0.7 (0.54-0.9); 0.006	0.47 (0.39-0.57); <.0001
ESA	1.02 (0.85-1.21); 0.8504	0.4 (0.29-0.54); <.0001	0.3 (0.18-0.51); <.0001	0.53 (0.35-0.8); 0.0024
Black	0.59 (0.46-0.76); <.0001	1.02 (0.76-1.38); 0.8901	0.56 (0.32-0.97); 0.0378	0.78 (0.51-1.18); 0.2411
Other	1.02 (0.85-1.23); 0.8359	1.32 (1.04-1.68); 0.0233	1.08 (0.73-1.58); 0.7048	1.63 (1.22-2.17); 0.001
Multiracial	1.24 (1.04-1.48); 0.0164	1.3 (1.02-1.65); 0.032	1.41 (0.99-1.99); 0.0534	1.48 (1.12-1.96); 0.0065
School Size (increments of 200)	1.01 (0.97-1.04); 0.7968	1.05 (0.97-1.13); 0.2431	0.93 (0.84-1.02); 0.1189	0.95 (0.86-1.05); 0.3073
Median Income (increments of $10,000)	1.02 (0.99-1.05); 0.3023	1.05 (0.98-1.11); 0.151	0.93 (0.86-1); 0.0578	1.03 (0.95-1.12); 0.4177
Rural	0.95 (0.8-1.13); 0.5626	0.99 (0.72-1.37); 0.9632	1.38 (0.95-2); 0.0907	1.46 (0.99-2.17); 0.058

Table 6.2B School Belonging Model (reference=Low SU/High MH). Reported as Odds Ratios (95% Confidence Interval); p-value.

Reference Group: Low SU/High MH	Low SU/ MH	High HEDCAN/ Moderate MH	High HEDTOB/ Moderate MH	High SU/MH
Belonging	1.28 (1.25-1.3); <.0001	1.06 (1.03-1.08); <.0001	1.01 (0.98-1.05); 0.4299	0.94 (0.91-0.96); <.0001
Female	0.54 (0.49-0.6); <.0001	0.44 (0.38-0.51); <.0001	0.51 (0.42-0.63); <.0001	0.41 (0.35-0.49); <.0001
Age	0.93 (0.89-0.96); <.0001	1.43 (1.36-1.51); <.0001	1.39 (1.28-1.5); <.0001	1.32 (1.24-1.4); <.0001
Family Assets	1.02 (0.97-1.08); 0.3947	1.09 (1.01-1.18); 0.0286	0.98 (0.89-1.09); 0.7709	0.88 (0.82-0.96); 0.003
1st gen	1.15 (0.97-1.36); 0.1164	0.54 (0.41-0.71); <.0001	0.83 (0.55-1.23); 0.3495	0.47 (0.33-0.67); <.0001
2nd gen	1.08 (0.95-1.24); 0.2353	0.85 (0.7-1.04); 0.1173	0.69 (0.51-0.94); 0.0194	0.54 (0.42-0.69); <.0001
2 parents	1.22 (1.08-1.38); 0.0012	0.68 (0.58-0.81); <.0001	0.66 (0.52-0.84); 0.0007	0.69 (0.57-0.83); 0.0001
Parents PS	1.15 (1.01-1.31); 0.036	0.76 (0.64-0.91); 0.0033	0.8 (0.61-1.04); 0.0991	0.54 (0.44-0.66); <.0001
ESA	0.95 (0.8-1.13); 0.5834	0.38 (0.27-0.53); <.0001	0.29 (0.17-0.49); <.0001	0.5 (0.33-0.76); 0.0013
Black	1.64 (1.28-2.1); <.0001	1.7 (1.2-2.39); 0.0026	0.93 (0.52-1.66); 0.8116	1.29 (0.82-2.01); 0.2655
Other	0.97 (0.8-1.17); 0.7534	1.29 (0.99-1.68); 0.0615	1.05 (0.71-1.56); 0.8082	1.58 (1.16-2.15); 0.0036
Multiracial	0.8 (0.67-0.96); 0.0146	1.04 (0.81-1.34); 0.7571	1.13 (0.79-1.61); 0.5027	1.18 (0.88-1.58); 0.2576
School Size (increments of 200)	1 (0.96-1.04); 0.9606	1.04 (0.97-1.13); 0.2668	0.92 (0.84-1.02); 0.1009	0.95 (0.86-1.05); 0.2885
Median Income (increments of $10,000)	0.98 (0.95-1.01); 0.2627	1.03 (0.97-1.09); 0.3982	0.91 (0.84-0.98); 0.0174	1.01 (0.94-1.1); 0.72
Rural	1.05 (0.88-1.25); 0.5973	1.03 (0.75-1.43); 0.8393	1.43 (0.99-2.07); 0.0536	1.53 (1.04-2.25); 0.0323

Table 6.2C School Belonging Model Gender Interaction Model. Reported as Odds Ratios (95% Confidence Interval); p-value.

Reference: Low SU/MH	Low SU/High MH	HEDCAN/Moderate MH	HEDTOB/Moderate MH	High SU/MH
Belonging	0.79 (0.76-0.81); <.0001	0.87 (0.84-0.9); <.0001	0.87 (0.83-0.91); <.0001	0.76 (0.73-0.79); <.0001
Female	2.07 (1.56-2.76); <.0001	1.75 (1.19-2.58); 0.0046	3.19 (1.89-5.38); <.0001	1.32 (0.89-1.96); 0.1743
Belonging*Female	0.99 (0.95-1.03); 0.5664	0.9 (0.86-0.95); <.0001	0.84 (0.78-0.9); <.0001	0.93 (0.88-0.98); 0.0064
Age	1.09 (1.05-1.12); <.0001	1.54 (1.47-1.62); <.0001	1.5 (1.39-1.61); <.0001	1.42 (1.34-1.51); <.0001
Family Assets	0.98 (0.93-1.03); 0.4095	1.06 (0.99-1.14); 0.1011	0.96 (0.87-1.06); 0.4238	0.86 (0.8-0.93); 0.0002
1st gen	0.87 (0.73-1.03); 0.098	0.47 (0.36-0.61); <.0001	0.73 (0.5-1.08); 0.1191	0.42 (0.3-0.58); <.0001
2nd gen	0.92 (0.8-1.05); 0.193	0.79 (0.66-0.94); 0.0083	0.64 (0.47-0.86); 0.0033	0.5 (0.39-0.63); <.0001
2 parents	0.82 (0.72-0.92); 0.0012	0.56 (0.48-0.65); <.0001	0.54 (0.43-0.68); <.0001	0.56 (0.47-0.68); <.0001
Parents PS	0.87 (0.77-1); 0.044	0.67 (0.57-0.79); <.0001	0.7 (0.54-0.9); 0.0064	0.47 (0.39-0.58); <.0001
ESA	1.02 (0.85-1.21); 0.8455	0.4 (0.3-0.55); <.0001	0.31 (0.18-0.52); <.0001	0.53 (0.35-0.8); 0.0028
Black	0.59 (0.46-0.76); <.0001	1.02 (0.76-1.38); 0.8921	0.56 (0.32-0.96); 0.0365	0.78 (0.51-1.18); 0.2391
Other	1.02 (0.85-1.23); 0.8336	1.32 (1.04-1.68); 0.0237	1.08 (0.73-1.59); 0.6977	1.62 (1.22-2.17); 0.0011
Multiracial	1.24 (1.04-1.48); 0.0183	1.3 (1.02-1.65); 0.0311	1.42 (1.01-2.02); 0.0462	1.48 (1.12-1.96); 0.0063
School Size	1.01 (0.97-1.04); 0.7965	1.05 (0.97-1.13); 0.2308	0.93 (0.84-1.02); 0.1272	0.95 (0.86-1.05); 0.306
Median Income	1.02 (0.99-1.05); 0.3025	1.04 (0.98-1.11); 0.1649	0.92 (0.85-1); 0.053	1.03 (0.95-1.12); 0.4283
Rural	0.95 (0.8-1.12); 0.5481	0.99 (0.72-1.37); 0.9709	1.39 (0.95-2.01); 0.0871	1.47 (0.99-2.17); 0.0572

Table 6.2D School Belonging Model <u>Female</u> Model (reference=Low SU/MH). Reported as Odds Ratios (95% Confidence Interval); p-value.

Reference Group: Low SU/MH	Low SU/High MH	High HEDCAN/ Moderate MH	High HEDTOB/ Moderate MH	High SU/MH
Belonging	0.77 (0.76-0.79); <.0001	0.78 (0.76-0.81); <.0001	0.73 (0.7-0.77); <.0001	0.71 (0.68-0.74); <.0001
Age	1.05 (1.01-1.1); 0.0294	1.54 (1.43-1.66); <.0001	1.36 (1.22-1.52); <.0001	1.27 (1.16-1.39); <.0001
Family Assets	1 (0.93-1.07); 0.9288	1.03 (0.92-1.16); 0.5633	0.93 (0.79-1.08); 0.3225	0.78 (0.69-0.89); 0.0001
1st gen	0.89 (0.71-1.12); 0.3238	0.47 (0.31-0.7); 0.0002	0.84 (0.48-1.47); 0.5403	0.52 (0.31-0.87); 0.0118
2nd gen	0.98 (0.82-1.16); 0.8113	0.84 (0.65-1.1); 0.2075	0.71 (0.48-1.07); 0.0998	0.51 (0.36-0.73); 0.0002
2 parents	0.8 (0.68-0.93); 0.0051	0.54 (0.43-0.68); <.0001	0.69 (0.49-0.97); 0.0304	0.51 (0.39-0.67); <.0001
Parents PS	0.93 (0.79-1.1); 0.4034	0.77 (0.6-0.98); 0.0321	0.53 (0.38-0.74); 0.0002	0.47 (0.36-0.62); <.0001
ESA	0.86 (0.68-1.08); 0.1992	0.3 (0.18-0.48); <.0001	0.19 (0.08-0.44); 0.0001	0.13 (0.05-0.33); <.0001
Black	0.47 (0.34-0.65); <.0001	0.69 (0.43-1.11); 0.1303	0.54 (0.26-1.1); 0.09	0.38 (0.19-0.76); 0.0065
Other	0.89 (0.69-1.15); 0.3844	1.26 (0.88-1.81); 0.2145	0.8 (0.44-1.46); 0.4653	1.33 (0.85-2.06); 0.2093
Multiracial	1.26 (1-1.57); 0.0464	1.2 (0.85-1.69); 0.3009	1.43 (0.89-2.29); 0.1411	1.48 (0.99-2.19); 0.0545
School Size (increments of 200)	1 (0.95-1.05); 0.878	1.07 (0.97-1.16); 0.1656	0.93 (0.82-1.06); 0.2697	0.97 (0.86-1.09); 0.6204
Median Income (increments of $10,000)	1.01 (0.97-1.05); 0.5535	1.02 (0.95-1.1); 0.6153	0.94 (0.85-1.05); 0.2781	1.03 (0.94-1.14); 0.5385
Rural	0.91 (0.73-1.13); 0.3825	0.98 (0.67-1.43); 0.9121	0.92 (0.55-1.52); 0.7394	1.17 (0.73-1.88); 0.5102

Table 6.2E School Belonging Model Male Model (reference=Low SU/MH). Reported as Odds Ratios (95% Confidence Interval); p-value.

Reference Group: Low SU/MH	Low SU/High MH	High HEDCAN/ Moderate MH	High HEDTOB/ Moderate MH	High SU/MH
Belonging	0.79 (0.77-0.81); <.0001	0.87 (0.84-0.9); <.0001	0.87 (0.83-0.92); <.0001	0.76 (0.73-0.79); <.0001
Age	1.12 (1.06-1.18); <.0001	1.56 (1.46-1.67); <.0001	1.63 (1.47-1.8); <.0001	1.59 (1.46-1.72); <.0001
Family Assets	0.95 (0.88-1.03); 0.2002	1.09 (0.99-1.2); 0.0758	0.99 (0.87-1.14); 0.9381	0.9 (0.82-1); 0.0556
1st gen	0.85 (0.66-1.11); 0.2359	0.47 (0.33-0.67); <.0001	0.63 (0.37-1.07); 0.0901	0.33 (0.21-0.52); <.0001
2nd gen	0.84 (0.68-1.04); 0.1124	0.74 (0.58-0.95); 0.0159	0.56 (0.36-0.87); 0.0096	0.46 (0.33-0.65); <.0001
2 parents	0.84 (0.69-1.02); 0.0757	0.56 (0.45-0.7); <.0001	0.43 (0.32-0.59); <.0001	0.63 (0.49-0.82); 0.0005
Parents PS	0.77 (0.62-0.95); 0.0166	0.6 (0.47-0.75); <.0001	1 (0.67-1.5); 0.9984	0.47 (0.36-0.62); <.0001
ESA	1.24 (0.96-1.62); 0.1052	0.48 (0.32-0.72); 0.0003	0.44 (0.22-0.86); 0.016	0.98 (0.61-1.59); 0.9429
Black	0.75 (0.51-1.1); 0.1446	1.32 (0.89-1.95); 0.166	0.51 (0.21-1.23); 0.135	1.25 (0.73-2.12); 0.4157
Other	1.21 (0.91-1.6); 0.1935	1.36 (0.98-1.89); 0.0664	1.35 (0.81-2.24); 0.2492	1.87 (1.27-2.77); 0.0016
Multiracial	1.16 (0.86-1.56); 0.3295	1.37 (0.98-1.9); 0.0644	1.36 (0.82-2.24); 0.2343	1.36 (0.91-2.03); 0.1379
School Size (increments of 200)	1.02 (0.97-1.08); 0.4797	1.03 (0.94-1.14); 0.4845	0.91 (0.81-1.03); 0.1404	0.94 (0.83-1.05); 0.2565
Median Income (increments of $10,000)	1.02 (0.98-1.07); 0.301	1.06 (0.98-1.15); 0.1169	0.9 (0.82-0.99); 0.0361	1.02 (0.93-1.12); 0.651
Rural	0.98 (0.77-1.25); 0.864	0.99 (0.67-1.48); 0.9793	1.92 (1.27-2.89); 0.0019	1.7 (1.1-2.62); 0.0165

Table 6.3A School Safety Model (reference=Low SU/MH). Reported as Odds Ratios (95% Confidence Interval); p-value.

Reference Group: Low SU/ MH	Low SU/ High MH	High HEDCAN/ Moderate MH	High HEDTOB/ Moderate MH	High SU/MH
Safety	0.86 (0.85-0.88); <.0001	0.97 (0.95-0.99); 0.002	0.89 (0.86-0.91); <.0001	0.86 (0.84-0.88); <.0001
Female	1.94 (1.76-2.13); <.0001	0.87 (0.76-0.99); 0.0341	1 (0.82-1.23); 0.9674	0.85 (0.72-0.99); 0.043
Age	1.16 (1.12-1.2); <.0001	1.59 (1.51-1.67); <.0001	1.57 (1.46-1.69); <.0001	1.52 (1.43-1.61); <.0001
Family Assets	0.97 (0.92-1.02); 0.2995	1.05 (0.97-1.12); 0.2184	0.95 (0.86-1.05); 0.3237	0.85 (0.79-0.92); <.0001
1st gen	0.94 (0.8-1.12); 0.492	0.5 (0.38-0.65); <.0001	0.79 (0.53-1.16); 0.2255	0.46 (0.33-0.64); <.0001
2nd gen	0.94 (0.83-1.07); 0.3614	0.79 (0.66-0.94); 0.0083	0.65 (0.48-0.87); 0.0044	0.5 (0.39-0.64); <.0001
2 parents	0.76 (0.67-0.86); <.0001	0.52 (0.44-0.61); <.0001	0.51 (0.4-0.64); <.0001	0.52 (0.43-0.62); <.0001
Parents PS	0.85 (0.75-0.97); 0.0155	0.64 (0.54-0.75); <.0001	0.68 (0.53-0.88); 0.0028	0.45 (0.37-0.55); <.0001
ESA	0.91 (0.77-1.08); 0.2757	0.39 (0.29-0.53); <.0001	0.27 (0.16-0.46); <.0001	0.47 (0.31-0.71); 0.0003
Black	0.6 (0.47-0.76); <.0001	1.11 (0.83-1.5); 0.4837	0.56 (0.32-0.97); 0.0385	0.78 (0.51-1.19); 0.2522
Other	1.02 (0.85-1.23); 0.8222	1.39 (1.09-1.76); 0.0075	1.08 (0.73-1.59); 0.6969	1.65 (1.24-2.2); 0.0006
Multiracial	1.22 (1.02-1.44); 0.027	1.33 (1.05-1.69); 0.0173	1.37 (0.97-1.94); 0.0741	1.45 (1.1-1.92); 0.0078
School Size (increments of 200)	0.99 (0.96-1.03); 0.643	1.03 (0.96-1.11); 0.3844	0.91 (0.83-1); 0.0624	0.93 (0.85-1.03); 0.1505
Median Income (increments of $10,000)	1.04 (1.01-1.07); 0.0082	1.05 (0.99-1.12); 0.0841	0.94 (0.87-1.02); 0.1212	1.05 (0.97-1.13); 0.2125
Rural	0.98 (0.84-1.14); 0.7914	1.01 (0.74-1.39); 0.937	1.41 (0.97-2.04); 0.0706	1.51 (1.03-2.2); 0.0357

Table 6.3B School Safety Model (reference=Low SU/High MH). Reported as Odds Ratios (95% Confidence Interval); p-value.

Reference Group: Low SU/High MH	Low SU/ MH	High HEDCAN/ Moderate MH	High HEDTOB/ Moderate MH	High SU/MH
Safety	1.16 (1.14-1.18); <.0001	1.12 (1.1-1.15); <.0001	1.03 (1-1.06); 0.0853	1 (0.97-1.02); 0.7431
Female	0.52 (0.47-0.57); <.0001	0.45 (0.39-0.52); <.0001	0.52 (0.42-0.64); <.0001	0.44 (0.37-0.52); <.0001
Age	0.87 (0.84-0.9); <.0001	1.38 (1.31-1.45); <.0001	1.36 (1.27-1.47); <.0001	1.32 (1.24-1.4); <.0001
Family Assets	1.03 (0.98-1.08); 0.289	1.08 (0.99-1.16); 0.0667	0.98 (0.88-1.09); 0.669	0.87 (0.81-0.95); 0.0011
1st gen	1.06 (0.89-1.25); 0.5224	0.53 (0.4-0.7); <.0001	0.83 (0.55-1.24); 0.3572	0.48 (0.34-0.69); <.0001
2nd gen	1.06 (0.93-1.2); 0.4145	0.83 (0.68-1.02); 0.0734	0.69 (0.51-0.94); 0.0178	0.53 (0.41-0.68); <.0001
2 parents	1.31 (1.16-1.48); <.0001	0.68 (0.57-0.81); <.0001	0.67 (0.53-0.85); 0.0009	0.68 (0.56-0.82); <.0001
Parents PS	1.18 (1.04-1.34); 0.0118	0.75 (0.62-0.9); 0.0017	0.8 (0.61-1.04); 0.0922	0.53 (0.44-0.65); <.0001
ESA	1.07 (0.9-1.28); 0.4135	0.42 (0.3-0.59); <.0001	0.29 (0.17-0.5); <.0001	0.5 (0.33-0.77); 0.0016
Black	1.64 (1.28-2.08); <.0001	1.84 (1.3-2.6); 0.0005	0.93 (0.52-1.66); 0.806	1.29 (0.83-2.02); 0.2627
Other	0.97 (0.81-1.17); 0.746	1.35 (1.03-1.76); 0.0273	1.05 (0.71-1.57); 0.7984	1.61 (1.18-2.19); 0.0026
Multiracial	0.82 (0.69-0.98); 0.0258	1.09 (0.85-1.41); 0.494	1.13 (0.79-1.6); 0.5127	1.19 (0.89-1.6); 0.233
School Size (increments of 200)	1.01 (0.98-1.05); 0.4744	1.04 (0.97-1.13); 0.2538	0.92 (0.84-1.01); 0.0979	0.94 (0.86-1.04); 0.2306
Median Income (increments of $10,000)	0.96 (0.93-0.99); 0.0105	1.01 (0.95-1.08); 0.652	0.91 (0.84-0.98); 0.0121	1.01 (0.94-1.09); 0.792
Rural	1.02 (0.86-1.2); 0.8207	1.03 (0.75-1.42); 0.8573	1.43 (0.99-2.07); 0.0587	1.53 (1.05-2.23); 0.0285

Table 6.3C School Safety Gender Interaction Model (reference=Low SU/MH). Reported as Odds Ratios (95% Confidence Interval); p-value.

