

## RESEARCH ARTICLE

# Substance use and psychiatric phenotypes of youth experiencing homelessness: A cluster analysis

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## Abstract

**Background and Objectives:** Due to the complex interactions of psychopathology, psychosocial stressors, and risk behaviors, characterizing high-risk phenotypic groups of transitional-age youth experiencing homelessness (TAY-EH) for targeted interventions remains difficult. We aimed to uncover specific phenotypes of TAY-EH based upon psychiatric and substance use disorder (SUD) diagnoses, and to assess relationships between these phenotypes and negative outcomes including suicidality and high-risk behaviors.

**Methods:** Participants ( $N = 140$ ; 57% male, 54% Black) were individuals aged 16–25 years accessing support at a psychosocial agency in the U.S. Northeast. Data were gathered via structured assessment. Cluster analysis identified sub-groups of TAY-EH with differing diagnostic patterns. Bivariate analyses examined associations between cluster membership and target outcomes.

**Results:** A four-cluster solution was identified. Cluster 1 (*Co-occurring*;  $N = 33$ ) was characterized by high levels of comorbidity (i.e., major depressive disorder (MDD), SUD, and notable levels of other diagnoses). Clusters 2 (*MDD alone*;  $N = 47$ ) and 3 (*SUD alone*;  $N = 18$ ) were characterized by single diagnoses. Cluster 4 (*None*;  $N = 42$ ) was characterized by low levels of psychopathology. Clusters differed significantly on several variables including suicidality, adverse childhood experiences, and social connectedness. Comorbid MDD and SUD were most strongly associated with high-risk behaviors and suicidality.

**Discussion and Conclusions:** These results highlight the importance of diagnosis and targeted interventions for co-occurring MDD and SUD to address the crisis of early mortality and other negative outcomes among TAY-EH.

**Scientific Significance:** This study is the first to identify specific high-risk psychiatric and psychosocial phenotypes among the highly complex group of TAY-EH based upon structured diagnostic assessments.

Transitional-age youth experiencing homelessness (TAY-EH; youth between the ages of 16 and 25) represent a marginalized and understudied population with complex mental health and social needs. Four percent of individuals ages 13–17 years and 10% of individuals

ages 18–25 experience homelessness each year.<sup>1</sup> TAY-EH have notably elevated rates of psychiatric and substance use disorders (SUDs) compared with stably housed peers.<sup>1–4</sup> Without adequate psychological support, these youth experience markedly greater risk

for negative outcomes including persistent housing instability.<sup>4,5</sup> Perhaps most notably, TAY-EH have a greater than tenfold increased risk of early mortality compared with their stably housed peers, with suicide and overdose being the first and second leading causes, respectively, of early mortality in this group.<sup>6,7</sup> However, TAY-EH are a heterogeneous<sup>5</sup> and consistently changing group.<sup>7</sup> Targeted research is needed to identify high-risk groups of TAY-EH based on diagnostic and psychosocial characteristics to enhance services and prevent premature morbidity and mortality in this group.

Prior research describing TAY-EH suggests that these youth often meet criteria for multiple psychiatric and/or substance use disorders (SUDs) of varying severities.<sup>3,6</sup> For example, Whitbeck and colleagues (2004) reported that adolescents experiencing homelessness were 6 times more likely to meet criteria for two or more psychiatric disorders in comparison to their stably housed peers.<sup>8</sup> Similarly, we previously highlighted the complexity of overlapping conditions facing TAY-EH, as more severe SUD including cannabis use disorder (CUD) and/or alcohol use disorder (AUD) is associated with a greater burden of co-occurring psychiatric conditions among TAY-EH.<sup>2</sup> However, little is known about disorder-specific patterns of co-occurrence that might increase the risk of negative outcomes.

