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Premorbid Adjustment, Cannabis Use and Global, Role, and Social Functioning in Individuals at
Clinical High Risk for Psychosis

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An abstract of
a thesis submitted to the Faculty of Emory College of Arts and Sciences
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Abstract:

The use of cannabis is associated with mixed outcomes in individuals at clinical high risk (CHR) for developing a psychotic disorder. While several studies have observed an increase in psychosis conversion rates and severity of positive symptoms, other research suggests that cannabis use is associated with reduced negative symptoms and improved cognitive performance in a CHR population. Several hypotheses aim to explain this discrepancy in findings, some arguing that cannabis itself has enhancing effects, while others argue that CHR individuals with higher pre-existing functioning are more likely to use cannabis. Important indices of prodromal course, such as global, social, and role functioning, have yet to be explored in relation to cannabis use in a CHR sample. The sample for the present study is from the third wave of the North American Prodrome Longitudinal Study- 3rd cohort (NAPLS-3) and includes 710 participants who have been classified as clinical high risk (CHR) for developing a psychotic disorder. Cannabis use frequency at baseline was assessed using the Alcohol/Drug Use Scale and the three post-baseline variables were measured from the Global Functioning – Social (GF-S), and Global Functioning – Role (GF-R) scales. Premorbid Adjustment as a covariate was measured with the Premorbid Adjustment Scale (PAS). Linear regression analyses were conducted to test the relation of cannabis use with role and social functioning, controlling for premorbid functioning. A repeated measures ANCOVA, controlling for pre-baseline functioning tested the relation of cannabis use with global, role, and social functioning from baseline through the 2- and 4-month follow-up visits. Cannabis use prior to and/or at baseline was associated with significantly higher premorbid and baseline social functioning scores. Moderate cannabis users demonstrate significantly higher baseline social and role functioning scores compared to never and heavy users. Greater cannabis use levels significantly predicted higher baseline social and role functioning scores with and without controlling for premorbid social and scholastic adjustment scores. Baseline cannabis use predicted significantly greater improvement over four months in social, but not role functioning, after baseline. Findings appear to support the social skills hypothesis given the significant positive relationship between cannabis use and baseline and subsequent social functioning. Cannabis itself does not appear to exert a protective effect, given that moderate users demonstrate better outcomes than heavier users. Given that obtaining cannabis generally requires interpersonal relationships, it appears that the higher functioning exhibited by moderate cannabis use is more likely a reflection role played by social adjustment in access to the social connections and/or motivations required for access to cannabis.

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Introduction:

Schizophrenia is a psychotic disorder that is severe, often chronic and affects an estimated 1% of the global population (Dixon, 2017). It exhibits substantial symptom heterogeneity. Symptoms of schizophrenia are classified into four domains: positive, negative, and disorganized. In order to meet diagnostic criteria for schizophrenia, an individual must exhibit two of the five core symptoms (hallucinations, delusions, disorganized speech, gross disorganization, diminished emotional expression) for a period of at least one month with continuous signs of the disturbance for at least 6 months. (5th ed.; DSM-5; American Psychiatric Association, 2013). At least one of the symptoms, must be hallucinations, delusions, or disorganized speech, thus negative symptoms are not required for the diagnosis. Schizophrenia treatment is challenging and expensive, with an estimated \$60 billion cost to the US national healthcare system annually (Fitch et al. 2014). Individuals with a psychotic disorder additionally face a myriad of adverse health effects and life outcomes compared to the general population. Among patients diagnosed with schizophrenia, only an estimated 10-15% are currently employed (Dixon, 2017). Additionally, a recent systematic review found that individuals with schizophrenia experience elevated rates of early mortality, increased rates of psychiatric and somatic comorbidities, as well as a dramatically higher risk of suicide (Crespo-Facorro et al. 2021) than the general population. Current etiological research on psychosis estimates that a proportion of the variability in risk for schizophrenia can be attributed to genetic predisposition (Blokland et al. 2017), but adverse prenatal and life events are also significantly associated with an increased risk for the development of schizophrenia and other psychotic disorders (Powers et al. 2016).

Individuals with a psychotic disorder are also at an increased likelihood of meeting criteria for a concurrent psychiatric diagnosis, of which a substance use disorder is one of the most common. An estimated 30-66% of individuals with a psychotic disorder have been dually diagnosed with a substance use disorder (Prat et al. 2021). These disorders include abuse and dependence on alcohol, cannabis, nicotine, and a number of other addictive substances. In comparison, the prevalence of substance use disorders within the general population is estimated to be around 10% (Prat et al. 2021). A concurrent substance use disorder in psychosis is associated with a myriad of additional health risks and barriers to treatment, rendering it an important dual diagnosis to investigate. Compared to those with a sole diagnosis of schizophrenia or another psychosis, patients with a comorbid substance use disorder diagnosis demonstrate a markedly higher rate of hospitalizations, suicide attempts, mortality, and additional psychiatric comorbidities (Lahtenvuo et al. 2021). If multiple substances are abused, the risk of hospitalizations, suicide and mortality is further increased.

Cannabis use/abuse and psychosis.

Cannabis use has historically been a substance of interest in psychosis because it is the most commonly used recreational drug linked with psychosis risk. Though typically seen as exerting a wholly negative effect on psychosis symptoms and outcomes, more recent literature presents a more complex picture. A large body of literature does suggest that cannabis use may be associated with an increased risk for developing a psychotic disorder, particularly at an early age of onset as well as with high potency varieties that contain a high level of tetrahydrocannabinol (THC) which is the main psychoactive compound in cannabis (Sideli et al. 2019, Colizzi & Bhattacharyya, 2020, Ortiz-Medina et al. 2018). Cannabis use has, therefore,

become an important focus of current research on substance use and psychosis not only due to its increased accessibility with legalization expanding, but also because it is one of the most commonly used illicit substances in individuals with psychosis (Koskinen et al. 2010). Heavy cannabis use has also been shown to exacerbate subthreshold psychotic symptoms in a healthy community samples (Yucel et al. 2008). Estimates for past year use and abuse of cannabis amongst individuals with a psychotic disorder are 29% and 19%, with lifetime rates of 42% and 23% (Green et al. 2005). This is greater than the rate of use in comparable age groups of healthy individuals, in which the lifetime rate of cannabis use disorder is an estimated 3% (Haberstick et al. 2014).

There are several potential mechanisms of action for the effect of cannabis on psychosis. For example, it has been suggested that exposure to THC affects both cortical and sub-cortical regions, including the prefrontal cortex (PFC) and mesolimbic DA pathway, that are associated with abnormalities in patients with psychosis. Specifically, prefrontal cortical GABAergic hypofunction, which is linked with psychosis, may cause dysfunction of the PFC in regulating sub-cortical DA neurotransmission (Renard et al. 2018). Alternatively, experimental studies have documented that THC can dose-dependently contribute to social deficits and abnormal dopamine neuron activity in the ventral tegmental area of the brain (Seillier et al. 2020). While a comprehensive review of the neural mechanisms linking THC with brain dysfunction is beyond the scope of this paper, it is important to acknowledge that there a variety of potential neural pathways.

The relationship between cannabis use and psychosis outcomes has been investigated in both prospective and retrospective studies. Recent integrative reviews of the literature indicate

that the risk for psychosis is higher among individuals who use cannabis (Hasan et al., 2020; Livne et al., 2022). Further, an earlier age of cannabis use onset (prior to the age of 15) is associated with an earlier prodromal and full psychosis onset (Leeson et al. 2012). Cannabis use onset occurs an average of 6.3 years prior to clinical psychosis onset in those who develop the condition (Leeson et al. 2012). Progression from a lower to higher frequency use decreases the time it takes an individual to reach prodromal and clinical psychosis status (Compton et al. 2009).

Despite the findings implicating cannabis use as a risk factor for psychosis onset and a poorer prognosis, it has also been found that psychosis patients who moderately use cannabis exhibit better overall social functioning (Salyers & Mueser, 2001). Additionally, ratings of premorbid social adjustment and estimated IQ have been found to be significantly higher in cannabis using individuals with psychosis compared to non-users (Leeson et al. 2012). Brain abnormalities typically associated with psychosis also appear to be less marked in comorbid cannabis users, with one study demonstrating less gray matter in the left middle and inferior frontal gyrus as well as the left hippocampus in first episode psychosis patients who abstained from cannabis compared to those who were users (Cunha et al. 2013).

Clinical high-risk samples (CHR).

A crucial, under-researched population to study are individuals who meet standardized criteria for being at clinical high risk (CHR) for developing a psychotic disorder. Individuals receive this classification based on a documented history of attenuated psychotic symptoms, brief intermittent psychotic symptoms, or a familial history with a period of decline in adolescence or early adulthood (Addington et al. 2020). Depending on the length of the follow-

up period, it is estimated that 19-39% of individuals who are classified as CHR go on to meet diagnostic criteria for a full psychotic disorder (Ruhrmann et al. 2010).

