Evaluating the yield of brain CT examinations in patients presenting with first onset seizures at the Groote Schuur Hospital, Cape Town

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DECLARATION

I, Innocent Vusumusi Ncube, hereby declare that the work on which this dissertation/thesis is based is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

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List of abbreviations:

ACEP: American College of Emergency Physicians

CECT: Contrast Enhanced Computed Tomography

CT: Computed Tomography

ECG: Electrocardiography

ED: Emergency Department

EEG: Electroencephalography

HIV: Human Immunodeficiency Virus

MRI: Magnetic Resonance Imaging

MRN: Medical Record Number

NECT: Non-enhanced Computed Tomography

PACS: Picture Archiving and Communications System

TB: Tuberculosis

Abstract:

Background: Seizures are a frequent and potentially significant presenting complaint to the emergency department (ED). Determining the underlying cause for seizures is important in guiding further clinical management of patients. ED physicians at Groote Schuur Hospital, Cape Town, South Africa routinely request Computed Tomography (CT) brain scans in the work-up of patients presenting with first onset seizures.

Objectives: To determine the number and proportion of CT scan examinations with abnormal findings in patients presenting with first onset seizures at the Groote Schuur Hospital ED, Cape Town, South Africa and to identify the range of CT abnormalities.

Method: A retrospective study was carried out in the Division of Radiology, Groote Schuur Hospital. Patients who presented to the ED with first onset seizures and who underwent brain CT examination as part of their work up between 1 January 2013 and 31 December 2016 were enrolled. All patients presenting to the ED with first onset focal or grand mal seizures were included. Patients with recent trauma and those with previously diagnosed epilepsy were excluded.

Results: A total of 200 patients were eligible for the study. Of these, 92 (46%) patients with first onset seizures had an abnormality or abnormalities on brain CT scan. Of those patients whose HIV status was known, 50% of HIV positive and 53% of HIV negative patients had abnormal CT scans. 54% of patients with focal seizures and 38% with generalised seizures had an abnormality on CT scan. Abnormalities found on CT scans included chronic cerebral infarction (7.5%), acute or subacute cerebral infarction (4.5%), neurocysticercosis (7.0%), other infections (6.5%), haemorrhage and

other vascular lesions (6.5%), post-traumatic encephalomalacia (6.5%), primary brain tumours and metastases (based on CT characteristics) (7.0%).

Conclusion: Forty-six (46%) of patients presenting to the Groote Schuur Hospital ED, Cape Town, South Africa with first onset seizures had an abnormality on their brain CT scans. Brain CT scan is therefore recommended in patients presenting to the ED department with first-onset seizures, irrespective of their HIV/ neurological status.

CHAPTER 1: LITERATURE REVIEW

Background

A seizure is defined as a finite event of abnormal cerebral function due to excessive and abnormal electrical activity of the brain cells (1). Seizures can be classified as either generalized or focal (partial) by mode of presentation. A generalised seizure involves both cerebral hemispheres, whereas a focal seizure involves one area of the brain. Generalised seizures usually present with loss of consciousness, tonic-clonic whole body movements, loss of muscle tone and myoclonic jerking (this involves a single muscle or group of muscles without loss of consciousness). Focal seizures often have variable presentation, including autonomic, sensory or motor disturbances. A focal seizure may have secondary generalisation, in which case there may also be associated loss of consciousness (2).

Classification of unprovoked seizures into cryptogenic (unknown cause), remote symptomatic (associated brain injuries or other cerebral lesions), or idiopathic (with potential underlying genetic association) has been proposed (3).

Epidemiology

It is estimated that about 5 to 11% of the population will experience at least one episode of a non-febrile seizure at some point during their lifetime(4, 5).

First onset seizures are a frequent and important cause for presentation to the ED, being estimated to account for approximately 1% of all ED visits(4, 6). Various studies have examined the investigation and management of adult first onset seizures, with little agreement among the different investigators (7). Consequent to the variations in findings and hence recommendations by various studies regarding the appropriate investigations and resultant management of adult first onset seizures, it has been suggested that treatment should be individualised and local guidelines for referral be agreed upon between the local ED physicians and neurologists (8).

Impact of HIV and TB

Seizures commonly occur in HIV-infected patients, and in this patient group approximately 75% have an identifiable cause on brain imaging in some studies [9]. Seizures are a relevant presentation during the course of HIV infection. The seizures often result from the direct effects of the HIV virus itself on the brain or alternatively secondary effects from opportunistic infections (including viral, bacterial, fungal and protozoal infections) as well as brain tumours[10-12]. In addition to the recognised increased prevalence of primary central nervous system lymphoma in HIV infected individuals, there is increasing evidence that this patient group is also at increased for developing primary brain gliomas[13]. Most patients with new onset seizures in the setting of HIV will eventually develop epilepsy and may require prolonged anticonvulsant medication. Intravenous drug abuse and the presence of non-HIV-associated risk factors for epilepsy appear to be linked to the development of chronic seizures in this patient group[10].

The use of neuroimaging with brain CT or MRI may identify abnormalities that could necessitate a change in management with 15% of patients admitted in one series who would have otherwise been discharged if they had not been imaged[14].

Tuberculosis of the central nervous system has also been associated with first onset seizures. This may be due to several effects of TB on the brain which include the development of space-occupying lesion (tuberculoma), inflammation of the meningeal coverings of the brain (meningitis), infarcts from localised vasculopathy (particularly affecting the basal ganglia), cerebritis and development of tuberculous abscess[11].

Review

Several authors agree that detailed clinical evaluation of a patient presenting to the ED with a first onset seizure is mandatory to determine the type of seizure, the

potential seizure-provoking events and underlying aetiology. This helps to guide clinical management and prevention of seizure recurrence.

The evaluation of patients presenting to the ED with first onset seizures should include careful history taking (including collateral history if required), thorough clinical examination and ancillary investigations. Some of the investigations that are routinely performed include blood tests (blood glucose levels, urea and electrolytes for kidney function evaluation, toxicology screen and other biochemistry tests), electroencephalography (EEG) and neuroimaging with brain CT scan or magnetic resonance imaging (MRI). In certain situations, some guidelines advocate further tests such as the chest x-ray and electrocardiography (ECG) (7, 15-17). More extensive laboratory testing in first seizure patients has been associated with a low yield unless indicated by a suggestive history or physical examination (18).

