THE PROFILE OF NEUROCOGNITIVE DISORDERS IN PATIENTS ATTENDING PSYCHIATRIC OUTPATIENT SERVICES AT A TERTIARY LEVEL ACADEMIC HOSPITAL IN JOHANNESBURG.

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A research report submitted to the Faculty of Health Sciences, University of the Witwatersrand, in fulfilment of the requirement for the degree of Master of Medicine in the Department of Psychiatry.

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DECLARATION

I, Peacemaker Samukelisiwe Mngomezulu, declare that this research report is my own work. It is being submitted to the Faculty of Health Sciences, University of the Witwatersrand, Johannesburg in requirement for the degree of a Master of Medicine in the Department of Psychiatry. It has not been submitted for any degree or examination at this or any other University.

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Student number 0601059H

15th day of October 2020_____in Johannesburg

DEDICATION

To my husband, Mr Siphamandla Mngomezulu and the rest of my family who have been a pillar of strength.

PRESENTATION ARISING FROM THIS RESEARCH PROJECT

- Witwatersrand University, Division of Psychiatry, 31st Annual Research Day held on the 19th June 2019.

ABSTRACT

Mild or major neurocognitive disorders (NCDs) are a group of non-communicable diseases presenting with acquired cognitive decline. They are usually complex, chronic and progressive in nature. NCDs are classified into primary NCDs and secondary NCDs. They are a growing public health concern globally, with the worldwide prevalence of approximately 46.8 million people in 2015. The estimate is expected to increase to 74.7 million by 2030 and 131.5 million in 2050 respectively.

The aim of the study was to describe the profile of NCDs in patients attending tertiary level psychiatric outpatient department. The study was a descriptive-retrospective record review of the files of patients who attended the Charlotte Maxeke Johannesburg Academic Hospital (CMJAH) psychiatric outpatient department. Out of 6 879 psychiatric patients that were older than 18 years seen between 01 January 2015 and 31 December 2017, only 145 (2.1%) had a diagnosis of NCD according to DSM IV-TR/DSM-5 criteria. The majority were elderly patients from the 61 - 80 years age group 67 (46.2%), female gender 87 (60%) and of black ethnicity 68 (47%). Most patients presented with major NCDs i.e.129 (89%). Most were secondary in nature 118 (81.1%). Of the primary NCDs frontotemporal NCDs occurred commonly 2 (1.4%). With regards to, secondary NCDs, vascular NCDs 54 (37.2%) and NCDs due to HIV infection 21 (14.5%) were most significantly represented. Cardiovascular diseases 88 (77%), psychotic disorders 54 (39.7%) and major depressive disorders 42 (30.9%) were the most common comorbidities.

The study described NCDs in terms of demographic profile, psychiatric and medical comorbidities. The findings support early standardised neurocognitive screening of psychiatric

patients for NCDs, to identify those at risk and to prevent rapid progression of those already diagnosed.

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LIST OF ABBREVIATIONS

AIDS	Acquired Immune-Deficiency Syndrome
ART	Antiretroviral Therapy
CT	Computerized Tomography
CMJAH	Charlotte Maxeke Johannesburg Academic Hospital
CEO	Chief Executive Officer
DSM-IV-TR	Diagnostic and Statistical Manual of mental disorders, fourth Edition – text revised
DSM-V	Diagnostic and Statistical Manual of mental disorders, fifth edition
EEG	Electroencephalography
HIV	Human Immuno-Deficiency Virus
IHDS	International HIV Dementia Scale
MMSE	Folstein's Mini-Mental State Examination
MoCA	Montreal Cognitive Assessment
MRI	Magnetic Resonance Imaging
MCI	Mild cognitive impairment
NCDs	Neurocognitive Disorders
RSA	Republic of South Africa
TBI	Traumatic Brain Injury
WHO	World Health Organization

CHAPTER ONE

1.1 Introduction

Mild or major neurocognitive disorders (NCDs) are a group of non-communicable diseases presenting with acquired cognitive decline. They are usually complex, chronic and progressive in nature.[1] Neurocognitive disorders are classified into primary and secondary NCDs.[3] This classification focuses mainly on the multiple aetiological factors associated with NCDs. Primary NCDs are progressive neurodegenerative diseases which are characterised by selective neuronal loss. Possible causes of primary NCDs are Alzheimer's disease, frontotemporal, Lewy body, and prion disease.[2,3]

Secondary NCDs are associated with secondary cerebral or systemic causes.[2] They may be as a result of various diseases including human immuno-deficiency virus (HIV), traumatic brain injury (TBI), strokes, chronic alcohol abuse or other substances/medication, Huntington's disease, Parkinson's disease and other medical conditions such as vitamin B12 deficiency, endocrine dysfunction, neurosyphilis, etc.[1,3] Most importantly, NCDs may be due to multiple aetiological factors.[1] Furthermore, NCDs can also be classified into cortical, subcortical and cortico-subcortical NCDs, which indicate the affected brain regions and possible associated clinical features respectively. These classifications are useful for diagnostic and management purposes as well as epidemiological studies.[4]

Historically, the Diagnostic and Statistical Manual of Mental Disorders (DSM), Fourth Edition (IV) Text revision (TR), broadly referred to major NCDs as “dementia” which is described as a degenerative disorder typically seen in the elderly population affecting a range of cognitive functions such as memory, learning, language, orientation, attention, social cognition and executive functioning.[5] In addition, the mental function must be noted to decline below the

pre-morbid level, irrespective of the previous level of intellectual capacity and achievement as well as impairment of social or occupational functioning.[3] However, the fifth edition of Diagnostic and Statistical Manual of Mental Disorders (DSM-5) subsumed dementia under the newly named entity of neurocognitive disorders with a specification of the severity being mild or major.[1] Mild or major NCDs encompasses acquired cognitive disorders of all age groups with the diagnosis supported by standardised neuropsychological tests. There is a notable paucity of published research on the prevalence of NCDs in the Republic of South Africa (RSA).[4,5,9,13] Few available studies have focused more on NCDs in the elderly population whilst there is increasing evidence of NCDs in the younger population in RSA, particularly due to the high prevalence of HIV, chronic alcohol abuse and TBI.[6,13]

1.2 Literature review

1.2.1 Description of relevant terminology

1.2.1.1 Mild Cognitive Impairment (MCI)

Mild Cognitive Impairment (MCI) is defined as the presence of mild cognitive decline that does not warrant the diagnosis of mild or major NCD and has preserved basic activities of daily living. MCI is also known as age-associated cognitive decline.[10,55] The term MCI was suggested as a diagnostic category designed to fill the gap between cognitive changes associated with ageing and cognitive impairment suggestive of major NCD/dementia. Most of these patients often present with memory complaints preferably confirmed by the informant where possible, objective memory impairment for age and education, preserved general cognitive function and intact activities of daily living.[55] It is important to note that this term does not have an official international diagnostic criterion and it has been regarded as the prodromal stage for Alzheimer's disease, frontotemporal and vascular NCDs.[55] One-third of

patients with MCI are more likely to progress to have major NCD especially those with multiple-domain MCI.[55]

1.2.1.2 Mild and major neurocognitive disorders (NCDs)

a) Mild neurocognitive disorders (NCDs)

The term mild NCD was first introduced in DSM-IV under the category of 'Cognitive Disorder Not Otherwise Specified'.[5] This was essentially defined by neuropsychological testing or by quantitative clinical assessment whereas the DSM-5 version of mild NCD is based on several cognitive and related criteria which resemble clinical features of MCI.[1,5] For example, subjective complaints by the patients, objective findings by the informant or clinician and preferably confirmed by a neuropsychological test. The main difference between these terms is that MCI is common in the elderly population whilst mild NCD encompasses acquired cognitive disorders of all age groups.[55]

b) Major neurocognitive disorders (NCDs)

Major NCD is a term that is used synonymously with dementia.[1] The key distinction between mild and major NCDs is the loss of independence, functional decline and profound cognitive decline in major NCDs compared to mild NCD.[1,5,55] Both mild and major NCDs have similar aetiological factors.[1] These conditions can present with several behavioural abnormalities such as psychotic or mood symptoms, sleep disturbances, agitation, apathy etc. but these behavioural disturbances are more common in major NCDs.[55] The diagnosis of NCDs is based on a detailed history taking, proper physical and neurological examination, mental status examination, bedside neurocognitive testing, standardised neuropsychological tests, comprehensive laboratory work-up to detect reversible causes of NCDs and neuro-imaging to identify the subtype of NCDs.[55]

1.2.2 Prevalence of NCDs worldwide

NCDs are a growing public health concern globally, with a worldwide prevalence of approximately 46.8 million people in 2015. This is estimated to increase to 74.7 million by 2030 and 131.5 million in 2050 respectively.[7] The prevalence of NCDs has shown a rapid increase from 2% to 3% among those aged between 70 and 75 years and 20% to 25% among those aged 85 years or older.[8] The World Alzheimer's Report 2009 showed an increase in the prevalence of NCDs in developed countries such as Europe and East Asia from 4.98% to 6.99%.[7] The higher prevalence of NCDs in developed countries was mainly noted in the elderly population and may be due to increased cardiovascular risk factors, longer life expectancy and well-established health facilities with more accurate statistics being documented or updated.[7,18] An increase in the prevalence of NCDs in developing countries (Sub-Saharan Africa) was noted to be from 2.07% to 4.76%.[7] The prevalence of NCDs in the younger population is expected to rise due to the increased burden of NCDs due to HIV, TBI and chronic alcohol abuse.[9,10]

1.2.3 Prevalence of NCDs in the Republic of South Africa

The prevalence of NCDs in the Republic of South Africa (RSA) has not been established conclusively.[4] Recent studies emerging in RSA suggest that the prevalence of NCDs may be higher than previously thought.[10] Studies have reported consistently lower rates of NCDs in developing countries compared to developed countries, which has been attributed to differential survival rates; non-presentation of cases of mental illness at service facilities owing to stigma and other reasons; access barriers to health care; symptoms and signs of NCDs being accepted by sufferers' families as normal ageing; and preferential use of traditional healing or complementary medicine.[4]

In the South African context, vascular NCDs followed by NCDs due to Alzheimer's disease are common in the elderly population.[10] A survey of individuals aged >60 years in Durban residential homes found 7.9% of residents with NCDs in 2014.[11] Two similar findings emerged from prevalence studies done at the University of the Free State, which investigated NCDs in the urban black community. The first study was conducted amongst indigenous Sotho-speaking elderly black people in 2012 and a prevalence of 7.7% was reported.[12] The second study done in 2015 reported a prevalence of 6% from a small study sample of 200 elderly individuals.[13] However, most studies done previously in RSA have been limited to old age homes thus focusing on the elderly population which made them age biased. [11,13]

NCDs in a younger population are increasingly recognized as an important clinical and social problem, with frequently devastating consequences for both the patient and the caregiver. [65] The majority of these patients often experience a full course of NCD, particularly NCD due to HIV infection is common in the younger population. [10] In addition, drugs and toxic exposures should always be considered in a younger population with NCDs. In approximately 10% of cases of patients with NCDs in this population is a consequence of chronic alcohol abuse. There is dearth of research performed in a younger population with NCDs. [65] This is despite the fact that RSA continues to battle with a unique burden of diseases among the younger population that may result in secondary causes of NCDs.[11,13]

1.2.4 Psychiatric disorders and NCDs

Patients with NCDs usually present to different fields of medicine due to the nature of their comorbidities. High numbers of these patients are seen in Psychiatry, Medicine and Neurology Departments.[55] Up to 90% of patients with NCDs have psychiatric comorbidities.[14] However, there is a paucity of studies to confirm the prevalence of patients with NCDs who later develop

psychiatric illnesses and vice versa. It is common that patients with NCDs have neuropsychiatric manifestations, but some types of NCDs develop psychiatric illnesses earlier than others and they are associated with certain types of psychiatric illnesses. For example, patients with post-stroke vascular NCDs are more likely to suffer from major depressive disorders (MDD). NCD due to Alzheimer's disease often present with a prodrome MDD.[14]

The assessment and treatment of psychiatric symptoms in patients with NCDs have become complex because of the increased sensitivity to psychotropic medication; and adverse effects such as falls and over-sedation. These may further worsen the neurocognitive function. Neuropsychiatric symptoms that include depression, psychosis, anxiety and agitation/aggression are often first signs of cognitive disorders and are correlated with faster progression to NCDs.[14]

a) Affective disorders

Affective disorders are associated with cognitive disturbances that are not just limited to acute mood episodes. Even after a major depressive episode has remitted, patients show impairment in executive function and attention. Depressive symptoms can be initial manifestations of NCD and may fluctuate over time.[14,55] Assessing for depression in patients with NCDs poses challenges because they do not often have classic presentation of MDD hence the diagnosis maybe difficult .[14,55] Compared with older patients with intact cognition, patients with NCDs are more likely to report a diminished ability to concentrate or indecisiveness during a major depressive episode. On the other hand, patients with NCDs are less likely to report

insomnia/hypersomnia, feelings of worthlessness and guilt, or suicide thoughts.[14] These are some of the reasons that depression is often missed in patients with NCDs.