TAY-EH also faces a complex array of psychosocial adversity, which further complicates the identification of high-risk phenotypes. TAY-EH experiences high rates of adverse childhood experiences (ACEs),<sup>9,10</sup> that have been found to predict poor mental health outcomes.<sup>11,12</sup> Further, adverse experiences contribute to social isolation that furthers the development of adult psychiatric morbidity<sup>13</sup> and hinders recovery from mental illness.<sup>14</sup>

High-risk behaviors and patterns of victimization also contribute to TAY-EH's complexity. A greater burden of psychopathology has been associated with increased high-risk behaviors such as violent or sexual risk behaviors among youth experiencing homelessness.<sup>15</sup> Conversely, sexual risk behaviors and violence victimization can increase the risk for traumatic experiences and thus the development or worsening of psychopathology.<sup>16,17</sup> Due to the complex interactions of psychopathology, ACEs, social connectedness, and risk behaviors, characterizing particular groups of TAY-EH for potential targeted interventions has been fraught with difficulties.

To this end, we aimed to uncover specific phenotypes of TAY-EH based on psychiatric diagnoses to assess relationships between these phenotypes and negative outcomes including high-risk behaviors, social connectedness, and suicidality. Our goal was to identify high-risk subgroups of TAY-EH to inform targeted diagnosis, interventions, and deployment of public health resources for this marginalized population. To achieve this aim and illuminate the complex lived experience of TAY-EH, we examined how co-occurring patterns of psychiatric diagnoses relate to behavioral outcomes for TAY-EH. We hypothesized that TAY-EH with more complex and severe psychiatric phenotypes would exhibit greater levels of early-life adversity, poorer social functioning, and greater endorsement of suicidality and other risk behaviors.

## METHODS

Participants were individuals aged 16–25 years accessing any level of support at Bridge Over Troubled Waters (BOTW), a psychosocial support agency serving TAY-EH in the Northeast U.S. BOTW is the largest provider of drop-in services, transitional housing, counseling/support, rapid re-housing, and educational/vocational services for youth experiencing homelessness in its region, and is the primary collaborating site in our academic-community partnership focused on the health and well-being of TAY-EH. Youth accessing any level of services were eligible to participate. Exclusion criteria included youth experiencing acutely unstable medical and/or psychiatric symptoms that limited engagement in interview, youth unable to communicate in English, and youth with limited capacity to complete rating scales with staff assistance. The methodology, study population, and characteristics of this sample have been described in detail elsewhere.<sup>2</sup> Briefly, study participants were recruited in person at BOTW, and data were collected via secure video visits utilizing computer equipment located on-site at BOTW between April 2020 and July 2021. All research methods and materials were approved by the Mass General Brigham Institutional Review Board, and a federal Certificate of Confidentiality was secured for this study.

## Measures

Demographic and psychosocial information was gathered via self-reported, structured assessment and included questions on race, ethnicity, sex, gender identity, educational and occupational status, and a range of other information related to childhood development and psychiatric history/treatment.

## Clustering variables

Comprehensive psychiatric and SUD diagnostic data were gathered via the Mini International Neuropsychiatric Interview (MINI) with supplemental ADHD module.<sup>18</sup> Data were gathered for all disorders with the exception of eating disorders. Due to the low prevalence of social anxiety disorder, panic disorder, and agoraphobia, these variables were combined with generalized anxiety disorder into a single anxiety disorder variable.<sup>2</sup> We selected structured, DSM-based diagnostic tools to inform evidence-based clinical psychiatric and psychosocial interventions for TAY-EH, many of which are validated and approved according to DSM diagnostic criteria.

## Wellbeing and risk factors

### *Suicidality*

Suicidality was measured using the MINI suicidality module. Specifically, participants were asked “In your lifetime: Did you ever make a suicide attempt (try to kill yourself)?” and responded either yes or no.

### Adverse childhood experiences

Adverse childhood experiences were measured using the 2019 ACE module of the CDC Behavioral Risk Factor Surveillance System.<sup>19</sup> The ACE survey contains 11 items covering various types of adverse experiences occurring before the age of 18 including emotional, physical, or sexual abuse, and household dysfunction. All positive endorsements of any occurrence of an adverse experience were summed to create a composite ACE score, with scores ranging from 0 to 11 and higher scores indicating more ACEs.