The period preceding the onset of a psychotic disorder is referred to as the prodrome, and is generally marked by a gradual increase in attenuated positive symptoms and a decline in psychosocial functioning and other health measures (Schothorst et al. 2006). Structured diagnostic interviews and rating systems have been developed to rate the presence and severity of subclinical psychotic symptoms. Using current standardized measures, such as the Structured Interview for Prodromal Syndromes (SIPS), prospective studies of CHR individuals are diagnosed as “converting” to psychosis when they receive a score on a 6-point scale for one of the following symptoms: unusual thought content, suspiciousness, grandiose ideas, perceptual abnormalities, or disorganized communication. Furthermore, they must report conviction about their perceptual abnormalities (hallucinations) or unusual (delusional) ideations and exhibit this for an average of one hour per day at least four days per week over the previous month (Addington et al. 2020). There is an emerging body of research dedicated to assessing the effects of cannabis use patterns in CHR samples and how it is associated with risk of conversion to meeting diagnostic criteria for a psychotic disorder.

Research conducted with CHR samples has yielded a mix of findings associated with cannabis use. A recent systematic review of 36 cannabis CHR studies found an association between cannabis use and increased risk of transitioning to psychosis, but the pooled relative risk (RR) was not statistically significant (Ferris et al. 2020). In contrast, a recent study that divided CHR cannabis users by frequency of use into categories of use, abuse, and dependence found that only abuse and dependence were associated with an increased likelihood of conversion to

psychosis. Cannabis use was also associated with an increase in positive symptom ratings in a dose-response fashion. CHR cannabis users are also more likely than healthy control cannabis users to have a younger age of onset use, use alone, and use during the daytime (Buchy & Cadenhead et al. 2015). Baseline cannabis use levels in CHR individuals were not associated with likelihood of conversion, but an increase in usage over time was an independent risk factor (Buchy & Cadenhead et al. 2015). Contemporary research has subsequently focused on factors that may moderate an association between CHR cannabis use and earlier psychosis conversion. A recent meta-analysis reported that age of onset, frequency of use, and amount of childhood trauma moderated the relationship between cannabis use and conversion (Kiburi et al. 2021).

The neurophysiological and neuroanatomical effects of cannabis have additionally been a recent focus of research in CHR individuals. A recent study of CHR participants used EMG technology to measure neural responses to pulse stimuli. One variable of interest, startle latency, is the time elapsed prior to the point of greatest magnitude of neural response. A slower startle latency is thought to be a general indicator of cognitive impairment and was found to be a predictor of increased risk for conversion to psychosis (Cadenhead et al. 2020). Among CHR cannabis users, startle latency was faster than in non-users, suggesting a cognitive advantage in this population (Cadenhead et al. 2020). Prepulse inhibition is an index of sensorimotor gating, and is seen to be increased in individuals with psychosis and is a risk factor for conversion in CHR populations (Cadenhead, 2011). In the recent study by Cadenhead et al. (2020), cannabis use was associated with a higher prepulse inhibition. Additionally, disrupted thalamic connectivity, another abnormality found in individuals with psychosis (Woodward et al. 2012), was found to not be associated with cannabis use at any quantity in a CHR population in a recent

study (Buchy & Cannon et al. 2015). Earlier age of onset of cannabis use, though, was significantly associated with impaired thalamic connectivity, suggesting that earlier cannabis use may be a specific risk factor for psychosis conversion (Buchy & Cannon et al. 2015). Volumetric reductions in the thalamus, hippocampus, and amygdala are additionally frequent biomarkers of psychosis, and research on a healthy sample has shown cannabis use is associated with similar reductions (Buchy et al. 2016). These brain regions did not differ significantly in a recent study comparing a CHR sample with healthy controls, but amongst the CHR sample, increased cannabis use was significantly associated with a reduction in amygdala volume, but not in the other two regions of interest (Buchy et al. 2016). These inconsistent neuroanatomical findings align with similar mixed results in research focusing on the influence of cannabis on clinical outcomes in CHR samples.

CHR cannabis users perform better on cognitive assessments than non-cannabis users, aligning with the aforementioned findings in clinical psychosis patients (Buchy & Seidman et al. 2015). Cannabis using CHR individuals exhibited significantly stronger premorbid social adjustment and IQ scores than non-users. This disparity in IQ between cannabis users and non-users is present even at baseline and even amongst those who only used cannabis once. Age of onset was also associated with higher IQ in that those who initiated cannabis use at a later age received higher IQ scores than those with an earlier initiation (Buchy & Seidman et al. 2015). Cannabis use is associated with less severe negative symptoms of psychosis, such as anhedonia, amotivation, and affective flattening, in CHR individuals (Yucel et al. 2012). Conversely, positive symptoms of psychosis, such as hallucinations and delusions, appear to be more severe in CHR cannabis users than non-users. There is a linear relationship between lifetime exposure to

cannabis and severity of positive symptoms, which is even more pronounced in users of high-potency cannabis (Quattrone et al. 2021). Based on these findings, it appears cannabis may have an effect that reduces negative symptom severity, but may also produce thought disturbances and abnormalities that relate to psychosis development.

Accounting for the relation between cannabis and psychosis

Neuroprotective hypothesis

Researchers have formulated several hypotheses to account for the association between cannabis use and improved cognition and reduced negative symptom presentation. The neuroprotective hypothesis asserts that cannabis itself may have a neurocognitive enhancing effect that produces improvements in psychosis symptoms and cognitive functioning. Evidence for this hypothesis stems from findings that cannabinoid could stimulate prefrontal neurotransmission to enhance cognitive functions (Coulston et al. 2007), but long-term repeated administration may result in detrimental cognitive effects (Solowjj, 2007). This hypothesis accounts for the findings that cannabis users with psychosis perform cognitively better at baseline, but functioning gradually declines over time. There is little evidence, though, suggesting that cannabis use actually causally improves cognition, and once premorbid IQ was controlled for, the association between cannabis use and better cognitive performance was no longer apparent (Yucel et al. 2012). Lower frequency use was also associated with stronger cognitive performance than high frequency use (Leeson et al. 2012). Furthermore, in patients with psychosis, previous but now abstinent cannabis users displayed comparable IQ and other measures of cognition compared to continued users, but also reduced positive symptoms and days of hospitalization, suggesting cannabis may not be neuroprotective in itself (Leeson et al.

2012 & Weibell et al. 2019). Long term clinical outcomes were also improved in those who quit cannabis immediately following diagnosis when compared to continued users (Addington & Addington, 2007).

Social skills hypothesis and Differential vulnerability hypotheses

The social skills hypothesis assumes that better social skills are what enable cannabis users with psychosis to obtain illicit substances and maintain their habit over time (Potvin et al. 2008). This would explain the better cognition and premorbid social functioning demonstrated in comorbid cannabis users, but still requires additional research.

The third primary hypothesis, which is not mutually exclusive from the social skills hypothesis, is that high frequency cannabis use increases vulnerability for psychosis in a subgroup of otherwise less cognitively and genetically vulnerable individuals. This less vulnerable group is also more likely to demonstrate superior social functioning, rendering them more likely than more vulnerable individuals to be able to form the relationships needed to obtain and maintain cannabis use over time. Cannabis itself then induces psychotic symptoms in this population who may have otherwise not have developed symptoms. This is compared to individuals with lower premorbid adjustment, who may have an increased predisposed vulnerability that are likely to develop psychosis regardless of whether they use cannabis. This less vulnerable CHR subgroup demonstrates higher levels of premorbid adjustment and intelligence. Premorbid social adjustment scores are extremely strong predictors of baseline social functioning in CHR populations (Tarbox et al. 2013). Since, according to the social skills hypothesis, CHR individuals with better social functioning are more likely to use cannabis, this results in an apparent association between cannabis use and positive outcomes. Cannabis itself,

though, does not produce this effect, but rather it confounds the relationship between premorbid adjustment and current functioning. (Yucel et al. 2012, Schnell et al. 2009). Support for this hypothesis largely derives from the findings suggesting that premorbid adjustment remains the most crucial predictor of disease prognosis, regardless of substance use (Weibell et al. 2019). A recent study found that any previous differences in cognitive performance between users and non-users disappeared once premorbid IQ was controlled (Ringen et al. 2013). Furthermore, a growing body of literature is focusing on polygenic risk scores (PRS) to determine an individual's cumulative genetic vulnerability for psychosis. A recent PRS study found that cannabis use was associated with psychotic like experiences (PLEs) regardless of an individual's PRS (Elkrief et al. 2021), suggesting that cannabis in itself may induce greater vulnerability for psychosis in an otherwise non-genetically vulnerable population, providing additional support for this hypothesis.

Evidence for these hypotheses has been limited in CHR populations. Furthermore, the current body of research largely focuses on the relationship between cannabis use and cognitive outcomes. Additional crucial measures, such as social and role functioning are each strongly predictive of psychosis prognosis. Global functioning, as rated by the Global Assessment of Functioning (GAF) scale, is an indicator an individual's symptom severity and overall life adaptation level. It is significantly associated with symptom severity and conversion from CHR to psychosis, making it a crucial variable to investigate in relation to cannabis use. Role functioning, as measured by the Global Functioning-Role scale, indicates an individual's ability to perform the duties of their occupation (e g., work, school). It has not been examined in relation to cannabis use in CHR samples and is an important factor in determining an

individual's overall level of functioning. Social functioning, as measured by the Global Functioning – Social scale, is an index of one's social involvement and capabilities. Declines in social functioning are a major risk factor for psychosis conversion, rendering social functioning an important category to measure in relation with cannabis use as well (Carrion et al. 2019).

