TRAJECTORIES OF CANNABIS USE DISORDER: RISK AND DEVELOPMENTAL

FACTORS, CLINICAL CHARACTERISTICS, AND OUTCOMES

by

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DISSERTATION ABSTRACT

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Title: Trajectories of Cannabis Use Disorder: Risk and Developmental Factors, Clinical
Characteristics, and Outcomes

Efforts to objectively inform cannabis discourses include research on the
epidemiology of cannabis abuse and dependence disorders or, collectively, cannabis use
disorder (CUD). For my dissertation I identified classes of individuals based on
intraindividual CUD trajectory patterns and contrasted trajectory classes with respect to
clinical characteristics of CUD, developmental risk factors, and psychosocial outcomes.
Identifying differences between trajectory classes provides evidence for the validity of
trajectory-based CUD constructs and informs the development of comprehensive models
of CUD epidemiology and trajectory-specific intervention approaches.

My dissertation used data from the Oregon Adolescent Depression Project, a
prospective epidemiological study of the psychiatric and psychosocial functioning of a
representative community-based sample randomly selected from nine high schools across
western Oregon. Four waves of data collection occurred between mid-adolescence and
early adulthood and included diagnostic interviews and self-report questionnaires. Onset
and offset ages of all CUD episodes were recorded. The reference sample included 816
participants who completed all diagnostic interviews.

A series of latent class growth models revealed three distinct CUD trajectory classes through age 30: (1) a persistent increasing risk class; (2) a maturing out class, marked by increasing risk through age 20 and then a decreasing risk through early adulthood; and (3) a stable low risk class. Rates of cannabis dependence were similar across the persistent increasing and the maturing out classes. Trajectory classes characterized by a history of CUD were associated with a variety of childhood risk factors and measures of psychosocial functioning during early adulthood. Participants who were male, had externalizing disorders, and had psychotic experiences during early adulthood discriminated between the persistent increasing and the maturing out classes.

Future research based on more diverse samples is indicated, as are well-controlled tests of associations between risk factors, trajectory class membership, and psychosocial outcomes. A better understanding of these relationships will inform etiological theories of CUD and the development of effective intervention programs that target problematic cannabis use at specific developmental stages. Designing targeted versus undifferentiated interventions for those at greatest risk for adult psychosocial impairment could be a cost-effective way to mitigate the consequences of CUD.

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CHAPTER I

INTRODUCTION

Cannabis is the subject of a contemporary social and political debate due to its changing legal status, controversies concerning its medicinal utility, and numerous reports on the pervasiveness (Boden, Fergusson, & Horwood, 2006; Moffitt et al., 2010; Wittchen et al., 2007) and potentially adverse consequences (Bolla, Brown, Eldreth, Tate, & Cadet, 2002; Hubbard, Franco, & Onaivi, 1999; Lehman & Simpson, 1992; Lynskey & Hall, 2000) of hazardous cannabis use. Recent efforts to objectively inform cannabis discourses and the development of evidence-based prevention and treatment programs include research on the epidemiology of cannabis abuse and dependence disorders or, collectively, cannabis use disorder (CUD), including intraindividual CUD trajectory patterns and their associated developmental risk factors and psychosocial outcomes (Brook, Lee, Brown, Finch, & Brook, 2011b; Flory, Lynam, Milich, Leukefeld, & Clayton, 2004; Kandel & Chen, 2000; Windle & Wiesner, 2004).

It is well established that, on average, risk for problematic substance use increases during adolescence, declines during early adulthood, and remains stable during later adulthood (e.g., Johnston, O'Malley, Bachman, & Schulenberg, 2013a, 2013b). Identifying this population-average longitudinal trajectory is an important contribution to the literature, but there is additional evidence that trajectories of problematic substance use are systematically heterogeneous among populations with more homogeneous subgroups defined by specific patterns in the timing, duration, and consequences of substance abuse or dependence. Commonly identified subgroups based on intraindividual substance use trajectory patterns include a low incidence or non-using subgroup, a

chronically or persistently high incidence subgroup, a subgroup characterized by high use that declines over time, and a subgroup characterized by low use that increases over time (Sher, Jackson, & Steinley, 2011). Relative to the extensive research literature on the longitudinal trajectory patterns of alcohol and general substance abuse and dependence, limited cannabis-specific research indicates that adolescent and young adults who use or abuse cannabis also cannot easily be regarded as a single, homogeneous group (Babor, Webb, Burleson, & Kaminer, 2002; Baggio et al., 2014; Brook et al., 2011b; Flory et al., 2004; Hix-Small, Duncan, Duncan, & Okut, 2004; Kandel & Chen, 2000; Windle & Wiesner, 2004).

A primary reason for studying specific intraindividual patterns of CUD over time is to understand the profiles of individuals in trajectory subgroups with respect to their different risk factors and outcomes. Individuals in a chronically or persistently CUD subgroup, for example, may demonstrate distinct background characteristics and greater psychosocial impairment later in life compared to those in non-abusing or maturing out subgroups. Identifying differences between CUD trajectory subgroups with respect to etiologically-relevant developmental factors and outcomes provides evidence for the construct validity of trajectory-based patterns (Babor et al., 2002) and informs the development of comprehensive models of CUD epidemiology and trajectory-specific intervention approaches (Schulenberg, Maggs, Steinman, & Zucker, 2001). The overarching goal associated with this dissertation is to identify subgroups based on intraindividual CUD trajectory patterns and to contrast these subgroups in terms of clinical characteristics of CUD, risk factors, and psychosocial outcomes. This study used data from the Oregon Adolescent Depression Project (Lewinsohn, Hops, Roberts, Seeley,

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& Andrews, 1993), a prospective epidemiological study of the psychiatric and

psychosocial functioning of a community-based cohort between adolescence and early

adulthood.

CHAPTER II

LITERATURE REVIEW

Before reviewing the literature on trajectory-based patterns of cannabis use and CUD, it is necessary to distinguish between the various cannabis use variables that are frequently considered in the literature (Conway, Compton, & Miller, 2006). Common variables include initiation, use in the past year, frequency of use, quantity consumed, and the clinical diagnosis of CUD as defined by the *Diagnostic and Statistical Manual of Mental Disorders, 3rd edition* (*DSM-III*; American Psychiatric Association, 1980), *4th edition* (*DSM-IV*; American Psychiatric Association, 1994) and *5th edition* (*DSM-5*; American Psychiatric Association, 2013). Because of the various operational definitions of cannabis use and abuse, cannabis research must be carefully interpreted because there are likely distinct epidemiological findings with respect to longitudinal trajectories, risk factors, and psychosocial outcomes as a function of the specific cannabis use variables under investigation. Indeed, von Sydow, Lieb, Pfister, Höfler, and Wittchen (2002) demonstrated that unique risk factors predicted cannabis initiation, severity of use, and disorder-level abuse and dependence.

According to *DSM-IV*, cannabis abuse is characterized by:

"a maladaptive pattern of [cannabis] use manifested by recurrent and significant adverse consequences related to the repeated use of [cannabis]. There may be may be failure to fulfill major role obligations, repeated use in situations in which it is physically hazardous, multiple legal problems, and recurrent social and interpersonal problems" (p. 182).

Cannabis dependence is characterized by:

> "a cluster of cognitive, behavioral and physiological symptoms indicating that
> the individual continues use of [cannabis] despite significant [cannabis-related]
> problems. There is a pattern of repeated self-administration that can result in
> tolerance, withdrawal and compulsive drug-taking behavior" (p. 176).

DSM-IV further specifies that if an individual has a history of cannabis dependence, any future patterns of use that meet criteria for abuse should be coded as dependence.

Recent research has demonstrated the lack of discriminant validity between cannabis abuse and cannabis dependence categories (Lynskey & Agrawal, 2007), and the distinction has been discontinued in *DSM-5* in favor of a single "use disorder" category. Consequently, for purposes of this literature review and increased statistical power in subsequent analyses, I combine cannabis abuse and dependence diagnoses into a single category (CUD) to indicate patterns of continued cannabis use that might result in significant functional impairment in social or occupational settings. However, due to the paucity of research on the developmental trajectories of CUD, I review below more general literature on developmental trajectories of cannabis use more broadly defined (e.g., initiation, frequency of use, and quantity consumed).

Developmental Perspective on Cannabis Abuse and Dependence

This research is guided by a developmental psychopathology perspective (Cicchetti, 2006) that emphasizes multiple levels of influence (e.g., individual and family characteristics) on specific developmental trajectories of CUD and their associated outcomes. This perspective aligns with contemporary views that risk for substance abuse disorders is multiply determined, and from these unique or partially overlapping

developmental factors distinct substance use trajectories emerge (Zucker, Donovan, Masten, Mattson, & Moss, 2009; Zucker & Gomberg, 1986). Identifying distinct trajectories of CUD and their associated risk factors and outcomes through a developmental perspective requires an integration of variable-centered and person-centered quantitative methodologies (Bates, 2000).

Variable-centered analytic approaches typically involve descriptive statistics and general or generalized linear models to make inferences about overall associations between independent and dependent variables in a population. Some studies that utilize variable-centered approaches also report results disaggregated by observed individual-level traits such as sex, ethnicity, or other measurable characteristics. Variable-centered investigations represent much of the cannabis literature and have been instrumental in advancing theory and intervention development. However, variation in intraindividual patterns of CUD over time is not adequately addressed with variable-centered analyses alone.

Person-centered analytic approaches, such as latent class growth modeling and growth mixture modeling, represent complementary modeling frameworks that can be used to reveal the heterogenous nature of individuals' trajectories on variables of interest (Bergman, von Eye, & Magnusson, 2006; Cairns, Bergman, & Kagan, 1998; Hinde & Dennis, 1986). A person-centered CUD trajectory analysis, for example, explicitly models interindividual variation in intraindividual patterns of CUD risk over time and identifies classes of individuals who are similar with respect to CUD trajectories. The identification of these classes facilitates inquiry into risk factors and outcomes of CUD as

a function of specific classes of trajectories, which is not possible with variable-centered analyses alone (Bates, 2000).

Recent advances in analytic techniques and the software used to implement them have made integrated variable-centered and person-centered approaches more accessible (Asparouhov & Muthén, 2014; Bates, 2000; Muthén & Muthén, 2000). These novel applications can be used to better understand trajectories of CUD and the generality versus specificity of their risk factors and outcomes. In the following sections I review contemporary literature in these areas. I conclude with a summary of the limitations of existing literature and define my research questions that aim to address important gaps in the literature.