Reference: Low	Low SU/High MH	HEDCAN/Moderate MH	HEDTOB/Moderate MH	High SU/MH
Safety	0.85 (0.83-0.87); <.0001	0.98 (0.95-1.01); 0.1777	0.92 (0.89-0.96); 0.0001	0.88 (0.85-0.9); <.0001
Female	1.6 (1.16-2.22); 0.0044	1.29 (0.77-2.15); 0.3365	2.89 (1.49-5.61); 0.0017	1.45 (0.88-2.42); 0.1483
Safety *Female	1.02 (0.99-1.05); 0.1889	0.97 (0.93-1.01); 0.1198	0.91 (0.86-0.96); 0.001	0.95 (0.91-0.99); 0.0292
Age	1.16 (1.12-1.2); <.0001	1.59 (1.51-1.67); <.0001	1.57 (1.46-1.69); <.0001	1.52 (1.43-1.61); <.0001
Family Assets	0.97 (0.92-1.02); 0.2938	1.05 (0.97-1.12); 0.225	0.95 (0.86-1.05); 0.3375	0.85 (0.79-0.92); <.0001
1st gen	0.95 (0.8-1.12); 0.5086	0.5 (0.38-0.64); <.0001	0.78 (0.53-1.15); 0.2126	0.46 (0.32-0.64); <.0001
2nd gen	0.94 (0.83-1.07); 0.372	0.79 (0.66-0.94); 0.0082	0.65 (0.48-0.87); 0.004	0.5 (0.39-0.64); <.0001
2 parents	0.76 (0.68-0.86); <.0001	0.52 (0.44-0.6); <.0001	0.51 (0.4-0.64); <.0001	0.52 (0.43-0.62); <.0001
Parents PS	0.85 (0.75-0.97); 0.0154	0.64 (0.54-0.75); <.0001	0.68 (0.53-0.88); 0.0028	0.45 (0.37-0.55); <.0001
ESA	0.91 (0.76-1.07); 0.2528	0.39 (0.29-0.53); <.0001	0.27 (0.16-0.47); <.0001	0.47 (0.31-0.72); 0.0004
Black	0.59 (0.47-0.76); <.0001	1.12 (0.83-1.5); 0.4712	0.57 (0.33-0.98); 0.044	0.79 (0.52-1.21); 0.2839
Other	1.02 (0.85-1.23); 0.8331	1.39 (1.09-1.76); 0.0074	1.08 (0.74-1.59); 0.6934	1.66 (1.24-2.21); 0.0006
Multiracial	1.21 (1.02-1.44); 0.029	1.33 (1.05-1.68); 0.0179	1.38 (0.97-1.94); 0.071	1.46 (1.11-1.92); 0.0074
School Size	0.99 (0.96-1.03); 0.6476	1.03 (0.96-1.11); 0.3877	0.91 (0.83-1); 0.0596	0.93 (0.84-1.03); 0.147
Median Income	1.04 (1.01-1.07); 0.0096	1.05 (0.99-1.12); 0.0809	0.94 (0.87-1.02); 0.1368	1.05 (0.97-1.14); 0.1968
Rural	0.98 (0.84-1.14); 0.7774	1.01 (0.74-1.39); 0.9335	1.42 (0.98-2.05); 0.0659	1.51 (1.03-2.21); 0.0353

7. Methodological Recommendations from Halladay, J., et al. (2020). Patterns of substance use among adolescents: A systematic review. *Drug and Alcohol Dependence*, 108222.

Clear reporting of cluster-based methodological decisions	Statistical fit across 3 domains: absolute, relative, and predictive probabilities	yes
	Evaluation of local independence	N/A traditional LPA
	Transparent discussion regarding final model selection and competing models (including presenting patterns for competing models).	yes
Substance use indicator decisions	Separate indicators for alcohol, cannabis, and tobacco should be included	yes
	Using continuous indicators, as opposed to dichotomous or categorical	yes
	Indicators related to mental health symptomatology	yes
	Maximizing consistency and comparability across studies: 1) standardized substance use measures, 2) cross-replication (across samples and clustering techniques)	1 – no (not available) 2 – yes – split half sample cross-replication
Additional relevant items from Guidelines for Reporting on Latent Trajectory Studies	Statistical software used	yes - Mplus & SAS
	Are alternate shape/functional forms described?	yes
	If covariates have been used, can analyses still be replicated?	yes

(GRoLTS) Checklist	Is information reported about the number of random start values and final iterations included?	yes
	Are model comparison and selection tools described from a statistical perspective?	yes
	Are the total number of fitted models reported, including a one-class solution?	yes
	Is entropy reported?	yes
	Is a plot of the final model/means included?	yes
	Are characteristics of the final class solution numerically described? (means, SD/SE, n, CI, etc.)?	yes
	Are syntax files available (either in appendix, supplementary materials, or from the authors)?	yes, upon request
Follow STROBE guidelines (See full checklist) www.strobe-statement.org	**Note**: Ensure clear and comprehensive reporting of response rates and missingness, including approaches for dealing with missing data	yes

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Chapter 4: The CAMP Study: Feasibility and Clinical Correlates of Standardized Assessments of Substance Use in a Youth Psychiatric Inpatient Sample

Halladay, J., Horricks, L., Amlung, M., MacKillop, J., Munn, C., Nasir, Z., Woock, R., Georgiades, K. (2021). The CAMP study: Feasibility and clinical correlates of standardized assessments of substance use in a youth psychiatric inpatient sample. *Child and Adolescent Psychiatry and Mental Health, 14*, 48. https://doi.org/10.1186/s13034-021-00403-4

Highlights:

- This study provides preliminary evidence that use of standardized substance use and mental health assessments during youth psychiatric hospitalization is both feasible and acceptable to youth and staff.
- Substance use is common among youth experiencing psychiatric hospitalization and is associated with increased severity and complexity of presentation and repeat hospital visits.
- Frontline staff support the need for standardized comprehensive assessments of substance use to improve clinical conceptualization and quality of care.
- Integrating routine, standardized electronic self-reported substance use and mental health assessments into care can enhance clinical practice and promote quality assurance and research in clinical settings.

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Child and Adolescent Psychiatry and Mental Health

RESEARCH ARTICLE Open Access

The CAMP study: feasibility and clinical correlates of standardized assessments of substance use in a youth psychiatric inpatient sample

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Abstract

Background: To determine: (a) the feasibility and acceptability of administering a standardized electronic assessment of substance use and other mental health concerns to youth admitted to an inpatient psychiatric unit, and (b) the prevalence and clinical correlates of substance use in this sample.

Methods: The sample included 100 youth between the ages of 13 to 17 years admitted to an inpatient psychiatric unit in Ontario, Canada between September and November 2019 (78% response rate). Youth data were comprised of electronic self-reported assessments (during hospitalization and 6-months following) and chart reviews (99% consented; historical and prospective). Frontline staff completed a self-report survey assessing their perceptions of the need for standardized substance use assessments, training, and interventions on the unit (n = 38 Registered Nurses and Child and Youth Workers; 86% response rate). Analyses included descriptive statistics, correlations, regression, and qualitative content analysis.

Results: Feasibility of standardized youth self-reported mental health and substance use assessments was evident by high response rates, little missing data, and variability in responses. 79% of youth had used at least one substance in their lifetime; 69% reported use in the last 3 months. Substance use was positively correlated with severity of psychiatric symptoms (τb 0.17 to 0.45) and number of psychiatric diagnoses (τb 0.17 to 0.54) at index. Based on prospective and retrospective data, substance use was also positively related to mental health symptom severity at follow-up and repeat mental health related hospital visits. Frontline staff reported a need for standardized assessment, training, and interventions on the unit, indicative of acceptability.

Conclusions: This study demonstrated the feasibility, acceptability and clinical importance of administering a standardized mental health and substance use assessment among youth experiencing psychiatric hospitalization.

Keywords: Adolescent, Cannabis, Alcohol drinking, Substance-related disorder, Psychiatric Hospitals

Background

Most mental illnesses emerge in childhood and adolescence, and suicide is the second leading cause of death during adolescence [1, 2]. Although substance use disorders (SUDs) often emerge later than other mental illnesses, most individuals who use substances initiate

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use prior to age 20 [3]. Cannabis and alcohol are two of the most commonly used substances [4], and accumulating evidence suggests use of cannabis and alcohol may precede the onset or worsening of psychiatric and suicide-related outcomes [5–7]. Regardless of temporal sequencing, co-occurrence of mental health and substance use problems is common [8]. Although help-seeking among adolescents with substance use concerns is low, many engage with psychiatric services prior to substance use treatment [9, 10]. This presents a critical opportunity for prevention and early identification in psychiatric settings.

Assessing and addressing substance use may be particularly important during psychiatric hospitalizations given the acuity of youth presentations, access to multidisciplinary teams, and treatment recommendations and community referrals often facilitated upon discharge. However, standardized instruments, designed to assess substance use and mental health concerns, are not routinely administered in youth psychiatric settings [11–14]. There is emerging but limited evidence suggesting that individuals with mental illnesses who use cannabis or alcohol may experience more severe and complex symptoms, greater functional impairment, and poorer prognosis [7, 9, 15, 16]. This evidence is primarily drawn from work in outpatient settings and is not routinely collected as a means to provide robust insight.

When considering youth populations from the perspective of those presenting to health services with substance use concerns, there is data available on the co-occurrence of mental health problems. In Canada between 2017 and 2018, about 70% of youth hospitalizations for substance use involved concurrent psychiatric concerns [17]. Similarly, a majority of adolescents attending a large outpatient substance use program in Toronto, Ontario, endorsed high levels of internalizing (72%) and externalizing (83%) psychopathology [18]. These findings have been replicated among youth attending substance use treatment in the US [10, 19]. Of note, cannabis typically accounts for the largest proportion of substance use related service use among youth [17–19].

There are significant challenges navigating and securing services for youth that address both mental health and substance use in North America [9, 20]. Longstanding gaps in youth addiction services have been recognized by governments and there have been calls for increased capacity to treat SUDs and psychiatric disorders concurrently across all sectors of youth care [20]. Both Canadian and US governments have recognized the need to identify substance use problems early, especially among those with psychiatric concerns, and have indicated a need for integrated and coordinated treatments [21–23]. This is echoed in various clinical best practice guidelines (BPGs) which recommend assessing for substance use prior to diagnosing mental illnesses and treating concurrently if co-presenting [24–27]. Despite the recognition of this problem, this gap in service persists. Common healthcare provider reported barriers to addressing substance use include time constraints, lack of training, stigma, and uncertainty about how to interpret and apply results of screening assessments [13, 28, 29]. Notably, a recent systematic review of concurrent disorder recommendations within existing BPGs found a lack of specificity and consistency regarding recommendations, as well as low levels of rigor and stakeholder input when developing the guidelines [30]. Further, no specific guidelines address the management of youth substance use on inpatient psychiatric units, which were not built or funded to address both issues. As such, further research and stakeholder input are critical to inform guidelines and advocate for funding and system changes where it is most needed.

The Cannabis, Alcohol, Mental Health, and Patterns of Service Use (CAMP) study was a pilot study to determine the feasibility and acceptability of collecting and integrating substance use, mental health, and hospitalization data among youth admitted to an inpatient psychiatric unit through both primary data collection methods (i.e., self-reported youth electronic clinical assessments, stakeholder surveys) and secondary linkages to medical records by research personnel. Our results can inform subsequent: (1) clinical research studies, designed to assess the feasibility, acceptability, utility and cost-effectiveness of integrating routine substance use and mental health assessments directly within clinical practice; and (2) methods for larger scale research studies within clinical programs. The specific feasibility objectives included [31]: (1) *process* outcomes, i.e., ability to recruit (patient willingness); (2) *resource and management* outcomes, i.e., youth and staff burden and extent of missing data, refusal, and retention; (3) *scientific* outcomes, including prevalence and variability in substance use and preliminary insight into correlates between substance use and psychiatric severity (i.e., intensity of symptoms), complexity (i.e., comorbidity), and health service use (i.e., length of stay and readmission); and (4) *staff acceptability* outcomes, including staff perceptions regarding substance use assessment and intervention on the inpatient unit, including its importance, facilitators, and barriers.

Methods

Design and setting

The CAMP study was a feasibility observational cohort study conducted on a large Child and Youth Mental Health Inpatient Unit in a large urban city in Ontario, Canada. The unit services youth up to the age of 18 years. The purpose of admission includes emergent psychiatric

assessments, crisis stabilization, acute treatment delivery including pharmacological and nonpharmacological approaches (e.g., daily structured individual and/or group psychotherapeutic programming), and coordinated post-discharge planning with community partners. In general, roughly 50% of beds on this unit are occupied by youth experiencing internalizing symptoms (e.g., depression, anxiety, trauma), 23% by youth with primary personality disorder related symptoms (e.g., borderline personality disorder, oppositional defiant disorder), and 27% by highly acute youth (e.g., psychotic and manic episodes). The average length of stay is 7–10 days, appreciating the vast majority of treatment provision occurs post-crisis in the community. Developed 12 years ago, the units focus has been on the acute stabilization of psychiatric presentations. Over the past 12 years, the unit has admitted youth with concurrent disorders, and openly acknowledges it is not a designated concurrent disorders unit and therefore does not provide specific treatments for SUDs.

The study consisted of 4 parts: (1) a self-reported electronic youth assessment during hospitalization; (2) a 6-month follow-up assessment; (3) retrospective (3 years) and prospective (6 months) chart reviews; and (4) frontline staff surveys. The staff component combined cross-sectional and qualitative description designs in survey format [29]. All study objectives and procedures were iteratively refined with feedback from frontline staff, unit leadership, and the Child and Youth Mental Health Research Advisory Committee. Of note, the selected clinical indicators related to severity, complexity, and health service utilization align with provincially defined clinical indicators for child and youth mental health services [32, 33].

Participants

The target population for the youth component was all youth 12–17 years of age admitted to the unit. The sample included 100 youth recruited on a rolling basis. Youth were excluded if they were: unable to provide informed consent, unable to complete a 30-min assessment (due to attention, cognitive, or safety concerns), or experiencing acute psychotic symptoms based on clinical staff evaluations. Substance use was not required. Recruitment occurred between September 9, 2019 and November 26, 2019. The target population for the staff component was all frontline full-time and part-time Registered Nurses (RNs) and Child and Youth Workers (CYWs) as of September 2020.

Measures

Youth self-report measures

The youth assessment was based on a clinical screening tool used on the adult Concurrent Disorders units in Hamilton (St. Joseph's Healthcare Hamilton), adapted for youth. To facilitate comparisons, all measures were selected based on pre-piloted and/or psychometrically validated measures for youth used in large population surveys including the Ontario Student Drug Use and Health Survey (OSDUHS) [4] and the Ontario Child Health Study (OCHS) [34]. The assessment measured demographic characteristics, substance use with a particular focus on cannabis and alcohol use, psychiatric symptomatology, and mental health service utilization. The adapted interview tool was piloted and revised to ensure clarity and minimal burden. See Table 1 for a summary of measures (see Additional file 1 for a PDF of the assessment).

Youth chart reviews

Person-level, *health service utilization* data was collected on prior (past 3 years) and follow-up (6 months post-discharge) psychiatric and substance use related emergency department (ED) presentations and inpatient psychiatric admissions at the hospital. The hospital for data collection is the only pediatric hospital in the city but it is possible for youth in surrounding cities to present to EDs at other hospitals and then get transferred to this inpatient unit (i.e., direct admission). ED visits were identified in Canadian Institute for Health Information (CIHI) National Ambulatory Care Reporting System (NACRS) database using the Canadian Emergency Department Information System (CEDIS) presenting complaints alongside the most responsible diagnosis code for each ED encounter at the hospital site. Inpatient admissions and associated length of stay were identified in CIHI Discharge Abstract Database (DAD) by the most responsible discharge diagnosis code for each inpatient encounter. Substance use and mental health codes were included. Data on *severity and complexity* included documentation by clinicians on harm to self, harm to others, property damage, symptoms of psychosis, substance use, and discharge diagnoses (for a complete list of codes and extraction content, see Additional file 2). Substance use information came from existing semi-structured interviews documented in patient charts by either the nurse upon admission to the unit, or the psychiatrist during the psychiatric assessment. Interviews included open-ended questions related to substances used and patterns of use prior to the inpatient admission. However, these interviews were not standardized and did not utilize validated measures, consistent historical timelines, or systemized probes or response options. Additionally, the documentation system had sections with limited character counts.

Table 1 Summary of key measures in the youth electronic assessment

General construct	Specific variables
Demographics	Age, gender, sex, race/ethnicity, immigrant status, subjective social status [4, 48]
Substance use variables	
Cannabis use	• Frequency of use [4, 58] • Symptoms of cannabis use disorder (CUDIT-R) [59] • Age of onset [4, 58] • Percentage of typical THC/CBD, grams per use day, cost per week/month • Coping motives scores [60] • Proportion of time spent using with others [61] • Co-use with alcohol and co-use with tobacco [4]
Alcohol use	• Frequency of any use [4, 58] • Frequency of heavy episodic drinking (HED; 5+ drinks in a sitting) [4] • Symptoms of alcohol use disorder (AUDIT) [62] • Coping motives scores [63] • Proportion of time spent using with others [61]
Smoking	• Frequency of smoking cigarettes/cigars [4, 58] • Frequency of e-cigarette use and types of substances in e-cigarettes [4, 58]
Prescription drug misuse	Frequency of [4, 58, 64]: • Prescription stimulants • Prescription opioids • Prescription sedatives
Other drug use	Frequency of [4, 58, 64]: • Cocaine • Methamphetamine • Solvents • Hallucinogens • Street opioids • Steroids
Psychiatric clinical severity and complexity	
Severity of psychological distress	The Kessler 6 (K6) [65] provided a dimensional measure of non-specific psychological distress. Previously derived cut-offs of ≥ 13 which indicate serious mental illness were used
Internalizing symptom severity	The OCHS Emotional Behavioral Scales (OCHS-EBS) [66] dimensional measure captured symptoms of internalizing disorders including: • Major depressive episode (MDE; of note, suicide item removed) • Generalized anxiety disorder (GAD) • Social phobia (SP)
Externalizing symptom severity	The OCHS-EBS [66] dimensional measure captured symptoms of externalizing disorders including: • Oppositional defiant disorder (ODD) • Conduct disorder (CD) • Attention deficit hyperactivity disorder (ADHD)
Youth derived clinical complexity	Clinical cut-offs for OCHS-EBS disorder scores based on prevalence estimates derived from a diagnostic structured interview in the original OCHS general population sample were used to generate categorical prevalence of disorders [34]. The number of cut-offs youth exceeded were summed to derive number of internalizing, externalizing, and total disorders as indicators of youth reported clinical complexity.
Symptoms of psychosis	A pre-existing symptom scale adapted from the Diagnostic Interview Schedule [67] provided a dimensional measure of symptoms of psychosis

Staff self-report measures

The staff survey was informed by previous research [13, 28, 29] alongside consultations with the CAMP study team, unit management and leadership, and senior front-line staff. The staff survey included 14 closed and open-ended questions related to standardized youth substance use assessment, treatment planning, training/education, and potential barriers and facilitators to addressing these on the unit (see Additional file 3 for a PDF of the survey).

Recruitment and data collection

Youth

The study Research Assistants (RAs) were trained on general reasons for admission, unit staffing model,

common clinical presentations, and specific items about their role in the maintenance of environmental safety. Unit staff were informed about the study through emails and staff meetings beginning one month prior to recruitment through to completion of baseline data collection. Patients were recruited primarily through a one-on-one discussion with an RA. Alternative methods included RAs providing a brief study overview during morning group on a semi-weekly basis and study posters. The RAs consulted with nursing staff about eligible patients in advance of meeting with the patient, to ensure eligibility, safety, appropriate timing, and capacity to consent. Data was collected on an iPad using Qualtrics CoreXM, which is a secure online survey platform and database (Qualtrics, Provo, UT). The RA supervised the youth as they completed the assessments. For youth who consented, a 6-month follow-up assessment was sent to their phones and/or emails (with one reminder) and chart reviews were done to obtain information before, during, and after their index hospital admission. Youth were able to consent to partake in 1, 2 or all 3 parts of the study (i.e., baseline, follow-up, chart reviews), and received a $10 gift card for each component (up to $30).