Furthermore, several studies on diagnosed psychosis patients have observed that premorbid adjustment may partially determine the risk imparted by cannabis on the severity of psychosis symptoms (Leeson et al. 2012), but this has yet to be tested in a CHR population. Therefore, it is important to assess whether any association between cannabis use and short-term functional outcomes is still maintained once premorbid adjustment is controlled. If a significant positive association remains, it would suggest that cannabis is linked with ongoing (i.e., both pre-baseline and post-baseline) differences in levels of functioning. If the strength of the association of cannabis use with post-baseline functioning is positive, but reduced in strength, it would support the differential vulnerability hypothesis and indicate that positive associations with cannabis use are partially a reflection of its association with higher levels of premorbid adjustment.

Conversely, if cannabis use levels are associated with poorer baseline and post-baseline social and role functioning even after controlling for premorbid adjustment, it would indicate an adverse effect of cannabis use on these outcome measures. Furthermore, if cannabis use is significantly associated with social adjustment and functioning, it would support the social skills hypothesis and suggest that there is a large social component that may be related to the obtaining and maintaining cannabis use over time. Given that premorbid adjustment scores are predictive of current functioning in CHR users, it is also important to know whether controlling for premorbid functioning eliminates or reverses the association between cannabis use and the level

and/or course of post-baseline functioning, this suggests that differences in premorbid functioning may determine baseline cannabis use but is detrimental to subsequent functioning.

The present research utilizes data from a large, multi-site longitudinal study of youth who manifest clinical risk signs for psychosis; the North American Prodrome longitudinal Study (NAPLS). NAPLS is one of several such studies currently ongoing countries around the world. The clinical high risk (CHR) youth who are the focus of this research are identified based on the presence of subclinical psychotic symptoms measured with a structured diagnostic interview administered at baseline. Then they are followed prospectively to determine the clinical course, including transition to clinical psychosis. In the NAPLS project, data on substance use, including cannabis use, are also collected at baseline and subsequent follow-ups. In addition, retrospective data on pre-baseline functioning, including pre-baseline social and academic functioning are collected.

Using this longitudinal dataset, the present study will expand upon previous research conducted on the relationship between cannabis use and functional outcomes in a CHR population. Namely, it will measure how cannabis use influences role and social functioning as well as how controlling for measures of premorbid adjustment influence this relationship. This analysis will provide additional insights addressing the aforementioned hypotheses underlying the relationship between cannabis use and positive outcomes in a CHR population. Using retrospective and prospective methods, the aims of this longitudinal study are to determine the relation of cannabis use with psychosis vulnerability. The present study will 1) test the social skills hypothesis by assessing whether cannabis use is associated with elevated premorbid functioning levels, as well as baseline social and role functioning in a CHR population, 2) assess

the degree to which premorbid adjustment scores influence the predictive power of cannabis use frequency on baseline social and role functioning, with and without controlling for ratings of premorbid adjustment 3) assess whether baseline cannabis use frequency predicts significant differences in social and role functioning change from baseline to the 4 month follow-up.

Based on previous evidence on the clinical profiles of CHR cannabis users, it is predicted that ever cannabis users will demonstrate significantly higher premorbid adjustment scores and social and role functioning scores at baseline. We additionally predict that greater cannabis use will predict higher social and role functioning at baseline, but once premorbid adjustment is controlled for, cannabis use will no longer significantly predict these outcomes. Lastly, we predict that higher baseline cannabis use severity will predict greater declines in social, and role functioning at the 4 month follow-up appointment.

Method:

Participants

Participants were recruited for the third phase of the North American Prodromal Longitudinal Study (NAPLS-3) (Addington et al. 2020). The NAPLS-3 sample is comprised of participants at CHR for psychosis, and healthy controls. Only participants classified as CHR were included in the analyses for this study. To meet CHR criteria, participants must meet the Criteria for Psychosis Risk Syndromes (COPS) based on the Structured Interview for Psychosis Risk Syndromes (SIPS) (McGlashan et al. 2010). Inclusion criteria are age between 12 and 30 years at the time of enrollment and no history of a psychotic disorder, neurological disorder, or serious head injury.

Clinical and biomarker assessments are administered at baseline, and at 2, 4, 6, 8, 12, 18, and 24 month follow-ups. However, due to attrition, which is common in longitudinal clinical research, the present study uses only the baseline, 2 and 4 month ratings in order to enhance the sample size. Retrospective family and clinical history measures are administered at baseline. If a participant converts to meeting full diagnostic criteria for a psychotic disorder, they receive biomarker and clinical assessments at that time, and at a one-year follow up appointment (Addington et al. 2020).

At all of the eight NAPLS-3 research sites, the CHR diagnostic interview and the measures described below were administered by graduate or postdoctoral students in psychiatry or psychology who were trained to meet standards of reliability in the administration of the measures.

Measures:

Demographics:

Participant demographic data was obtained via the NAPLS-3 Demographic scale. The present study collected data pertaining to participant sex, race, age, household income, and educational attainment. Demographic characteristics of the sample are presented in Table 1.

Alcohol/Drug Use Scale (AUS/DUS)

The Alcohol/Drug Use Scale is a measure of the one's frequency of use and dependence on nearly a dozen common substances in the past month. Participants are given a score for each of the included substances based on reported frequency that also takes into account demonstrated impairment levels in response to substance use. Scores range from 1 (no use) to 5 (daily use). A score of 2 would indicate use several times per month, a 3 would indicate several times per

week, and a 4 would nearly daily use. With scores awarded based on frequency, clinicians can be trained to effectively rate an individual's substance use levels using the AUS/DUS (Drake et al. 1996). Although a dozen substances are included in this scale, only cannabis use at baseline is the focus of this study. In this study, due to a low number of scores in the 4-5 range, all scores in this category were combined and recoded as scores of 3 for the analysis, and all scores in the 2-3 range were recoded as 2. Based on the cannabis data from this scale, two cannabis use variables were derived; never- *versus* ever-used at baseline, and frequency of use no use, moderate use (2-3), and heavy use (4-5).

Global Assessment of Functioning (GAF) Scale

The Global Assessment of Functioning (GAF) Scale is an indicator of an individual's current level of overall functioning which takes into account the degree to which psychosocial and occupational stressors adversely influence one's functioning (Schwartz, 2007). and participants are given a rating on a scale from 0 (extreme dysfunction) to 100 (strong functioning) based on a comprehensive assessment of overall functionality as indicated by a number of criteria, including occupational status, symptom severity, and social functioning. Our study uses the GAF as an index of cumulative wellbeing. The GAF is demonstrated to be extremely reliable and valid for assessing functional status in psychotic disorders (Startup et al. 2002) and lower GAF scores are associated with an increase in psychosocial and occupational stressors (Schwartz, 2007). NAPLS-3 participants are given a functioning rating at baseline, as well as 2, 4, 6, 8, 12, 18, and 24 month follow-ups.

Global Functioning - Role (GF-R) Scale

The Global Functioning - Role (GF-R) Scale (see Appendix B) is an assessment derived as a sub-score of the GAF that specifically assesses one's current level of occupational functioning. The scale categorizes roles into four primary role types: school, work, homemaker, and part time school + part time work which participants receive prior to their overall rating. Considerations are additionally given to the level of support received as well as the individual's overall performance in their given role. The GF-R is a 10 point scale, with 10 indicating superior role functioning and 1 indicating role dysfunction. Each administration of the GF-R produces 3 scores, one of which is lowest functioning in the past month, deemed current functioning. Ratings of the highest and lowest scores in the previous year are also made, but are not used in the present analyses. The GF-R has high interrater reliability, with a score of 0.93 (Cornwall et al. 2007). Current ratings from baseline, as well as the two and four month follow-up will be used in the analysis.

Global Functioning - Social (GF-S) Scale

The Global Functioning - Social (GF-S) scale (see Appendix A) is an assessment derived originally from the GAF that specifically measures quantity and quality of peer relationships, relationship conflicts, and level of involvement with family members (Cornwall et al. 2007). The GF-S is a 10 point scale, with 10 indicating superior social functioning and 1 demonstrating dysfunction. Ratings are awarded independent of clinical symptomatology. Ratings are given based on subject interviews. Each administration of the GF-S produces 3 scores, one of which is lowest social functioning in the past month, deemed current functioning, as well as the highest and lowest scores in the previous year. Clinicians are trained with detailed descriptions for each rating interval in order to increase interrater reliability. Interrater reliability for the GF-S is an

estimated 0.85, and it also demonstrates strong construct validity with other measures of negative symptoms, including social withdrawal (Cornwall et al. 2007). The GF-S provides a reliable indicator of social functioning in CHR individuals. Current level scores from baseline, as well as the 2 and 4 month follow-ups were used for analysis.

Cannabis Scale

The Cannabis Scale is a six-question self-report inventory that is only administered to participants at baseline. The first question asks if an individual has ever used cannabis, and if they respond no, they are not asked the following five questions. For participants who have used cannabis, they are asked if they are a current (within the past month) or former user. They are additionally asked to estimate the number of times they have used cannabis in the previous 6 months on a scale of 0-180, and additionally the age in which they first used cannabis. The final two questions ask about current or past usage frequency on an 7 point scale, from 1 (everyday use) to 8 (once or twice total). The first question of whether an individual has ever used cannabis will be used for analysis of between group differences between never and ever cannabis users on current social and role functioning as well as premorbid adjustment scales.

