The diagnostic yield of computerised tomography in human immunodeficiency virus (HIV) positive psychiatric patients at a tertiary hospital in the Western Cape.

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Dissertation submitted in part fulfilment of the degree MMed (Psychiatry)

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DECLARATION

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ABSTRACT

Background. HIV infection increases the risk for mental illness. Neuroimaging is an important part of the diagnostic workup in HIV+ psychiatric patients. Computerised tomography (CT) is the most widely neuroimaging modality available in resource limited settings. However, not every affected individual requires brain imaging, and no clear guidelines exist for the use of CT in psychiatric settings. This retrospective study aimed to explore the diagnostic yield of CT brain (CTB) scans in human immunodeficiency virus positive (HIV+) psychiatric patients referred to Groote Schuur Hospital Department of Psychiatry, as well as demographic and clinical associations.

Methods. Clinical and radiological data for HIV+ psychiatric patients who received a CTB scan during admission were obtained and analysed for the period January 2013 – June 2015. The diagnostic yield- scans with positive findings versus no findings- was established and differences between these groups compared.

Results. A total of 65 patients met the inclusion criteria. The mean age of the participants in this study was 36.2 years (range 18 – 64). The most common presenting psychiatric symptoms were psychosis (81.54%), cognitive deficits (72.41%) and mood symptoms (69.23%). CT scan results consisted of 29 (44.62%) normal scans and 36 (55.38%) abnormal scans. Atrophy was the most common (72%) radiological finding in abnormal CT scans. No associations were found between current proposed CT guidelines in psychiatric patients with and without abnormal CT scans, although a history of previous traumatic brain injury (TBI) approached significance ($p = .054$). There was a significant correlation between abnormal CT scans and past or current substance use ($X^2 = 5.9508$ $P = .015$). Abnormal CT findings increased with the Centers for Disease Control and Prevention (CDC) HIV immunological stage progression. The management of 9 patients changed; 7 of these CT scans were abnormal.

Conclusion. In this study of CTB scans in HIV+ psychiatric inpatients, previously suggested criteria proposed in guidelines for imaging were not associated with abnormal CT findings. Current or previous substance use correlated with significant higher rates of abnormal CT findings. Due to the high yield of abnormal CT scans in this study, it is suggested that HIV+ psychiatric inpatients with previous or current substance use, a history of TBI or HIV immunological stages B or C, are considered for imaging as a priority. It is recommended that further studies with larger sample sizes, consisting of inpatient and outpatient populations, with control groups be conducted to investigate current or previous substance use as an indication in guidelines for CTB scan in HIV+ psychiatric patients.

ACKNOWLEDGEMENTS

1. Professor John Joska (Research supervisor)
2. Anneli Hardy (Statistical consultant, Department of Statistical Science, University of Cape Town)

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ABBREVIATIONS

AIDS – acquired immunodeficiency syndrome
ARV – antiretroviral
CAT – computerised axial tomography
CD4 - cluster of differentiation 4
CMV – cytomegalovirus
CNS – central nervous system
CSF – cerebral spinal fluid
CT – computerised tomography/computed tomography
CTB – computerised tomography/computed tomography of the brain
CVA – cerebral vascular accident
EBV – Epstein-Barr virus
EEG – Electroencephalogram
ELISA – enzyme-linked immunosorbent assay
FES – first episode psychosis
GSH – Groote Schuur Hospital
HAD – human immunodeficiency virus associated dementia
HAND – HIV associated neurocognitive disease
HIV – human immunodeficiency virus
HIV-1 – human immunodeficiency virus type 1
HIV-2 – human immunodeficiency virus type 2
HIV+ - human immunodeficiency virus positive
HSV – herpes simplex virus
IHDS – International HIV dementia scale
JCV – John Cunningham virus
MRI – magnetic resonance imaging
NHLS – National Health Laboratory Service
OR – odds ratio
PML – Progressive multifocal leukoencephalopathy
RLS – resource-limited settings
SA – South Africa
SMI – serious mental illness
TB – tuberculosis
TBI – traumatic brain injury
UCT – University of Cape Town
VL – viral load

CHAPTER 1

INTRODUCTION

Background and context

Human immunodeficiency virus (HIV) emerged as a novel infection more than 35 years ago. Southern Africa is currently the epicentre of the HIV global epidemic, with South Africa (SA) among the worst affected countries.[1] According to the latest mid-year population estimates released by Statistics SA it is estimated that for 2016, 12.7% of the total population is infected with HIV. The total number of HIV infected persons in SA in 2016 is estimated at 7.03 million compared to the 4.02 million estimated in 2002. HIV is currently one of the 5 overall leading causes of death in SA. HIV was the leading cause of death in the Cape Winelands in the Western Cape according to stats SA's 2013 report on mortality and causes of death in SA.[2]

HIV can be staged according to clinical and/or immunological features. Clinical features are used to stage HIV into 3 main clinical stages: (1) primary HIV infection, (2) latent stage HIV/early symptomatic disease and (3) acquired immunodeficiency syndrome (AIDS). AIDS is defined as the development of specific AIDS related opportunistic infections or malignancies.[3] Cluster of differentiation 4 (CD4) T-lymphocyte count is used for immunological staging. A fall in CD4 T-lymphocytes is a hallmark feature of HIV infection. The CD4 count (measured in cells per microliter) predicts the development of opportunistic infections in HIV positive (HIV+) individuals. Immunological stages set out by the Centers for Disease Control and Prevention (CDC) are (1) category A, with a CD4 count of more than 500, (2) category B, with a CD4 count between 200-500 and (3) category C, with a CD4 count below 200. Immunological stages (category A, B and C) correspond to clinical stages (primary HIV, latent/early stage HIV and AIDS).[3,4]

The brain is a major target in HIV infection. Cerebral spinal fluid (CSF) analysis has indicated that HIV enters the central nervous system (CNS) early in the course of the infection. HIV CNS pathogenesis occurs through two possible mechanisms, firstly direct invasion of the virus and secondly by activation of immune competent cells that result in damaging immunological processes within the CNS. CNS complications in HIV are estimated at 60-70%.[5]

CNS abnormalities in HIV infection can be grouped under 3 main categories: (1) HIV-associated CNS lesions, (2) HIV-associated opportunistic infections and (3) HIV-associated neoplasms.[5] Common opportunistic infective agents in AIDS include toxoplasmosis, cryptococcus, herpes simplex virus (HSV), John Cunningham virus (JCV), cytomegalovirus (CMV), Epstein Barr virus (EBV) and mycobacterium tuberculosis (TB). TB caused by mycobacteria tuberculosis remains a significant threat to HIV+ individuals. [6,7]

HIV infection causes a multitude of both neurological and psychiatric manifestations that can present along the entire disease trajectory. HIV and mental illness are responsible for a substantial proportion of the total burden of disease in developing countries especially in Sub-Saharan Africa. Mental illness and HIV/AIDS will both be in the top 10 causes of mortality and morbidity by the year 2020 as estimated by the Global Burden of Disease Survey.[8]

Mental illness and HIV/AIDS

HIV+ patients are at an increased risk for mental illness**.** In general, psychiatric illness in HIV+ patients is associated with worse psychiatric and HIV outcomes. HIV-associated neuropsychiatric disorders may result from organic brain disease, psychosocial factors or a combination of both. Advances in antiretroviral treatment are responsible for shifts in incidence and prevalence rates of HIV associated neuropsychiatric conditions. Neuropsychiatric conditions may occur at any stage of the disease.[8]

Mood, anxiety and substance use disorder are common in HIV+ patients. Depressive disorders are the most common psychiatric manifestation in HIV+ patients. Prevalence rates of major depressive disorder of up to 50% have been reported. Unrecognised and untreated depression is associated with poor medication adherence and disease progression.[9]

Psychosis in HIV+ patients can either be primary, secondary or a combination of both. Patients with a primary psychotic disorder are more likely to engage in high-risk behaviour and therefore are at an increased risk for contracting HIV.[9]

Older HIV+ patients (>50 years) present with additional challenges. This group is more at risk of developing side effects from antiretroviral and psychotropic medication. The concept of accelerated aging through on-going increased inflammatory processes in this group has been proposed. Accelerated aging is associated with higher rates of psychiatric disorders.[10]

HIV associated neurocognitive disorder (HAND) is characterised by progressive deterioration in neurocognitive functioning. The incidence of HAND has decreased but the prevalence is increasing worldwide due to highly affective antiretroviral (ARV) treatment. HAND was diagnosed in up to 23.5% patients attending HIV clinics in SA. Neurocognitive impairment is classified according to severity in (1) asymptomatic neurocognitive impairment, (2) mild neurocognitive impairment and (3) HIV associated dementia (HAD). Cognitive impairment can occur at any stage of HIV disease but generally symptomatic stages are associated with later stages of HIV disease.[6,11]

Delirium is a syndrome often diagnosed in HIV+ psychiatric patients referred to psychiatry. More subtle forms of delirium can be present in HIV+ patients. These subtle presentations are often difficult to diagnose.[10]

Neuroimaging in general psychiatry

Severe mental disorders requiring in-patient care are costly to manage and specialized investigations like neuroimaging studies often form part of the diagnostic workup for psychiatric patients. The use of neuroimaging in psychiatry has increased over the last decade due to technological advances made in the field of imaging techniques. Imaging modalities are generally structural in nature, functional in nature or a combination of both. Three imaging modalities that are currently most used in the clinical setting are: CT, magnetic resonance imaging (MRI) and perfusion studies.[12]

MRI images of the brain are of higher resolution compared to CT images. However, in clinical settings CT does provide some advantages over MRI:

- CT imaging is less expensive and more widely available
- CT has fewer contraindications and greater accessibility.[12]

Currently no clear concise guidelines exist for the use of CT scans in psychiatric settings. Several studies have attempted to generate guidelines for the use of imaging studies in psychiatric patients. These studies are however limited to the study population and generalisability of the findings remain a limitation. General guidelines common to these studies recommend the use of CTB in the following situations: (1) a history of head injury, neurological disease, stroke and dementia, (2) an abnormal neurological examination, (3) the presence of confusion or cognitive decline, (4) first onset psychosis or personality changes after the age of 50 years and (5) any atypical presentations.[13]

Neuroimaging studies are also utilised to improve diagnostic accuracy in certain neuropsychiatric disorders by identifying specific affected brain areas and possible causes. Improved diagnostic accuracy is important in neuropsychiatric disorders like dementia and white matter disease. Neuroimaging studies may also be used to monitor disease progression.[5,12]

A literature search was conducted on the proposed research topic. The aim of the search was to establish current knowledge on the study topic. Various databases were searched using key words in different combinations. The following databases were used: PsychInfo, PubMed and Medline. Key words that were used: CT, computerised tomography, computed tomography, head, brain, neuroimaging, indications, guidelines, diagnostic, yield, HIV, human immunodeficiency virus, AIDS, acquired immunodeficiency syndrome, psychiatry, psychiatric, mental illness, mental disorder, atrophy, alcohol, illicit substances . A total of 267 articles were retrieved applying a filter for only human studies. Title and abstracts were reviewed - articles most relevant to this research topic were selected – these articles are listed in the reference section. Studies that investigated CT in HIV populations were separated from studies investigating psychiatric populations – these studies are tabled in Table 1 and Table 2.

CT yield in general psychiatry

The yield of abnormal CTB scans in psychiatric patients is highly variable. Three previous studies reported abnormal CTB at 6.8%, 35% and 49.8% respectively.[13,14,15] Several factors contribute to the variability of abnormal CTB findings, including selection bias and differences in study populations. Brain atrophy is a common shared finding amongst these and other studies that investigated CTB scans in a psychiatric population.[13,14,15,16]

Various studies have been conducted to investigate different aspects of imaging in psychiatric patients. These studies often focussed on first episode psychosis (FES) and the value of routine CTB scans as part of the initial workup. Agzarian (2006) investigated the use of routine computerised tomography brain scanning of psychiatry patients. This prospective study excluded psychiatric patients with focal neurological signs. In this study 20 out of a total of 397 or 5% of CTB scans were abnormal. The lower yield of abnormal CTB scans in this study population is most likely attributed to the exclusion of patients with focal neurological signs.[17]

Bain (1998) conducted a retrospective study at a military hospital. CTB scans of patients with FES and good general health were analysed. In this retrospective study 123 out of 127 CTB scans were normal with 4 incidental findings. The study concluded that routine CTB scans for index psychosis may not be justifiable.[18] Battalgia (1988) had a similar finding from their prospective study on psychiatric inpatients with FES.[18] In contrast, Gewirtz (1994) supported FES as an indication for ordering CTB scans. In this cohort study 168 CTB scans were performed. Diffuse atrophy was found in 40% of all scans and other abnormalities in 6.6%.[20]

An explorative study done by Jeenah (2007) investigated CTB scans at Chris Hani Baragwanath hospital in South Africa. All mentally ill inpatients age 18 years and older admitted during the study period were eligible for CT scans. Inclusion criteria were (i) first episode psychosis, (ii) psychotic patients with features of delirium, focal physical or neurological signs and/or (iii) abnormal special investigations. A total of 20 out of 55 or 36% of CTB scans were abnormal.[21]

Larson (1981) conducted a retrospective study to determine the diagnostic yield of CTB scans in patients with psychiatric illness. This study investigated the findings of a group of consecutive patients referred for CTB scans with a psychiatric illness. In their study 6 out of 123 CTB scans were assessed as a true positive finding suggesting that a 'rule in approach' based on the presence of focal neurological signs may increase the diagnostic yield of CTB scans.[22]

In a retrospective study on CT and MRI scans in first presentation to psychiatric inpatient and outpatient services, Mueller (2006) reviewed 280 CTB scans of which 161 CTB scans were normal, 52 abnormal and 67 equivocal. Focal neurological signs and advanced age were associated with higher abnormal imaging studies. This study highlighted the need for clear indications for neuroimaging studies in psychiatric inpatients.[23]

Ananth (1993) signified the importance of clinical findings to guide the use of CTB scans in order to clarify or compliment findings in psychiatric patients. This prospective study randomised hospitalised psychiatric patients to investigate the clinical use of CTB scans. A total of 34 CTB scans were performed of which 9 were abnormal.[24]

Two separate studies concluded that specific risk factors could be used as guidance in ordering CTB scans in psychiatric patients. Moles (1998) conducted a prospective study on psychiatric inpatients to identify clinical factors associated with increased CTB abnormalities. This study reported 53% of 150 CTB as abnormal. Organic mental syndromes and advanced age (60 years and above) were associated with higher abnormal CTB scans.[25] In a retrospective study by Hollister (1991) reviewing 140 CTB scans over a 3-year period, several suggested indications for ordering CTB scans in psychiatric patients were identified; (i) History of head injury, stroke, neurological disease, (ii) presence of abnormal neurological signs or organic mental signs, (iii) first psychotic break or personality change after age 50 years.[13]

In summary, CTB is used to exclude organic pathology in patients presenting to psychiatry. CT is the primary neuroimaging study available in resource limited settings. Clear guidelines for the use of CTB in psychiatric populations are still

lacking. Current suggested indications for CTB in psychiatric patients are derived from studies where generalisability is limited to those study populations. Table 1 provides a summary of the findings from the various studies that investigated CTB scans in psychiatric patients.