Depression affects 20% to 32% of patients with NCDs.[14] The prevalence is higher in patients with vascular NCDs than in patients with Alzheimer's disease and Parkinson's disease.[1,14] Previous systematic review studies have noted that a chronic history of depression poses a risk of NCDs at the later stage.[20] It was believed that the cognitive and functional deficits seen in pseudodementia could be entirely restored to normal after successful treatment of depression.[20] In contrast, this concept has been progressively abandoned since cognitive dysfunction may not be totally reversed by antidepressant treatment and more than 40% of patients with pseudodementia eventually develop NCDs. Clinical monitoring of cognition may be warranted in these patients.[1,5,20,55] Hence it is important to screen for depression in every patient with NCD regardless of the stage of the illness and screening for NCDs in all chronic severely depressed patients is valid.

Numerous studies have shown that young and older patients with bipolar disorders have significant cognitive impairment, especially deficits with executive function and processing speed. [66] These cognitive deficits are more pronounced in older individuals because of a higher rate of medical and neurological comorbidities. The presence of cognitive impairment in patients with bipolar disorders is associated with greater disability and increased mortality. [66] Some patients with bipolar disorders in remission had deficits in verbal declarative memory and executive function and others improved over time. [15] There is a limited data of prevalence of NCDs in patients with bipolar mood disorders. [10, 66]

b) Psychotic disorders

Psychotic features are shown to be present in 14% to 18% of patients with NCDs in community-based cohort studies done in America.[14] They are common in NCDs, particularly at the mild to moderate stages of NCDs due to Alzheimer's disease, Lewy body, and frontotemporal lobe degeneration.[1] The previous study conducted by Ku et al found that the prevalence of NCDs in patients with schizophrenia was four times higher than the prevalence of those without schizophrenia. [16] The study noted that 9.9% of patients with schizophrenia were diagnosed with NCDs versus 2.2% of patients without schizophrenia.[16] A significant number of patients with schizophrenia and NCDs were noted in elderly females (12%) than in males (7.8%). The most common type of NCD was Alzheimer's disease (20.7%) followed by vascular NCDs (4.8%).[16] The reason for the high risk of NCDs in patients with schizophrenia were unknown but there was a hypothetical link between long term use of antipsychotics and cognitive decline.[16,20]

c) Anxiety disorders

The probability of primary anxiety disorders in patients with NCDs is nearly 20%.[14] Generalised anxiety disorder is one of the more frequently diagnosed anxiety disorders and it occurs in 5% of patients with NCDs due to Alzheimer's disease.[14] Estimates of clinically significant anxiety features are as high as 70% particularly in vascular NCDs and frontotemporal NCDs.[14]

d) Personality changes

Personality changes in individuals with NCDs are distressing to their families. Pre-existing personality traits are usually more prominent after the NCD diagnosis.[55] They may become introverted and seem to be less concerned than they previously were about the effects of their behaviour on others. Individuals with frontal and temporal involvement are likely to have

marked personality changes and they may be irritable and explosive.[55] The prevalence of agitation or aggression among individuals with NCDs is 27%.[14] The prevalence increases as NCD progresses (13% in mild NCD and 29% in major NCD).[14] In patients with NCDs, agitation may manifest in a variety of behavioural disturbances. These behaviours may include intermittent psychomotor hyperactivity, disinhibition to physical aggression and combativeness, [14] to a point of resisting caregiving duties such as bathing and dressing.[1] Other important behavioural disturbances in NCDs include apathy, wandering, excessive eating, sleep disturbance and hoarding.[1] These features have been shown to increase caregiver burden and this is more likely the reason these patients end up in care facilities.

1.2.5 Medical comorbidities in NCDs

A significant number of patients with NCDs often present initially to health care centres with chronic medical illnesses with the NCD diagnosis being discovered later. These medical comorbidities may cause or exacerbate the progression of NCDs.[51] Cardiovascular diseases have been implicated to increase the risk of NCDs due to the reduced blood supply to the brain. They are associated with vascular NCDs and NCDs due to Alzheimer's disease. Cardiovascular risk factors exponentially increase with age and are often overlooked as a source of cognitive changes or major NCDs.[51] These risk factors include stroke, hypertension, hypercholesterolaemia, diabetes mellitus, obesity and smoking. NCDs develop earlier in patients with severe or recurrent major strokes.[51] The previous literature has highlighted the increased risk of epilepsy in patients with a stroke or post head trauma. Importantly, some findings also suggest that older patients with epilepsy are at a higher risk of developing cognitive impairment and ultimately major NCDs. The chronic epilepsy history from a young age is associated with some form of NCDs later in life.[1,5,51,55]

There is growing evidence linking alterations in the endocrine system to the pathogenesis of NCDs due to Alzheimer's disease and other major NCDs. Insulin resistance, elevated cortisol and low oestrogen and testosterone levels have all been implicated by multiple studies in the development of major NCDs.[41] Clinical hypothyroidism and hyperthyroidism have been recognised as potential causes of reversible NCDs and the serum thyroid stimulating hormone (TSH) level has become a standard screening test for the routine evaluation of patients with suspected NCDs.[41] There are other multiple medical illnesses such as neurosyphilis, vitamin B12 deficiency etc. that pose a risk of NCDs. There have been inconclusive results to suggest respiratory and gastrointestinal diseases as aetiological factors of NCDs. However, there are a few research projects highlighting mid-life obstructive lung disease and inflammatory bowel disease as a possible cause of impaired cognitive function later in life.[51,55] Therefore, full medical evaluation is recommended in all patients presenting with NCD features so that reversible and exacerbating factors may be treated timeously.

1.2.6 Primary NCDs

1.2.6.1 NCDs due to Alzheimer's disease

In 1970, Alois Alzheimer first described the condition that later assumed his name.[55] Alzheimer's disease (AD) is a progressive degenerative disease of the brain that has an insidious onset and gradual progression of impairment in one or more cognitive domains.[4] AD presents with various psychiatric symptoms such as apathy, depression, anxiety, irritability, agitation, and delusions. Hallucinations and mania are uncommon in AD.[64] Alzheimer's disease is the most common cause of NCDs in the elderly population, accounting for 60% to 80% of cases of late-life cognitive decline worldwide.[17] The duration of the illness may be as short as 6 months or as long as 20 years, with an average of 12 years.[1,10]

Younger individuals are more likely to survive the full course of the disease, while older individuals are more likely to have multiple medical comorbidities that affect the course and the management of the illness.[1] The prevalence of Alzheimer's disease has been observed in elderly females over the age of 85 years.[10] This may be due to a longer life expectancy in females than males. The literature suggests that there is a decreased risk of NCDs due to Alzheimer's disease in people with at least a high school education. This is attributed to cognitive stimulation that assists in building healthy brain cell connections.[10,17] Risk factors of Alzheimer's disease include a positive family history of Alzheimer's disease, metabolic syndrome, stroke or previous head trauma.[10,17] There is a paucity of published prevalence studies of Alzheimer's disease in South Africa. However, according to estimates in the World Alzheimer's Report 2015, there were almost 186 000 people living with Alzheimer's disease in RSA, of those, nearly 75% were elderly females. This number is expected to rise to nearly 275 000 by 2030.[18,19] A pilot study conducted in 2016 in a rural black community of 2000 households in Bloemfontein (RSA) showed a prevalence of 6.4% of Alzheimer's disease.[17] This may suggest that NCDs due to Alzheimer's disease is significantly high in RSA and is common in elderly females with a low level of education.

1.2.6.2 Frontotemporal NCDs

Frontotemporal lobes degenerative NCD (FTD) is the term preferred over Pick's disease to describe the spectrum of non-Alzheimer's NCDs characterised by focal atrophy of the frontal and anterior temporal brain regions.[22] These regions have neuronal loss, gliosis and neuronal Pick's bodies, which are masses of cytoskeletal elements.[22,55] The cause of Pick's disease is unknown but it constitutes approximately 5% of all irreversible major NCDs.[55] The estimated prevalence is 15 to 22/100,000 and survival varies widely from 3 to 14 years. The prevalence of frontotemporal NCDs is substantial, though specific figures vary in different studies.[20] It

occurs usually in an age range of 35 to 75 years and among these patients, 20% to 40% have a positive family history of frontotemporal NCDs.

Risk factors associated with this disorder include head trauma and a genetic predisposition.[20] FTD is characterised by gross decline in conduct (i.e. the behavioural variant) or speech and language (the language variant). The behavioural variant of FTD typically presents as a combination of socially inappropriate behaviour(s), loss of manners or decorum, impulsivity, stereotyped behaviours, apathy, loss of sympathy or empathy, hyperorality and dietary changes, dysexecutive syndrome etc. Many of these patients do not have noticeable cognitive deficits until illness is established.[64]

1.2.6.3 NCDs due to Lewy body disease

The few population-based prevalence estimates for NCDs due to Lewy body disease (NCDLB) available range from 0.1% to 5% of the general elderly population and from 1.7% to 30.5% of all NCDs cases. [1] It is common in males compared to females with a ratio of approximately 1.5:1. [1] NCDLB is characterised by cognitive, behavioural and physical features in varying combinations.[1,4,55] The classical triad of symptoms of NCDLB comprises of fluctuating cognitive impairment, parkinsonism and visual hallucinations. The fluctuation may be day to day or even hour to hour and it may resemble delirium. Cognitive impairment and psychiatric symptoms present early in the course of the disease and parkinsonism follows almost a year later.[1,2] Illusions and visual hallucinations in NCDLB are florid, persistent and in many cases they are associated with misidentification, persecutory delusions and anxiety.[64] Patients suffering from Lewy body disease often present with Capgras syndrome (delusion in which patients believe that someone they know has been replaced by an imposter) and depression.[1,55]

The disorder has an insidious onset and gradual progression. Individuals with NCDLB frequently experience repeated sleep disturbance, falls, syncope and transient episodes of unexplained loss of consciousness.[1] Autonomic dysfunction such as orthostatic hypotension and urinary incontinence may be observed.[1] Patients are particularly sensitive to developing extrapyramidal side effects (EPSEs) and also to the potentially fatal complication of neuroleptic sensitivity (neuroleptic malignant syndrome), which affects approximately 50% of NCDLB patients.[61] Therefore, a need exists for antipsychotic drugs with less propensity to induce EPSEs and reduced affinity for dopamine and acetylcholine receptors. Suggested antipsychotics to manage debilitating psychiatric symptoms in NCDLB are low doses of quetiapine and clozapine.[39] This suggests that NCDLB may present as a complex picture that requires reasonable experience in NCDs for a clinician to diagnose and to manage it.

1.2.6.4 NCDs due to prion disease

The classification of NCD due to prion disease is caused by transmissible agents known as prion proteins. These proteins aggregate on the membrane of the neurons forming large plaques that are toxic to the brain tissue.[1] It causes brain tissue to degenerate and look like a sponge. The most common cause of NCD due to prion disease is Creutzfeldt-Jakob disease (CJD) which has four different types, namely familial CJD, variant CJD, iatrogenic CJD and sporadic CJD.[1,55] Prion disease may develop at any age in adults and the peak age for sporadic Creutzfeldt-Jacob disease is approximately 67 years.[1] It has an insidious onset and rapid progression which may worsen within 6 months. Apart from the cognitive decline, this condition often presents with predominant motor features such as myoclonus or ataxia, chorea, dystonia and startle reflexes.[1,55] Patients may present with psychiatric manifestations such as depressed mood, withdrawal from others and anxiety. Prion disease can be confirmed only by biopsy or autopsy.[1,55] There is a general dearth of literature on NCD due to prion disease.[1]

1.2.7 Secondary NCDs

1.2.7.1 NCDs due to HIV infection

NCDs due to HIV infection is usually prevalent in individuals with prior episodes of severe immunosuppression or indicators of AIDS. Some individuals with HIV infection develop NCD which generally shows a subcortical pattern with prominently impaired executive function.[1] The pivotal role of HIV in the burden of NCDs cannot be underestimated in the South African context.