### Social connectedness

Social connectedness was measured using the 8-item Social Connectedness Scale (SCS).<sup>20</sup> Example items include "I feel disconnected from the world around me" and "I have no sense of togetherness with my peers." As opposed to the typical six-item Likert scale, in the present study participants were presented with the answer choices "yes" and "no" for each item to reduce overall survey burden. All items were reverse-coded and summed to create a composite score of social connectedness, with greater scores indicating greater social connectedness. The measure demonstrated high internal consistency, with a Cronbach's  $\alpha$  of 0.81 as evidenced by the current study's collected data, in accordance with the literature ( $\alpha = .91$ ).

### Risk behaviors

Risk behaviors were measured using items adapted from the CDC's 2019 National Youth Risk Behavior Survey.<sup>21</sup> Items used in the current study included 6 questions regarding violence-related behaviors. Participants were asked the number of days in the past month on which they carried a weapon and the number of days in the past month on which they avoided regular activities (i.e., work, school, etc.) due to feeling unsafe. Participants were also asked how many times they were threatened or injured with a weapon, how many times they were in a physical fight, and how many times they were physically hurt by a romantic partner in the past 12 months. Finally, participants were asked if they had ever been forced to have sexual intercourse. Each item was scored as either 0 or 1 if a participant endorsed a particular behavior/experience having occurred at least once. All items were analyzed separately.

## Analytic strategy

To identify sub-groups of TAY-EH with differing patterns of diagnoses, we used hierarchical agglomerative cluster analysis using Ward's minimum variance method based on the squared Euclidean distance.<sup>22</sup> In this analysis, individuals of the closest distance to each other, or individuals for whom the degree of difference on the clustering variables is minimized, are joined. Mathematically, groups of individuals (i.e., clusters) are then continuously joined, one at a time, until a single cluster remains containing all participants. Smaller 'distances' across which clusters are joined are indicative of greater cluster likeness. For interpretational purposes, a cut-point is chosen at which the merging process stops, so that clusters that are 'distant'

to each other are not joined, resulting in a distinct number of unjoined clusters.<sup>23</sup> In this study, we used the following criteria to select the optimal number of clusters to retain: inverse screen test,<sup>24</sup> gap statistic method,<sup>25</sup> and inspection of the dendrogram. The clustering variables were not standardized as all variables utilized the same measurement scale (i.e., 0 = diagnosis is absent, 1 = diagnosis is present), and their numerical values relative to each other capture meaningful variation.

To test if identified sub-groups varying in nature and complexity of psychiatric diagnoses differed from each other in terms of their demographics, adverse childhood experiences, and recent violence-related behaviors, we used chi-square tests and one-way analyses of variance (ANOVAs). Cluster group membership served as the only independent variable in these analyses. To account for multiple testing, we used Bonferroni's correction for multiple comparisons.<sup>26</sup> Analyses were conducted using R statistical software and SPSS, and all tests were evaluated for significance at  $\alpha = .05$ . Effect sizes were calculated using Cramer's  $V$  ( $V$ ) and eta squared ( $\eta^2$ ).

## RESULTS

Of the 147 individuals enrolled in the study, 140 (95%) participants had complete data and were included in analyses. No TAY-EH were excluded from study entry due to exclusion criteria, and no screened TAY-EH declined to enter the study. The demographics of this study population have been described previously.<sup>2</sup> Briefly, participants had a mean age of 21 years. Fifty-seven percent identified as male and 42% as female, with less than 1% identifying as genderqueer/gender non-conforming or nonbinary. A majority (53%) identified as Black or African American; 16% identified as Hispanic or Latino, and 12% as White. Additional sample characteristics can be found in Table 1.