Table 1: A summary of previous studies investigating CT in psychiatric patients

Study reference	Study setting	CT findings	Conclusion
Larson EB, Mack LA, Watts B, Cromwell LD. Computed tomography in patients with psychiatric illnesses: advantage of a 'rule in' approach. Ann Intern Med 1981;95(3):360-364.	Retrospective study to determine the diagnostic yield of CTB scans in patients with a psychiatric illness.	123 CTB scans performed. 62 (50%) normal CTB scans. 43 (35%) CTB scans with atrophy. 6 (5%) true positive CTB scans.	Ordering of CTB scans as a "rule in approach" based on the presence of focal neurological signs would be less expensive and more effective.
Battalion J, Spector IC. Utility of the CAT scan in a first psychotic episode. Gen Hosp Psychiatry1998;10(6):398-401.	Prospective study on psychiatric inpatients admitted for FES.	45 CTB scans performed. 42 (93%) normal CTB. 3 (7%) abnormal CTB.	CTB scans for FES should be based on clinical judgement not according to protocol.
Hollister LE, Boutros N. Clinical use of CT and MR scans in psychiatric patients. J Psychiatry Neurosci 1991;16(4):194-198.	Retrospective study reviewing neuroimaging studies requested at a psychiatric hospital over a 3-year period.	Total of 140 CTB scans performed. 78 (56%) normal CTB scans. 4 (3%) equivocal CTB scans. 58 (41%) abnormal CTB scans.	Suggested indications for ordering CTB scans in psychiatric patients: (i) History of head injury, stroke, neurological disease, (ii) presence of abnormal neurological signs or organic mental signs, (iii) first psychotic break or personality change after age 50 years.

Study reference	Study setting	CT findings	Conclusion
Ananth J, Gamal R, Miller M, Wohl M, Vandewater S. Is the routine CT head scan justified for psychiatric patients? A prospective study. J Psychiatry Neurosci 1993;18(2):69-73.	Prospective study of randomized hospitalised psychiatric patients to investigate the clinical use of CTB head scans.	34 CTB scans performed. 9 (26%) abnormal CTB scans.	Clinical findings should guide the use of CTB scans to clarify or compliment the findings.
Gewirtz G, Squires-Wheeler E, Sharif Z, Honer WG. Results of computerised tomography during first admission for psychosis. Br J Psychiatry 1994;50:789-795.	Cohort study of 168 patients that underwent CTB scans on first admission.	168 CTB scans performed. Diffuse atrophy found in 40% of scans. Abnormalities other that atrophy found in 6.6%	Study supporting CTB scans for first onset psychosis.
Bain BK. CT scans of first-break psychotic patients in good general health. Psychiatr Serv1998;49:234–235.	Retrospective study on psychiatric patients evaluated for a psychotic illness at a military hospital that received a CTB scan.	127 CTB scans performed. 123 (97%) normal CTB. 4 (35%) incidental findings.	Study supports the finding that CTB scans for all newly psychotic patients may not be justifiable.
Moles JK, Franchina JJ, Sforza PP. Increasing the clinical yield of computerized tomography for psychiatric patients. Gen Hosp Psychiatry 1998;20(5):282-291.	A prospective study on psychiatric inpatients to identify clinical factors associated with increased CT abnormalities.	150 CTB scans performed. 53% of CTB scans abnormal. 11% influenced patient care. 2% potentially reversible lesions.	Specific clinical risk factors can be used as guidance in ordering CTB scans in psychiatric patients to increase the yield. The incidence of abnormal CTB scans is increased in patients over 60 years and in organic mental syndromes.

Study reference	Study setting	CT findings	Conclusion
Agzarian MJ, Chryssidis S, Davies CH, Pozza CH. Use of routine computed tomography brain scanning of psychiatry patients. Australas radiol 2006;50(1):27-28.	To evaluate the usefulness of CTB in psychiatric conditions without focal neurological signs. Prospective study on psychiatric inpatient and outpatients referred for CT scans.	397 CTB performed. 337 (95%) normal CTB. 20 (5%) abnormal CTB.	Probability of finding lesions in psychiatric patients is not greater than for the general population.
Mueller C, Rufer M, Moergeli H, Bridler R. Brain imaging in psychiatry – a study of 435 psychiatric in-patients at a university clinic. Acta Psychiatr Scand 2006,114(2):91-100.	Retrospective study on CT and MRI head scans performed on first presentation to psychiatric inpatient and outpatient services.	280 CTB scans performed. 161 (57.5%) normal CTB scans. 52 (18.5%) abnormal CTB scans. 67 (24%) equivocal scans.	The need exists for clear indications for neuroimaging studies in psychiatric inpatients. Focal neurological signs and advanced age are associated with increased abnormal imaging studies.
Jeenah FY, Moosa MYH. CT scans in psychiatric patients - An exploratory study at Chris Hani Baragwanath Hospital. S Afr J Psychiatr 2007;13(1):22-25.	Prospective explorative study to determine the CT brain yield on psychotic inpatients.	55 CTB scans performed. 20 (36%) abnormal CTB scans. 35 (64%) normal CTB scans.	Psychiatric patients have a larger incidence of CTB abnormalities especially FES. Clinical abnormalities may not be a reliable predictor for abnormal CTB scans.

CT brain yield in HIV

CTB is a valuable tool used in the evaluation of HIV+ patients. Despite extensive research on CT abnormalities in HIV+ patients, clear guidelines for the use of CTB scans in this population are also lacking.[26]

CTB scan findings in HIV+ patients often correspond to the level of immunosuppression. Opportunistic infections are more common in those patients with a CD4 of less than 200. Specific CTB findings are often useful in the diagnosis of the type of opportunistic infection.[7,27]

Cerebral atrophy is also a common finding in CTB scans of HIV+ patients. Atrophy in tissue implies the loss of cells. The national institute of neurological disorders and stroke defines brain atrophy as a loss of neurons and the connections between them.[34] Brain atrophy can be generalised (affecting the whole brain) or focal (affecting only specific areas). Brain atrophy can be visualised on CTB scans by increased ventricular size and widening of sulci with diminished grey matter size. Atrophy in HIV is nonspecific and thus cannot currently be differentiated from other causes of atrophy, such as herpes encephalitis.[7] In a study conducted by Pfefferbaum (2012) investigating the effects of AIDS, alcohol and age in HIV infection, advanced CDC HIV staging revealed higher cerebral volume deficits in the HIV only group. Atrophy was also found to be related to several HIV-related factors including CD4 cell-count nadir and a history of an AIDS-defining event.[28]

CTB scans are often part of the initial diagnostic workup in HIV+ patients who present to psychiatry.[3] The shift of HIV to a chronic illness means that more neuroimaging studies, like CTB scans, will be performed in the future as part of the chronic management plan of these patients.[29]

A study by Seth (1991) investigated all HIV/AIDS patients with a psychiatric illness referred to liaison psychiatry. A total of 23 CTB scans were ordered of which 17 or 73.9% were abnormal. In this study patients that progressed to AIDS were 5 times more likely to be referred to liaison psychiatry services. Study findings also indicated a high diagnostic yield of CTB abnormalities in HIV+/AIDS psychiatric patients.[30]

Hongsakul (2008) investigated findings of CTB scans in HIV+ homosexual men. A randomly selected sample from a cohort of HIV+ homosexual men was selected and 195 CT scans were performed. HIV encephalopathy was the most common brain finding affecting 59% of the study population. Toxoplasmosis was the most common opportunistic infection affecting 22%. Other CT findings were cryptococcoma (9%), tuberculous meningitis (5%), tuberculoma (4%), progressive multifocal leukoencephalopathy (PML) (3%) and lymphoma (2%).[31] This study reflects the high incidence of abnormal CT findings in HIV+ patients.

Mundinger (1992) investigated the use of CTB and MRI scans as a prognostic tool in patients with AIDS and neurological deficit. Imaging studies of AIDS patients with only focal brain lesions and/or atrophy were reviewed. The study concluded that the mean survival time of patients with initial normal imaging studies were higher than those with initial abnormal imaging studies. Patients with both focal brain lesions and atrophy had the shortest survival time. The risk of death in these patients was 19.3 times higher compared to patients with normal initial neuroimaging studies. This

study proposed that CTB and MRI scans could be used to identify AIDS related brain pathology that may assist in AIDS prognosis.[32]

Robert (1986) reviewed 200 consecutive AIDS patients with CTB scans. The study population consisted of homosexual men with AIDS and neurological symptoms ranging in age from 23 to 60 years. 81 of the 200 CTB scans were normal, 75 had atrophy and 44 had a focal lesion. The study findings suggested that MRI might be a valuable supplement to CTB in patients with generalised atrophy as MRI may reveal lesions not seen on CBT scans.[33]

In summary, CTB is an invaluable tool in the diagnostic workup of HIV+ patients in resource limited settings. Toxoplasmosis is the most common opportunistic infections identified on CT in HIV+ populations. Atrophy is a common nonspecific finding with possible prognostic implications.
Table 2 provide a summary of these studies. [27,31,32]

Table 2: Previous studies investigating CT yield and clinical correlates in HIV+ patients

Study reference	Study setting	CT findings	Conclusion
Robert M, Rosenbloom S, Perrett LV. Neuroradiological findings in AIDS: A review of 200 cases. AJNR Am J Neuroradiol 1986;7:833-839.	Neuroradiological studies of 200 consecutive homosexual men with AIDS and neurological symptoms were reviewed.	200 CTB scans reviewed. 81 (41%) normal CTB scans. 75 (38%) CTB scans indicating atrophy. 44 (22%) CTB scans with focal lesions.	The study indicated that patients with AIDS might have normal CTB scans. AIDS patients with evidence of diffuse cerebral atrophy are more likely to progress both neurological and radiological.
Seth R, Granville-Grossman K, Goldmeier S, Lynch S. Psychiatric illnesses in patients with HIV infection and AIDS referred to the liaison psychiatrist. Br J Psychiatry 1991;159:347-350.	Psychiatric illness in HIV/AIDS patients referred to liaison psychiatric in- and outpatient services.	23 CTB scans performed. 17 (74%) abnormal CT scans. 6 (26%) normal CTB scans. 11 (48%) CTB scans indicated atrophy. 4 (17%) CTB scans with PML.	The proportion of AIDS patients referred to liaison psychiatry was 5 times more than HIV+ patients.
Mundinger A, Adam T, Ott D, Dinkel E, Beck A, Peter HH, Volk B. CT and MRI: prognostic tools in patients with AIDS and neurological deficits. Neuroradiology 1992;35(1):75-78.	To determine if CT and MRI are of better prognostic value than clinical status in AIDS patients with neurological signs. Imaging studies of AIDS patients with only focal lesions and/or atrophy were reviewed.	26 CTB scans performed.	Mean survival time of patients with initial normal imaging studies was higher than that of patients with isolated focal lesions or atrophy. Atrophy with focal lesions correlates with the shortest mean survival time. CT and MRI scans allow identification of brain

Study reference	Study setting	CT findings	Conclusion
			changes that may be of prognostic value.
Hongsakul K, Laothamatas . Computer tomographic findings of the brain in HIV+ patients at Ramathibodi Hospital. J Med Assoc Thai 2008; 91(6):895-907.	Randomly selected sample from a cohort study of HIV+ homosexual men to evaluate the accuracy of CTB lesions.	195 CTB scans performed. 59% were HIV encephalopathy, 22% toxoplasmosis, 9% cryptococcoma, 5% tuberculous meningitis, 4% tuberculoma, 3% PML, 2% lymphoma, and 1% normal. In non-specified causes (from CTB scan), 33% were meningitis, 4% cerebritis, and 5% infarction.	HIV encephalopathy is the most common brain finding in HIV. Toxoplasmosis is the most common opportunistic infection.

AIMS AND OBJECTIVES

Study aims

The aim of the study was to determine the diagnostic yield of abnormal CTB scans in HIV+ psychiatric patients, who received a CTB scan during the study period and to describe these abnormalities.

Study objectives

Primary objectives:

1) To determine the yield of abnormal CTB scans in HIV+ psychiatric patients,
2) To describe these abnormalities.
3) To describe demographic and clinical variables associated with an abnormal CTB scan in HIV+ patients with a psychiatric disorder.

METHODS

Study design:

A retrospective exploratory folder review.

Study setting

The study was conducted in the department of Psychiatry at Groote Schuur Hospital in Cape Town, Western Cape. Groote Schuur Hospital (GSH) is an academic teaching hospital affiliated to the University of Cape Town (UCT).

Study population and sampling

The study investigated all psychiatric inpatients, confirmed to be HIV+, who received one or more CTB scans during the study period (1st January 2013 to 30st June 2015).
Psychiatric inpatients comprised of inpatients from either male or female acute units, neuropsychiatric and liaison-therapeutic units. Current suggested guidelines for CTB scans in psychiatric patients serve as a guide for ordering CTB in these units.

Inclusion criteria:

1. Male and female psychiatric inpatients,
2. above 18 years of age,
3. who presented at Groote Schuur Hospital
4. during the study period (1st January 2013 to 30st June 2015).
5. Confirmed HIV seropositive by laboratory HIV enzyme-linked immunosorbent assay (ELISA) or detectable HIV viral load.
6. Patients who received one or more CTB scan (contrasted or uncontrasted) at or during their admission within the study period.

