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Comparison of co-morbid psychiatric diagnoses in male adolescent in-patients with a history of cannabis use with those without cannabis use

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A Research Report (in the format of a 'submissible' paper) submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, in partial fulfilment of the requirements for the degree of Master of Medicine (Psychiatry)

Johannesburg, 2020

DECLARATION

I, Stacey-Leigh Lintnaar, declare that this research report is my own, unaided work. It is being submitted for the degree of Master of Medicine in Psychiatry (in submissable format with my protocol) in the branch of Psychiatry at the University of the Witwatersrand, Johannesburg. This research report has not been submitted before for any degree or examination at any other University.

(Signature of candidate)

29 day of October 2020

CONTRIBUTION OF THE CANDIDATE TO THE PAPER

Declaration: Student's contribution to article(s) and agreement of co-author(s)

I, Stacey-Leigh Lintnaar, student number 1730739, declare that this Research Report is my own work and that I have contributed significantly towards the research findings presented in the paper intended for publication below.

Signature of Student: _____ Date: 29/10/2020

Name of Supervisor: Doctor Wendy Friedlander

Signature of Supervisor: _____ Date: 29/10/20

Agreement of co-authors: By signing this declaration, the co-authors listed below agree to the use of the article by the student as part of her Research Report. In cases where the student is not the first author of a published article, the primary supervisor must explain (under comments) why the student is entitled to use the paper for her degree purposes.

Article title: Comparison of co-morbid psychiatric diagnoses in male adolescent in-patients with a history of cannabis use

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ABSTRACT

Background: Globally, cannabis is one of the most commonly used substances and it is perceived to be harmless. However, research confirms that the onset of cannabis use before the age of 16 may predispose the individual to a range of severe psychiatric illnesses.

Objective: The aim of this study was to determine the prevalence of cannabis use disorder, to describe the local demographic profile of the participants and to examine the co-morbid psychiatric diagnoses in adolescents admitted to a psychiatric unit.

Methods: This was a retrospective record review of male adolescents aged 13 to 18 years admitted as in-patients to the psychiatric ward at the Chris Hani Baragwanath Academic Hospital.

Results: The study sample comprised of 51 male adolescents admitted during an 18-month period. The majority, 84%, were diagnosed on admission with cannabis use disorder. In the cannabis use disorder group (n = 43) the mean level of education was grade 9 and the mean age was 16 years. There was an association found between cannabis use disorder and substance induced psychotic disorder.

Conclusion: The most common diagnosis recorded in this study was substance induced psychotic disorder. The findings highlight the need for more integrated services, such as educational initiatives and dual diagnosis treatment programmes, targeted particularly at psychiatrically vulnerable adolescents.

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RESEARCH REPORT IN THE FORMAT OF A "SUBMISSIBLE" PAPER

Comparison of co-morbid psychiatric diagnoses in male adolescent in-patients with a history of cannabis use with those without cannabis use

Introduction

Adolescence is the period of progression through puberty characterised by marked changes within an individual and in the individual's environment. Adolescence typically describes the years between ages 13 and 18. Physiologically, the adolescent develops an advancement in cognitive abilities, and socially, transformations are occurring in both parental and peer relationships.[1] Therefore, it is not surprising that with all these changes, adolescence is a period where the risk for substance use and other psychiatric disorders begins to establish itself. Delaying the onset of substance use could change the prevalence and nature of adult substance use.[2]

There are many reasons why adolescents are particularly vulnerable to substance use disorders due to developmental processes that occur during this transitional stage. Firstly, cognitive development occurs during adolescence and partaking in risky behaviours is increased due to differences in the rate of development of the limbic/para-limbic system and the prefrontal cortex. This causes an imbalance between impulse control and sensation-seeking. Secondly, neural development ensues during this period. Significant changes take place in neural maturation of the hippocampus and the prefrontal cortex, thus making adolescents vulnerable to injury caused by the acute and chronic effects of substance use. Memory and learning may also be affected. Substance dependence develops due to chronic use of a substance, which is associated with neural changes in the reward pathways of the brain. Thirdly, a large amount of changes happen socially; this is marked by the transition from primary school to high school that results in adolescents broadening their peer groups, less supervision from teachers and less time spent with family members. During early and mid-adolescence, the effects of peer pressure are most influential, and association with peers who use substances results in an increased risk of substance use, misconduct and other risky behaviours.[2]

Globally, cannabis is the most commonly used drug, excluding alcohol and tobacco. In South Africa, cannabis was the primary substance of abuse that persons under the age of 20 sought treatment for in 2018.[3] Typically, the use of cannabis is initiated in adolescence because of its easy obtainability and the misconception that it is harmless.[4] Research confirms that the onset of cannabis use before the age of 16 may predispose the individual to a range of severe psychiatric illnesses such as substance use disorders, psychotic disorders, mood disorders, anxiety and personality disorders.[4]

In addition to psychiatric consequences, adolescents may suffer other devastating consequences as result of early onset cannabis use. A review done in the early 2000's examined the cannabis use trends in South Africa. It revealed cannabis use to be lower in rural areas compared to urban areas and lower in females compared to males. Cannabis use was associated with increased trauma admissions for physical injuries and medical admissions for certain conditions such as epilepsy. The increasing potency of cannabis consumed, and the earlier onset of cannabis use were listed as possible reasons for seizures. People living with HIV and AIDS were more likely to use cannabis than people without HIV. Cannabis use was linked to risky behaviours resulting in crime and incarceration.[5]