Trajectories of cannabis use. Research on cannabis use between adolescence and adulthood has generally suggested significant heterogeneity in the longitudinal patterns of cannabis use. Kandel and Chen (2000), for example, used a four-wave longitudinal correlational design and a latent class analysis (LCA) to identify classes of cannabis users between ages 15 and 34 among a representative community-based New York cohort. Variables used for classifying individuals into subgroups were self-report age of onset, persistence of use, and temporal stability of heavy use. Four classes were identified: *late onset-light use* (i.e., mean age of initiation = 20 years, 21% daily users, and 1% using at the time of last assessment), *early onset-light use* (i.e., mean age of initiation = 15 years, 50% daily users, and 10% using at the time of last assessment), *mid onset-heavy use* (i.e., mean age of initiation = 16 years, 67% daily users, and 100% using at the time of last assessment), and *early onset-heavy use* (i.e., mean age of initiation = 15 years, 100% daily users, and 50% using at the time of last assessment). The classes were

further differentiated by several baseline risk factors. The early onset-heavy use class, compared to the mid onset-heavy use class, demonstrated significantly higher rates of psychiatric disorders prior to the first assessment. Heavy use classes, compared to light use classes, demonstrated significantly higher levels of childhood delinquency. Early onset classes, compared to late onset classes, demonstrated significantly higher rates of initiation of other substances.

Flory et al. (2004) also used a longitudinal correlational design and applied LCA techniques to model self-report frequency of cannabis use between ages 10 and 20 among a mostly white cohort of youth from Kentucky. Three trajectory classes were identified: *non-users*, *late onset* (i.e., initiation between age 13 and 16), and *early onset* (i.e., initiation by age 12). Cannabis trajectory classes differed in a linear fashion on baseline risk factors, with early onset classes demonstrating significantly lower levels of academic achievement, self-esteem, family relations, and higher levels of conduct problems prior to the first assessment point. Both early and late onset classes demonstrated significantly greater levels of antisocial and substance abuse symptomology compared to the non-user class twelve months prior to the last assessment point.

Researchers have begun using growth mixture modeling (GMM) techniques to identify distinct classes among cannabis users with respect to longitudinal trajectories. Windle and Wiesner (2004), for example, examined longitudinal trajectories of self-report frequency of cannabis use over a two-year period between the ages of 15 and 17 among a cohort of youth from mostly white suburban high schools in western New York. They reported five trajectory classes based on frequency of cannabis use: *abstainers*, *experimental users* (i.e., used cannabis approximately one time per month over the course

of the study), *decreasers* (i.e., used cannabis approximately 12 times per month at baseline, gradually decreasing to three times per month by the last assessment point), *increasers* (i.e., used cannabis approximately two times per month at baseline, gradually increasing to 14 times per month by the last assessment point), and *high chronic users* (i.e., used cannabis daily over the course of the study). These trajectory classes were further distinguished by a variety of risk factors assessed at the first assessment point and psychosocial outcomes assessed at age 23. Findings indicated that the high chronic class, relative to the other trajectory classes, had significantly higher baseline levels of alcohol initiation, delinquency, academic impairment, and stressful life events. All classes characterized by cannabis use, relative to the abstainers, were associated with significantly higher lifetime rates of alcohol use disorders and lower levels of educational attainment.

Finally, Brook et al. (2011b) used a four-wave longitudinal correlational design and a GMM analysis to model trajectories of self-report frequency of cannabis use over a 15 year period between ages 14 and 29 among a sample of African-American and Puerto Rican participants. Four classes were identified: *non-users or low-users* (i.e., used cannabis a few times a year or less across the course of the study), *maturing out* (i.e., used cannabis a few times a year or less around age 14, more than several times a month around age 19, once a month around age 24, and a few times a year or less around age 29), *late initiation* (i.e., used cannabis a few times a year or less between ages 14 and 19, more than several times a year around age 24, and several times a month around age 29), and *chronically high use* (i.e., used cannabis a few times a year or less around age 14, more than once a month around age 19, and more than several times a month between

ages 24 and 29). Classes characterized by use, versus non-use, had significantly greater adverse outcomes including higher levels of internalizing symptoms, interpersonal difficulty, occupational impairment, and marital problems. The chronically high class was associated with significantly higher levels of adult antisocial behavior.

Additional cannabis-related risk factors and outcomes. More general epidemiological research has indicated various risk factors for cannabis initiation and CUD that were not evaluated in the trajectory-based studies reviewed in the previous section. For example, sex (Brook, Lee, Finch, Koppel, & Brook, 2011a), parental divorce and poor family relations (Butters, 2002; Flewelling & Bauman, 1990; Hayatbakhsh, Najman, Jamrozik, Mamun, & Alati, 2006), and maltreatment during childhood (Oshri, Rogosch, Burnette, & Cicchetti, 2011) have all been associated with CUD and cannabis initiation.

Previous research has also indicated that there may be psychosocial consequences of hazardous cannabis use that were not evaluated in previous trajectory-based studies. Poor employment outcomes are more frequent among those who initiate cannabis use during early to mid-adolescence (Lehman & Simpson, 1992) and cannabis use has also been associated with impaired social relations including isolation or withdrawal (Ashton, 2001; Diego, Field, & Sanders, 2003), engagement in risky or potentially harmful behavior (Hall & Babor, 2000), and psychotic-like experiences (Mackie, Castellanos-Ryan, & Conrod, 2011).

The extent to which these risk factors and outcomes operate uniformly across the population of persons with histories of CUD is unclear. As noted previously, there is

limited research indicating that differences in risk factors and outcomes are associated with specific CUD trajectory classes.

The Current Study

In my review of the literature I did not find a single study that evaluated the heterogeneity of trajectories of clinically defined CUD. Instead, all trajectory-based studies I reviewed used self-report data concerning age of initiation, frequency of use, or quantity consumed. Moreover, studies completed to date have evaluated a limited variety of risk factors and psychosocial outcomes associated trajectory class membership. Addressing these limitations will increase our knowledge regarding the heterogeneous nature of the development of CUD, normative versus non-normative development, and developmental risk factors and psychosocial outcomes associated with CUD trajectory classes.

For the current study, data were drawn from the Oregon Adolescent Depression Project (OADP; Lewinsohn et al., 1993), a prospective community-based study of the psychiatric and psychosocial functioning of a community-based cohort between adolescence and early adulthood. OADP includes diagnostic information for a range of Axis I psychiatric disorders expressed in person-months from adolescence through early adulthood. Earlier work with OADP indicated that 19% of participants developed a CUD (Farmer et al., 2015) and that histories of social phobia, mood disorders, conduct disorder, and alcohol use disorder were associated with CUD onset by age 30 (Buckner et al., 2008). In the current study, I attempted to extend these findings and address the limitations of previous research by answering the following research questions:

1. What are the parametric characteristics of the average intraindividual growth trajectories (e.g., intercept, linear and quadratic slopes) of CUD from childhood through early adulthood?

2. Is there significant heterogeneity in intraindividual trajectory patterns from childhood through early adulthood that define distinct classes of individuals with more homogeneous intraindividual trajectory patterns? If so, how many distinct classes emerge?

3. Do clinical characteristics of CUD discriminate between trajectory patterns, such as age of initial onset, total number of episodes, cumulative duration across episodes, and criteria for cannabis dependence?

4. Do participant and family characteristics predict trajectory classes of CUD from childhood through early adulthood?

5. Are intraindividual trajectory classes of CUD from childhood through early adulthood associated with differential psychosocial functioning later in life?

CHAPTER III

METHOD

Participants

The OADP was a four-panel epidemiological study (T_1 to T_4) of a convenience sample of adolescents selected between 1987 and 1989 from nine high schools in two urban communities and three rural communities across western Oregon. Schools were chosen because they were located less than 100 miles from project headquarters in Eugene, Oregon. School characteristics were unavailable for reporting. The T_1 sample consisted of 1,709 adolescent youth (mean age = 16.6, SD = 1.2), with an overall participation rate of 61% of the sampling frame. A previous study reported on the representativeness of the T_1 sample relative to the larger western Oregon geographical region (Lewinsohn et al., 1993). No statistically significant differences were observed between the T_1 sample and the corresponding 1980 census data on sex, ethnic status, or parental education. Additionally, no statistically significant differences were observed between the T_1 sample and those who declined participation on sex of head of household, family size, or number of parents in the household. While decliners' mean socioeconomic status was significantly lower than that of the participants', both were reflective of middle class.

Approximately one year following T_1, 1,507 participants (88% of the T_1 sample) participated in a T_2 assessment (mean age = 17.7, SD = 1.2). Approximately 7 years following T_2, a stratified sampling procedure was implemented to increase the diversity and variability within the sample whereby eligible T_3 participants included all ethnic and racial minorities, all persons with a positive history of a psychiatric diagnosis by T_2 (n =

644), and a randomly selected subset of participants with no history of mental disorder by T_2 ($n = 457$ of 863 persons). Of the 1,101 participants recruited for a T_3 interview, 941 (85%) completed the evaluation (mean age = 24.6, $SD = 0.6$). Approximately 6 years after T_3 (mean age = 30.5, $SD = 0.7$), 816 of the 941 T_3 participants (87%) participated in the T_4 diagnostic evaluation. Given the sample stratification procedures implemented at T_3 and high rates of missing data for the T_1 sample, results reported and interpreted in the current study are based on the 816 T_4 participants with complete diagnostic data through age 30. Table 1 summarizes means or percentages for demographic characteristics of this sample.

Previous analyses of participant attrition revealed bias related to study discontinuation between T_1 and T_4 (Farmer et al., 2015; Farmer, Kosty, Seeley, Olino, & Lewinsohn, 2013; Lewinsohn et al., 1993). In a comparison between the T_4 panel and those who dropped out from the study after T_1, no significant differences were found with respect to history of CUD at T_1 ($p = .53$), any lifetime psychiatric disorder at T_1 ($p = .96$), or the cumulative number of lifetime disorders at T_1 ($p = .23$). Wave-to-wave analyses, though, revealed several significant differences: participants with disruptive behavior disorders were more likely to drop out from T_1 to T_2 (17% vs. 11%), men were more likely to drop out from T_2 to T_3 (19% vs. 11%) and from T_3 to T_4 (16% vs. 11%), and participants with a history of substance use disorders, including CUD, were more likely to dropout from T_3 to T_4 (17% vs. 11%). This differential attrition confounds the interpretation of findings reported in the current study.

Prior research has reported epidemiological parameters for CUD in the 816 participants included in the current study (Farmer et al., 2015). The lifetime prevalence of

CUDs was 19.1% with an average onset age of 18.6 years. Findings indicated that ages

14 to 25 were a period of increasing risk for initial CUD onset, yet this risk diminished

after age 25. These patterns are consistent with recent national surveys conducted in the

United States that reported annual cannabis use prevalence rates of 11% at age 14, 36% at

age 18, 34% at age 22, 26% at age 26, and 20% at age 30 (Johnston et al., 2013a, 2013b).

Table 1

Sample Demographic Characteristics (n = 816)

Variable	*M* (*SD*) or % (*SE*)
Age at T_1, *M* (*SD*)	16.6 (1.2)
Male, % (*SE*)	43.9 (1.7)
Non White, % (*SE*)	7.7 (1.0)
Raised in dual parent household, % (*SE*)	57.3 (1.7)
At least one parent with bachelor's degree, % (*SE*)	45.0 (1.8)
Ever married by T_4, % (*SE*)	66.9 (1.7)
Years of education by T_4, *M* (*SD*)	14.6 (1.9)

Note. *M* = mean; *SD* = standard deviation; *SE* = standard error.

