A Mixed-Method Approach to Assessing the Need and Capacity for Epilepsy Surgery in a National Referral Hospital in Uganda

by

Prince Antwi

Duke Global Health Institute
Duke University

Defense Date: March 22, 2024

Approved:

Michael M. Haglund, Co-Advisor

Nathan Thielman, Co-Advisor

Kearsley Stewart

Deborah Koltai

Thesis submitted in partial fulfillment of the requirements for the degree of Master of Science in the Duke Global Health Institute in The Graduate School of Duke University
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ABSTRACT

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Abstract

Background: An estimated 80% of patients with epilepsy reside in LMICs, where surgical options for treating medication refractory epilepsy (MRE) may not be readily available. This study assesses the need for an epilepsy surgery program in Uganda and evaluates the current capacity for implementing such a program at the nation's largest hospital, the Mulago National Referral Hospital (MNRH).

Methods: Medical records of 183 adult patients receiving care for epilepsy at the Bosa Psychiatric Clinic between January and April 2021 were retrospectively reviewed to determine patterns of medical management of epilepsy. 13 clinicians across Psychiatry, Neurology, and Neurosurgery were interviewed; these interviews were analyzed thematically to address the subjects of need and capacity for epilepsy surgery at MNRH. 41 patients and 63 caregivers were surveyed on their perceptions and attitudes toward surgery as a potential treatment for epilepsy.

Results: Nearly half (49%) of patients receiving care at the Bosa Clinic had been treated on two or more anti-epileptic drugs (AEDs) over the course of their disease, with Carbamazepine, Sodium Valproate, and Phenytoin being the most commonly prescribed medications. Only few patients had records of prior brain imaging (8.2%) and EEG (21%) in their medical charts, and no patient had prior referral for surgical evaluation. The interviewed clinicians noted that there is a need for an epilepsy surgery program to augment the current medical practice. They identified infrastructure, cost, further specialized training, and public perception as factors to address in implementing a sustainable epilepsy surgery program locally. 53.3% of patients and 58.5% of caregivers would consider epilepsy surgery only after they had tried 5 or more AEDs without resolution of seizures, citing complications and cost as deterrents.

Conclusions: Both clinical records and clinician interviews demonstrated a need for a surgical option for treating idiopathic epilepsy among Ugandans with medication refractory epilepsy. Investigative modalities such as EEG, CT, and MRI are locally accessible for preliminary evaluation of surgical candidacy. A future pilot program could serve as a platform for training personnel to sustain an epilepsy surgery program at MNRH, and patients and caregivers would subscribe to surgical treatment if a local program is affordable and has a low complication rate.

Contents

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Abbreviations

AEDs	Anti-epileptic drugs
ATL	Anterior Temporal Lobectomy
BDI	Beck's Depression Inventory
CAH	Cortico-Amygalohippocampectomy
CT	Computerized Tomography
EEG	Electroencephalogram
LMIC	Low- and middle-income country
MNRH	Mulago National Referral Hospital
MRE	Medication refractory epilepsy
MRI	Magnetic Resonance Imaging
PET	Positron Emission Tomography
QOLIE	Quality of Life in Epilepsy
SAH	Selective Amygdalohippocampectomy
SPECT	Single-Photon Emission Computerized Tomography

Operational Definitions

Seizure: Paroxysmal, hypersynchronous neuronal discharge

Epilepsy: A chronic, non-communicable disease of the nervous system characterized by recurrent unprovoked seizures

Medication refractory (or drug resistant) epilepsy: Failure of adequate trials of two tolerated, appropriately chosen and used antiepileptic drug schedules (whether as monotherapies or in combination) to achieve sustained seizure freedom [1]

Acknowledgements

Apart from Me you can do nothing (rf. John 15:5). My foremost gratitude is to the Most High God who has ordered my steps throughout my life, and ultimately brought me into the Duke Global Health Pathway. I must thank my precious wife, Ama Annama Antwi, and my daughters, Phoebe and Princess Antwi, for being my biggest cheerleaders during my academic and career pursuits at Duke University. To my extended family and friends who have encouraged me and prayed for me, thank you and God bless you.

I would like to thank Drs. Michael Haglund, Anthony Fuller, and Nathan Thielman for your mentorship in global health. In large part, I came to Duke Neurosurgery because I wanted to learn from Dr. Haglund how to improve neurosurgical care in less resourced settings; I am indebted to his mentorship. Dr. Thielman's guidance, encouragement, and friendship have been invaluable in navigating the Global Health Pathway. An immense gratitude goes to the Chair of Duke Neurosurgery, Dr. Gerald Grant, for his support of my interest in global neurosurgery.

Navigating this work in Uganda would have been impossible without the help of Dr. Deborah Koltai, Tara Pemble, Beth Baltes, and Christine Muhumuza, and my research assistant Mr. Emmanuel Tumuhimbise. My immense gratitude goes to collaborators at the Mulago National Referral Hospital, particularly Drs. Joel Kiryabwire and Oscar Obiga, and to the patients, caregivers and clinicians who participated in the study. My hope is that soon surgical treatment will be an option for Ugandans living with refractory epilepsy.

I greatly appreciate Prof. Kearsley Stewart for her mentorship on this project; she has taught me the most of what I know in global health ethics and in quantitative analysis. Lastly, I am very grateful to the U_Epilepsy_Surgery subgroup in DGNN, including Dr. Alvan Ukachukwu, for your support in this endeavor. I look forward to continued work to help improve epilepsy care across Africa.

1. Introduction:

Characterized by recurrent episodes of unprovoked seizures, epilepsy creates a significant global health challenge and contributes to social stigma, impaired quality of life, lost productivity, comorbid medical and psychiatric conditions, burgeoning health care costs, and even premature death.[2–8] The World Health Organization (WHO) estimates that about 50 million people worldwide live with epilepsy, and approximately 80% of these individuals live in low- and middle-income countries (LMICs).[9] A recent meta-analysis of 167 articles estimated the incidence of epilepsy in Africa at 84.8 cases per 100,000 person-years, with an active prevalence of 729.5 cases per 100,000 persons.[10]

Anti-epilepsy drugs (AEDs) represent the first line of treatment for epilepsy; if correctly diagnosed and appropriately treated with AEDs, an estimated 70% of all persons with epilepsy (PWE) could live free of seizures.[9] Nearly 30% of persons with epilepsy will have disease refractory to medical management. Multiple studies have demonstrated the role of surgery in managing these patients whose epilepsy may be refractory to adequate and well-tolerated AEDs.[11–13] A majority of patients with previously intractable epilepsy who ultimately undergo surgery for epilepsy achieve significant freedom from disabling seizures which conceivably translates into decreased social stigma, improved quality of life, and increased productivity.[14] In the last two decades, the modalities available for surgically managing patients with intractable epilepsy have greatly expanded to include less morbid surgical procedures, neurostimulation, and laser ablation, among others.[14,15]

Despite the advances in the medical and surgical management of refractory epilepsy, there is still a large treatment gap globally.[16] In more developed parts of the world, there is a reported 5-20 year delay between when patients demonstrate having medication-refractory disease and when

they ultimately are considered for surgical evaluation.[17–19] Not only is this delay likely more pronounced in LMICs, but barriers such as social stigma around epilepsy, limited options for AEDs, and limited infrastructure and personnel account for an even greater treatment gap for medication refractory epilepsy in LMICs. In Africa alone, Vaughan et al., in 2019, estimated a burden of surgically treatable epilepsy of 213,157 new individuals per annum, with a current estimated surgical volume of 1,819,067 cases across the continent.[10] One must consider this large surgical disease burden in the context of the limited opportunities for neurosurgery across Africa. Notably, in a 2021 survey of providers from 51 African countries, only seven countries had prior experiences with epilepsy surgery programs, some of which are no longer in continuity due to terminated international collaborations.[20]

In an effort to close this epilepsy treatment gap in LMICs, it is imperative to assess the current need and capacity for epilepsy surgery in the public health systems of respective countries.