Many South Africans live in townships and informal settlements. The increase of substance use in these areas correlates with unemployment, academic decline, poverty and maladjusted family life. These communities often seek escape from the harsh realities of social injustice by using substances. There are limited treatment programmes for substance rehabilitation available in these areas, which perpetuates the endless cycle of substance use and poverty. Cannabis is used widely in traditional communities and the use of cannabis is governed by the elders. With communities migrating more to townships and informal settlements it became increasingly difficult to control use. This resulted in increased cannabis use, especially amongst the adolescent population.[6]

Psychotic disorders are the psychiatric pathology most frequently associated with cannabis use disorder. The use of cannabis is an independent risk factor for developing psychosis, and early-onset cannabis use is associated with a two-fold risk of developing schizophrenia later in life.[7]

Temperament and personality mediate the genetic risk of adolescent substance use and, to some extent, co-occurring disorders.[2] Extrinsic factors that influence the progression of initial recreational substance use to abuse include: poor socio-economic status, a history of trauma, inadequate parental monitoring, an unstable family environment and associations with deviant peers.[8-10]

The aim of this study was to determine the prevalence of cannabis use disorder, to describe the local demographic profile of the participants and to examine the co-morbid psychiatric diagnoses in adolescents admitted to a psychiatric unit.

Methods

Study design

This study was a retrospective record review of male adolescents aged 13 to 18 years admitted to a psychiatric ward as in-patients.

Setting

The study took place at the Chris Hani Baragwanath Academic Hospital situated in Soweto, Gauteng. Chris Hani Baragwanath Academic Hospital is a tertiary academic hospital that provides both in-patient and out-patient psychiatric services to Soweto and surrounding areas. The in-patient psychiatric facility includes an exclusive ten-bed adolescent male ward.

Study population and sampling strategy

All adolescent male psychiatric patients who were admitted between 1 January 2018 and 30 June 2019 were included in this study. The patients meeting the inclusion criteria were identified through the hospital's admission records. All had been assessed by a psychiatrist during their admission.

Data collection

Data was collected from the relevant clinical files and recorded in a structured data sheet after all patient files had been reviewed by the principal investigator. The following details were documented: demographic data, employment status of the primary caregiver, psychiatric diagnosis and substance history. It is noted that the clinical records did not consistently provide all information regarding religion and employment status of the adolescent's primary caregiver.

Data analysis

Data was captured using Microsoft Excel spreadsheet software. Variables were illustrated by percentage (categorical variables) and mean and standard error (continuous variables), and represented as pie charts or bar charts. Statistical analyses were conducted using R software (R version 3.5.1; https://www.r-project.org). Tests were two-tailed probability values, and statistical significance was accepted when $\alpha \leq 0.05$.

Statistical analysis used for each of the three objectives are as follows:

1. Chi-squared contingency tests were used to determine the prevalence of cannabis and other substances used by male adolescents admitted to the adolescent psychiatric ward at Chris Hani Baragwanath Academic Hospital during the study period.

2. The demographic profile variables of male adolescents who had been diagnosed with cannabis use disorder were compared to those without cannabis use disorder. Analyses of categorical data were done using chi-squared contingency tests. Continuous variables were tested for normality using QQ-plots and then analysed using t-tests.

3. The co-morbid psychiatric diagnosis variables of male adolescents who had been diagnosed with cannabis use disorder were compared to those without cannabis use disorder. Also, cannabis use disorder was compared with other substance use disorders. All variables were categorical and analysed using chi-squared contingency and Fisher's tests (p values shown only).

Sample size

From an assessment of Z-scores of expected frequencies, a minimum sample size of 150 adolescents (75 per cannabis use disorder/without cannabis use disorder group) was likely to detect statistically significance at the 5% level. Unfortunately, this sample size was not reached because only 51 adolescents who met the inclusion criteria were admitted to the adolescent unit during the 18-month study period.

Ethical considerations

Permission to conduct the study and ethical clearance was obtained from the University of Witwatersrand Health Research Ethics Committee (Appendix C). Permission to do the study at Chris Hani Baragwanath Academic Hospital was approved by the medical advisory committee of the hospital (Appendix B).

Consideration was given regarding patients' confidentiality. Hence, random numbers were assigned to the case files of patients who were selected for the study to protect their names and hospital numbers. Patients' personal information was always protected and remains anonymous.

Results

Participants

The total study sample comprised of 51 male adolescents admitted to the adolescent psychiatric ward at Chris Hani Baragwanath Academic Hospital over 18-months. The analyses were restricted to these patients.

Prevalence of cannabis use and other substance use disorders

The diagnosis of cannabis use disorder was made on the history obtained from the participants at the time of admission. Of the 51 participants, significantly more (84%; n = 43) were diagnosed with cannabis use disorder (Figure 1; $\chi^2_1 = 24.02$, $p < 0.001$). Henceforth, "group 1" refers to the group with cannabis use disorder and "group 2" the group without cannabis use disorders.