Exclusion criteria:

1. Patients below 18 years,
2. CTB scans performed outside of Groote Schuur Hospital.
3. HIV status not confirmed by laboratory HIV ELISA or HIV viral load.

Sample size
The sample consisted of all psychiatric inpatients who met the inclusion and exclusion criteria. The total sample size was 65.

Study procedures
All final CTB scan reports were reviewed by qualified radiologists.

Medical records and radiological reports of all patients who met the inclusion and exclusion criteria were obtained and reviewed in detail. Referral documents, admission notes, progress notes, prescriptions, order instructions and discharge reports were reviewed from medical records. Electronic entries and reports, obtained from patient databases through intranet access within GSH was also reviewed to subtract any relevant information. The three electronic databases that was used were Clinicom, National Health Laboratory Service (NHLS) and Isite. Relevant data was grouped under the following categories:

- Demographical data and history
- Clinical data
- Radiological data
- Other special investigations

Data for each patient was captured on pre coded data capturing sheets. (Copy included in appendix)

Demographic data and history:

- Demographic data was collected on age, gender, relationship status and ethnicity.
- Any significant history of current or previous alcohol or illicit substance use was recorded. Significant substance use included any recorded entries on substance use that were deemed to be excessive or problematic at the time the entry was made.
- A history of seizure activity, traumatic brain injury (TBI) and cerebral vascular accidents (CVA) was recorded.
- All index presentations to psychiatry was recorded.

Clinical data:
Relevant clinical data that was extracted:

- Clinical data on presenting psychiatric symptoms before CTB scans. Presenting psychiatric symptoms were grouped as affective (mood) symptoms, psychotic symptoms, anxiety and post-traumatic symptoms, cognitive symptoms and other symptoms. A cluster approach was used to group psychiatric symptom presentation in clusters.

Cognitive testing and screening tests for HIV associated dementia with scores were recorded. The Mini Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA) are two commonly used validated tests performed to assess cognitive functioning. The international HIV dementia scale (IHDS) is a validated rapid screening test for HIV associated dementia. [11] Studies by Joska (2011) and Goodkin (2014) investigated the validity of the IHDS in a South African population. These studies however suggested adding brief tests of executive functioning and increasing the cut-off score of the IHDS respectively. [35,36]

Education and cultural factors including language influence MMSE and MoCA scores. Score adjustments are made based on level of education however, limited information is available

on allowances made when scoring tests performed in a language other than the first language. [11]

- Pharmacological treatment at the time of CTB scans.
- Date of confirmed HIV status (confirmation by HIV ELISA or detectable HIV viral load), initiation of ARVs, HIV treatment failure, and compliance with ARVs and immunological stages at the time of CTB scan were recorded.
- The presence of any focal neurological findings on the neurological examination before the CTB scans. An abnormal neurological examination was defined as any abnormality or deficit in cranial nerve, motor, sensory or reflexes function.
- Other comorbid medical conditions at the time of the scan (excluding psychiatric conditions or HIV infection).
- Any complications as a direct result of CTB scans performed.

Other special clinical investigations:

- Most recent CD4 count and viral load before the CT scan.
- CSF findings.
- Electroencephalogram (EEG) findings.

Radiological findings:
The final CT brain report for the 1st CTB scan performed on or during admission for each patient within the study period was reviewed to extract relevant data:

- The department that requested the initial CTB scan during the study period.
- Indications for CTB scans.
- CTB scan findings were recorded as normal (negative) or abnormal (positive) and contrasted or uncontrasted. A positive finding was regarded as abnormal intracranial findings noted on CTB reports. The presence of any atrophy on CTB scans was regarded as a positive finding. Different methods have been proposed to quantify atrophy. These methods however are not commonly used in clinical settings especially with lower resolution CT imaging.

Medical records of all patients with an abnormal CTB scan reports within the study period were reviewed for 2 weeks for any change in management following the date of the CTB scan report. A change in management was defined as any change in the diagnosis, treatment or prognosis as a result of the CTB scan report. Changes in management included any special orders or additional special investigations ordered after the CTB scan was performed as a direct result of CTB findings.

STUDY RATIONALE

The diagnostic yield of CTB scans in HIV+ psychiatric patients in this population was unknown. No study known to the research team has been done in SA that investigated CT scans specifically in HIV+ psychiatric patients. Also, no clear guidelines exist to help identify those patients with HIV and mental illness who will benefit most from CTB scans in a resource-limited setting. In order to address this gap, we aimed to determine the yield of abnormal CTB scans in HIV+ psychiatric patients and to describe these abnormalities including demographic and clinical variables associated with an abnormal CTB scan.

REFERENCES

1. The Joint United Nations Programme on HIV and AIDS Fact sheet: 2016 statistics. 2016.
   Available from:
   http://www.unaids.org/sites/default/files/media_asset/UNAIDS_FactSheet_en.pdf
2. Statistics South Africa. Mid-year population estimates. 2015.
   Available from: http://www.statssa.gov.za/publications/P0302/P03022016.pdf
3. Centers for Disease Control and Prevention. Revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. 1993. Available from:
   http://www.cdc.gov/mmwr/preview/mmwrhtml/00018871.htm
4. Offiah, CE, Turnbull IW. The imaging appearances of intracranial CNS infections in adult HIV and AIDS patients. Clin Radiol 2015;61(5):393–401. Available from: https://doi.org/10.1016/j.crad.2006.01.008
5. Thurnher, MM, Donovan Post MJ. 2008. Neuroimaging in the Brain in HIV-1-Infected Patients. Neuroimaging Clin North Am 2008;18(1):93-117. Available from: https://doi.org/10.1016/j.nic.2007.12.013
6. Corr, P. Imaging of neuro-AIDS. J Psychos Res 2006;61(3):295-299. Available from: https://doi.org/10.1016/j.jpsychores.2006.05.011
7. Ramsey RG, Germia GK. CNS complications of AIDS: CT and MR findings. Am J Roentgenol 1998;151(3):449-454. Available from: https://doi.org/10.2214/ajr.151.3.449
8. Myer L, Smit J, Le Roux L, Parker S, Stein DJ, Seedat S. Common mental disorders among HIV-infected individuals in South Africa: prevalence, predictors, and validation of brief psychiatric rating scales. AIDS Patient Care STDS 2008;22(2):147–158. Available from: https://doi.org/10.1089/apc.2007.0102
9. Gaynes BN, Pence BW, Eron JJ, Miller WC. Prevalence and comorbidity of psychiatric diagnoses based on reference standard in an HIV+ patient population. Psychos Med 2008;70(4):505–511. Available from: https://doi.org/10.1097/psy.0b013e31816aa0cc
10. Treisman GJ, Watkins CC. Neuropsychiatric complications of aging with HIV. J Neurovirol 2002;18(4):277-290. Available from: https://doi.org/10.1007/s13365-012-0108-z
11. Joska JA, Fincham DS, Stein D, Paul RH, Seedat S. Clinical correlates of HIV-associated neurocognitive disorders in South Africa. AIDS Behav 2010;14(2):371-378. Available from: https://doi.org/10.1007/s10461-009-9538-x
12. Malhi GS, Lagopoulos J. Making sense of neuroimaging in psychiatry. Acta Psychiatr Scand 2008;117(2):100-117. Available from: https://doi.org/10.1111/j.1600-0447.2007.01111.x
13. Hollister LE, Boutros N. Clinical use of CT and MR scans in psychiatric patients. J Psychiatry Neurosci 1991;16(4):194-198.
14. Larson EB, Mack LA, Watts B, Cromwell LD. Computed tomography in patients with psychiatric illnesses: advantage of a 'rule in' approach. Ann Intern Med 1981;95(3):360-364. Available from: https://doi.org/10.7326/0003-4819-95-3-360
15. Roberts JKA, Lishman WA. The use of the CAT head scanner in clinical psychiatry. Br J Psychiatry 1984;145(2):152-158. Available from: https://doi.org/10.1192/bjp.145.2.152

16. Kim DM, Tien R, Byrum C, Krishnan KR. Imaging in acquired immune deficiency syndrome dementia complex (AIDS dementia complex): a review. Prog Neuropsychopharmacol Biol Psychiatry 1996;20(3):349-370. Available from: https://doi.org/10.1016/0278-5846(96)00002-4
17. Agzarian MJ, Chryssidis S, Davies CH, Pozza CH. Use of routine computed tomography brain scanning of psychiatry patients. Australas radiol 2006;50(1):27-28. Available from: https://doi.org/10.1111/j.1440-1673.2005.01542.x
18. Bain BK. CT scans of first-break psychotic patients in good general health. Psychiatr Serv 1998;49:234–235. Available from: https://doi.org/10.1176/ps.49.2.234
19. Battalion J, Spector IC. Utility of the CAT scan in a first psychotic episode. Gen Hosp Psychiatry1998;10(6):398-401. Available from: https://doi.org/10.1016/0163-8343(88)90062-x
20. Gewirtz G, Squires-Wheeler E, Sharif Z, Honer WG. Results of computerised tomography during first admission for psychosis. Br J Psychiatry 1994;50:789-795. Available from: https://doi.org/10.1192/bjp.164.6.789
21. Jeenah FY, Moosa MYH. CT scans in psychiatric patients - An exploratory study at Chris Hani Baragwanath Hospital. S Afr J Psychiatr 2007;13(1):22-25. Available from: https://doi.org/10.4102/sajpsychiatry.v13i1.7
22. Larson EB, Mack LA, Watts B, Cromwell LD. Computed tomography in patients with psychiatric illnesses: advantage of a 'rule in' approach. Ann Intern Med 1981;95(3):360-364. Available from: https://doi.org/10.7326/0003-4819-95-3-360
23. Mueller C, Rufer M, Moergeli H, Bridler R. Brain imaging in psychiatry – a study of 435 psychiatric in-patients at a university clinic. Acta Psychiatr Scand 2006, 114(2):91-100. Available from: https://doi.org/10.1111/j.1600-0447.2006.00848.x
24. Ananth J, Gamal R, Miller M, Wohl M, Vandewater S. Is the routine CT head scan justified for psychiatric patients? A prospective study. J Psychiatry Neurosci 1993; 18(2):69-73.
25. Moles JK, Franchina JJ, Sforza PP. Increasing the clinical yield of computerized tomography for psychiatric patients. Gen Hosp Psychiatry 1998;20(5):282-291. https://doi.org/10.1016/s0163-8343(98)00040-1
26. Rothman RE, Keyl PM, McArthur JC, Beauchamp NJ, Danyluk T, Kelen GD. A decision guideline for emergency department utilization of noncontrast head computed tomography in HIV-infected patients. Acad Emerg Med 1999;6(10):1010–1019. Available from: https://doi.org/10.1111/j.1553-2712.1999.tb01184.x
27. Thurnher MM, Thurnher SA, Schindler E. CNS involvement in AIDS: spectrum of CT and MR findings. Eur Radiol 1997;7(7):1091-1097. Available from: https://doi.org/10.1007/s003300050260
28. Pfefferbaum A, Rosenbloom, MJ, Sassoon SA, et al. Regional Brain Structural Dysmorphology in HIV Infection: Effects of AIDS, Alcoholism, and Age. Biol Psychiatry 2012;72(5):361–370. Available from: https://doi.org/10.1016/j.biopsych.2012.02.018
29. Lund C, Petersen I, Kleintjes S, Bhana A. Mental Health Services in South Africa: Taking stock. Afr J Psychiatry 2012;15:402-405. Available from: https://doi.org/10.4314/ajpsy.v15i6.48
30. Seth R, Granville-Grossman K, Goldmeier S, Lynch S. Psychiatric illnesses in patients with HIV infection and AIDS referred to the liaison psychiatrist. Br J Psychiatry 1991;159:347-350. Available from: https://doi.org/10.1192/bjp.159.3.347
31. Hongsakul K, Laothamatas. Computer tomographic findings of the brain in HIV+ patients at Ramathibodi Hospital. J Med Assoc Thai 2008;91(6):895-907.

32. Mundinger A, Adam T, Ott D, Dinkel E, Beck A, Peter HH, Volk B. CT and MRI: prognostic tools in patients with AIDS and neurological deficits. Neuroradiology 1992;35(1):75-78. Available from: https://doi.org/10.1007/bf00588284
33. Robert M, Rosenbloom S, Perrett LV. Neuroradiological findings in AIDS: A review of 200 cases. AJNR Am J Neuroradiol 1986;7:833-839. Available from: https://doi.org/10.2214/ajr.147.5.977
34. National institute of neurological disorders and stroke. Cerebral atrophy information page. Available from: https://www.ninds.nih.gov/Disorders/All-Disorders/Cerebral-Atrophy-Information-Page
35. Joska J, Westgarth-Taylor J, Hoare J, Thomas K, Paul R, Myer L, Stein D. Validity of the International HIV Dementia Scale in South Africa. AIDS patient care and STDs 2011;25(2):95-101. Available from: https://doi.org/10.1089/apc.2010.0292
36. Goodkin K, Hardy DJ, Singh D, Lopez E. Diagnostic utility of the International HIV Dementia Scale for HIV-associated neurocognitive impairment and disorder in South Africa. J Neuropsychiatry Clin Neurosci 2014;26(4):352-358. Available at https://doi.org/10.1176/appi.neuropsych.13080178

CHAPTER 2

ARTICLE TITLE

The diagnostic yield of computerised tomography in human immunodeficiency virus (HIV) positive psychiatric patients at a tertiary hospital in the Western Cape.

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ETHICAL APPROVAL

Ethics approved by Human Ethics Research Committee University of Cape Town
Date approved: 11 December 2015
HREC reference number: 892/2015
(copy included in appendix)

REVIEW JOURNAL

South African Medical Journal (SAMJ)
Instructions for authors available at:
http://www.samj.org.za/index.php/samj/about/submissions#authorGuidelines
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The diagnostic yield of computerised tomography in human immunodeficiency virus (HIV) positive psychiatric patients at a tertiary hospital in the Western Cape

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ABSTRACT

Background. HIV infection increases the risk for mental illness. Neuroimaging is an important part of the diagnostic workup in HIV+ psychiatric patients; CT is the primary neuroimaging modality available in resource limited settings. Despite advances in neuroimaging no clear guidelines exist for the use of CT in psychiatric settings.