Measures

Diagnostic interviews. For the first three waves, psychiatric disorders among

participants were assessed with the Present Episode and Epidemiologic versions of the

Schedule for Affective Disorders and Schizophrenia for School-Age Children (Chambers,

1985; Orvaschel, Puig-Antich, Chambers, Tabrizi, & Johnson, 1982). At T_4, the

Structured Clinical Interview for Axis I *DSM-IV* Disorders–Non-Patient Edition (First,

Spitzer, Gibbon, & Williams, 1994) was used. These interviews were supplemented with

the Longitudinal Interval Follow-Up Evaluation (Keller et al., 1987) to assess disorder

presence and course since the previous assessment. Symptom reports were evaluated with respect to *DSM-IV* criteria and decision rules at each assessment wave.

Recorded interviews were randomly selected from each assessment wave and evaluated for inter-rater reliability: $T_1 = 263$ (15%), $T_2 = 162$ (11%), $T_3 = 190$ (20%), and $T_4 = 124$ (15%) of interviews. The level of agreement among raters for CUD since the previous interview was moderate to high across study waves (Cohen's kappas: $T_1 = .72$, $T_2 = .93$, $T_3 = .83$, $T_4 = .82$). Additional information about the reliability procedures used in the OADP can be found in previous reports (Farmer, Seeley, Kosty, & Lewinsohn, 2009; Seeley, Kosty, Farmer, & Lewinsohn, 2011).

Cannabis Use Disorder. The OADP dataset includes onset and offset ages for each CUD diagnosis and other psychopathology. This feature of the dataset allowed me to compute a series of dummy coded variables to indicate period prevalence of CUD within the following age-based intervals: age 14 to 15.9, 16 to 17.9, 18 to 19.9, 20 to 21.9, 22 to 23.9, 24 to 25.9, 26 to 27.9, and 28 to 29.9. A value of 0 was assigned if CUD was not present in a given interval and a value of 1 was assigned if CUD was present. These prevalence variables were used as indicators in the trajectory analyses described in subsequent sections.

Risk factors. I evaluated the following variables as putative risk factors for longitudinal trajectory patterns of CUD.

Participant and family characteristics. Participant and family characteristics that were assessed at T_1 included sex (coded 1 "male" or 0 "female"), pubertal timing relative to peers (coded 1 "early", 2 "on time", or 3 "late"), growing up in a single parent

household (coded 1 "yes" or 0 "no"), and history of repeating a grade before age 12 (coded 1 "yes" or 0 "no").

Psychiatric disorders. Period prevalence of other psychiatric disorders prior to age 14 was calculated using diagnostic age of onset data. Consistent with findings associated with comorbidity and aggregation patterns of psychiatric disorders among the OADP sample (Farmer et al., 2013; Farmer et al., 2009; Seeley et al., 2011), I collapsed *DSM*-defined disorders into internalizing and externalizing disorder domains for risk factor and outcome analyses. Diagnostic categories that contributed to the *internalizing domain* were mood disorders (major depressive; dysthymia; bipolar spectrum inclusive of bipolar I, bipolar II, and cyclothymic disorders) and anxiety disorders (separation anxiety, simple/specific phobia, generalized anxiety, obsessive–compulsive, panic, agoraphobia without panic, post-traumatic stress, social phobia). Disorders that contributed to the *externalizing domain* were disruptive behavior disorders (attention deficit/hyperactivity, oppositional defiant, conduct) and non-cannabis-related substance use disorders (alcohol abuse or dependence diagnoses, hard drug abuse or dependence other than alcohol). For each domain, a value of 0 was assigned if a given disorder was not diagnosed and a value of 1 assigned if a given disorder was diagnosed.

Substance use initiation. In addition to diagnostic data detailed above, T_1 interviews included questions regarding substance use initiation, defined by five or more occurrences of use. I calculated a summary variable to indicate alcohol, tobacco, or illicit drug use initiation prior to the T_1 assessment and evaluated this variable as a predictor of CUD trajectory patterns.

Depressive symptoms. The 20-item Center for Epidemiological Studies Depression Scale (Radloff, 1977) was used to assess depressive symptoms at T_1. Items were rated on a scale from 0 "rarely or none of the time" to 3 "most or all of the time." Higher scores indicated greater depressive symptomology. This measure had a coefficient alpha of .90 in the current sample and has been correlated (r's = .50 to .80) with other measures of depression (Weissman, Sholomskas, Pottenger, Prusoff, & Locke, 1977).

Major life events. Eleven negative life events were selected from several life events inventories and assessed at T_1 (Dohrenwend, Krasnoff, Askenasy, & Dohrenwend, 1978; Holmes & Rahe, 1967; Sandler & Block, 1979). Major life events included death of a loved one, major illness, victim of violence, legal troubles, lost job, fighting, used drugs or alcohol, attempted suicide, moved residence, victim of theft, and vehicular accident. The total number of major life events was used in subsequent analyses. This measure had a coefficient alpha of .78 in the current sample. Currently, no validity coefficients are available for this measure.

Daily hassles. Twenty items from the Unpleasant Events Schedule (Lewinsohn, Mermelstein, Alexander, & MacPhillamy, 1985) were administered at T_1 to assess daily hassles in the last month. Items were rated on a scale from 1 "not at all" to 5 "about every day." Higher scores indicated greater daily hassles. This measure had a coefficient alpha of .89 in the current sample and has been correlated (r = .63) with self-monitoring of the same events over a one month period (Lewinsohn et al., 1985).

Childhood maltreatment. Childhood physical and sexual abuse were assessed retrospectively at T_3 using 12 items from the Assessing Environment II (Berger, Knutson, Mehm, & Perkins, 1988) and five items from the Childhood Trauma Questionnaire

(Bernstein, Fink, Handelsman, & Foote, 1994). Items were rated on a scale from 1 "never true" to 5 "very often true." A composite measure of childhood maltreatment was computed as the mean across z-score transformations of physical abuse and sexual abuse scale scores. Higher scores indicated greater levels of abuse. This measure had a coefficient alpha of .71 for physical abuse and .96 for sexual abuse in the current sample. Currently, no validity coefficients are available for this measure.

Psychosocial functioning at T$_4$. I evaluated the following variables as putative distal outcomes of longitudinal trajectory patterns of CUD.

Participant characteristics. The T$_4$ survey included questions concerning years of education (reported on a scale from 1 "high school diploma" to 7 "doctorate degree"), weeks unemployed during the past year (reported on a scale from 1 "0 weeks" to 6 "52 weeks"), marital history (coded 1 "ever married" or 0 "never married"), history of divorce or separation (coded 1 "yes" or 0 "no"), and history of biological parentage of a child (coded 1 "yes" or 0 "no").

Psychopathology between ages 24 and 30. Period prevalence of externalizing and internalizing disorder categories between ages 24 and 30 was calculated using diagnostic episode data (i.e., age of onset and duration of episode).

Relationship quality. Twenty items from the Perceived Social Support scale (Procidano & Heller, 1983) were administered at T$_4$ to assess perceived social support from family and friends. Lower scores indicated poorer relationship quality. This measure had a coefficient alpha of .90 in the current sample and has been correlated (r's = .13 to .43) with other measures of social asset traits (Procidano & Heller, 1983).

Social adjustment. Fifty-four items from the Social Adjustment Scale (Weissman & Bothwell, 1976) were used to assess social adjustment during the two weeks preceding the T_4 interview. Higher scores indicated poorer adjustment. This measure had a coefficient alpha of .70 in the current sample and yields similar results to those obtained by the interview format of the instrument (Weissman, Prusoff, Thompson, Harding, & Myers, 1978).

Life satisfaction. Fifteen items related to general feelings of happiness and contentment (Andrews & Withey, 1976; Campbell, Converse, & Rodgers, 1976) were used to assess life satisfaction at T_4. Higher scores indicated greater life satisfaction. This measure had a coefficient alpha of .87 in the current sample. Currently, no validity coefficients are available for this measure.

Depressive symptoms. The 20-item Center for Epidemiological Studies Depression Scale was also assessed at T_4 and had a coefficient alpha of .93 in the current sample.

Psychotic experiences. Thirteen items adapted from the Wisconsin Manual for Assessing Psychotic-Like Experiences (Kwapil, Chapman, & Chapman, 1999) were used to assess whether participants experienced thought transmission, passivity experiences, thought withdrawal, auditory experiences, personally relevant aberrant beliefs, visual experiences, or deviant olfactory experiences during the year prior to the T_4 interview. Higher scores indicated more frequent psychotic experiences. This measure had a coefficient alpha of .74 in the current sample. Currently, no validity coefficients are available for this measure.

Risky sexual behavior. The T_4 assessments also included items assessing high-risk sexual behavior during the past year. A composite measure of high-risk sexual behavior was computed as the mean across *z*-score transformations of the number of concurrent partners in the past year and total number of partners in the past year. A higher score indicates more risky sexual behavior. Currently, no reliability or validity coefficients are available for this measure.

Analytic Procedures

My dissertation involved four sets of exploratory analyses described in detail below. First, I identified CUD trajectory classes through age 30 using observed indicators of the presence versus absence of CUD within specific time-based intervals. Second, I evaluated the associations between clinical characteristics of participants' CUD and trajectory class membership. Third, I evaluated the associations between putative risk factors and trajectory class membership. Fourth, I evaluated the associations between latent class membership and psychosocial outcomes measured at age 30. These analyses involved many statistical tests. Thus, readers concerned with increased Type I error rates associated with multiple testing should apply the Bonferroni correction when interpreting subsequent results. The largest family of statistical tests was the class contrasts with respect to risk factors and outcomes (*n* = 13 tests each). Therefore, the family-wise Bonferroni corrected alpha is .05/13 = .004.

Cannabis use disorder trajectory classes. An initial unconditional latent class growth model (LCGM) with a one-class solution was estimated to reflect the overall population CUD trajectory over time. The basic one-class LCGM included an intercept factor (initial probability of meeting criteria for CUD) and linear slope factor (rate of

change in probability of meeting criteria for CUD over time) predicting CUD at each defined interval. An additional one-class LCGM was estimated that included an intercept factor and linear and quadratic slope factors. A chi-square difference test based on log-likelihood values and scaling correction factors was used to determine whether a linear or curvilinear functional form resulted in superior model fit.

After describing the overall population trajectory, I explored potential heterogeneity in trajectories of CUD within a series of unconditional LCGMs in which the number of latent classes sequentially increased, beginning with a two-class solution and moving to three classes, then four classes, and so on, until model convergence criteria were not met. The number of latent classes in the final LCGM solution was guided by interpretability, the statistical significance of the Lo-Mendell-Rubin adjusted Likelihood Ratio Test that compared the $n - 1$ and n-class solutions (Yungtai, Mendell, & Rubin, 2001), and Akaike's information criterion (AIC; Burnham, Anderson, & Huyvaert, 2011). Lower values of AIC indicate greater parsimony and fit, or a more optimal balance between under- and over-fitted models. Figure 1 provides a path diagram of an unconditional LCGM with n classes.