1.1 Overview of epilepsy prevalence and management in Uganda

The estimated incidence of epilepsy in Africa is 84.8 cases per 100,000 person-years, with an active prevalence of 7.3 cases per 1,000 persons. [10] Although Duke Global Neurosurgery and Neurology (DGNN) is currently conducting a prevalence study across the country, the true prevalence of epilepsy in Uganda is challenging to determine. That said, in one study surveying 64,172 residents in the Iganga/Mayuge Health Demographic Surveillance Site in Uganda, the prevalence of "active convulsive epilepsy" was estimated at 10.3 cases per 1,000 persons (95% confidence interval [C.I]: 9.5-11.1/1000 persons), after adjusting for nonresponse and sensitivity of the screening tool which involved two questions.[21] The true estimate of the prevalence of epilepsy across the country is likely higher as the study did not account for patients with non-convulsive seizure semiology. Further, nearly 70% of people with epilepsy were unaware of their

diagnosis, suggesting low awareness of the disease in Iganga - and potentially across Uganda. Concerning treatment, the researchers found that while 49.3% of respondents with epilepsy were receiving traditional medicine treatments, only 21.2% (95% C.I: 16.5-25.8%) were receiving anti-epilepsy drugs.[21] Among individuals with epilepsy in Uganda who sought biomedical clinical care at three major public referral hospitals in Uganda, 46% and 37% were treated with one or two AEDs, respectively.[22] Carbamazepine, sodium valproate, and phenytoin were the most commonly prescribed AEDs, with other AEDs being relatively uncommon. While the study demonstrated a trend toward improved seizure severity with treatment at these public referral hospitals, more than half of the patients had sub-therapeutic levels of their medications. This concern of suboptimal seizure control has similarly been demonstrated by Atugonza and colleagues: of 139 children receiving medical treatment for epilepsy at the Mulago National Referral Hospital (MNRH) Pediatric Neurology Clinic, 32.4% were on multiple AEDs and 59.7% of the children had sub-therapeutic drug levels. [23] The authors attributed this suboptimal seizure control on AEDs to lack of adequate supply of AEDs in their setting, an apparent tendency to prescribe multiple AEDs instead of titrating up a monotherapy to achieve therapeutic level, and challenges with continuity of care as their clinic was often run by senior house officers on a rotational basis.

As mentioned, even with optimal medical treatment of seizures, nearly a third of patients have MRE, which often is responsive to surgical treatment.[14] In a setting like the public health sector in Uganda, where many patients demonstrably have sub-therapeutic drug levels, it is conceivable that many PWEs have suboptimal seizure control.[23,24]

1.2 Published experiences in epilepsy surgery in Africa

A July 2022 database search in PubMed/MEDLINE and Google Scholar, identified eight full-text articles that reported on either seizure outcomes and/or quality of life outcomes after

epilepsy surgery in Africa (Figure 1). These eight publications represented results from seven unique cohorts from the seven African countries - including Uganda - that reported epilepsy surgery programs in the recent survey by Kissani and colleagues.[20] The reported clinical outcomes of these prior reports of epilepsy surgery on the continent are summarized below and in Table 1.

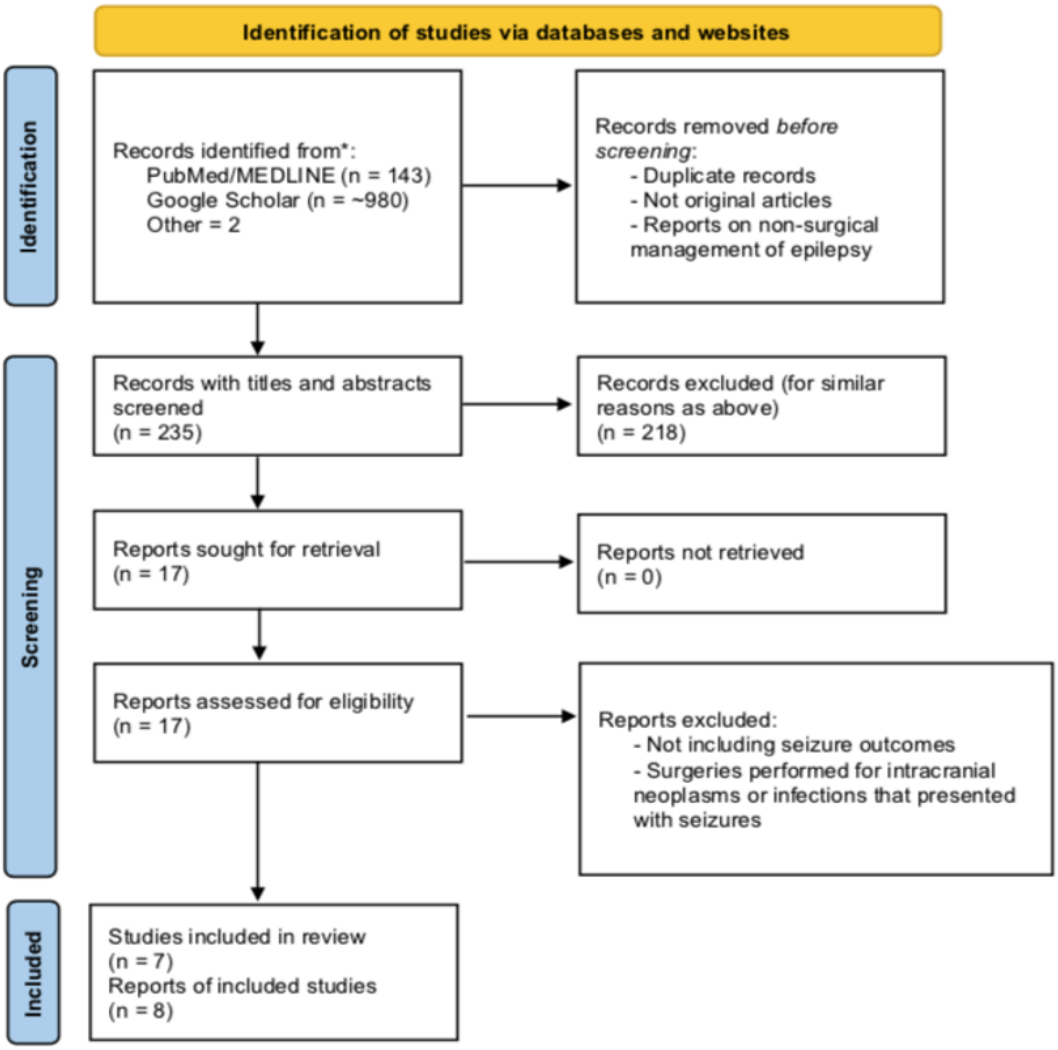


Figure 1: Methodology of literature search and selection of eligible articles

1.2.1 Geographic distribution and collaborations in published experiences in epilepsy surgery in Africa

The geographic distribution of the publications included in this review is of interest. Most of the studies were conducted in North Africa, with reports from Tunisia, Algeria, Egypt, and Morocco.[25–27] The reports by Dr. Ruberti in Kenya and the reports from Dr. Boling's team in Uganda represent contributions from East Africa.[28–30] Deliperi and Butler's works are contributions from South Africa. [31,32] Conspicuously, as of the time of the literature review there was no published report from West Africa on outcomes following epilepsy surgery.