Descriptive summaries of the variables used in the cluster analysis are presented in Table 1. Results of hierarchical agglomerative cluster analysis indicated a four-cluster solution for the data set. Clusters were labeled based on the most prevalent psychiatric diagnoses (Figure 1). Cluster 1 (*Co-Occurring*;  $N = 33$ , 24%) is marked by high levels of MDD and SUD (CUD and/or AUD), and notable levels of other diagnoses including bipolar disorder, attention-deficit/hyperactivity disorder (ADHD), posttraumatic stress disorder (PTSD), and anxiety disorders. Cluster 2 (*MDD Alone*;  $N = 47$ , 34%) is marked by high levels of MDD and low levels of other diagnoses. Cluster 3 (*SUD Alone*;  $N = 18$ , 13%) is marked by high levels of SUD and low levels of other diagnoses. Cluster 4 (*None*;  $N = 42$ , 30%) is marked by low levels of any psychiatric diagnoses.

### Cluster differences in demographic characteristics

Demographic characteristics per cluster are presented in Table 2, including any pairwise significant differences. Sex at birth significantly predicted cluster membership such that the *MDD alone* cluster had a significantly higher proportion of individuals assigned female at

**TABLE 1** Demographic characteristics, social/occupational functioning, and psychiatric profiles ( $N = 140$ ).

	Mean	SD
Age (years)	20.9	2.0
	N (%)	%
Gender identity		
Male	79	56%
Female	59	42%
Genderqueer/Gender nonconforming	2	1%
Sex assigned at birth		
Male	80	57%
Female	59	42%
Not reported	1	1%
Race		
American Indian or Alaska Native	2	1%
Asian	1	1%
Black or African American	74	53%
Hispanic or Latino	22	16%
White	17	12%
More than one	20	14%
Not reported	4	3%
Currently enrolled in school	48	34%
Highest level of education		
Some high school	55	39%
Graduated high school	51	36%
Some college or community college	31	22%
Graduated college	2	1%
Not reported	1	1%
Currently employed	49	35%
Primary caretaker in childhood		
Single parent	69	49%
Two parents	33	24%
Other family members	20	14%
Foster family	9	6%
Other	9	6%
Current contact with family (any contact with blood relative in the past 6 months)	105	75%
Current behavioral health treatment (engagement with therapist, mental health counselor, or psychiatrist)	55	39%
Current living situation (majority of nights in the past week)		
Bridge Over Troubled Waters (BOTW)	92	66%

**TABLE 1** (Continued)

	N (%)	%
Street	17	12%
Shelter (not BOTW)	15	11%
Staying with friends	7	5%
Staying with family	5	4%
Own house/apartment	2	1%
Other	2	1%
Psychiatric and substance use disorder diagnoses		
Major depressive disorder	73	52%
Cannabis use disorder	62	44%
Attention-deficit/hyperactivity disorder	33	24%
Bipolar disorder	31	22%
Any anxiety disorder <sup>a</sup>	30	21%
Alcohol use disorder	29	21%
Obsessive-compulsive disorder	23	16%
Antisocial personality disorder	20	14%
Posttraumatic stress disorder	20	14%