An important characteristic of LCGMs is that the variances of the intercept and slope parameters are fixed to zero; in contrast to models like growth mixture models (GMMs) that allow within-class variation in growth parameters. In the current study, GMMs with more than one trajectory class failed to meet convergence criteria, even with empirically derived start values, so I employed the more restrictive LCGMs for final interpretation and reporting. While LCGMs are useful for identifying latent trajectory classes when GMMs do not converge, they provide incomplete information about intra-

and inter-individual variability in trajectories and, therefore, provide an incomplete

understanding of trajectory classes. To explore within class variability in trajectories of

CUD I modeled risk for CUD over time within each latent class obtained in the LCGM

using multilevel longitudinal analyses (Raudenbush & Bryk, 2002), with age-based

intervals nested within individuals.

Figure 1. Model specification for a latent class growth model of cannabis use disorder
across *t* intervals with *n* latent classes. A latent class growth model fixes the growth
factor variances and covariances (Φ coefficients) to equal zero.

Clinical characteristics of cannabis use disorder and trajectory class

membership. I used a discriminant function analysis to predict CUD trajectory class

membership using age of initial CUD onset, total number of CUD episodes, cumulative

duration across CUD episodes, and the presence versus absence of a cannabis

dependence disorder as defined by *DSM-IV*.

Risk factors associated with cannabis use disorder trajectory classes. I employed

multinomial logistic regression to regress the latent trajectory class variable on each

putative risk factor, separately, using a three-step approach recommended by Asparouhov

and Muthén (2014). Briefly described, three-step approaches first require estimating a

mixture model using the latent class indicator variables. In the second step, a nominal

most likely class variable (N) is computed for each subject based on the posterior

distribution of the latent class variable (C_1) estimated in the LCGM. Because the

probability of being in a particular class is seldom 1.0, the casewise probabilities of being

in each latent class are also computed to characterize the misclassification of N. In the

third step, a mixture model using N as an indicator of a new latent class variable (C_2) is

specified with the mixture parameters fixed according to the misclassification of N

calculated in step 2. In this final step multinomial logistic regression is used to regress C_2

on the predictor of class membership. Three-step approaches have two primary

advantages compared to single-step approaches or analyses conducted without taking

uncertainty in class membership into account (McIntosh, 2013). First, they account for

error in latent class membership when estimating associations between a predictor and

the latent class variable. Second, they do not affect latent class formation as defined by

the solution of the unconditional mixture model. Figure 2 provides path diagrams for the

first and third steps of the three-step approach for evaluating predictors of latent class

membership. Odds ratios (*OR*) were computed for each risk factor to characterize the

relative risk of belonging to each trajectory class compared to the others.
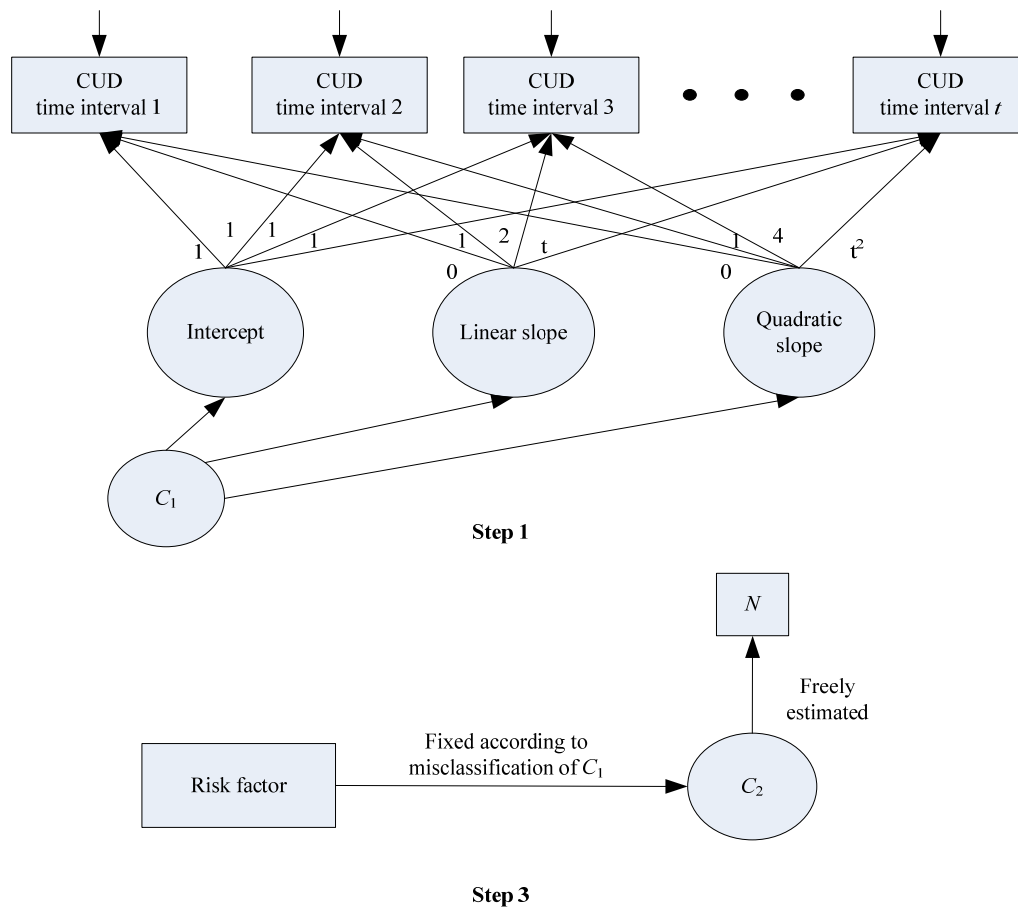
Figure 2. Path diagrams for the first and third steps of the three-step approach for evaluating predictors of latent class membership.

Outcomes associated with cannabis use disorder trajectory classes. I tested for equality of means for continuous psychosocial outcomes and proportions for binary psychosocial outcomes across the latent trajectory classes. These analyses used a similar three-step approach as described above and relied on Wald tests of equality across classes. Cohen's *d* effect sizes (Cohen, 1988) and *OR*s were computed to characterize the magnitude of associations between latent trajectory classes and continuous and binary outcomes, respectively. Cohen's *d* values of 0.2, 0.5, and 0.8 correspond to small, medium, and large effects, respectively.

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Statistical estimation methods. LCGMs were conducted using Mplus statistical software version 7.11 (Muthén & Muthén, 1998-2012), and model parameters were estimated using full information maximum likelihood estimation with robust standard errors. Because LCGMs are susceptible to converging on local solutions, multiple random starting values were used and solutions were considered non-convergent if random starts did not result in consistent log likelihood values. Multilevel longitudinal analyses within trajectory classes were completed using HLM 7.0 (Raudenbush, Bryk, Cheong, Congdon, & du Toit, 2011), the penalized quasi-likelihood estimator for binary outcomes, and specification of the intercept and the linear and quadratic growth parameters as random effects. To accommodate the dichotomous nature of the observed indicators of trajectory classes, the logit link function was used in the LCGMs and multilevel longitudinal analyses. By transforming dichotomous data, the logit link function imposes a threshold model that assumes an underlying normally distributed liability, or risk, for having a dichotomous trait. Within this normal distribution a threshold denotes the presence versus absence of a trait such as CUD. Variance in the liability for dichotomous traits can be modeled in similar ways as variance in continuous variables.

Participant weighting. Caucasians without a history of psychiatric diagnosis by T_2 were under sampled at T_3 by way of the stratified sampling procedure described earlier. To adjust for this in the analyses, a sampling weight was used such that Caucasian participants without a lifetime diagnosis by T_2 were assigned a weight of 2.05, a value that reflects the probability of this subgroup being sampled at T_3. In contrast, all participants with a psychiatric diagnosis and all non-Caucasian participants were assigned

a weight of 1.0. All analyses accounted for the stratified sampling procedure implemented at T_3.

Missing data. Diagnostic and substance use initiation data were available for all participants who were included in the reference sample for the current study (i.e., $n = 816$ who completed the T_4 assessment). Minimal missing data (< 1%) was observed for all risk factors used to predict trajectory class membership except the childhood maltreatment variable, for which 12% missing data was observed. All psychosocial outcome variables measured at T_4 had rates of missing data between 5% and 8%. See Appendix for rates of missing data for each self-report measure used in subsequent analyses.

Although methods for handling missing data typically assume data are missing at random (MAR), it is not possible to directly test this assumption when the values of the missing data are unavailable. Instead, I tested whether this assumption was tenable in the reference sample using *t*-tests and chi-square tests for differences in continuous and categorical self-report measures, respectively, by completion status of each self-report measure with missing data. Given the large number of statistical tests conducted in this analysis (> 150), I focused on patterns of systematic missing data rather than individual statistical significance tests. No strong patterns of systematic missing data were observed, suggesting that the MAR assumption was tenable. However, the more conservative assumption that data were missing completely at random (MCAR) was not tenable according to Little's MCAR test (χ^2 [723] = 18831.65, $p < .001$).

Multiple imputation (MI) in Mplus was used to impute missing values (up to 12%) on *risk factors* used to predict class membership. MI is an acceptable solution for

dealing with missing data regardless of whether the data are MAR (Rubin, 1996; Tabachnick & Fidell, 2007) and has been demonstrated to produce similar results across data that are missing completely at random, MAR, and not missing at random (Gadbury, Coffey, & Allison, 2003). The MI procedure I used in the current study generated 10 complete data sets using all available self-report measures as predictors of missing values. Analyses were conducted for each predictor of class membership across each of the 10 imputed data sets and pooled estimates are reported in the results.

Single imputation based on the expectation maximization algorithm as implemented in the SPSS Missing Value Analysis module was used to impute missing values (between 5% and 8%) on the *psychosocial functioning outcomes* because MI procedures were not supported by the three-step procedure for evaluating distal outcomes of class membership when sampling weights are applied. All self-report measures were included as auxiliary variables in the single imputation procedure to help reduce potential bias if the MAR assumption was violated (Allison, 2009).