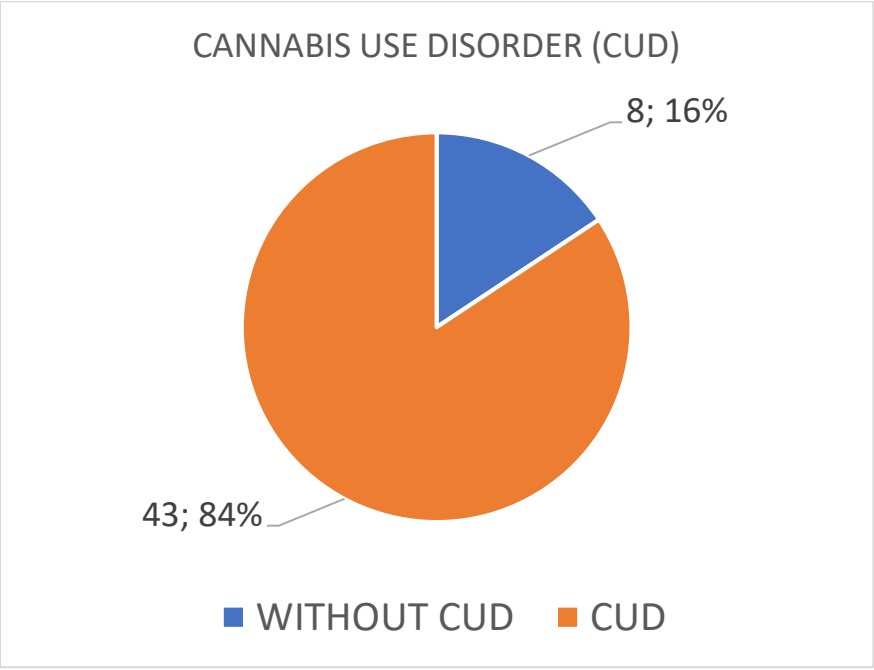

Figure 1. The number of male adolescents with and without cannabis use disorder (CUD) as diagnosed on admission.

Other substance use disorders documented in the records were associated with alcohol, opioid, stimulant and inhalant use. 53% (n = 27) of participants diagnosed with cannabis use disorder had a diagnosis of another substance use disorder as well.

Demographic profile

The 51 participants were black African males.

Age

The participants were between 13 and 18 years of age. The ages of group 1did not differ significantly from group 2 ($t_{49} = -0.10$, $p = 0.919$; Table 1). The mean age for both groups was 16 years.

Highest level of education

The mean highest level of education at the time of admission of the majority of group 1 was grade nine ($\chi^2_8 = 19.45$, $p = 0.013$; Table 1). Of the 51 participants, seven had records that did not state their level of education.

Duration of admission

The duration of admission did not vary significantly between group 1 and group 2 ($\chi^2_2 = 0.08$, $p = 0.963$). Although duration of admission was similar between the two groups, group 1were more likely to be admitted for less than one week compared to group 2 or those using other substances ($\chi^2_2 = 17.26$, $p < 0.001$).

Table 1: Sample characteristics and prevalence of cannabis use disorder.

Variable	**Group 1 CUD+ (n=43)**		**Group 2 CUD- (n=8)**		**P-value**
	n	**%**	**n**	**%**	
Mean age in years (s.d)	16.38	84.31	16.42	15.69	0.919
Highest level of education					0.013
Grade 5-7	4	9.30	-		
Grade 8	5	11.62	-		
Grade 9	11	25.58	-		
Grade 10	8	18.60	1	12.5	
Grade 11	3	6.98	1	12.5	
Grade 12	3	6.98	2	25.0	
Special needs education	2	4.65	4	50.0	
Unknown	7	16.28	-		
Duration of admission in weeks					0.963
<1	7	16.27	1	12.5	
1 to 4	15	34.88	3	37.5	
>4	21	48.83	4	50.0	

Table 2: Psychiatric diagnosis and prevalence of cannabis use disorder.

Variable	**Group 1 CUD+ (n=43)**		**Group 2 CUD- (n=8)**		**P-value**
	n	**%**	**n**	**%**	
Psychiatric diagnosis					
Psychotic disorder	14	32.56	1	12.50	0.410
Bipolar disorder I	3	6.98	1	12.50	0.506
Major depressive disorder	1	2.33	-	-	1.000
Conduct disorder	2	4.65	-	-	1.000
Intellectual disability	2	4.65	1	12.50	0.401
Reactive attachment disorder	2	4.65	-	-	1.000
Substance induced psychotic disorder	19	44.19	-	-	0.020
Psychotic disorder due to another medical condition	-	-	3	37.50	0.003
Other	-	-	2	25.00	0.022

Psychiatric profile

Only the primary psychiatric diagnoses on discharge were considered (Table 2). The majority of the participants (n = 19; 44.19%) had a diagnosis of substance induced psychotic disorder. For this sample, psychotic disorders included 14 participants with schizophrenia and one with brief psychotic disorder. Three participants admitted were diagnosed with bipolar I disorder. One participant admitted was diagnosed with major depressive disorder.

The percentage of participants with and without psychotic disorder due another medical condition [AMC] varied significantly by cannabis use (p = 0.003; Table 2). Participants from group 2 were 15.36 times more likely to have a psychotic disorder due to AMC compared to participants from group 1.

The percentage of participants with “other” psychiatric disorder varied significantly by cannabis use (p = 0.022; Table 2). Participants from group 2 were 13.46 times more likely to have “other” psychiatric disorder compared to participants from group 1. The two participants whose diagnosis was recorded as “other” both had autism spectrum disorder (Table 2).

No further statistical correlations could be demonstrated between participants from group 1 and 2.