Of further interest is the role of external collaborations in accomplishing epilepsy surgery in Africa. Dr. Ruberti trained and practiced in Italy before moving to Kenya, where his contribution included his report on performing temporal lobectomies, callosotomies, and lesionectomies for patients with intractable epilepsy.[30] The pilot study conducted by Dr. Boling and colleagues in Uganda relied on a partnership between local staff in Uganda and colleagues in the United States and Canada: Ugandan staff were trained in EEG technology at the Montreal Neurological Institute and Stellate, Inc. to help care for patients in the epilepsy monitoring unit, whereas EEG data were transferred to West Virginia University to be interpreted by experts.[28] The work in Tunisia was accomplished in collaboration between providers in the Neurological Department of Charles Nicolle Hospital of Tunis and providers at the neurophysiological Department of Charles Nicolle Hospital in Rouen, France, via the EUMEDCONNECT network project.[25]

1.2.2 Determining candidacy for epilepsy surgery

Following compelling results from studies in high income countries (HICs), current teaching is that patients with medication refractory epilepsy - formally defined as failure to achieve sustained seizure freedom in spite of adequate trials of two well tolerated and appropriately chosen AEDs - may be evaluated for epilepsy surgery.[11,13] In HICs such as the United States, evaluation

for epilepsy surgical candidacy follows strict algorithms that routinely involve clinical assessments by neurologists, neuropsychologists and neurosurgeons, video-EEGs, epilepsy-protocol MRIs, and on some occasions PET and SPECT scans; some patients may then proceed to invasive neurophysiological monitoring such as stereo-EEG and subdural grids and strips.[14]

In determining the candidacy of patients for possible surgical management of their intractable epilepsies, all the studies included here employed a combination of noninvasive modalities comprising the clinical history and examination, neuropsychological assessment, the EEG (although not always clear how long patients were monitored on video-EEG), and neuroimaging (CTs for the studies before 2010 and MRIs for the studies since 2010). Although there are reports in the literature of the use of functional MRI and invasive EEG monitoring in presurgical evaluation in South Africa, none of the studies included in this current report employed either modality in presurgical assessment.[20,33] The 2013 report from the team in Egypt is the only one that utilized PET and SPECT in presurgical evaluation, demonstrating that a multimodal imaging approach boosts lateralization of the pathologic substrate in patients with intractable temporal lobe epilepsy, especially in cases where the MRI is not definitive in showing an epileptogenic substrate.[27]

1.2.3 Procedures performed and results reported

With some of the studies describing the respective surgical procedures as “lesionectomy”, “resective surgery”, and simply “surgery for temporal lobe epilepsy”, it is challenging to determine the exact proportions of the surgical procedures performed for temporal lobe epilepsy versus extratemporal lobe epilepsy. Regardless, the number of patients treated for temporal lobe epilepsies constitutes most of the patients included in the published reports, with the Egypt study being the largest with 137 patients (Table. 1). For temporal lobe epilepsy, the teams varied in their surgical

approaches with some performing cortico-amygdalohippocampectomies (CAH) and others performing selective amygdalohippocampectomies (SAH). Ruberti is the only author to report performing hemispherectomies (in seven patients) and callosotomies (in seven patients).[30] Surgical procedures reported included resections of lesions such as cavernous malformations and "post-traumatic scars", among others, that had been associated with intractable seizures.

The duration of follow-up varied among the various published reports, ranging from 2 months to 11 years when reported. Using the Engel classification of seizure freedom, 60-100% of patients undergoing surgery for intractable epilepsy achieved good outcomes (often defined as Engel I or II; see classification system in Table 2). The Tunisian cohort had a remarkable 100% of its 10 patients achieving Engel I outcome.[25] The Ugandan cohort had 60% of 10 patients achieving Engel I outcome at the 1-year follow-up, but that improved to 70% at the eight-year follow-up, with one of the previously Engel II patients ultimately becoming free of seizures.[28,29] Kassem and colleagues found that in patients with "positive" localizing MRIs, 75% had good seizure outcomes after surgery compared to 60% in those patients with "negative" MRIs despite using PET/SPECT as part of their multimodal approach for lateralizing epileptogenic foci.[27] The South African studies were the only ones to compare seizure freedom outcomes between selective amygdalohippocampectomy (SAH) and anterior temporal lobectomy (ATL). In their cohort of 32 patients randomized to either SAH or ATL of the dominant hemisphere, Engel I outcome was reported in 65% and 81% of patients in the SAH and ATL arms, respectively, although that difference was not statistically significant ($p = 0.31$).[31]

Although the scope of functions assessed on neuropsychological testing in these studies have been limited, the reported results in suggest that quality of life, as measured with the QOLIE-31 or QOLIE-89, improves after surgery for intractable temporal epilepsy (Table 3).[30,31] In the South African studies, this improvement remained true in both SAH and ATL. When reported, the

severity of depression nominally improved following surgery for intractable temporal lobe epilepsy with a 2.2 to 4.7 points decrease on the Beck's Depression Inventory (BDI).[30,31] Regarding neurocognition after surgery, Dr. Boling and team had one patient with a significant decline in post-surgical assessments (on the mini-mental state examination, MMSE) between the 6- and 12- month postoperative period.[23] Specifically, in the South African randomized study, visual naming similarly declined in both the SAH and ATL groups, but auditory naming improved in both groups with significantly better improvement in the SAH group.[31]

Notably, there is very limited reporting of complications associated with these surgical procedures performed in Africa for medication-refractory epilepsy. Boling et al. reported one case of a postoperative wound infection treated with debridement and antibiotics.[28] Ruberti reports having no complications in his cohort, as did Khiari and colleagues in their Tunisian study. [25,30] The remaining reports do not discuss any postoperative complications.

Table 1. Summary of published articles on epilepsy surgery in Africa

Authors, Year	Country	Number of Patients	Preoperative assessment			Surgery	Follow up	Seizure Outcome
			Video-EEG	Imaging	Neuropsychologic evaluation			
Ruberti R.F., 1997	Kenya	97	_	CT	Yes	Lesionectomy (64pts); temporal lobectomy (19pts); hemispherectomy (7pts); anterior callosotomy (7pts)	_	_
Boling et al., 2009; Fletcher et al., 2015	Uganda	10	Yes	CT	Yes	CAH	Mean of 1 year, then 8 years	60% Engel I at 1 year; 70% Engel I at 8 years
Khiari et al., 2010	Tunisia	10	Yes	MRI	Yes	Temporal lobectomy	At least, 4pts followed	100% Engel I outcome

							for 2 years	
Lagha et al., 2012	Algeria	19	Yes	MRI	Yes	ATL (11 pts); Lesionectomy (8pts)	5-11 years for 7pts; 2-15 months for 12pts	89.5% Engel I/II
Kassem et al., 2013	Egypt	137	Yes	MRI, PET, SPECT	_	"Surgery for temporal lobe epilepsy"	> 12 months for each patient	MRI-positive (104pts) - 75% Engel I/II; MRI-negative (33pts) - 60% Engel I/II
Souirti et al., 2016	Morocco	7	Yes	MRI	Yes	"Resective surgeries"	_	71.4% Engel I/II
Deliperi and Butler, 2017*	South Africa	25	Yes	MRI	Yes	SAH; ATL	1 year	64% Engel I, 24% Engel II
Deliperi and Butler, 2021*	South Africa	32	Yes	MRI	Yes	SAH; ATL	1 year	SAH - 65% Engel I; ATL - 81% Engel I

CAH – corticoamygdalohippocampectomy; SAH- selective amygdalohippocampectomy; ATL – anterior temporal lobectomy; pts – patients

* Unclear if the patients in 2017 were included in the 2021 study

Table 2. Engel's classification of postoperative clinical seizure outcome.