Frontline staff

Staff were recruited through personalized cards in their staff mailbox, emails, posters, and reminders during morning rounds. Data was also collected using Qualtrics CoreXM. All staff received a $20 gift card regardless of participation to keep responses anonymous.

Ethics and reporting guidelines

Ethics approval was obtained from the Hamilton Integrated Research Ethics Board (ID 7075) and study procedures were approved by the Child and Youth Mental Health Research Advisory Committee. Consent to participate was obtained directly from youth, and not parents, in order to mitigate bias in reporting substance use [35, 36], and to maintain parameters of confidentiality. Our focus on capacity rather than age, is consistent with the Tri-Council Policy Statement, Health Care Consent Act, and previous research demonstrating that youth 12 years of age or older are often capable of consent [37]. Methods and reporting follow pilot study guidelines [31], Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines, and Reporting of Studies Conducted Using Observational Routinely-Collected Health Data (RECORD) guidelines (for reporting checklists, see Additional file 4).

Statistical analyses

Youth component

This paper examines feasibility outcomes [31], predominantly operationalized as: (1) recruitment of 100 youth within 4 months with a response rate greater than 75%; (2) at least 80% of youth consenting to chart reviews and follow-up assessments; (3) over 80% of consenting youth completing their 6-month follow-up assessment; and (4) at least 20% of youth reporting monthly cannabis and/or heavy alcohol use. Thresholds for adequate response rates come from Risk of Bias tools [38]. Using representative general population data [39], we estimated the prevalence of monthly cannabis use to be 1.7 times greater and heavy drinking to be 1.5 times greater for youth experiencing high levels of psychiatric symptomatology, compared to those with no or few symptoms.

Descriptive statistics were used for feasibility outcomes and to characterize the sample including substance use prevalence estimates with 95% Confidence Intervals (CIs) calculated for proportions [31]. Bivariate Kendall's Tau (τb) correlations using a $p<0.05$ to denote significance were used to examine associations between self-reported substance use variables and clinical severity and complexity. Logistic regressions were conducted to explore associations between substance use and any ED visit or inpatient admission, adjusted for type of index admission (e.g., whether patients were directly admitted or went through the local ED). Linear regressions were done to examine associations between self-reported substance use at index and psychiatric symptomatology at follow-up, adjusted for symptomatology at index. All analyses were done using complete cases, after pro-rating summative scales for up to 3 missing items.

Staff component

Descriptive statistics were used to provide frequencies and averages of closed-ended response options. Two researchers (JH and RW) used qualitative content analysis to code all open-ended data manually through adding index labels, which were then counted and inductively categorized based on regularities and patterns in the topic codes [40]. Final categories evolved through refinement of codes by re-reading, discussions, and consultations with the larger research team [41]. Results from the quantitative and qualitative items were deliberately integrated and merged during the analysis and interpretation phase to obtain a more complete picture of staff perspectives [42].

Results

Youth component

Response rates and retention

During the 3-month data collection period, of the 128 youth that met inclusion criteria, 111 were invited to

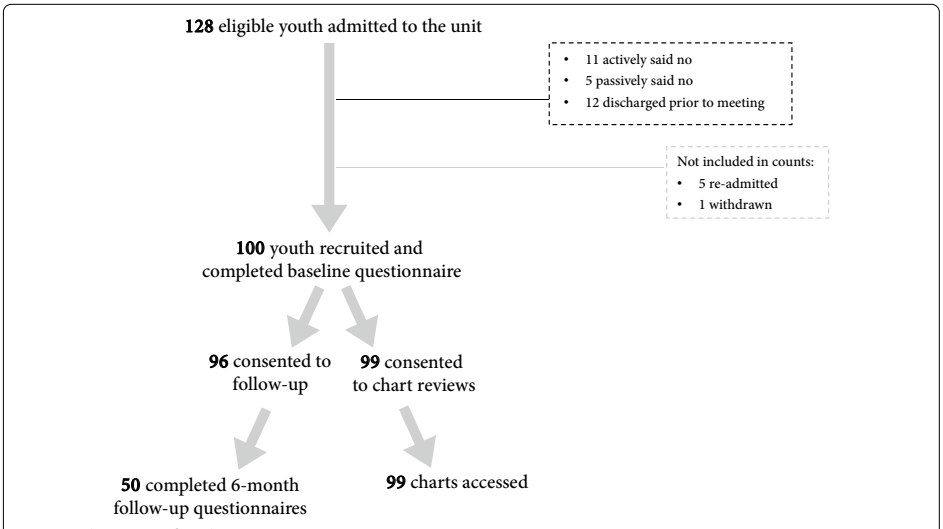

Fig. 1 Youth participant flow chart

participate in the study, and 100 youth consented to be involved in the study (78% [95% CI 70% to 86%] response rate of all eligible youth, 90% response rate of those invited). For baseline assessments, 77% of youth completed all items with the remaining missing 3 or fewer items. Almost all youth consented to follow-up assessments (96% [CI 92% to 100%]) and chart reviews (99% [CI 97% to 100%]). 50 (52% [CI 42% to 62%]) youth responded to the follow-up assessments within 3 weeks of their 6-month follow-up date.[1] At follow-up, 78% had complete data with the remaining missing 4 or fewer items. The study surpassed all a priori feasibility criteria, with the exception of the follow-up rate (52% vs. proposed >80%) which was likely influenced by the COVID19 pandemic. Of note, only higher psychological distress (Odds Ratio [OR] = 0.913, p = 0.034) and prior mental health ED visits (OR = 0.420, p = 0.036) were associated with a lower odds of missing at follow-up; no other indicators of severity, complexity, service use, substance use, or demographic characteristics predicted missingness. See Fig. 1 for a participant flow chart.

[1] 1 youth submitted 2 follow-up assessments with multiple discrepancies and another youth submitted 2 months after their follow-up time (not included in follow-up rates). Thus, the follow-up analyses were based on a sample size of n = 49.

Recruitment and data collection strategy

Recruitment and data collection processes were efficient and acceptable. Interactions between RAs and staff took on average 5 min per interaction and staff did not express concerns about time taken away from clinical care. RAs typically took 30–40 min to discuss the study and thoroughly review the consent forms with youth. Baseline assessments took youth on average 13 min to complete, with a minimum of 5 and maximum of 33 min (variability due to skip patterns). Of youth included in follow-up assessments, 23 (47%) completed via email and 26 (53%) via smartphones, thus supporting the inclusion of both options.

Demographics

Youth were on average 15.4 years of age (age range, 13–17 years). Most youth were female gender (65%). With 2 outliers removed, the average length of stay for index admissions was 8.4 days (shortest 1 day, longest 21 days). In the 3 years prior to index, 44% of the sample had an ED visit for mental health concerns and 40% had a psychiatric admission at the data collection site. In the 6 months following index, 27% re-presented to ED and 24% were re-admitted for mental health concerns at the data collection site. See Table 2 for demographic characteristics.

Mental health symptomatology

Using clinician-identified most responsible (one per youth) discharge diagnosis, depressive-related (29%), anxiety and obsessive–compulsive related (22%), and trauma and stressor related (21%) disorders were the most common. When using diagnoses taken from discharge summary notes, in which multiple diagnoses could be identified, the most common disorders were: anxiety and obsessive–compulsive related (64%), depressive related (43%), borderline personality, cluster B, and emotion dysregulation related (41%), and trauma and stressor related (31%). Of note, 10% of youth had a discharge diagnosis of a SUD, none of which were the most responsible diagnosis. Using self-reported symptom scores, 87% surpassed cut-offs for at least one mental health disorder. Specifically, 75% and 49% surpassed thresholds for at least 1 internalizing or externalizing disorder, respectively, with 37% meeting criteria for both. See Table 2 for mental health symptomatology and diagnostic characteristics.

Substance use

69% of youth had used at least one substance in the 3 months prior to their psychiatric admission. The most common substances used among youth in the 3 months prior to admission were alcohol, cannabis, tobacco, e-cigarettes, and opioids. Use of multiple substances was common, whereby 50% of youth were using more than one substance prior to admission. Co-use was common, with 24 youth (60%) combining alcohol and cannabis and 25 youth (63%) combining tobacco and cannabis. See Table 3 for prevalence of substance use at index. Self-reported substance use in assessments was higher than documented use in clinical notes—especially when compared to nursing assessments done on admission. These discrepancies could be due to differential reporting by the youth in confidential self-reported assessments versus clinical interviews, but it is more likely that discrepancies arise given differences in content coverage between assessments (i.e., specific questions, timelines, probing, response options, etc.). For example, the electronic self-reported assessment provided examples of each substance type and response options to aid with recall, which were not standardized in clinical interviews.

Cannabis The average age of initiation among all youth who reported lifetime cannabis use was 13.3 years. Of the 50% of youth who reported cannabis use in the 3 months prior to admission, 32 (64%) had CUDIT-R scores indicative of hazardous cannabis use (mean = 12.4; SD = 7.4) and 23 (46%) had recently thought about cutting down or stopping use. Of the 45% of youth who endorsed past month use, 25 (55%) reported using alone half of the time or more, 35 (78%) reported using to cope most or all of the time, and 18 (40%) reported daily use. Notably, frequency of cannabis use and using for coping purposes accounted for 60% of the variance in CUDIT-R scores. Prevalence of monthly cannabis use was 3.2 times greater than prevalence in the general population of grade 7–12 students (14.1%) [4], surpassing a priori feasibility thresholds.

Alcohol Of the 51% who reported using alcohol in the 3 months prior to admission, 23 (47%) had AUDIT scores indicative of hazardous alcohol use (mean = 8.4, SD = 6.3). Of these youth, 12 (24%) reported someone being injured as a result of their drinking and 7 (14%) were currently concerned about their drinking. Of the 46% of youth who endorsed past month use, 11 (24%) reported using alone half of the time or more, 30 (65%) reported using to cope most or all of the time, and 29 (63%) reported heavy episodic drinking (HED). Questions regarding past month drinking and HED alongside drinking coping motives explained 58% of the variance in AUDIT scores. Prevalence of monthly HED was 1.9 times greater than the general population (15%) [4], surpassing a priori feasibility thresholds.

Cigarettes and E-cigarettes 14% endorsed daily use of tobacco cigarettes and 14% endorsed daily use of e-cigarettes. Types of e-cigarettes were clarified at follow-up, where most youth reported using e-cigarettes with nicotine (79%) and about a third (32%) reported use with cannabis.

Other drug and prescription drug misuse When other drugs were used in the 3 months prior to admission, most youth endorsed using the substance 1 or 2 times with no more than 3% endorsing 10 or more times for any individual substance (3% cocaine, 2% solvents, 2% hallucinogens). Misuse of prescription drugs 10 or more times was more common with youth endorsing frequent use of prescription stimulants (4%), sedatives (5%), and/or opioids (5%).

Clinical correlates of substance use

The magnitude, significance, and precision of effects varied across different substance types (e.g., alcohol, cannabis, cigarettes, e-cigarettes, prescription, other) and substance-related variables (e.g., frequency, AUDIT/CUDIT-R, coping motives, using alone) for different clinical indicators. However, significant correlations emerged between at least one substance use variable and: (1) self-reported externalizing (all substances; significant r_b from 0.17 to 0.45) and internalizing symptomatology (select substances; significant r_b from 0.17 to 0.40); (2) clinician-reported aggressive behaviors

Table 2 Demographic and clinical characteristics of youth participants

Sample characteristics	Mean (SD) or %
Demographic characteristics	
Age	15.4 (1.2)
Perceived social status	5.5 (1.7)
Female sex	82%
Female gender	64%
Transgender and gender diverse	19%
White race/ethnicity	72%
Mixed race/ethnicity	17%
Lived in Canada whole life	91%
One or more parents born outside of Canada	25%
Positive screening on self-reported psychiatric symptom scales	
Generalized anxiety disorder (GAD)	69%
Social phobia (SP)	22%
Major depressive episode (MDE)	50%
Attention deficit hyperactivity disorder (ADHD)	32%
Oppositional defiant disorder (ODD)	37%
Conduct disorder (CD)	32%
At least one internalizing disorder (GAD, SP, and/or MDE)	75%
At least one externalizing disorder (ADHD, ODD, and/or CD)	49%
At least one internalizing and one externalizing disorder	37%
Any internalizing or externalizing disorder	87%
Serious mental illness (K6)	85%
Most responsible physician discharge diagnosis (primary diagnosis, youth only have one)	
Depressive related disorders	29%
Anxiety and obsessive–compulsive related disorders	22%
Trauma and stressor related disorders	21%
Borderline, cluster B, and emotion dysregulation disorders	5%
ADHD and other neurodevelopmental disorders	5%
Other (for complete list, see Additional file 3, available online)	17%
Discharge summary diagnoses[a]	
Depressive related disorders	43%
Anxiety and obsessive–compulsive related disorders	64%
Trauma and stressor related disorders	31%
Borderline personality, cluster B, and emotion dysregulation disorders	41%
ADHD and other neurodevelopmental disorders	20%
Problems with family relations	17%
Eating disorders	12%
SUDs	10%
Other	14%
Number of any discharge diagnoses	2.9 (1.5)
Number of categories of discharge diagnoses (excluding other)	2.5 (1.2)
Hospital contacts prior to and following index	
Any ED visit in prior 3 years	44%
Any ED visit in prior 6 months	25%
Any ED re-presentations in following 6 months	27%
Any admission in prior 3 years	40%
Any admission in prior 6 months	21%
Any re-admission in following 6 months	24%

[a] Discharge summary diagnoses are not mutually exclusive, and youth can have multiple

Table 3 Prevalence of youth substance use prior to index admission

Substance	Time period or type of use	Total sample (n = 100)
Alcohol	Lifetime	73% (64 to 82)
	Past 3 months	51% (41 to 61)
	HED past month	29% (20 to 38)
	AUDIT 8–15 "risky"[a]	17 (33% [20 to 46])
	AUDIT ≥ 16 "harmful and high risk"[a]	6 (12% [3 to 21])
Cannabis	Lifetime	66% (57 to 75)
	Past 3 months	50% (40 to 60)
	Daily past month	18% (10 to 26)
	CUDIT 8–11 "hazardous"[a]	5 (10% [2 to 18])
	CUDIT ≥ 12 "possible CUD"[a]	27 (54% [40 to 68])
Tobacco	Lifetime	47% (37 to 57)
	Past 3 months	33% (24 to 42)
	Daily past month	14% (7 to 21)
E-cigarettes	Lifetime	42% (32 to 52)
	Past 3 months	34% (25 to 43)
	Daily past month	14% (7 to 21)
Prescription opioids	Lifetime	22% (14 to 30)
	Past 3 months	18% (10 to 26)
Sedatives	Lifetime	22% (14 to 30)
	Past 3 months	14% (7 t 21)
Prescription stimulants	Lifetime	21% (13 to 29)
	Past 3 months	11% (5 to 17)
Cocaine	Lifetime	18% (10 to 26)
	Past 3 months	8% (3 to 13)
Hallucinogens	Lifetime	22% (14 to 30)
	Past 3 months	14% (7 to 21)
Solvents	Lifetime	10% (4 to 16)
	Past 3 months	4% (0 to 8)
Any prescription drug	Lifetime	35% (26 to 44)
	Past 3 months	24% (16 to 32)
Any illicit substance use	Lifetime	34% (25 to 43)
	Past 3 months	17% (10 to 24)
Any substance use	Lifetime	79% (71 to 87)
	Past 3 months	69% (60 to 78)

Methamphetamines, street opioids, steroids, and synthetic cannabinoids were not included uniquely as prevalence was < 4%

[a] For those who endorsed use in the 3 months prior to index visit

(most substances; significant τb from 0.21 to 0.32); (3) number of youth-reported psychiatric disorders (all substances; significant τb from 0.19 to 0.43); (4) number of physician-reported discharge diagnoses (select substances; significant τb from 0.17 to 0.54); (5) mental health related ED visits 3 years prior and 6 months after index (select substances); and (6) psychiatric admissions in the 3 years prior to index (all substances). Additionally, those who completed the 6-month follow-up who used cannabis, alcohol, cigarettes, or e-cigarettes prior to index endorsed significantly higher psychiatric symptoms at follow-up. This serves as preliminary exploratory evidence of correlations between substance use and clinical severity, complexity, service use, and poorer prognosis. See Table 4 for select correlations between substance use and severity and complexity variables. More comprehensive details and results are presented in Additional file 5.

Staff component

There was an 86% response rate (37/43) with roughly half RNs (49%) and half CYWs (51%). Over half (54%) of the staff participating in the survey had been working on the unit 5 years or longer with only 2 staff reporting less than

Table 4 Selected Kendall's tau correlations between substance variables and clinical severity and complexity outcomes

	Youth-reported psychiatric symptomatology as per OCHS-EBS							Physician-reported	
	SP	GAD	MDE	ADHD	ODD	CD	Total # surpassing clinical thresholds	Aggressive threats and behaviors	Total # of discharge diagnoses based on categories
Frequency									
Cannabis	−0.076	0.007	0.075	0.128	0.266[b]	0.309[b]	0.212[b]	0.227[a]	0.117
Alcohol	0.054	0.038	0.105	0.073	0.210[b]	0.250[b]	0.200[a]	0.212[a]	0.093
Cigarette	0.005	0.069	0.071	0.185[a]	0.295[b]	0.447[b]	0.280[b]	0.324[b]	0.167
E-cigarette	−0.021	0.05	0.107	0.14	0.259[b]	0.300[b]	0.284[b]	0.136	0.141
Prescription	0.208[a]	0.245[b]	0.279[b]	0.168[a]	0.230[b]	0.319[b]	0.360[b]	0.262[b]	0.197[a]
Other	0.081	0.137	0.174[a]	0.206[a]	0.274[b]	0.374[b]	0.341[b]	0.282[b]	0.200[a]
Coping motives									
Cannabis coping motives	0.293[b]	0.398[b]	0.206	0.001	0.052	0.04	0.229[a]	−0.068	0.358[a]
Alcohol coping motives	0.128	0.302[b]	0.236[a]	0.320[b]	0.299[b]	0.316[b]	0.412[b]	0.159	0.540[b]
Substance use disorder scores									
CUDIT total score	−0.094	0.015	0.072	−0.041	0.002	−0.005	0.005	0.039	0.116
AUDIT total score	0.02	0.123	0.186	0.289[b]	0.336[b]	0.444[b]	0.396[b]	0.281[a]	0.442[b]
Using substances with others									
Using cannabis with others	−0.172	−0.14	−0.112	0.049	0.054	0.108	−0.043	−0.085	0.049
Using alcohol with others	−0.103	−0.167	−0.067	−0.111	−0.143	−0.117	−0.187	−0.113	−0.205

More detailed results in Additional file 5, available online

[a] Correlation is significant at the 0.05 level (2 tailed)

[b] Correlation is significant at the 0.01 level (2-tailed)

1 year experience. The main findings were that: (1) staff believe substance use is important and common among youth on the unit and want to improve how they assess and address substance use; (2) staff have ideas about how to facilitate improvements in quality of care including greater standardization of assessments and interventions, separate cohorting and staffing for youth with more severe co-occurring problems, more direct substance related interventions, and more indirect facilitation of appropriate and supportive conversations; and (3) staff want more education and training to increase knowledge, confidence, and standardization of practices. Of note, lack of training (81%) and time pressures (64%) were the most commonly reported barriers to comprehensive assessment while facilitators included standardization, adding designated spaces in documentation, and training on conducting assessments and addressing positive screens.

Discussion

The CAMP study examined the feasibility of administering a standardized electronic assessment to measure mental health and substance use on an inpatient youth psychiatric unit and provides insight into the prevalence and correlates of substance use among youth in this acute setting. Collecting this data as part of a research study proved feasible, with high recruitment and response rates, and little participant and staff burden. The high prevalence of substance use provides evidence of the feasibility of general consecutive sampling and reinforces the importance of routine substance use assessments within this context.

Overall, comorbid substance use was the norm, not the exception. A majority of youth had used at least one substance prior to their admission, and substance use correlated with more severe psychiatric symptoms, greater complexity, and more mental health related hospital visits. Youth using substances were often using in ways that have been associated with higher risk of experiencing substance-related problems, including early age of initiation, frequent use, using multiple substances, using alone or for coping purposes, and co-using substances. Despite the unit not being designated as a concurrent disorders unit, youth with substance concerns are admitted. As such, frontline staff recommended adopting a comprehensive approach to substance use among youth admitted to hospital for psychiatric concerns, including adoption of standardized assessments, more training,

and enhanced patient conceptualization and intervention which include substance use considerations. Standardized screening and assessments can facilitate efficient identification of patients requiring more thorough SUD clinical assessments or immediate withdrawal management and can support comprehensive patient conceptualization, integrated treatment planning, and referral pathways.