Discussion

To the primary investigator's knowledge, this is the first study looking specifically at the prevalence of cannabis use disorder and associated co-morbid psychiatric diagnoses in adolescent male in-patients in Johannesburg, South Africa. The study found a prevalence of 84% of participants with a diagnosis of cannabis use disorder with a mean age of 16 in this sample. The duration of admissions for the participants with cannabis use disorder were similar than for participants without cannabis use. This may be due to the symptoms of intoxicated patients being severe enough to warrant a hospital admission but resolving rapidly once the individual is no longer exposed to the substance. Substance intoxication may present with symptoms similar to a major psychiatric disorder and create a diagnostic dilemma at the time of admission. There was an association found between cannabis use disorder and substance induced psychotic disorders.

Cannabis use amongst the adolescent South African population is an escalating problem. The prevalence rate in this study is higher compared to 73% that was recorded by the national survey in South Africa in 2018, which falls within the study's reference period.[3] This prevalence is similarly higher than the previously recorded percentage of 40-50% for the period June to December 2017, the period preceding the commencement of this study.[11]. The most likely explanation for the high prevalence of cannabis use disorder is due to this study being conducted in a hospital rather than in the community. Additionally, it is postulated that the increase in prevalence may be as a result of misinterpretation of the Cape High Court ruling related to the decriminalisation of cannabis that occurred in late 2017.[12] This ruling is frequently misinterpreted as the use of cannabis being legalised in the country. In the United States of America, there was a notable increase in the prevalence of cannabis use amongst adolescents in certain states where cannabis was decriminalised.[13] Previous studies found the prevalence rate of cannabis use in this study to be comparable to other African countries but higher than other South African provinces. [14-16] The prevalence rate in other provinces where studies were done on a similar in-patient adolescent group were 61.4% in KwaZulu Natal and 67% in the Western Cape. [15-16]

The majority of the study population were black African males and reflected the ethnicity demographics of the population served by the site where the study was conducted. The mean age of adolescents with cannabis use disorder is comparable to the findings of both other local and African studies.[14,15]

The mean highest level of education amongst the study population with a diagnosis of cannabis use disorder was grade nine, which is lower than the assumed grade ten when considering the mean age of 16. This could be indicative of poor academic performance, the reasons for which are multifaceted.[17] However, this study does demonstrate an association between cannabis use and suboptimal educational achievement. This corroborates an existing concerning factor that ongoing substance use may affect the highest level of education reached by individuals.[16]

The most common diagnosis amongst the participants in this study was substance induced psychotic disorder. This is not surprising since substance abuse triggers the onset of substance induced psychiatric illnesses. Rates of substance use have been reported to be higher in people at risk of developing psychosis. Some evidence suggests that the rate of substance use may be higher in those who convert to psychosis.[18,19] It would be interesting to follow these patients after discharge to determine if this admission were a prodrome or first presentation of other psychotic spectrum disorder. These patients need close monitoring because the onset of psychosis in adolescents with cannabis use is associated with a poor prognosis, more severe symptoms, poor inter-episodic functioning and impaired level of functioning.

Three participants were diagnosed with a psychotic disorder due to another medical condition. However, this result may be an under-representation since studies have found that adolescents admitted with psychotic symptoms may be inadequately investigated to exclude medical co-morbidity.[15] Important investigations, such as an HIV test, thyroid function tests and imaging studies, are often omitted if the physical examination is within normal limits.

Additional evidence suggests that anxiety disorders, conduct disorder, attention deficit hyperactivity disorder and intellectual disability have a high prevalence amongst adolescents and often co-occur with substance use, particularly cannabis use.[1; 18; 19; 20] These conditions are most likely to be seen in out-patient settings, and

therefore, are not adequately represented in this study. Due to the difficulty in diagnosing a mood disorder in patients using cannabis, frequently an extended duration of time from onset of mood symptoms to initiation of treatment occurs, as documented in the literature.[18] Patients may present with manic, depressive or psychotic symptoms. The presenting symptoms may be obscured by the substance use and evolve over time. The onset of mood disorders is typically in adolescence, but patients may only present in adulthood and this might account for the low prevalence of mood disorders in this study population. Depressive disorders are often not recognized amongst the community, therefore, patients with these disorders are less likely to seek help or present to hospital. This may be because of lack of awareness surrounding symptoms of depression and the perception that depressive disorders are less important than other psychiatric disorders.

The biopsychosocial risk factors for the origin of primary psychiatric disorders and substance-induced disorders are similar. The development of mental illness is dependent on the interaction of various risk factors. Ongoing cannabis use prolongs psychiatric symptoms and influences adherence negatively. This, in turn, negatively influences the prognosis, reduces functional capacity and increases the burden of care. [7]

Limitations

In a retrospective record review, the information available is dependent on the quality of the patient records. The data was collected by a single investigator in an attempt to improve uniformity. The sample size and control group of this study was small, and this impacted on the statistical analysis. The psychiatric co-morbidities in the population described may limit generalisation to other adolescent populations due to the sample size and pattern of service use in the community. Cultural norms for seeking help, especially for mental illness, may have impacted the size of the sample. The data was collected at a tertiary-level hospital, hence those patients presenting for primary or secondary level care, which is appropriate for this type of pathology, were not included.

Conclusion

The rate of cannabis use was found to be high amongst in-patient male adolescents, and the most common diagnosis recorded in this study was substance induced psychotic disorder. The findings of this study highlight the need for more integrated services to address the high rates of cannabis use before more long-term sequelae are present. These include educational initiatives in schools and dual diagnosis treatment programmes, targeted particularly at psychiatrically vulnerable adolescents.