In 2015, the estimated overall prevalence of HIV was approximately 11.2% [21] and in 2017 there was a notable increase to 12.6% of the total South African population.[59] For the younger population aged 15 to 49 years, an estimated 16.6% was HIV positive (2015) and invariably this involved the brain.[21] Previous studies suggest that up to 60% of people living with HIV/AIDS are at risk of developing some form of NCD in their lifetime.[22] Grant [23] found that the prevalence of NCDs due to HIV infection was between 15% and 30% in untreated individuals while the prevalence in individuals receiving ART was 10%, with an annual incidence of 1 %.

There were identified risk factors that cause early onset of NCD in HIV and faster progression of the disease. These risk factors include advanced age, a low CD4 count of <200, high viral load, previous history of significant TBI, alcohol abuse and low level of education. The aetiological mechanism of these risk factors was poorly understood.[6,23] The literature suggests that even though the risk of NCDs due to HIV infection seems to be high, the progression of cognitive decline in patients receiving ART is slower than those who are not receiving ART.[13,22,60]

1.2.7.2 NCDs due to traumatic brain injury

Traumatic brain injury (TBI) occurs when an external force impacts the head causing the brain to move excessively within the skull thereby disrupting normal brain function.[24] It results in neurodegeneration and progressive brain atrophy that may be observed at least one year after the injury.[24] TBI seems to be a major problem in modern societies, primarily as a consequence of motor vehicle accidents and falls. TBI appears to be a leading cause of death and disability for persons between the ages of 1 and 44 years.[24] An estimated 10 million people in 2015 were affected annually by TBI worldwide.[24] However, this figure was likely underestimated because it did not include patients with mild TBI who frequently dismissed their symptoms and never sought medical attention (25%) or those who were seen in private clinics or by primary care physicians (14%).[24]

In 2009, an internal audit conducted at Groote Schuur Hospital, Cape Town, revealed that among the total of 10 046 trauma patients admitted, approximately 24% were classified as head-injury patients and 654 (6.5%) patients had a moderate to severe TBI. This audit also identified that 82% of assault-related head trauma was experienced by young black and coloured men.[25] Multiple studies have shown that experiencing TBI early in adulthood is associated with increased risk of NCDs later in life. There is no evidence that a single mild TBI episode increases NCD's risk. However, it has been acknowledged that multiple repetitive mild TBIs as observed in contact sport players may have serious long-term consequences. It is important to note that not all individuals who experience head injury develop NCDs.[24] A meta-analysis of 15 case-control studies estimated that individuals who suffered head injuries of sufficient severity to result in a loss of consciousness had approximately a 50% increased risk of NCDs.[24] This shows that TBI is a significant aetiological risk factor of NCDs, depending on its severity and recurrence.

1.2.7.3 Vascular NCDs

Vascular NCD is known as cortico-subcortical NCD. Major subtypes of vascular NCDs are multi-infarct NCDs, vascular NCDs due to lacunar lesions and Binswanger's disease. Cortical multi-infarct NCDs are due to large cerebral vessels' pathologies.[55] Binswanger's disease and lacunae are subcortical in nature. Binswanger's disease is also known as subcortical arteriosclerotic encephalopathy.[55] It derives from pathological changes affecting the long perforating vessels to the deep white matter and subcortical nuclear masses resulting in small areas of infarction (lacuna) together with the cardinal feature of diffuse axonal demyelination of the white matter.[2]

The risk of NCDs increases substantially after multiple strokes and a single major stroke may manifest similarly. Some patients may present with haemorrhagic strokes due to brain trauma or vasculopathy. Furthermore, a patient with an underlying primary degenerative major NCD such as Alzheimer's disease may have one or more strokes and present with features that overlap with vascular NCDs.[26] The research suggests that vascular NCDs contribute to the second highest cause of NCDs worldwide. However, in RSA vascular NCD is a leading cause followed by NCDs due to Alzheimer's disease with risk factors including stroke, hypertension, diabetes mellitus, obesity, cardiac diseases, hypercholesterolaemia and smoking.[1,6,10,26]

Approximately one-third of individuals over 85 years of age in developed countries have NCDs, and of those 4% to 5% are vascular in nature.[26] However, prevalence estimates of vascular NCDs in developing countries range from 0.6% to 2.1% in the elderly population (>65 years).[26] This discrepancy may be due to a high prevalence of cardiovascular diseases in developed countries compared to developing countries.[26] Vascular NCDs present with many

of the same psychiatric symptoms as Alzheimer's disease especially apathy, depression, anxiety, and irritability.[64]

1.2.7.4 Alcohol induced NCDs

Epidemiological studies suggest that excessive and prolonged use of alcohol may lead to structural and functional damage of the brain that is permanent in nature.[27] In 2010 the Global Status Report on alcohol estimated a population prevalence of 5.6% of alcohol use disorder. The frequency of alcohol dependence was 2.4% (males 4.2%, females 0.7%).[28] High risk of alcohol abuse has been observed in young males between the ages of 18 and 49 years.[27] Alcohol remains the dominant substance of abuse in RSA. The WHO Global Status Report on alcohol (2014) indicated that RSA has the highest use of alcohol in Africa, especially in the population aged 15 years and older.[28] Several reviews reported a high prevalence of alcohol abuse in patients with NCDs ranging from 9% to 22%.[27] They also estimated that 10% to 24% of alcohol abusers develop NCDs later in life.[27] The above literature suggests that alcohol may be an aetiological and exacerbating factor in NCDs, especially amongst the younger population.

1.2.7.5 NCDs with movement disorders

a) NCDs due to Huntington's disease

George Huntington's description of Huntington's disease (HD) in 1872 remains the basic pillar of the diagnosis.[29] HD is an inherited disease (autosomal dominant gene on chromosome-4) characterised by degeneration of the basal ganglia and cerebral cortex.[10] Huntington's disease features a triad of cognitive, affective and motor phenomena.[29, 64] The motor features, typically chorea, athetosis, tics, bradykinesia, incoordination, and ideomotor apraxia, are preceded by executive dysfunction, apathy, irritability, depression, and anxiety. Such cognitive deficits and behavioural symptoms may begin about 15 years prior to the motor diagnosis.[64] In

asymptomatic Huntington's disease mutation carriers, the earliest cognitive deficits are found in attention, working memory, verbal learning, verbal long-term memory, and learning of random associations.[64]

Huntington's disease is considered rare among Black South Africans, with an estimated prevalence of 1 per 10 million.[29] It has been reported that the risk of Huntington's disease in Caucasians and mixed races is approximately 20 to 30 times higher than Black South Africans.[30] Age of onset is between 15 and 50 years when choreiform movements and progressive NCD are identified. The NCD due to Huntington's disease initially presents as a sub-cortical NCD before affecting the cortex as the illness progresses.[10] No cure is currently available and death is likely to occur within 15 to 20 years.[10]

b) NCDs due to Parkinson's disease

Parkinson's disease is a progressive debilitating degenerative disorder with no known cure.[1,31] Similarly to Huntington's disease, Parkinson's disease affects basal ganglia and is associated with depression.[55] Parkinson's disease risk factors are genetically and environmentally related. NCD due to Parkinson's disease manifests with illusions, hallucinations, paranoia, and delusions very late in the illness, usually many years after the development of the motor symptoms, subclinical cognitive dysfunction, anxiety, and depression.[64] In NCD due to Parkinson's disease, visual hallucinations, paranoia, and anxiety often arise as complications of dopaminergic therapy.[64] The general prevalence of Parkinson's disease is approximately 1%

of individuals aged >65 years, increasing to 4% in individuals aged >80 years.[31] It is more common in males than females.[1]

A study conducted in Tygerberg hospital in 2012 found that Parkinson's disease is associated with a genetic predisposition in elderly male patients.[31] Among individuals with Parkinson's disease, as many as 75% will develop major NCD sometime in the course of their disease.[1] The prevalence of mild NCD in Parkinson's disease has been estimated to be 27%.[1] There is still a scarcity of research conducted on NCDs due to Parkinson's disease in RSA.

1.2.7.6 Secondary NCDs due to other cerebral and medical conditions

Secondary NCDs may also be as a result of other multiple cerebral pathologies. These include direct tissue damage, changes in intracranial contents and distorting brain structures as well as systematic diseases affecting the brain. Examples of those causing direct brain tissue damage are neurosyphilis, Wilson's disease, and brain tumours such as glioblastoma. Those that result in changing intracranial contents and distorting brain structures include normal pressure hydrocephalus and primary or metastatic brain tumours. Systemic diseases affecting the brain are vitamin B12 deficiency, endocrine diseases such as hypothyroidism or hyperthyroidism, and systemic lupus erythrametosus.[1,3,10]

1.2.8 Investigations in NCDs

Diagnosing NCDs requires a comprehensive history taken from the caregiver and the patient, a thorough clinical examination that includes both a physical and neurological examination, mental state examination, bedside neurocognitive screening tests, standardised neuropsychological tests, special blood investigations, neuroimaging and functional

neuroimaging if available.[4,10] Occupational therapy functional assessments are also used to substantiate the diagnosis.[10]

1.2.8.1 Bedside neurocognitive screening tools

Information regarding different cognitive function domains can be obtained from bedside assessments. In RSA, the commonly used screening tools include Folstein's Mini–Mental State Examination (MMSE), Montreal Cognitive Assessment Test (MoCA) and International HIV Dementia Scale (IHDS). These are useful neurocognitive screening tools but they are not considered as diagnostic tools. [11]

a) Folstein's Mini-Mental State Examination

MMSE is a 30-point questionnaire that is used extensively in clinical and research settings to measure cognitive impairment. Cognitive domains assessed are registration, attention and calculation, recall, language, ability to follow simple commands and orientation. It is the widely used cognitive test for detecting cortical NCDs. According to multiple studies, demographic variables, especially advanced age and low level of education, influence MMSE results and cause false-positive cases.[10] The following abnormal MMSE scores are of patients with at least seven years of education or higher. The score of mild NCD ranges between 21 and 24, moderate NCD (11 and 20) and severe NCD (0 and 10). Despite the MMSE being a useful tool, researchers have cautioned against its use as a stand-alone assessment test.[10]

b) Montreal Cognitive Assessment

MoCA is a 30-point test aimed at assessing several cognitive domains including visuospatial abilities, executive functioning, short-term memory, attention/working memory, language and orientation. It is useful in detecting both cortical and subcortical NCDs. Research suggests that

MoCA has higher sensitivity compared to the MMSE in detecting mild cognitive impairment (MCI).[32] This was supported by Nasreddine et al. [33] who found that MMSE had a sensitivity of 18% in detecting MCI whereas MoCA detected 90% of MCI cases. Most individuals meeting the clinical criteria for MCI scored above 26 on the MMSE, which is in the range of a normal score in elderly individuals.[33] To address this problem, MoCA was developed as a tool to screen patients who present with mild cognitive complaints and usually perform in the normal range on the MMSE.[33] However, the phonemic fluency task and sentence repetition task remain problematic due to high rates of illiteracy and low level of education in RSA as the MoCA requires at least twelve years of education. The language barrier may also prove to be challenging as there are eleven official languages in South Africa. The MoCA score of 26 and higher is regarded as normal.[32]

c) International HIV Dementia Scale

IHDS was designed specifically to assess the subcortical NCDs due to HIV infection and for use across cultures. It can be used by non-neurologists in resource-limited communities. It is a 12-point screening tool which measures motor speed, psychomotor speed and memory-recall. It is a brief neurocognitive test to administer and it does not require English language proficiency but it requires the additional use of a clock. [32,34] A patient with a score of ten or less should be evaluated further for a possible NCD due to HIV infection.[32,33] Sacktor et al. [34] found that IHDS had a sensitivity of 45% and specificity of 79% at a cut-off score of ten compared to other neurocognitive screening tools.