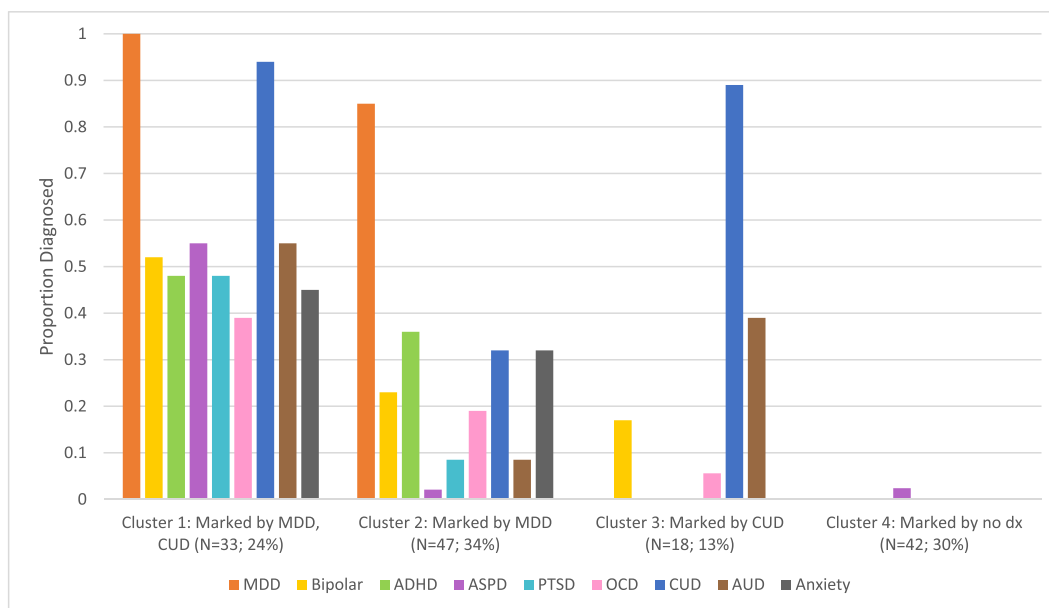
<sup>a</sup>Any anxiety disorder includes: generalized anxiety disorder, social anxiety disorder, panic disorder.

birth than the *SUD alone* cluster. No significant differences were found based on race and ethnicity. All clusters differed significantly from each other on the total burden of psychopathology (i.e., the mean number of psychiatric and SUD diagnoses). The *Co-Occurring* cluster had the highest average number of diagnostic criteria met ( $M = 5.4$ ), followed by the *MDD alone* cluster ( $M = 2.5$ ), the *SUD alone* cluster ( $M = 1.5$ ), and the *None* cluster ( $M = 0.02$ ).

### Cluster differences in adverse experiences and behaviors

Score distributions per cluster on adverse experiences and behaviors are presented in Table 2, including any pairwise significant differences. Cluster 1 (*Co-Occurring*) was associated with high rates of ACEs, risk behaviors, and suicidality, and low levels of social connectedness. This profile was statistically similar to Cluster 2 (*MDD Alone*) but differed significantly from Cluster 4 (*None*) across almost all variables. Additionally, Cluster 1 significantly differed from Cluster 3 (*SUD alone*) on a number of variables including ACEs, social connectedness, and suicidality.

Similar to Cluster 1 (*Co-Occurring*), Cluster 2 (*MDD Alone*) significantly differed from Cluster 4 (*None*) across multiple variables. Specifically, Cluster 2 had significantly greater suicidality, higher levels of ACEs, poorer social connectedness, and elevated levels of multiple risk behaviors. Cluster 2 differed significantly from Cluster 3



**FIGURE 1** Prevalence of psychiatric diagnoses within each identified sub-group.

(*SUD Alone*) only on levels of social connectedness, with Cluster 2 exhibiting poorer social connectedness.

Cluster 3 (*SUD Alone*) was associated with relatively low suicidality, moderate levels of ACEs, better social connectedness, and fewer risk behaviors compared with Clusters 1 (*Co-Occurring*) and 2 (*MDD Alone*). This profile was statistically similar to Cluster 4 (*None*) and only significantly differed on endorsement of having been in a physical fight.

## DISCUSSION

The results of our study support our hypothesis in revealing multiple distinct phenotypes of TAY-EH based upon diagnostic features, with significantly different profiles of risk behaviors, victimization experiences, early life adversity, and suicidality. Notably, results revealed markedly higher rates of suicidality among young people with complex co-occurring disorders and those with MDD alone, and lower suicidality among those with SUD alone and no psychiatric diagnoses. While not all sequential pairwise comparisons reached statistical significance, these findings suggest that the presence of MDD may be an important factor associated with suicidality, and that the co-occurrence of SUD and MDD may be particularly pernicious in the high risk for suicide in this group, with a striking 58% of the subjects in this group having attempted suicide. Similar trends held in analyses of ACEs, social connectedness, and experience of sexual abuse (having been forced to have intercourse), wherein the *MDD Alone* group was surpassed only by the *Co-Occurring* group in rates of negative outcomes.