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APPENDIX A: Approved research protocol with appendices

RESEARCH PROTOCOL

Title: Comparison of co-morbid psychiatric diagnoses in male adolescent in-patients with a history of cannabis use with those without cannabis use

Introduction

Adolescence is the period of progression through puberty characterised by marked changes within an individual and in the individual's environment. Adolescence typically describes the years between ages 13 and 18. Physiologically the adolescent develops an advancement in cognitive abilities and socially there are transformations happening in both parental and peer relationships (1). Therefore, it is not surprising that with all the changes occurring, adolescence is a period where risk for substance use and other psychiatric disorders begin to establish itself. By delaying the onset of substance use it could possibly change the prevalence and nature of adult-onset substance use (2).

Three developmental processes occur during adolescence that increase the risk of evolving substance use.

Cognitive development: Partaking in risky behaviours is increased during adolescence due to differences in the rate of development of two neurobiological systems which causes an imbalance between arousal and regulation. The limbic/para-limbic system is responsible for social and emotional regulation and is more rapidly developing resulting in increased sensation seeking. Cognition, self-regulation and impulse control, only develop toward the end of adolescence and young adulthood in the internal, prefrontal and parietal cortices (2).

Neural development: During adolescence important changes take place in neural maturation of the hippocampus and prefrontal cortex thus making adolescents vulnerable to injury caused by acute and chronic effects of substance use (2). Chronic exposure to substance use is similarly associated with neural changes in the reward pathways of the brain (2).

Social development: Transition from primary school to high school result in adolescents broadening their peer groups, less supervision from teachers and less time spent with family (2). During early and mid-adolescence effects of peer pressure are at its strongest. Association with peers who use substances results in increased risk of substance use, misconduct and other risky behaviours (2).

Scope of substance use in South African adolescents

SACENDU (South African Community Epidemiology Network of Drug Use) is a sentinel surveillance system project for alcohol and other drug abuse which is operational in 9 provinces in South Africa (3). The system monitors trends in alcohol and other drug use and associated consequences on a six-monthly basis from specialist alcohol and other drugs treatment programmes. According to their report from July to December 2017 persons under the age of 20 attending 80 specialist alcohol and other drug abuse treatment programs ranged from 19-32% (3). Persons under the age of 20 sought help for the following substances: 40-50% for cannabis; 30-40% for alcohol; 10-20% for methamphetamine and heroin and less than 10% for cocaine, mandrax, over the counter medication and CAT (3). What could account for the high proportion of heroin amongst youth is the use of Nyaope of which cannabis and heroin are the main narcotic ingredients. One of the topics selected for further research was to determine what is driving codeine use in this age group (3). All centres reported the proportion of African people seeking treatment as considerably lower than would be expected for the underlying demographics of the population (3).

Risk factors for substance use

Temperament and personality mediate the genetic risk of adolescent substance use and to some extent co-occurring disorders (2).

Inherited susceptibility often plays a role once a person begins to use substances, usually during adolescence. Adolescents that have a greater genetic predisposition to develop substance abuse may be more susceptible to the influence of substance use (4). Exposure to substances may trigger the turning on of genes and in turn drive the mechanism of substance abuse (4). Vulnerability to drug use usually occurs after

a person is persistently exposed to substance and would typically have an effect later in adulthood. Biological susceptibility may also influence the early onset of substance use (4).

According to Widome, substance use is more prevalent amongst socio-economically disadvantaged populations and is associated with lower socio-economic position (5). Widome postulates that cannabis use is highest amongst adults who had no secondary education (5).

Male and female adolescents initiate substance use at comparable rates, but males increase use faster (6). Sex/gender differences exist in neurobiologic factors mediating both reinforcement and aversiveness as well as intrinsic factors (personality, psychiatric co-morbities) and extrinsic factors (history of abuse, environment especially peer and family) which influences the progression of initial use to abuse (6). Same sex peer risk factor is higher in males than in females and romantic partners abusing substances increases the risk for female substance use (6).

Parental monitoring and deviant peer association were predictive of substance use in early adolescence, but family relationship quality was a significant predictor across the transition to high school and continued to predict use in later adolescence, as did association with deviant peers (7). Family context was found to be an important aspect in influencing choice of friends and peer group composition (7).

Co-morbidities associated with cannabis use

Psychosis

Rates of substance use have been reported to be higher in people at risk of developing psychosis and some evidence suggests that substance use may be higher in those who convert to psychosis (8).

Use of cannabis during the first episode of psychosis is related to earlier age of onset of the first episode, while ongoing cannabis use predicts poorer outcome (9). The earlier the age of onset, the greater the risk of developing psychosis. In addition, early onset cannabis use is associated with a two-fold risk of developing

schizophrenia later in life (9). Adolescents with a history of cannabis use are reported to have more positive psychotic symptoms and greater illness severity at onset. Cannabis use is furthermore an independent risk factor for developing psychosis (9).

Mood disorders

Cannabis use prior to onset of symptoms of bipolar disorder is associated with younger age of onset and increased manic episodes (9). One furthermore has to consider that patients with bipolar disorder are at increased risk of substance use and abuse (9).

Depression and substance use often occur simultaneously obscuring the treatment of both the substance use and depression (10). Wymbs reports that the most reliable risk factor for developing depressive symptoms are the early age of onset of substance use (11). The physiological and psychological effects of alcohol and cannabis use may present as depressive symptoms (11). Depressive symptoms are exaggerated by substance use that causes cognitive impairment and interpersonal difficulties (11).