Objective. To determine the diagnostic yield of CT brain (CTB) scans in HIV+ psychiatric patients and to describe these abnormalities as well as demographic and clinical variables associated with abnormal CT scans.

Methods. A retrospective study was conducted at the Department of Psychiatry and Mental illness at Groote Schuur Hospital, Cape Town, South Africa. Clinical and radiological data for HIV+ psychiatric patients who received a CTB scan during admission were analysed for the period January 2013 – June 2015.

Results. A total of 65 patients met the inclusion criteria. The mean age of the participants in this study was 36.2 years (range 18 – 64). The most common presenting psychiatric symptoms were psychosis (81.54%), cognitive deficits (72.41%) and mood symptoms (69.23%). CT scans results consisted of 29 (44.62%) normal scans and 36 (55.38%) abnormal scans. Atrophy was the most common (72%) radiological finding in abnormal CT scans. No associations were found between current proposed CT guidelines in psychiatric patients, although a history of previous traumatic brain injury (TBI) approached significance ($p = 0.054$). There was a significant correlation between abnormal CT scans and past or current substance use ($X^2 = 5.9508$ $P = .015$). Abnormal CT findings increased with the Centers for Disease Control and Prevention (CDC) HIV immunological stage progression. The management of 9 patients changed; 7 of these CT scans were abnormal.

Conclusion. In this study of CTB scans in HIV+ psychiatric inpatients, previously suggested criteria proposed in guidelines for imaging were not associated with significantly higher rates of abnormal CT findings. Current or previous substance use correlated with significant higher rates of abnormal CT findings. Due to the high yield of abnormal CT scans in this study, it is suggested that HIV+ psychiatric inpatients with previous or current substance use, a history of TBI or HIV immunological stages B or C, are considered for imaging. It is recommended that further studies with larger sample sizes, consisting of inpatient and outpatient populations, with control groups be conducted to investigate current or previous substance use as an indication in guidelines for CTB scan in HIV+ psychiatric patients.

INTRODUCTION

The impact of the human immunodeficiency virus (HIV) pandemic on world-wide health care systems is substantial with resource-limited settings (RLS) most affected. South Africa (SA) is located at the epicentre of the pandemic, with 12.7% of total population in 2016 infected with HIV.[1]

HIV positive (HIV+) patients are at an increased risk for mental illness. The brain is a target of HIV infection early on in the disease and neuropsychiatric disorders may occur at any stage of the disease. Neuroimaging investigations are often part of the diagnostic workup in HIV.[2] The shift of HIV to a chronic illness also means that more neuroimaging investigations, such as CT scans, will be performed in the future as part of the management plan of these patients.[3] Computerised tomography (CT) and magnetic resonance imaging (MRI) are structural neuroimaging modalities most often used in clinical settings. MRI is regarded as the neuroimaging modality of choice as it produces higher resolution images, especially of the sub-cortex. However, in RLS, CT does provide some advantages over MRI as it is less expensive, is more widely available and has fewer contraindications.[4] Despite the availability of CT, it remains a restricted resource, and it is not clear whether every patient with HIV and a serious mental illness (SMI) requires a CT brain (CTB) scan.

No clear guidelines exist for the use of CTB scans in psychiatric inpatient and outpatient populations. Several studies have attempted to generate guidelines for the use of imaging studies in psychiatric populations: Generally, studies recommend CTB scans for patients with (i) a history of head injury, (ii) abnormal neurological examination, (iii) the presence of confusion or cognitive decline, (iv) first onset psychosis or personality change after the age of 50 years and (v) any atypical presentation.[5] These studies are however limited to the respective study populations reported on and therefore generalisability remains a limitation. The yield of abnormal CTB scans in psychiatric patients is also highly variable, ranging from 7% to 53%[6,7]. Factors contributing to the variability including selection bias, differences in defining CTB abnormalities and unique differences in study populations.

Groote Schuur Hospital is a tertiary hospital in the Western Cape in a RLS. CT is the primary neuroimaging modality as access to MRI remains restricted. No clear guidelines are available as to which HIV+ psychiatric patients will benefit most from CTB scans. As many patients with both HIV and psychiatric disorder are seen and managed, a targeted approach to requesting CTB is desirable, in order to set priorities and plan investigations during admission (i.e. urgent vs non-urgent scans). This study was conducted to provide information on the current CTB scan yield of HIV+ psychiatric patients as an essential initial step for guideline development in this sub-population.

In order to address this gap, we aimed to explore the following (i) to determine the yield of abnormal CTB scans in HIV+ psychiatric patients, (ii) to describe these abnormalities and (iii) to describe demographic and clinical variables associated with an abnormal CTB scan in HIV+ patients with a psychiatric disorder.

METHODS

Study setting

A retrospective folder review was conducted in the clinical Department of Psychiatry and Mental Health at Groote Schuur Hospital (GSH) in Cape Town. GSH is an academic teaching hospital affiliated to the University of Cape Town (UCT). The department provides services at secondary and tertiary level, including service at the Emergency Unit, as well as neuropsychiatric and liaison-therapeutic admissions. The study was approved by the Human Research Ethics committee (HREC) of the UCT.

Criteria for eligibility

The study investigated all psychiatric inpatients, confirmed to be HIV+, who received a CTB scan during the study period January 2013 to June 2015. Inclusion criteria were: (i) male and female psychiatric inpatients, (ii) above 18 years of age, (iii) who presented at GSH, (iv) during the study period, (v) confirmed HIV seropositive by laboratory HIV enzyme-linked immunosorbent assay (ELISA) or detectable HIV viral load, (vi) who received one or more CTB scan (contrasted or uncontrasted) at or during their admission within the study period. Exclusion criteria were: (i) patients below 18 years, (ii) CTB scans performed outside of GSH and (iii) HIV status not confirmed by laboratory HIV ELISA or HIV viral load.

Study Procedures

Medical records and radiological reports of all patients that met the inclusion an exclusion criteria were obtained and reviewed. Data were grouped as: (i) demographic data and history, (ii) clinical data, (iii) other special investigations, (iii) radiological data and (iv) a change in management. Psychiatric symptoms were grouped into clusters of affective (mood), psychotic, anxiety, post-traumatic, cognitive and other psychiatric symptoms. The Mini Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA) and The International HIV Dementia Scale (IHDS) scores were recorded as evidence for cognitive impairment. The final CTB report for the first CTB scan performed for each patient was reviewed. The validity of these scales in a South African population have been investigated in studies by Joska (2011) and Goodkin (2014). [8,9] CTB scan findings were recorded as normal (negative) or abnormal (positive). The presence of atrophy on CTB scans was regarded as a positive finding. Different methods have been proposed to quantify atrophy, however these methods are not commonly used in clinical settings especially with lower resolution CT imaging. Cluster of differentiation 4 (CD4) T-lymphocyte count was used for immunological staging. Immunological stages set out by the Centers for Disease Control and Prevention (CDC) are (1) category A, with a CD4 count of more than 500, (2) category B, with a CD4 count between 200-500 and (3) category C, with a CD4 count below 200.[10] Medical records of all patients with abnormal CTB scan reports were reviewed for a change in management. A change in management was defined as any change in the diagnosis, treatment or prognosis as a result of the CTB scan report.

Statistical analysis

We calculated percentages, minimum and maximum values, 95% confidence intervals, medians and means including standard deviations. The Chi-square test was used to explore differences between categories of abnormal and normal CTB scans. The association between categorical characteristics of the group with normal CTB scans and the group with abnormal CTB scans were determined using Pearson’s correlation co-efficient. Cramér's V was used to

measure the strength of association between variables. Data analysis was done using STATA data package. A P value of $P < 0.05$ was considered statistically significant.

RESULTS

Sample characteristics

During the 30-month study period, 65 patients met the study inclusion criteria of which 26 (40%) were male and 39 (60%) female. Patients ranged in age from 19 to 64 years (mean=36.2; SD=10.4). The males were generally older: Nearly half of male patients (46.15%) were in the age category 31 – 40 years and very few (7.69%) in the age category 18 – 30 years. In contrast, almost half (48.72%) of females were in the age category 18 – 30 years and fewest (5.13%) in the age category 51 – 65 years. The study population consisted of 73.85% black, 16.92% coloured, 7.69% white and 1.54% and mixed race patients.

The most common presenting psychiatric symptoms overall were psychosis (81.54%), cognitive deficits (72.41%) and mood symptoms (69.23%). In the study population 9 patients were newly diagnosed HIV+, 13 defaulted ARV treatment and 17 had a detectable viral load. CTB scan results consisted of 29 (44.62%) normal scans and 36 (55.38%) abnormal scans.

Imaging findings

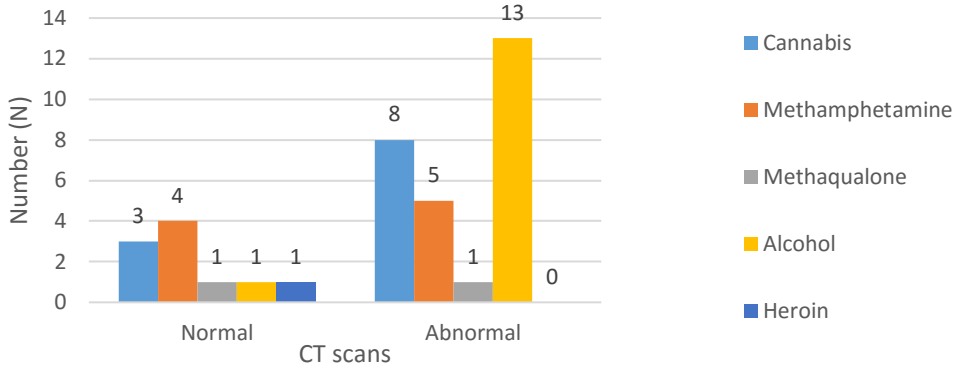
More than half of CTB scans (55.38%) were reported as abnormal. Details of the abnormal findings are listed in **Table 1.** No adverse events were documented for any of the CTB scans performed.

Table 1
Abnormal CTB findings

Details	*Number (N)*
Atrophy	28
Findings consistent with neurocysticercosis	4
Encephalomalacia	1
Nonspecific white matter lesions	2
Nonspecific calcified granulomas	4

Nearly two thirds of male patients (61.54%) had abnormal scans- see **Table 2**. In the group with abnormal scans the gender distribution was similar, 18 (75%) had a history of current or previous substance use, 8 (53.33%) had a history of seizures, 7 (87.50%) had a history of traumatic brain injury (TBI) and for 16 (50%) patients, this was the index presentation to psychiatry. Details of the type of substance use, and substance use by age groups are indicated in **figure 1**.

Figure 1 Current or previous substance use



There was no significant difference between the abnormal and normal CTB scan groups with regard to a history of seizures, TBI or an index presentation to psychiatry.
There was however a significant correlation between abnormal CT scans and past or current substance use (X^2 = 5.9508 P = .015). **Table 2** reflects demographic, clinical and disease variables, commonly listed as key variables supporting the need for CTB in general or HIV populations. Although the numbers of patients with a history of TBI was small, this characteristic approached significance (p = .054).

Table 2
Characteristics of the study sample

Characteristics	*Number (N)*	*Normal CTB (N=29)*	*Abnormal CTB (N=36)*	*Statistical analysis*
Demographic data:				
Gender				X^2 = 0.6641 P = .415
-male	26	10 (38.46)	16 (61.54)	
-female	39	19 (48.72)	20 (51.28)	
Ethnicity				X^2 = 0.8806 P = .830
-black	48	22 (45.83)	26 (54.17)	
-coloured	11	5 (45.45)	6 (54.55)	
-white	5	2 (40.00)	3 (60.00)	
-mixed	1	0	1	
Current or previous substance use	24	6 (25.00)	18 (75.00)	**X^2 = 5.9508 P = .015**
Current or past seizures	15	7(46.67)	8 (53.33)	X^2 = 0.5307 P = .466
History of traumatic brain injury	8	1 (12.50)	7 (87.50)	**X^2 = 3.7187 P = .054**
Current or past tuberculosis	24	12 (50.00)	12 (50.00)	X^2 = 1.7830 P = .410
-current	9	6 (66.67)	3 (33.33)	
-past	15	6 (40.00)	9 (60.00)	
Index presentation to psychiatry	32	16 (50.00)	16 (50.00)	X^2 = 0.7722 P = .380
Older than 50 years and index presentation	1	0	1	X^2 = 0.6000 P = .439
Clinical data:				
Presenting psychiatric symptoms				
-mood	45	18 (40.00)	27 (60.00)	X^2 = 1.2608 P = .262
-psychotic	53	23 (43.40)	30 (56.60)	X^2 = 0.1727 P = .678
-delirium	5	4 (80.00)	1 (20.00)	X^2 = 2.7447 P = .098
-other	15	5 (33.33)	10 (66.67)	X^2 = 1.0045 P = .316
Cognitive deficits	21	8 (38.10)	13 (61.90)	X^2 = 0.0009 P = .976
Focal neurological signs	6	4 (66.67)	2 (33.33)	X^2 = 1.2183 P = .270
Newly diagnosed HIV	9	6 (66.67)	3 (33.33)	X^2 = 2.0557 P = .152
Defaulted ARVs	13	4 (30.77)	9 (69.23)	X^2 = 0.5989 P = .439

Table 2 Characteristics of the study sample				
Other special investigations:				
Immunological stage	64			$X^2 = 0.8417$ P = .656
-stage A	15	8 (53.33)	7 (46.67)	
-stage B	28	12 (42.86)	16 (57.14)	
-stage C	21	8 (38.10)	13 (61.90)	
HIV viral load	30			$X^2 = 1.0860$ P = .297
-detectable	17	7 (41.18)	10 (58.82)	
-lower than detectable	13	3 (23.08)	10 (76.92)	
EEG	10			$X^2 = 0.9105$ P = .340
-normal	10	3 (30.00)	7 (70.00)	
-abnormal	0	0	0	
CSF	54			$X^2 = 3.5609$ P = .169
-normal	38	20 (52.63)	18 (47.37)	
-abnormal	16	4 (25.00)	12 (75.00)	
-not performed	10	4 (40.00)	6 (60.00)	

There were no significant differences in the distribution of presenting psychiatric symptom clusters across normal and abnormal scan groups. There were higher proportions of patients with mood disorders (60 vs 40%) and cognitive deficits (61.90 vs 38.10%) but these were not significant. Of note, a higher number of patients with delirium had normally reported scans (80 vs 20%) but the numbers were very small. These proportions are shown in **Figure 2**. Focal neurological deficits were present in 6 patients of which only 2 (33.33%) had abnormal scans. Of the 9 newly diagnosed HIV+ patients, 3 (33.33%) had abnormal scans. The majority of patients (69.23%) who defaulted ARV treatment had abnormal scans. (**Table 2**).