CHAPTER IV

RESULTS

Cannabis Use Disorder Trajectory Classes

Estimation processes for the one-class LCGMs with linear and quadratic functional forms terminated normally. A visual inspection of the data describing risk for CUD by age interval and a likelihood ratio test based on the likelihood values suggested that including a linear and quadratic growth factor resulted in significantly better fit compared to a linear-only model ($p = .003$). The linear and quadratic slope coefficients were statistically significant (linear slope $= 0.27$, $t = 3.59$, $p < .001$; quadratic slope $= -0.03$, $t = -3.28$, $p = .001$) and the threshold was estimated at 2.92 ($t = 21.33$, $p < .001$). These results translate into probabilities of developing CUD of .051 between ages 14 and 15.9, .064 between 16 and 17.9, .075 between 18 and 19.9, .082 between 20 and 21.9, .085 between 22 and 23.9, .082 between 24 and 25.9, .075 between 26 and 27.9, and .065 between 28 and 30. Figure 3 depicts the observed and model-implied overall population trajectory of CUD risk from age 14 to 29.9.
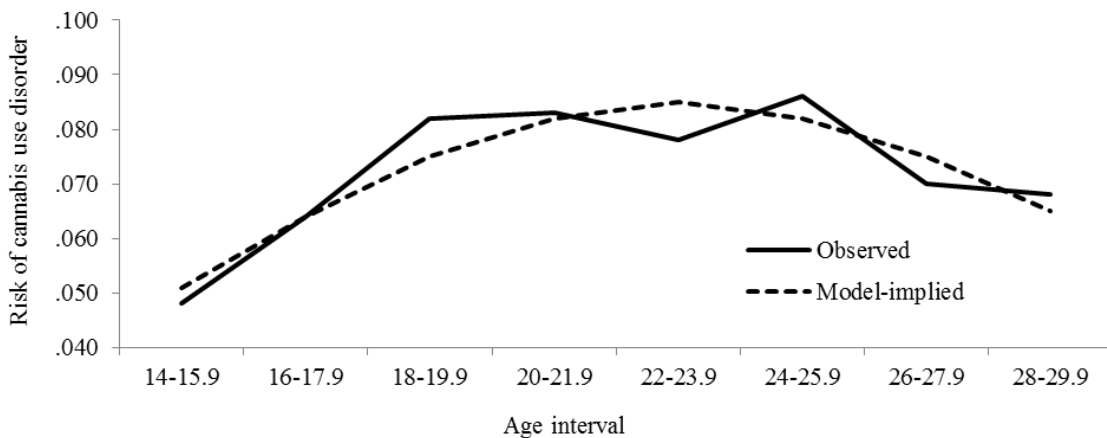

Figure 3. Risk probability of cannabis use disorder by age interval.

Heterogeneity in trajectory patterns was explored in a series of unconditional LCGMs with two, three, four, and five latent trajectory classes. Table 2 summarizes the model selection criteria for each unconditional LCGM that was used to determine the number of classes to use in subsequent analyses. The five-class solution failed to converge and was not evaluated for model fit. The smallest AIC value was obtained with the four-class solution (AIC = 2129.33). However, the Lo-Mendell-Rubin adjusted Likelihood Ratio Test indicated that the increase in goodness-of-fit from the three-class solution to the four-class solution was not statistically significant ($p = .577$), whereas the goodness of fit from the two-class solution to the three-class solution was statistically significant ($p < .001$). The four-class solution was conceptually similar to the three-class solution. In the four-class solution, however, the smallest subgroup formed by the three-class solution was subdivided into two classes ($n = 28$ in each class). The distinguishing feature between these two classes was the point at which risk for CUD began to increase (age 14 versus age 22). Given these results, I chose the three-class solution as the final model based on the interpretability of the latent class trajectories, parsimony, adequate class sizes for subsequent risk factor and outcome analyses, and the results of the Lo-Mendell-Rubin adjusted Likelihood Ratio Tests.

Table 2

Criteria for Class Formation for the Unconditional Latent Class Growth Model

Number of Classes	LR χ^2	df	p	AIC	LMR LRT	Entropy
1	929.86	252	<.001	3385.09	--	--
2	497.67	248	<.001	2346.39	<.001	.952
3	304.82	244	.005	2178.92	<.001	.960
4	226.65	240	.691	2129.33	.577	.964

Note. LR = likelihood ratio; AIC = Akaike's information criterion; LMR LRT = Lo-Mendell-Rubin likelihood ratio test; *df* = degrees of freedom. The five class solution did not converge.

Results of the final unconditional three-class LCGM are presented in Table 3. Table entries include class-specific group sizes, longitudinal course descriptors, growth parameter estimates in log odds scale, and point estimates in probability scale. Three trajectory classes were distinguished: a persistent increasing risk class (Class 1, $n = 58$), a maturing out class (Class 2, $n = 76$), and a stable low risk class (Class 3, $n = 682$). For illustrative purposes, risk probability results are summarized in Figure 4, showing the risk for CUD across age intervals for each of the three trajectory classes. For Class 1, risk persistently increased from 17% between ages 14 to 15.9 to 97% between ages 28 to 29.9. For Class 2, risk increased from 26% between ages 14 to 15.9 to 61% between ages 18 to 19.9, then risk decreased to less than 1% between ages 28 to 29.9. For Class 3, risk was less than 2% across all age intervals through age 30.

Because of concerns about participant attrition introducing substantial bias into latent class formation, I repeated the primary trajectory analyses summarized above using the full T_1 sample ($n = 1,709$). This sensitivity analysis revealed the same number of optimal trajectory classes with equivalent functional characteristics as the results based on the T_4 panel. However, the proportion of participants belonging to the stable increasing class was attenuated in the analysis based on the T_1 panel, likely given the profiles of participants who dropped out between the first (T_1) and last assessment (T_4) were associated with increased risk for CUD.

Table 3

Summary of the Final Unconditional Latent Class Growth Model with Three Classes

Class Characteristic	Class 1	Class 2	Class 3
n (%)	58 (7.1%)	76 (9.3%)	682 (83.6%)
Longitudinal course	Persistent increasing risk	Maturing out	Stable low risk
Parameter estimates			
Intercept	2.66***	3.22***	0.00 [a]
Linear slope	0.18	1.26***	-0.83
Quadratic slope	0.08*	-0.26***	0.08
Threshold	4.25***	4.25***	4.25***
Risk by age interval in probability scale			
14-15.9	.169	.263	.014
16-17.9	.208	.493	.007
18-19.9	.285	.610	.004
20-21.9	.416	.598	.002
22-23.9	.597	.457	.002
24-25.9	.784	.219	.002
26-27.9	.912	.053	.002
28-29.9	.972	.006	.002

Note. [a] Intercept for Class 3 fixed to zero by default.

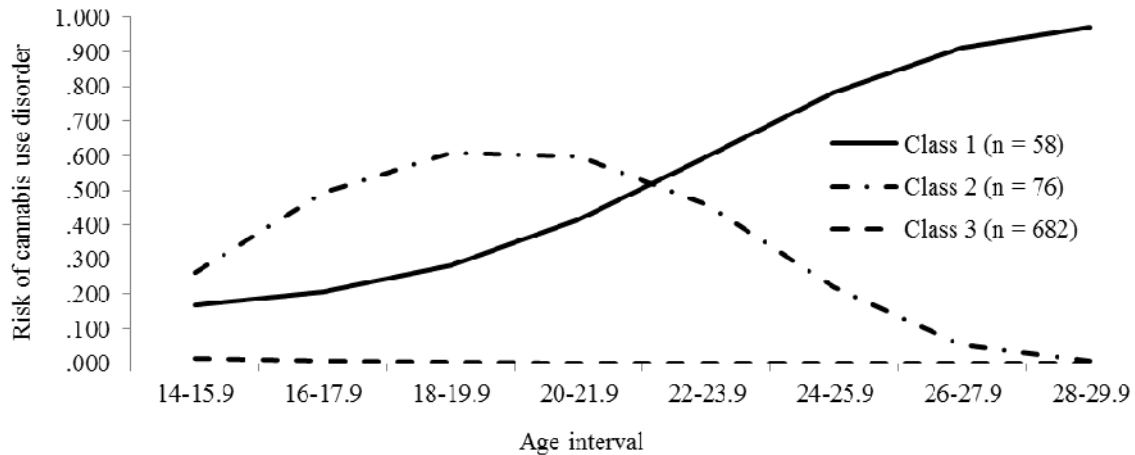* $p < .05.$ ** $p < .01.$ *** $p < .001.$

Figure 4. Risk probability of cannabis use disorder by age interval and latent class. Class 1 = persistent increasing risk over time; Class 2 = maturing out; Class 3 = stable low risk over time.

Within class variability in growth parameters. I estimated an unconditional random effects model for each latent CUD trajectory class to explore within class variability in CUD trajectories. Estimated individual trajectories within each trajectory class are illustrated in Figure 5. Within the persistent increasing trajectory class (Class 1) there was significant variability in the intercept (χ^2 [57] = 80.34, p = .049) but not in the linear or quadratic slopes (χ^2 [57] = 78.07, p = .069 and χ^2 [57] = 72.47, p = .149; respectively). Within the maturing out trajectory class (Class 2) there was significant variability in the intercept (χ^2 [75] = 155.19, p < .001), linear slope (χ^2 [75] = 140.41, p < .001), and quadratic slope (χ^2 [75] = 106.77, p = .034). Within the stable low trajectory class (Class 3) none of the growth parameters demonstrated significant variability (p's > .500).
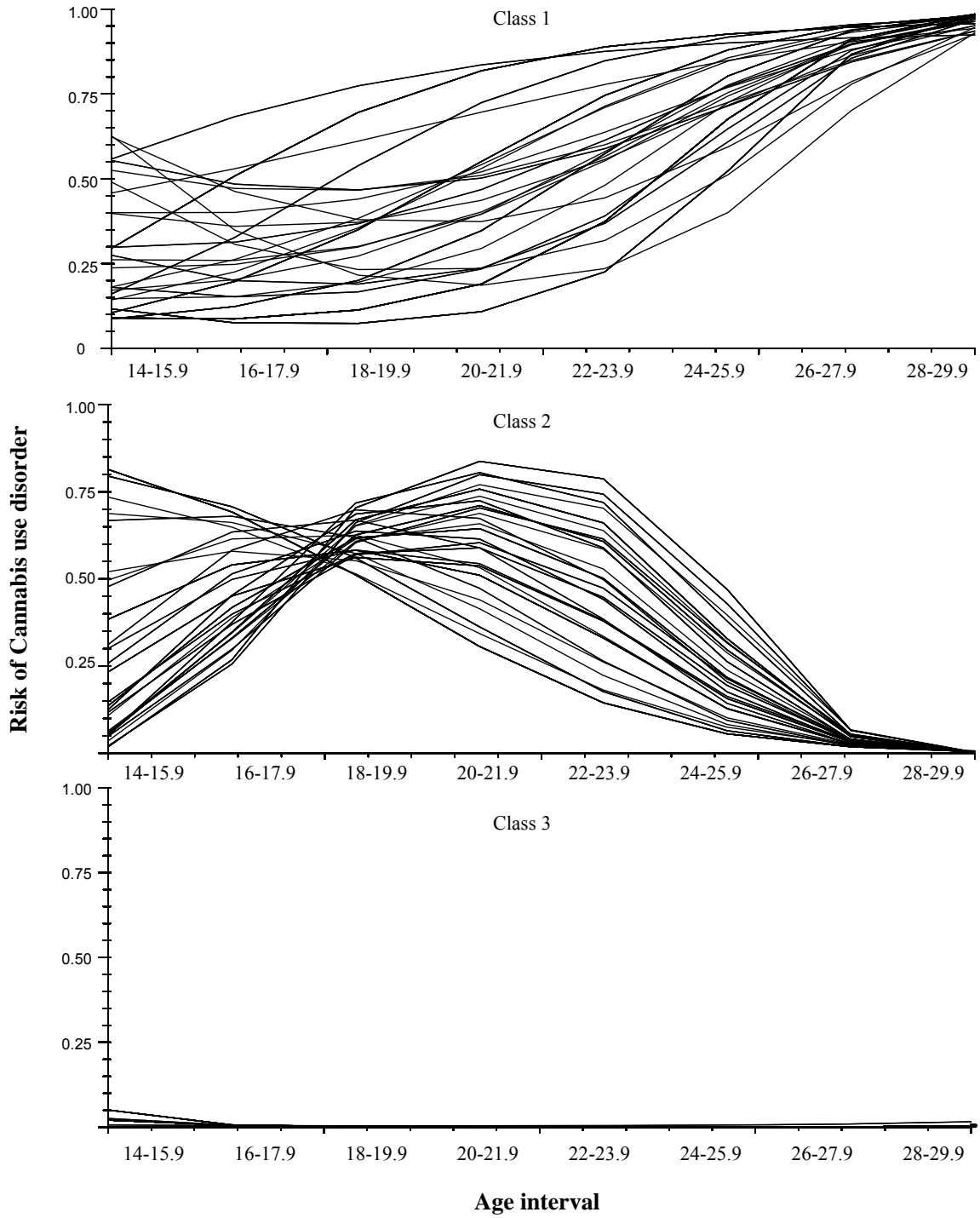
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Figure 5. Estimated individual trajectories within cannabis use disorder trajectory classes. Class 1 = persistent increasing risk over time; Class 2 = maturing out; Class 3 = stable low risk over time.