Depression is often associated with suicidality and suicide remains an important cause of mortality in adolescents and a high number of adolescents have suicidal ideation (9).

Anxiety disorders

Anxiety disorders are more prevalent during adolescence and individuals who experience high levels of anxiety may use substances to lessen the symptoms (1). Anxiety and substance use tend to co-occur during adolescence. Individuals with higher levels of social anxiety and separation anxiety will use less substances, whereas generalized anxiety disorder and panic disorder will use more substance (1). The type of anxiety disorder may influence the amount of time spent with peers and therefore influence the amount of substance use (1).

Conduct disorder

Evidence suggests that substance use predicts the development of conduct disorder (11). Conduct features during adolescents may be precipitated by early initiation of substance use and substance use may perpetuate such features (11).

Conduct features, such as violence and juvenile offending in adolescence, and antisocial personality disorder in adulthood are increased with adolescent cannabis use (11).

ADHD (Attention deficit hyperactivity disorder)

A higher rate of adolescent substance use has been associated with a diagnosis of ADHD in childhood (12). An adolescent with ADHD and co-morbid diagnosis of conduct disorder are at an even higher risk of adolescent substance use (12). In approximately 30-50% of adolescents diagnosed with ADHD a co-morbid diagnosis conduct disorder is present (12).

Intellectual disability

Substance use is an increasing problem amongst adolescents with mild to moderate intellectual disability. This is concerning because substance use has more negative consequences amongst individuals with an intellectual disability and this group is at higher risk of developing a substance use disorder (13).

Review of the literature point to risk factors and possible psychiatric co-morbities to consider in cases of adolescents with a history of cannabis use. Due to the increasing rate of cannabis use amongst this age group it is therefore important to establish an understanding of the prevalence of co-morbid psychiatric diagnosis in South African context. Predicted outcomes of this study will be a high incidence of cannabis use disorders with co-morbid psychotic disorders in adolescent male in-patients.

Study Objectives

- To determine the prevalence of cannabis use disorders amongst adolescents admitted to the adolescent psychiatric ward at Chris Hani Baragwanath Academic Hospital

- To compare the demographic profiles of adolescents with cannabis use disorders versus those without cannabis use
- To compare co-morbid psychiatric diagnosis associated with cannabis use disorders in adolescents versus those without cannabis use

Methodology

Study site:

The study will take place at Chris Hani Baragwanath Academic Hospital situated in Soweto, Gauteng province. Chris Hani Baragwanath Academic Hospital is a tertiary hospital that provides both in-patient and outpatient psychiatric services to Soweto and surrounding areas. In-patient psychiatric services include an exclusive 10 bed adolescent male ward, which was started in January 2018. The ward was started due to increase number of adolescent male patients' admissions to psychiatry and this age group required specialized care that could not be offered in general male psychiatric wards.

Sample sizes

From an assessment of Z scores of expected frequencies, a minimum sample size of 150 adolescents (75 per cannabis use/other substance use group) is likely to detect statistically significance at the 5% level.

Inclusion criteria

- Male adolescents between the ages of 13 to 18 years old that have been admitted to the adolescent psychiatric ward at Chris Hani Baragwanath Academic Hospital

Exclusion criteria

- Male adolescents admitted older than the age of 18 or younger than 13

Data collection

Case files for adolescents admitted to the Adolescent ward will be identified via the admissions book in Zebra ward, the psychiatric admission ward at Chris Hani Baragwanath Academic Hospital. Data will be collected from clinical records of in-patients that were admitted from 1 January 2018- 30 June 2019.

Data will be collected from the relevant files and recorded on a data sheet. The following details will be documented: demographic data, employment status of primary caregiver, psychiatric diagnosis and substance history. (see appendix 1)

Study design: The study will be a retrospective record review of adolescents aged 13 to 18 years old admitted as inpatients.

Data analysis

The questionnaire data will be captured in Microsoft Excel spreadsheets. Categorical variables will be summarised and tabulated by frequency (numbers of occurrence) and illustrated in bar charts. All statistical analyses will be conducted using R software (R version 3.5.1; https://www.r-project.org). Tests will be two-tailed probability values, and statistical significance accepted when $\alpha \leq 0.05$. The data set for this study will be generated from assessments of categorical scores.

Statistical analyses used in each of the three objectives are outlined below.

Objective 1. To determine the prevalence of cannabis use disorders, a chi-squared contingency test to analyse the numbers of male adolescents involved with substance abuse vs the total male adolescents admitted to the adolescent psychiatric ward at Chris Hani Baragwanath Academic Hospital will be used.

Objective 2. the demographic profile of male adolescents with and without cannabis use disorder will be assessed by comparing the proportion of adolescents falling into the following demographic parameters: level of education; home language; employment status of the primary caregiver; and receipt of a child care grant. Analyses will involve a logistic regression (GLZ with a binomial error structure), in which substance abuse and non-abuse patients be included as the dependent variable and demographic parameters included as fixed factors.

Objective 3. To analyse the co-morbid psychiatric diagnoses associated with substance use disorders, a logistic regression (GLZ with a binomial error structure) will be used to analyse the effects of several continuous predictors, including psychotic disorders, bipolar disorder, depressive, disorder, anxiety disorder, ADHD, conduct disorder, ODD, ID, DMDD, SIPD, SIMD, psychotic disorder due to AMC, and mood disorder due to AMC, on the substance abuse and non-abuse patients (dependent variable).