The associations between MDD and negative outcomes in this sample, and the additive correlates of co-occurring SUD and mood disorders, are in line with findings from prior epidemiologically

derived (non-homeless) youth samples. In housed samples, exhibiting depressive symptoms in childhood was correlated with greater suicidal ideation and psychiatric comorbidities later in life.<sup>27,28</sup> This established risk for negative outcomes following MDD onset is particularly relevant for TAY-EH, who often report mental illness, specifically mood disorders, as a reason for current homelessness.<sup>29</sup> The findings of the current study support the extant literature not only through the high prevalence of MDD endorsed by TAY-EH, but also in the increased likelihood of adverse behaviors and experiences in comparison to the groups without MDD. Indeed, co-occurring MDD and SUD (representing 24% of the current sample) has been consistently associated with more severe functional impairment, greater vulnerability to additional psychopathology, and increased rates of suicide attempts in comparison to either MDD or SUD alone.<sup>30-32</sup> This study meaningfully extends this prior literature by identifying patterns of complex co-occurring disorders appearing alongside MDD and SUD which appear to amplify risk even further in the highly marginalized population of TAY-EH.

The phenotypes uncovered in this investigation rely upon varied factors including early life experiences, engrained risk/coping behaviors, and psychiatric and SUD diagnoses. As such, this model does not rely solely on potentially transient states of housing instability and may have applicability beyond the TAY-EH population. Given the highly complex and overlapping trajectories of youth into and out of homelessness,<sup>33,34</sup> these results may apply equally to other high-risk groups of youth in child welfare and foster care, criminal justice, and high-adversity community psychiatric settings—all settings into and out of which TAY-EH cycle frequently.<sup>35</sup> The extent to which these phenotypes are stable across broader populations of marginalized young people merits further study.

The current findings highlight complexities in diagnosis and treatment planning for marginalized young people. Notably, we