The two major modalities employed for imaging of the brain are computed tomography (CT) and magnetic resonance imaging (MRI). Guidelines vary on what modality is to be employed for imaging the patient presenting with first onset seizures in the ED. However, most researchers have demonstrated that CT scan has a high diagnostic yield although this varies widely in the published data.

Routine use of brain CT imaging in the evaluation of all patients presenting to the ED with first onset seizures remains an ongoing controversial issue (19). Early investigators proposed that brain CT imaging is recommended in all first onset seizures, regardless of neurological status on examination. This was because brain CT and MRI found between 2,4% and 20,3% rates of focal cerebral lesions despite normal neurological examination (6). Subsequently, most investigators now agree that neuroimaging is an integral part of the evaluation of a first onset seizure although there is still lack of agreement regarding the appropriate timing and type of imaging to be employed (18, 20).

Neuroimaging with brain CT or brain MRI is important in the diagnosis, classification and consequently treatment of patients with seizures. When an adult patient presents to the ED with a first onset seizure, the ED clinician should request brain imaging to determine the potential cause of the seizure and guide further management including the decision regarding the need for hospitalisation for instance in patients presenting in status epilepticus(21, 22).
Approximately 10 to 24% of patients received important therapeutic intervention resulting from the findings on brain CT examination after presenting to the ED with first onset seizure(23).

The American College of Emergency Physicians (ACEP) recommends head CT imaging for all patients presenting to the ED with first onset seizures despite the presence of only non-focal symptoms (24). Other ACEP recommendations are that those patients that return to baseline neurological status may be discharged and scheduled for elective neuroimaging as outpatients, while HIV positive patients should all be imaged with brain CT(14, 25). In their study of the investigations carried out in ED's for patients presenting with first onset seizures in some selected Western Cape Emergency Centres, Smith AB et al found wide variations for all the types of investigations and they subsequently recommended that local guidelines should be developed and followed to allow uniformity in management of these patients (26).

The request or need for urgent neuroimaging is best guided by the history, clinical presentation, presence of co-morbid conditions (including HIV infection, tuberculosis, known primary malignancy), neurological status, type of seizures and potential difficulty in follow-up of the patient (7).

Many previous various studies report CT brain abnormalities in patients with first onset seizures that range from 20% to 60%. The patient demographics as well as the

spectrum of causative pathologies also varied widely. Of the brain CT scans with positive findings, abnormalities found ranged from infection (neurocysticercosis, TB, toxoplasmosis), tumours (cysts, primary glial, meningeal and metastatic tumours) and other structural lesions (6, 22, 24, 27, 28). Positive findings on neuroimaging have been associated with a high risk of seizure recurrence and are used to guide treatment with long term or sometimes lifelong anticonvulsant therapy. Seizure recurrence has been found to be lower in patients with idiopathic seizures, that is, those with no causative lesions found on imaging (27, 29).

The choice of whether brain CT or brain MRI is requested for a patient presenting with first onset seizures varies among physicians, between centres and across different guidelines. Brain MRI is generally accepted as being more sensitive in identifying likely causative pathology due to superior soft tissue resolution in comparison to brain CT. However, in the acute setting brain CT imaging is generally regarded as sufficient to identify life-threatening conditions. Most catastrophic conditions presenting with seizures are related to intracranial haemorrhage, brain swelling, mass effect, herniation syndromes or hydrocephalus. Hence a brain CT scan without contrast (NECT) may be all that is required in the emergency setting to make a prompt diagnosis and allow emergent life-saving intervention if required. After the initial NECT, further evaluation with contrast-enhanced CT (CECT) or MRI can then be decided upon depending on the findings (28). In patients in whom MRI is contraindicated, such as those with pacemakers, claustrophobic patients and patients with ferromagnetic objects in the body (such as aneurysmal clips, cochlear implants, retained metallic foreign objects, etc), a CT scan with or without intravenous contrast injection has been recommended. In addition, CT offers several advantages over MRI including lower cost, faster scanning (ideal for emergency situations) and ease of use and interpretation (30). However, when compared to brain MRI, brain CT imaging is associated with exposure to ionising radiation which is absent with MRI imaging.

The decision to use intravenous iodinated contrast or not depends on the clinical suspicion for possible aetiology and the presence of co-morbid conditions. In patients with suspected intracranial haemorrhage, patients with a remote history of trauma or those in whom contrast administration is not desirable (usually because of impaired kidney function or previous allergic reaction to iodinated contrast agent) a NECT will suffice. In HIV positive patients and those in whom an infectious or neoplastic cause for seizures is suspected, a CECT will be a good starting point (1, 7, 20).

Conclusion

In the ED at Groote Schuur Hospital, Cape Town, patients with first-onset seizures have brain CT requested as part of their workup to find a possible aetiology for the seizures. Given the high volume of CT examinations requested for patients with first-onset seizures, and the associated cost to the local government, as well as radiation dose to patients, it is important to determine the positive yield that brain CT examination provides in the evaluation for the seizure aetiology, as well as to evaluate the spectrum of positive findings. We therefore carried out a 4-year retrospective study to assess the yield of CT brain examination and the spectrum of findings in patients with first-onset seizures presenting to the Groote Schuur Hospital ED (Ward C15).

In summary, there is general consensus for the need for neuroimaging in the adult patient who presents with first onset seizures to the ED, although variations in timing and the specific type of imaging exist (1, 7, 20, 26). The aims of imaging such patients are to exclude brain pathology, identify treatable or reversible causes, to aid the clinician in making a prompt and correct diagnosis that may guide further management as well as prediction of seizure recurrence.

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CHAPTER 2: FULL TEXT JOURNAL ARTICLE FOR SUBMISSION.

Evaluating the yield of brain CT examinations in patients presenting with first onset seizures at the Groote Schuur Hospital, Cape Town

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Abstract:

Background: Seizures are a frequent and potentially significant presenting complaint to the emergency department (ED). Determining the underlying cause for seizures is important in guiding further clinical management of patients. ED physicians at Groote Schuur Hospital, Cape Town, South Africa routinely request Computed Tomography (CT) brain scans in the work-up of patients presenting with first onset seizures.

Objectives: To determine the number and proportion of CT scan examinations with abnormal findings in patients presenting with first onset seizures at the Groote Schuur Hospital ED, Cape Town, South Africa and to identify the range of CT abnormalities.