Premorbid Adjustment Scale (PAS)

The premorbid adjustment scale (PAS) (see Appendix C) is an measure that provides an estimate of an individual's premorbid functioning levels in four different domains: sociability and withdrawal, peer relationships, scholastic performance, and adaptation to school. The scale includes 26 questions that are used to award participant scores in each of the four aforementioned domains. The scale is subdivided into four age ranges, childhood (<11 years), adolescence (12-15 years), late adolescence (16-18 years), adulthood (19+). For the present

analyses, however, only the childhood and adolescent scores were used to increase the number of subjects with complete data. Participants are given a score of 0 (optimal functioning) to 6 (poor functioning) for each of the domains in each of the age ranges. If a participant has not yet reached one of the age ranges, they are not scored for that specific range. PAS sociability and peer relations demonstrate strong validity indicated by 0.76 and 0.80 correlations, respectively with the Draft Board social behavior scale. PAS scholastic performance and adaptation to school had 0.71 and 0.72 correlations with the Draft Board Functioning in Structured Environments scale (Brill et al. 2008). The PAS scale additionally demonstrates an interrater reliability of 0.77, making it a reliable index of early life functioning in individuals at CHR for psychosis (Rabinowitz et al. 2007). Additionally, for the present study, social withdrawal and peer relationship scores were combined for several analyses as a cumulative premorbid social score. Scholastic performance and adaptation to school were similarly added to form a cumulative premorbid scholastic score. Only PAS-A (childhood) and PAS-B (adolescence) scores were included in analysis so that CHR participants across the age-range could be included in the analyses.

Statistical Analyses

First, one-way ANOVAs were conducted to determine significant differences between reported ever-used and never-used cannabis groups on premorbid social and scholastic adjustment sub scores for childhood and adolescence as well as baseline social and role functioning. Additionally, ANOVAs were conducted to look for significant between group differences in present cannabis use levels (no use, moderate use, heavy use) on baseline social and role functioning as well as premorbid adjustment.

Multiple linear regression analyses were conducted to test the predictive power of baseline cannabis use on ratings of baseline role and social functioning with and without controlling for premorbid adjustment scores. Without controlling for premorbid adjustment, the first block of the linear model contained demographic covariates sex, age, race, household income, and educational attainment, while the second block contained cannabis use frequency. In my analyses controlling for premorbid adjustment scores, PAS scores were included in the first block with cannabis use frequency in the second block. Separate analyses were conducted controlling for different premorbid adjustment scores. Total PAS-A (childhood) and PAS-B (adolescence) scores were separately controlled, as well as each PAS sub score individually for both the childhood and adolescent ranges.

Lastly, in order to test the relation of cannabis use with change in functioning over time, a repeated measures, ANCOVA was conducted to test the relationship of baseline cannabis use with role and social functioning at the baseline, and 2 and 4 month follow-up visits. Interaction effects between baseline cannabis use and premorbid functioning on outcome variables were additionally tested.

Results:

Demographics, Cannabis Use Patterns, and Functional Outcomes

Demographic data for the sample are presented in Tables 1 and 2. The average age of the sample is 18.19.

Table 1.
Sample characteristics (n=710)

Age, years (mean \pm SD)	18.19 \pm 4.04
----------------------------	------------------

Sex, n(%)	
Male	385 (54.2%)
Female	325 (45.8%)
Race, n(%)	
First Nations	14 (2.0%)
East Asian	42 (5.9%)
Southeast Asian	11 (1.5%)
South Asian	22 (3.1%)
Black	82 (11.5%)
Central/South American	41 (5.8%)
West/Central Asian and Middle Eastern	7 (1.0%)
White	392 (55.2%)
Native Hawaiian or Pacific Islander	2 (0.3%)
Interracial	95 (13.4%)
Max. Education n(%)	
Some high school	376 (53.0%)
High school	260 (36.6%)
College	34 (4.8%)
Technical school	3 (0.4%)
University	32 (4.5%)
Grad school	5 (0.7%)
Household Income (USD), n(%)	
<10,000	63 (8.9%)
10,000 – 19,999	42 (5.9%)
20,000 – 39,999	63 (8.9%)
40,000 – 59,999	70 (9.9%)
60,000 – 99,999	100 (14.1%)
100,000+	205 (28.9%)
No answer	162 (22.8%)
Baseline Cannabis Use Level, n(%)	
None	447 (63.9%)
Mild/moderate	234 (33.4%)
Heavy	19 (2.7%)
Ever Cannabis Use	356 (50.9%)

Table 2.
Descriptive Statistics of Study Variables (n=710)

<i>Variable</i>	<i>Mean</i>	<i>SD</i>	<i>Range</i>
PAS-A (Childhood)			
Social	3.02	2.55	0-12
Scholastic	2.82	2.41	0-12
PAS-B (Adolescence)			
Social	3.67	2.63	0-12
Scholastic	3.78	2.66	0-12
Global Functioning			
Role	6.21	2.22	1-10
Social	6.42	1.52	1-10

Note: Lower PAS-A and PAS-B scores indicate better functioning. Higher social and global role functioning indicate better functioning.

Relationship Between Cannabis Use and Social Outcome Variables

Ever cannabis users, compared to never users, exhibited significantly higher baseline social functioning ($F = 18.301, p < 0.001$) but not role functioning ($F = 0.163, p = 0.687$) scores. Cannabis use is also associated with significantly higher total premorbid functioning scores in childhood ($F = 6.334, p = 0.012$) and early adolescence ($F = 10.836, p = 0.001$). After dividing premorbid functioning into social versus scholastic domains, only childhood ($F = 13.771, p < 0.001$) and adolescent social ($F = 17.476, p < 0.001$) subscales remained associated with cannabis use. Childhood scholastic ($F = 2.077, p = 0.150$) and adolescent scholastic ($F = 0.075, p = 0.784$) subscales were not significantly associated with ever cannabis use. These results are displayed in Table 3. When present cannabis use was divided into no use, moderate use, and heavy use,

moderate cannabis users reported higher social and role functioning as well as premorbid adjustment compared to non-users and heavy users. These results are shown in Table 4.

Table 3.
Between Group Differences in Never and Ever Cannabis Users on Outcome Variables and Premorbid Assessment Ratings

Variable	Mean Square	df	F	Sig
GF-R	0.799	698	0.163	0.687
GF-S	41.213	698	18.301	<0.001
PAS-A Social	88.390	690	13.771	<0.001
PAS-A School	0.439	688	0.075	0.784
PAS-B Social	116.890	687	17.476	<0.001
PAS-B School	14.686	686	2.077	0.150

Table 4.
Outcome Variables Means by Baseline Cannabis Use Levels

	<i>No use</i>	<i>Mild/Moderate use</i>	<i>Heavy use</i>	<i>F</i>	<i>Sig.</i>
GF-R	6.11	6.36	6.21	1.002	0.368
GF-S	6.24	6.74	6.21	8.525	<0.001
PAS-A Social	3.12	2.82	2.94	1.047	0.352
PAS-A Scholastic	2.91	2.65	3.00	0.951	0.387
PAS-B Social	3.83	3.36	3.50	2.558	0.078
PAS-B Scholastic	3.87	3.57	4.33	1.340	0.262

Note: Lower PAS-A and PAS-B scores indicate better functioning. Higher social and global role functioning indicate better functioning.

Relationship Between Baseline Cannabis Use and Functional Outcome Variables

As shown in Tables 5-8, baseline cannabis use significantly predicted baseline social functioning ($B = 0.168, p < 0.001$) and role functioning ($B = 0.095, p = 0.023$). After controlling for childhood social and scholastic adjustment scores, cannabis use severity remained a significant predictor of higher baseline role ($B = 0.091, p = 0.029$) and social ($B = 0.153, p < 0.001$) functioning scores. After controlling for early adolescent social and scholastic adjustment, cannabis use severity remained a significant predictor of higher baseline role ($B = 0.098, p = 0.015$) and social ($B = 0.151, p < 0.001$) functioning scores.

In addition to total childhood and early adolescent premorbid adjustment scores being included in the linear model, specific sub-scores were also separately added as covariates to determine the specificity of the premorbid behavioral domains (sociability, peer relationships, adaptation to school, and scholastic performance) relationships with cannabis use and functional outcome variables. Baseline cannabis use remained a significant predictor of baseline role functioning when childhood sociability ($B = 0.095, p = 0.025$), peer relationships ($B = 0.097, p = 0.021$), scholastic performance ($B = 0.092, p = 0.028$), and adaptation to school ($B = 0.098, p = 0.020$) were separately included in the same linear model. Baseline cannabis use was additionally a significant predictor of baseline social functioning when early childhood sociability ($B = 0.155, p < 0.001$), peer relationships ($B = 0.159, p < 0.001$), scholastic performance ($B = 0.163, p < 0.001$), and adaptation to school ($B = 0.173, p < 0.001$) were each included in the model.