**TABLE 2** Cluster differences in demographic characteristics and psychometric assessments.

Variable	Cluster 1 (Co-Occurring) 24%	Cluster 2 (MDD Alone) 34%	Cluster 3 (SUD Alone) 13%	Cluster 4 (None) 30%	Test statistic*	p value	Effect size
<i>Demographic variables</i>							
Female sex at birth, n (%)	12 (36%) <sup>a,b</sup>	27 (57%) <sup>a</sup>	3 (17%) <sup>b</sup>	17 (40%) <sup>a,b</sup>	$\chi^2 = 9.8$	<b>p = .02</b>	V = 0.27
<i>Race/ethnicity, n (%)</i>							
American Indian/Alaskan Native	0	1 (2%)	0	1 (2%)		pNS	
Asian	1 (3%)	0	0	0		pNS	
Black or African American	14 (42%)	27 (57%)	8 (44%)	25 (60%)		pNS	
Hispanic or Latino	9 (27%)	5 (11%)	2 (11%)	6 (14%)		pNS	
White	4 (12%)	6 (13%)	3 (17%)	4 (10%)		pNS	
More than one	5 (15%)	7 (15%)	4 (22%)	4 (10%)		pNS	
Other/Declined	0	1 (2%)	1 (6%)	2 (5%)		pNS	
Psychiatric burden (# of diagnoses), M (SD)	5.4 (1.4) <sup>a</sup>	2.5 (1.2) <sup>b</sup>	1.5 (0.7) <sup>c</sup>	0.02 (0.2) <sup>d</sup>	F = 173.9	<b>p &lt; .001</b>	$\eta^2 = 0.83$
<i>Adverse experiences/behaviors</i>							
Suicidality, n (%)	19 (58%) <sup>a</sup>	23 (49%) <sup>a,b</sup>	3 (17%) <sup>b,c</sup>	5 (12%) <sup>c</sup>	$\chi^2 = 23.7$	<b>p &lt; .001</b>	V = 0.41
ACEs <sup>†</sup> , M (SD)	7.1 (2.2) <sup>a</sup>	5.9 (2.3) <sup>a,b</sup>	4.3 (3.1) <sup>b,c</sup>	3.3 (2.6) <sup>c</sup>	F = 16.4	<b>p &lt; .001</b>	$\eta^2 = 0.27$
SCS <sup>†</sup> , M (SD)	3.5 (1.9) <sup>a</sup>	4.5 (2.3) <sup>a</sup>	6.8 (1.7) <sup>b</sup>	5.9 (2.6) <sup>b</sup>	F = 11.6	<b>p &lt; .001</b>	$\eta^2 = 0.20$
<i>Risk Behaviors, n (%)</i>							
Carried a weapon (past 30 days)	13 (39%) <sup>a</sup>	10 (21%) <sup>a,b</sup>	6 (33%) <sup>a,b</sup>	4 (10%) <sup>b</sup>	$\chi^2 = 10.7$	<b>p = .014</b>	V = 0.28
Avoided regular activities (past 30 days)	10 (30%) <sup>a</sup>	6 (13%) <sup>a</sup>	2 (11%) <sup>a</sup>	6 (14%) <sup>a</sup>	$\chi^2 = 5.3$	pNS	
Threatened/injured with weapon (past 12 months)	15 (45%) <sup>a</sup>	20 (43%) <sup>a</sup>	4 (22%) <sup>a,b</sup>	7 (17%) <sup>a</sup>	$\chi^2 = 10.7$	<b>p = .013</b>	V = 0.28
Physical fight (past 12 months)	23 (70%) <sup>a</sup>	27 (57%) <sup>b</sup>	13 (72%) <sup>b</sup>	12 (29%) <sup>a</sup>	$\chi^2 = 17.7$	<b>p &lt; .0001</b>	V = 0.36
Intimate partner violence (past 12 months)	13 (39%) <sup>a</sup>	8 (17%) <sup>a</sup>	4 (22%) <sup>a</sup>	6 (14%) <sup>a</sup>	$\chi^2 = 8.4$	<b>p = .039</b>	V = 0.25
Forced to have intercourse (ever)	16 (48%) <sup>a</sup>	16 (34%) <sup>a,b</sup>	5 (28%) <sup>a,b</sup>	7 (17%) <sup>a</sup>	$\chi^2 = 8.6$	<b>p = .034</b>	V = 0.25

Note: Clusters that share a superscript are not pairwise statistically significant from each other. Bold values indicate a statistically significant difference with a p value < .05.

$\alpha = .05$ .

\*Test statistics used include Chi-Squared analyses ( $\chi^2$ ) and on-way ANOVAs (F).

<sup>†</sup>ACEs: adverse childhood experiences; SCS: social connectedness.

identified that 24% of our sample represented a high-risk subset of TAY-EH who met criteria for an average of five distinct psychiatric/SUD diagnoses. This finding invites further inquiry into the stability of psychiatric and SUD diagnoses as youth enter and exit homelessness during critical developmental windows, and the extent to which psychosocial and life stressors impact responsiveness to standard disorder-based treatments. These results suggest the need for integrated treatment interventions that can target psychiatric disorders, SUD, and psychosocial stressors concurrently to address all facets of impairment in this complex population. Additionally, these findings

highlight the importance of using structured and detailed diagnostic instruments in studying marginalized populations to capture the full complexity of disorders present in these groups. The use of structured diagnostic assessments in TAY-EH research is relatively rare in recent years,<sup>3</sup> though challenging in the historically hard-to-reach TAY population, this study reaffirms the feasibility of using structured diagnostic assessments with TAY-EH and the potential for highly informative phenotyping that can arise from such efforts.