Prevalence and frequency of substance use far surpassed that found in the general population of Ontario youth in grades 7–12. Not only were youth in this study more likely to use substances, but these youth also reported more frequent use, more co-use of substances, and more symptoms related to Alcohol Use Disorder and Cannabis Use Disorder compared to the general population. In particular, almost 1 in 5 youth in the present study reported using cannabis daily and 1 in 7 smoked tobacco products daily, frequencies which are roughly 8 to 9 times greater than general population estimates [4]. Further, this sample reported an age of initiation of cannabis about 2 years younger than the general population (13.3 CAMP vs. 15.4 OSDUHS) and similar to the age of initiation among youth who present to an outpatient concurrent disorders program in Toronto (13.6) [18]. Earlier age of cannabis initiation has been related to a greater likelihood of using multiple substances and developing a SUD [43, 44], experiencing cognitive impairment, lower academic achievement, and dropping out of school [43, 45, 46], having more criminal and legal involvement, and experiencing more concurrent mental health symptomatology [47]. Although there are differences in sampling strategies and characteristics, this provides general evidence of higher prevalence and risky use in clinical samples consistent with existing studies of youth with high levels of psychiatric symptomatology and suicidality [5–8, 48, 49].

Most clinical guidelines indicate the need to assess the role of substances prior to diagnosing and determining treatment for mental illnesses [24–27]. This study demonstrates it is feasible to collect self-reported substance use data electronically from youth experiencing acute psychiatric concerns. Electronic assessments have shown validity, acceptability, and greater efficiency as compared to clinical interviews [50]. Further, the high frequency of substance use seen in this sample demonstrate that a non-negligible proportion of youth admitted to the hospital for psychiatric concerns may be at risk of withdrawal during admission [51]. The most common withdrawal symptoms for cannabis and nicotine are behavioral and emotional, which may bias diagnostic assessments and interfere with care while on an inpatient unit if substance use is not assessed systematically and comprehensively [51]. Thus, screening and assessment should not be reserved only for research studies but rather must be integrated into routine clinical care and treatment planning.

Given neurodevelopmental vulnerability, any and all substance use among adolescents merits clinical intervention, especially among those with comorbid psychiatric concerns [26]. Early intervention has the potential to reduce the severity and persistence of substance use related problems [52]. The inpatient unit also provides a unique opportunity where motivation to change behavior may be higher and access to substances is limited, likely resulting in at least temporary cessation of use. Further, given there is evidence that youth present to mental health services before substance use services [9, 10], psychiatric hospitalizations may present a key opportunity for early intervention and/or referral to treatment. There is a critical need for further research of substance use on youth in psychiatric inpatient settings to inform the development of best practice guidelines and standardized clinical practices.

The existing study was a pilot study of 100 youth and 38 RNs and CYWs at a single institution. Generalizability of findings pertaining to youth is limited due to the small sample size, predominately female sex and White race, and data collection and visit history only obtained at one hospital site. While youth 12 years of age were eligible to participate, no 12 year olds were recruited into the study. This is likely due to the older age distribution of youth admitted to the inpatient units in Canada, where 15–17 year olds account for the highest rates of psychiatric hospitalizations (72%) [17]. Additionally, no youth with a diagnosis of psychosis or bipolar disorder were included in the final sample. In Canada and the US, depression is typically the most common reason for psychiatric hospitalization among adolescents [33, 53–56], which was also found in our sample. In 2019 across Canada, psychotic disorders represented a small proportion of psychiatric admissions for adolescents (< 5%) [17]. Thus, we believe our sample is representative of the majority of adolescent psychiatric hospitalizations in Canada but does not generalize to a small proportion of youth unable to safely and cognitively consent or provide accurate histories, potentially due to young age (≤ 12) and altered mental status such as acute symptoms of mania and/or symptoms of psychosis (based on our study inclusion criteria). Future studies should consider developing and evaluating alternative assessments methods for patients who do not meet these criteria. Further, although we had high frontline staff response rates, generalizability of the staff results is also limited due to the small sample size at a single institution, in addition to only including regular full-time and part-time RNs and CYWs (to preserve anonymity). Future work should

include staff feedback from the broader multidisciplinary and leadership team. Overall, recruitment rates were high among those meeting eligibility criteria, increasing confidence in the local representativeness of the sample.

Regarding measurement, gold standard urine drug screens, timeline follow-back, and clinical diagnostic interviews were not used to assess substance use and mental health concerns, but psychometrically validated measures were used alongside chart reviews providing multiple sources for information. Social desirability bias is of particular concern for self-reported data and may have resulted in underestimations of substance use [57]. Although we were unable to completely eliminate risk of social desirability bias, strategies to mitigate bias were used including exclusively requiring youth consent to participate (and not parent) [35, 36], using self-reported as opposed to interview-administered measures, and incorporating reminders about privacy and confidentiality during the consent process and embedded reminders throughout the assessment [12]. Of note, the willingness to complete may have been influenced by confidentiality and the provision of a $10 incentive, which is not viable in routine clinical practice. However, information collected directly by clinical staff can support direct use of this data to inform treatment planning, referrals, and shared decision making with patients that may increase patient engagement without the need for an incentive. Additionally, clinical correlations should be interpreted as preliminary evidence and require further examination in larger samples with multivariable adjustments for potential confounders.

Conclusions

In conclusion, the present study found that a majority of youth presenting to an inpatient psychiatric unit were engaging in recent substance use, often involving multiple substances, and provides preliminary evidence which supports the use of standardized substance use and mental health assessments during youth psychiatric hospitalizations. Subsequent studies should examine the feasibility and associated costs of having clinicians conduct standardized assessments, versus research assistants. Frontline staff in this study saw the need for standardized comprehensive assessments to improve clinical conceptualization and quality of care. By embedding standardized assessments directly into clinical practice, data becomes useful for: (1) direct patient care, by informing patient conceptualization, treatment pathways, and discharge planning; (2) program evaluation, by characterizing patients and providing insight into quality improvement strategies; and (3) enabling comprehensive and sustainable integration of research. Future work should include co-development and refinement of standardized assessments and related clinical uses with youth, staff, and their families. Combining research and clinical practice will facilitate bridging current policy and clinical gaps while efficiently addressing and mitigating critical research gaps.

Abbreviations

ADHD: Attention Deficit Hyperactivity Disorder; AUDIT: Alcohol Use Disorder Identification Test; BPG: Best Practice Guideline; CAMP: Cannabis, Alcohol, Mental health, and Patterns of service use; CD: Conduct Disorder; CEDIS: Canadian Emergency Department Information System; CIHI: Canadian Institute for Health Information; CYW: Child and Youth Worker; CUDIT-R: Cannabis Use Disorder Identification Test-Revised; DAD: Discharge Abstract Database; ED: Emergency Department; GAD: Generalized Anxiety Disorder; HED: Heavy Episodic Drinking; K6: Kessler-6; MDE: Major Depressive Episode; NACRS: National Ambulatory Care Reporting System; OCHS: Ontario Child Health Study; OCHS-EBS: Ontario Child Health Study-Emotional Behavioural Scales; ODD: Oppositional Defiant Disorder; OSDUHS: Ontario Student Drug Use and Health Survey; RA: Research Assistant; RECORD: REporting of studies Conducted using Observational Routinely-collected health Data; RN: Registered Nurse; SP: Social Phobia; STROBE: Strengthening the Reporting of Observational Studies in Epidemiology; SUD: Substance Use Disorder.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13034-021-00403-4.

Additional file 1. Youth baseline survey.

Additional file 2. Chart reviews.

Additional file 3. Staff survey.

Additional file 4. Reporting guidelines.

Additional file 5. Detailed methods and results.

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Authors' contributions

JH conceived of and designed the study. JH led the data collection, data analysis, and writing of the paper. RW assisted with youth and staff primary data collection and analysis. ZN assisted with chart reviews and descriptive analysis. LH, CM, JM, MA, and KG provided methodological and substantive support throughout the study design and manuscript process. All authors read and approved the final manuscript.

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Availability of data and materials

The data used for this study are not publicly available due to its sensitive clinical nature. Data are available from the corresponding author upon reasonable request and will be subject to further ethics approval.

Declarations

Ethics approval and consent to participate
Ethics approval was obtained from the Hamilton Integrated Research Ethics Board (ID 7075) and study procedures were approved by the Child and Youth Mental Health Research Advisory Committee. Informed consent was obtained directly from youth, and not parents, in order to mitigate bias in reporting substance use [31, 32], and to maintain parameters of confidentiality. Our focus on capacity rather than age, is consistent with the Tri-Council Policy Statement, Health Care Consent Act, and previous research demonstrating that youth 12 years of age or older are often capable of consent [33]. All methods were carried out in accordance with relevant guidelines and regulations.

Consent for publication
Not applicable.

Competing interests
JM is a principal and senior scientist in BEAM Diagnostics, Inc; no BEAM products or services were used in the current work. JH, LH, MA, CM, ZN, RW, and KG have no competing interests to declare.

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Publisher's Note

Chapter 4: Select Supplementary Materials

All additional files available here: https://doi.org/10.1186/s13034-021-00403-4

Additional File 2: Chart Reviews

2.1 Summary of Visit History Methods

The list of 99 study participants provided by the researcher was linked, by chart number, to CIHI DAD (inpatient) and NACRS (ambulatory) databases to identify visits within 3 years prior and 6 months following the index visit, that met the following criteria:

1. **DAD**: 3-year prior visits = inpatient encounters where the index admit date - prior admit date < 1096 days; 6-month readmissions = inpatient encounters where the index discharge date - readmit date < 184 days. Include mental health and substance misuse encounters coded with any one of the following most responsible diagnoses (MRDx): Mental health codes (F*), Problems related to living in resd inst (Z593), Oth symptoms signs inv emotional state (R458), Probs relationship w parents & in laws (Z631), Poisoning by drugs, medications and biological substances (self-harm) (T36-T50), Stress not elsewhere classified (Z733).
2. **NACRS:** 3-year prior visits = ED visits where the index admit date - ED triage date < 1096 days; 6 months revisits = ED visits where the index discharge date - ED triage date < 184 days. Includes mental health and substance misuse ED visits coded with any one of following presenting complaint groupings, presenting complaints, or most responsible diagnoses (MRDx): Presenting complaint groupings related to Mental Health (351–400) and Substance Misuse (751–800); Presenting complaint of Anorexia; MRDx including Mental health codes (F*) and Oth symptoms signs inv emotional state (R458).

2.2 Summary of Data Extraction Content

Data type	Time	Content
Service utilization	Prior to hospitalization	Mental health ED presentations
		Psychiatric emergency admissions
		Inpatient psychiatric admissions
		Any previous mental health inpatient admission
		If the youth was connected to an outpatient mental health service or family physician prior to their admissions
	Current hospitalizations	Length of stay
	6-month follow-up	# of total ED presentations
		# psychiatric emergency admissions
		# psychiatric inpatient admissions
		For psychiatric emergency and inpatient admits: length of stay
Clinical severity and complexity	Current hospitalization (Clinical chart review from inpatient admission)	Suicidal ideation and/or attempt
		Medical instability from attempt
		Non-suicidal self-harm
		# of previous suicide attempts
		Admission homicidal behaviours or thoughts
		Historical homicidal behaviours or thoughts
		Aggressive behaviours
		Admission symptoms of psychosis
		#/types/reasons for restraints
		#/reasons egregious behavioural analyses (EBA)
		Substance use information
		Working admission diagnosis
		Discharge diagnoses
	6-month follow-up	For mental health related admissions: discharge diagnosis

2.3 Discharge Diagnoses (Summary Note)

Discharge Diagnoses According to Discharge Summary Notes		
Category	**# patients >= 1 within category**	**Discharge Diagnosis**
Borderline personality, Cluster B, and emotion dysregulation related diagnoses	41	Borderline personality disorder; Borderline personality disorder features/traits; Borderline personality traits (with dissociative symptoms); Borderline personality disorder (with significant emotional dysregulation and poor impulse control); Emerging borderline personality traits; Borderline personality disorder with features of PTSD; Cluster B/C traits or mixed personality traits (Borderline, Obsessive compulsive traits); Cluster B/C traits(prominent OCP traits); Cluster B traits/features; Cluster B (emotional dysregulation); Cluster B (with gender dysphoria); emotional dysregulation
Depressive-related diagnoses	43	[chronic] Major Depressive Disorder; Major depressive disorder; Major depressive episode; Persistent depressive disorder; Unspecified depressive disorder vs. major depressive disorder; [unspecified] depressive disorder; Depression; Depressive symptoms
Anxiety and OCD Related Disorders	64	Social anxiety disorder; [unspecified] anxiety disorder; General anxiety disorder; "high" anxiety; School phobia; Anxiety; Social anxiety disorder (with symptoms of GAD); Social anxiety disorder (with panic attacks); General anxiety disorder (with panic attacks); Panic attacks; Panic disorder; Severe obsessive compulsive disorder; Obsessive compulsive disorder; body dysmorphic disorder

Trauma and stressor related disorders	31	(historic) PTSD; PTSD; PTSD features complex trauma; *borderline personality disorder with features of PTSD acute stress disorder; Unspecified trauma and stressor related disorder; Adjustment disorder; Chronic adjustment disorder; Adjustment disorder with disturbance of mood and conduct; Adjustment disorder with depressive symptoms/depressive symptoms; Adjustment disorder with depressed mood; Adjustment disorder secondary to unresolved grief; Adjustment disorder with depressed social anxiety disorder; [insecure] attachment disorder
ADHD and other neurodevelopmental disorders	20	ADHD; ADHD (combined); Historic/previous ADHD; Learning disorder; Learning disorders (areas of reading and math); Comorbid NVLD; intellectual difficulties
Eating disorders	12	anorexia nervosa; anorexia nervosa (restrictive type); atypical anorexia nervosa; anorexia nervosa (binge/purge subtype); [unspecified] eating disorder; OFSED
Problems with family relations	17	Parent-child relational difficulties/conflict; Child conflict; Significant Family stressors and conflict
SUDs	10	Substance use disorder; Poly-substance use disorder (cannabis and alcohol); Cannabis use disorder; Alcohol use disorder; Nicotine use disorder
Other	14	Gender dysphoria, Cluster C personality disorder, somatic symptom and related disorders disruptive, impulsive control, and conduct disorders, neurocognitive disorders, or no direct disorder.

2.4 Most Responsible Discharge Diagnosis

Collapsed Discharge Diagnoses	n	Specific Index discharge diagnosis	Fcode
Depressive-related disorders	29	Depressive episode unspecified	F329
		Sev. depressive episode wo psych symptoms	F322
		Rec depressive disrd curr. episode mod	F331
Anxiety and OCD related disorders	22	Anxiety disorder (unspecified)	F419
		Generalized anxiety disorder	F411
		Panic disrd [ep paroxysmal anxiety]	F410
		Social anxiety disorder of childhood	F932
		Other specified anxiety disorders	F418
		Obsessive compulsive disorder NOS	F429
Trauma and stressor disorder	21	Adjustment disorder(s)	F432
		Post-traumatic stress disorder	F431
		Acute stress reaction	F430
Borderline personality, Cluster B, and emotion dysregulation related diagnoses	5	Emotionally unstable personality disrd	F603
ADHD and other neurodevelopmental disorders	5	Disturbance of activity and attention	F900
		Development disrd scholastic skills NOS	F819
Other	17	Feeding and eating disorders, substance use and addictive disorders, somatic symptoms and related disorders, disruptive, impulsive control and conduct disorders or other reasons that did not directly map on to a specific psychiatric disorder	F500, F501, F989, F949, K922, F649, F129, F129, R458, G9388, T432, F459, F452, F388, F913, F919

Additional File 5: Detailed Methods & Results

1. Pilot Sample Size Calculations

Pilots do not require sample size calculations and do not need to be adequately powered for a particular effect sizes[48]. Therefore, we aimed to recruit a sample large enough to provide enough information to guide the methods and processes for a future full-scale study. Firstly, we considered prevalence of cannabis and alcohol use. Among a general population sample of grade 7-12 students in Ontario during the 2016/2017 academic year, 12.1% and 16.9% endorsed using cannabis and engaging in heavy drinking in the past month respectively[53]. Cannabis and heavy drinking are even more common among individuals with mental health concerns[7]. Of note, prevalence of cannabis use has been increasing among Canadian youth in recent years[107]. Further, using the School Mental Health Surveys - a similar representative sample of grade 6-12 students across Ontario during the 2014/2015 academic year - prevalence estimates of occasional or regular cannabis use and heavy drinking were, respectively, 1.7 and 1.5 times more compared to the general population among youth endorsing high levels of internalizing and externalizing symptoms (i.e., 1 SD or greater than the general sample). Given general population estimates, we anticipated that among 100 youth, a minimum of 20 and 25 youth would endorse at least monthly cannabis use and heavy drinking respectively. We anticipated these numbers would be higher given recent increasing trends in youth cannabis use alongside national cannabis legalization and the acuity of the sample. Secondly, we considered precision around feasibility estimates, basing success of the pilot around the 95% confidence interval (CI) of recruitment and follow-up[48].

Of note, using G*Power software[108], it was determined that a total sample size of 1230 will be required for the full study to analyze associations between substance use and clinical characteristics and service use, assuming a small difference in means (d=0.2), using a 2-sided independent t-test, with an a=0.05, B=0.2, and 4:1 difference in group membership (i.e. if n_{nouse}=80% and n_{use}=20%, the allocation ratio n_{nouse}/ n_{use}=4). Estimates of effect sizes come from a recent meta-analysis of the general population which found point estimates between cannabis use and developing depression, anxiety and suicidal

ideation to be 1.37, 1.18, and 1.5 respectively[109]. Therefore, our study represents less than 10% of the target sample size for an adequately powered analysis to find a small significantly difference between youth who use cannabis versus those that do not, although this may be an underestimation of prevalence of youth in this sample and effect estimates in the target acute population.

2. Follow-up Missingness Analysis

Univariable logistic regressions predicting 6-month follow-up missingness (missing=1).