For the analyses for objectives 2 and 3, c2 statistics will be used for overall model significance. Z statistics, including beta estimates, SE values and confidence intervals (CI), will be generated for specific components of fixed factors. Here, reference categories will be selected using sequential entry and/or based on logically meaningful categories to obtain Z statistics for each component. Relative Risks (RR) for an abuse vs no abuse scores for each of the significant fixed factors will be calculated by dividing the % value per component of a factor by the % value of the reference category.

Limitations

As this a retrospective study and the results are dependent on clinical records, incomplete or unavailable data will be the major obstacle.

Adolescents using substances such as nyaope, a mixture of cannabis and heroin, will be classified as cannabis use disorder and this might impact on the results.

Ethics

The protocol will be submitted to the ethics committee for approval before data can be collected. Permission to conduct the study will be sought from the CEO of the hospital.

Consideration will be given regarding patients' confidentiality. Patients' personal information will be protected at all times and remain anonymous. Random numbers

will be assigned to case files of patients selected for the study in order to protect patient names and hospital numbers.

Timing

Data collection will commence as soon as the protocol I approved by the Postgraduate Committee and the Ethics Committee.

June-October 2018: Literature review and protocol preparation

November 2018: Presentation to Postgraduate Committee

January 2019: Presentation to Ethics Committee

February-March 2019: Data collection

April-May 2019: Data capturing and analysis

June- September 2019: write up of thesis and review by supervisor

Funding

Due to low costs nature of the study, all cost will be borne by the researcher

ITEMS	ESTIMATED AMOUNT
Travel costs	R1500
Photocopying and stationary	R1500
Statistician	R2000
Other	R1000
Total budget	R6000

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APPENDIX 1: DATA COLLECTION SHEET

Case number _____

Demographic data

Age	Gender	Level of education-
Religion		

Duration of stay

Less than one week	One-four weeks	More than four weeks

Psychiatric diagnosis [tick appropriate box]

Psychotic disorder	Bipolar Disorder	Depressive disorder
Anxiety disorder	ADHD	CD
ODD	ID	Attachment disorder
DMDD	SIPD	SIMD
Psychotic D/O due to AMC	Mood D/O due to AMC	Other

Primary caregiver employed?

Yes	No	Child support grant

Substance history

Cannabis use	Other substance use	Both

APPENDIX B: Permission to conduct research

GAUTENG PROVINCE

MEDICAL ADVISORY COMMITTEE

CHRIS HANI BARAGWANATH ACADEMIC HOSPITAL

PERMISSION TO CONDUCT RESEARCH

Date: 18th March 2019

TITLE OF PROJECT: Comparison of co-morbid psychiatric diagnoses in male adolescent in-patients with a history of cannabis use with those without cannabis.

UNIVERSITY: Witwatersrand

Principal Investigator: Dr S Lintnaar

Department: Psychiatry

Supervisor : Dr W Friedlander

Permission Head Department (where research conducted): Yes

The Medical Advisory Committee recommends that the said research be conducted at Chris Hani Baragwanath Academic Hospital. The CEO / management of Chris Hani Baragwanath Academic Hospital is accordingly informed and the study is subject to:-

- Permission having been granted by the Committee for Research on Human Subjects of the University of the Witwatersrand.
- The Hospital will not incur extra costs as a result of the research being conducted on its patients within the hospital
- The MAC will be informed of any serious adverse events as soon as they occur
- Permission is granted for the duration of the Ethics Committee Approval.

Recommended
(On behalf of the MAC)
Date: 18/03/2019

Approved/~~Not Approved~~
Hospital Management
Date: 19/03/2019

APPENDIX C: Ethical clearance certificate

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R14/49 Dr Stacey-Leigh Lintnaar

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M190478

NAME: (Principal Investigator)	Dr Stacey-Leigh Lintnaar
DEPARTMENT:	Psychiatry Chris Hani Baragwanath Academic Hospital
PROJECT TITLE:	Comparison of co-morbid psychiatric diagnosis in male adolescent in-patients with a history of cannabis use with those without cannabis use
DATE CONSIDERED:	26/04/2019
DECISION:	Approved unconditionally
CONDITIONS:	
SUPERVISOR:	
APPROVED BY:	Dr CB Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	30/05/2019

This clearance certificate is valid for 5 years from date of approval. Extension may be applied for.

DECLARATION OF INVESTIGATORS

To be completed in duplicate and **ONE COPY** returned to the Research Office Secretary on the Third Floor, Faculty of Health Sciences, Phillip Tobias Building, 29 Princess of Wales Terrace, Parktown, 2193, University of the Witwatersrand. I/we fully understand the conditions under which I am/we are authorized to carry out the above-mentioned research and I/we undertake to ensure compliance with these conditions. Should any departure be contemplated, from the research protocol as approved, I/we undertake to resubmit the application to the Committee. **I agree to submit a yearly progress report**. The date for annual re-certification will be one year after the date of convened meeting where the study was initially reviewed. In this case, the study was initially reviewed in **April** and will therefore be due in the month of **April** each year. Unreported changes to the application may invalidate the clearance given by the HREC (Medical).