Figure 2 Presenting psychiatric symptoms

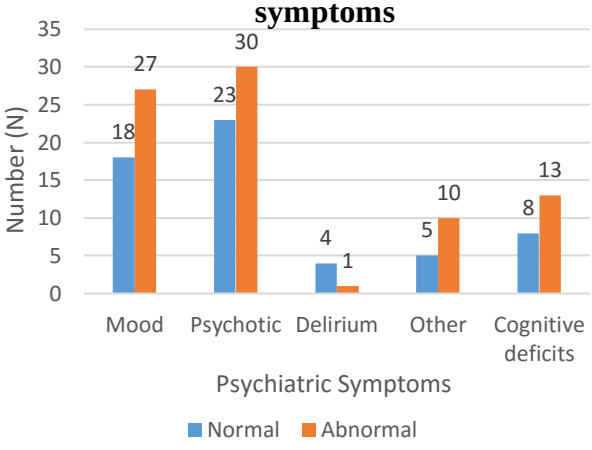
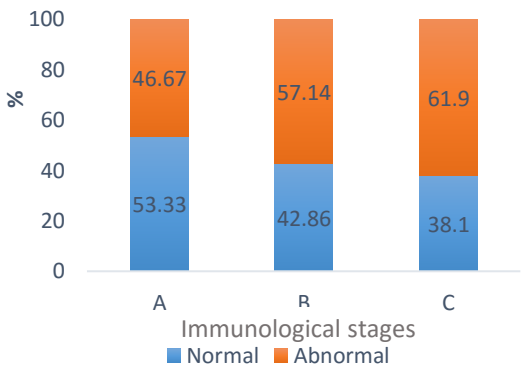


Figure 3 Normal and abnormal scans according to immunological stages



HIV disease characteristics

Nearly half of patients (43.75%) with a known CD4 count were classified as stage B according to the CDC immunological classification of HIV. In the group with abnormal CTB scans 7 (19.44%) of the 36 with abnormal scans were classified stage A, 16 (44.44%) stage B and 13 (36.11%) stage C. The majority (61.90 vs 38,10%) of the stage C had abnormal CTB scans. **Table 3** and **Figure 3** set out the characteristics of the study sample associated with the HIV immunological stages. The proportion of normal scans decreased with disease stage progression. Of the female patients, there were more with stage B and stage C disease. More patients with an index presentation were in these later stages of disease and more patients with current tuberculosis (TB) had late stage disease. A significant correlation was found

between index presentation to psychiatry and CDC HIV immunological stages ($X^2 = 9.1101$ P = .011).

Table 3
Characteristics of the study sample associated with HIV immunological stages

Characteristic	*Number (N)*	*Stage A*	*Stage B*	*Stage C*	*Statistical analysis*
Gender					$X^2 = 5.5943$ P =.061
-male	26	9 (34.62)	7 (26.92)	10 (38.46)	
-female	38	6 (15.79)	21 (55.26)	11 (28.95)	
Current or previous substance use	24	5 (20.83)	12 (50.00)	7 (29.17)	$X^2 = 0.7670$ P = .681
Index presentation to psychiatry	31	3 (9.68)	14 (45.16)	14 (45.16)	**$X^2 = 9.1101$ P = .011**
Newly diagnosed HIV	8	1 (12.50)	4 (50.00)	3 (37.50)	$X^2 = 0.6095$ P = .737
Defaulted ARVs	13	3 (23.08)	6 (46.15)	4 (30.77)	$X^2 = 0.1478$ P = .929
Previous ARV treatment failure	11	0	8 (72.73)	3 (27.27)	$X^2 = 5.5552$ P = .062
Presence of focal neurological signs	13	5 (38.46)	6 (46.15)	2 (15.38)	$X^2 = 3.1135$ P = .211
Tuberculosis	24				$X^2 = 9.0081$ P = .061
-current	9	0	3 (33.33)	6 (66.67)	
-previous	15	3 (20.00)	8 (53.33)	4 (26.67)	
Atrophy	28	4 (14.28)	13 (46.43)	11 (39.29)	$X^2 = 1.8295$ P = .767

An equal distribution was found in the group with abnormal CTB scans with a detectable and a lower than detectable viral load. The majority (58.82%) of patients with a detectable viral load had abnormal CTB scans. Electroencephalograms (EEGs) were requested for 10 patients – and all were reported as being within normal limits. CSF analysis were done on 54 patients of which 16 (29.63%) had abnormal results. The majority of patients with abnormal CSF results (75%) had abnormal CTB scans. These differences, however, did not reach statistical significance. No significant difference was found between the abnormal and normal group with regard to data on special investigations (**Table 2**).

Outcomes of imaging

A total of 9 patients had a change in their management associated with the CTB scan findings. All except 1 of these CTB scans were abnormal. A brain MRI scan was requested for the patient with the normal CTB scan – the MRI was reported as normal. Details of the type the management change are listed in **Table 4**.

Table 4
Change in patient management associated with CTB findings

Characteristics	*Normal CT (N)*	*Abnormal CT (N)*	*Statistical analysis*
Change in management as a direct result of CT scan findings	1	8	$X^2 = 4.7456$ P = .029
Type of management change			
-additional special investigations requested	1	3	
-change in diagnosis	0	4	
-other management changes	0	1	

Table 5 compare the study results with current recommended guidelines advocating CTB scans in psychiatric patients. None of these variables were significant – a previous history of TBI approached significance level.

Table 5
Results according to current recommendations for CTB in psychiatric patients (N (%))

Recommended indication	*Total*	*CTB Normal (N)*	*CTB Abnormal (N)*	*Statistical analysis*
Previous significant traumatic brain injury	8	1 (12.50)	7 (87.50)	**X^2 = 3.7187 P = .054**
Focal neurological signs	6	4 (66.67)	2 (33.33)	X^2 = 1.2183 P = .270
Presence of cognitive decline	21	8 (38.10)	13 (61.90)	X^2 = 0.0009 P = .976
First onset psychosis after the age of 50 years	1	0	1	X^2 = 0.6000 P = .439

DISCUSSION

The overall yield of abnormal CTB scans in this study was high (55.38%). Atrophy was the most common (72%) radiological finding in abnormal CTB scans. A significant correlation was found between abnormal CTB scans and current or previous substance use. In this retrospective study, we did not find associations between proposed CTB guidelines in psychiatric patients, although a history of previous TBI neared significance.

The high yield of abnormal CTB scans indicate that our study population should be considered at high risk for abnormal CTB scans. Other studies that investigated CTB in psychiatric patients had similar high yields at 35%, 53% and 49.8%.[6,11,12] The reason for the high yield is probably related to the sample taken from a tertiary hospital population. It is likely that the yield would be lower in non-inpatient samples and primary health care settings. In our study, as HIV immunological stage progressed abnormal CTB scans increased. Similarly, as HIV immunological stage progressed the psychiatric symptom cluster presentations increased. Therefore, in our study HIV immunological stage progression, CDC B and C, was associated with higher abnormal CTB scans and psychiatric symptom clusters presentation.

Cerebral atrophy is a common finding in CTB scans of HIV+ patients.[13] In a study conducted by Pfefferbaum (2012) that investigated the effects of AIDS, alcohol and age in HIV infection, advanced CDC HIV stages revealed higher cerebral volume deficits in the HIV only group.[18,19] In our study a higher proportion of atrophy was present in immunological stages B and C. The incidence of atrophy in our study (43.08%) was similar to previous studies. Previous studies investigating CTB findings in HIV+ populations found atrophy in 38% and 45% of CTB scans, while in general psychiatric populations atrophy has been reported in 35% and 40% of CTB scans respectively.[14,15,16,17] Both of these studies, in general psychiatric populations, were conducted in inpatient populations with first episode psychosis and other SMI requiring admission. In addition to the presence of SMI contributing to CT changes, neuroimaging studies have also reported structural brain changes associated with substance and alcohol use. Common findings include diffuse atrophy and nonspecific lesions.[19] Combinations of these factors in our population, including the high prevalence of substance use most likely explain why atrophy was the most common finding in abnormal CTB scans.

A study conducted by Patel (2002) indicated that neurocognitive deficits significantly correlated with brain atrophy in a cohort of HIV+ and noninfected indiviuals. The study found that atrophy predicted a poor neuropsychological test score performed by using a standard battery of eight tests (NPZ-8 test battery).[20] Cognitive impairement in HIV+ individuals is a significant barrier to the management of risk behaviour and is associated with suboptimal adherence to treatment. The presence of brain atrophy must therefore be taken into account in the management of HIV+ psychiatric patients as adherence strategies should be stepped up to ensure adequate follow up and treatment adherence.[21]

The small sample size probably limited our study from finding associations with previous suggested guidelines for CTB scans in psychiatric patients. A history of TBI is a salient finding on history taking and therefore one of the proposed indications for CTB scans in psychiatric patients likely to be recorded. This may account for the near significance finding despite our small sample size.

Generalisability of this study is limited due to the focused population - consisting of a unique subset within a psychiatric population treated at a tertiary hospital. The majority of previous studies investigated the yield of CTB scans in general psychiatric populations and therefore comparing study results with other studies may not represent an accurate finding. The incidence of HIV associated opportunistic infections and other neurological disease entities in this study may not be a true reflection of the population incidence, as this group of patients are primarily referred to neurology for management. Finding statistically significant associations between groups was limited by the small sample size and therefore the measure of association between a history of substance use and atrophy could not established. Nonetheless, the study findings provide essential data on the population subset not previously know.

Previous studies that investigated CTB in psychiatric patients were able to recruit higher sample sizes from general psychiatric populations, however limited data was generated on HIV within these populations. In our study we were able to generate data on HIV+ psychiatric patients, however the sample size was affected by narrowing the inclusion criteria.

Our study results indicate that past or current substance use and a history of TBI increase the probability of abnormal CTB findings in HIV+ psychiatric inpatients.

CONCLUSION

In this study of CTB in HIV+ psychiatric inpatients, we note that previously suggested criteria proposed as a guideline for imaging were not associated with significantly higher rates of abnormal CTB findings, although the presence of previous TBI neared significance. We did find that current or previous substance use was associated with significant higher rates of abnormal CTB findings. Abnormal CTB findings increased with CDC HIV immunological stage progression. Atrophy was the most common finding in abnormal CTB scans. The data may be limited by the sample size due to the narrow inclusion criteria. Due to the high yield of abnormal CTB scans in this study, it is suggested that HIV+ psychiatric inpatients with previous or current substance use, a history of TBI or HIV immunological stages B or C, are considered for imaging as those with abnormal findings are highly likely to undergo a change in management.

It is recommended that further studies with larger sample sizes, consisting of inpatient and outpatient populations, with control groups be conducted to investigate current or previous substance use as a proposed indication for CTB scan in HIV+ psychiatric patients.

REFERENCES

1. Statistics South Africa. Mid-year population estimates. 2015. Available from: http://www.statssa.gov.za/publications/P0302/P03022016.pdf
2. Myer L, Smit J, Le Roux L, Parker S, Stein DJ, Seedat S. 2008. Common mental disorders among HIV-infected individuals in South Africa: prevalence, predictors, and validation of brief psychiatric rating scales. AIDS Patient Care STDS 2008; 22(2):147–158. Available from: https://doi.org/10.1089/apc.2007.0102
3. Lund C, Petersen I, Kleintjes S, Bhana A. Mental Health Services in South Africa: Taking stock. Afr J Psychiatry 2012;15:402-405. Available from: https://doi.org/10.4314/ajpsy.v15i6.48
4. Malhi GS, Lagopoulos J. Making sense of neuroimaging in psychiatry. Acta Psychiatr Scand 2008;117(2):100-117. Available from: https://doi.org/10.1111/j.1600-0447.2007.01111.x
5. Thurnher, MM, Donovan Post MJ. Neuroimaging in the Brain in HIV-1-Infected Patients. Neuroimaging Clin N Am 2008;18(1):93-11. Available from: https://doi.org/10.1016/j.nic.2007.12.013
6. Hollister LE, Boutros N. Clinical use of CT and MR scans in psychiatric patients. J Psychiatry Neurosci 1991;16(4):194-198.
7. Battalion J, Spector IC. Utility of the CAT scan in a first psychotic episode. Gen Hosp Psychiatry1998;10(6):398-401. Available from: https://doi.org/10.1016/0163-8343(88)90062-x
8. Joska J, Westgarth-Taylor J, Hoare J, Thomas K, Paul R, Myer L, Stein D. Validity of the International HIV Dementia Scale in South Africa. AIDS patient care and STDs 2011;25(2):95-101. Available from: https://doi.org/10.1089/apc.2010.0292
9. Goodkin K, Hardy DJ, Singh D, Lopez E. Diagnostic utility of the International HIV Dementia Scale for HIV-associated neurocognitive impairment and disorder in South Africa. J Neuropsychiatry Clin Neurosci 2014;26(4):352-358. Available at https://doi.org/10.1176/appi.neuropsych.13080178
10. Centers for Disease Control and Prevention. Revised classification system for HIV infection and expanded surveillance case definition for AIDS among adolescents and adults. 1993. Available from: http://www.cdc.gov/mmwr/preview/mmwrhtml/00018871.htm
11. Moles JK, Franchina JJ, Sforza PP. Increasing the clinical yield of computerized tomography for psychiatric patients. Gen Hosp Psychiatry 1998;20(5):282-291. Available from: https://doi.org/10.1016/s0163-8343(98)00040-1
12. Jeenah FY, Moosa MYH. CT scans in psychiatric patients - An exploratory study at Chris Hani Baragwanath Hospital. S Afr J Psychiatr 2007;13(1):22-25. Available from: https://doi.org/10.4102/sajpsychiatry.v13i1.7
13. Ramsey RG, Germia GK. CNS complications of AIDS: CT and MR findings. Am J Roentgenol 1998;151(3):449-454. Available from: https://doi.org/10.2214/ajr.151.3.449
14. Robert M, Rosenbloom S, Perrett LV. Neuroradiological findings in AIDS: A review of 200 cases. AJNR Am J Neuroradiol 1986;7:833-839. Available from: https://doi.org/10.2214/ajr.147.5.977
15. Seth R, Granville-Grossman K, Goldmeier S, Lynch S. Psychiatric illnesses in patients with HIV infection and AIDS referred to the liaison psychiatrist. Br J Psychiatry 1991;159:347-350. Available from: https://doi.org/10.1192/bjp.159.3.347
16. Larson EB, Mack LA, Watts B, Cromwell LD. Computed tomography in patients