Class	Postoperative clinical seizure outcome
I	Completely free of disabling seizures, may have auras
II	Rare disabling seizures
III	Worthwhile reduction in seizures
IV	No appreciable reduction in seizures

Modified from Kivelev et al. Neurosurgery 2009 [34]

Table 3. Summary of seizure freedom, quality of life, and neurocognitive outcomes after surgery for medication refractory epilepsy in Africa

Authors, year	Country	Number of Patients	Surgery	Follow up	Effect on QOL	Effect on Depression	Effect on Neurocognition
Fletcher et al., 2015	Uganda	10	CAH	8 years	76.15 points increase on QOLIE-31	_	_
Ives-Deliperi and Butler, 2017	South Africa	25	Dominant temporal lobe resection	1 year	17.2 points increase on QOLIE-89	4.7 points decrease on BDI	4.6 points decline on BNT
Ives-Deliperi and Butler, 2021	South Africa	32	SAH, ATL	1 year	On QOLIE-89, 15 and 18 points increases after SAH and ATL respectively	On BDI, 2.2 and 4.6 points decrease on BDI after SAH and ATL respectively	On BNT, 6.3 and 5.5 points decrease after SAH and ATL respectively; on ANT, 5.2 and 0.2 points increase after SAH and ATL respectively

CAH – corticoamygdalohippocampectomy; SAH- selective amygdalohippocampectomy; ATL – anterior temporal lobectomy; QOLIE – Quality of Life in Epilepsy; BDI – Beck's Depression Inventory; BNT – Boston Naming Test; ANT – Auditory Naming Test

1.3 Study purpose, aims, and hypothesis

As noted above, in 2009, Dr. Boling and colleagues from the United States partnered with the CURE International Hospital in Mbale, Uganda, to perform temporal lobectomies for 10 patients with medication-refractory epilepsy.[28] Of these patients, 60% were free of seizures by 1 year after surgery, and at 8-year follow-up, that number had improved to 70%.[29] While that work was notably successful, it was limited in scope and duration, and piloted only one surgical

technique for TLE. Given the high number of persons with medication refractory epilepsy in Uganda, continued exploration of the value of surgical management is warranted.

The Duke Division of Global Neurosurgery and Neurology (DGNN) has collaborated with neurosurgeons at MNRH to establish a neurosurgical residency training program. Subsequently, with support from the King Baudouin Foundation, DGNN worked with faculty at the Mbarara Regional Referral Hospital and Mbarara University of Science and Technology to open a dedicated Epilepsy Clinic. These progresses make way for the possibility of an epilepsy surgery program in the public health sector of Uganda, though much work needs to be done. This study will support these progresses by: estimating the prevalence of medication-refractory epilepsy, assessing the available resources for evaluating patients with epilepsy for possible surgical candidacy, and characterizings the current needs that require attention if epilepsy surgery is to established in Uganda. Knowledge from such need assessment may also inform future endeavors to introduce or improve epilepsy surgery in other LMICs. In light of this, the present study sought to accomplish the following objectives:

1. Determine available assessment tools (such as video-EEG and MRI) and personnel (such as neurologists and radiologists) for evaluating patients with medication refractory epilepsy for potential surgical candidacy at the Mulago National Referral Hospital (MNRH)
2. Identify existing barriers to providers and patients accessing the needed studies and expert examinations.
3. Determine patient and caregiver perspectives on surgery as a potential treatment for epilepsy
4. Estimate the prevalence of MRE among patients receiving epilepsy care at MNRH

We hypothesized that: 1) there are limited resources for presurgical evaluation of patients with medication-refractory epilepsy, 2) providers do not feel adequately trained/experienced to

perform epilepsy surgery procedures independently, 3) patients and caregivers have significant reservations about surgery as a treatment for epilepsy, and 4) most patients who likely have medication-refractory epilepsy have not been duly/thoroughly evaluated for possible surgically-treatable pathologies.

2. Methods

To accomplish the afore-listed objectives, this study employed a mixed-methods approach. Specifically:

- Qualitative data on the current needs and capacity for epilepsy surgery was gathered using semi-structured interviews of clinicians within the public health sector at MNRH in Kampala, Uganda.
- Qualitative and quantitative data on attitudes and perceptions of patients and caregivers toward epilepsy surgery was gathered through in-person surveys
- Quantitative data on treatment patterns of patients with epilepsy was gathered through:
    - Retrospective review of patients' medical records
    - In-person surveys of patients and caregivers

2.1 Setting

All elements of this study were conducted at the 1500+ bed Mulago National Referral Hospital (MNRH), the largest national referral hospital in Uganda. MNRH is affiliated with the nation's oldest and largest tertiary education institution, the Makerere University. This study was primarily set within the Departments of Neurosurgery, Neurology (adult and child), and Psychiatry at MNRH as clinicians from these departments are most likely to manage the care of patients with epilepsy. Much of epilepsy care happens in the outpatient setting - often with inpatient care reserved for patients in status epilepticus; thus, this study attended to the outpatient clinics. Clinician interviews were conducted on both the wards and in the clinics; however, the surveys of patients and caregivers were conducted at the Bosa Psychiatry Clinic and the

Paediatric Neurology Clinic at MNRH. Further, the medical records reviewed as part of the study consisted of those maintained at the Bosa Clinic.

2.2 Participants

Healthcare providers practicing in Neurosurgery, Neurology (both adult and pediatric), and Psychiatry were invited to participate in the semi-structured interviews. Attending physicians, resident physicians, and clinical officers within these departments were eligible if they had experience caring for patients with epilepsy at MNRH.

Patients aged 18 years or older attending the outpatient Psychiatry and Neurology clinics with primary diagnosis of epilepsy during the study period, and their caregivers if accompanied by any, were recruited to complete study surveys. If an adult participant had limited competence due to the effects of their seizure disorder, only his/her caregiver was enrolled. In the Pediatric Neurology clinic, adult caregivers of children with epilepsy were recruited for the study.

All adult patients treated for epilepsy at the Bosa Clinic within the study period were candidates for the retrospective chart review.

2.2.1 Sample selection

The sample of healthcare providers to complete the interviews was determined by purposive sampling. Emails and WhatsApp messaging were used to contact eligible candidates. Further, eligible providers met on the wards or in clinics were asked in person to consider participating in study. The sample of patients and caregivers to complete the surveys was established via convenience sampling with the support of clinic nurses. Head nurses at the clinics were informed of the study and the target population. They subsequently directed patients who came to clinics during the study period for epilepsy treatment to the study team to discuss potential participation in the study. For the retrospective chart review, the records of all adult

patients who had received treatment for epilepsy at the Bosa Clinic at MNRH between January and April 2021 were reviewed.