Method: A retrospective study was carried out in the Division of Radiology, Groote Schuur Hospital. Patients who presented to the ED with first onset seizures and who underwent brain CT examination as part of their work up between 1 January 2013 and 31 December 2016 were enrolled. All patients presenting to the ED with first onset focal or grand mal seizures were included. Patients with recent trauma and those with previously diagnosed epilepsy were excluded.

Results: A total of 200 patients were eligible for the study. Of these, 92 (46%) patients with first onset seizures had an abnormality or abnormalities on brain CT scan. Of those patients whose HIV status was known, 50% of HIV positive and 53% of HIV negative patients had abnormal CT scans. 54% of patients with focal seizures and 38% with generalised seizures had an abnormality on CT scan. Abnormalities found on CT scans included chronic cerebral infarction (7.5%), acute or subacute cerebral infarction (4.5%), neurocysticercosis (7.0%), other infections (6.5%), haemorrhage and other vascular lesions (6.5%), post-traumatic encephalomalacia (6.5%), primary brain tumours and metastases (based on CT characteristics) (7.0%).

Conclusion: Forty-six (46%) of patients presenting to the Groote Schuur Hospital ED, Cape Town, South Africa with first onset seizures had an abnormality on their brain CT scans. Brain CT scan is therefore recommended in patients presenting to the ED department with first-onset seizures, irrespective of their HIV/ neurological status.

Introduction:

First onset seizures are a frequent and important cause for presentation to the ED, estimated to account for approximately 1% of all ED visits[1].

The evaluation of patients presenting to the ED with first onset seizures should include careful, detailed history taking, clinical examination and investigations including blood tests, EEG and brain imaging[2-4].

Neuroimaging with CT or MRI scan is important in the diagnosis, classification and treatment of patients with seizures. When a patient presents to the ED with a first onset seizure, the clinician should request brain imaging to determine the cause of the seizure[5-7].

Multiple abnormalities that may cause seizures can be detected on brain CT scan imaging and this can potentially lead to early, accurate diagnosis that can guide further clinical management of the patient[1, 8-10].

There is consensus in literature for the need for neuroimaging in the adult patient who presents with first onset seizures to the ED, however variations in timing and type of imaging exist[2, 6, 11, 12]. Consequently, it has been suggested that individualised treatment and referral guidelines be agreed upon between the local ED physicians and neurologists[13].

In the ED at Groote Schuur Hospital, Cape Town, patients with first-onset seizures have brain CT requested as part of their workup to find a possible aetiology for the seizures. We carried out a 4-year retrospective study to assess the yield of CT brain examination and spectrum of findings in patients with first-onset seizures presenting to the Groote Schuur Hospital ED.

Methods:

Study design

A prospective, cross-sectional study design was used.

Study setting and population

A retrospective study was performed in the Division of Radiology, Groote Schuur Hospital, Cape Town, South Africa. The Radiology Division at Groote Schuur Hospital maintains a database of all examinations and reports in the department through the Picture Archiving and Communications (PACS) system. This database, which includes radiological images and their associated reports, was accessed after Ethics and hospital approval.

Inclusion criteria were all patients who presented with first-time seizures and underwent brain CT examination in the 4-year period of the study. Only CT scans that were reported by a consultant radiologist or a radiology registrar and subsequently approved by a consultant radiologist were considered. A total of 2 577 patients satisfied the initial search within the database. The initial search of radiology reports used the phrases 'first-time seizures and first-onset seizures' and was limited to ward C15 (the Groote Schuur Hospital ED ward for adult medical/ non-trauma cases). The search was conducted using a search tool on iSite (a component of PACS Philips). Patients were then randomized using the medical record numbers (MRN). The first 200 patients of the 2577 who satisfied the inclusion criteria were identified and the findings recorded.

All patients with a history of traumatic head injury in the preceding three months were excluded, as their symptoms may be related to the trauma. Registrar only reports were also excluded. Patients with a known seizure disorder or a known diagnosis of epilepsy were also excluded from the study.

Radiology reports of patients who satisfied the inclusion criteria were retrieved from iSite and the findings noted. Patients with abnormal brain findings on CT scan that were deemed to explain the cause of the seizures were recorded as being positive. CT scans of patients who showed no abnormality were recorded as negative.

Statistical Analysis

Descriptive statistics were reported using histograms, frequencies and percentages. Where appropriate means and standard deviations were reported. Relationships were tested using cross tabulation with the Chi-squared test. Fischer exact test was also calculated for 2 x 2 tables.

Ethical consideration

Ethical approval to conduct the study was obtained from the Faculty of Health Sciences Human Research Ethics Committee of the University of Cape Town (HREC reference number: 434/2017) and the hospital.

Results

A total of 200 patients who met the inclusion criteria were identified and the consultant-approved findings were recorded.
Patients who were excluded were those with a known seizure disorder, history of trauma in the preceding 3 months and CT scans not approved by a consultant radiologist.

Some patients had two or more aetiologies as a possible cause for the seizures. In these patients, each aetiology was recorded separately as a possible cause for the seizures. This resulted in the total percentage of the possible causes for seizures exceeding the overall forty-six percent (46.0%).

A coincidental equal gender distribution of male and female patients was found in our study (Fig.1), with a mean age of 43.2 years (standard deviation +/- 18.29) (Fig 2).
72 patients (36.0%) presented with generalised seizures, 26 patients (13.0%) had focal seizures whilst 3 patients (1.5%) had focal seizures with secondary generalisation (Fig 3). In 99 patients (49.5%) the seizure type was not documented.
CT scanning identified abnormalities of the brain in 27 patients (38.0%) with generalised seizures and in 14 patients (54.0%) with focal seizures (Fig 4).