When assessing the influence of early adolescent adjustment scores, baseline cannabis use was a significant predictor of baseline role functioning when early adolescent sociability ($B = 0.091, p = 0.029$), peer relationships ($B = 0.091, p = 0.030$), scholastic performance ($B = 0.099, p = 0.016$), and adaptation to school ($B = 0.014, p = 0.010$) were included in the linear

model. Baseline cannabis use was a significant predictor of baseline social functioning when controlling for early adolescent sociability ($B = 0.152$, $p < 0.001$), peer relationships ($B = 0.151$, $p < 0.001$), scholastic performance ($B = 0.174$, $p < 0.001$), and adaptation to school ($B = 0.173$, $p < 0.001$).

Table 5:

The relation of Baseline Social Functioning with Baseline Cannabis Use, controlling for Childhood Premorbid Adjustment and Demographics

		<i>Unstandardized Coefficients</i>		<i>Standardized coefficients</i>	<i>Sig.</i>	<i>R2</i>
<i>Step</i>			<i>Std. error</i>	<i>Beta</i>		
1	(Constant)	6.475	0.430		>0.001	0.012
	Sex	0.078	0.116	0.026	0.502	
	Age	-0.040	0.020	-0.109	0.043	
	Education	0.161	0.079	0.108	0.042	
	Income	0.034	0.032	0.042	0.285	
	Race	0.050	0.063	0.031	0.428	
2	Constant	7.408	0.428			0.017

	PASA-Social	-0.156	0.023	-0.265	>0.001	
	PASA-School	-0.062	0.024	-0.099	0.011	
3	Constant	7.209	0.427			0.125
	Cannabis	0.429	0.113	0.153	>0.001	

Table 6.
The relation of Baseline Social Functioning with Baseline Cannabis Use, controlling for Adolescent Premorbid Adjustment and Demographics

		<i>Unstandardized Coefficients</i>	<i>Std. error</i>	<i>Standardized Coefficients Beta</i>	<i>Sig.</i>	<i>R2</i>
<i>Step</i>						
1	(Constant)	6.516	0.432		>0.001	0.006
	Sex	0.082	0.116	0.027	0.482	
	Age	-0.044	0.020	-0.117	0.029	
	Education	0.170	0.079	0.114	0.032	

	Sex	0.404	0.166	0.092	0.015	
	Age	-0.095	0.029	-0.176	>0.001	
	Education	0.345	0.113	0.160	0.002	
	Income	0.072	0.045	0.063	0.110	
	Race	-0.031	0.090	-0.013	0.725	
2	Constant	7.233	0.635		>0.001	0.057
	PASA-Social	-0.018	0.034	-0.021	0.598	
	PASA-School	-0.138	0.036	-0.153	>0.001	
3	Constant	7.062	0.638		>0.001	0.064
	Cannabis	0.370	0.169	0.091	0.029	

Table 8.

The relation of Baseline Role Functioning with Baseline Cannabis Use, controlling for Adolescent Premorbid Adjustment and Demographics

		<i>Unstandardized Coefficients</i>	<i>Std. error</i>	<i>Standardized coefficients</i>	<i>Sig.</i>	<i>R2</i>
<i>Step</i>				<i>Beta</i>		
1	(Constant)	6.573	0.621		>0.001	0.036
	Sex	0.410	0.167	0.093	0.014	
	Age	-0.102	0.029	-0.188	>0.001	
	Education	0.369	0.114	0.170	0.001	
	Income	0.078	0.045	0.067	0.086	
	Race	-0.036	0.090	-0.015	0.686	
2	Constant	8.109	0.622		>0.001	0.127
	PASB-Social	-0.066	0.032	-0.079	0.036	
	PASB-School	-0.228	0.032	-0.276	>0.001	
3	Constant	7.933	0.624		>0.001	0.135
	Cannabis	0.401	0.164	0.098	0.015	

Relationship Between Baseline Cannabis Use and Post-Baseline Social and Role Functioning

A repeated measures ANCOVA test found that there were not significant between group differences between baseline cannabis users and non-users in role functioning ($F = 0.118$, $p = 0.731$) from baseline to four months after controlling for childhood social and scholastic adjustment scores. There were also no significant between group differences in role functioning over time after controlling for early adolescent social and scholastic adjustment ($F = 0.205$, $p =$

0.651). Baseline cannabis users, compared to non-users, did exhibit significantly better social functioning ($F = 8.188, p = 0.005$) from baseline to four months, after controlling for childhood social and scholastic adjustment. Similarly, cannabis users exhibited significantly greater social functioning improvement ($F = 8.613, p = 0.004$) from baseline to four months when controlling for early adolescent social and scholastic adjustment. These results are displayed in Tables 9 and 10 as well as Figures 1-4.

Table 9.

Between Group Differences in Baseline Cannabis Use and Variation in Social and Role Functioning at Four Month Follow-Up Controlling for Childhood Adjustment Scores

	<i>Role Functioning</i>			<i>Social Functioning</i>		
<i>Mean square</i>	<i>F</i>	<i>Sig.</i>	<i>Mean square</i>	<i>F</i>	<i>Sig.</i>	

Between subjects effects						
PASA-Social	32.997	2.576	0.110	85.694	16.380	<0.001
PASA-School	137.285	10.719	0.001	6.819	1.303	0.255
Cannabis	1.516	0.118	0.731	42.834	8.188	0.005
Within subjects effects						
PASA-Social	0.418	0.449	0.638	0.008	0.021	0.979
PASA-School	1.143	1.228	0.294	0.288	0.779	0.459
Cannabis Use	0.537	0.576	0.562	0.089	0.240	0.787

Table 10.

Between Group Differences in Baseline Cannabis Use and Variation in Social and Role Functioning at Four Month Follow-Up Controlling for Adolescent Adjustment Scores

	<i>Role Functioning</i>			<i>Social Functioning</i>		
	<i>Mean square</i>	<i>F</i>	<i>Sig.</i>	<i>Mean square</i>	<i>F</i>	<i>Sig.</i>
Between subjects effects						
PASB-Social	46.982	4.077	0.044	183.607	38.031	<0.001
PASB-School	395.373	34.309	<0.001	4.769	0.988	0.321
Cannabis Use	2.358	0.205	0.651	41.582	8.613	0.004

Within subjects effects

PASB-Social		0.430	0.651	0.253	0.683	0.505
PASB-School	2.696	2.902	0.056	0.013	0.035	0.965
Cannabis Use	0.885	0.953	0.386	0.152	0.411	0.663

Cannabis Use and the Relationship Between Premorbid Adjustment and Baseline Functioning

Premorbid childhood social adjustment sub scores significantly predicted baseline global (B = -0.173, p < 0.001) and social (B = -0.295, p < 0.001), but not role (B = 0.068, p = 0.073) functioning. When controlling for baseline cannabis use, childhood social adjustment still significantly predicted baseline global (B = -0.170, p < 0.001) and social (B = -0.0288, p < 0.001), but not role (B = -0.063, p = 0.096) functioning. Premorbid childhood scholastic scores significantly predicted baseline global (B = -0.094, p = 0.016), role (B = -0.161, p < 0.001), and social (B = -0.184, p < 0.001) functioning. When controlling for cannabis use frequency, premorbid childhood scholastic scores still significantly predicted baseline global (B = -0.093, p < 0.001), role (B = -0.158, p < 0.001), and social (B = -0.180, p < 0.001) functioning. Adolescent social adjustment scores significantly predicted baseline global (B = -0.248, p < 0.001), role (B = -0.155, p < 0.001), and social (B = -0.385, p < 0.001). When controlling for cannabis use frequency, adolescent social adjustment still significantly predicted baseline global (B = -0.244, p < 0.001), role (B = -0.151, p < 0.001), and social (B = -0.378, p < 0.001). Adolescent scholastic adjustment scores significantly predicted baseline global (B = -0.166, p < 0.001), role (B = -0.301, p < 0.001), and social (B = -0.172, p < 0.001). When controlling for cannabis use

frequency, adolescent scholastic adjustment still significantly predicted baseline global ($B = -0.168, p < 0.001$), role ($B = -0.300, p < 0.001$), and social ($B = -0.171, p < 0.001$).

Discussion:

Interpretations

This study investigated the influence of cannabis use on role and social functioning in a population at clinical high risk for psychosis, building upon a body of previous CHR literature that has largely focused on the relationship between cannabis and cognitive performance. In our analysis, compared to non-users, ever-cannabis users exhibited significantly higher levels of premorbid childhood and adolescent social functioning and baseline social functioning. Cannabis users did not demonstrate higher levels of premorbid childhood and adolescent scholastic functioning or baseline role functioning. These findings support the social skills hypothesis in that social ability predicts whether an individual has ever used cannabis at or prior to baseline. This suggests that in order to obtain cannabis, an individual must have the capability of forming relationships with others. Interestingly, premorbid scholastic functioning did not predict cannabis use, supporting the assumption that social and scholastic adjustment are separate entities that predict different future behavioral domains. It has previously been shown that higher social functioning in CHR samples is associated with reduced negative and disorganized symptoms, both of which are positively associated with poorer long-term prognosis (Corcoran et al. 2011). High negative symptom severity ratings, particularly social withdrawal, are one of the primary risk factors for future conversion to psychosis (Piskulic et al. 2012). These findings do suggest that the improved functioning demonstrated in clinical high risk cannabis

users may at least partially be a function of enhanced social relationships and the resulting benefits.