with psychiatric illnesses: advantage of a ‘rule in’ approach. Ann Intern Med 1981;95(3):360-364. Available from: https://doi.org/10.7326/0003-4819-95-3-360
17. Gewirtz G, Squires-Wheeler E, Sharif Z, Honer WG. Results of computerised tomography during first admission for psychosis. Br J Psychiatry 1994;50:789-795. Available from: https://doi.org/10.1192/bjp.164.6.789
18. Pfefferbaum A, Rosenbloom MJ, Sassoon SA, et al. Regional Brain Structural Dysmorphology in HIV Infection: Effects of AIDS, Alcoholism, and Age. Biol Psychiatry 2012;72(5):361–370. Available from: https://doi.org/10.1016/j.biopsych.2012.02.018
19. Geibprasert S, Gallucci M, Krings T. Alcohol-induced changes in the brain as assessed by MRI and CT. Eur Radiol 2010;20(6):1492-1501. Available from: https://doi.org/10.1007/s00330-009-1668-z
20. Patel SH, Kolson DL, Matozzo I, et al. Correlation between percentage of brain parenchymal volume and neurocognitive performance in HIV-infected patients. AJNR Am J Neuroradiol 2002;23(4):543-549.
21. Anand P, Springer SA, Copenhaver MM, Altice FL. Neurocognitive impairment and HIV risk factors: A reciprocal relationship. AIDS behav 2010;14(6):1213-1226. Available from: https://doi.org/10.1007/s10461-010-9684-1

APPENDIX

DATA CAPTURE SHEET

STUDY NUMBER - - -	
DATE OF ADMISSION	*(dd/mm/yr)* —/—/—
DATE OF CT	*(dd/mm/yr)* —/—/—
CT FINDINGS	NORMAL ABNORMAL
14 DAYS POST CT	*(dd/mm/yr)* —/—/—
CHANGE IN MANAGEMENT	YES NO

COMMENTS:

DEMOGRAPHIC DATA			
AGE (on admission)	DATE OF BIRTH (dd/mm/yr) ___/___/___ YEARS _____		[ ] 18-30 [ ] 31-40 [ ] 41-50 [ ] 51-65 [ ] > 65
HIGHEST LEVEL OF EDUCATION	[ ] STANDARD _____ [ ] GRADE _____ [ ] OTHER _____ [ ] NOT KNOWN		[ ] < GRADE 5 [ ] GRADE 5 - 9 [ ] GRADE 10 - 12 [ ] > GRADE 12 [ ] NOT KNOWN
GENDER			[ ] MALE [ ] FEMALE [ ] OTHER
RELATIONSHIP STATUS (on admission)	[ ] SINGLE [ ] MARRIED [ ] DIVORCED [ ] WIDOWED [ ] NOT KNOWN		[ ] SINGLE [ ] NON-SINGLE [ ] NOT KNOWN
ETHNICITY			[ ] BLACK [ ] COLOURED [ ] WHITE [ ] ASIAN [ ] MIXED [ ] OTHER _____ [ ] NOT KNOWN
SUBSTANCE HISTORY	ILLICIT: [ ] Yes [ ] No [ ] Not known ALCOHOL: [ ] Yes [ ] No [ ] Not known	list Illicit substances: _____ _____ _____ _____ _____ _____ _____ _____ _____ _____ _____ _____ _____ _____ _____ _____ _____	SUBSTANCE: [ ] Yes [ ] No [ ] Not known
SEIZURE HISTORY			[ ] YES [ ] NO [ ] NOT KNOWN
TRAUMATIC HEAD INJURY HISTORY			[ ] YES [ ] NO [ ] NOT KNOWN

DEMOGRAPHIC DATA			
CEREBRAL VASCULAR ACCIDENT HISTORY			[ ] YES [ ] NO [ ] NOT KNOWN
INDEX PRESENTATION TO PSYCHIATRY			[ ] YES [ ] NO [ ] NOT KNOWN

CLINICAL DATA			
PRESENTING PSYCHIATRIC SYMPTOMS (before date of CT)	MOOD/AFFECTIVE: [ ] Depressive [ ] Dysthymic [ ] Hypomanic [ ] Manic [ ] Mixed PSYCHOTIC [ ] Thought disordered [ ] Delusions [ ] Perceptual disturbances [ ] ANXIETY [ ] PTSD [ ] OCD [ ] COGNITIVE [ ] OTHER	list other symptoms: _____ _____ _____ _____ _____ _____ _____ _____ _____ _____ _____ _____ _____ _____ _____ _____ _____ ___	[ ] MOOD/ AFFECTIVE [ ] PSYCHOTIC [ ] ANXIETY [ ] PTSD [ ] OCD [ ] COGNITIVE [ ] OTHER
COGNITIVE TESTING AND SCREENING TESTS (during admission)	[ ] MMSE __/__ [ ] > 26 (normal) [ ] 24 - 26 (mild cognitive impairment) [ ] < 24 (cognitive impairment) [ ] MoCA __/__ [ ] 18-26 (mild cognitive impairment) [ ] 10-17 (moderate cognitive impairment) [ ] < 10 (severe cognitive impairment. [ ] IHDS __/12 [ ] >10 (normal) [ ] 10 or less (positive)		NEUROCOGNITIVE DEFICITS [ ] Present [ ] Absent

CLINICAL DATA			
PHARMACO LOGICAL TREATMENT (on date of CT)	ARVs [ ] Yes [ ] No [ ] Not known PSYCHIATRIC [ ] Antidepressants [ ] Antipsychotics [ ] Anxiolytics [ ] Mood stabilisers (including anti-convulsants used for mood stabilizing properties) [ ] Other psychiatric OTHER [ ] Anti-convulsants (used specifically for seizure disorders) [ ] TB Rx	list psychotropics: _____	ARVs [ ] Yes [ ] No [ ] Not known PSYCHOTROPICS [ ] Yes [ ] No [ ] Not known
HIV	CONFIRMED DATE: *(mm/yr)* ___/___ [ ] NOT KNOWN CONFIRMATION TEST: [ ] ELISA [ ] Viral load ARV START DATE *(mm/yr)* ___/___ [ ] Not known COMPLIANT-ARVs [ ] Yes [ ] No [ ] Not known PREV ARV Rx FAILURE [ ] Yes [ ] No [ ] Not known	LAST CD COUNT: _____ Date *(mm/yr)* ___/___ [ ] Not known IMMUNOLOGICAL STAGE: [ ] A CD4 >500 [ ] B CD4 200-500 [ ] C CD4 < 200	ARVs initiated [ ] < 6 week prior to date of admission [ ] > 6 weeks prior to date of admission [ ] not known COMPLIANT-ARVs [ ] Yes [ ] No [ ] Not known PREV ARV Rx FAILURE [ ] Yes [ ] No [ ] Not known IMMUNOLOGICAL STAGE [ ] Not known [ ] A [ ] B [ ] C

CLINICAL DATA			
COMORBID CONDITIONS (CURRENT EXCLUDING HIV AND PSYCHIATRIC)	NEUROLOGICAL CONDITION [ ] Yes [ ] No [ ] Not known FOCAL NEUROLOGICAL SIGNS [ ] Yes [ ] No [ ] Not known TB [ ] Yes [ ] No [ ] Not known OTHER [ ] Yes [ ] No [ ] Not known	list focal neurological signs: _____ _____ _____ _____ _____ _____ _____ _____ _____ _____ _____ _____ _____ _____ _____ _____ _____	COMORBID CONDITIONS [ ] Yes [ ] No [ ] Not known FOCAL NEUROLOGICAL SIGNS [ ] Yes [ ] No [ ] Not known
COMPLICATIONS FROM CTs			[ ] Yes [ ] No [ ] Not known
PSYCHIATRIC DIAGNOSIS	AT TIME OF CT: _____ _____ _____ _____ _____ _____ _____ _____ _____ _____	AT DISCHARGE: _____ _____ _____ _____ _____ _____ _____ _____ _____ _____ __	CHANGE IN DIAGNOSIS [ ] Yes [ ] No [ ] Not known

OTHER SPECIAL INVESTIGATIONS			
CD4	LATEST CD4 _____ DATE *(mm/yr)* ___/___/___ [ ] Not known		CD4 [ ] < 200 [ ] 200-500 [ ] > 500 [ ] Not known
VIRAL LOAD (VL)	LATEST VL _____ DATE *(mm/yr)* ___/___/___ [ ] Not known		VL [ ] Detectable [ ] Lower than detectable [ ] Not known
CEREBRAL SPINAL FLUID (CSF) (during admission)	CSF [ ] Done [ ] Not done [ ] Not recorded	list CSF findings: _____ _____ _____ _____ _____ _____ _____ _____ _____ _____ _____	CSF [ ] Normal [ ] Abnormal [ ] Not known
ELECTRO ENCEPHALOGRAM (EEG) (during admission)	EEG [ ] Done [ ] Not done [ ] Not known	list EEG findings: _____ _____ _____ _____ _____ _____ _____ _____	EEG [ ] Normal [ ] Abnormal

RADIOLOGICAL FINDINGS			
COMPUTERISED TOMOGRAPHY (CT)	DATE *(dd/mm/yr)* ___/___/___ DEPARTMENT [ ] Psychiatry [ ] Emergency department [ ] Neurology [ ] Other _____ [ ] CONTRASTED [ ] UNCONTRASTED ATROPHY [ ] No [ ] Yes [ ] Age appropriate atrophy [ ] age inappropriate atrophy	list CTB abnormal findings: _____	CT findings [ ] Normal [ ] Abnormal [ ] Inconclusive

CHANGE IN MANAGEMENT			
DATE OF CT	*(dd/mm/yr)* ___/___/___		
14 DAYS POST CT	*(dd/mm/yr)* ___/___/___		
CHANGE IN MANAGEMENT	CHANGE IN MANAGEMENT [ ] No [ ] Yes [ ] Diagnosis [ ] Treatment [ ] Prognosis [ ] Special investigations [ ] Special orders [ ] Other	List changes in management: _____ _____ _____ _____ _____ _____ _____ _____ _____ _____ _____ _____	Change in management [ ] Yes [ ] No

ETHICS APPROVAL LETTER

UNIVERSITY OF CAPE TOWN
Faculty of Health Sciences
Human Research Ethics Committee

Room E52-24 Old Main Building
Groote Schuur Hospital
Observatory 7925
Telephone [021] 406 6338 • **Facsimile** [021] 406 6411
Email: sumayah.ariefdien@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

11 December 2015

HREC REF: 892/2015

Prof J Joska
Division of Psychiatry-Neuropsychiatry
Room 69
J-Block
GSH

Dear Prof Joska

PROJECT TITLE: THE DIAGNOSTIC YIELD OF COMPUTERIZED TOMOGRAPHY IN HUMAN IMMUNODEFICIENCY VIRUS (HIV) POSITIVE PSYCHIATRIC PATIENTS AT A TERTIARY HOSPITAL IN THE WESTERN CAPE (MMeD-candidate-Dr J Berwers)

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee (HREC) for review.

It is a pleasure to inform you that the HREC has **formally approved** the above-mentioned study.

Approval is granted for one year until the 30th January 2017.

Please submit a progress form, using the standardised Annual Report Form if the study continues beyond the approval period. Please submit a Standard Closure form if the study is completed within the approval period.
(Forms can be found on our website: www.health.uct.ac.za/fhs/research/humanethics/forms)

We acknowledge that the following student:- Dr J Berwers is also involved in this project.

Please quote the HREC reference no in all your correspondence.

Please note that the ongoing ethical conduct of the study remains the responsibility of the principal investigator.

Yours sincerely

pp T Burgess
PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE
Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938

Hrec/ref:892/2015

This serves to confirm that the University of Cape Town Research Ethics Committee complies to the Ethics Standards for Clinical Research with a new drug in patients, based on the Medical Research Council (MRC-SA), Food and Drug Administration (FDA-USA), International Convention on Harmonisation Good Clinical Practice (ICH GCP) and Declaration of Helsinki guidelines.

The Research Ethics Committee granting this approval is in compliance with the ICH Harmonised Tripartite Guidelines E6: Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95) and FDA Code Federal Regulation Part 50, 56 and 312.

Hrec/ref:892/2015

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- Quotes should be placed in single quotation marks: i.e. The respondent stated: '...'
- Round brackets (parentheses) should be used, as opposed to square brackets, which are reserved for denoting concentrations or insertions in direct quotes.
- If you wish material to be in a box, simply indicate this in the text. You may use the table format –this is the *only* exception. Please DO NOT use fill, format lines and so on.

SAMJ is a generalist medical journal, therefore for articles covering genetics, it is the responsibility of authors to apply the following:

- Please ensure that all genes are in italics, and proteins/enzymes/hormones are not.
- Ensure that all genes are presented in the correct case e.g. TP53 not Tp53.

**NB: Copyeditors cannot be expected to pick up and correct errors wrt the above, although they will raise queries where concerned.