Clinical Characteristics of Cannabis Use Disorder and Trajectory Class

Membership

I used a discriminant function analysis to examine the extent to which clinical characteristics of CUD discriminated between the persistent increasing and maturing out trajectory classes. Predictors included age of initial CUD onset, total number of CUD episodes, cumulative duration across CUD episodes, and the presence versus absence of a cannabis dependence disorder as defined by *DSM-IV*. While the log determinants were similar across classes (6.0 vs. 6.5 for the persistent increasing and maturing out trajectory classes, respectively), Box's *M* test indicated that the assumption of equality of covariance matrices was violated (Box's $M = 27.90$, $p = .003$). Therefore, separate group covariance matrices were analyzed in the following discriminant function analysis.

Wilk's test of multivariate significance indicated that trajectory class membership was significantly related to the weighted multivariate combination of the clinical characteristics of CUD ($\Lambda = .29$, $\chi^2 [4] = 161.37$, $p < .001$, $\eta^2 = .71$). The rate of correct classification was 95%. Average age of initial CUD onset was significantly greater for participants in the persistent increasing class compared to participants in the maturing out class (20.8 years [$SD = 4.1$] vs. 17.6 years [$SD = 3.1$]; $F [1, 131] = 25.97$, $p < .001$, $\eta^2 = .16$). Participants in the persistent increasing class had, on average, significantly more CUD episodes compared to participants in the maturing out class (1.5 episodes [$SD = 0.7$] vs. 1.2 episodes [$SD = 0.5$]; $F [1, 131] = 4.84$, $p = .030$, $\eta^2 = .03$). Average cumulative duration across CUD episodes was also greater in the persistent increasing class compared to the maturing out class (90.6 months [$SD = 45.6$] vs. 40.2 months [$SD = 39.9$]; $F [1, 131] = 46.29$, $p < .001$, $\eta^2 = .26$). Rates of cannabis dependence were not

significantly different between the persistent increasing class and the maturing out class (56% and 54%, respectively; F [1, 131] = 0.05, p = .824, η^2 < .01). Examination of the standardized function coefficient matrix revealed that age of initial CUD onset (coefficient = 1.48), cumulative duration across CUD episodes (coefficient = 1.23), and number of CUD episodes (coefficient = 0.95) were most important in forming the function that discriminated between the trajectory classes.

Risk Factors Associated with Cannabis Use Disorder Trajectory Classes

In the next set of exploratory analyses I examined how putative risk factors related to latent trajectory classes. Table 4 summarizes results of a multinomial logistic regression using a three-step approach that evaluated what variables independently predicted the relative risk of belonging to each trajectory class. Table entries include odds ratios (OR) and their 95% confidence intervals (CI_{95}). All three pairwise comparisons of the latent classes were conducted. Male sex was related to nearly 3 times higher odds of persistent increasing class membership compared to the maturing out class (Class 1 vs. 2; p = .018) and the stable low class (Class 1 vs. 3; p = .001). Growing up in a dual parent household was related to 2.6 times lower odds of maturing out class membership compared to the stable low class (Class 2 vs. 3; p = .001). Period prevalence of externalizing psychiatric disorders prior to age 14 were related to 2.75 times higher odds of persistent increasing class membership compared to the stable low class (Class 1 vs. 3; p = .009). Substance use initiation before age 14 was related to 3.6 times higher odds of persistent increasing class membership (Class 1; p = .021) and 4.0 times higher odds of maturing out class membership (Class 2; p = .013) compared to the stable low class (Class 3). Each major life event was related to 1.1 times higher odds of persistent

Table 4

Multinomial Logistic Regression Results Predicting Latent Cannabis Use Disorder Trajectory Class using Putative Risk Factors

Risk Factor	Latent Class Contrast, OR [CI_{95}]		
	Class 1 vs. 2	Class 1 vs. 3	Class 2 vs. 3
Participant and family characteristics			
Male	2.57* [1.17, 5.61]	2.78** [1.52, 5.06]	1.08 [0.63, 1.87]
Pubertal timing			
Early vs. on-time	0.68 [0.26, 1.78]	0.88 [0.42, 1.87]	1.31 [0.67, 2.56]
Late vs. on-time	1.37 [0.46, 4.08]	1.62 [0.77, 3.41]	1.18 [0.49, 2.84]
Early vs. late	0.49 [0.13, 1.82]	0.54 [0.22, 1.38]	1.10 [0.40, 3.01]
Dual versus single parent household	1.92 [0.89, 4.13]	0.75 [0.43, 1.32]	0.39** [0.22, 0.69]
History of repeating grade before age 12	1.64 [0.59, 4.53]	1.86 [0.93, 3.74]	1.14 [0.50, 2.60]
Psychiatric disorders before age 14			
Internalizing domain	0.44 [0.16, 1.22]	0.61 [0.26, 1.42]	1.38 [0.74, 2.57]
Externalizing domain	1.47 [0.52, 4.14]	2.75** [1.29, 5.87]	1.87 [0.82, 4.24]
Substance use initiation before age 14	0.90 [0.19, 4.16]	3.59* [1.21, 10.64]	4.01* [1.33, 12.07]
Depressive symptoms	1.00 [0.97, 1.03]	1.01 [0.99, 1.04]	1.02 [1.00, 1.04]
Major life events	1.02 [0.97, 1.09]	1.06* [1.01, 1.11]	1.03 [0.99, 1.08]
Daily hassles	1.01 [0.98, 1.04]	1.02 [1.00, 1.04]	1.01 [0.99, 1.03]
Childhood maltreatment	1.16 [0.79, 1.71]	2.14*** [1.57, 2.91]	1.84*** [1.34, 2.51]

Note. OR = odds ratio; CI_{95} = 95% confidence interval. Separate models were conducted for each risk factor. Class 1 = persistent increasing risk over time; Class 2 = maturing out; Class 3 = stable low risk over time. The second class of each contrast is the reference category.

* $p < .05$. ** $p < .01$. *** $p < .001$.

increasing class membership compared to the stable low class (Class 1 vs. 3; $p = .016$).

Each unit increase in childhood maltreatment was related to 2.1 times higher odds of

persistent increasing class membership (Class 1; $p < .001$) and 1.8 times higher odds of

maturing out class membership (Class 2; $p < .001$) compared to the stable low class

(Class 3). Class contrasts were not significant for pubertal timing, history of repeating a

grade, internalizing psychiatric disorders prior to age 14, depressive symptoms, or daily

hassles.

Outcomes Associated with Cannabis Use Disorder Trajectory Classes

Table 5 summarizes descriptive statistics for adult psychosocial outcomes by

CUD trajectory class; the results of Wald tests of equality of CUD trajectory class means

or proportions for each outcome, with one degree of freedom; and available normative

comparison data based on United States census (U.S. Census Bureau, 2015) and

instrument validation studies (Radloff, 1977; Weissman et al., 1978). When compared to

the maturing out class and the stable low class, participants in the increasing class had a

higher likelihood of experiencing an externalizing disorder between ages 24 and 30

(Wald test $= 7.29$, $p = .007$, $OR = 2.64$ and Wald test $= 60.56$, $p < .001$, $OR = 11.59$;

respectively) and greater levels of psychotic symptomology in the past year at T_4 (Wald

test $= 5.79$, $p = .016$, Cohen's $d = 0.44$ and Wald test $= 14.06$, $p < .001$, Cohen's $d = 0.74$;

respectively). Participants in the increasing class also had a lower likelihood of being

married by T_4 (Wald test $= 6.46$, $p = .011$, $OR = 0.48$), a higher likelihood of divorce or

separation by T_4 (Wald test $= 5.52$, $p = .019$, $OR = 2.38$), and poorer social adjustment at

T_4 (Wald test $= 5.45$, $p = .020$, Cohen's $d = 0.29$) than did participants in the stable low

class. Participants in the maturing out class had fewer years of education (Wald test $=$

Table 5

Wald Tests of Equality of Cannabis Use Disorder Trajectory Class Means or Proportions on Adult Psychosocial Outcomes

Psychosocial functioning measure	Trajectory class			Wald pairwise class comparisons	Normative comparison data
	Class 1 ($n = 58$)	Class 2 ($n = 76$)	Class 3 ($n = 682$)		
Participant characteristics at T_4					
Years of education, M (SD)	14.3 (2.1)	13.8 (1.9)	14.6 (1.9)	2 < 3	12.0
Weeks unemployed in past year, M (SD)	1.8 (1.5)	2.2 (1.6)	1.7 (1.4)	2 > 3	NA
Ever married, % (SE)	50.9 (6.7)	58.3 (6.1)	68.5 (1.8)	1 < 3	65%
History of divorce or separation, % (SE)	30.2 (6.2)	16.2 (4.6)	15.4 (1.4)	1 > 3	12%
History of biological parentage of a child, % (SE)	37.4 (6.5)	51.9 (6.2)	49.2 (1.9)	NS	53%
Psychiatric disorders between 24 and 30, % (SE)					
Internalizing domain	41.4 (6.6)	53.9 (6.2)	32.1 (1.8)	2 > 3	NA
Externalizing domain	64.4 (6.4)	40.6 (6.0)	13.5 (1.3)	1 > 2, 3; 2 > 3	NA
Relationship quality with family and friends at T_4, M (SD) [a]	16.6 (4.1)	16.9 (4.4)	17.4 (3.9)	NS	NA
Social adjustment at T_4, M (SD) [b]	1.8 (0.3)	1.8 (0.4)	1.7 (0.3)	1 > 3	1.6
Life satisfaction at T_4, M (SD) [a]	30.9 (8.6)	29.8 (8.2)	28.9 (8.4)	NS	NA
Depressive symptoms at T_4, M (SD) [b]	12.0 (8.4)	11.4 (10.6)	9.7 (9.4)	NS	9.3, clinical cutoff = 16
Psychotic experiences in past year at T_4, M (SD) [b]	2.9 (2.9)	1.8 (2.4)	1.5 (1.8)	1 > 2, 3	NA
High-risk sexual behavior in past year at T_4, M (SD) [b]	0.3 (1.5)	0.2 (1.2)	-0.1 (0.6)	NS	NA

Note. M = mean; SD = standard deviation; SE = standard error; NS = no statistically significant pairwise class comparisons. Separate models were conducted for each outcome variable. Class 1 = persistent increasing risk over time; Class 2 = maturing out; Class 3 = stable low risk over time. [a] Higher scores indicated greater adjustment. [b] Lower scores indicated greater adjustment. Comparative average is based on United States census data (U.S. Census Bureau, 2015) and instrument validation studies (Radloff, 1977; Weissman et al., 1978). NA = not available.