Our analysis also divided current cannabis use into three severity levels: no use, moderate use, and heavy use. Of the three groups, moderate users exhibited significantly higher social and role functioning scores at baseline compared to never and impaired users. Moderate users additionally demonstrated higher premorbid social adjustment scores than heavy users. Heavy cannabis users reported the lowest premorbid scholastic functioning, while moderate users reported the highest. These findings suggest that premorbid social and scholastic adjustment may predict the degree to which an individual is able to moderate their cannabis use, making them susceptible to the adverse effects of cannabis. It may also suggest that cannabis use does not produce as significantly negative outcomes when one uses with others or otherwise has strong relationships. This also suggests that there may be a dose-response effect of cannabis use, meaning that moderate usage may partially reflect increased social interaction without the possible adverse effects of greater cannabis use.

Once integrated into a linear model controlling for demographic covariates, baseline cannabis use severity was a significant predictor of higher social and role functioning scores at baseline. Given the demonstrated association with ever-cannabis use and premorbid functioning levels in childhood and adolescence, these were integrated into our linear model. When controlling for total childhood and adolescent adjustment scores, cannabis use remained a significant predictor of role and social functioning. As expected, the predictive power of cannabis use is notably stronger for social functioning than role functioning, which may reflect social relationships facilitating the ability to regularly obtain and use cannabis. Cannabis use

better predicted social and role functioning when not controlling for premorbid adjustment in all cases. This suggests that premorbid functioning does partially account for the strength of the association between cannabis use and improved post-baseline functional outcomes, and that cannabis use predicts improved functioning regardless of one's childhood and adolescent adjustment levels.

Baseline cannabis use did not significantly predict role functioning improvement from baseline to four months. Although cannabis users did display greater improvement in this domain, it appears to be better accounted for by premorbid scholastic adjustment rather than being related to cannabis use itself. Conversely, baseline cannabis use did significantly predict greater social functioning improvement at four months, even after controlling for premorbid social and scholastic adjustment. This could be for a number of reasons, namely that cannabis chemically may reduce certain negative symptoms of psychosis that result in poorer social functioning, produce social anhedonia, or that obtaining and maintaining cannabis use may create more opportunities for social interaction which results in social functioning improvement.

Limitations

There were several limitations in the investigation. Cannabis use frequency was initially measured on a 5 point Likert scale, but responses from the 3,4, and 5 levels indicating highest frequency of use were converted into a single variable due to a small sample size for each. Additionally, each score roughly equates to no use, weekly use, and daily use. Although a rough indicator of total frequency of use, this study did not include a precise indicator of quantity and frequency of use that may have provided additional insight into a possible dose-response relationship between cannabis use and functioning.

Premorbid adjustment levels were used as a best marker of early life functioning and estimated inherent psychosis vulnerability levels. Although a useful indicator, there are likely other factors that could have been accounted for, such as genetic and other biomarkers that would have produced a more comprehensive psychosis risk profile. This would have allowed for a more precise allocation of participants into higher and lower risk groups which in turn would have allowed us to better assess if cannabis appears to be related to a significant decline in a lower risk group. Ultimately the differential vulnerability hypothesis is extremely difficult to test, as there is a spectrum of psychosis vulnerability that furthermore is influenced by a host of additional environmental factors other than cannabis use that may be associated with increasing psychosis risk over time.

This study did not take into account age of cannabis use onset, which previous research has suggested is an important factor in predicting the degree to which cannabis exerts an influence on neurodevelopment. Late onset cannabis users with psychosis score higher on cognitive performance measures and premorbid intelligence than early onset users, who subsequently score better than non-users (Prat et al. 2021). This indicates that the substance itself may exhibit a neurotoxic effect if used for a long period of time, and that users versus non-users may comprise two distinctive categories of premorbid vulnerability. Additionally, early onset of cannabis use before the age of 15 is associated with a greater risk of developing a psychotic disorder, even controlling for preexisting psychotic symptoms (Arseneault et al. 2002), suggesting cannabis may induce psychotic symptoms even in populations who otherwise may have been less vulnerable. Controlling for age of onset of cannabis use in our analysis may have altered our findings, particularly for our over time analysis. Future research may examine

whether younger users exhibit more pronounced functional changes over time as a result of cannabis use severity.

Additionally, we did not take into consideration the amount of time an individual had been using cannabis, or if they had previously been a user and since stopped. More specific details about the form or THC concentration of the individual's cannabis is another important factor to take into consideration. Due to sample size restraints, we additionally were not able to assess the influence of baseline cannabis use on time points beyond the four month follow-up. Measuring this relationship at further time points is necessary to determine the long-term effects of cannabis on functional outcomes.

Taken together, our findings suggest that the association between cannabis use and improved functioning is likely a result of CHR cannabis users having higher pre-existing levels of functioning. Therefore, cannabis use likely confounds the relationship between these two variables. Although premorbid adjustment levels did not significantly alter the predictive power of cannabis use frequency on our three outcome variables, this is likely due to other factors that were not controlled for. Our study did not take into account total years of usage nor age of onset, both of which have been observed in previous research to be important factors in predicting one's susceptibility to cannabis usage. Furthermore, premorbid adjustment scores were much stronger predictors of current functioning than cannabis use, and cannabis use did not appear to alter this relationship when controlled for in the linear model. Ever cannabis use was also associated with significantly higher premorbid and current functioning. Given the increased likelihood of higher functioning individuals to use cannabis, our findings likely reflect the interrelationship between cannabis use and premorbid adjustment. This relationship explains why

cannabis use appears to predict positive functional outcomes. These likely do not reflect the effects of cannabis itself, but rather users with higher pre-existing functioning, but determining whether cannabis itself exerts an enhancing effect is challenging given the number of potential confounding factors.

Conclusion:

The relationship between cannabis use, functioning, and premorbid adjustment appears to be complex. Although our findings somewhat counterintuitively suggest that cannabis use is associated with generally more positive outcomes, it is additionally observed that there may be a “sweet-spot” cannabis use frequency in which an individual retains social benefits but avoids adverse effects of high cannabis use. Cannabis use appears to predict an increase in functional outcomes regardless of premorbid adjustment, suggesting the effect occurs across all clinical high risk individuals. Future research is necessary to better understand whether cannabis itself exerts this positive influence, or if it is other confounding factors that are highly interrelated with cannabis use such as social functioning.

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Figures

Figure 1:

Post Baseline Social Functioning by Baseline Cannabis Use Controlling for Childhood Adjustment

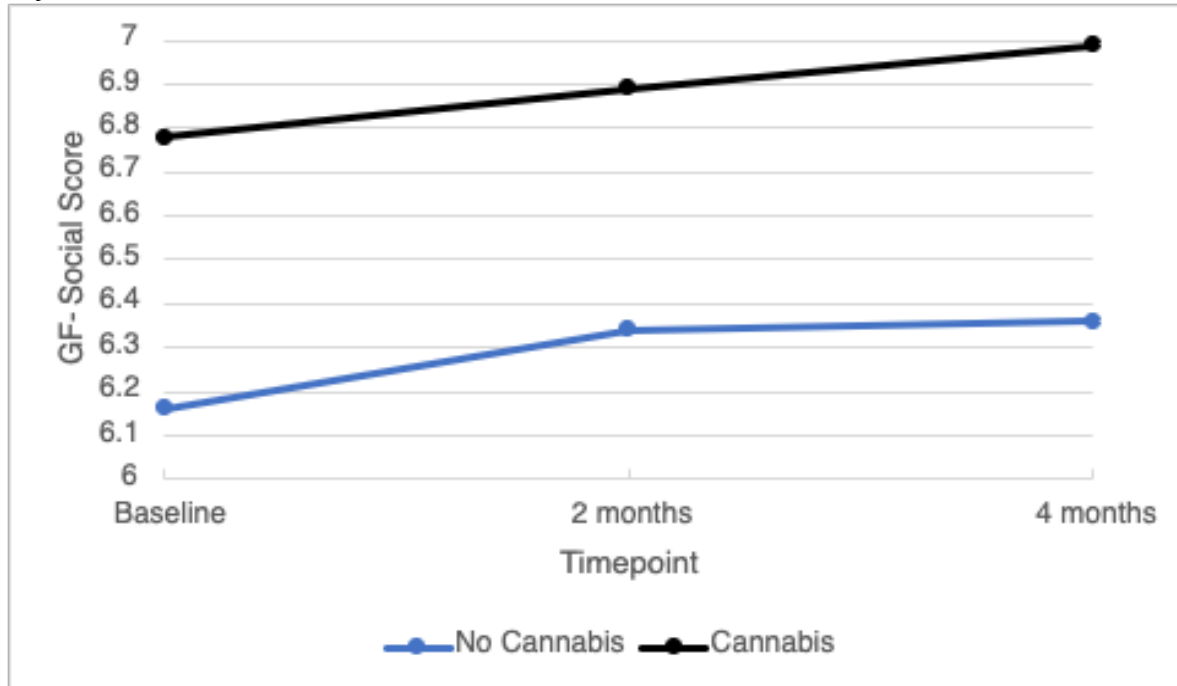


Figure 2

Post Baseline Role Functioning by Baseline Cannabis Use Controlling for Childhood Adjustment