	OR (SE)	**P value**
Mental Health Severity		
Total OCHS-EBS	1.00 (0.015)	0.989
Internalizing OCHS-EBS	0.948 (0.030)	0.079
Externalizing OCHS-EBS	1.03 (0.022)	0.180
Psychological distress (K6)	0.913 (0.043)	0.034
Psychosis symptoms	1.05 (0.047)	0.302
Nonsuicidal self-injury	0.605 (0.277)	0.070
Suicide attempt	0.775 (0.267)	0.388
Aggression	1.197 (0.239)	0.451
Mental Health Complexity		
OCHS diagnosis count (self-reported)	0.994 (0.12)	0.960
Physician reported diagnoses count (physician-reported)	1.066 (0.134)	0.635
Hospital Service Use History		
Prior psychiatric inpatient admission	0.690 (0.411)	0.368
Prior psychiatric ED visit	0.420 (0.414)	0.036
Substance Use Frequency		
Cannabis	0.914 (0.180)	0.617
Alcohol	0.755 (0.174)	0.108
Tobacco Cigarettes	1.021 (0.183)	0.908
E-cigarettes	0.928 (0.178)	0.676
Prescription Drug Misuse	0.796 (0.237)	0.337
Other Drug use	0.760 (0.264)	0.299
Demographics		
Female Gender (ref male)	0.684 (0.451)	0.401
Transgender or Gender Diverse (ref male)	0.353 (0.945)	0.270
Female Sex	0.606 (0.532)	0.346
Age	0.924 (0.166)	0.632
Self-Reported Social Status	0.971 (0.121)	0.808
White Race/ethnicity	0.579 (0.453)	0.228

3. Substance Use Disaggregated by Sex and Gender

Substance	**Time Period** (ref to index)	**Total Sample** (n=100)	**Female Sex** (n=82)	**Male Sex** (n=18)	**Transgender or Gender Diverse** (n=19)	**Cisgender** (n=81)
Alcohol	lifetime	73%	61 (74%)	12 (67%)	16 (84%)	57 (70%)
	3 months	51%	42 (51%)	9 (50%)	12 (63%)	39 (48%)
	HED past month	29%	24 (29.3%)	5 (27.8%)	4 (21.1%)	25 (30.9%)
	AUDIT>=8 (for those who used)	23 (47%)	21 (52.5%)	2 (22.2%)	5 (45.5%)	18 (47.4%)
Cannabis	lifetime	66%	53 (65%)	13 (72%)	13 (68%)	53 (65%)
	3 months	50%	39 (48%)	11 (61%)	9 (47%)	41 (51%)
	daily past month	18%	14 (17.1%)	4 (22.2%)	3 (15.8%)	15 (18.5%)
	CUDIT>=8 (of those how have used)	32 (64%)	24 (61.5%)	8 (72.7%)	6 (66.7%)	26 (63.4%)
Tobacco	lifetime	47%	39 (48%)	8 (44%)	8 (42%)	39 (48%)
	3 months	33%	29 (35%)	4 (22%)	7 (37%)	26 (32%)
	daily past month	14%	14 (17.1%)	0	4 (21.2%)	10 (12.3%)
E-cigarettes	lifetime	42%	34 (42%)	8 (44%)	7 (37%)	35 (43%)
	3 months	34%	29 (35%)	5 (28%)	5 (26%)	29 (36%)
	daily past month	14%	13 (15.9%)	1 (5.6%)	2 (10.5%)	12 (14.8%)
Prescription Opioids	lifetime	22%	17 (21%)	5 (28%)	4 (21%)	18 (23%)
	3 months	18%	14 (18%)	4 (22%)	4 (21%)	14 (18%)
Any Alcohol, Cannabis, or Tobacco	3 months	66%	52 (63%)	14 (78%)	14 (74%)	53 (64%)
Any Prescription drug	3 months	24%	18 (22%)	6 (33%)	4 (21%)	20 (25%)
Any Illicit substance use	3 months	17%	14 (17%)	3 (17%)	2 (11%)	15 (19%)
Any substance use	3 months	69%	55 (67%)	14 (78%)	15 (79%)	54 (67%)

4. Substance Use Disorder Scores and Exploration

Table 4.1. Correlations between CUDIT scores and other cannabis and substance use variables.

	Kendall's Tau	Baseline CUDIT total score
Baseline frequency of cannabis use	Correlation Coefficient	.542**
	Sig. (2-tailed)	.000
	N	50
How old were you the first time you used cannabis?	Correlation Coefficient	-.037
	Sig. (2-tailed)	.726
	N	50
What percentage of THC is in the cannabis you usually use?	Correlation Coefficient	.108
	Sig. (2-tailed)	.544
	N	19
What percentage (%) of CBD is in the cannabis you usually use?	Correlation Coefficient	.025
	Sig. (2-tailed)	.909
	N	14
Baseline Marijuana Coping Motives Score	Correlation Coefficient	.250*
	Sig. (2-tailed)	.021
	N	45
Coping Motive Item 1: To forget my worries	Correlation Coefficient	.248*
	Sig. (2-tailed)	.032
	N	45
Coping Motive Item 2: Because it helps me when I feel depressed or nervous	Correlation Coefficient	.252*
	Sig. (2-tailed)	.030
	N	45
Coping Motive Item 3: To cheer me up when I am in a bad mood	Correlation Coefficient	.380**
	Sig. (2-tailed)	.001
	N	45
Coping Motive Item 4: To forget about my problems	Correlation Coefficient	.283*
	Sig. (2-tailed)	.015
	N	45
Coping Motive Item 5: Because I feel more self-	Correlation Coefficient	.097
	Sig. (2-tailed)	.402
	N	45

confident and sure about myself		
Baseline frequency of alcohol use	Correlation Coefficient	.194
	Sig. (2-tailed)	.075
	N	50
Baseline past month any alcohol use or binge drinking	Correlation Coefficient	.106
	Sig. (2-tailed)	.349
	N	50
Baseline Alcohol Coping Motives Score	Correlation Coefficient	.003
	Sig. (2-tailed)	.981
	N	40
Tobacco use at Baseline	Correlation Coefficient	.131
	Sig. (2-tailed)	.232
	N	50
E-cigarette use at Baseline	Correlation Coefficient	.121
	Sig. (2-tailed)	.272
	N	50
Any prescription drug misuse in 3months prior to admission	Correlation Coefficient	.151
	Sig. (2-tailed)	.208
	N	50
Any illicit substance use in 3months prior to admission	Correlation Coefficient	.182
	Sig. (2-tailed)	.129
	N	50

Predicting CUDIT Scores

Using forward selection based on bivariate correlations, linear regression revealed that questions regarding frequency of cannabis use and coping motives explain 60.4% of the variance (adjusted R^2 0.585). This model fit better than frequency of cannabis alone (adjusted R^2 0.501). Adding frequency of using with others did not increase adjusted variance explained (adjusted R^2 0.582). Among those who also used tobacco, frequency of co-use was not significant after adjusting for frequency and motives.

Table 4.3. Correlations between AUDIT scores and other alcohol and substance use variables.

	Kendall's Tau	Baseline AUDIT total score
Baseline frequency of alcohol use	Correlation Coefficient	.537**
	Sig. (2-tailed)	.000
	N	49
Baseline past month any alcohol use or binge drinking	Correlation Coefficient	.551**
	Sig. (2-tailed)	.000
	N	49
Baseline Alcohol Coping Motives Score	Correlation Coefficient	.541**
	Sig. (2-tailed)	000
	N	44
Motives Item 1. To forget my worries	Correlation Coefficient	.451**
	Sig. (2-tailed)	.000
	N	44
Motives Item 2. Because it helps me when I feel depressed or nervous	Correlation Coefficient	.475**
	Sig. (2-tailed)	.000
	N	44
Motives Item 3. To cheer me up when I am in a bad mood	Correlation Coefficient	.481**
	Sig. (2-tailed)	.000
	N	44
Motives Item 4. To forget about my problems	Correlation Coefficient	.457**
	Sig. (2-tailed)	.000
	N	44
Motives Item 5. Because I feel more self-confident and sure about myself	Correlation Coefficient	.501**
	Sig. (2-tailed)	.000
	N	44
Are other people with you when you drink alcohol?	Correlation Coefficient	-.209
	Sig. (2-tailed)	.083
	N	44
Baseline frequency of cannabis use	Correlation Coefficient	.204
	Sig. (2-tailed)	.054
	N	49

How often did you use alcohol and cannabis on the same occasion?	Correlation Coefficient	.337**
	Sig. (2-tailed)	.008
	N	38
Tobacco use at Baseline	Correlation Coefficient	.424**
	Sig. (2-tailed)	.000
	N	49
E-cigarette use at Baseline	Correlation Coefficient	.295**
	Sig. (2-tailed)	.008
	N	49
Any prescription drug misuse in 3 months prior to admission	Correlation Coefficient	.212
	Sig. (2-tailed)	.082
	N	49
Any illicit substance use in 3 months prior to admission	Correlation Coefficient	.234
	Sig. (2-tailed)	.055
	N	49

Predicting AUDIT scores

Using forward selection based on bivariate correlations, linear regression revealed that questions regarding past month drinking (split into none, any but no HED, and HED) alongside coping motives for drinking explain 57.7% of the variance (adjusted R^2 0.557). This model fit better than past month drinking/HED alone (R^2 0.379) or coping motives alone (R^2 0.407). Adding frequency of tobacco use to the regression did not improve the model (adjusted R^2 0.553). Among those who also used cannabis, frequency of co-use slightly improved prediction to 59.9% (adjusted R^2 0.564). Of note, frequency of solitary use did not improve model fit.

5. Substance Use and Clinical Severity

Part A: Substance use and clinical severity at index

Indicators of clinical psychiatric severity were operationalized based on clinician-reports from chart reviews and based on youth self-reported surveys.

Severity indicators from charts used for correlation analyses included:

1. Suicide plan (1) and attempt (2) compared to ideation or none (0). Response options of none and suicidal ideation were collapsed as only 1 patient indicated no suicide related thoughts or behaviours.
2. Self-harm previous (1) and current (2) versus none (0).
3. Aggression categories were collapsed based on overlap and frequencies into aggressive threats or aggression without harm (1), aggression resulting in property damage or harm to others (2), and none (0). Some youth fell into multiple domains and the highest level of aggression reported was coded in this indicator.

Several severity indicators from chart reviews were not included in subsequent analyses due to low frequency counts and/or missing data/lack of clarity, including:

- Patient (19 missing), parent (33 missing), and clinician (n<10) reported psychosis, bizarre, or disorganized behaviour documented in the medical record.
- Homicidal ideation, plans, or attempts (n<10) documented in medical record.
- Use of restraints (n<10) or an egregious behaviour analyses (n<10) while on the unit documented in medical record.

Severity indicators from self-reported youth surveys included: 1) OCHS-EBS measures for Social Phobia (SP), Generalized Anxiety Disorder (GAD), Major Depressive Disorder (MDE), Attention Deficit Hyperactivity Disorder (ADHD), Oppositional Defiant Disorder (ODD), Conduct Disorder (CD); 2) K6 for general psychological distress; 3) Psychosis symptoms score.

Kendall's Tau correlations		suicidal ideation, plan, & attempt	Non-suicidal self-harm	Aggressive threats & behaviours
Cannabis use	Correlation	0.167	0.128	.227*
	Sig. (2-tailed)	0.057	0.159	0.016
	N	98	94	87
Alcohol use	Correlation	0.15	0.063	.212*
	Sig. (2-tailed)	0.087	0.486	0.025
	N	98	94	87
Tobacco use	Correlation	.227*	0.142	.324**
	Sig. (2-tailed)	0.011	0.126	0.001
	N	98	94	87
E-cigarette use	Correlation	0.094	0.092	0.136
	Sig. (2-tailed)	0.295	0.322	0.159
	N	98	94	87
Prescription drug misuse	Correlation	0.136	0.113	.262**
	Sig. (2-tailed)	0.142	0.24	0.009
	N	98	94	87
Illicit drug misuse	Correlation	0.044	0.131	.282**
	Sig. (2-tailed)	0.631	0.169	0.005
	N	98	94	87
Cannabis Coping Motives Score	Correlation	-.059	-.012	-.068
	Sig. (2-tailed)	.636	.921	.595
	N	44	44	41
Alcohol Coping Motives Score	Correlation	-.019	.117	.159
	Sig. (2-tailed)	.881	.347	.215
	N	45	45	42
CUDIT	Correlation	.160	-.110	.039
	Sig. (2-tailed)	.165	.347	.749
	N	49	49	44
AUDIT	Correlation	.148	.094	.281*
	Sig. (2-tailed)	.206	.431	.022
	N	48	47	44
Using cannabis with others	Correlation	-.073	-.126	-.085
	Sig. (2-tailed)	.574	.342	.530
	N	44	44	41
Using alcohol with others	Correlation	-.074	-.205	-.113
	Sig. (2-tailed)	.582	.130	.416
	N	45	45	42

Kendall's Tau Correlations (self-report severity)		SP	GAD	MDE	ADHD	ODD	CD	Psychosis	K6
Cannabis use (n=100)	Correlation Coefficient	-0.076	0.007	0.075	0.128	.266**	.309**	0.028	0.035
	Sig. (2-tailed)	0.346	0.93	0.344	0.102	0.001	0	0.721	0.652
Alcohol use (n=100)	Correlation Coefficient	0.054	0.038	0.105	0.073	.210**	.250**	0.059	0.152
	Sig. (2-tailed)	0.502	0.632	0.186	0.35	0.008	0.002	0.456	0.051
Tobacco use (n=100)	Correlation Coefficient	0.005	0.069	0.071	.185*	.295**	.447**	0.133	0.065
	Sig. (2-tailed)	0.952	0.397	0.377	0.021	0	0	0.099	0.412
E-cigarette use a(n=100)	Correlation Coefficient	-0.021	0.05	0.107	0.14	.259**	.300**	0.083	0.115
	Sig. (2-tailed)	0.802	0.543	0.188	0.081	0.001	0	0.304	0.149
Prescription drug misuse (n=100)	Correlation Coefficient	.208*	.245**	.279**	.168*	.230**	.319**	0.116	.195*
	Sig. (2-tailed)	0.014	0.004	0.001	0.042	0.005	0	0.163	0.017
Illicit drug use (n=100)	Correlation Coefficient	0.081	0.137	.174*	.206*	.274**	.374**	0.129	0.04
	Sig. (2-tailed)	0.338	0.102	0.037	0.012	0.001	0	0.122	0.627
Cannabis coping motives (n=45)	Correlation Coefficient	.293**	.398**	0.206	0.001	0.052	0.04	-0.014	.301**
	Sig. (2-tailed)	0.009	0	0.065	0.992	0.635	0.714	0.897	0.006
Alcohol coping motives (n=46)	Correlation Coefficient	0.128	.302**	.236*	.320**	.299**	.316**	0.137	.276*
	Sig. (2-tailed)	0.259	0.007	0.033	0.004	0.007	0.004	0.216	0.012
AUDIT total score (n=49)	Correlation Coefficient	0.02	0.123	0.186	.289**	.336**	.444**	.364**	0.157
	Sig. (2-tailed)	0.853	0.25	0.077	0.006	0.001	0	0.001	0.134
CUDIT total score (n=50)	Correlation Coefficient	-0.094	0.015	0.072	-0.041	0.002	-0.005	0.136	0.105
	Sig. (2-tailed)	0.371	0.885	0.488	0.686	0.987	0.96	0.189	0.304
Using cannabis with others (n=45)	Correlation Coefficient	-0.172	-0.14	-0.112	0.049	0.054	0.108	-0.164	-0.138
	Sig. (2-tailed)	0.148	0.234	0.34	0.671	0.642	0.352	0.159	0.234
Using alcohol with others (n=46)	Correlation Coefficient	-0.103	-0.167	-0.067	-0.111	-0.143	-0.117	-.470**	-.298*
	Sig. (2-tailed)	0.405	0.174	0.579	0.353	0.232	0.325	0	0.013

Part B: Substance use and clinical severity at follow-up

6-month follow-up self-reported psychiatric symptoms as per the OCHS-EBS were predicted by frequency of the most commonly used substances at index admission (i.e., cannabis, alcohol, tobacco cigarettes, and e-cigarettes) and whether youth increased, decreased, or kept their use the same at 6-month follow-up. Linear regressions were performed adjusting for index psychiatric symptoms.

	Follow-up Internalizing Symptoms		Follow-up Externalizing Symptoms		Follow-up Total symptoms	
Baseline Cannabis	1.9 (0.7) p=0.013	2.2 (0.8) p=0.008	0.89 (0.99) p=0.372	1.1 (1.0) p=0.297	2.4 (1.5) p=0.032	3.8 (1.6) p=0.023
Increased (n=10)		0.5 (2.1) p=0.809		2.9 (2.6) p=0.256		3.9 (4.0) p=0.333
Decreased (n=8)		-3.0 (2.5) p=0.232		-2.4 (3.0) p=0.426		-5.0 (4.7) p=0.288
Baseline Alcohol	1.3 (0.7) p=0.091	1.6 (0.9) p=0.066	0.8 (0.9) p=0.373	1.5 (1.1) p=0.189	2.5 (1.4) p=0.096	3.6 (1.7) p=0.038
Increased (n=13)		0.1 (2.1) p=0.977		-0.6 (2.5) p=0.805		-0.9 (4.0) p=0.830
Decreased (n=15)		-1.9 (2.4) p=0.443		-3.0 (2.8) p=0.293		-5.8 (4.4) p=0.199
Baseline Tobacco cigarettes	2.2 (0.8) p=0.006	1.7 (0.9) p=0.066	1.9 (1.0) p=0.059	1.7 (1.2) p=0.162	4.6 (1.5) p=0.004	4.1 (1.8) p=0.031
Increased (n=7)		2.9 (2.5) p=0.24		3.4 (2.9) p=0.251		6.1 (4.6) p=0.187
Decreased (n=9)		1.9 (2.5) p=0.451		0.7 (3.1) p=0.833		2.3 (4.8) p=0.629
Baseline E-cigarettes	1.8 (0.7) p=0.018	1.9 (0.7) p=0.016	0.5 (0.9) p=0.599	0.8 (0.9) p=0.394	2.7 (1.5) =0.077	3.0 (1.4) p=0.043
Increased (n=11)		4.0 (2.0) p=0.050		5.4 (2.5) p=0.034		10.4 (3.7) p=0.008
Decreased (n=8)		0.5 (2.3) p=0.842		-0.4 (3.0) p=0.890		1.5 (4.5) p=0.734

6. Substance Use and Clinical Complexity

Indicators of clinical psychiatric complexity were operationalized based on clinician-diagnoses from chart reviews and based on youth self-reported surveys.

Complexity indicators from the charts included:

- Number of diagnoses at discharge
- Number of categories of diagnoses at discharge (excluding other)
    - Categories included: anxiety and OCD, depressive related, cluster-B/BPD, trauma and stressor related, ADHD and neurodevelopmental, Eating disorders, Problems with family relations, and SUDs.

Complexity indicators from the youth survey included:

- Number of OCHS-EBS symptom scores surpassing population thresholds
    - Total number (i.e., GAD, SP, MDE, ADHD, ODD, and CD)
    - # internalizing (i.e., GAD, SP, MDE)
    - # externalizing (i.e., ADHD, ODD, CD)
    - INT & EXT

With the exception of INT&EXT, conservative non-parametric Kendall's Tau correlations (τb) were performed, whereby $p<0.05$ indicated significant correlations. Point-biserial (r_{pb}) were used for INT&EXT correlations.

Kendall's Tau & Point-biserial correlations for complexity		self-report total count	self-report int count	self-report ext count	self-report int & ext	total physician count	category physician count
Cannabis use (n=100)	Correlation Coefficient	.212**	0.029	.289**	.209*	0.04	0.117
	Sig. (2-tailed)	0.009	0.727	0.001	0.037	0.63	0.162
Alcohol use (n=100)	Correlation Coefficient	.200*	0.09	.215*	0.181	0.009	0.093
	Sig. (2-tailed)	0.013	0.285	0.012	0.071	0.911	0.269
Tobacco use (n=100)	Correlation Coefficient	.280**	0.049	.367**	.357**	0.122	0.167
	Sig. (2-tailed)	0.001	0.571	0	0	0.147	0.05
E-cigarette use (n=100)	Correlation Coefficient	.284**	0.083	.324**	.286**	0.074	0.141
	Sig. (2-tailed)	0.001	0.335	0	0.004	0.382	0.1
Prescription drug misuse (n=100)	Correlation Coefficient	.360**	.334**	.229*	.321**	.173*	.197*
	Sig. (2-tailed)	0	0	0.012	0.001	0.047	0.026
Illicit drug use (n=100)	Correlation Coefficient	.341**	.191*	.317**	.273**	0.114	.200*
	Sig. (2-tailed)	0	0.031	0	0.006	0.189	0.023
Cannabis coping motives (n=45)	Correlation Coefficient	.229*	.383**	-0.02	.331*	0.091	.358*
	Sig. (2-tailed)	0.044	0.001	0.868	0.027	0.43	0.016
Alcohol Coping Motives (n=46)	Correlation Coefficient	.412**	0.222	.372**	.539**	.297*	.540**
	Sig. (2-tailed)	0	0.058	0.002	0	0.01	0
CUDIT total score (n=50)	Correlation Coefficient	0.005	0.07	-0.029	0.126	0.12	0.116
	Sig. (2-tailed)	0.959	0.52	0.791	0.382	0.268	0.422
AUDIT total score (n=49)	Correlation Coefficient	.396**	0.132	.431**	.417**	0.121	.442**
	Sig. (2-tailed)	0	0.237	0	0.003	0.271	0.001
Using cannabis with others (n=45)	Correlation Coefficient	-0.043	-0.137	0.103	0.054	-0.064	0.049
	Sig. (2-tailed)	0.721	0.27	0.41	0.723	0.598	0.747
Using alcohol with others (n=46)	Correlation Coefficient	-0.187	-0.138	-0.134	-0.224	-0.12	-0.205
	Sig. (2-tailed)	0.129	0.28	0.298	0.135	0.34	0.172

7. Substance Use and Service Use

Methods. **Repeat ED visits and hospitalizations** were obtained through administrative records. Timelines were operationalized as: (1) 3 years prior to index; (2) 6 months prior to index; and (3) 6 months after index. ED visits and psychiatric hospitalizations were analyzed separately. Any mental health related ED visit was created through combining mental health and substance use ED visits. Any mental health inpatient admissions were identified by combining discharges from the Child and Youth Mental Health Inpatient unit and the Eating Disorder Inpatient unit. There may have been some youth who were discharged from other non-mental health related units who were missed – i.e., transferred to a medical unit prior to discharge – however, this is extremely rare and typically it occurs in the reverse whereby youth are medically cleared on a medical unit first and subsequently transferred to the mental health unit. **Logistic regressions** were conducted predicting any ED visit or any inpatient admission. All analyses were adjusted for whether the index admission was a direct admission (proxy for out of city) or through the local ED. Independent variables included: substance use frequencies (measure categorically and continuously), cannabis and alcohol coping motives scores, CUDIT and AUDIT scores, and proportion of time spent using cannabis and alcohol with others (whereby lower scores are reflective of a greater frequency of solitary use). ***Results.*** When looking at substance use frequencies, all substances (i.e., alcohol, cannabis, tobacco, e-cigarettes, prescription drugs, and illicit drugs) were significantly related to a higher likelihood of having had an inpatient admission in the 3 years prior. Prescription drug misuse was additionally related to a higher likelihood of ED presentations in the 3 years prior. E-cigarette use was additionally related to a higher likelihood of an ED visit 6 months after index. For cannabis and alcohol, coping motives and AUDIT/CUDIT scores were not related to hospital contacts. However, using alcohol alone was related to a greater likelihood of re-presenting to ED within 6 months and a having a prior inpatient admission in the past 3 years and 6 months. Using cannabis alone was related to a greater likelihood of an ED visit in the past 3 years and 6 months. Other visit types and timelines were not significant. Please see the table for full results.