1.2.8.2 Special blood investigations

Special blood investigations help to rule out potentially reversible or exacerbating causes of NCDs. Haematological work-up may include a full blood count, vitamin B12, serum folate,

HIV test, CD4 count, viral load and autoimmune screen. Indications of performing these tests will depend on the clinical profile of each patient.[10,17,19]

1.2.8.3 Neuro-imaging

Neuro-imaging investigations remain important diagnostic tools in NCDs. The computed tomography (CT) and magnetic resonance imaging (MRI) of the brain are generally useful to diagnose organic cerebral pathology and they have been proven to be powerful neuropsychiatric research tools.[35,55] MRI of the brain is generally regarded as a superior tool for brain parenchyma as compared to the CT brain due to the absence of ionising radiation, increased imaging flexibility and better tissue contrast in MRI scans.[35]

a) CT of the brain

CT of the brain provides information on the structure of the brain, meninges and soft tissues of the head. It may reveal pathologies such as abnormal calcifications, involutional changes and abnormalities of cerebrospinal fluid space.[35] Patients with acute haemorrhages or hematomas must continue to be assessed using CT brain but these patients present infrequently in psychiatric settings.[55] Advantages of CT are lower cost, shorter acquisition time (15-30 minutes), easier to conduct in patients who are poorly co-operative and the possibility that it can be performed in patients with metal devices such as a pacemaker. In contrast to MRI scans, CT scans have poorer soft-tissue contrast abilities and fail to diagnose lesions with the same densities as surrounding tissues. In order to visualise these lesions and diagnose infections, the iodinated contrast medium is often injected intravenously and it carries a risk of permanent renal impairment and allergic reaction.[35]

b) MRI of the brain

The MRI of the brain provides a higher resolution and a greater sensitivity to the underlying tissue structures and water content. It allows for the detection of subtle anatomical and vascular changes associated with cognitive decline.[35] MRI better discriminates the interface between grey and white matter and it is useful in detecting a variety of white matter lesions in the periventricular and subcortical regions.[55] White matter abnormalities are detected in young patients with HIV and older patients with hypertension, vascular NCDs and NCDs due to Alzheimer's disease.[55] Both CT and MRI can demonstrate a flattening of gyri, widening of sulci, atrophied medial temporal lobes and enlarged ventricles that are mainly noted in patients with Alzheimer's disease.[10] Recent developments in MRI allow the direct measurement of structures such as the thalamus, basal ganglia, hippocampus and amygdala as well as temporal and epical areas of the brain and structures of the posterior fossa.[55] Disadvantages of MRI scans may be related to higher costs and availability is limited to tertiary hospitals. MRI scans are contra-indicated in patients with pacemakers, which are commonly found in the elderly population due to ischaemic heart diseases.[35]

1.2.8.4 Neurophysiological test

Electroencephalography (EEG) is a relatively simple, easily accessible and inexpensive diagnostic tool. It has a high sensitivity for diffuse organic encephalopathy of various aetiologies but rather with a low specificity for multiple types of NCDs.[36,55] The highest sensitivity is shown in NCDs due to Alzheimer's disease and Parkinson's disease. The early stage consists of reduction of alpha activity, which may sometimes disappear entirely. Later in the course of Alzheimer's disease, EEG often shows diffuse slow waves, irregular theta activity with superimposed runs of delta wave.[2] Focal or paroxysmal features are rare, even in patients with epileptic fits. Quantitative EEG may be useful in diagnosing certain cases.[2] NCDs

associated with seizures are seen in approximately 10% of patients with NCDs due to Alzheimer's diseases and 20% in vascular NCDs.[55] Among these conditions, the degree of EEG abnormalities is correlated with disease severity. NCDs with predominantly frontal pathology show much less EEG abnormalities, and in these conditions, the EEG is often normal despite obvious NCDs' clinical features.[36]

2. CHAPTER TWO: RESEARCH METHODOLOGY

2.1 Aim

The aim of the study was to describe the profile of NCDs in patients attending tertiary level psychiatric outpatient department.

2.2 Study questions

1. How many patients referred to a psychiatric outpatient department were diagnosed with NCDs?
2. Of these patients with NCDs, what type of NCDs did they present with i.e. primary or secondary NCDs?
3. What was their demographic profile and comorbidities i.e. psychiatric and/or medical?

2.3 Objectives

- To determine the percentage of NCDs in patients that attended the psychiatric outpatient department at the tertiary academic hospital over a three-year period.
- To determine the types of NCDs in the study population i.e. primary NCDs versus secondary NCDs and the possible aetiology were applicable and/or documented
- To describe the demographic profile related to NCDs.
- To describe any medical and psychiatric comorbidities which may or may not be related to NCDs.

2.4 Study method

The study was a descriptive-retrospective record review of files of patients who attended at CMJAH psychiatric outpatient department. Patients that were diagnosed with NCDs

according to DSM IV-TR/DSM-5 criteria between 01 January 2015 and 31 December 2017 were included in the study. Files of patients with NCDs seen during the study period were collected. The information was captured on a data collection sheet attached in Appendix A and B.

2.4.1 Exclusion criteria

Patients who did not meet the diagnostic criteria for NCDs according to DSM IV-TR/DSM-5 criteria.[1,5]

2.4.2 Inclusion criteria

- Patients were 18 years and older.
- Patients in psychiatric outpatient department that were diagnosed with NCDs according to DSM IV-TR/DSM-5 criteria. [1,5]
- Patients were seen during the study period.

2.5 Sample size

Since the main aim of the study was the descriptive reporting of percentages, a sample size estimation was based on a 5% precision and at 95% confidence level. From a previous study, the prevalence of neurocognitive disorders was reported to be 7.7%.[32] Using the Fishers calculation, the sample size for this study was calculated to be 109 using the formula:

$n = \frac{Z^2 P(1-P)}{d^2}$ $n = \frac{1.96^2 x\ 0.077(1-0.077)}{0.05^2}$ n=109

n = sample size,

Z = Z-statistic for the chosen level of confidence, (z=1.96)

P = expected prevalence or proportion (from previous study p=7.7%)

d = precision (d=0.05)

Therefore, the period of data collection for this study was estimated to be from 01 January 2015 to 31 December 2017.

2.6 Data analysis

Data was captured on data collection sheets (Appendix A and B) and entered into Microsoft Office Excel 2013. Study codes were assigned to enable the creation of a link to files used in the study. Descriptive analyses of the data were carried out as follows: Since all variables were categorical, they were summarized using frequencies and percentages. Tables, bar graphs and pie charts were used to present these results. Comparisons of types of NCDs by different aetiologies, demographic profiles, medical and psychiatric comorbidities were carried out using Fisher's exact test because expected frequencies were less than five in most comparisons. Data analysis was carried out in STATA software version 13 and the 5% statistical significance level was used.[37]

2.7 Ethics approval

The study was a retrospective review of files, and as such, anonymity of patients was maintained. The primary investigator was the only person who had access to patients' medical records for the purpose of this study. All this information was securely stored. Ethical approval was obtained from the University of the Witwatersrand's Human Research Ethics Committee on the 29th of August 2016 and the clearance certificate number was M160822 (appendix C). In addition, permission to conduct the study was also obtained from the Chief Executive Officer (CEO) of CMJAH (appendix D).

2.8 Material

Facilities of the CMJAH was utilized. The study was self-funded with the estimated cost detailed below (Table 2.8.1). Own transport was used.

Table 2.8.1: Study material and costs

ACTIVITY	**ESTIMATED COST**
Transport	R2000
Stationary	R1500
TOTAL	R3500

3. CHAPTER THREE: RESULTS

A total of 6 879 patients were seen in CMJAH general psychiatric clinic between the 01st of January 2015 and the 31st of December 2017. Out of the total number of patients who were seen during this period, 145 (2.1%) patients had a diagnosis NCD.

3.1 Demographic profile of patients

Figure 3.1.1 shows that out of the 145 patients, majority 67 (46.2%) were from the 61 - 80 years age group, followed by those from the 41 – 60 years age group 53 (36.6%) and the least of all were those above 80 years 11 (7.6%).

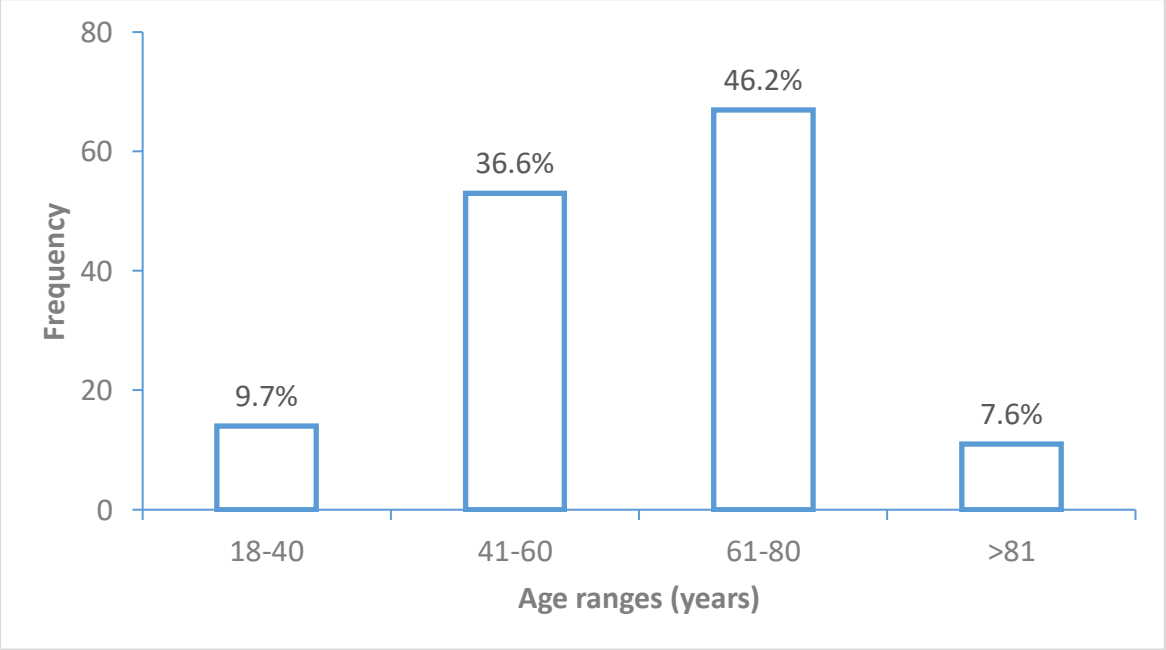

Figure 3.1.1: Age distribution of patients with NCDs

Figure 3.1.2 shows that a larger proportion of individuals were females 87 (60%) while 58 (40%) were males.

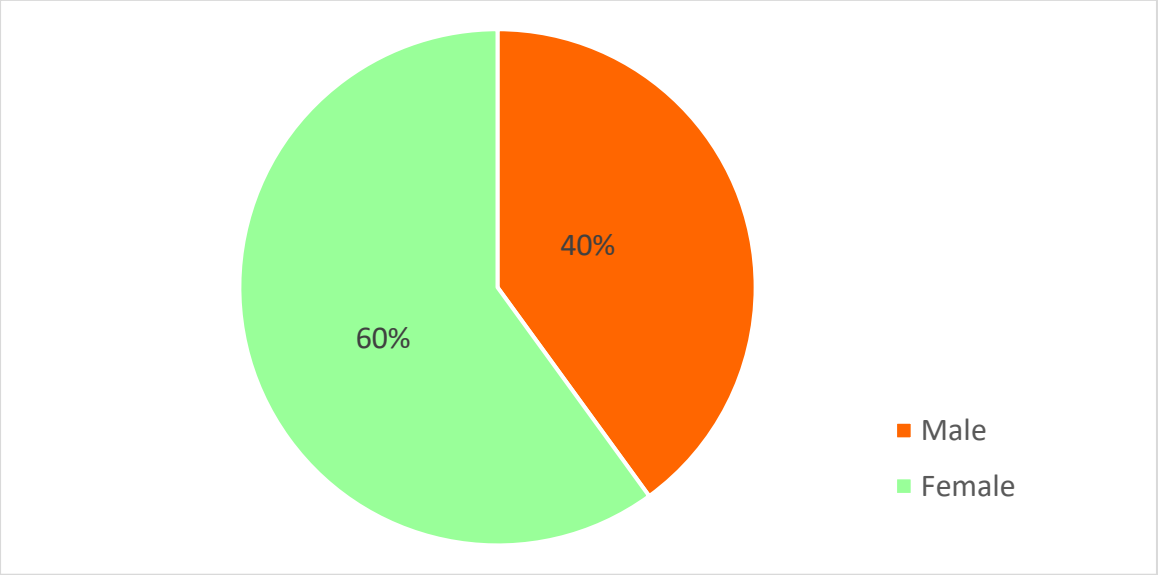

Figure 3.1.2: Distribution of patients with NCDs by gender

Figure 3.1.3 shows that majority of patients 68 (47%) were of Black ethnicity, followed by Whites 49 (34%), Indians 21 (15%) and least of all were the Coloured participants 7 (5%).