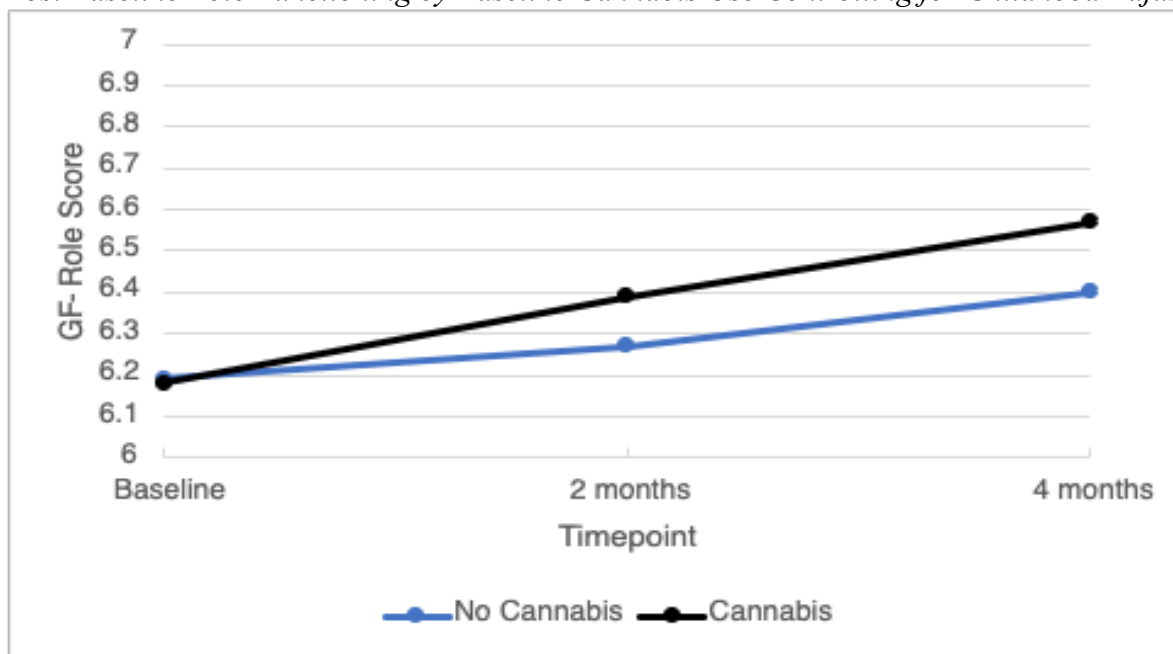


Figure 3

Post Baseline Social Functioning by Baseline Cannabis Use Controlling for Adolescent Adjustment

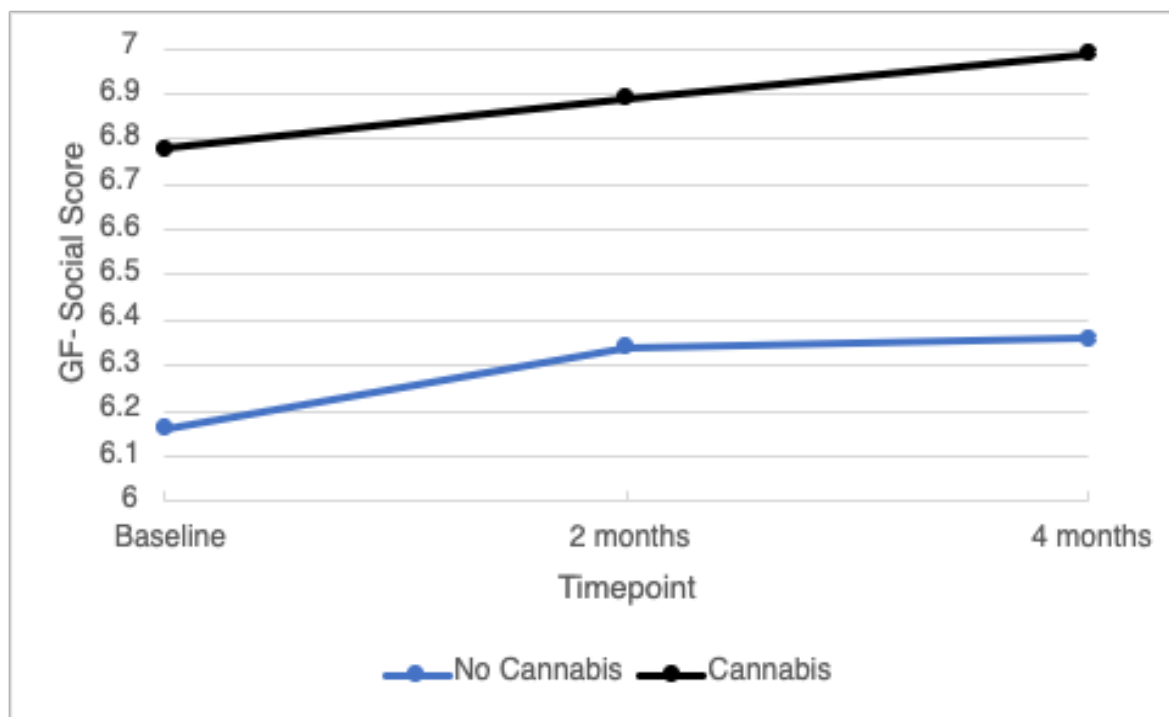
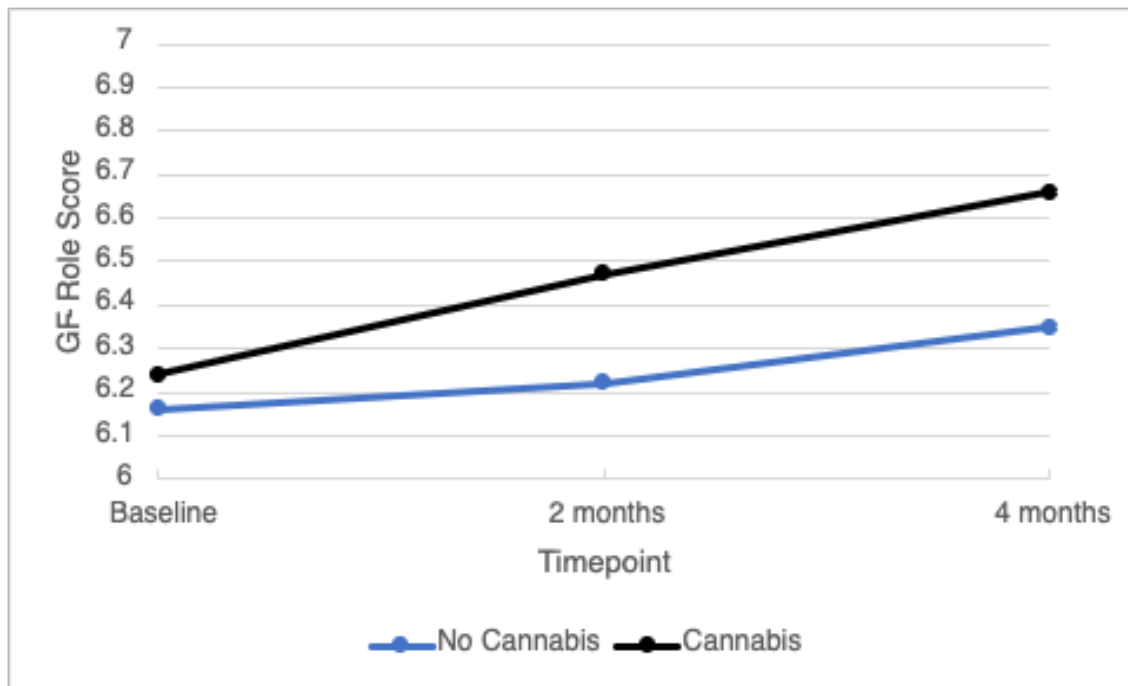


Figure 4

Post Baseline Role Functioning by Baseline Cannabis Use Controlling for Adolescent Adjustment



Appendix A:

Global Functioning – Social Scale

CURRENT _____ Range 0-10 LOWEST PAST YEAR _____ Range 0-10 HIGHEST PAST YEAR _____ Range 0-10

Please rate the patient's most impaired level of social functioning for the specified time period by selecting the lowest level which describes his/her functioning within that time frame. For current, rate most impaired level of functioning in the past month. Rate actual functioning regardless of etiology of social problems.

Note: The emphasis is on social contact/interactions with people other than family members, unless these are the only interpersonal contacts a person has (e.g., the lower end of the scale). Also note that ratings of intimate relationships are secondary to the rating of primary friendships and should take into account the age of the individual. For example, older individuals may be expected to have intimate relationships involving steady dating, cohabitation, or marriage whereas younger individuals may be expected to have only romantic interests (i.e., flirtations or crushes) or close friendships.

SUPERIOR SOCIAL/INTERPERSONAL FUNCTIONING

Criteria:

10

Superior functioning in a wide range of social and interpersonal activities. Frequently seeks out others and has multiple satisfying interpersonal relationships, including multiple close and casual friends. Is sought out by others because of his or her many positive qualities. Age appropriate involvement in intimate relationships.

ABOVE AVERAGE SOCIAL/INTERPERSONAL FUNCTIONING

Criteria:

9

Good functioning in all social areas, and interpersonally effective. Interested and involved in a wide range of social and interpersonal activities, including both close and casual friends. Age appropriate involvement in intimate relationships. No more than everyday interpersonal problems or concerns (e.g., an occasional argument with spouse, girlfriend/boyfriend, friends, co-workers, or classmates). Able to resolve such conflicts appropriately.