Logistic regressions predicting any ED visit or any inpatient admission. All analyses adjusted for whether the index admission was a direct admission or through local ED. Presented as adjusted OR (95% CI); p value.

	ED visits			Inpatient Admissions		
	3-year prior	**6-months prior**	**6-months post**	**3-year prior**	**6-months prior**	**6-months post**
Substance use Factors						
Cannabis						
not past month (ref=never)	2.66 (0.81,8.77); p=0.108	1.83 (0.53,6.29); p=0.338	3.33 (0.91,12.12); p=0.069	7.65 (2.15,27.22); p=0.002	4.03 (1.01,16.08); p=0.048	1.71 (0.52,5.62); p=0.38
past month but not every day (ref=never)	1.43 (0.47,4.32); p=0.53	0.52 (0.13,2.06); p=0.353	1.66 (0.45,6.07); p=0.444	4.19 (1.31,13.41); p=0.016	2.57 (0.66,10.02); p=0.175	0.46 (0.13,1.71); p=0.249
daily (ref=never)	1.95 (0.57,6.68); p=0.289	0.8 (0.19,3.32); p=0.758	1.18 (0.27,5.18); p=0.828	3.65 (1.01,13.25); p=0.048	0.87 (0.14,5.34); p=0.883	0.54 (0.13,2.32); p=0.407
Continuous frequency score	1.18 (0.81,1.73); p=0.392	0.83 (0.54,1.29); p=0.412	1.03 (0.67,1.58); p=0.891	1.45 (1,2.11); p=0.048	1.03 (0.66,1.59); p=0.899	0.75 (0.49,1.15); p=0.191
Cannabis coping motives	0.99 (0.9,1.08); p=0.763	1 (0.9,1.12); p=0.965	1.08 (0.97,1.21); p=0.178	1.1 (0.99,1.21); p=0.062	1.01 (0.91,1.13); p=0.81	1.11 (0.95,1.28); p=0.186
CUDIT score	1.03 (0.95,1.12); p=0.47	1.02 (0.93,1.13); p=0.664	0.95 (0.87,1.04); p=0.274	1.06 (0.98,1.14); p=0.174	0.98 (0.89,1.07); p=0.615	1.03 (0.93,1.15); p=0.566
Frequency of use with others	0.58 (0.35,0.96); p=0.035	0.51 (0.26,1); p=0.049	0.62 (0.35,1.08); p=0.088	0.7 (0.44,1.11); p=0.126	0.56 (0.3,1.02); p=0.058	0.74 (0.4,1.37); p=0.336
Alcohol						
not past month (ref=never)	4.49 (1.3,15.47); p=0.017	1.29 (0.34,4.82); p=0.709	3.8 (0.98,14.71); p=0.053	10.87 (2.86,41.3); p=0	2.4 (0.53,10.91); p=0.258	1.26 (0.39,3.99); p=0.701
past month but not heavy (ref=never)	2.17 (0.56,8.34); p=0.261	1.41 (0.33,6.05); p=0.646	0.86 (0.16,4.53); p=0.86	3.14 (0.73,13.47); p=0.123	2.42 (0.46,12.62); p=0.294	0.73 (0.18,2.93); p=0.652
past month heavy (ref=never)	1.36 (0.42,4.41); p=0.612	0.87 (0.24,3.2); p=0.832	1.32 (0.35,5.04); p=0.684	4.69 (1.28,17.21); p=0.02	2.8 (0.65,12.08); p=0.168	0.27 (0.06,1.16); p=0.078
Continuous frequency score	1 (0.7,1.44); p=0.983	0.95 (0.64,1.43); p=0.813	0.94 (0.63,1.41); p=0.775	1.31 (0.92,1.85); p=0.135	1.31 (0.86,2.01); p=0.207	0.67 (0.44,1.01); p=0.057
Alcohol coping motives	0.98 (0.9,1.06); p=0.631	0.94 (0.85,1.03); p=0.172	1.06 (0.97,1.16); p=0.207	1.1 (1.01,1.2); p=0.023	1.06 (0.97,1.16); p=0.204	1.12 (0.99,1.27); p=0.085
AUDIT score	0.95 (0.85,1.07); p=0.397	0.95 (0.83,1.07); p=0.374	1.04 (0.93,1.16); p=0.486	1.06 (0.97,1.17); p=0.206	1.08 (0.97,1.2); p=0.15	0.98 (0.87,1.11); p=0.775

Frequency of use with others	0.79 (0.46,1.36); p=0.399	0.61 (0.35,1.07); p=0.083	0.52 (0.29,0.92); p=0.025	0.52 (0.29,0.92); p=0.025	0.42 (0.22,0.78); p=0.006	0.53 (0.27,1.04); p=0.066
Tobacco cigarettes						
less than monthly (ref=never)	1.08 (0.36,3.21); p=0.89	1.66 (0.51,5.35); p=0.398	1.89 (0.57,6.25); p=0.296	1.85 (0.65,5.31); p=0.25	1.54 (0.44,5.35); p=0.499	1.67 (0.55,5.07); p=0.369
monthly but less than daily (ref=never)	0.93 (0.24,3.59); p=0.921	0.96 (0.21,4.38); p=0.961	2.57 (0.62,10.64); p=0.193	3.45 (0.94,12.6); p=0.061	1.58 (0.35,7.12); p=0.552	1.11 (0.26,4.78); p=0.887
daily (ref=never)	2.15 (0.6,7.72); p=0.24	0.52 (0.1,2.76); p=0.439	0.99 (0.22,4.47); p=0.99	4.46 (1.28,15.54); p=0.019	2.01 (0.5,8); p=0.322	0.56 (0.11,2.83); p=0.479
frequency	1.2 (0.82,1.77); p=0.348	0.88 (0.56,1.37); p=0.564	1.14 (0.74,1.74); p=0.553	1.7 (1.16,2.49); p=0.007	1.26 (0.82,1.93); p=0.289	0.91 (0.59,1.4); p=0.654
E-cigarettes						
less than monthly (ref=never)	4.63 (1.04,20.62); p=0.045	2.18 (0.55,8.58); p=0.267	2.06 (0.47,8.95); p=0.337	3.11 (0.87,11.13); p=0.081	1.42 (0.32,6.21); p=0.642	0.63 (0.12,3.22); p=0.577
monthly but less than daily (ref=never)	0.6 (0.17,2.11); p=0.426	0.67 (0.16,2.83); p=0.584	1.99 (0.52,7.64); p=0.317	1.94 (0.61,6.17); p=0.262	1.54 (0.41,5.81); p=0.528	1.14 (0.31,4.16); p=0.84
daily (ref=never)	0.99 (0.27,3.63); p=0.987	0.63 (0.12,3.35); p=0.584	5.76 (1.31,25.4); p=0.021	3.04 (0.9,10.2); p=0.072	1.35 (0.31,5.82); p=0.692	1.26 (0.34,4.72); p=0.732
frequency	0.95 (0.65,1.38); p=0.783	0.87 (0.55,1.37); p=0.549	1.67 (1.08,2.58); p=0.022	1.44 (1.01,2.07); p=0.046	1.14 (0.75,1.75); p=0.535	1.07 (0.72,1.6); p=0.737
Prescription drug misuse						
not past 3 months (ref=never)	5.86 (1.28,26.87); p=0.023	1.23 (0.27,5.71); p=0.79	1.24 (0.26,5.79); p=0.785	2.63 (0.72,9.64); p=0.145	0.99 (0.19,5.23); p=0.988	0.57 (0.11,2.9); p=0.497
past 3 months (ref=never)	1.28 (0.46,3.52); p=0.635	0.74 (0.24,2.3); p=0.598	1.13 (0.38,3.32); p=0.832	3.16 (1.18,8.49); p=0.022	1.6 (0.53,4.82); p=0.401	0.51 (0.15,1.71); p=0.272
Illicit and other drug use						
not past 3 months (ref=never)	2.53 (0.78,8.2); p=0.121	1.5 (0.42,5.31); p=0.53	1.68 (0.47,6.07); p=0.429	7.41 (2.14,25.68); p=0.002	1.97 (0.57,6.79); p=0.282	1.52 (0.46,5.04); p=0.497
past 3 months (ref=never)	0.93 (0.3,2.95); p=0.905	0.89 (0.24,3.3); p=0.862	2.47 (0.74,8.3); p=0.143	1.57 (0.52,4.72); p=0.423	1.34 (0.37,4.88); p=0.662	1.52 (0.46,5.04); p=0.495

8. Staff Survey Detailed Summary of Results

There was an 86% response rate (37/43) with almost half RNs (49%) and half CYWs (51%). Differences between RNs and CYWs are to be expected in all domains given different scopes of practice, however both RNs and CYWs have a high degree of patient exposure and thus increased knowledge and confidence related to substance use would be prudent across both roles. Over half (54%) of the staff participating in the survey had been working on the unit 5 years or longer with only 2 staff reporting less than 1 year on the unit. Given the mandate of this unit is outside the scope of a substance treatment facility, specialized substance use training is not a requirement for the staff. As such, 84% of the staff had never received specialized substance use training. All closed ended questions had no missing data (with the exception of one item missing one respondent). Open ended questions were answered by 63% to 83% of the sample. Open-ended responses ranged from 1 to 6 sentences or bullet points, with typical responses to all questions being 2-3 sentences.

A majority of staff reported feeling fairly or completely **confident** in their knowledge of how alcohol, cannabis, and nicotine/tobacco impacted youth on the unit (RNs 56 to 78%; CYWs 68 to 74%), however, for other prescription and illicit drug misuse a minority of staff reported high confidence (RNs 22 to 50%; CYWs 16 to 37%). Open ended responses further elucidated higher confidence in assessing and addressing alcohol, cannabis, and tobacco/nicotine may be due to more frequent use by youth and existing protocols for Nicotine Replacement Therapy (NRT) on the unit and a greater need for education on other drugs and co-use of substances. Overall, staff expressed perceived importance of considering both occasional and regular substance use in the clinical conceptualization of youth admitted to the unit.

All staff indicated at least one barrier to a hypothetical incorporation of comprehensive substance use **assessments**, with the most common barriers being lack of training (RNs 72%; CYWs 95%) and time pressures (RNs 72%; CYWs 63%). No staff stated they felt uncomfortable talking about substances. Of note, RNs indicated conducting substance use screening during admission but identified areas to improve

comprehensiveness including more question prompts and space to document in the electronic medical record (EMR). Thus, many staff indicated that adding designated space in the Kardex (i.e., patient summary sheet) and EMRs alongside training of assessments and interventions for those who screen positive would facilitate comprehensive assessments if deemed necessary and appropriate for an inpatient setting.

Regarding **withdrawal**, roughly half of RNs reported feeling confident in identifying and responding to withdrawal for alcohol, cannabis, nicotine, opioids, and sedatives (50 to 67%) while less than one third (28%) reported confidence for other illicit drugs. CYWs were explicitly asked about psychotherapeutic and supportive withdrawal interventions, and few reported high levels of confidence across all substances (11 to 39%). RNs reported existing withdrawal protocols, including COWS (opioids), CIWA (alcohol and benzos), and NRT (nicotine). Both RNs and CYWs reported uncertainty regarding non-pharmacological management of withdrawal.

Very few staff reported high levels of confidence in delivering brief psychoeducation or brief motivational **interventions**. Of RNs, 50% reported high levels of confidence for psychoeducation related to tobacco/nicotine (in alignment with existing protocols) while for the other substances, high confidence in psychoeducation was only reported by 17-33%. High confidence in psychoeducation was also highest for tobacco/nicotine among CYWS (47%) while only 21% and 26% reported high confidence for psychoeducation related to alcohol and cannabis respectively and no CYWs reported high confidence related to opioids, sedatives, or other drugs. Related to brief motivational interventions, no staff reported being completely confident with only 22% of RNs and 16% of CYWs reporting feeling fairly confident. Staff do lead a bi-weekly group on substance use which uses evidence-based strategies focused predominantly on alcohol, cannabis, and nicotine. Staff made suggestions for more training and standardization regarding facilitating appropriate conversations about substance use in the milieu, more psychoeducational materials, and more targeted interventions for youth using substances.

Overall: (1) staff believe substance use is important and common among youth on the unit and want to improve how they assess and address substance use (e.g., withdrawal management, brief interventions, unit structures and programming); (2) staff have ideas about how to facilitate improvements in quality of care including greater standardization of assessments and interventions, separate cohorting and staffing for youth with more severe co-occurring problems, more direct substance related interventions, and more indirect facilitation of appropriate and supportive conversations; and (3) staff are open to and want more education and training to increase knowledge, confidence, and standardization of practices. Specific quotes supporting these domains available upon request.

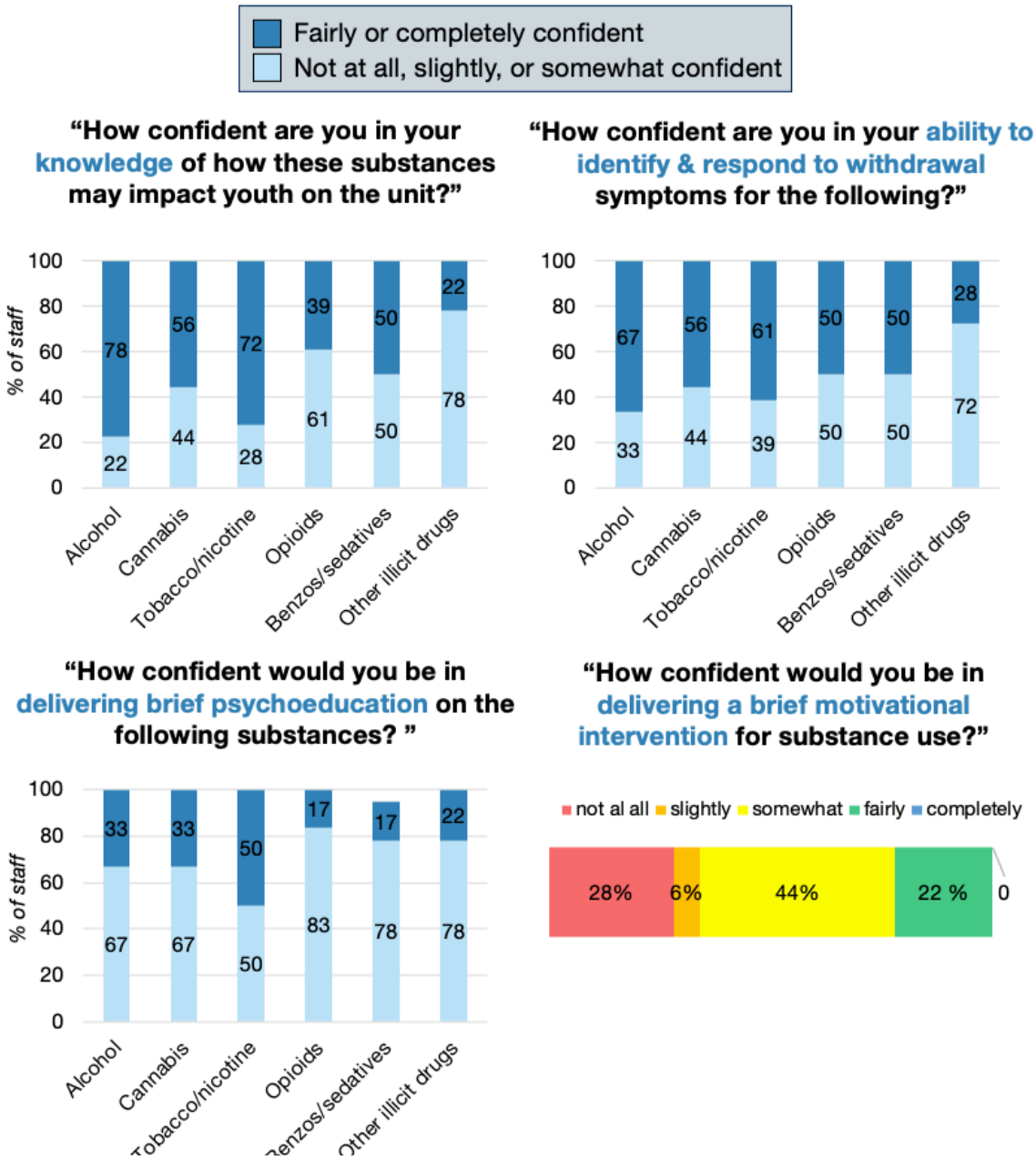
Percentage of staff endorsing each facilitator

Facilitators	RNs	CYWs	All staff
Adding a space in the Kardex to flag substance use concerns	89%	89%	89%
Training on how to deliver psychoeducation	83%	95%	89%
Training on psychotherapeutic approaches for substance use	83%	89%	87%
Adding specific questions to the electronic medical record	72%	89%	84%
Training on pharmacological options for addressing substance use	89%	79%	84%
Training on how to ask questions related to substance use	72%	79%	76%