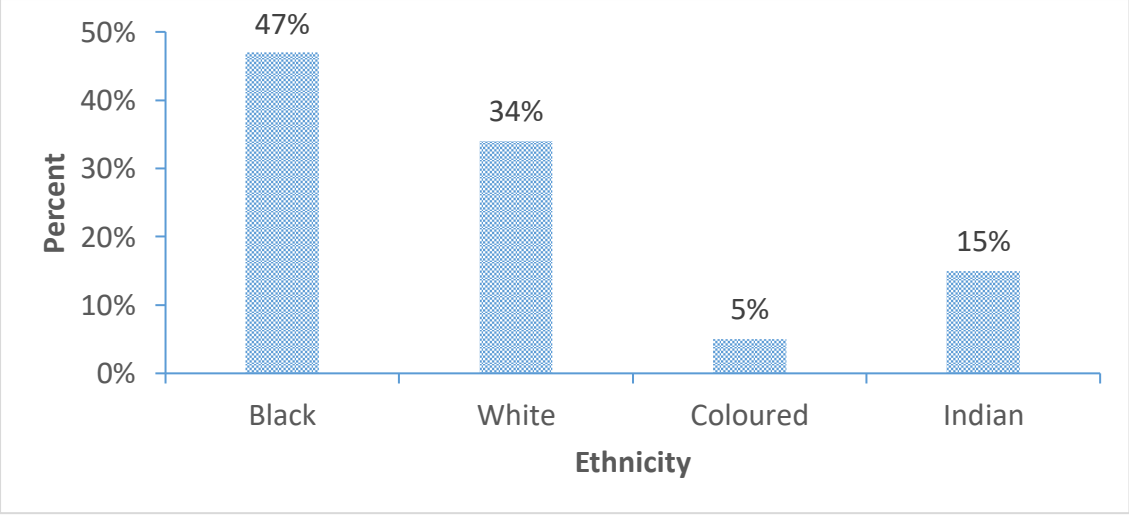

Figure 3.1.3: Distribution of patients with NCDs by ethnicity

The majority of patients 52 (36%) were married, followed by 36 (25%) who were single, 26 (18%) who were divorced and least of all were 2 (1%) who were cohabiting (see figure 3.1.4).

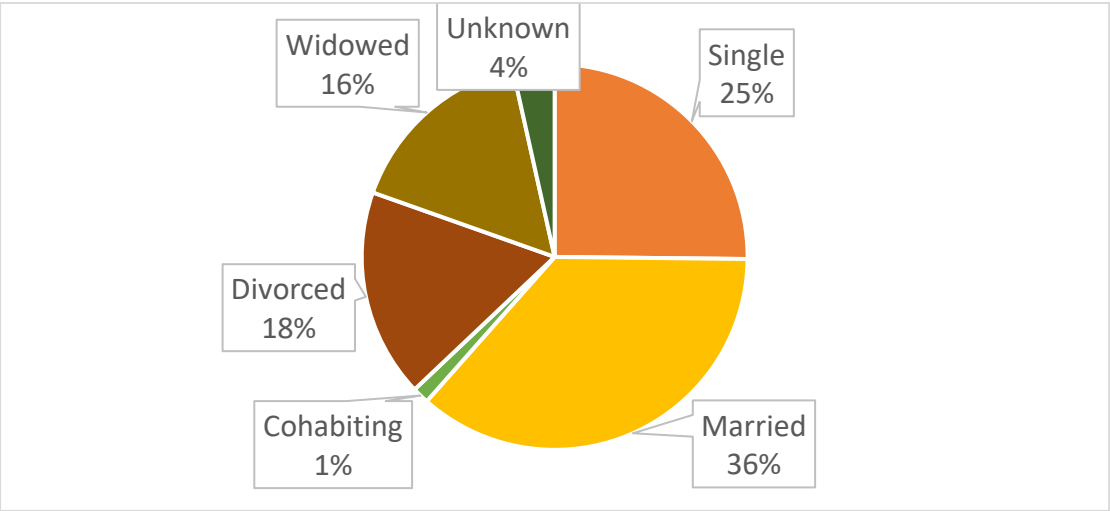

Figure 3.1.4: Distribution of patients with NCDs by marital status

In terms of employment status, most of the patients 60 (41%) were pensioners, 42 (29%) were unemployed, 16 (11%) were employed and a similar number were on disability grants (see figure 3.1.5).

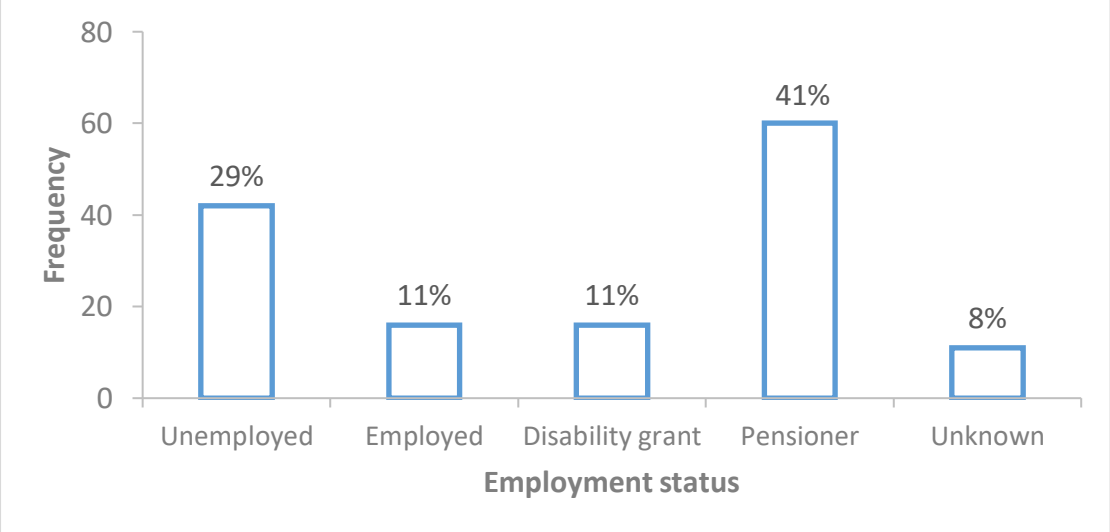

Figure 3.1.5: Distribution of patients with NCDs by employment status

Figure 3.1.6 shows that the larger percentage of patients 62 (43%) had attained secondary level of education, 26 (18%) had up to tertiary level, 23 (16%) up to primary level while 3 (2%) had no formal education at all.

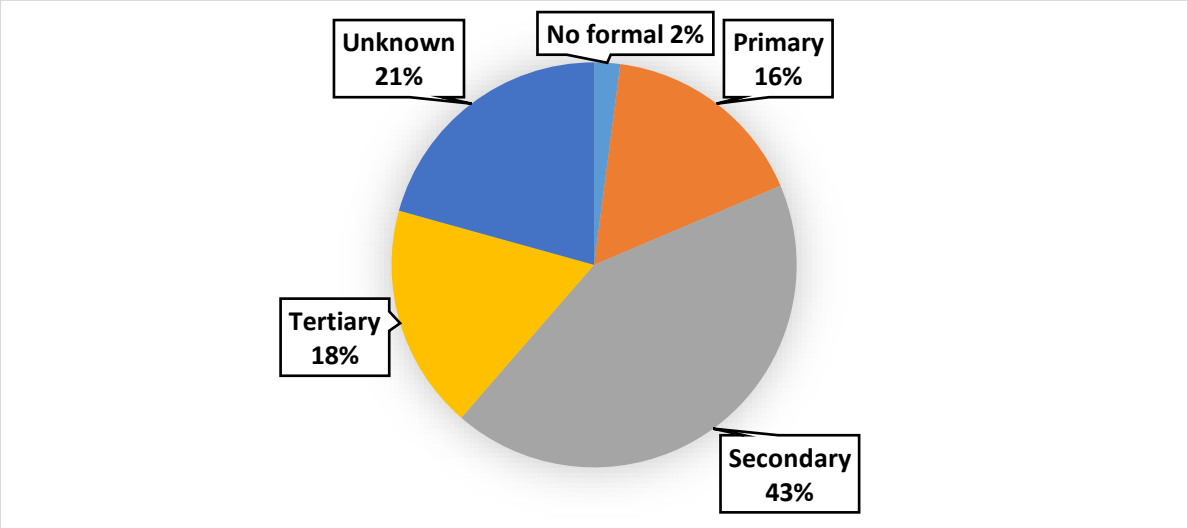

Figure 3.1.6: Distribution of patients with NCDs by highest level of education

From figure 3.1.7, it is evident that most of the caregivers 44 (30%) were spouses, followed by children 34 (23%), care facilities 24 (17%) and parents 9 (6%). It was noted that the caregiver status was not documented on 29 (20%) patients' files.

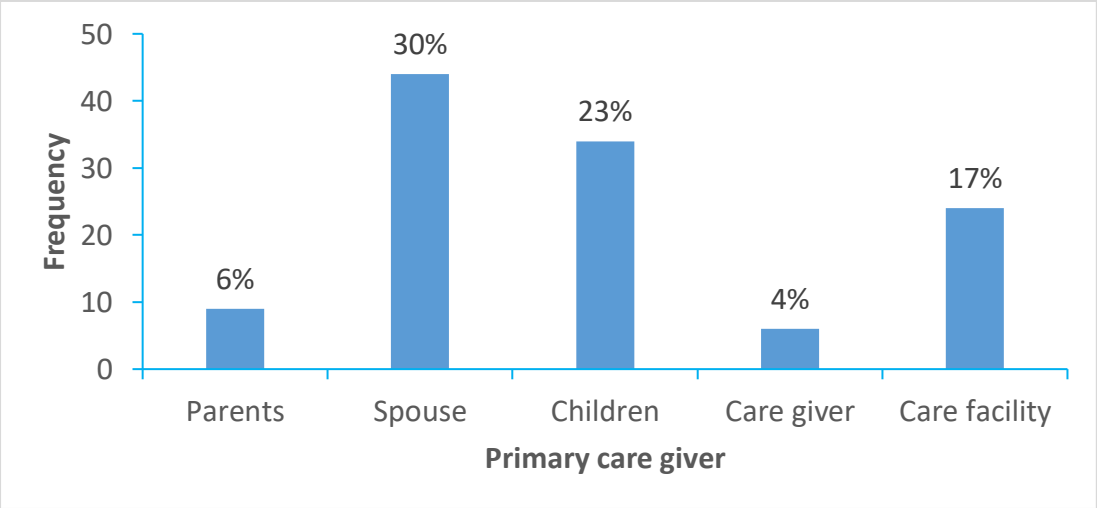

Figure 3.1.7: Distribution of patients with NCDs by primary caregiver

3.2 DSM-5 diagnosis - Neurocognitive disorders

Of the reported NCDs, 129 (89%) were of major severity while 13 (9%) were characterized as mild NCDs. By type, 118 (81.4%) of patients had secondary NCDs, while 3 (2.1%) had primary NCDs and 5 (3,4%) had both primary and secondary NCDs (mixed NCDs) (see Table 3.2.1). Of the patients who had primary NCDs, 1 (0.7%) had NCDs due to Alzheimer's disease and 2 (1.4%) had frontotemporal NCD. (see Table 3.2.1).

Of the patients who had secondary NCDs, the largest percentage 54 (37.2%) had vascular NCDs, followed by 21 (14.5%) of NCDs due to HIV infection, 20 (13.8%) were NCDs due to multiple aetiologies, 8 (5.5%) were due to alcohol induced NCDs, while the least of all were those from endocrine cause 1 (0.7%) (see Table 3.2.1).

Table 3.2.1: Categorization of NCDs by severity and type

Categorisation		Number	%
Severity of NCDs			
Mild		13	9%
Major		129	89%
Unknown		3	2%
Types NCDs			
Primary NCDs 3 (2.1%)	Alzheimer's disease	1	0.7%
	Frontotemporal NCD	2	1.4%
Secondary NCDs 118 (81.4%)	HIV	21	14.5%
	TBI	7	4.8%
	Alcohol	8	5.5%
	Parkinson's disease	4	2.8%
	Vascular	54	37.2%
	Vitamin B12 deficiency	3	2.1%
	Endocrine	1	0.7%
	Multiple aetiologies	20	13.8%
Mixed NCDs 5 (3.4%)	Lewy body NCD and vascular NCD	1	0.7%
	Alzhemier's disease and vascular NCD	1	0.7%
	Alzhemier's disease and multiple aetiologies	1	0.7%
	Frontotemporal NCD and multiple aetiologies	2	1.4%
Unknown NCDs 19 (13.1%)		19	13.1%

3.3 Psychiatric comorbidities

A larger percentage of the patients 136 (94%) had psychiatric comorbidities (see table 3.3.1). Major depressive disorders (MDD) were more common than bipolar disorders 42 (30.9%) and 32 (23.5%) respectively. Of the other psychiatric illnesses investigated, psychotic disorders were the most common comorbidity 54 (39.7%), followed by other unspecified disorders 23 (16.9%), anxiety disorders 15 (11%) and substance/medication induced disorders 3 (2.2%) (see table 3.3.1).