92 CT scans (46.0%) showed abnormalities that were deemed as a possible cause for the patient's seizures (Fig 5).
Abnormal findings on CT scans in our patients with generalised and focal seizures included chronic cerebral infarcts (CCI) 15 patients (7.5%), various stages of neurocysticercosis 14 patients (7.0%), intracranial bleeding and other vascular lesions (berry aneurysms, classic pial arteriovenous malformations, and dural arteriovenous fistulae) 13 patients (6.5%), acute and subacute infarcts 9 patients (4.5%), primary and

secondary brain tumours 14 patients [9 + 5 patients] (4.5% and 2.5% respectively), and calcified granulomas other than neurocysticercosis 6 patients (3.0%). Cerebral oedema 4 patients (2.0 %), hydrocephalus 3 patients (1.5 %), demyelinating processes 1 patient (0.5%) and brain abscess 1 patient (0.5%) accounted for a total of 9 patients (4.5%) of abnormal CT findings, assigned as "other" in Fig 5. Acute, subacute and chronic infarcts accounted for the highest total percentage (12%) of abnormal findings on CT scans in patients presenting with seizures.

In 141 patients (70.5%), the HIV status was unknown at the time of requesting the CT scan. Of these, 61 patients (43.3%) had abnormalities of the brain on CT scan. 44 patients (22.0%) were HIV positive, and of these 22 patients (50.0%) had an abnormality on CT scans (Fig 6). 15 patients (7.5%) were HIV negative, and of these 8 (53.3%) had abnormal CT scans.

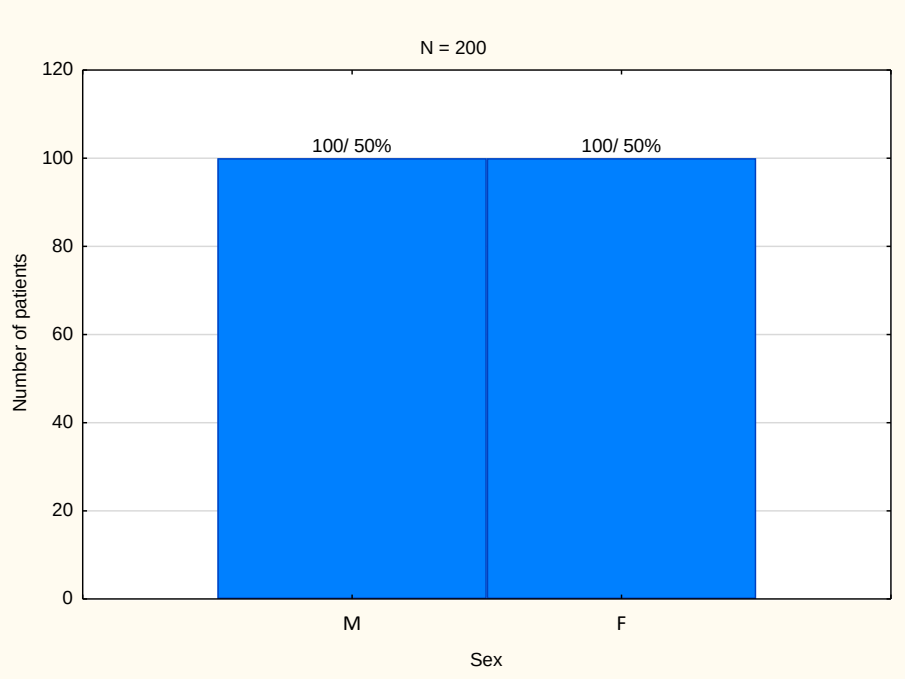

Figure 1: Gender distribution

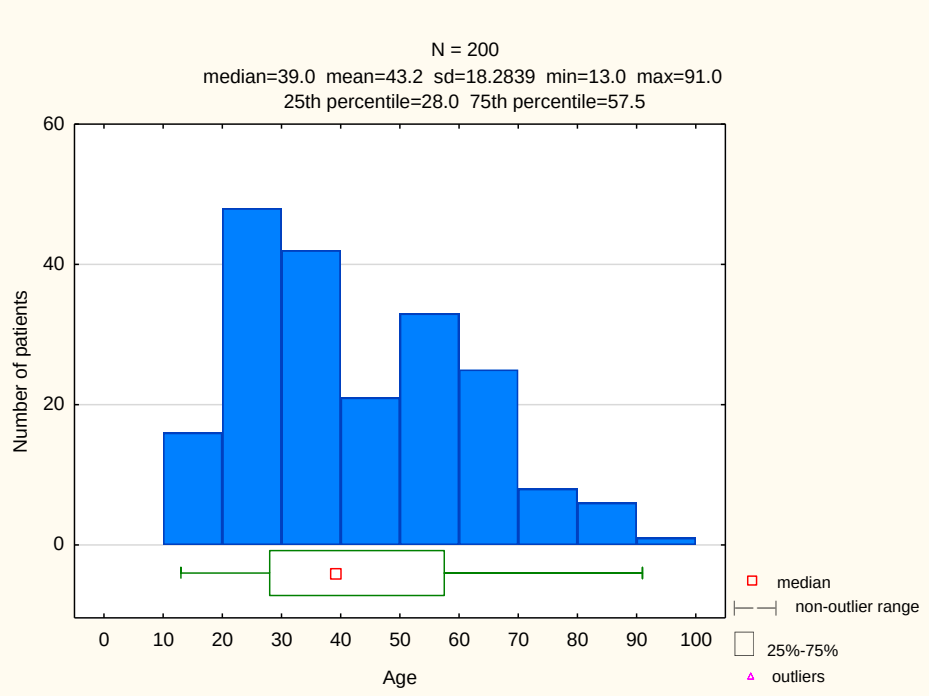

Figure 2: Age distribution.