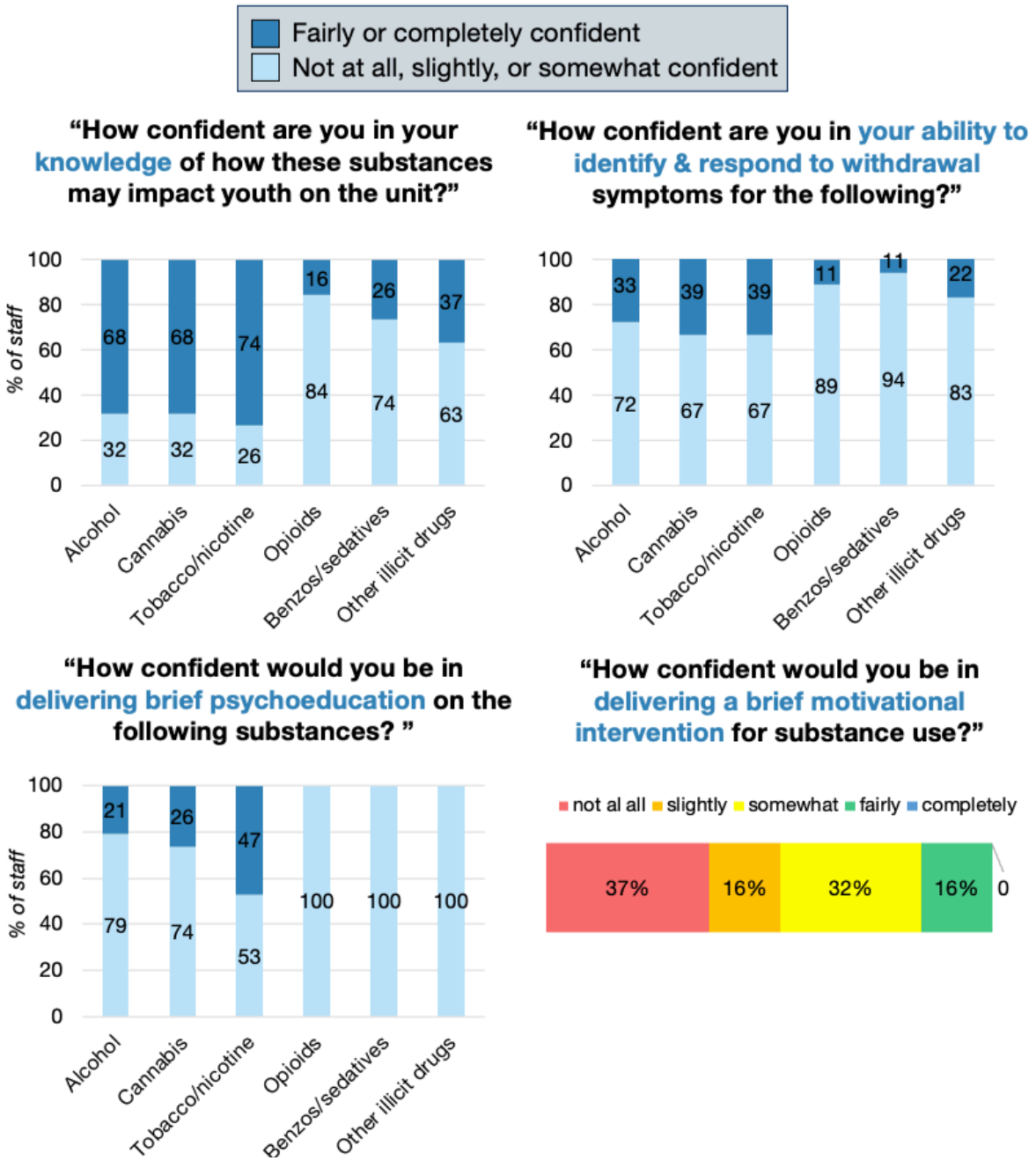
Percentage of staff endorsing each barrier

Barriers	RNs	CYWs	All staff
Lack of training	72%	95%	81%
Time pressures	72%	63%	68%
Unfamiliar with treatment resources in the community	56%	53%	54%
Youth do not often tell the truth about their substance use	33%	58%	43%
Do not know what to do if youth screen positive while on the unit	39%	37%	38%
Screening for substance use is the function of other health services	11%	37%	24%
Uncertainty regarding the effectiveness of available treatments	11%	26%	19%
Lack of funds to make system changes	6%	32%	19%
Do not want youth to worry about who will be informed about their substance use	11%	16%	14%
Lack of space and privacy for conversations	6%	11%	8%
Documentation of substance use problems in the medical record may adversely affect youth	0%	11%	5%
Personally uncomfortable talking about substance use with youth	0%	0%	0%
I do not foresee any barriers to changing screening procedures	0%	0%	0%

Confidence Reported by Registered Nurses



Confidence Reported by Child and Youth Workers



Chapter 5: Discussion

This dissertation deepens our understanding of the patterns and correlates of co-occurring substance use and mental health symptoms among adolescents and within schools, how to collect relevant data on inpatient units, and how to rigorously analyze and report findings. The program of work synthesizes, identifies, and explores this co-occurrence through various methods including a systematic review and meta-synthesis, secondary analysis of large population survey data, and primary data collection on a psychiatric inpatient unit. Despite a number of policy and practice guidelines highlighting the need to identify and treat substance use early and concurrently with other mental health concerns, efforts remain uncoordinated, and guidelines lack specificity. Our current lack of understanding about co-occurrence hinders our ability to effectively address these concerns early in the life course when they first emerge. This program of work is designed to provide novel, timely, and actionable insight into the patterns, correlates, and potential targets for assessment and intervention related to adolescent substance use and co-occurring mental health symptoms.

Summary of key findings

Chapter 2

Given substance use rarely occurs in isolation, it is becoming increasingly important to consider patterns of use rather than modeling substances individually. Chapter 2 reports results from a systematic review of 70 cluster-based studies on adolescent substance use (70), which comprehensively summarizes complex patterns of multiple (multi-) substance use and co-occurring mental health symptoms and identifies critical methodological and statistical limitations of existing evidence. A series of concrete methodological recommendations are made to improve quality, transparency, rigor, replicability, and generalizability of future work. With over half of the included

studies published in the five years prior to the search, summarizing the state of the work substantively and methodologically was critically needed to guide ongoing research.

Substantively, this review found consistent thematic substance use patterns across studies that can be used as targets for future etiological, prevention, and early intervention research including: 1) low use; 2) single or dual substance use, including (in descending order of frequency) alcohol, cannabis with alcohol, tobacco with alcohol, and tobacco; 3) moderate general multi-use; and 4) high multi-use. Various demographic correlates are also summarized, with age, sex, and gender being the most commonly explored correlates. Findings predominantly reveal multi-use as being more common among older adolescents and males. These finding suggests a need to shift from separate, single substance use prevention and intervention efforts to a focus on dual cannabis and alcohol use and/or general multiple substance use concurrently especially among older adolescents. This is in line with the common liability to addiction model (34) that proposes individuals have underlying risk and resiliency factors that relate to their propensity to initiate *any* substance use and propensity to experience various levels of severity of substance use problems, broadly.

This review is the first to characterize mental health considerations in relation to patterns of multiple substance use, highlighting the common, but not inevitable, co-occurrence of substance use and mental health symptoms among adolescents. Similarities are drawn between the identified patterns of co-occurrence and the four-quadrant model of concurrent disorders (32) whereby: quadrant 1 reflects low substance use and mental health symptoms; quadrant 2 reflects low substance use but high mental health symptoms; quadrant 3 reflect high substance use but low mental health symptoms; and quadrant 4 reflects high substance use and mental health symptoms. Notably, nuanced sex and gender differences emerge when mental health indicators are included. Though distinct patterns are found, insight into specific, replicable patterns of co-occurrence remains limited as few studies include internalizing symptoms as indicators (k=4) and, though externalizing symptoms are more commonly included (k=18), these are predominantly represented by single behavioral indicators (e.g., truancy, fighting). Further, no papers

included in this review used samples of youth in acute psychiatric settings and only two papers used samples of youth in outpatient mental health settings (71, 72), both of which were US-based with data collected over 20 years ago and neither included mental health indicators in their cluster analyses.

Overall, this review synthesizes common patterns of multiple substance use and co-occurring mental health symptoms, though few systematically integrate mental health symptoms. Thus, next steps for this line of research include: 1) more explicitly examining patterns of co-occurrence including multiple substances (at minimum, alcohol, cannabis, and tobacco as separate indicators) and mental health symptoms (both internalizing and externalizing symptoms using psychometrically sound scales); 2) identifying correlates related to these patterns to inform prevention and early intervention efforts; and 3) establishing feasible approaches to standardized measurement of substance use and mental health symptoms in treatment settings to inform practice.

Chapter 3

Chapter 3 reports on a multilevel latent profile analysis (MLPA) and subsequent series of multilevel multinomial regressions using a large, representative sample of Ontario secondary students and schools. Findings reveal (73): 1) five substance use and mental health latent student profiles, invariant across gender; 2) three school substance use and mental health typologies, with rural schools disproportionately represented in the high-risk type; and 3) individual and contextual correlates related to these patterns, including protective effects of school belonging, safety, and climate. These findings reflect the largest epidemiological MLPA to date that provides a population-level characterization of the overlap and separation of common substance use and mental health symptoms among adolescents and across schools.

The identified student profiles can serve as *targets* for tailored and combined prevention and early interventions. First, around 40% of adolescents in this sample experience some elevations in substance use and mental health symptoms and these elevations are not defined by a single substance or mental health symptom indicator.

Second, the patterns of substance use map onto the core thematic patterns identified in the systemic review including dual cannabis and alcohol (9.7%), dual tobacco and alcohol (3.7%), and general multi-use (6.5%). This further provides support for targeting dual or multiple substance use, as opposed to single substance focused prevention and intervention efforts. Third, the co-occurring patterns reflect 3 of the 4 quadrants in the concurrent disorders model suggesting a need to further delineate the etiological and prognostic differences between adolescents who experience elevations in mental health symptoms but do not use substances, compared to those who do use substances.

Schools are identified as important *contexts* for interventions, with multilevel clustering identifying select schools that may benefit from more intensive, targeted prevention and early intervention efforts. Several targets for action set out by Public Health Agency of Canada (41) map onto universal and malleable aspects of a school's social environment, that can serve as Tier 1 targets, including: school climate, school belonging, and school safety. In line with these guidelines, chapter 3 found improving school climate, belonging, and safety may be key *processes* to focus on for interventions. These school social environmental factors appear to be associated with a lower likelihood of both substance use and mental health symptoms. In particular, belongingness yields greater protective effects for female students compared to males, suggesting gender is important to consider when creating and implementing prevention strategies to equitably support all adolescents. Future work should focus on the development, implementation, and evaluation of specific interventions and policies to improve these school social environmental factors. Additionally, repeating the School Mental Health Surveys (or a sub-set of the items) at the beginning and several years into implementing the Blueprint can serve as a natural experiment.

Chapter 4

Lastly, chapter 4 reports results from a pilot study called the Cannabis, Alcohol, Mental Health, and Patterns of Service Use (CAMP) study. The CAMP study demonstrates the feasibility, acceptability, and importance of administering a

standardized mental health and substance use assessment among 100 adolescents (13–18 years of age) experiencing psychiatric hospitalization (74). This work is grounded in close collaborations with unit staff and management and combines findings from primary patient (intake and 6-month follow-up) and staff surveys (closed and open-ended questions), chart reviews, and health administrative data.

Almost all (79%) patients in the sample indicate using substances in their lifetime with 69% reporting use in the 3 months prior to their admission. Early age of initiation of substance use, using for coping purposes, solitary use, multi-use, and co-use are commonly reported. These indicators of risky substance use and prevalence in this clinical sample are much higher than what is seen in the general Ontario adolescent population, with prevalence estimates ranging from 1.9 to 9 times greater in the CAMP sample (3). Substance use prior to admission is also correlated with various indicators of mental health symptom severity, clinical diagnostic complexity (ascertained through the number and types of clinician-reported discharge diagnoses and self-reported symptoms surpassing clinical cut-points), and frequency of hospital contacts. Further, frequent use is most commonly reported for cannabis (18% using daily), cigarettes (14% using daily), and e-cigarettes (14% using daily) though a non-negligible proportion of adolescents indicate recent misuse of illicit or prescription drugs 10 or more times (3-5%). Frequent use is of particular relevance on inpatient units due to the chance of withdrawal that can result in immediate physical safety concerns and/or emotional and behavioural disturbances that may influence accurate diagnostic assessments during admission.

Currently, on inpatient adolescent psychiatric units, standardized mental health and substance use assessments are uncommon. The inpatient unit provides a unique opportunity for temporary cessation, brief interventions with trained multidisciplinary staff, and referrals to outpatient services. Reports from frontline staff surveys indicated staff were concerned about patient substance use and saw the inpatient unit as an important place for concurrent assessment and treatment. However, staff reported wanting more training, education, and standardized practices (including assessment and subsequent interventions). Standardized assessments can facilitate consistent early

identification of adolescents with substance use concerns, assist with treatment planning, and inform population monitoring and research. Overall, the CAMP study establishes that the collection of this type of information using standardized self-report electronic assessments is feasible, acceptable to staff, and clinically important.

Strengths

This program of work takes a novel, foreword-thinking perspective to understanding co-occurring substance use and mental health symptoms among adolescents. Research and practice related to mental health and substance use has largely remained siloed, despite continuous calls for integrated thinking and approaches. Thus, the substantive findings in this dissertation are responsive to the longstanding policy and practice calls to action to better understand co-occurrence. Methodologically, the major strengths of this dissertation are the: 1) in-depth appraisal of current methods for evidence collection, synthesis, and evaluation in relation to adolescent substance use and mental health symptoms; 2) application of contemporary and rigorous analytic approaches using a large representative sample of adolescents and schools across Ontario; and 3) high local response rate and mixed-methods approaches on an adolescent psychiatric inpatient unit, alongside the establishment of close partnerships with key clinical stakeholders through the research process.

Cluster-based methods presented in chapter 2 (70) and chapter 3 (73) are used to provide a person-centered non-linear conceptualization of co-occurrence, in this case, in relation to multiple substance use and co-occurring mental health symptoms. As indicated by the systematic review (70), use of cluster-based methods has rapidly grown in popularity in recent years in an effort to better represent and explain complexity and co-occurrence. Cluster analyses identify homogenous subgroups (or categories) of people from a set of indicators; many current studies use categorical indicators (i.e., latent class analysis [LCA]) rather than dimensional indicators (i.e., latent profile analysis [LPA]). Substance use and mental health can be thought of as both categorical (i.e., whether a person meets diagnostic criteria, whether a person uses any substances) or dimensional

(i.e., number and frequency of symptoms, frequency of substance use) (75, 76). However, part of the methodological recommendations in the review was to use dimensional indicators where possible. We may lose information and power when categorizing a dimensional construct, especially when measuring mental health in the general population with self-reported symptom checklists as was typically the case in included studies (76). Dimensional measures of mental health symptoms also tend to yield better psychometric properties (e.g., reliability and validity) (77). SUDs typically do not have their onset until mid-20s (2) and, among adolescents with SUDs, the phenomena appears to be better reflected dimensionally (75). Relatedly, chapter 4 of this dissertation (74) found a high prevalence of substance use and related risk factors (e.g., early age of onset, using to cope, solitary use) that correlated with other mental health symptom severity, comorbidity, and service use among a clinical sample of youth, despite few having a clinician diagnosed SUD (10%). As such, the multilevel latent profile analysis presented in chapter 3 demonstrated the ability to identify distinct profiles of students, with varying levels of dimensional symptoms and frequency of substance use (73). Modeling complexity and patterns of multiple substance use with and without co-occurring mental health symptoms lacks a single "dimension," and thus, categorization in the context of capturing these patterns remains empirically and theoretically useful.

Further strengths specific to chapter 3, include the use of a contemporary multilevel latent profile approach to identify profiles of co-occurrence at both student and school levels and subsequent multilevel multiple imputation and multinomial regression. Beyond critical statistical reasons for accounting for non-independence of students in schools (78-80), taking a multilevel approach provides insight into the importance of social and environmental contexts (in this case, schools) on student outcomes (in this case, patterns of co-occurrence); contextual variation is critical to our understanding of casual mechanisms, not merely statistical error (81). As schools are increasingly being highlighted as key contexts for prevention and intervention, these approaches will help inform what student outcomes schools can influence, potential targets for interventions, and guide identification of schools that may need more supports.

Reproducibility and replication issues have recently been discussed specifically in the field of addictions, with two key papers highlighting the importance of: 1) selecting which studies should be replicated (e.g., key trials, papers with high impact/citations, core theoretical papers) and how (i.e., whether direct or conceptual); and 2) applying and combining multiple different replication statistics to interpret results of replications, given differing results depending on the approach and no universally used replication statistic (82, 83). This dissertation addresses replication in multiple ways. Chapter 2 highlights current non-replicability issues and provides concrete recommendations to support improvements in replication of future cluster-based studies (70). This review also found that replication was particularly needed to evaluate co-occurring substance use and mental health profiles and a broader range of correlates, notably including tests of measurement invariance (or stratifying clusters) for gender and age (or school level). Chapter 3 directly includes a split-half cross-sample replication and tested for gender-invariance (73). Lastly, methodological decisions and results are comprehensively and transparently reported across all chapters with specific and explicitly stated next steps for research.

Partnerships with clinical stakeholders in chapter 4 enabled detailed consideration of research burden unique to psychiatric inpatient units. Every effort was made to involve frontline staff from the outset of the study, including study conceptualization and design, and to receive ongoing feedback and engagement through recruitment and data collection. The CAMP study team worked with staff to reduce burden, on both patients and the clinical team, and facilitate uptake of assessment. This study was a success primarily due to the explicit integration of research within a clinical program through careful planning and establishment of strong stakeholder engagement and partnerships. Support and interest from clinical staff led not only to high patient recruitment, but also high participation in the staff survey and interest in utilizing research findings to inform practice change. Further, findings related to the importance of assessing substance use on inpatient psychiatric units was strengthened by combining quantitative insights regarding the prevalence of substance use and clinical correlates with qualitative insights from

frontline providers about the perceived importance and clinical utility of assessing and addressing substance use in this setting.

Limitations

Key limitations include: 1) current limits of existing cluster-based methodologies regarding standardized reporting and decision making, and a lack of meta-analytical techniques to synthesize results; 2) cross-sectional nature of most data and analyses, limiting any inferences regarding causality or directionality; 3) most data (with the exception of follow-up surveys in chapter 4, which had low response rates) were collected prior to the emergence of the COVID-19 pandemic, and thus results may not generalize to the current context; 4) inability to robustly disentangle certain demographic subpopulations; and 5) limitations of secondary data analysis.

Limitations regarding current cluster-based methodologies, which are discussed at length in chapter 2 and mentioned in chapter 3, are worth reiterating. There are currently no standardized reporting guidelines for cluster analyses, limitations with current model fit indices that do not consistently converge on the same solutions, and no guidelines for synthesizing work coming from use of these methods (including a lack of meta-analytical software or approach to pooling results). Thus, theoretical, and subjective interpretations of models play a key role in model selection. All methodological recommendations made in chapter 2 were implemented in chapter 3, though theoretical rationale was still required for final model selection due to these limitations. This is a call for quantitative psychologists to update and/or create new model fit indices to improve objective model selection, and to create meta-analytical software to pool results. These statistical ambiguities may bias within-study model selection, between-study comparisons, and broader generalizability of findings. That being said, this method still provides promise for allowing us to model and understand the inherent comorbidity and complexity in the field that has historically been ignored.

Much of the work in this dissertation focuses on snapshots of co-occurrence at one point in time, rather than on the causal development of comorbidity pathways and related

risk and resiliency factors. Future work should collect and leverage longitudinal data to disentangle the developmental patterns of comorbid substance use and mental health symptoms across different developmental stages; there remains no single causal theory and directionality may change across developmental stages, particularly from adolescence (ages 12-17) to emerging adulthood (ages 18-25) (84-86). It has been proposed that existing gaps in the literature may be due to limitations with current statistical methods (84, 87, 88) - namely an inability to adequately tease apart within from between-person relationships over time - that can be overcome with novel approaches such as Autoregressive Latent Trajectory Modeling with Structured Residuals (84, 87-89). Further, longitudinal studies or cluster-based trials within school settings will provide insight into temporality and causality of school contextual factors (such as climate, belonging, and safety) related to the development and maintenance of student substance use and mental health patterns. Lastly, repeated assessments within clinical samples will provide greater insight into prognostic implications and clinical interconnectedness of substance use and mental health symptoms. Though chapter 4 did have a 6-month follow-up, response rates were low (possibly due to the beginning of the COVID-19 pandemic) and thus longitudinal findings were limited due to sample size (i.e., underpowered) and lack of representativeness (i.e., limited generalizability). Therefore, using contemporary statistical approaches with longitudinal data are recommended next steps to advance theory and inform evidence-based prevention and early interventions.

All the data used throughout this dissertation was collected prior to the global COVID-19 pandemic. Since March 2020, the global COVID-19 pandemic has destabilized life for adolescents and contributed to increased healthcare pressures. Though the global crisis prompted a rapid accumulation of research related to the impacts of COVID-19 on mental health and substance use, many *current* (as of January 2022) peer-reviewed publications are based on cross-sectional convenience samples collected during the initial wave(s) early in the pandemic (90-95). Preliminary results suggest a sub-set of adolescents may have increased their substance use (~20%), and this appears to have been more likely among adolescents with mental health symptoms. However,

findings are inconsistent. Further, though overall numbers of youth presenting to the hospital for mental health and substance use concerns may not have increased (96), the severity and types of presentations may have changed (for example, (97)). It remains uncertain what the realized and lasting impact of this pandemic will be on the mental health and substance use patterns and trajectories of our young people. Therefore, a limitation of the work in this dissertation may not generalize to the current pandemic context, though this remains largely unclear.