Table 3.3.1: Psychiatric comorbidities

Categorisation	Number	%
Were there psychiatric comorbidities?		
Yes	136	94%
No	9	6%
Mood disorders	74	54.4%
Bipolar	32	23.5%
MDD	42	30.9%
Other psychiatric illnesses	95	69.8%
Psychotic disorders	54	39.7%
Anxiety disorders	15	11%
Substance/Medication induced disorders	3	2.2%
Other disorders	23	16.9%

3.4 Medical comorbidities

Table 3.4.1 shows that 114 (79%) patients had medical comorbidities while 31 (21%) of them did not. Of the other medical comorbidities investigated, cardiovascular diseases were reported the most 88 (77%), followed by other unspecified conditions 39 (34%), neurological diseases 25 (21.9%) and respiratory diseases 8 (7%) (see table 3.4.1). Some patients in table 3.4.1 with medical comorbidities had multiple medical conditions.

Table 3.4.1: Medical comorbidities

Categorisation	Number	%
Medical comorbidities present?		
Yes	114	79%
No	31	21%
Medical comorbidities		
Cardiovascular diseases	88	77%
Respiratory diseases	8	7%
GIT diseases	3	2.6%
Neurological diseases	25	21.9%
Other medical conditions	39	34%
Unknown	3	2.6%

3.5 Investigations

Table 3.5.1 summarizes the investigations that were performed. It shows that 114 (78.6%) of patients had neurocognitive screening tests done. Of these tests, the larger number of patients 82 (71.9%) completed MoCA test, followed by MMSE test 52 (45.6%) and 17 (14.9%) of them completed the IHDS test. A number of patients completed more than one neurocognitive test. Of the patients who had neuroimaging, a larger percentage 99 (68.3%) had CT scans of the brain while 24 (16.6%) had MRI brain scan. Functional neuroimaging was performed on 7 (4.8%) patients. FBC was the most commonly performed blood test 128 (88.3%) patients followed by other blood tests 51 (35.2) and CD4 counts on 22 (15.2%) patients (Table 3.5.1).

Table 3.5.1: Investigations

Categorisation	Number	%
Neurocognitive tests done?		
Yes	114	78.6%
No	12	8.3%
Unknown	19	13.1%
Test done		
MMSE	52	45.6%
IHDS	17	14.9%
MoCA	82	71.9%
Specialized neurocognitive tests.	53	46.5%
Neuroimaging		
CT scan	99	68.3%
MRI	24	16.6%
Functional neuroimaging	7	4.8%
EEG		
Yes	40	27.6%
No	71	49%
Unknown	34	23.4%
Common blood investigations		
FBC	128	88.3%
CD4 count	22	15.2%
Vitamin B12 Deficiency	10	6.9%
Autoimmune screen	2	1.4%
Other blood	51	35.2%

3.6 Associations between demographic profile and the category of NCDs

Table 3.6.1 shows the cross-tabulations of demographic variables with the type of NCDs reported. Fisher's exact test was used to establish whether there were any statistical associations between the demographic variables and the classification of NCDs by type.

Only gender and ethnicity were significantly associated with the type of NCDs (p-value = 0.004 for each association). It was observed that three patients who had only primary NCDs were all females while five patients who had mixed NCDs (i.e. both primary and secondary) were all males (see table 3.6.1).

In terms of ethnicity, two of the three patients who had only primary NCDs were of Coloured ethnicity while one was of Indian ethnicity. Of the five patients with mixed NCDs, two were Indians, two were Whites while one was Black. In the category of secondary NCDs, the majority of the patients were of Black ethnicity (51%) followed by Whites (32%) (see table 3.6.1).

Table 3.6.1: Associations between demographics and type of NCDs

Type of NCDs							
	Primary		**Secondary**		**Mixed**		
Demographics	**No**	**%**	**No**	**%**	**No**	**%**	**p-value**
Age in years							
18 -40	0	0	13	12	0	0	0.759
41 – 60	2	67	38	34	2	40	
61 – 80	1	33	54	48	2	40	
>81	0	0	8	7	1	20	
Gender							
Male	0	0	48	42	5	100	**0.004**
Female	3	100	65	58	0	0	
Ethnicity							
Black	0	0	50	51	1	20	**0,004**
White	0	0	32	32	2	40	
Coloured	2	67	4	4	0	0	
Indian	1	33	13	13	2	40	
Marital Status							
Single	0	0	30	27	0	0	0,328
Married	1	33	36	32	4	80	
Cohabiting	0	0	2	2	0	0	
Divorced	2	67	18	16	0	0	
Widowed	0	0	20	18	1	20	
Unknown	0	0	5	5	0	0	
Employment status							
Unemployed	1	33	32	29	1	20	0,184
Employed	0	0	14	13	0	0	
Disability grant	2	67	9	8	1	20	
Pensioner	0	0	48	43	3	60	
Unknown	0	0	9	8	0	0	
Highest level of education							
No formal	0	0	2	2	0	0	0,495
Primary	1	33	19	17	2	40	
Secondary	2	67	48	43	1	20	
Tertiary	0	0	20	18	0	0	
Unknown	0	0	22	20	2	40	
Primary caregiver							
Parents	0	0	9	10	0	0	0,564
Spouse	1	33	29	33	4	80	
Children	2	67	24	27	0	0	
Care giver	0	0	5	6	0	0	
Care facility	0	0	21	24	1	20	

*p-value from Fisher's exact test, significant value highlighted in bold.

3.7 Associations between psychiatric/medical comorbidities and category of NCDs

Table 3.7.1 shows the cross-tabulations of psychiatric or medical comorbidities with the type of NCDs reported. Fisher's exact test was again used to establish whether there were any statistical associations between the presence or absence of psychiatric or medical comorbidities and the classification of NCDs by type.

The presence of psychiatric comorbidities was significantly associated with the type of NCDs (p-value= 0.046). All three patients who had only primary NCDs had psychiatric comorbidities as well. Of the 5 patients who had mixed NCDs, three of them had psychiatric comorbidities. A larger percentage of patients who had secondary NCDs also had psychiatric comorbidities (see table 3.7.1).

The association between the presence and absence of medical comorbidities and type of NCDs was not statistically significant especially respiratory and GIT diseases. It is worth noting though, that the majority of patients with medical comorbidities had cardiovascular and neurological diseases (see table 3.7.1).

Table 3.7.1: Associations between existence of comorbidities and type of NCDs

Type of NCDs							
Comorbidities	**Primary**		**Secondary**		**Mixed**		
Yes/No	**No.**	**%**	**No.**	**%**	**No**	**%**	**P-value**
Psychiatric comorbidities present?							
Yes	3	100	107	95	3	60	**0.046**
No	0	0	0	5	2	40	
Medical comorbidities present?							
Yes	3	100	88	78	5	100	0.627
No	0	0	25	22	0	0	

*p-value from Fisher's exact test, significant value is highlighted in bold.

4. CHAPTER FOUR: DISCUSSION

The aim of the study was to describe the profile of NCDs in patients attending the tertiary level psychiatric outpatient department at CMJAH. It further aimed to investigate the proportion of primary and secondary NCDs among the target population as well as describing the respective differences in their demographic profile. To the researcher's knowledge, there is no such study conducted in RSA focusing on this aspect of a psychiatric outpatient group. There are other international studies conducted in this area [48] but none focused on describing NCDs among the vulnerable psychiatric population.[6,13]

4.1 Prevalence of NCDs

The findings of this study indicated that 2.1% of psychiatric patients in the sample population had NCDs. This is in keeping with the prevalence of NCDs conducted in 2013 in developing countries (Sub-Saharan Africa) which was noted to range from 2.07% to 4.76%.[7] In contrast, previous South African studies conducted in Durban noted a prevalence of 7.9% [11] and two studies in the Free State noted 6% and 7.7% respectively.[12,13] It is vital to note that these studies were age biased as they targeted the elderly population hence it is difficult to generalise their results.

Possible reasons of low prevalence of NCDs in this study are that it was conducted at a tertiary academic hospital, the sample was therefore biased towards complex clinical patients whereas most patients with uncomplicated clinical features are generally seen in the primary health care. The other possible reasons are that family members are not reporting minor cognitive symptoms until the condition is severe. Additionally, standardised neurocognitive screening tools may not be routinely performed during clinical assessments resulting in a low detection rate of NCDs. Lastly, patients may not seek medical attention because signs and symptoms of

NCDs are still accepted by sufferers' families as part of normal ageing and preferential use of traditional healing or complementary medicine are considered first.[4]

4.2 Demographic profile and NCDs

4.2.1 Age profile

The majority of patients was in the 61 – 80 years age group 67 (46.2%) and the smallest group of patients was 80 years and older 11 (7.6%). The low number of patients over 80 years was probably due to most people dying before the 80th decade. This can be extrapolated from the five-year mortality rate estimate in South Africa which showed the highest percentage of deaths observed for age groups 60–64 with proportions rising from 7,4% to 8,1% in 2017 compared to other age groups. Life expectancy in South Africa was also estimated to be 57,9 in 2010. [59] In the study conducted in South Africa in 2015, found that there were about 4.42 million people older than 60 years, representing 8 % of the total population. [68] Similar findings regarding an age bias were explicated from the study conducted in the elderly population in Durban (SA) in 2013 by Ramlall et al. which showed that the rate of NCDs increases with age (mean age: 75.2 years).[38] However, the study conducted by Ramlall et al. targeted the elderly population as opposed to a general psychiatric clinic hence it was more likely to be age biased.[38] The results of this study suggest an increased risk of developing NCDs in the elderly population as the advanced age has been identified as the 'most consistent risk factor for NCDs worldwide'.[12,13]

This study demonstrates a significant number of young individuals with NCDs in an age group of 41-60 years 53 (36.6%) and 18-40 years 11 (9.7%) respectively. In South Africa, there is a reported high prevalence of NCDs due to HIV infection, alcohol use disorder and TBI in a younger population (<65 years) but none of the studies provide conclusive results. [10,22,24,27] The significant proportion of HIV infections 21 (14.5%), alcohol use disorder 8 (5.5%) and TBI 7

(4.8%) as aetiological factors of NCDs in this sample possibly justifies the high number of young individuals with NCDs in the study. There is a paucity of data currently to affirm whether the NCD prevalence is increasing or stabilising among the younger population.

4.2.2 Gender profile

This study showed that a larger proportion of patients were female gender 87 (60%) compared to male gender (40%). The study by Ramlall et al. found similar findings in that NCDs were more common in females (69.3%) than males (30.7%).[38] The most proposed mechanism of NCD likelihood in elderly female individuals is the post-menopausal loss of oestrogen protection and related hormones. There is sufficient evidence that oestrogen has some neuro-protective properties, particularly against amyloid-induced neurotoxicity.[2,12] Additional explanations for gender being a confounding variable in the context of this study may have been the influence of high health-seeking behaviour and a longer life expectancy among the female population compared to male population. A study was conducted in 2012 comparing health seeking behaviour among elderly women and men in urban communities and rural communities of South Africa. This study found that women have high health seeking behaviour both in urban communities (female 53.6% vs male 46.4%) and in rural communities (female 66.7% vs male 33.3%) respectively. In addition, life expectancy was found to be longer in females (66,7 years) than in males (61,2 years) in South Africa in the mid-year population estimate conducted in 2017. [59] Whilst this study validated the high prevalence of NCDs in elderly females, Ogunniyi et al. in their NCD prevalence study done in a rural Nigerian community observed a high male preponderance among those diagnosed with NCDs.[56] Hence gender association of NCDs has not been a consistent finding in all studies.