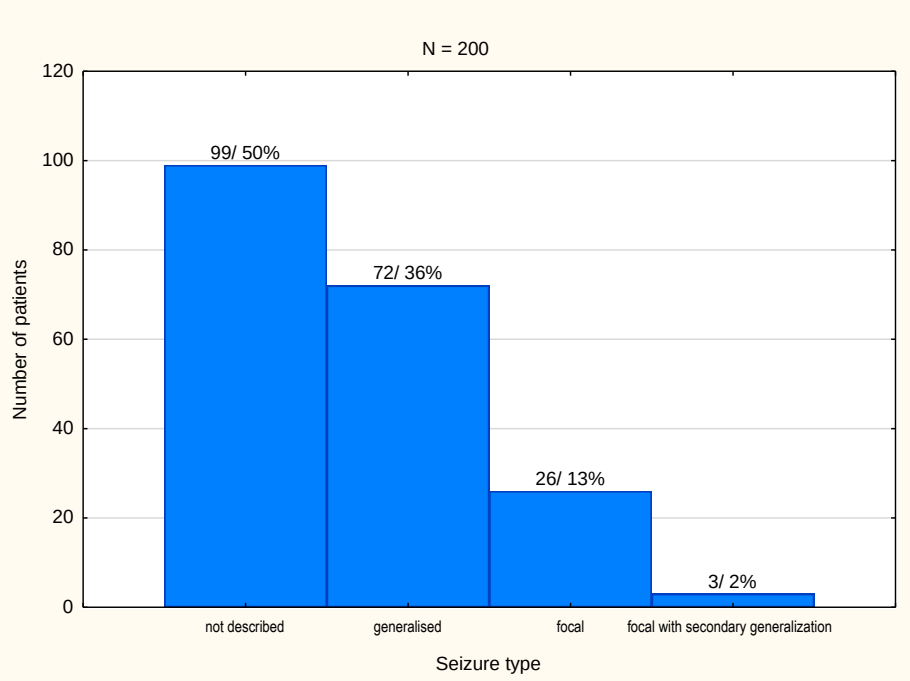

Figure 3: Seizure type

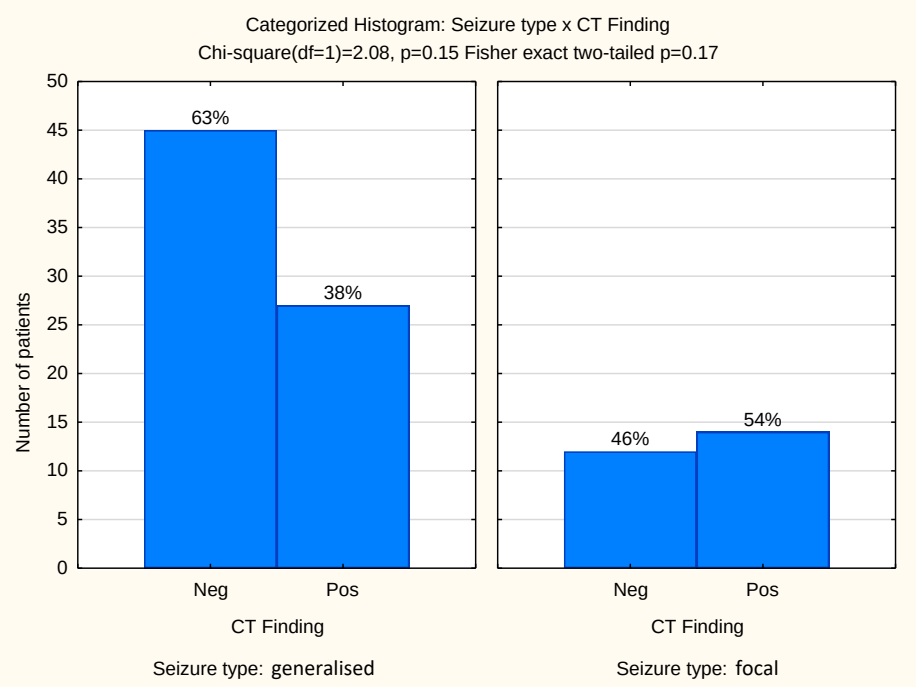

Figure 4: %age of abnormal and normal CT findings vs generalised/ focal seizure type