There is a complicated interaction between sociocultural gender-related factors and neurobiological sex differences related to substance use and mental health outcomes. General population studies clearly demonstrate differences in the prevalence of SUDs and other mental disorders between males and females. Males are more likely to use substances and have a SUD, whereas females are more likely to have depression and anxiety (98), progress from substance use to SUD more quickly (i.e., telescoping) (99), experience higher degrees of craving (100-103), more severe withdrawal (104), and poorer substance use prognosis (105, 106). These differences may be both in part due to: sex-differences, related to hormones, genes, physiology, anatomy, and neurobiology; and/or gender-differences, related to values, beliefs, preferences, stigma, discrimination, bullying, and social acceptability that are related to gender identity, roles, and marginalization (107).

Collectively, this dissertation found female adolescents were more likely to report high internalizing symptoms (70, 73, 74) with (70) and without (70, 73, 74) co-occurring substance use compared to male adolescents, and that school belonging may yield greater benefits for female students (73). However, there were several instances in the dissertation when sex and gender were not explicitly separated, predominantly driven by using previously collected data (chapter 2 and 3). Broadly, substance use research has not routinely differentiated sex and gender as distinct constructs, which impacted inferences that could be drawn in the review. Where possible, sex and gender were collected and reported separately (74), and suggestions were made for future work to report sex and gender separately following international guidelines (108). Notably, 19% of the youth in

the inpatient sample in this dissertation were transgender or gender diverse (74) and recent population estimates have found that between 3% and 8% of children and adolescents in the general population are transgender or gender diverse (109, 110). Youth who are transgender or gender diverse experience greater vulnerability to substance use and mental health concerns (111) with a recent Canadian study finding transgender adolescents have 5 to 7.6 times the risk for suicidal ideation and attempts respectively (112). Continued misclassification of youth when only binary response options are used for gender, and when gender is not reported separately from sex, reduces our ability to identify mechanisms driving differences and results in a complete inability to identify high risk groups that warrant evidence-based mental health supports.

Race and ethnicity are distinct social constructs that infer a level of power and privilege that have historically been used interchangeably. Race is defined based on perceived differences in physical appearance while ethnicity is a multidimensional concept related to shared culture (113). Systematic racism and discrimination are known to negatively impact mental health care access, experiences, and outcomes among Canadian youth (114). Further, of relevance to adolescent substance use, certain cultures have distinct parenting practices and family dynamics, which are known to be closely tied to whether or not an adolescent initiates substance use (115). The Canadian Institute for Health Information (CIHI) recently published a guideline for collecting race and ethnicity data in healthcare settings (113). Notably, the response options for the suggested race-based question map onto the categories asked and reported on throughout this dissertation; however, the question stems differ whereby CIHI asks about "race or racial background" whereas questions and results reported across this dissertation asked about "race or culture" (informed by Statistics Canada questions) or "background" (using OSDUHS questions). Thus, "race and ethnicity" is reported as a combined construct across studies in this dissertation. Moving forward, research needs to disaggregate across these characteristics to enable the examination of differential underlying causal pathways to target outreach and prevention efforts more accurately. Further, not only should race

and ethnicity be examined separately, but also the intersectionality that exist between them (116).

Related to limitations with previously collected demographics are the broader issues associated with secondary data analysis and data harmonization practices. In chapter 2, findings in the systematic review were restricted to what was collected and reported in prior research studies resulting in a lack of specificity, consistency, and generalizability in demographic predictors (70). In chapter 3, the variables included to identify and characterize profiles in the MLPA study were limited to what was collected in the original research study (73). This resulted in an inability to differentiate between sex and gender and race and ethnicity. Further, the primary objective of the original study was not related to adolescent substance use, and thus there were limited questions related to substance use including no questions on illicit or prescription drug misuse. For chapters 2 and 3, there were also limits to how stakeholders could be involved (as the primary studies were complete) and thus stakeholders were not directly involved in the co-design. It would have been possible to co-design and co-interpret the secondary research questions, though more limited than typically desired, which was not done in this dissertation. There are plans for stakeholder involvement in end-of-study knowledge translation with youth, schools, and policymakers (117). Lastly, in chapter 4, many measures were selected as they had been previously used in adolescent population studies – both to capitalize on validated scales and items and to enable comparisons of study findings to general population studies (74). Overall, secondary data and data harmonization presents tensions between our contemporary understandings and the desire to leverage existing data to maximize prior research, participant investments, comparability of findings across studies, and evidence syntheses.

Opportunities for future work

In addition to the future work to bridge existing limitations, next steps for this program of work include: 1) developing and evaluating a measurement-based care (MBC) system, including assessment and early interventions, for adolescent psychiatric inpatient

units; 2) exploring contexts and developmental stages for prevention and early intervention related to co-occurrence; and 3) examining patterns of co-occurrence over time and related correlates, including before, during, and after the COVID-19 pandemic. For all work moving forward, it will be important to include youth, clinicians, and other stakeholders from the beginning of study conceptualization and design, during interpretation, and through to knowledge mobilization. This can be accomplished by embedding co-development approaches into future work.

Co-development: "Nothing about us without us"

Future work regarding understanding co-occurrence and developing prevention, clinical assessments, and early interventions need to prioritize and include end-user engagement (e.g., youth, loved ones, clinicians). Following integrated knowledge translation approaches (118), there are several national standards for youth engagement to guide co-development and co-interpretation of research results (119-121) and tools to assess the quality of public and patient engagement in research (122). Future researchers should consider not only implementing participatory research approaches (e.g., Patient Oriented Research [SPOR], community based participatory research [CBPR], Integrated Knowledge Translation) but also integrating Human Centred Design (or co-design) approaches to maximize research, clinical, and public health impact (123). Both participatory research and co-design approaches are systematic, and iterative processes that share a common purpose and set of values based on developing close collaborations between researchers and stakeholders (fostering equal partnerships), deliberate co-creation and end-user engagement throughout the whole process of identifying issues and selecting and testing possible solutions, and mutual benefits of the work (123). In particular, combining the rapid design solutions of co-design and Design Thinking (DT) with the rigor of research-related stakeholder engagement approaches will be critical to efficiently creating effective solutions. All approaches are guided by the notion of, "nothing about us without us" (119, 120) or "shifting from designing *for* users, to *with* users" (124).

There are many different co-design models, and related toolkits, to guide creative thinking about complex problems; no gold-standard approach currently exists (104). All models aim to accelerate the identification, visualization, and creation of innovations to allow non-designers to leverage the key skills, strategies, and processes of designers (124). IDEO is a leading global design thinking company, whose core 3-I model has three distinct phases: Inspiration (identifying a problem and building empathy), Ideation (generating ideas for solutions), and Implementation (prototyping, updating, and scaling-up) (125) (see Chen, Leos (102) for connections between 3 I's and CBPR). Another common co-design model is the 5-stage model from the Hasso Plattner Institute of Design at Stanford, including: Empathize (understanding lived experience, storyboarding), Define (root problems and barriers), Ideate (brainstorm solutions), Prototype (rapid, small scale, low-fidelity testing), and Test (large scale testing) (126). To note, Foundry and the Canadian Centre for Substance use and Addiction (CCSA) have partnered on a combined CBPR and co-design project to create youth-centric opioid service innovations using this 5-stage process (127). Their protocol paper provides direct connections between principles of CBPR and co-design, and a comprehensive description of methods (including end-user worksheets and workshop structures) that can guide future work for youth substance use and mental health co-design research projects (127). Overall, the co-design approaches will facilitate rapid generation of creative, iterative, and stakeholder-driven solutions and these approaches are gaining rapid popularity in the public health and health services field.

Another way of systematically collecting and synthesizing stakeholder input is through a multi-staged consensus-based survey approach called Delphi (128, 129). Given the clinical providers in the CAMP study only included nurses and child and youth workers from one hospital (74), the Delphi approach can be used to gather broader, multidisciplinary perspectives on the importance and feasibility of assessing and addressing substance use on inpatient youth psychiatric units across Canada (and globally). Additionally, adolescents and their caregivers can, and should, be involved in their own Delphi's to form consensus within stakeholder groups. Cleverley, McCann

(130) demonstrates how to conduct a Delphi study with clinicians, administrators, youth, and caregivers to inform priorities for improving transitions from pediatric to adult mental health care. Further, the Delphi approach can be applied outside of the healthcare system, such as to gain feedback from students, caregivers, teachers, school mental health providers, and school administrators regarding conceptualizing co-occurrence among students in schools and priorities for school-based prevention initiatives.

Implementing and evaluating measurement-based care

The CAMP study established the feasibility of administering a standardized tool to assess substance use and mental health symptoms in an adolescent psychiatry inpatient unit (74). Given a number of policy recommendations and practice guidelines suggest assessing and addressing substance use concurrently with mental health concerns, and there are neurodevelopmental concerns with any substance use among adolescents, further research should be considered concurrent with policy and practice changes. One such approach to achieving these aims simultaneously is through measurement-based care (MBC).

MBC is a contemporary approach to simultaneous patient assessment, ongoing monitoring, and evaluation within healthcare systems. MBC involves routine measurement through rating scales and tools integrated into care, followed by both clinician and patient reviews of the findings to guide collaborative, timely, patient-centered, measurement-based treatment planning (131). MBC provides a decision-support system that assists clinicians and patients to accurately and comprehensively identify presenting issues and helps provide empirical decision support to tailor initial treatment planning, ongoing monitoring and adjustments, and final outcome evaluation. MBC has been associated with multi-faceted clinical benefits, including greater retention, engagement, and therapeutic alliances during treatment with better patient outcomes that occur more quickly and last longer than traditional care (132-135). Further, MBC can simultaneously be used for direct patient care, program monitoring and quality improvement, and research. Unfortunately, MBC is underutilized in mental health and

substance use treatment (136). Collectively, these benefits may help improve immediate treatment outcomes among adolescents accessing psychiatric services while contributing to the limited research in this setting to empirically inform future system reform and guideline development.

The CAMP study sets the foundation for future exploration and research into the utility of a MBC approach, though additional steps are required for developing and providing evidence for wider-spread MBC. Next steps include: 1) collecting feedback from a wider range of multidisciplinary providers across multiple institutions (such as through the Delphi approach); 2) co-developing and refining standardized assessments and related clinical uses (such as clinician and patient feedback reports) with youth, staff, and their families; 3) assessing the feasibility and associated costs of fully clinically integrated standardized assessments across multiple institutions; 4) providing more precise estimates of the clinical importance of assessing substance use in this context (i.e., associations with clinical severity, complexity, and service use); and 5) determining whether or not MBC leads to better outcomes on adolescent psychiatric inpatient units. As noted in the CAMP Study (74), precise estimates of the prevalence and clinical impacts of substance use on various aspects of youth psychiatric hospitalizations will require large samples. Thus, taking an MBC approach earlier in these "next steps" may allow practice and research to evolve side by side; using what we know now, while improving collection of standardized clinical data to answer what we do not yet know.

Prevention and intervention across contexts and stages of development

In addition to adolescent psychiatric hospital settings, this dissertation focuses on adolescents in secondary schools. In line with findings from chapter 3 (73) and PHAC's recent recommendations (41), future school-based research should focus on co-developing and evaluating school-based prevention interventions to target climate, belonging, and safety. More broadly, other targets set by PHAC for substance use prevention should be further explored and evaluated in the context of substance use and co-occurring mental health symptoms. For example, school-based preventative models

(41, 42) often seek to increase involvement in substance-free prosocial activities, such as involvement in extracurriculars like sports or clubs. This is similar to other evidence-based approaches for substance use including the adolescent community reinforcement approach (ACRA) (137) and behavioural economic approaches for addiction (138) that (in part) aim to reduce substance-related reinforcement while maximizing substance-free reinforcements (138). Further, relationships between school-activities (such as extracurriculars) and school environmental factors (such as belonging) as they relate to co-occurrence should be considered.

There are other contexts and developmental stages important to concurrent prevention and intervention. *First*, substance use prior to age 14 has been associated with greater risks of experiencing later substance use disorders and related problems (5, 7, 139-141) and there is a notable increase in substance use occurs around age 14, corresponding to the transition from elementary (up to grade 8) to secondary (grades 9-12) schooling (3). Thus, research focused on substance use initiation, mental health correlates, school contextual factors (including factors related to transitioning to secondary school), and targeted early intervention in elementary student and school samples will be important for future work.

Second, given substance use disorders are typically diagnosed during the early to mid-twenties (2) and rates of concurrent disorders are highest among emerging adults (~18-25 years of age) (23), transitions from pediatric to adult healthcare, developmentally tailored substance use treatment programs, and post-secondary factors (including social context and student services) are also important for future work. Notably, this healthcare transition represents a collision of fragmented mental health and addiction services in both pediatric and adult systems with unsupported navigation into adult systems of care and increasing service disengagement among an already low help-seeking population (142, 143). Thus, more insight into the needs of this population is needed to reduce the number of young people "falling through the cracks."

Third, within our current health system landscape, general health providers (such as family physicians) are the most likely professionals to be able to provide ongoing,

accessible mental health care for young people across the transition from pediatric to adult healthcare systems (144). Young people who have seen a family physician (or pediatrician, or psychiatrist) for their mental health prior to turning 18 are more likely to remain connected to physicians-related mental health supports following the transition to adult services, compared to young people who attended no services or only accessed other community mental health agency supports (145). Thus, primary care clinics are likely key contexts for interventions. In order to support primary care physicians to do this work, increased access to collaborative care models and streamlined access to mental health and substance use consultations are essential.

Fourth, more broadly, collaborative care models involving both physicians and other community mental health services may be a key factor in providing comprehensive early outpatient care for adolescents and emerging adults with co-occurring substance use and mental health difficulties, including co-location of multidisciplinary service providers and offering care beyond 18 years of age (145). This concept is in line with the "hub" model currently being evaluated across Canada (i.e., Access Open Minds, Foundry, Youth Hubs Ontario), which is based on established *headspace* centres in Australia and *Jigsaw* centres in Ireland (146). Notably, the hub model prioritizes co-design and often has MBC embedded into their care and evaluation approach (147-149).

Understanding co-occurrence over time

As previously mentioned, the COVID-19 pandemic may impact patterns of co-occurrence and we do not yet know the impacts on adolescents. However, it is important to recognize that patterns of comorbidity were changing even prior to the COVID-19 pandemic. As such, at a population level, there is emerging interest in examining whether joint associations between substance use and mental health have changed over time. Current studies have produced mixed results depending on age, sex and gender, specific substance, and frequency of use (150-157). For example, among US adolescents the associations between binge drinking and depression appear to be weakening (156) but cannabis and depression are strengthening (157). These trends are important to unpack

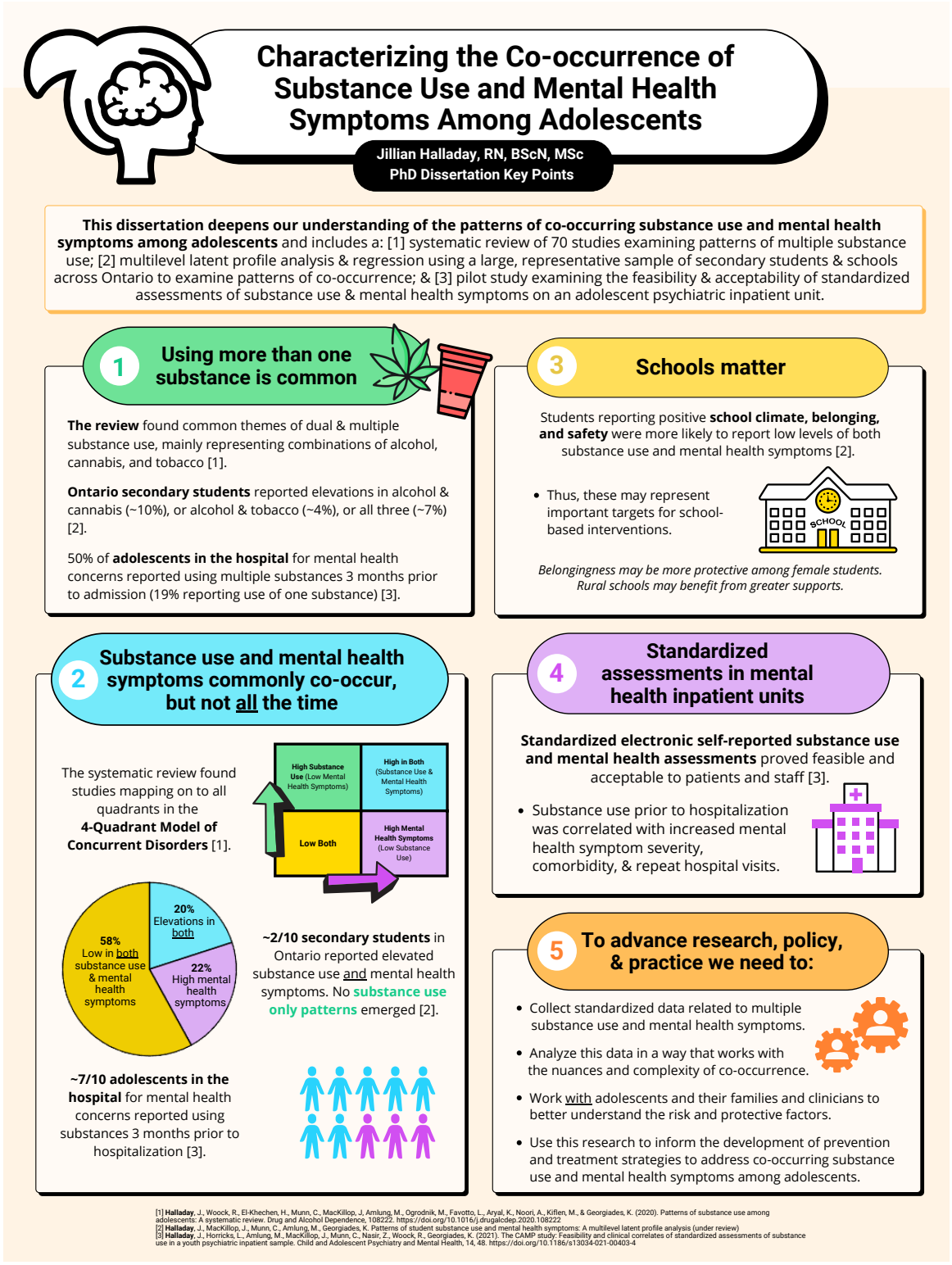
given the possibility that youth still engaging in substance use - despite average population-level declines – may be particularly vulnerable and in need of integrated care. However, few existing studies examine trends separately for adolescents or emerging adults, a minority are conducted outside the US, and most use statistical approaches that obstruct our ability to observe natural fluctuations in associations over time. A novel flexible non-parametric regression-based approach has been developed to analyze complicated time-trend data called Time-Varying Effect Modeling (TVEM) (88), which can provide new insight into temporal changes in joint associations. We also require deeper explorations of the mechanisms behind any observed trends (i.e., whether changing trends are explained by population changes in average ages of onset and/or perceptions related to harms, disapproval, availability of substances, and/or drug policies). This knowledge will help pinpoint targets for future prevention policy and interventions (156). This is particularly important with changing cannabis legislation and public perceptions regarding substance use internationally, as well as changes due to the pandemic.

Conclusions

Overall, this dissertation provides a deeper understanding of how substance use and mental health symptoms co-occur among adolescents and how to rigorously model these patterns, insight into correlates, and evidence to support concurrent assessment and care within inpatient psychiatric youth settings. Collectively, the key substantive findings of this program of work include: 1) multiple substance use is common, and thus interventions targeting multiple substances (rather than substances separately) should be prioritized; 2) co-occurrence of substance use and mental health symptoms is common, though not universal among adolescents; 3) substance use may be related to mental health symptom severity, comorbidity, and hospital service use and thus integrated and concurrent care is needed; 4) schools are important contexts for prevention, with climate, belonging, and safety being possible targets for interventions; and 5) adolescent psychiatric hospitalizations may be important contexts for assessment of early substance

use and delivery of early interventions, though more professional training and standardization in assessments and interventions are needed. Methodologically, cluster-based analyses may provide a unique, and foreword thinking approach to modeling complexity and co-occurrence, though currently these methods have notable limitations regarding generalizability. Additionally, self-report electronic standardized assessments show promise for collecting data on adolescent psychiatric inpatient units that can be leveraged simultaneously for direct patient care, program evaluation, and research to better inform specific best practice guidelines. Youth cannot wait, and thus policy and practice change should move forward alongside progress in research. We need to improve system navigation and the ability for adolescents to access services for both mental health and substance use concerns, and better integrate concurrent disorder perspectives across prevention and intervention strategies.

Figure 1. Summary of Key Dissertation Findings



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