4.2.3 Ethnicity profile

NCDs were found to be more prevalent among patients of Black ethnicity accounting for 68 (47%) followed by White ethnicity 49 (34%) and the least was of Coloured ethnicity 7 (5%). This might be explained by the national population estimates in RSA in mid-2017.[59] It showed that the African population was the majority (45.7 million) and constituted approximately 81% of the total South African population.[59] The White population was estimated at 4.5 million, the Coloured population at 5 million and the Indian/Asian population at 1.4 million.[59] Despite the Black population being approximately ten times the size of the White population, they did not represent a corresponding greater proportion of the study participants. This was probably due to the fact that CMJAH is not the main referral hospital for a large percentage of Black communities who tend to populate hospitals located within the proximity of the townships, where the majority of this population group reside. Cultural factors such as family tolerance and prioritizing traditional health seeking behaviours before presenting to health care centres may also explain the comparative under-representation of Black ethnicity patients with NCDs in this sample. This study's results do however substantiate findings from Glymour et al.[57] who investigated NCD incidence estimates for African Americans, Mexican Americans, and Japanese Americans. The study found that NCD risk was high among African Americans (38%) compared with White Americans (30%).[57]

In a study conducted by Shadlen et al.[58] Black ethnicity was also associated with greater risk of NCDs even after adjustment for education and other potential confounders. In contrast, the study conducted by Ramlall et al.[38] in the residential homes for the elderly population showed different results of ethnicity distribution of people with NCDs. Their study sample consisted of 140 participants comprising 46.4% White, 29.3% Coloured, 20% Asian and 4.3% Black participants.[38] It must, however, be noted that Ramlall et al.'s study was conducted specifically

at the old age home where there was a high population of people of White ethnicity as compared to Black ethnicity.[40] In contrast, the current study was done at the general psychiatric outpatient department where residents from old age institutions were less likely to constitute the study population. Importantly, there is also a paucity of literature interrogating the prevalence of NCDs among the Black ethnicity.[57,58]

4.2.4 Marital status profile

Previous studies concluded that marriage may result in more frequent social contact, which is associated with reduced NCD risk [46] and reduced harmful lifestyle behaviours.[45] Furthermore, marriage may improve cognitive reserve and a greater ability to cope with neuro-pathological damage by using compensatory cognitive approaches from a physically more resilient brain to maintain cognitive ability and daily function.[44,45] Meanwhile, bereavement or divorce in people who had been married may promote NCD development through stress, which is pathogenic and associated with increased NCD risk.[45] Being unmarried is associated with adverse health behaviours and a range of poorer health outcomes.[45] The above is reflected in this study which found a high rate of unmarried patients in different stages of life namely, single 36 (25%), divorced 26 (18%), and widowed 11 (16%) as compared to married individuals 52(36%).

4.2.5 Caregiver profile

It is evident that most of the caregivers were spouses 44 (30%) and the least of them were supervised by caregivers 5 (4%). A meta-analysis found that NCD family caregivers are more significantly stressed than non-NCD caregivers and they suffer more serious depressive and anxiety symptoms as well as physical problems such as hypertension.[61] Similarly, physical conditions such as hyperlipidaemia, hyperglycaemia and insufficiency of the cellular immune system may also develop as a consequence of the caregiving burden.[62] Common feelings of

caregiver burden are relationship strain, social isolation and emotional strain. These changes are likely to occur if there is a full dependency on a caregiver and there are significant NCD associated behavioural disturbances such as aggression, psychosis, poor sleep patterns, etc.[61] Caregivers who are heavily burdened by the needs of the patient may opt for institutionalisation of the relative as an alternative.[61] Unfortunately, while much is known about caregiving burden and its consequences, there is a paucity of information on the caregivers' demographic differences.[62]

This study shows that, regardless of the caregiver's heavy social and financial burden of caring for individuals with major NCDs, the majority of patients were still being cared for by their family members. This was also noted in the study conducted in the memory clinic in Cape Town (2010) where the majority of individuals with NCDs were cared for by their family members and the least were living in care facilities.[6] The comparatively low number of institutionalised patients could be due to cultural preferences, economic factors and availability of care from family members.[6]

4.2.6 Education profile/Employment Status

Education is thought to either protect or provide resilience against NCD-related pathology. It is related to a higher socioeconomic status, a healthy lifestyle and less exposure to environmental toxins. All these may prevent the development of cerebral pathology and consequent NCDs, particularly vascular cerebral diseases.[12,43] A larger percentage of patients 62 (43%) from the current study had attained a secondary level of education. In contrast, previous studies suggest that high school educational attainment is associated with lower risks of developing NCDs.[12,43]

It is not surprising that most patients were pensioners as the higher percentage of participants were above the age of 60 years. However, only 16 (11%) of patients with NCDs were employed. Possible explanations for this low percentage are three-fold. Firstly, all of those participants who were employed had mild NCDs and supposedly could perform their occupational roles adequately. Secondly, the unemployment rate in South Africa rose to 30.1% in the first quarter of 2020 and has shown an increase of 5% over the last 10 years. Thirdly, the low level of education seen in particularly disadvantaged communities plays a major role in finding permanent employment in RSA. [67] This also justifies the significant number of patients 42 (29%) that were unemployed and on disability grants 16 (11%).

4.3 Types of NCDs

The majority of reported NCDs were major NCDs which were 129 (89%). This could suggest that a significant number of patients with mild NCDs may be seen in the primary healthcare as compared to those with major NCDs being seen at a tertiary level due to the complexity of their medical and psychiatric comorbidities. Additionally, in this study primary NCDs appear to be less common in clinical practice compared to secondary NCDs. In the current study, frontotemporal NCD was the most common type of NCD in the category of primary NCDs whilst vascular NCDs were the most common type in secondary NCDs followed by NCDs due to HIV infection, multiple aetiologies and a small difference between alcohol and TBI causes. This is in keeping with the available literature which indicates that in RSA vascular NCD is a leading cause of all NCDs due to the high risk of metabolic diseases, cardiac diseases and stroke in the elderly population.[6,10,13,26] This is the reason for physical and mental exercise, balanced diet, social engagement and stress management being important factors in maintaining cognitive vitality and possibly protecting against the development of NCDs.[12]

The current study showed that NCDs due to HIV infection was the second most common cause 21 (14.5%) and it was noted in a younger population. The NCDs due to multiple aetiologies included mainly the combination of HIV, alcohol use disorders, TBI and few with other aetiological factors. This is in line with a previous study which asserted that up to 60% of people living with HIV/AIDS (PLWHA) are at risk of developing some form of NCD in their lifetime especially in a younger population aged between 15 to 49 years.[22] Grant [23] found that the prevalence of NCDs due to HIV infection was between 15% and 30% in untreated individuals while the prevalence in individuals receiving ART was 10%, with an annual incidence of 1 %. This shows that ARTs play a significant role in delaying the onset of NCDs or the prevention of rapid progression in those who are already diagnosed with NCD due to HIV infection.

4.4 Psychiatric comorbidities in NCDs

Neuropsychiatric symptoms (NPS), such as psychosis, affective disorders, apathy, anxiety, personality changes, aberrant motor activity, sleep disturbance and eating disorders, often occur in patients with NCD.[63] Psychiatric symptoms in NCD have also been linked to more severe cognitive decline, functional disabilities, faster progression to severe NCD and increased mortality rate.[64]

In this study, a large proportion, 136 (94%) of patients with NCDs seen at the general psychiatric clinic had psychiatric comorbidities. This is unsurprising as the study was conducted in the psychiatric clinic that treats patients with psychiatric pathology. It does, however, concur with a study done by de Jager et al[13] which suggested that up to 90% of patients with NCDs have psychiatric comorbidities. In the current study, major depressive disorders (MDD) were more common than bipolar disorders 42 (30.9%) and 32 (23.5%)

respectively. Affective disorders are frequent in NCDs and often precede or worsen cognitive dysfunction. The risk for NCD appears to be higher in individuals with more severe depressive symptoms and appears to be associated with the frequency of admissions to psychiatric wards for depression and bipolar disorders.[64] Whether the risk for NCD is greater for young-onset versus late-onset depression is still unclear as studies have yielded mixed results.[64] Depressive symptoms may appear in the NCD as prodrome.[64] Ghika[49] suggested that patients with NCDs due to Alzheimer's disease, Parkinson's disease and vascular NCDs are at risk of MDD whereas those with NCDs due to HIV infection are at risk of bipolar disorders. The study further asserted that approximately 40% to 70% of the elderly population had affective disorders, and among them, 15% to 25% had MDD.[49]

Psychotic disorders were also prominent in the current study 54 (39.7%), followed by anxiety disorders 15 (11%). Psychosis is associated with more rapid cognitive decline. [1, 55] This concur with a study conducted by Ku et al[16] that found the increased prevalence of NCDs in patients with schizophrenia (9.9%) compared to those without schizophrenia (2.2%).[16]

Defining anxiety in people living with NCDs is complicated due to the overlap in symptoms of anxiety disorders, MDD and NCDs. The study done by Shub et al.[14] estimated the clinical anxiety features to be as high as 70% especially in vascular NCDs and frontotemporal NCDs.[14] It was unclear from the data whether participants presented with anxiety disorders first and later developed NCDs or vice versa as this aspect was beyond the scope of the study. What may be proposed is that the disease burden of a dual diagnosis of anxiety disorders and NCDs is complex and as such may have necessitated their management in a tertiary psychiatric institution such as CMJAH.

4.5 Medical comorbidities

There is a strong association between NCDs and medical comorbidities, more importantly, cardiovascular diseases. These medical comorbidities cause or exacerbate the progression of NCDs and some of them often cause reversible NCDs. In the current study there was a high prevalence of cardiovascular disease 88 (77%) and reflected vascular NCDs as the commonest type of NCDs. Some cases of NCDs in the current study had comorbid neurological diseases 25 (21.9%), most of which was contributed to by adult-onset epilepsy mostly due to stroke. This concur with other studies which suggested that adult-onset epilepsy is associated with multiple causes of NCDs such as Alzheimer's disease, Huntington's diseases, post-stroke adult epilepsy and TBI.[51,55] In addition, childhood chronic epilepsy imposes a risk of NCDs later in life. The reason for this is unclear.[51,55]

4.6 Investigations

Investigations in patients suspected to have NCDs remain a gold standard of practice as they assist in detecting the possible cause of NCDs. In the current study, the majority of patients 114 (78.6%) performed neurocognitive tests and the most performed test was MoCA 82 (71%) which was helpful to detect both cortical and subcortical NCDs.[33] Ideally, all patients attending the clinic should have been screened for neurocognitive difficulties but proposed limitations to not performing some of neurocognitive testing in some patients might have been due to the language barrier, a low level of education and the fact that most standardised neurocognitive tests are not normed for a diverse South African population, and therefore may not yield the desired results.

Regardless of the high costs associated with neuroimaging in RSA, patients were fairly well investigated. In this regard, in this study, 99 (68.3%) of patients underwent CT scans of the

brain, 24 (16.6%) for MRI scans of the brain and 7 (4.8%) received functional neuroimaging investigations including PET/SPECT scans. CT scans of the brain were performed frequently compared to other neuroimaging because of their multiple advantages related to cost-effectiveness and accessibility. They are also effective in demonstrating various cerebral pathologies even though other scans, such MRI, take precedence to detect minute cerebral pathologies, but their high cost and low availability remain a challenge. [35] A low number of patients with more complex NCDs diagnosis were seen by the Neuropsychiatrist who generally performed more intensive investigations while other patients were seen by medical officers and psychiatry registrars supervised by a specialist Psychiatrist. This may provide an explanation as to the lower number of overall neurocognitive tests done, as well as the variability of intensive high-level investigations like MRI Brain scans and functional neuroimaging. Some aetiological factors of NCDs such as vascular related conditions, atrophy etc, were easily diagnosed on the CT scan of the brain and it would have not contributed further to the management of NCDs to perform other expensive neuroimaging investigations.

Blood investigations were done when an indication arose and each set of bloods was individualised according to the patient's clinical diagnosis. Full blood count (FBC) was done to the majority of patients 128 (88.3%), followed by other bloods 51 (35.2%) which included thyroid function tests, renal function tests, liver function tests, syphilis tests, etc. CD4 count was done on 22 (15.2%) of patients and vitamin B12 10 (6.9%). The CD4 count was measured in all patients with an HIV diagnosis even though it was not measured regularly as per HIV guidelines because these patients were also monitored closely at their ARV clinics. It is recommended to test for vitamin B12 deficiencies in patients diagnosed with NCDs to rule out vitamin B12 deficiency as an aggravating and reversible factor. Unexpectedly, in the study the number of patients who were tested for vitamin B12 was significantly low. It is unclear why

this should be the case but the author postulates that a standardised haematological work-up for NCDs was not always followed. Other blood tests were performed more frequently with an intention of monitoring chronic medical comorbidities such as renal failure from hypertension, liver dysfunction from chronic alcohol abuse, metabolic diseases, psychotropic adverse effects etc.