2.2.2 Sample size estimation

Treating the healthcare providers as a homogenous group, it was estimated that after 12-16 interviews the study would reach 90% saturation in identifying themes surrounding the need and capacity for epilepsy surgery at MNRH. Nielsen and Landauer evaluated six different projects and determined via mathematical models that 90% of usability challenges in a system can be uncovered after 12 interviews.[35] This has similarly been demonstrated by works of other authors suggesting 90% saturation can be achieved in qualitative analysis using in-depth interviews.[36,37]

For the surveys, all eligible and consenting patients and caregivers attending the clinics during the study period were to be included in the sample. To identify the rate of medication refractory epilepsy among patients receiving outpatient epilepsy care at MNRH, we estimated that medical records of 323 patients with epilepsy would be reviewed to identify the reported 30% rate of MRE in the literature and assuming a 5% margin of error and a 95% confidence interval. The calculation of this estimate is as follows:

$$n \geq \left(\frac{z}{m}\right)^2 \times \hat{p}(1-\hat{p})$$

$$= n \geq (\frac{1.96}{0.05})^2 \times 0.3 \times 0.7 = 322.694 \approx 323 \quad .$$

2.3 Procedures

2.3.1 Ethical Approval

The protocol and instruments (ie. survey tools, interview guide, and consent forms) for this study were reviewed and approved by the Duke University Medical Center Institutional

Review Board (IRB; protocol ID Pro00112845) and the Mulago National Referral Hospital Research Ethics Committee (REC; protocol ID MHREC-2023-94). The study was exempted from seeking consent from patients whose medical records were reviewed as part of the study. Clinicians granting interviews and patients and caregivers completing the study surveys provided written informed consent; completed consent forms were maintained at MNRH. A research assistant fluent in the local language was always present to discuss the study with potential participants prior to consenting for the study.

2.3.2 Data collection

All semi-structured interviews were conducted in-person using an interview guide created by a team of researchers at Duke University (Appendix A). The author of this thesis (PA) conducted all interviews. The interview guide covered topics ranging from healthcare providers' perceived need for epilepsy surgery at MNRH, availability of personnel and infrastructure to evaluate patients for surgical candidacy and conduct surgeries, and providers' perceived priority of epilepsy surgery within the context of the current needs of the health system at MNRH and in Uganda at large. All interviews were conducted in English and took place at the provider's chosen site of meeting. The interviews were recorded with an audio recording device and then uploaded for storage on Duke Box.

A team of researchers - composed of the author of this thesis (PA), a DGNN faculty member (Dr. Anthony Fuller), and two medical students (Kevin Bode-Padron and Adhith Palla) - created the survey tools completed by patients and caregivers (Appendices B and C respectively). Specifically, the surveys assessed the duration of patients' disease course, treatment history, awareness of epilepsy surgery as a treatment option for refractory disease, and perceptions of the risks and benefits of undergoing surgery to treat epilepsy. The surveys were hosted on Duke Qualtrics and completed on a dedicated study iPad.

Retrospective chart review using a chart review data collection guide (Appendix D) was conducted, with data elements collected into a Microsoft Excel sheet securely hosted on the study's folder in Duke Box.

2.4 Measures

From the qualitative aspect of the study, themes were gathered regarding providers' perspectives surrounding the following variables:

1. Availability of resources (such as trained workforce, video-EEG, MRI, PET/SPECT scanners, etc) for evaluation for evaluation of surgical candidacy of patients with medication refractory epilepsy
2. Barriers to implementing an epilepsy surgery program at MNRH, including stigma, workforce and resource unavailability, and those barriers intrinsic to the hospital and national health system and its processes
3. Perception of providers, patients and caregivers regarding brain surgery as a treatment modality for refractory epilepsy

The quantitative instruments of the study measured variables such as:

1. Duration of epilepsy in patients receiving care at MNRH
2. History of prior epilepsy-related evaluation (particularly with EEG and MRI) and medical treatment
3. Knowledge, perceptions and attitudes regarding surgery as a treatment modality for refractory epilepsy

2.5 Analysis

2.5.1 Qualitative analysis

Audio recordings of the interviews of healthcare providers were transcribed verbatim in English. The interview transcripts were coded using Nvivo14 (QSR International Pty Ltd, Victoria, Australia) and Microsoft Excel (Microsoft, Washington, USA) for thematic analysis as described by Braun and Clarke.[38–41] All interview transcripts were read for data familiarization and relevant data pertaining to the research questions were organized into codes with the author defining each code. Subsequently the codes were clustered into themes related to epilepsy care and implementation of epilepsy surgery in Uganda. All themes and the data were reviewed for thematic validity, prior to defining each theme. The frequency of themes were tabulated; code frequencies were calculated as the ratio of the number of transcripts in which the code appeared to the total number of transcripts. The author of this thesis performed the interviews, transcriptions, coding, and thematic analysis. Visualization of the analysis and selected segments of the interview transcripts are included in this report (see example word tree below for "priority of epilepsy surgery"; Figure 2).

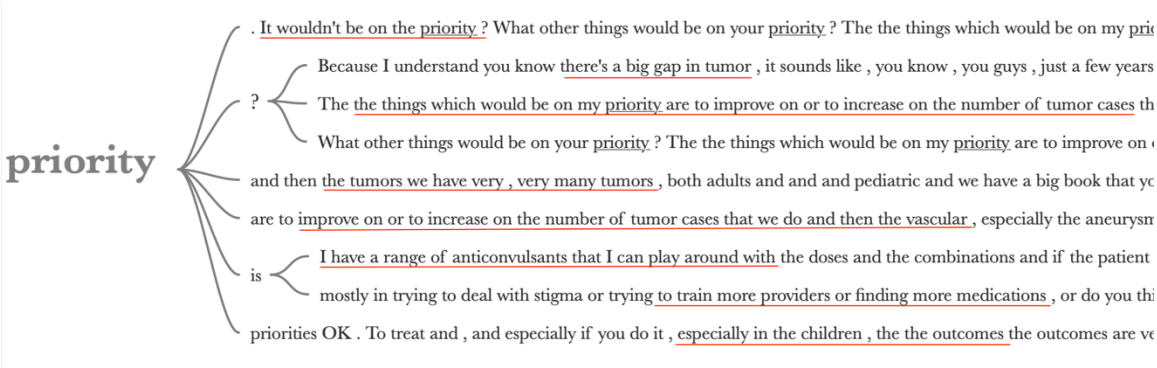


Figure 2. Word tree of "priority" as it appeared in interviews.

2.5.2 Quantitative analysis

Quantitative analysis in this study was completed with R studio (Posit Software, PBC, Massachusetts, USA) and Microsoft Excel (Microsoft, Washington, USA). Demographic information of study participants was described using descriptive statistics. Frequency of survey

responses were tabulated. The Pearson's chi-squared test and the Fisher-exact test were used to compare survey responses of patients and caregivers, assessing for statistically significant differences in attitudes and perceptions between the two categories of respondents to the survey.