- Define all genes, proteins and related shorthand terms at first mention, e.g. '188del11' can be glossed as 'an 11 bp deletion at nucleotide 188.'
- Use the latest approved gene or protein symbol as appropriate:

- Human Gene Mapping Workshop (HGMW): genetic notations and symbols
- HUGO Gene Nomenclature Committee: approved gene symbols and nomenclature
- OMIM: Online Mendelian Inheritance in Man (MIM) nomenclature and instructions
- Bennet et al. Standardized human pedigree nomenclature: Update and assessment of the recommendations of the National Society of Genetic Counselors. J Genet Counsel 2008;17:424-433: standard human pedigree nomenclature.

Preparation notes by article type

- Research
- Editorials
- CME
- In Practice and Case reports
- Reviews
- Clinical trials
- Correspondence
- Obituaries
- Book reviews
- Guidelines

Research

Guideline word limit: 4 000 words

Research articles describe the background, methods, results and conclusions of an original research study. The article should contain the following sections: introduction, methods, results, discussion and conclusion, and should include a structured abstract (see below). The introduction should be concise – no more than three paragraphs – on the background to the research question, and must include references to other relevant published studies that clearly lay out the rationale for conducting the study. Some common reasons for conducting a study are: to fill a gap in the literature, a logical extension of previous work, or to answer an important clinical question. If other papers related to the same study have been published previously, please make sure to refer to them specifically. Describe the study methods in as much detail as possible so that others would be able to replicate the study should they need to. Results should describe the study sample as well as the findings from the study itself, but all interpretation of findings must be kept in the discussion section, which should consider primary outcomes first before any secondary or tertiary findings or post-hoc analyses. The conclusion should briefly summarise the main message of the paper and provide recommendations for further study.

Select figures and tables for your paper carefully and sparingly. Use only those figures that provided added value to the paper, over and above what is written in the text.
Do not replicate data in tables and in text .

Structured abstract

- This should be 250-400 words, with the following recommended headings:
  - **Background:** why the study is being done and how it relates to other published work.
  - **Objectives:** what the study intends to find out
  - **Methods:** must include study design, number of participants, description of the intervention, primary and secondary outcomes, any specific analyses that were done on the data.
  - **Results:** first sentence must be brief population and sample description; outline the results according to the methods described. Primary outcomes must be described first, even if they are not the most significant findings of the study.
  - **Conclusion:** must be supported by the data, include recommendations for further study/actions.
- Please ensure that the structured abstract is complete, accurate and clear and has been approved by all authors.
- Do not include any references in the abstracts.

Here is an example of a good abstract.

Main article

All articles are to include the following main sections: Introduction/Background, Methods, Results, Discussion, Conclusions.
The following are additional heading or section options that may appear within these:

- Objectives (within Introduction/Background): a clear statement of the main aim of the study and the major hypothesis tested or research question posed
- Design (within Methods): including factors such as prospective, randomisation, blinding, placebo control, case control, crossover, criterion standards for diagnostic tests, etc.
- Setting (within Methods): level of care, e.g. primary, secondary, number of participating centres.
- Participants (instead of patients or subjects; within Methods): numbers entering and completing the study, sex, age and any other biological, behavioural, social or cultural factors (e.g. smoking status, socioeconomic group, educational attainment, co-existing disease indicators, etc)that may have an impact on the study results. Clearly define how participants were enrolled, and describe selection and exclusion criteria.
- Interventions (within Methods): what, how, when and for how long. Typically for randomised controlled trials, crossover trials, and before and after studies.
- Main outcome measures (within Methods): those as planned in the protocol, and those ultimately measured. Explain differences, if any.

Results

- Start with description of the population and sample. Include key characteristics of comparison groups.
- Main results with (for quantitative studies) 95% confidence intervals and, where appropriate, the exact level of statistical significance and the number need to treat/harm. Whenever possible, state absolute rather than relative risks.
- Do not replicate data in tables and in text.
- If presenting mean and standard deviations, specify this clearly. Our house style is to present this as follows:
- E.g.: The mean (SD) birth weight was 2 500 (1 210) g. Do not use the ± symbol for mean (SD).
- Leave interpretation to the Discussion section. The Results section should just report the findings as per the Methods section.

Discussion

Please ensure that the discussion is concise and follows this overall structure – sub-headings are not needed:

- Statement of principal findings
- Strengths and weaknesses of the study
- Contribution to the body of knowledge
- Strengths and weaknesses in relation to other studies

- The meaning of the study – e.g. what this study means to clinicians and policymakers
- Unanswered questions and recommendations for future research

Conclusions

This may be the only section readers look at, therefore write it carefully. Include primary conclusions and their implications, suggesting areas for further research if appropriate. Do not go beyond the data in the article.

Editorials

Guideline word limit: 1 000 words

These opinion or comment articles are usually commissioned but we are happy to consider and peer review unsolicited editorials. Editorials should be accessible and interesting to readers without specialist knowledge of the subject under discussion and should have an element of topicality (why is a comment on this issue relevant now?) There should be a clear message to the piece, supported by evidence.
Please make clear the type of evidence that supports each key statement, e.g.:

- expert opinion
- personal clinical experience
- observational studies
- trials
- systematic reviews.

CME (by invite only)

CME is intended to provide readers with practical, up-to-date information on medical and related matters. It is aimed at those who are not specialists in the field.
From January 2016, all CME articles will be printed in full in the *SAMJ*. Please try to adhere strictly to the guidelines on word count as we have a page limit for the print issue of the *SAMJ*. We reserve the right to place some tables and reference lists online if this is necessary for space.
In practice, this means that each CME topic usually covers two issues of the print issue of the *SAMJ*.

The guest editor, in consultation with the editor, is responsible for convening a team of authors, deciding on the subjects to be covered and for reviewing the manuscripts submitted. The suggestion is for 4 - 5 articles, although there is some room for flexibility contingent on discussions with the editor.

For queries about these guidelines please feel free to contact the CME editor, Dr Bridget Farham, by email (ugqirha@iafrica.com) or telephone (+27 (0)21 789 2331).

Review process

The guest editor reviews the articles and returns them to the CME editor for review and final approval.

Guest editorials

Guideline word limit: 1 000 words

- Include the guest editor's personal details (qualifications, positions, affiliation, e-mail address, and a short personal profile (50words)).
- If possible, include a photograph of the author(s) at high enough resolution for print. It is preferable to provide two guest editorials, one for each issue, so that the content of the articles in each issue is covered.

Articles

Guideline word limit: 2 000 - 3 000 words

- Each article requires an abstract of ±200 words.
- The editor reserves the right to shorten articles but will send a substantially shortened article back for author approval.

Personal details

Please supply: Your qualifications, position and affiliations and MP number (used for CPD points); Address, telephone number and fax number, and your e-mail address; and a short personal profile (50words)and a few words about your current fields of interest.

In Practice

Guideline word limit: 2 000 - 3 000words

This section includes articles that would previously have been accepted into the Forum section, and case reports.
In practice articles are those that draw attention to specific issues of clinical, economic or political interest regarding medicine and healthcare in southern Africa. They are assigned to a topic:

- Case report
- Clinical practice
- Clinical alert
- Issues in medicine
- Issues in public health
- Healthcare delivery
- Consensus/Position statement
- Medicine and the environment
- Medicine and the law
- Cochrane corner

An In Practice article should follow the following format – sub-headings are not necessary, but may be used for clarity:

- Author affiliations and qualifications: to be the same as for Research. Provide all authors' names and initials, qualifications and full affiliations, and corresponding author.
- Short abstract: does not need to be structured, but should capture the essential features of the article
- Introduction: the reason for the article and the issue being addressed
- Recent research, discussion, local policy around the issue – include your own research where appropriate
- All statements should be referenced and, if opinion only, this should be stated
- Discussion: how this article adds to the discussion around a particular topic
- If a clinical practice or policy point is at issue, this needs to be emphasised, using a box with highlights if appropriate.

Essentially In practice is an opportunity for a more discursive approach to topics of clinical, economic or political importance in southern African health systems. It is not an opportunity to put forward unsubstantiated opinions!

Case reports

The *SAMJ* has recently started to accept case reports. The cases must come from Africa, preferably southern Africa unless the condition is common to all African countries, and must be either a completely new description of a clinical condition or result (use Google!) or a case that highlights important practice or management issues.

Please use the following format for case reports:

- Title of case: do not include the words 'a case report' in the title
- Summary/abstract: up to 150 words summarising the case presentation and outcome
- Background: why is this case important and why did you write it up?
- Case presentation: presenting features, medical, social, family history as appropriate
- Case management: should be according to best practice, and if not, please explain why
- Investigations, if relevant: save space by simply saying 'normal' if, for example, renal function was completely normal, rather than listing normal results, highlight the abnormal – or indeed the normal if this is clinically significant

- Differential diagnosis, if relevant
- Treatment, if relevant
- Outcome and follow-up
- Discussion – a VERY BRIEF review of similar published cases
- Teaching points: 3 - 5 bullet points
- References: as per the *SAMJ* house style
- Tables and figures: keep to a minimum. Use clinical images where relevant – we need hi-res versions for print, and identifiable persons must have a consent form
- Patient consent: please include a statement about patient consent to a written case report. This should be uploaded as a supplementary file.

Clinical trials

Guideline word limit: 4000 words

As per the recommendations published by the International Committee of Medical Journal Editors (ICMJE), clinical trial research is any research that assigns individuals to an intervention, with or without a concurrent comparison/control group to study the cause-and-effect relationship between the intervention and health outcomes. All clinical trials should be registered with the appropriate national clinical trial registry (or any international primary register, if relevant), and the trial registration number should be cited at the end of the abstract. Since 1st December 2005, all clinical trials conducted in South Africa have been required to be registered in the South African National Clinical Trials Register. The *SAMJ* therefore requires that clinical trials be registered in the relevant public trials registry at or before the time of first patient enrollment as a condition for publication. The trial registry name and registration number must be included in the manuscript.

Please refer to the general guidelines for all papers at the top of this article for additional requirements with respect to ethics approval, funding, author contributions, etc. The format of original research articles should be followed for reporting of clinical trial results.

Review articles

Guideline word limit: 4 000 words

These are welcome, but should be either commissioned or discussed with the Editor before submission. A review article should provide a clear, up-to-date account of the topic and be aimed at non-specialist hospital doctors and general practitioners.

Please ensure that your article includes:
- Abstract: unstructured, of about 100-150 words, explaining the review and why it is important
- Methods: Outline the sources and selection methods, including search strategy and keywords used for identifying references from online bibliographic databases. Discuss the quality of evidence.
- When writing: clarify the evidence you used for key statements and the strength of the evidence. Do not present statements or opinions without such evidence, or if you have to, say that there is little or no evidence and that this is opinion. Avoid specialist jargon and abbreviations, and provide advice specific to southern Africa.
- Personal details: Please supply your qualifications, position and affiliations and MP number (used for CPD points); address, telephone number and fax number, and your e-mail address; and a short personal profile (50 words) and a few words about your current fields of interest.

Correspondence (Letters to the Editor)

Guideline word limit: 500 words

Letters to the editor should relate either to a paper or article published by the SAMJ or to a topical issue of particular relevance to the journal's readership

- May include only one illustration or table
- Must include a correspondence address.

Book reviews

Guideline word limit: 400 words

Should be about 400 words and must be accompanied by the publication details of the book. Provide a hi-res image of the cover if possible (with permission from the copyright holder).

Obituaries

Guideline word limit: 400 words

Should be offered within the first year of the practitioner's death, and may be accompanied by a photograph.

Guidelines

Guidelines should always be discussed with the Editor prior to submission.

Because of the intensive review process required to ensure Guidelines are independent, evidence-based and free from commercial bias, they are usually published as a supplement to the *SAMJ*, the costs of which must be covered by sponsorship, advertising or payment by the guideline authors/association. We will provide a quote based on the expected length of the guideline and whether it is to appear online only, or in print, which must be accepted by the body putting the guidelines together before submitting the work to the SAMJ.

The Editor reserves the right to determine the scheduling of supplements. Understandably, a delay in publication must be anticipated dependent upon editorial workflow.

All guidelines should be structured according to Agree II.
Please access this website before putting the guidelines together, download the Agree 11 instrument and use this to put the guidelines together.
All submitted guidelines will be sent to the local Agree II appraisal committee for review and must be endorsed by an appropriate body prior to consideration and all conflicts of interest expressed.

A structured abstract not exceeding 400 words (recommended sub-headings: *Background, Recommendations, Conclusion*) is required. Sections and sub-sections must be numbered consecutively (e.g. 1. Introduction; 1.1 Definitions; 2.etc.) and summarised in a Table of Contents.

Illustrations/photos/scans

- If illustrations submitted have been published elsewhere, the author(s) should provide consent to republication obtained from the copyright holder.
- Figures must be numbered in Arabic numerals and referred to in the text e.g. '(Fig. 1)'.
- Each figure must have a caption/legend: Fig. 1. Description (any abbreviations in full).
- All images must be of high enough resolution/quality for print.
- All illustrations (graphs, diagrams, charts, etc.) must be in PDF form.
- Ensure all graph axes are labelled appropriately, with a heading/description and units (as necessary) indicated. Do not include decimal places if not necessary e.g. 0; 1.0; 2.0; 3.0; 4.0 etc.
- Scans/photos showing a specific feature e.g. *Intermediate magnification micrograph of a low malignant potential (LMP) mucinous ovarian tumour. (H&E stain).* –include an arrow to show the tumour.
- Each image must be attached individually as a 'supplementary file' upon submission (not solely embedded in the accompanying manuscript) and named Fig. 1, Fig. 2, etc.

Tables

- Tables should be constructed carefully and simply for intelligible data representation. Unnecessarily complicated tables are strongly discouraged.
- Large tables will generally not be accepted for publication in their entirety. Please consider shortening and using the text to highlight specific important sections, or offer a large table as an addendum to

the publication, but available in full on request from the author
- Embed/include each table in the manuscript Word file - do not provide separately as supplementary files.
- Number each table in Arabic numerals (Table 1, Table 2, etc.) and refer to consecutively in the text.
- Tables must be cell-based (i.e. not constructed with text boxes or tabs) and editable.
- Ensure each table has a concise title and column headings, and include units where necessary.
- Footnotes must be indicated with consecutive use of the following symbols: * † ‡ § ¶ ‖ then ** †† ‡‡ etc.