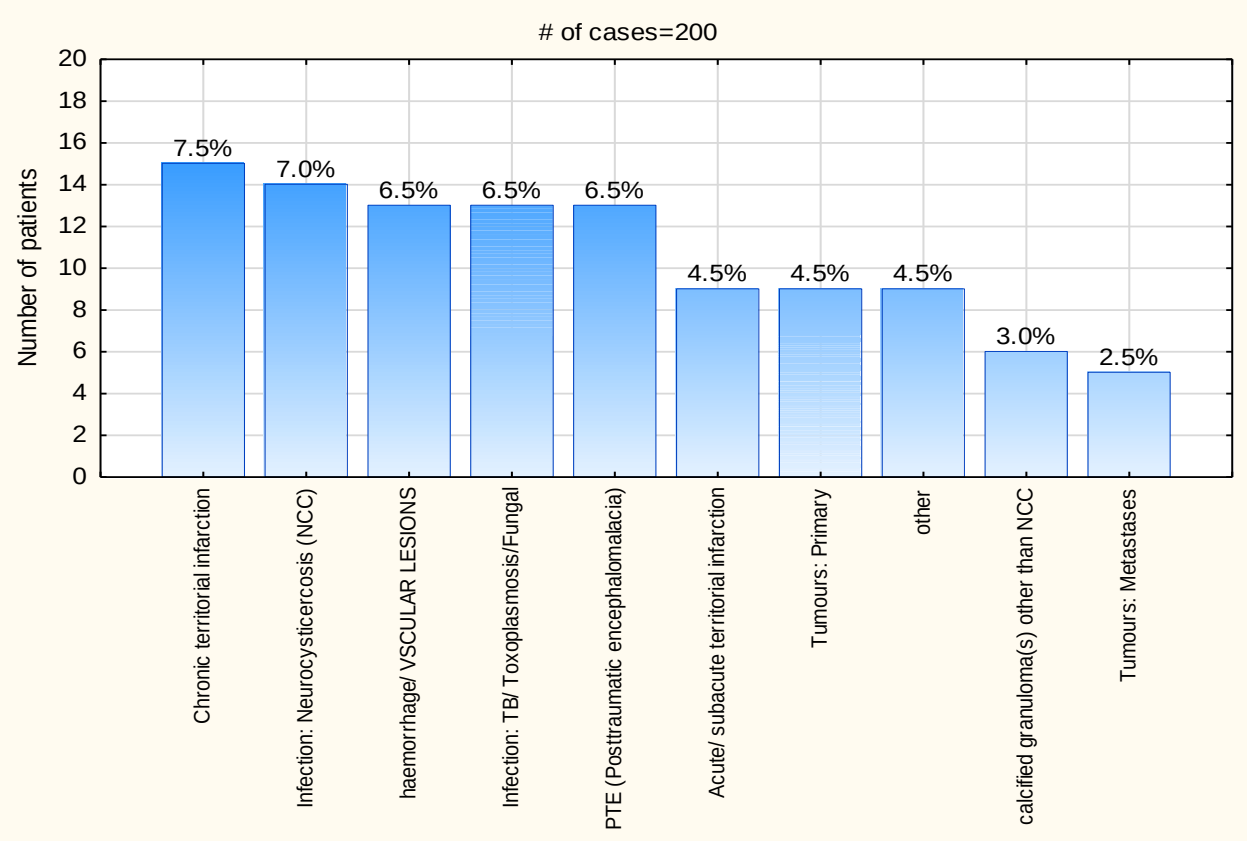

Figure 5: CT brain findings

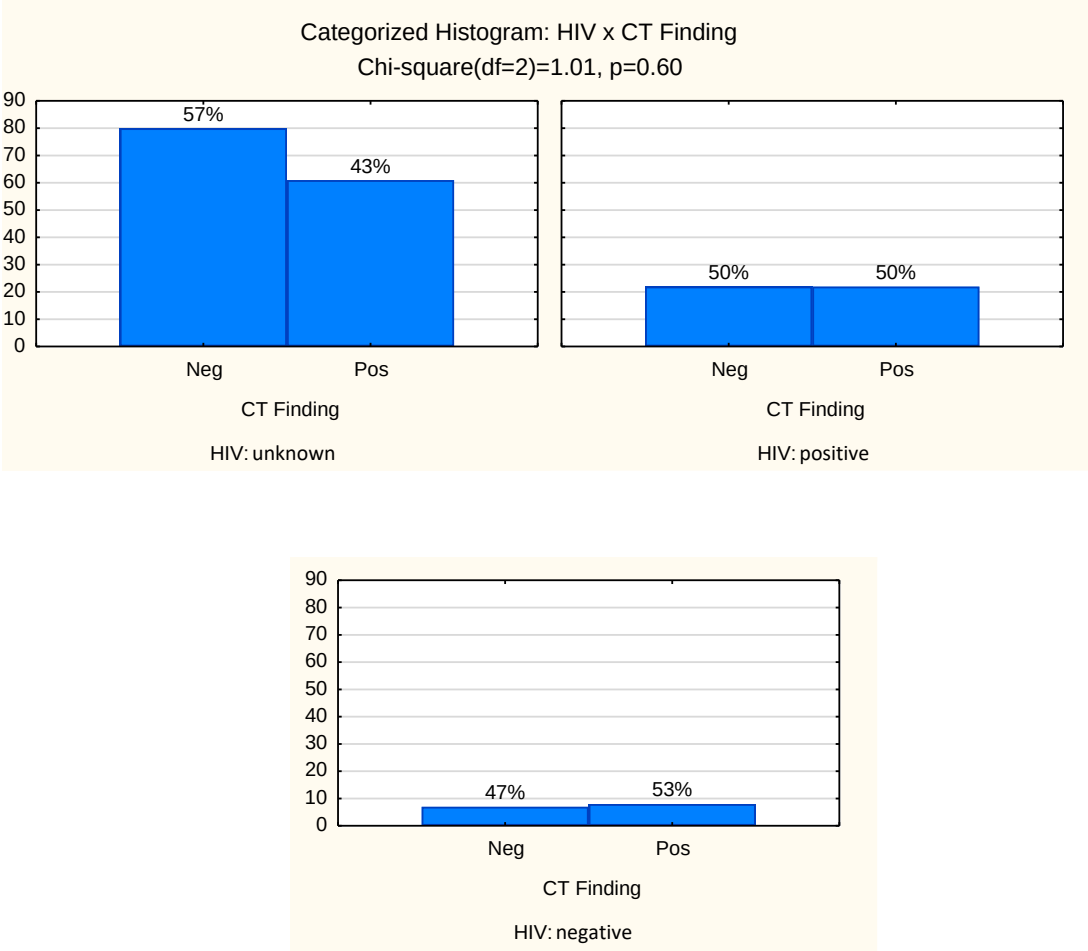

Figure 6: CT findings vs HIV status

Discussion

Our study did not demonstrate a variable gender predominance as was the case with previous studies [14-16], and instead an equal gender distribution of male and female patients was noted.

92 of the 200 patients (46%) presenting to the Emergency Department at Groote Schuur Hospital with first onset seizures were found to have an abnormal CT scan, compared to a previous study performed in the Western Cape (South Africa) which detected 59.6% abnormalities on CT scans.

The prevalence of abnormalities detected on CT scan examinations varied widely among investigators in other parts of the world. This variation may be attributed to different population samples with different genetic and environmental influences, differences in methodology and in the stratification of patients for imaging by the ED physicians.

Acute, subacute and chronic infarcts accounted for the highest total percentage (12%) of abnormal findings on CT scans in patients presenting with seizures. This may be attributed to the relatively high prevalence of hypertension and high body mass index (BMI) among the Western Cape population which may predispose to cerebrovascular disease (stroke) in this population subgroup [17], which in turn results in brain scarring and development of scar epilepsy [18].

There was no significant difference in the prevalence of the rest of the abnormalities detected on CT scans in patients presenting with seizures. The probability of finding an abnormal CT scan in a patient was independent of the HIV status of the patient, and this was found to be not statistically significant. This is probably due to the large number of patients whose HIV status was unknown at the time of scan.

Of those patients with described seizure type, the probability of finding an abnormality on CT scan was greater in patients with focal (54%) compared with those with generalised seizures (38%).

Investigation of patients with first onset seizures with brain CT assists ED physicians in making a diagnosis and may guide appropriate further clinical management. Patients can therefore be categorised into those that need admission for urgent treatment, those that can be managed non-urgently as hospital inpatients and those that can be discharged and followed up electively in the outpatient clinic. Advantages of this method of triaging of patients with first onset seizures by ED physicians include cost savings from unnecessary further investigations as well as hospital admissions.

Conclusion

Forty six percent (46%) of patients presenting to the ED at Groote Schuur Hospital with first onset generalised or focal seizures were found to have an abnormal CT scan. The management implications of these abnormal CT findings are detailed in the discussion.

CT scan identified a range of abnormalities in patients with first onset generalised and focal seizures which may guide clinicians in further patient management.

Acute, subacute and chronic infarcts accounted for the highest percentage (12%) of abnormalities on CT scans in patients presenting with first onset generalised or focal seizures.

Neuroimaging is therefore recommended in all patients presenting with first onset generalized or focal seizures to the ED at Groote Schuur Hospital regardless of the neurological status of the patient at the time of presentation.