Principal Investigator Signature Date

PLEASE QUOTE THE PROTOCOL NUMBER IN ALL ENQUIRIES

APPENDIX D: Turn-it-in report of Originality for Research Report in the format of a "submissible" paper

1730739:MMed_Research_report_.docx

by Stacey-Leigh Lintnaar

Submission date: 08-Oct-2020 09:45AM (UTC+0200)
Submission ID: 1408890923
File name: 3aab85b1-da22-4a13-9014-0dcf805504cc_MMed_Research_report.docx (551.73K)
Word count: 3696
Character count: 20815

1730739:MMed_Research_report_.docx

ORIGINALITY REPORT

14%	6%	13%	2%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	Machielsen, Marise, Suzanne van der Sluis, and Lieuwe de Haan. "Cannabis use in patients with a first psychotic episode and subjects at ultra high risk of psychosis: impact on psychotic- and pre-psychotic symptoms", Australian and New Zealand Journal of Psychiatry, 2010. Publication	2%
2	sajp.org.za Internet Source	1%
3	"Cannabis Use Disorders", Springer Science and Business Media LLC, 2019 Publication	1%
4	worldwidescience.org Internet Source	1%
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Exclude quotes	On	Exclude matches	Off
Exclude bibliography	On		

APPENDIX E: Guidelines for Authors submitting to the South African Journal of Psychiatry

Original Research Article full structure

Title: The article's full title should contain a maximum of 95 characters (including spaces).

Abstract: The abstract, written in English, should be no longer than 250 words and must be written in the past tense. The abstract should give a succinct account of the objectives, methods, results and significance of the matter. The structured abstract for an Original Research article should consist of six paragraphs labelled Background, Aim, Setting, Methods, Results and Conclusion.

- Background: Summarise the social value (importance, relevance) and scientific value (knowledge gap) that your study addresses.
- Aim: State the overall aim of the study.
- Setting: State the setting for the study.
- Methods: Clearly express the basic design of the study, and name or briefly describe the methods used without going into excessive detail.
- Results: State the main findings.
- Conclusion: State your conclusion and any key implications or recommendations. Do not cite references and do not use abbreviations excessively in the abstract.

Introduction: The introduction must contain your argument for the social and scientific value of the study, as well as the aim and objectives:

- Social value: The first part of the introduction should make a clear and logical argument for the importance or relevance of the study. Your argument should be supported by use of evidence from the literature.
- Scientific value: The second part of the introduction should make a clear and logical argument for the originality of the study. This should include a summary of what is already known about the research question or specific topic, and should clarify the

knowledge gap that this study will address. Your argument should be supported by use of evidence from the literature.

- Conceptual framework: In some research articles it will also be important to describe the underlying theoretical basis for the research and how these theories are linked together in a conceptual framework. The theoretical evidence used to construct the conceptual framework should be referenced from the literature.
- Aim and objectives: The introduction should conclude with a clear summary of the aim and objectives of this study.

Research methods and design: This must address the following:

- Study design: An outline of the type of study design.
- Setting: A description of the setting for the study; for example, the type of community from which the participants came or the nature of the health system and services in which the study is conducted.
- Study population and sampling strategy: Describe the study population and any inclusion or exclusion criteria. Describe the intended sample size and your sample size calculation or justification. Describe the sampling strategy used. Describe in practical terms how this was implemented.
- Intervention (if appropriate): If there were intervention and comparison groups, describe the intervention in detail and what happened to the comparison groups.
- Data collection: Define the data collection tools that were used and their validity. Describe in practical terms how data were collected and any key issues involved, e.g. language barriers.
- Data analysis: Describe how data were captured, checked and cleaned. Describe the analysis process, for example, the statistical tests used orsteps followed in qualitative data analysis.
- Ethical considerations: Approval must have been obtained for all studies from the author's institution or other relevant ethics committee and the institution’s name and permit numbers should be stated here.

Results: Present the results of your study in a logical sequence that addresses the aim and objectives of your study. Use tables and figures as required to present your findings. Use quotations as required to establish your interpretation of qualitative data. All units should conform to the **SI convention** and be abbreviated accordingly. Metric units and their international symbols are used throughout, as is the decimal point (not the decimal comma).

Discussion: The discussion section should address the following four elements:

- Key findings: Summarise the key findings without reiterating details of the results.
- Discussion of key findings: Explain how the key findings relate to previous research or to existing knowledge, practice or policy.
- Strengths and limitations: Describe the strengths and limitations of your methods and what the reader should take into account when interpreting your results.
- Implications or recommendations: State the implications of your study or recommendations for future research (questions that remain unanswered), policy or practice. Make sure that the recommendations flow directly from your findings.

Conclusion: Provide a brief conclusion that summarises the results and their meaning or significance in relation to each objective of the study.

Acknowledgements: Those who contributed to the work but do not meet our authorship criteria should be listed in the Acknowledgments with a description of the contribution. Authors are responsible for ensuring that anyone named in the Acknowledgments agrees to be named.
Also provide the following, each under their own heading:

- Competing interests: This section should list specific competing interests associated with any of the authors. If authors declare that no competing interests exist, the article will include a statement to this effect: *The authors declare that they have no financial or personal relationship(s) that may have inappropriately influenced them in writing this article.* Read our **policy on competing interests**.

- Author contributions: All authors must meet the criteria for authorship as outlined in the **authorship** policy and **author contribution** statement policies.
- Funding: Provide information on funding if relevant
- Disclaimer: A statement that the views expressed in the submitted article are his or her own and not an official position of the institution or funder.

References: Authors should provide direct references to original research sources whenever possible. References should not be used by authors, editors, or peer reviewers to promote self-interests. Refer to the journal referencing style downloadable on our *Formatting Requirements* page.