Do not: Use [Enter] within a row to make 'new rows':

Rather:

Each row of data must have its own proper row:

Do not: use separate columns for *n* and %:

Rather:

Combine into one column, *n* (%):

Do not: have overlapping categories, e.g.:

Rather:

Use <> symbols or numbers that don't overlap:

References

NB: *Only complete, correctly formatted reference lists in Vancouver style will be accepted. Reference lists must be generated manually and not with the use of reference manager software. Endnotes must* ***not*** *be used.*

- Authors must verify references from original sources.
- Citations should be inserted in the text as superscript numbers between square brackets, e.g. These regulations are endorsed by the World Health Organization,[2] and others.[3,4-6]
- All references should be listed at the end of the article in numerical order of appearance in the Vancouver style (not alphabetical order).
- Approved abbreviations of journal titles must be used; see the List of Journals in Index Medicus.
- Names and initials of all authors should be given; if there are more than six authors, the first three names should be given followed by et al.
- Volume and issue numbers should be given.
- First and last page, in full, should be given e.g.: 1215-1217 **not** 1215-17.
- Wherever possible, references must be accompanied by a digital object identifier (DOI) link). Authors are encouraged to use the DOI lookup service offered by CrossRef:
  - On the Crossref homepage, paste the article title into the 'Metadata search' box.
  - Look for the correct, matching article in the list of results.
  - Click Actions > Cite
  - Alongside 'url =' copy the URL between { }.
  - Provide as follows, e.g.: https://doi.org/10.7196/07294.937.98x

Some examples:

- *Journal references:* Price NC, Jacobs NN, Roberts DA, et al. Importance of asking about glaucoma. Stat Med 1998;289(1):350-355. http://dx.doi.org/10.1000/hgjr.182
- *Book references:* Jeffcoate N. Principles of Gynaecology. 4th ed. London: Butterworth, 1975:96-101.
- *Chapter/section in a book:* Weinstein L, Swartz MN. Pathogenic Properties of Invading Microorganisms. In: Sodeman WA, Sodeman WA, eds. Pathologic Physiology: Mechanisms of Disease. Philadelphia: WB Saunders, 1974:457-472.
- *Internet references:* World Health Organization. The World Health Report 2002 - Reducing Risks,

Promoting Healthy Life. Geneva: WHO, 2002. http://www.who.int/whr/2002 (accessed 16 January 2010).

- Legal references
- Government Gazettes:

National Department of Health, South Africa. National Policy for Health Act, 1990 (Act No. 116 of 1990). Free primary health care services. Government Gazette No. 17507:1514. 1996.
In this example, 17507 is the Gazette Number. This is followed by :1514 - this is the notice number in this Gazette.

- Provincial Gazettes:

Gauteng Province, South Africa; Department of Agriculture, Conservation, Environment and Land Affairs. Publication of the Gauteng health care waste management draft regulations. Gauteng Provincial Gazette No. 373:3003, 2003.

- Acts:

South Africa. National Health Act No. 61 of 2003.

- Regulations to an Act:

South Africa. National Health Act of 2003. Regulations: Rendering of clinical forensic medicine services. Government Gazette No. 35099, 2012. (Published under Government Notice R176).

- Bills:

South Africa. Traditional Health Practitioners Bill, No. B66B-2003, 2006.

- Green/white papers:

South Africa. Department of Health Green Paper: National Health Insurance in South Africa. 2011.

- Case law:

Rex v Jopp and Another 1949 (4) SA 11 (N)
Rex v Jopp and Another: Name of the parties concerned
1949: Date of decision (or when the case was heard)
(4): Volume number
SA: SA Law Reports
11: Page or section number
(N): In this case Natal - where the case was heard. Similarly, (C) woud indicate Cape, (G) Gauteng, and so on.
NOTE: no . after the v

- *Other references (e.g. reports) should follow the same format:* Author(s). Title. Publisher place: Publisher name, year; pages.
- Cited manuscripts that have been accepted but not yet published can be included as references followed by '(in press)'.
- Unpublished observations and personal communications in the text must **not** appear in the reference list. The full name of the source person must be provided for personal communications e.g. '...(Prof. Michael Jones, personal communication)'.

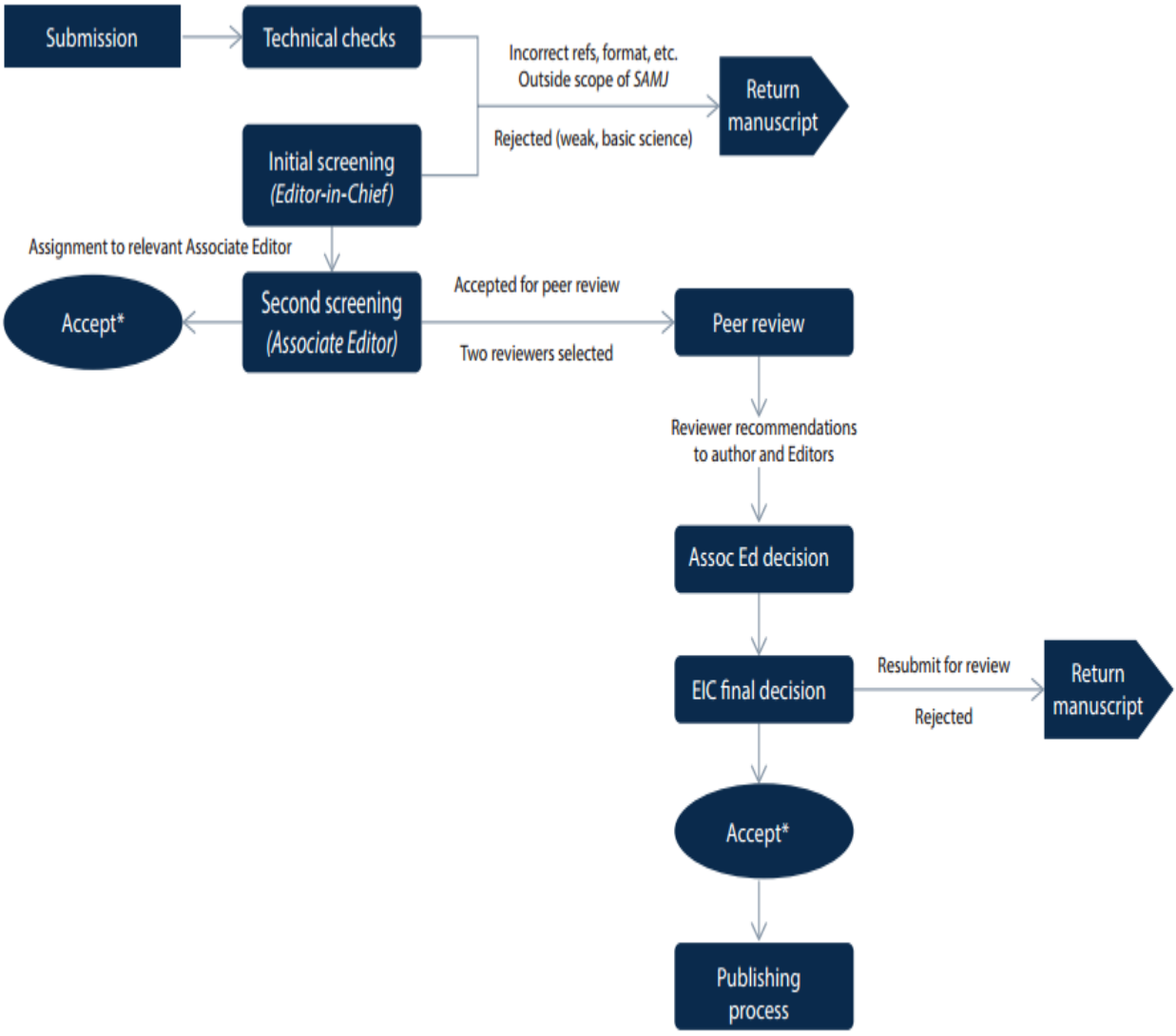
From submission to acceptance

Submission and peer-review

To submit an article:

- Please ensure that you have prepared your manuscript in line with the SAMJ requirements.
- All submissions should be submitted via Editorial Manager
- The following are required for your submission to be complete:
  - Anonymous manuscript (unless otherwise stated)
  - **Author Agreement form**
  - Manuscript
  - Any supplementary files: figures, datasets, patient consent form, permissions for published images, etc.
- Once the submission has been successfully processed on Editorial Manager, it will undergo a technical check by the Editorial Office before it will be assigned to an editor who will handle the review process. If the author guidelines have not been appropriately followed, the manuscript may be sent back to the author for correcting.

Peer-review process



*Manuscripts accepted at this point are limited to Editorials, Correspondence, Obituaries, Book reviews, Abstracts, CME
**Some minor revisions may be requested

Production process

The following process should usually take between 4 - 6 weeks:

1 An accepted manuscript is passed to a Managing Editor to assign to a copyeditor (CE).
2 The CE copyedits in Word, working on house style, format, spelling/grammar/punctuation, sense and consistency, and preparation for typesetting.
3 If the CE has an author queries, he/she will contact the corresponding author and send them the copyedited Word doc, asking them to solve the queries by means of track changes or comment boxes.
4 The authors are typically asked to respond within 1-3 days. Any comments/changes must be clearly indicated e.g. by means of track changes. Do not work in the original manuscript - work in the copyedited file sent to you and make your changes clear.
5 The CE will finalise the article and then it will be typeset.
6 Once typeset, the CE will send a PDF of the file to the authors to complete their final check, while simultaneously sending to the 2nd-eye proofreader.
7 The authors are typically asked to complete their final check and sign-off within 1-2 days. No major additional changes can be accommodated at this point.
8 The CE implements the authors' and proofreader's mark-ups, finalises the file, and prepares it for the

upcoming issue.

Changing contact details or authorship

Please notify the Editorial Department of any contact detail changes, including email, to facilitate communication.

Publication

Online v. print

The *SAMJ* is an online journal. The online version of the journal is the one that has the widest circulation, is indexed by bibliographic databases including PubMed and SciELO, and is accessible in academic libraries. A printed edition , containing material selected by the Editor is also published each month and distributed to the membership of the South African Medical Association.

Online

- The full text of all accepted articles is published in full online, open access, within 4 - 6 weeks of acceptance.
- Citation information of each article is based on its online publication.
- You may want to make use of the advantages of online publication e.g. specify web links to other sources, images, data or even a short video.

Print

- Not all articles will be selected for print.
- An article may be selected for print in a different month from that in which it was published online.
- Research articles will appear *in abstract form only*, if selected for a print edition.

Errata and retractions

Errata

Should you become aware of an error or inaccuracy in yours or someone else's contribution after it has been published, please inform us as soon as possible via an email to publishing@hmpg.co.za,including the following details:

- Journal, volume and issue in which published
- Article title and authors
- Description of error and details of where it appears in the published article
- Full detail of proposed correction and rationale

We will investigate the issue and provide feedback. If appropriate, we will correct the web version immediately, and will publish anerratum in the next issue. The correction will be indexed, as PubMed has a function for linking errata back to the original article. All investigations will be conducted in accordance with guidelines provided by the Committee on Publication Ethics (COPE).

Retractions

Retraction of an article is the prerogative of either the original authors or the editorial team of HMPG. Should you wish to withdraw your article before publication, we need a signed statement from all the authors.

Should you wish to retract your published article, all authors have to agree in writing before publication of the retraction.
Send an email to publishing@hmpg.co.za, including the following details:

- Journal, volume and issue to which article was submitted/in which article was published
- Article title and authors
- Description of reason for withdrawal/retraction.

We will make a decision on a case-by-case basis upon review by the editorial committee in line with international best practices. Comprehensive feedback will be communicated with the authors with regard

to the process. In case where there is any suspected fraud or professional misconduct, we will follow due process as recommended by the Committee on Publication Ethics (COPE), and in liaison with any relevant institutions.

When a retraction is published, it will be linked to the original article.

Indexing

The *SAMJ* has an impact factor of 1.5.
Published articles are covered by the following major indexing services. As such articles published in the *SAMJ* are immediately available to all users of these databases, guaranteed a global and African audience:

- Index Medicus (Medline/PubMed)
- ExcerptaMedica (EMBASE)
- Biological Abstracts (BIOSIS)
- Science Citation Index (SciSearch)
- Current Contents/Clinical Medicine
- Scopus
- AIM
- AJOL
- Crossref
- Sabinet
- Scielo

Sponsored supplements

Contact claudian@hmpg.co.za for information on submitting ad hoc/commissioned supplements, including guidelines, conference/congress abstracts, Festschrifts, etc.

Submission Preparation Checklist

As part of the submission process, authors are required to check off their submission's compliance with all of the following items, and submissions may be returned to authors that do not adhere to these guidelines.

1 Named authors consent to publication and meet the requirements of authorship as set out by the journal.
2 The submission has not been previously published, nor is it before another journal for consideration.
3 The text complies with the stylistic and bibliographic requirements in **Author Guidelines**.
4 The manuscript is in Microsoft Word or RTF document format. The text is single-spaced, in 12-point Times New Roman font, and contains no unnecessary formatting.
5 Illustrations/figures are high resolution/quality (not compressed) and in an acceptable format (preferably TIFF or PNG). These must be submitted individually as 'supplementary files' (not solely embedded in the manuscript).
6 For illustrations/figures or tables that have been published elsewhere, the author has obtained written consent to republication from the copyright holder.
7 Where possible, references are accompanied by a digital object identifier (DOI) and PubMed ID (PMID)/PubMed Central ID (PMCID).
8 An abstract has been included where applicable.
9 The research was approved by a Research Ethics Committee (if applicable)
10 Any conflict of interest (or competing interests) is indicated by the author(s).

Copyright Notice

submitted for publication elsewhere. Please inform the editorial team if the main findings of your paper have been presented at a conference and published in abstract form, to avoid copyright infringement.

Privacy Statement

The *SAMJ* is committed to protecting the privacy of the users of this journal website. The names, personal particulars and email addresses entered in this website will be used only for the stated purposes of this journal and will not be made available to third parties without the user's permission or due process. Users consent to receive communication from the *SAMJ* for the stated purposes of the journal. Queries with regard to privacy may be directed to publishing@hmpg.co.za.

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