3. Results

3.1 Retrospective chart review

The medical records of 183 adult patients who had received care for epilepsy at the Bosa Psychiatry Clinic between January and April 2021 were reviewed (see Table 4). One hundred and two (56%) of the patients were males. The median age at onset of seizures was 13 years (IQR = 5 - 21), the median age at time of last clinic visit was 24 years old (IQR = 18 - 30). Over the course of their care at the Clinic, 94 (51%) of the patients had been managed on one anti-epilepsy drug (AED), 61 (33%) on two AEDs, 19 (10%) on three AEDs. The most commonly prescribed AEDs were carbamazepine (used by 66% of patients), valproic acid (used by 34% of patients), and phenytoin (used by 36% of patients); only 1-6% of patients had been previously managed with newer AEDs such as levetiracetam, topiramate, and lamotrigine. At their last visits to the Clinic, 127 (70%) and 50 (27%) were being managed on one or two AEDs, respectively. Carbamazepine (66% of patients), valproic acid (26% of patients), and phenytoin (27% of patients) remained the three most frequently used AEDs at the last visits. Comparing previously tried AEDs to AEDs reported at last visit, 70 patients on AEDs at last visit had no documentation of previously tried AEDs, which could represent new initiation of treatment and/or other factors such as lapses in documentation, discontinuity in care across multiple facilities, or even missing prior medical charts. Of the remaining patients, 61 patients (including 11 patients on multiple AEDs) had no changes to their previously tried AEDs at the last visit. Unfortunately, there was no standardized way of documenting the frequency of seizures reported by patients; where available, patients were noted to have seizures as seldom as twice a year to as frequent as seven per day. Similarly, seizure frequencies at last visit were not consistently documented in medical records, with clinicians noting “much improvement”, “no seizures this year”, among others, when the patients had significant reduction in seizure frequency.

Regarding investigative studies for epilepsy, of the 183 patients only 38 (21%) had either EEG reports and/or summary of EEG studies in their medical charts at the Clinic. When available, these EEG studies were brief studies performed over 40-60 minutes. EEG findings included epileptiform discharges such as "bilateral generalized spike and wave [discharges] at 3Hz", focal sharp and wave complexes, central sharp waves, among others. Imaging of the brain was much less common as only one patient had an MRI report in the medical record and 14 patients had CT reports in their medical charts. All but one CT was read as "normal" with the exception being one CT study demonstrating global cerebral atrophy. Investigative studies such as PET and SPECT scans were not reported in the records of any of the patients. None of the records suggested that any of the 183 patients had been referred for neurosurgical evaluation and/or management.

Table 4. Summary of retrospective chart review on 183 adult patients receiving epilepsy care at Bosa Psychiatry Clinic between January and April 2021.

Table 4. Chart Review Descriptive Statistics	
Characteristic	N = 183[1]
Gender	
Female	81 (44%)
Male	102 (56%)
Age at Last Clinic Visit	24 (18 - 30)[1]
Median Age at Seizure Onset	13 (5 - 21)[2]
Number of AEDs Tried	
1	94 (51%)
2	61 (33%)
3	19 (10%)
4	2 (1.1%)
5	1 (0.5%)
Average Number of AEDs Tried	1.6 (0.77)[2]
AEDs tried	

Carbamazepine	120 (66%)
Valproic Acid	62 (34%)
Phenytoin	66 (36%)
Phenobarbital	10 (5.5%)
Diazepam	2 (1.1%)
Lamotrigine	6 (3.3%)
Levetiracetam	3 (1.6%)
Gabapentin	2 (1.1%)
Topiramate	1 (0.5%)
Number of AEDs at Last Visit	
1	127 (70%)
2	50 (27%)
Average Number of AEDs at Last Visit	1.3 (0.45)[2]
AEDs Reported at Last Visit	
Carbamazepine	120 (66%)
Valproic Acid	47 (26%)
Phenytoin	50 (27%)
Phenobarbital	1 (0.5%)
Diazepam	0 (0%)
Lamotrigine	4 (2.2%)
Levetiracetam	3 (1.6%)
Neurontin	1 (0.5%)
Topiramate	1 (0.5%)
EEG Completed	38 (21%)
Imaging Type	
CT	14 (7.7%)
MRI	1 (0.5%)
Neurosurgery Referral or Evaluation	
No	183 (100%)

[1] n (%), Median (IQR);
[2] Mean (SD)

3.2 Surveys of patients and caregivers

104 individuals - comprising 41 patients and 63 caregivers - completed the study surveys (see Table 5). As one would predict, the mean age of caregivers completing the survey was significantly higher than the mean age of patients completing the survey (37 years vs 28 years; $p < 0.001$). There were significant differences in the educational and employment statuses of the patients and caregivers completing the surveys. 81% of the caregivers had secondary or tertiary education, compared to 61% of patients (p-value = 0.007). Similarly, 77% of caregivers were either self-employed or employed full time; this was much lower for patients with only 44% of them reporting that they were either self-employed or working full time (p-value = 0.003).

Table 5. Summary of demographics of patients and caregivers completing study surveys.

Table 5. Patient and Relative Characteristics			
Characteristic	Patient, N = 41[1]	Relative, N = 63[1]	p-value[2]
Age at time of Survey	28 (8)	37 (11)	<0.001
Employment Status			0.003
Employed full time	9 (22%)	21 (33%)	
Employed part time	4 (9.8%)	1 (1.6%)	
Not employed	19 (46%)	13 (21%)	
Self employed	9 (22%)	28 (44%)	
Education			0.007
No education	1 (2.4%)	6 (9.5%)	
Primary education	15 (37%)	6 (9.5%)	

Secondary education (high school, technical school)	17 (41%)	32 (51%)	
Tertiary education (college, university, polytechnic)	8 (20%)	19 (30%)	

[1] Means (SD); n (%);

[2] Wilcoxon rank sum test; Fisher's exact test

Among the 41 patients completing the survey, there was a lag between onset of seizures (mean age of 12 years) and when the patients sought any medical attention (mean age of 16 years; Table 6). As noted in the retrospective chart reviews, the most commonly prescribed AEDs were carbamazepine (95% of the patients had been treated on this medication at one point in their disease course), phenytoin, and sodium valproate. Most of the patients (78%) reported having two or more seizures per month in spite of their ongoing treatments at the clinics where the study took place, suggesting a significant portion of this group could potentially meet criteria for medication refractory epilepsy. Fifty-one percent of the patients had been treated on two AEDs, 24% on 3 AEDs, and 7% on 4 AEDs. In addition to often requiring polytherapy to manage their seizures, the patients reported having notable side effects associated with their AEDs such as dizziness, sleep disturbances, headaches, blurry vision, and cognitive impairment.

Table 6. Epilepsy history among patients completing study surveys.

Table 6. Patient Seizure Characteristics	
Characteristic	Patient, N = 41[1]
Age at First Seizure	12 (10)

Age at First Neurology Visit	16 (10)
Estimated Seizures per Month	
1	9 (22%)
2-5	27 (66%)
> 5	5 (12%)
Anti-seizure Medications Taken Over Time	
0	1 (2.4%)
1	5 (12%)
2	21 (51%)
3	10 (24%)
4	3 (7.3%)
Anti-seizure Medications Currently Taking	
Carbamazepine	39 (95%)
Phenytoin	14 (34%)
Lamotrigine	3 (7.3%)
Topiramate	1 (2.4%)
Vigabatrin	1 (2.4%)
Diazepine	1 (2.4%)
Sodium Valproate	8 (20%)

Time Without a Seizure on Current Medication (months)	12 (12)
Side Effects on Current Medication	
Behavioral changes/Irritability	1 (2.4%)
Blurred vision/Diplopia	8 (20%)
Cognitive impairment	5 (12%)
Dizziness	25 (61%)
Fatigue	4 (9.8%)
Hallucinations	2 (4.9%)
Headache	10 (24%)
Hostility/Aggression	7 (17%)
Incoordination/Unsteadiness	1 (2.4%)
Increased salivation	2 (4.9%)
Insomnia/Sleep disturbance	13 (32%)
Nausea	2 (4.9%)
Vomiting	1 (2.4%)
Weight gain	3 (7.3%)
Other	6 (15%)
[1] Mean (SD); n(%)	