4.7 Association between demographics and category of NCD

The association of gender and advanced age with the type of NCDs has been consistent throughout the literature. This study suggested that gender and ethnicity were significantly associated with the type of NCDs. Several studies have shown that NCD risk increases in elderly female individuals and vascular NCDs remain the commonest type due to the increased incidence of cardiovascular diseases. More specifically, the current study found statistical associations between elderly female individuals and vascular NCDs. The current study also noted a possible increase of NCDs in the younger population. It is postulated from the study that the significant number of young individuals with NCDs were as a result of the high percentages of HIV infections, alcohol use disorders and TBI which represent the most common causes of NCDs in the younger population. There is, however, a scarcity of literature to provide comparable studies.

Caregivers of unmarried patients may be more likely to be distant relatives and remain poorly informed about the patient's condition. Hence these patients are at risk of neglect and abuse especially if NCDs are associated with behavioural disturbances and psychosis. The previous literature has highlighted less social and financial support of caregivers looking after individuals with NCDs in the RSA which increases an already unbearable burden on caregivers.[6] More advocacy, public awareness and government support to caregivers of NCD

sufferers is highly recommended to ease marked caregiver burden. There is a greater need for future epidemiological studies under the subject of NCDs to be conducted in the general psychiatric population to determine more demographic profiles associated with NCDs.[6,40]

4.8 Associations between psychiatric/medical comorbidities and category of NCD

A larger percentage of patients with NCDs had psychiatric and medical comorbidities. The presence of psychiatric comorbidities was significantly associated with the type of NCDs (p-value = 0.046). All three patients who had only primary NCDs had psychiatric comorbidities. Of the five individuals who had mixed NCDs, three of them had psychiatric comorbidities. A larger percentage of patients who had secondary NCDs also had psychiatric comorbidities. Major depressive disorders and psychotic disorders were the commonest in both primary and secondary NCDs.

The association between the presence and absence of medical comorbidities especially respiratory and GIT diseases and type of NCD was not statistically significant. Cardiovascular diseases were associated with vascular NCDs, neurological fallouts and major depressive disorders. There is still a dearth of research determining the percentage of individuals with psychiatric conditions who later developed NCDs and vice versa. Secondary NCDs may be preceded by psychiatric illnesses such as major depression disorder, schizophrenia and other psychiatric illnesses. These illnesses may mimic cognitive decline due to the chronic use of psychotropic medication, pseudodementia and other stressors related to psychiatric illnesses.[53]

5. CHAPTER FIVE: LIMITATIONS, CONCLUSION AND RECOMMENDATIONS

5.1 Limitations

The study may not represent other tertiary hospitals in South Africa which may have vastly different demographic patient profiles; and is therefore not generalizable. Although the sample size of the study was sizeable for psychiatric patients with NCDs, a larger sample size would have been beneficial in making the results more generalisable to a larger population. As the study was conducted at a tertiary academic hospital, the study sample was biased towards more complex clinical patients. As this was a retrospective study, there was a great reliance on diagnoses made by different clinicians; some of whom were more experienced than others and as such may have influenced the assessment and diagnoses assigned to these patients. In addition, the study was reliant on the accuracy of record-keeping and furthermore a limitation of the study was missing data, which was noted as 'unknown' on the data collection sheet.

General patients in medical and neurology out-patients departments were excluded. The net result is likely to be a reduced sample size. Patients seen in the neuropsychiatric clinic predominately presented with neuropsychiatric disorders which may have contributed further to bias with regard to over-representation of NCDs. These patients were seen by a specialist neuropsychiatrist hence bedside neurocognitive screening tools differed.

5.2 Conclusion

This study showed that NCDs in psychiatric patients were characterized by advanced age, single marital status, female gender and cardiovascular diseases as risk factors. The majority of psychiatric patients who were diagnosed with cardiovascular diseases and developed strokes, consequently suffered from vascular NCDs and adult-onset epilepsy.

There is a noticeably percentage of HIV infection, chronic alcohol abuse and TBI cases. The majority of patients with NCDs had major depressive disorders and psychotic disorders although it was not entirely clear which presentation was the preceding one. The MoCA screening tool was the most commonly used neurocognitive test as compared to MMSE because of its sensitivity to detect both cortical and subcortical NCDs. The CT scan of the brain was the most frequently used diagnostic neuroimaging tool as compared to MRI scan, due to its cost-effectiveness and accessibility. The study described NCDs in terms of demographic profile, psychiatric and medical comorbidities. The study findings of a 2.1% prevalence of NCDs is in keeping with previous prevalence studies that were conducted in the non-psychiatric population. The high percentage of elderly female patients was noted. However, there was a significant number of young people with NCDs. This probably reflects the high number of HIV infections, alcohol abuse and TBIs in the study sample and in the RSA in general. This is also slightly different from the previous literature that suggested NCDs as a condition for the elderly. Of consideration is that NCDs possibly always occurred in young people in the past but there were and still are few studies conducted to prove this. The study supports early standardised neurocognitive screening and management of patients with NCDs, or those at risk, to prevent rapid progression of the cognitive decline.

5.3 Recommendations

There are very few epidemiological studies done on NCDs in the general population and more importantly in vulnerable psychiatric populations worldwide. This emphasises a greater need for more research of NCDs in the psychiatric population to assist with identifying the trend which may help with better management of these patients. There is also a significant gap in the literature determining the quantitative risk of NCDs causing psychiatric comorbidities and vice versa. Further epidemiological studies of NCDs in a younger population are required to detect

whether the risk is increasing or stabilising in developing countries. Clinically, there is a notable rise of NCDs in the younger population but this has yet to be borne out in large scale studies. This population has received less attention compared to the elderly population and therefore warrants further investigations so that meaningful interventions can occur. Lastly, more studies that investigate the progression of NCDs due to HIV infection in patients as related to the use of ARTs will assist with better management of, and outcomes in these patients.

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Appendix A

DATA COLLECTION SHEET SAMPLE

Study code:
DEMOGRAPHIC DATA

AGE **In years**	18-40 1	41-60 2	61-80 3		>81 4	
SEX	Male= 1		Female= 2			
ETHNICITY	Black=1	White=2	Coloured=3		Indian=4	Other=5
LANGUAGE	English=1	Afrikaans =2	Nguni languages=3	Sotho Languages=4	Other=5	Unknown=6
MARITAL STATUS	Single=1	Married=2	Cohabiting=3	Divorced=4	Widowed=5	Unknown=6
EMPLOYMENT STATUS	Unemployed =1	Employed=2		Disability Grant=3	Pensioner=4	Unknown=5
HIGHEST LEVEL OF EDUCATION	No formal education=1	Primary school education=2	Secondary school education=3	Tertiary education=4		Unknown=5
PRIMARY CARE GIVER	Parents=1	Spouse=2		Children=3	Caregiver=4	Care facility =5

DSM-5 DIAGNOSIS

NEUROCOGNITIVE DIAGNOSIS								
Severity	**Mild=1**					**Major=2**	**Unknown=3**	
Primary NCDs	Alzheimer's disease=1		FTD=2	Lewy's body disease=3		Other=4		
Secondary NCDs	HIV =1	TBI =2	alcohol=3	Parkinson's disease=4	Huntington's disease=5	Vascular=6	Vitamin B12 deficiency= 7	Other=1
	Endocrine= 8		Specify=9			Multiple aetiologies =10		

PSYCHIATRIC COMORBIDITIES				
MOOD DISORDERS	Bipolar disorder=1		MDD=2	
OTHER PSYCHIATRIC ILLNESSES	Psychotic disorder=1	Anxiety disorder=2	Substance/Medication induced disorder=3	Other=4

MEDICAL COMORBIDITIES

MEDICAL COMORBIDITIES	Cardiovascular Diseases=1		Respiratory diseases=2	GIT diseases =3	Neurological diseases=4
OTHER MEDICAL CONDITIONS	Yes= 1		Elaborate=2	Unknown=3	
INVESTIGATIONS					
NEUROCOGNTIVE TESTS			Yes=1	No=2	Unknown=3
	MMSE=1	IHDS=2	MoCA=3	Specialized neuropsych tests=5	
NEURO-IMAGING	CT scan=1		MRI=2	Functional neuro-imaging=3	
EEG	Yes=1		No=2	Unknown=3	
COMMON BLOOD INVESTIGATIONS	FBC=1	CD4 count=2	Vitamin B12 deficiency=3	Autoimmune screen=4	Other=5

Appendix B

LINK FILE

STUDY CODE	HOSPITAL NUMBER

Appendix C

HREC APPROVAL

UNIVERSITY OF THE WITWATERSRAND, JOHANNESBURG

R14/49 Dr Peacemaker Samukelisiwe Mngomezulu

HUMAN RESEARCH ETHICS COMMITTEE (MEDICAL)

CLEARANCE CERTIFICATE NO. M160822

NAME: (Principal Investigator)	Dr Peacemaker Samukelisiwe Mngomezulu
DEPARTMENT:	Psychiatry Charlotte Maxeke Johannesburg Academic Hospital
PROJECT TITLE:	The profile of neurocognitive discorders in patients attending psychiatric outpatient services at a tertiary level academic hospital in Johannesburg
DATE CONSIDERED:	26/08/2016
DECISION:	Approved unconditionally
CONDITIONS:	Title and supervisor change 30/11/2018
SUPERVISOR:	Dr Anersha Pillay
APPROVED BY:	Dr C Penny, Chairperson, HREC (Medical)
DATE OF APPROVAL:	29/08/2016

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 in Room 301, 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 August and will therefore be due in the month of August 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

HOSPITAL CEO APPROVAL LETTER

GAUTENG PROVINCE
HEALTH
REPUBLIC OF SOUTH AFRICA

CHARLOTTE MAXEKE JOHANNESBURG ACADEMIC HOSPITAL

Enquiries:
Ms. N. Mzila
Office of the Clinical Director
Tell: (011): 488-4812
Email: Nolwazi.Mzila@gautemg.gov.za
27 February 2019

GP_201902_040

Dear Dr. P. S. Mngomezulu

STUDY TITLE: The Profile of Neurocognitive Disorders in Patients Attending Psychiatric Outpatient Services at a Tertiary Level Academic Hospital in Johannesburg.

Permission is granted for you to conduct the above recruitment activities as described in your request provided:

1. Charlotte Maxeke Johannesburg Academic Hospital will not anyway incur or inherit costs as result of the said study.
2. Your study shall not disrupt services at the study sites.
3. Strict confidentiality shall be observed at all times.
4. Informed consent shall be solicited from patients participating in your study.

Please liaise with the HOD and Unit Manager or sister in charge to agree on the dates and time that would suit all parties.

Kindly forward this office with the results of your study on completion of the research.

Supported / ~~**not supported**~~

Dr. M.I. Mofokeng
Clinical Director
DATE: 26/02/2019

Approved / **not approved**

Ms. G. Bogoshi
Chief Executive Officer
Date: 01.03.2019

Appendix: E

DEPARTMENT OF NEUROSCIENCES

Neurology, Neurological Surgery, Ophthalmology, Otorhinolaryngology, Psychiatry

School of Clinical Medicine, Faculty of Health Sciences,
7 York Road, Johannesburg 2193, South Africa
Tel: +27 11 717-2774 · Fax: +27 11 717 2775

Plagiarism declaration for written work

I Peacemaker Samukelisiwe Mngomezulu (student number: 0601059H) as a postgraduate student registered for a Degree of Master of Medicine in the Department of Psychiatry in 2016 at the University of the Witwatersrand declare the following:

- I am aware that plagiarism (the use of someone else's work without their permission and/or without acknowledging the original source) is wrong.
- I confirm that the work submitted for assessment for the above degree is my own unaided work except where I have explicitly indicated otherwise.
- I have followed the required conventions in referencing the thoughts and ideas of others.
- I understand that the University of the Witwatersrand may take disciplinary action against me if there is a belief that this is not my own unaided work or that I have failed to acknowledge the source of the ideas or words in my writing.
- I have included as an appendix a report from "Turnitin" (or other approved plagiarism detection) software indicating the level of plagiarism in my research document.

Signature ……..

Date 15/10/2020