10.50, $p = .001$, Cohen's $d = 0.42$), more weeks unemployed in past year at T_4 (Wald test $= 6.37$, $p = .012$, Cohen's $d = 0.34$), and a higher likelihood of experiencing internalizing (Wald test $= 11.10$, $p = .001$, $OR = 2.47$) and externalizing disorders (Wald test $= 19.15$, $p < .001$, $OR = 4.38$) between ages 24 and 30 than did participants in the stable low class. Class comparisons were not statistically significant for history of biological parentage of a child, relationship quality with family and friends at T_4, life satisfaction at T_4, depressive symptoms at T_4, or high-risk sexual behavior in past year at T_4.

CHAPTER V

DISCUSSION

The primary objective of my dissertation was to identify classes of individuals based on intraindividual trajectory patterns of cannabis use disorder (CUD) through age 30. In the current study, CUD diagnoses were based on meeting criteria for either cannabis abuse or dependence as defined by the *Diagnostic and Statistical Manual of Mental Disorders*, *4th edition* (*DSM-IV*; American Psychiatric Association, 1994). This definition is consistent with the recently released *DSM-5*, which also combines abuse and dependence criteria to form a single use disorder category (American Psychiatric Association, 2013). CUD is characterized by a pattern of cannabis use that either contributes to adverse consequences or continues despite cannabis-related problems. To evaluate the validity of CUD trajectories and the extent to which results were consistent with the *DSM* conceptualization of CUD I contrasted the trajectory classes on clinical characteristics of CUD episodes, developmental risk factors, and psychosocial outcomes. Person-centered latent class growth models integrated with variable-centered auxiliary analyses were used to address my research questions. Results were based on a representative community-based sample from western Oregon that participated in the Oregon Adolescent Depression Project (OADP; Lewinsohn et al., 1993).

Trajectory-based studies of CUD are rare, with previous studies of cannabis-related trajectories limited to cannabis initiation, use in the past year, frequency of use, and quantity consumed (Babor et al., 2002; Baggio et al., 2014; Brook et al., 2011b; Flory et al., 2004; Hix-Small et al., 2004; Kandel & Chen, 2000; Windle & Wiesner, 2004). Few studies included longitudinal data from adolescence through early adulthood

with detailed diagnostic information for a wide range of psychiatric disorder categories over the course of the study. My dissertation extended prior research on trajectories of cannabis use by utilizing the strengths of the OADP including its large-scale prospective evaluation of psychosocial functioning, assessment of *DSM*-defined psychiatric disorders through semi-structured diagnostic interviews, and extensive measurement of putative risk factors and outcomes. The OADP provided a unique opportunity to supplement the literature on risk factors, clinical characteristics, and psychosocial outcomes associated with developmental trajectories of CUD.

Summary of Findings

After conducting a series of latent class growth models, goodness of fit indices provided evidence that the best fitting model was composed of three latent classes. Through age 30, the three distinct CUD trajectory classes were interpreted as: (a) a class with persistent increasing risk over time; (b) a maturing out class, marked by increasing risk through approximately age 20 and declining risk from late adolescence through early adulthood; and (c) a generally non-abusing and non-dependent class marked by stable low risk over time. In her seminal review of longitudinal research on antisocial behavior, Moffitt (1993) described similar subgroups of individuals characterized by life-course persistent and adolescent-limited antisocial behavior patterns. Moffitt emphasized the importance of considering time-course variations in behavior patterns and the current findings support the taxonomies she proposed.

Previous studies of the developmental trajectories of self-reported cannabis use have yielded similar trajectory patterns (Brook et al., 2011b; Flory et al., 2004; Hix-Small et al., 2004; Kandel & Chen, 2000; Windle & Wiesner, 2004). In a study that included an

age range similar to the current study, Brook et al. (2011b) identified four trajectories of self-reported frequency of cannabis use characterized by non-users or low frequency users, maturing out users, users with late initiation, and chronically high users. Contrary to these findings the three-class solution I obtained did not include a chronically high use class. One possible explanation for this difference is that the clinically defined and more severe CUD indicator used in the current study limited the number of individuals who were at high risk during early adolescence relative to the less severe frequency of cannabis use indicator used by Brook and colleagues. Another possible explanation is that the chronic group might have been eliminated from the current study as an artifact of beginning trajectory-based analyses at age 14.

I examined the extent to which clinical characteristics of CUD discriminated between the persistent increasing and maturing out trajectory classes, including age of initial onset, number of episodes, cumulative duration across episodes, and rates of cannabis dependence versus cannabis abuse diagnoses. Constructing a screening index for CUD trajectory classes based on clinical characteristics was not my primary goal. However, the high classification accuracy based on clinical characteristics (95%) was validating. Compared to individuals in the maturing out class, the persistent increasing class demonstrated later initial CUD onsets on average (20.8 years of age vs. 17.6 years of age). This finding is consistent with those reported by Kandel and Chen (2000) wherein persistent and heavy users were not necessarily the earliest to initiate cannabis use and the early initiation group was less likely to persist using cannabis into adulthood. This supports other's findings that risk factors for substance use during adolescence, such as peer substance use and deviance or parental divorce, may not be associated with

continued use into adulthood (Bates & Labouvie, 1997). In the current study the persistent increasing class also demonstrated a greater average cumulative duration across CUD episodes (90.6 months vs. 45.6 months), which was expected given the functional forms of the relative trajectory classes. Interestingly, rates of cannabis dependence disorder were not significantly different between the persistent increasing class and the maturing out class (56% vs. 54%, respectively). Given that dependence is traditionally viewed as a more persistent and chronic form of a substance use disorder, this latter finding provides additional evidence for the lack of discriminant validity between cannabis abuse and cannabis dependence categories (Lynskey & Agrawal, 2007). Therefore, this study provides further empirical support for the combination of abuse and dependence categories into a single "use disorder" category in the *Diagnostic and Statistical Manual of Mental Disorders, 5th edition* (American Psychiatric Association, 2013).

Risk factors measured during early adolescence were evaluated as predictors of trajectory class membership in a set of univariate exploratory analyses. Male sex was related to nearly three times the odds of belonging to the persistent increasing class compared to both the maturing out class and the stable low class. Growing up in a single parent household was not associated with persistent increasing CUD risk but was associated with over two times the odds of belonging to the maturing out class compared to the stable low class. This finding suggests that parental divorce is a time-limited risk factor for CUD during adolescence but is not associated with continued risk into adulthood. Childhood externalizing psychiatric disorders, substance use initiation during childhood, and maltreatment during childhood generally differentiated trajectory classes

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characterized by a history of CUD but did not differentiate the persistent increasing class from the maturing out class. Overall, these findings are consistent with other epidemiological research on factors that predict cannabis initiation and CUD (Brook et al., 2011a; Butters, 2002; Farmer et al., in press; Flewelling & Bauman, 1990; Hayatbakhsh et al., 2006; Oshri et al., 2011). Namely, the presence of individual- and family-level risk factors substantially increases the risk for a sustained movement along the persistent increasing CUD trajectory through age 30. The extent to which these risk factors combine, or interact, to predict trajectory membership is unknown and warrants investigation in future studies.

Measures of psychosocial functioning later in life were compared across trajectory classes in a second set of exploratory analyses. Interestingly, the maturing out class completed the fewest years of education and reported the greatest amount of unemployment compared to the persistent increasing and stable low classes, with medium effect sizes obtained. These findings might be associated with a finding discussed earlier in which the average age of initial CUD onset coincided with high school years for the maturing out class, while the persistent increasing class typically did not meet criteria for CUD until after high school. Future research on CUD trajectories, the onset of CUD, and educational and occupational attainment might clarify these findings.

While results indicated nearly twice the odds of not marrying and divorce among the persistent increasing class compared to the class characterized by stable low risk for CUD, trajectory classes were not associated with self-report relationship quality with family and friends. These findings appear contradictory if one assumes marriage and divorce are positive and negative life events, respectively. However, a recent longitudinal

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study indicates that divorce, and perhaps choosing not to marry, can be positive for subjective well-being (Gustavson, Nilsen, Ørstavik, & Røysamb, 2014).

Social adjustment was significantly lower in the persistent increasing class compared to the stable low risk class (mean adjustment score = 1.8 vs. 1.7, respectively). However, the effect size was small and lesser in magnitude than that observed between individuals with alcoholism and non-mentally ill participants in a validation study of the social adjustment scale (mean adjustment score = 2.2 vs. 1.6, respectively). Therefore, the clinical significance of the observed difference in social adjustment between CUD trajectory classes is questionable.

Self-reported psychotic experiences were significantly greater in the persistent increasing class, while the maturing out and stable low risk classes reported similar levels of psychotic experiences. Although medium and large effect sizes were obtained in these class comparisons, it is difficult to determine the clinical significance of these differences due to the absence of normative data on the psychotic experiences measure used in this study. Studies often report positive associations between cannabis use and psychotic symptoms but the extent to which psychotic symptoms persist beyond transient cannabis intoxication is less clear (Moore et al., 2007). The current study provides evidence that psychotic experiences may be due directly to the effect of intoxication with cannabis rather than a more enduring effect of cannabis use by demonstrating similar levels of psychotic experiences in the stable low and maturing out CUD trajectory classes. It should be noted, however, that whether psychotic experiences are consequences of or risk factors for CUD cannot be determined from this study. Future studies should control for baseline psychotic experiences in the evaluation of these associations.

Although trajectory classes characterized by a history of CUD generally demonstrated lower levels of psychosocial functioning during early adulthood, there was variability in psychosocial outcomes within the maturing out and persistent increasing trajectory classes as evidenced by the standard deviations summarized in Table 5. Future research should evaluate predictors of within class variability in psychosocial functioning to further understand the nature of risk and protective factors for adverse consequences of CUD.