Knowledge, attitudes and perceptions regarding epilepsy surgery were largely similar among survey respondents, whether patients or caregivers (Table 7 and Figure 3). Less than half of patients (44%) and caregivers (30%) had any knowledge that epilepsy can sometimes be treated by a surgical procedure, suggesting a significant knowledge gap among the populace. The potential risks of living with uncontrolled seizures - such as injuries to self, difficulty maintaining relationships, difficulty maintaining employment - were well-recognized among both patients and caregivers. Despite this awareness of risks of poorly controlled seizures, a significant portion of respondents (37% of patients and 32% of caregivers) thought that brain surgery to treat epilepsy was "more dangerous" than continuing medications. Adverse outcomes that they associated with brain surgery as a potential treatment for epilepsy included hemiparesis/hemiplegia, memory loss, change in personality, and even death. Consequently, 53.3% of patients and 58.5% of caregivers thought epilepsy surgery should be considered only as a last resort or after trying five or more AEDs, evidence that the public has some hesitancy to surgical treatment of epilepsy. In spite of this apparent hesitation around surgery as a treatment option for epilepsy, most survey respondents (61% of patients and 70% of caregivers) would at least be interested in learning more about epilepsy surgery if their physician were to suggest it as a treatment option. One aspect of significant difference between patients and caregivers responding to the survey was the cadre of clinicians they would most trust to discuss surgery as a treatment option for epilepsy: 68% of caregivers would rather have that discussion with a neurosurgeon, whereas 64% of patients would rather listen to the recommendation of their general medical provider or even family and friends.

Patients and caregivers shared similar goals in the treatment of epilepsy. Virtually every respondent desired less frequent debilitating seizures for themselves or their relatives. Ninety-three percent of patients wished they could stop taking their AEDs, 63% would

like to be able to drive or operate heavy machines, and 61% wished they could plan for their futures without worrying about the impact of debilitating seizures. More than 80% of patients and caregivers would consider surgery as a treatment modality for epilepsy if it could be performed with no complications and had favorable outcomes in reducing seizure frequency. Their concerns in pursuing epilepsy, however, centered around potential complications (83% of patients, 86% of caregivers) and cost (78% of patients, 81% of caregivers) - both far more commonly reported than social concerns such as what family and friends would think about the patient.

Table 7. Comparison of survey responses between patients and caregivers.

Table 7. Survey Response: Comparisons Between Patients and Caregivers			
Characteristic	Patient, N = 41[1]	Relative, N = 63[1]	p-value[2]
Did you know that brain surgery is sometimes an option for treating epilepsy?	18 (44%)	19 (30%)	0.15
Which of these sources has made you aware of surgery as a possible treatment option for epilepsy?			0.58
Family/Friends	4 (9.8%)	4 (6.3%)	
Epilepsy support group	3 (7.3%)	5 (7.9%)	
General practitioner/family medicine physician/interest	6 (15%)	6 (9.5%)	
Community health worker	0 (0%)	2 (3.2%)	

Neurologist	6 (15%)	4 (6.3%)	
Internet	1 (2.4%)	1 (1.6%)	
I know someone who had surgery for epilepsy	0 (0%)	1 (1.6%)	
Other	23 (56%)	45 (71%)	
Which of these sources would you trust the most to discuss with you if brain surgery was an option for treating seizures?			<0.001
Family/friends	8 (20%)	6 (9.5%)	
General practitioner/family medicine physician/internist	18 (44%)	10 (16%)	
Neurologist	0 (0%)	4 (6.3%)	
Neurosurgeon	15 (37%)	43 (68%)	
In your opinion, which of these can occur to someone who has seizures?			0.54
Difficulty keeping a job and/or doing well in school	34 (83%)	39 (62%)	
Difficulty starting and/or maintaining relationships	26 (63%)	27 (43%)	
Feeling discriminated against by others in society (also called, stigma)	35 (85%)	44 (70%)	
Injury during seizure	38 (93%)	63 (100%)	
Not being allowed to drive or operate heavy machines	25 (61%)	29 (46%)	
Seizure that takes a long time to break and requires being hospitalized	29 (71%)	55 (87%)	

Side effects from anti-seizure medications	26 (63%)	40 (64%)	
Sudden unexpected death	35 (85%)	60 (95%)	
In your opinion, which of these can be negative effects of brain surgery for epilepsy?			0.84
Change in personality	9 (22%)	21 (33%)	
Death	32 (78%)	54 (86%)	
Difficulty seeing	6 (15%)	19 (30%)	
Difficulty speaking	7 (17%)	17 (27%)	
Loss of function of arm/leg on one side of body	27 (66%)	50 (79%)	
Memory loss	18 (44%)	38 (60%)	
Given the risks you may associate with brain surgery, in your opinion when should epilepsy surgery be considered?			0.62
As a first resort	17 (41%)	26 (41%)	
After trying one medication prescribed by the neurologist	1 (2.4%)	0 (0%)	
After trying 2-5 medications prescribed by the neurologist	1 (2.4%)	0 (0%)	
After trying more than 5 medications prescribed by the neurologist	3 (7.3%)	6 (9.5%)	
Only as a last resort	19 (46%)	31 (49%)	

In general, continuing to have seizures in spite of trying multiple medications is more dangerous than having surgery to treat seizures?			0.44
Strongly agree	5 (12%)	12 (19%)	
Somewhat agree	6 (15%)	14 (22%)	
Neutral	15 (37%)	17 (27%)	
Somewhat disagree	6 (15%)	12 (19%)	
Strongly disagree	9 (22%)	8 (13%)	
If one of your doctors was to suggest that you consider having surgery as a way to treat your seizures, what would be your first reaction?			0.64
Curious	4 (9.8%)	5 (7.9%)	
Discouraged	3 (7.3%)	1 (1.6%)	
Interested	25 (61%)	44 (70%)	
Refusal	5 (12%)	8 (13%)	
Suspicious	4 (9.8%)	5 (7.9%)	
If you were to consider surgery as a possible treatment for epilepsy, which person's opinion would matter most to you?			<0.001
Family/friends	17 (41%)	9 (14%)	
General practitioner/family medicine physician/internist	8 (20%)	6 (9.5%)	

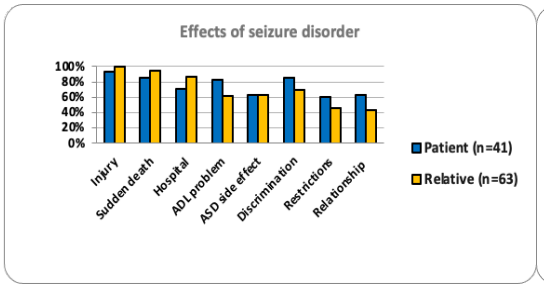
Neurologist	4 (9.8%)	1 (1.6%)	
Neurosurgeon	12 (29%)	47 (75%)	
If you were considering surgery as a treatment for epilepsy, which of these would you be worried about?			0.33
Developing a complication from the surgery	34 (83%)	56 (89%)	
How my friends/family will see me or feel about me	3 (7.3%)	1 (1.6%)	
How to pay for the care received (transportation	32 (78%)	51 (81%)	
What are your most important goals in the treatment of your epilepsy?			0.01
To be able to hold a job	22 (54%)	13 (21%)	
To be able to plan for the future	25 (61%)	31 (49%)	
To be able to start and/or maintain a relationship	17 (42)	6 (9.5%)	
To be allowed to drive and operate heavy machines	11 (27%)	7 (11%)	
To have improved memory and concentrations	26 (63%)	41 (65%)	
To have less frequent and/or fewer debilitating seizures	12 (29%)	15 (24%)	
To never have a seizure again	40 (98%)	63 (100%)	
To stop taking anti-seizure medications	38 (93%)	60 (95%)	
To take part in activities and hobbies without the uncertainty of having a seizure	25 (61%)	22 (35%)	