Our study showed that the probability of finding an abnormality on the CT scan was greater in patients with first onset focal seizures compared to those with generalised seizures.

No correlation between the patients' HIV status and an abnormality on CT scan was demonstrated in patients presenting with first onset generalised or focal seizures.

Study limitations

- The choice of sample size was noted to be small given the large number of abnormalities encountered.
- Patient level of consciousness (LOC) was not considered at the time of scan request. This was due to the fact that in the vast majority of requests the level of consciousness was not described in the clinical history, and reasons for reduced LOC may include post ictal status independent of underlying cause.
- The HIV status was not known in the majority of patients and this may have influenced the findings or number of abnormal CT scans in relation to the HIV status.
- Similarly, a significant proportion of patients did not have their seizure types described or stated in the radiology clinical request for the scan. This also may have affected the overall percentage findings of abnormal CT scans in relation to seizure type.

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Professor S. Beningfield (HOD, Division of Radiology, Groote Schuur Hospital) for critical appraisal of the manuscript.

Professor M. Kidd (Department of Statistics, University of Stellenbosch) for statistical support.

Competing interests

The authors declare that they have no financial or personal relationships that may have inappropriately influenced them in writing this article.

Authors' contribution

I.V Ncube was the lead author, N Ahmed was the supervisor.

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Appendix A: Ethical Approval

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 6492
Email: sumayah.ariefdien@uct.ac.za
Website: www.health.uct.ac.za/fhs/research/humanethics/forms

11 July 2017

HREC REF: 434/2017

Dr N Ahmed
Division of Radiology
C-8
NGSH

Dear Dr Ahmed

PROJECT TITLE: EVALUATING THE YIELD OF BRAIN CT EXAMINATIONS IN PATIENTS PRESENTING WITH FIRST ONSET SEIZURES AT THE GROOTE SCHUUR HOSPITAL, CAPE TOWN (MMeD-candidate- Dr I Ncube)

Thank you for submitting your study to the Faculty of Health Sciences Human Research Ethics Committee 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 July 2018.

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 I Ncube will also be involved in this study.

Please quote the HREC REF in all your correspondence.

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

Yours sincerely

Signature Removed

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE
Federal Wide Assurance Number: FWA00001637.
Institutional Review Board (IRB) number: IRB00001938
This serves to confirm that the University of Cape Town Human 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), South African Good Clinical Practice Guidelines (DoH

HREC 434/2017

Appendix B: Extension of Ethical Approval

HUMAN RESEARCH ETHICS COMMITTEE
21 MAY 2019
HEALTH SCIENCES FACULTY
UNIVERSITY OF CAPE TOWN

FHS017: Annual Progress Report / Renewal

Record Reviews/Audits/Collection of Biological Specimens/Repositories/Databases/Registries

HREC office use only (FWA00001637; IRB00001938)			
This serves as notification of annual approval, including any documentation described below.			
☑ Approved	Annual progress report	Approved until/next renewal date	30.05.2020
☐ Not approved	See attached comments		
Signature Chairperson of the HREC	Signature Removed	Date Signed	21/5/2019

Principal Investigator to complete the following:

1. Protocol information

Date (when submitting this form)	20/05/2019		
HREC REF Number	434/2017	Current Ethics Approval was granted until	30/07/18
Protocol title	EVALUATING THE YIELD OF BRAIN CT EXAMINATIONS IN PATIENTS PRESENTING WITH 1ST ONSET SEIZURES AT GSH		
Principal Investigator	N. AHMED		
Department / Office Internal Mail Address	DEPARTMENT OF RADIOLOGY, C16, GROOTE SCHUUR HOSPITAL, OBSERVATORY, 7925, CAPE TOWN		
1.1 Does this protocol receive US Federal funding?		☐ Yes	☑ No

2. Protocol status (tick ✓)

☐	Research-related activities are ongoing
☑	Data collection is complete, data analysis only
Please indicate (in the block below) the titles and HREC reference numbers of any projects currently making use of the Database/registry/repository.	
N/A	

3. Protocol summary

Total number of records or specimens collected, reviewed or stored since the original approval		200
Total number of records or specimens collected, reviewed or stored since last progress report		N/A
Have any research-related outputs (e.g. publications, abstracts, conference presentations) resulted from this research? If yes, please list and attach with this report.	☐ Yes	☑ No

4. Signature

Signature of PI	Signature Removed	Date	20 MAY 2019

Appendix C: Study Deviation

HUMAN RESEARCH ETHICS COMMITTEE
21 MAY 2019
HEALTH SCIENCES FACULTY
UNIVERSITY OF CAPE TOWN

UNIVERSITY OF CAPE TOWN
IYUNIVESITHI YASEKAPA • UNIVERSITEIT VAN KAAPSTAD

FACULTY OF HEALTH SCIENCES
Human Research Ethics Committee

Form FHS011: Study deviation

HREC office use only (FWA00001637; IRB00001938)			
This serves as acknowledgement of a protocol deviation as described below.			
Chairperson of the HREC signature	Signature Removed	Date	21/5/2019

Principal Investigator to complete the following:

1. Protocol information

Date (when submitting this form)	20/05/2019
HREC REF Number	434/2017
Project Title	EVALUATING THE YIELD OF BRAIN CT EXAMINATIONS IN PATIENTS PRESENTING WITH FIRST ONSET SEIZURES AT THE GROOTE SCHUUR HOSPITAL, CAPE TOWN
Protocol number (if applicable)	
Principal Investigator	NAZIR AHMED
Department / Office Internal Mail Address	DEPT OF RADIOLOGY, C16, GROOTE SCHUUR HOSPITAL, OBSERVATORY, 7925, CAPE TOWN

2. Protocol deviation description

Please describe the deviation below, including the reason why the deviation occurred.

THE PROJECT/RESEARCH WAS PUT ON HOLD WHILE MMED CANDIDATE WAS STUDYING FOR THE EXAMINATIONS. NO DATA COLLECTION WAS DONE OUTSIDE THE APPROVED PERIOD.

3. Follow-up actions

3.1 Please describe any follow-up action(s) taken or planned as a result of this deviation e.g. DSMB reporting, report to sponsor, informing participants.