Implications

The current findings regarding the trajectories of CUD from mid-adolescence to early adulthood parallel those reported in the broader field of antisocial behavior (Moffitt, 1993), a domain of psychopathology highly associated with substance use. Although the risk factors evaluated in this study generally failed to differentiate between the persistent increasing and maturing out CUD trajectory classes, future research with additional time-independent and time-varying risk factors is warranted.

Identifying CUD trajectory classes and their associated risk factors and outcomes can inform the development of comprehensive models of CUD etiology and, in turn, aid the development of trajectory-specific intervention approaches (Schulenberg et al., 2001). Identifying relatively benign trajectory classes, in particular, could have implications for public health perspectives and resource allocation for intervention services. Designing targeted versus universal interventions for those who are at greatest risk for CUD subtypes that manifest greater severity in psychosocial outcomes is a cost-effective way to mitigate the consequences of CUD. Findings from the current study suggest that altering the trajectories of CUD, especially persistent increasing trajectories, may be

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beneficial for reducing psychotic experiences and externalizing disorders during early adulthood. Still, the maturing out trajectory class was not exempt from psychosocial impairment during early adulthood despite the decreased risk for CUD. Opportune windows for successful intervention programs may, then, be during childhood or adolescence. Developmental transitions during these periods require consequential decisions concerning coping styles and other functional behaviors that might affect risk for CUD and more general health outcomes and well-being across the life span.

The findings that (a) other externalizing disorders during childhood were associated with the persistent increasing CUD trajectory class and (b) other externalizing disorders during early adulthood were associated with the persistent increasing and maturing out CUD trajectory classes is consistent with research on externalizing comorbidity (Farmer et al., 2009) and behavior theories of externalizing disorders (Hayes, Wilson, Gifford, Follette, & Strosahl, 1996). Behavior theory generally does not endorse the medical model of discrete psychiatric disorders. Instead, behaviorists often consider psychiatric comorbidity the manifestation of a functional response class (i.e., a set of topographically different behaviors that share the same maintaining consequence). Using cannabis and drinking alcohol, for example, have unique structural features and characteristics but often serve the same function of attenuating aversive internal stimuli such as painful emotions, thoughts, or memories. When experiential avoidance-related behaviors such as using cannabis and drinking alcohol are effective in attenuating or alleviating aversive stimuli they become negatively reinforced. Knowledge of setting events that occasion the response class and the behavioral function that the response class serves can be used to design effective intervention strategies that promote alternative,

healthier, and more socially acceptable responses (Farmer & Nelson-Gray, 2005). A recommendation for future research is to investigate the long-term effects of targeted behavioral interventions implemented during childhood and adolescence on the developmental trajectories of experiential avoidance-related behaviors including CUD and other externalizing disorders.

As researchers and practitioners explore cannabis as a biotechnology for treating medical conditions such as chronic pain, epilepsy, and asthma, it is necessary to consider adverse side effects of its sustained use. The current study may help to advance knowledge about who is at highest risk for adverse consequences of medicinal cannabis and the nature of those consequences. For example, patients with long-term prescriptions to medicinal cannabis might experience psychosocial consequences similar to individuals belonging to maturing out or persistent increasing trajectory classes identified in the current study. Practitioners who prescribe cannabis should be aware of the current study's findings when determining whether potential health benefits outweigh known consequences of sustained use, and potentially abuse, of medicinal cannabis.

Limitations

Limitations that impact the internal and external validity of the reported findings included relatively low participation rates, sample attrition and non-ignorable missing data, design features of the OADP, and statistical limitations. Although the demographic characteristics of the participating sample were similar to corresponding census data for the region (Lewinsohn et al., 1993), self-selection for study participation at the first and third assessment waves and participant attrition were sources of bias in the reported findings. Previous studies of the OADP have reported potential bias due to attrition,

including an increased propensity to discontinue study participation as a function of male sex, history of childhood disruptive behavior disorders, and history of substance use disorders including CUD (Farmer et al., 2015; Farmer et al., 2013; Lewinsohn et al., 1993). It is unknown what direction these self-selection and attrition biases operated in the analyses of CUD trajectory patterns and their correlates but a sensitivity analysis conducted in the current study revealed congruent trajectory patterns between analyses based on the T_1 ($n = 1,709$) and T_4 ($n = 816$) panels. It should be noted that the proportion of participants belonging to the stable increasing class was attenuated in the analysis based on the T_1 panel, likely given the profiles of participants who dropped out between the first and last assessment were associated with increased risk for CUD. Further exploration of self-selection and attrition mechanisms (Little, 1995) and their impact on the interpretation of the current findings should be explored in future research using techniques like propensity score analyses (Rosenbaum & Rubin, 1984) or complier-average causal effect modeling (Yau & Little, 2011).

Design features of the OADP also introduced several limitations. Causal associations between risk factors, trajectory class membership, and psychosocial outcomes could not be determined from the analyses due to the non-experimental nature of the study design. Historical, maturational, or cohort-specific effects such as cultural influences on cannabis use may have been sources of inferential bias associated with risk factors and outcomes and trajectory class formation (Shadish, Cook, & Campbell, 2002). Participants were relatively uniform with respect to race and geographic location. Consequently, the generalizability, or external validity, of the current findings to more diverse groups of individuals or locations is unclear. The timing of the four assessment

waves may have introduced increased retrospective recall bias in the measurement of CUD onset and offset ages for episodes that occurred further, in time, from the diagnostic interviews. I did not evaluate a comprehensive list of environmental influences on CUD development. Substance abuse or dependence in peers, for example, may exert a great influence on the risk for CUD (Verweij et al., 2010). Other potentially important variables were also omitted from the current analyses. Factors such as age of cannabis initiation, quantity of use, potency of cannabis used, or co-occurring substance use disorders including alcohol use disorder may further qualify trajectory classes and their correlates. Furthermore, associations between CUD trajectory classes, risk factors, and outcomes might be better accounted for by co-occurring substance use disorders such as alcohol use disorder. Finally, a number of self-report measures included in the current study lacked pre-established reliability and validity evidence, including the measure of psychotic experiences.

There were also limitations related to the statistical analyses applied in the current study. Risk factors and outcomes were evaluated using univariate tests when multivariate techniques, such as discriminant function analysis or multivariate analysis of variance, are typically more powerful and provide more information when addressing these types of research questions. The large number of statistical significance tests conducted for these analyses was also a concern. To acknowledge this limitation, I provided a Bonferroni adjusted alpha level (.004) to decrease Type I error rates. Interpretation based on this adjusted critical p value would eliminate some of the statistically significant associations between CUD trajectory classes and male sex, externalizing psychiatric disorders prior to age 14, substance use initiation before age 14, major life events,

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psychotic experiences, marital status, divorce or separation, social adjustment, and unemployment.

In addition, relatively few number of cases were classified into trajectory classes that were primarily of interest (i.e., $n = 58$ in the persistent increasing class and $n = 76$ in the maturing out class versus $n = 682$ in the stable low class). Limited statistical power associated with these small group sizes complicated my ability to detect statistically significant differences between classes on risk factors and outcomes. Moreover, at least one additional trajectory class was suggested by the significant variability in the intercept of the maturing out trajectory class illustrated in the second panel of Figure 5. Specifically, there may be two maturing out trajectories that are differentiated by the average age of onset and the timing at which the maturing out process begins. Future research, perhaps based on clinical samples with higher rates of CUD, should attempt to differentiate similar trajectory classes using risk factors and psychosocial outcomes and explore alternative longitudinal patterns of risk for CUD.

Finally, growth mixture models (GMMs) that allowed for within class variability in growth parameters failed to meet convergence criteria in the current study; likely due to incorrect model specification. Latent class growth models (LCGMs) that fixed within class variances of growth parameters to equal zero did meet convergence criteria and were therefore used for final interpretation. While LCGMs are useful for identifying latent trajectory classes when GMMs do not converge, they provide incomplete information about intra-class individual differences in trajectory patterns. I explored the within class variability in growth parameters using post hoc random effect multilevel models, but the extent to which risk factors and outcomes were associated with

individual-level growth was not evaluated in the current study. Estimating these associations using less restrictive mixture models would contribute to a greater understanding of risk factors and outcomes associated with CUD trajectory patterns. Future studies should consider applying empirically derived model specifications that allow for greater model flexibility and ensure that model convergence criteria are met. The current study, for example, indicates that the variability in the growth parameters should be fixed to zero for the stable low class and freely estimated for the persistent increasing and maturing out classes.

Conclusion

As findings from this study illustrated, there was substantial heterogeneity in intraindividual CUD trajectory patterns from childhood through early adulthood. Three trajectory patterns were interpreted: a class with persistent increasing risk over time; a maturing out class, marked by increasing risk through approximately age 20 and declining risk from late adolescence through early adulthood; and a generally non-abusing and non-dependent class marked by stable low risk over time. Compared to individuals in the maturing out class, the persistent increasing class demonstrated later average initial CUD onsets, greater average cumulative duration across CUD episodes, and similar rates of cannabis dependence versus abuse. Moreover, results partially supported distinctions between adolescent-limited and life-course persistent CUD trajectories with psychosocial differences evident in adulthood. For example, self-reported psychotic experiences were significantly greater in the persistent increasing class, while the maturing out and stable low risk classes reported similar levels of psychotic experiences.

Replications of these findings are needed, as is research on the validity of the trajectory-based constructs based on theoretically relevant variables such as treatment response and risk and protective factors not evaluated herein. Other areas for future investigation include the trajectories of specific CUD-related symptoms and their antecedents to better understand the function of the behavior and the progression from casual experimentation and recreational use to disorder-level abuse or dependence. Future research based on more diverse samples is indicated, as are well-controlled tests of associations between risk factors, trajectory class membership, and psychosocial outcomes. A better understanding of these issues will further the science of etiological theory and the development of effective intervention programs that target problematic cannabis use at specific developmental stages.

APPENDIX

RATES OF MISSING DATA FOR SELF-REPORT MEASURES

Study Variable	Number of Missing Cases	Rate of Missing Data
Risk factors		
Male	0	0.0%
Pubertal timing	6	0.7%
Dual versus single parent household	0	0.0%
History of repeating grade before age 12	1	0.1%
Substance use initiation before age 14	0	0.0%
Depressive symptoms	0	0.0%
Major life events	0	0.0%
Daily hassles	0	0.0%
Childhood maltreatment	95	11.6%
Psychosocial functioning measures		
Years of education	44	5.4%
Weeks unemployed in past year	64	7.8%
Ever married	44	5.4%
History of divorce or separation	44	5.4%
History of biological parentage of a child	49	6.0%
Relationship quality with family and friends at T_4	44	5.4%
Social adjustment at T_4	43	5.3%
Life satisfaction at T_4	43	5.3%
Depressive symptoms at T_4	44	5.4%
Psychotic experiences in past year at T_4	43	5.3%
High-risk sexual behavior in past year at T_4	44	5.4%

Note. The reference sample $n = 816$.

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