To our knowledge, there are no current organized state- or federal-level efforts to expand acceptable, effective, and tailored

psychiatric services for youth experiencing homelessness. Such services generally exist within academic-community partnerships, or within larger efforts to address the well-being of related populations including youth receiving child welfare services, justice-involved youth, and those receiving services at community mental health clinics. Providers and policy makers will benefit from the development, validation, and dissemination of evidence-based, acceptable, and effective tailored interventions based upon rigorous diagnostic data to optimize care tailored to the unique needs of TAY-EH.

The current study has several substantial limitations. The cross-sectional nature of our analysis limits inferences on causality and time-course of outcomes. Recruitment in a low-threshold service delivery setting may have biased recruitment toward help-seeking youth, theoretically excluding youth with higher or phenotypically different complexity who are not accessing services. Demographically, our sample had a very low proportion of trans and gender-diverse youth, which is in contrast with prior studies suggesting a disproportionate representation of LGBTQ+ youth among TAY-EH.<sup>1</sup> It is possible that this finding reflects trends in accessing drop-in services in our geographic region, a local temporal trend at the time of study recruitment, or some other unexamined factor which influenced the proportion of LGBTQ+ youth in our study sample. Our sample size may have limited our ability to detect statistically significant variance in outcomes among the four phenotypic groups. Unaccounted-for geographic or demographic characteristics in our single site may limit generalizability and warrant replication in larger and geographically diverse TAY-EH populations. Additional unexplored factors including duration of youths' homelessness, season, hunger, and other important variables may limit the contextual framing of our psychiatric findings. Our social connectedness measure focused on subjective feelings of belongingness and connections to peers, without explicit measure of connections to family or other potential support structures including mutual help organizations, and may thus represent an incomplete view of connectedness. Finally, the rater burden necessitated a limited assessment battery which did not capture variables such as family psychiatric history that likely contribute to TAY-EH psychiatric/SUD profiles and risk behaviors. Our determination of suicidality was derived from the MINI, which included a single item related to past suicide attempts and did not capture suicide more dimensionally. While we utilized a DSM-based diagnostic framework, which may inform clinical psychiatric and psychosocial interventions, we did not assess for trans-diagnostic or dimensional symptom groupings which may provide additional insights into risk and resilience phenotypes of TAY-EH. Future research might incorporate other variables likely contributing to the functioning of TAY-EH and more detailed risk behavior measures to further develop our understanding of the phenotypes identified in the current study.

## CONCLUSION

Despite these limitations, this study is the first to our knowledge to identify specific high-risk psychiatric, SUD, and psychosocial phenotypes among the highly complex group of TAY-EH based upon

structured diagnostic assessments. These results highlight the importance of diagnosis and targeted interventions for co-occurring MDD and SUD (particularly cannabis and alcohol use disorders) to address the crisis of early mortality and other negative outcomes among this group of marginalized youth. Further study is needed to identify psychosocially, culturally, and developmentally targeted treatment interventions for these disorders in this high-risk group.

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## DECLARATION OF INTEREST

*Timothy E. Wilens, MD:* Dr. Wilens has co/edited books: ADHD in Adults and Children (Cambridge University Press), Straight Talk About Psychiatric Medications for Kids (Guilford Press), An Update on Pharmacotherapy of ADHD (Elsevier Press). Dr. Wilens has a licensing agreement with Ironshore (BSFQ Questionnaire). He is a consultant for 3D Therapeutics and serves as a clinical consultant to the US National Football League (ERM Associates), U.S. Minor/Major League Baseball, Gavin Foundation and Bay Cove Human Services. He has received funding from NIDA grant UH3DA050252. No further disclosures or conflicts to report.

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## CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest. The authors alone are responsible for the content and writing of this paper, and the content and results have not been submitted or published elsewhere.

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