RESEARCH TO BE CONCLUDED NOW THAT CANDIDATE HAS COMPLETED HIS COLLEGE OF RADIOLOGY EXAMINATIONS

3.2 Please describe what action(s) have or will be taken to prevent similar deviations in future.

WE ARE READY TO CONCLUDE THE RESEARCH AND SUBMIT THE PROJECT FOR MMED ASSESSEMENT/THESIS

4. Principal Investigator's acknowledgement of responsibility

This signature indicates the PI has reviewed the deviation, taken appropriate follow-up action and implemented or plans to implement preventative steps where possible.

Signature of PI	Signature Removed	Date	20 MAY 2019

Appendix D: GSH Research Permission

Western Cape Government
Health

GROOTE SCHUUR HOSPITAL
Enquiries: Dr Bernadette Eick
E-mail : Bernadette.Eick@westerncape.gov.za

Dr Nazir Ahmed
DEPARTMENT OF RADIOLOGY

E-mail: nazir.ahmed@uct.ac.za / invcube83@gmail.com

Dear Dr Ahmed,

RESEARCH PROJECT: Evaluating The Yield Of Brain CT Examinations In Patients With First Onset Seizures At The Groote Schuur Hospital, Cape Town

Your recent letter to the hospital refers.

You are granted permission to proceed with your research, which is valid until **30 May 2020.**

Please note the following:

a) Your research may not interfere with normal patient care.
b) Hospital staff may not be asked to assist with the research.
c) No additional costs to the hospital should be incurred i.e. Lab, consumables or stationary.
d) **No patient folders may be removed from the premises or be inaccessible.**
e) Please provide the research assistant/field worker with a copy of this letter as verification of approval.
f) Confidentiality must always be maintained .
g) Should you at any time require photographs of your subjects, please obtain the necessary indemnity forms from our Public Relations Office (E45 OMB or ext. 2187/2188).
h) Should you require additional research time beyond the stipulated expiry date, please apply for an extension.
i) Please discuss the study with the HOD before commencing.
j) Please introduce yourself to the person in charge of an area before commencing.
k) On completion of your research, please forward any recommendations/findings that can be beneficial to use to take further action that may inform redevelopment of future policy / review guidelines.
l) Kindly submit a copy of the publication or report to this office on completion of the research.

I would like to wish you every success with the project.

Yours sincerely

Signature Removed

DR BERNADETTE EICK
CHIEF OPERATIONAL OFFICER
Date: 19 July 2019

C.C. Mr. L. Naidoo
Dr H. Aziz
Professor S. Beningfield

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Appendix E: South African Journal of Radiology Instructions to Authors

Original Research Article full structure

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

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

- Background: *Why do we care about the problem?* State the context and purpose of the study. (What practical, scientific or theoretical gap is your research filling?)
- Objectives: *What problem are you trying to solve*? What is the scope of your work (e.g. is it a generalised approach or for a specific situation)? Be careful not to use too much jargon.
- Method: *How did you go about solving or making progress on the problem*? State how the study was performed and which statistical tests were used. (What did you actually do to get the results?) Clearly express the basic design of the study; name or briefly describe the basic methodology used without going into excessive detail. Be sure to indicate the key techniques used.
- Results: *What is the answer*? Present the main findings (that is, as a result of completing the procedure or study, state what you have learnt, invented or created). Identify trends, relative change or differences on answers to questions.
- Conclusion: *What are the implications of your answer*? Briefly summarise any potential implications. (What are the larger implications of your findings, especially for the problem or gap identified in your motivation?)
  Do not cite references and do not use abbreviations excessively in the abstract.

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

- Social value: The first part of the introduction should make a clear and logical argument for the importance or relevance of the study. Your argument should be supported by use of evidence from the literature.

- Scientific value: The second part of the introduction should make a clear and logical argument for the originality of the study. This should include a summary of what is already known about the research question or specific topic, and should clarify the knowledge gap that this study will address. Your argument should be supported by use of evidence from the literature.
- Conceptual framework: In some research articles it will also be important to describe the underlying theoretical basis for the research and how these theories are linked together in a conceptual framework. The theoretical evidence used to construct the conceptual framework should be referenced from the literature.
- Aim and objectives: The introduction should conclude with a clear summary of the aim and objectives of this study.
  Research methods and design: This must address the following:
- Study design: An outline of the type of study design.
- Setting: A description of the setting for the study; for example, the type of community from which the participants came or the nature of the health system and services in which the study is conducted.
- Study population and sampling strategy: Describe the study population and any inclusion or exclusion criteria. Describe the intended sample size and your sample size calculation or justification. Describe the sampling strategy used. Describe in practical terms how this was implemented.
- Intervention (if appropriate): If there were intervention and comparison groups, describe the intervention in detail and what happened to the comparison groups.
- Data collection: Define the data collection tools that were used and their validity. Describe in practical terms how data were collected and any key issues involved, e.g. language barriers.
- Data analysis: Describe how data were captured, checked and cleaned. Describe the analysis process, for example, the statistical tests used orsteps followed in qualitative data analysis.
- Ethical considerations: Approval must have been obtained for all studies from the author's institution or other relevant ethics committee and the institution's name and permit numbers should be stated here.
  Results: Present the results of your study in a logical sequence that addresses the aim and objectives of your study. Use tables and figures as required to present your findings. Use quotations as required to establish your interpretation of qualitative data. All units should conform to the SI convention and be abbreviated accordingly. Metric units and their international symbols are used throughout, as is the decimal point (not the decimal comma).

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

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

  Acknowledgements: Those who contributed to the work but do not meet our authorship criteria should be listed in the Acknowledgments with a description of the contribution. Authors are responsible for ensuring that anyone named in the Acknowledgments agrees to be named. Also provide the following, each under their own heading:
- Competing interests: This section should list specific competing interests associated with any of the authors. If authors declare that no competing interests exist, the article will include a statement to this effect: *The authors declare that they have no financial or personal relationship(s) that may have inappropriately influenced them in writing this article.* Read our policy on competing interests.
- Author contributions: All authors must meet the criteria for authorship as outlined in the authorship policy and author contribution statement policies.
- Funding: Provide information on funding if relevant
- Disclaimer: A statement that the views expressed in the submitted article are his or her own and not an official position of the institution or funder.
  References: Authors should provide direct references to original research sources whenever possible. References should not be used by authors, editors, or peer reviewers to promote self-interests. Refer to the journal referencing style downloadable on our *Formatting Requirements* page.