GOOD SOCIAL/INTERPERSONAL FUNCTIONING

Criteria:

8

Some transient mild impairment in social functioning. Mild social impairment is present, but transient and expectable reactions to psychosocial stressors (e.g., after minor arguments with

spouse, girlfriend/boyfriend, friends, co-workers, or classmates). Has some meaningful interpersonal relationships with peers (casual and close friends), and/or age appropriate intimate relationships. Infrequent interpersonal conflict with peers.

MILD PROBLEMS IN SOCIAL/INTERPERSONAL FUNCTIONING

Criteria:

7

Some persistent mild difficulty in social functioning. Mild impairment present that is NOT just expectable reaction to psychosocial stressors (e.g., mild conflicts with peers, co-workers or classmates; difficulty resolving conflicts appropriately). Has some meaningful interpersonal relationships with peers (casual and/or close friends). Some difficulty developing or maintaining age appropriate intimate relationships (e.g., multiple short-term relationships).

MODERATE IMPAIRMENT IN SOCIAL/INTERPERSONAL FUNCTIONING

Criteria:

6

Moderate impairment in social functioning. Moderate impairment present (e.g., few close friends; significant but intermittent conflicts with peers, co-workers or classmates). Moderate difficulty developing age appropriate intimate relationships (e.g., infrequent dating). Occasionally seeks out others, but will respond if invited by others to participate in an activity.

SERIOUS IMPAIRMENT IN SOCIAL/INTERPERSONAL FUNCTIONING

Criteria:

5

Serious impairment in social functioning. No close friends or intimate partner, but has some casual social contacts (e.g., acquaintances, school/work friends only). Rarely seeks out others. Occasional combative or verbally argumentative behavior with peers. Beginning to withdraw from family members (e.g., doesn't initiate conversation with family, but will respond if addressed).

MAJOR IMPAIRMENT IN SOCIAL AND INTERPERSONAL FUNCTIONING

Criteria:

4

Major impairment in social functioning. Serious impairment in relationships with friends or peers (e.g., very few or no friends, frequent conflicts with friends, or frequently avoids friends). Frequent combative or verbally argumentative behavior with peers. Infrequent contact with family members (e.g., sometimes does not respond to family or avoids family members).

MARGINAL ABILITY TO FUNCTION SOCIALLY

Criteria:

3

Marginal ability to function socially or maintain interpersonal relationships. Frequently alone and socially isolated. Serious impairment in relationships with all peers, including acquaintances. Few interactions with family members (e.g., often alone in room). Serious impairment in communication with others (e.g., avoids participating in most social activities).

INABILITY TO FUNCTION SOCIALLY

Criteria:

2

Unable to function socially or to maintain any interpersonal relationships. Typically alone and socially isolated. Rarely leaves home. Rarely answers the phone or the door. Rarely participates in interactions with others at home or in other settings (e.g. work, school).

EXTREME SOCIAL ISOLATION

Criteria:

1

Extreme social isolation. No social or family member contact at all. Doesn't leave home. Refuses to answer the phone or door.

Appendix B:

Global Functioning – Role Scale

CURRENT _____ Range 0-10 LOWEST PAST YEAR _____ Range 0-10 HIGHEST PAST YEAR ____ Range 0-10

Please rate the patient's lowest level of functioning in occupational, educational, and/or homemaker roles, as appropriate, within specified time frame. For current, rate most impaired level of functioning for the past month. Rate actual functioning regardless of etiology of occupational/educational problems.

NOTE: This scale emphasizes the level of support provided within the individual's environment and the individual's performance given such support. The term "independently" as used throughout this instrument implies that an individual is functioning at an age-appropriate level without the assistance of external supports or accommodations. Examples of independent functioning include (1) age-appropriate functioning in a mainstream school without requiring extra help, special classes, or special accommodations for testing, (2) competitive full-time

employment without additional guidance, support, job coaching, or other forms of special assistance, and (3) full-time homemaker responsible for generating, organizing and pacing of household tasks and activities for a family without additional guidance, support or supervision.

SUPERIOR ROLE FUNCTIONING

Criteria:

10

Independently maintains superior functioning in demanding roles. Obtains only superior performance evaluations at competitive work placement. Obtains all A's in mainstream school. Generates, organizes & completes all homemaking tasks with ease.

ABOVE AVERAGE ROLE FUNCTIONING

Criteria:

9

Independently maintains very good functioning in demanding roles. Rarely absent or unable to perform. Obtains good to superior performance evaluations at competitive work placement. Obtains grades in A and B range in all courses in mainstream school. Generates, organizes and completes all homemaking tasks.

GOOD ROLE FUNCTIONING

Criteria:

8

Independently maintains good role functioning in demanding roles. Occasionally falls behind on tasks BUT always catches up. Obtains satisfactory performance evaluations at competitive work placement. Obtains grades of C and above in mainstream school. Occasional difficulty generating or organizing homemaking tasks. Or Maintains above average performance with minimal support (e.g. tutoring; reduced academic course load at 4-year university; attends community college; may receive additional guidance at work less than 1-2x week). Receives As & Bs, good work/school evaluations, completes all tasks with this level of support.

MILD IMPAIRMENT IN ROLE FUNCTIONING

Criteria:

7

Mildly impaired functioning in demanding roles independently. Frequently behind on tasks or unable to perform. Frequently obtains poor performance evaluations at competitive work placement or grades of Ds or better in mainstream school. Frequent difficulty generating or organizing homemaking tasks. Or Maintains good performance with minimal support (e.g. minimal accommodations in general education classroom; receives additional guidance/support at work 1-2x week). Receives Cs or higher, satisfactory work/school evaluations, and completes most homemaking tasks with this level of support.

MODERATE IMPAIRMENT IN ROLE FUNCTIONING

Criteria:

6

Moderate impairment independently. May receive occasional F in mainstream courses, persistently poor performance evaluations at competitive work placement, may change jobs because of poor performance, persistent difficulty generating or organizing homemaking tasks. Or Requires partial support (some resource or special education courses; receives guidance/support at work 2+ times/week). May requires less demanding or part-time jobs and/or some supervision in home environment BUT functions well or adequately given these supports (may fall behind but eventually completes as

SERIOUS IMPAIRMENT IN ROLE FUNCTIONING

Criteria:

5

Serious impairment independently. Failing multiple courses in mainstream school, may lose job, or unable to complete most homemaking tasks independently. Or In entirely special education classes, requires less demanding job/daily support or guidance, may require vocational rehabilitation , and/or some supervision in home environment BUT maintains above average performance - receives As & Bs, good evaluations at work/school, completes all tasks.

MAJOR IMPAIRMENT IN ROLE FUNCTIONING

Criteria:

4

Very serious impairment independently. All Fs in mainstream school or failing out of school. Can't obtain or hold independent job, or unable to complete virtually any homemaking tasks independently. Or Adequate to good functioning with major support. Requires assisted work environment, entirely special education classes, non-public or psychiatric school, home schooling for the purpose of a supportive school environment, and/or supported home environment BUT functions adequately given these supports (may fall behind but completes assigned tasks, obtains satisfactory performance evaluations at work or passing grades).

MARGINAL ABILITY TO FUNCTION

Criteria:

3

Impaired functioning with major support. Requires supported work environment, entirely special education classes, non-public or psychiatric school, home schooling for the purpose of a supportive school environment, and/or supported home environment BUT functions poorly despite these supports (persistently behind on tasks, frequently unable to perform, obtains poor performance evaluations at work or fails courses at school).

INABILITY TO FUNCTION

Criteria:

2

Disabled but participates in structured activities. On disability or equivalent non-independent status. Not working for pay, attending classes for grades, or living independently. Spends 5 or more hours a week in structured role-related activities (e.g. residential treatment, volunteering, tutoring, sheltered work programs).

EXTREME ROLE DYSFUNCTION

Criteria:

1

Severely disabled. On disability or equivalent non-independent status. Not working for pay, attending classes for grades, or living independently. Spends fewer than 5 hours a week in structured role-related activities.

Appendix C:

Premorbid Adjustment Scale

I. CHILDHOOD (up through Age 11) Range 0-6 NA

1. Sociability and withdrawal	0	1	2	3	4	5	6	NA
2. Peer relationships	0	1	2	3	4	5	6	NA
3. Scholastic performance	0	1	2	3	4	5	6	NA
4. Adaptation to school	0	1	2	3	4	5	6	NA

Childhood range 0-24

Subtotal Childhood= $\sum 1+2+3+4 / 24$

Subtotal Childhood range 0-1

II. ADOLESCENCE (early, ages 12-15) Range 0-6 NA

1. Sociability and withdrawal	0	1	2	3	4	5	6	NA
2. Peer relationships	0	1	2	3	4	5	6	NA
3. Scholastic performance	0	1	2	3	4	5	6	NA
4. Adaptation to school	0	1	2	3	4	5	6	NA
5. Social-sexual aspect of life	0	1	2	3	4	5	6	NA

Adolescence (early) range 0-30

Subtotal Adolescence (early) = $\sum 1+2+3+4 +5/ 30$

Subtotal Adolescence (early) range 0-1

Note: Lower scores indicate better levels of functioning