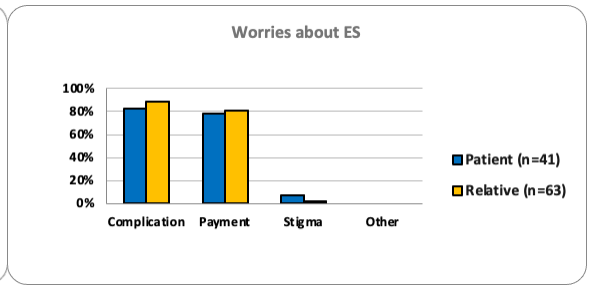
Other:	1 (2.4%)	0 (0%)	
I would rather try more anti-seizure medications than ever consider having surgery for epilepsy.			0.21
Strongly agree	10 (24%)	10 (16%)	
Somewhat agree	5 (12%)	9 (14%)	
Neutral	13 (32%)	11 (17%)	
Somewhat disagree	5 (12%)	16 (25%)	
Strongly disagree	8 (20%)	17 (27%)	
I would rather try alternative medicine (ie. herbal medicine, traditional healers) than ever consider having surgery for epilepsy.			0.1
Strongly agree	2 (4.9%)	1 (1.6%)	
Somewhat agree	1 (2.4%)	4 (6.3%)	
Neutral	11 (27%)	8 (13%)	
Somewhat disagree	1 (2.4%)	8 (13%)	
Strongly disagree	26 (63%)	42 (67%)	
Would you be willing to undergo surgery to treat your seizures if you were guaranteed that you will no longer have seizures after the surgery and will have no complication or brain injury?			0.27
Strongly agree	30 (73%)	47 (75%)	
Somewhat agree	3 (7.3%)	9 (14%)	

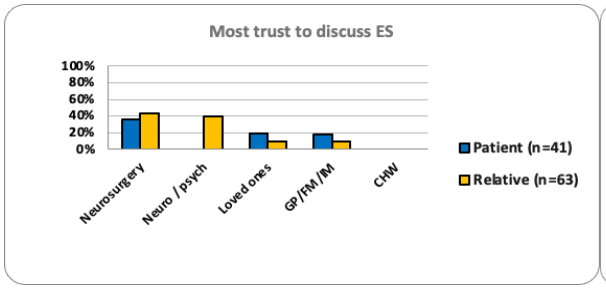
Neutral	7 (17%)	4 (6.3%)	
Strongly disagree	1 (2.4%)	3 (4.8%)	
Has your knowledge and/or perception of surgery as a treatment option for epilepsy changed after completing this questionnaire?			0.65
No	1 (2.4%)	4 (6.3%)	
Yes, I am more curious or interested in epilepsy surgery	40 (98%)	59 (94%)	

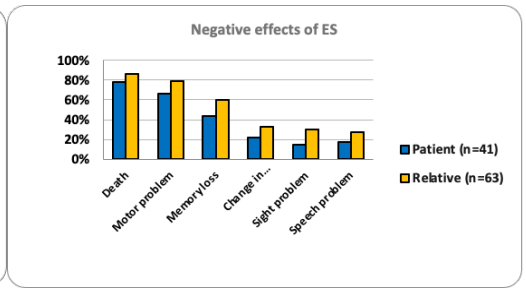
[1] n (%);

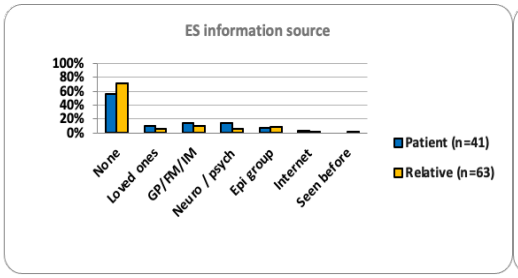
[2] Pearson's Chi-squared test; Fisher's exact test

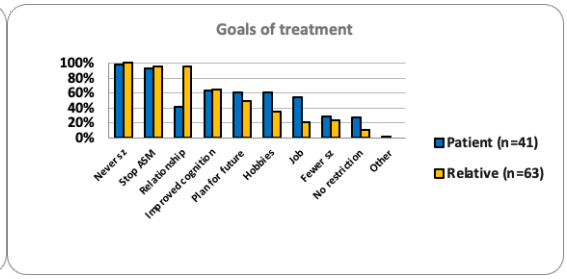

Effects of seizure disorder
100%
80%
60%
40%
20%
0%
Injury
Sudden death
Hospital
ADL problem
ASD side effect
Discrimination
Restrictions
Relationship
Patient (n=41)
Relative (n=63)

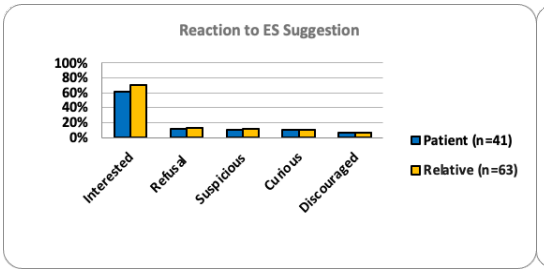

Worries about ES
100%
80%
60%
40%
20%
0%
Complication
Payment
Stigma
Other
Patient (n=41)
Relative (n=63)

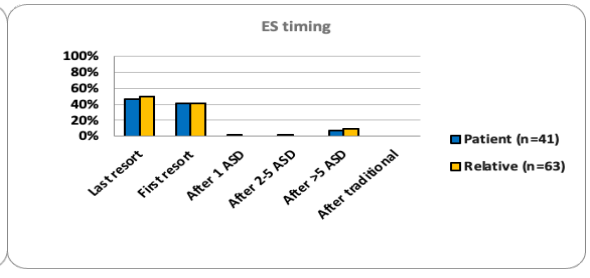

Most trust to discuss ES
100%
80%
60%
40%
20%
0%
Neurosurgery
Neuro / psych
Loved ones
GP/FM/IM
CHW
Patient (n=41)
Relative (n=63)


Negative effects of ES
100%
80%
60%
40%
20%
0%
Death
Motor problem
Memory loss
Change in...
Sight problem
Speech problem
Patient (n=41)
Relative (n=63)


ES information source
100%
80%
60%
40%
20%
0%
None
Loved ones
GP/FM/IM
Neuro / psych
Epi group
Internet
Seen before
Patient (n=41)
Relative (n=63)


Goals of treatment
100%
80%
60%
40%
20%
0%
Never sz
Stop ASM
Relationship
Improved cognition
Plan for future
Hobbies
Job
Fewer sz
No restriction
Other
Patient (n=41)
Relative (n=63)


Reaction to ES Suggestion
100%
80%
60%
40%
20%
0%
Interested
Refusal
Suspicious
Curious
Discouraged
Patient (n=41)
Relative (n=63)


ES timing
100%
80%
60%
40%
20%
0%
Last resort
First resort
After 1 ASD
After 2-5 ASD
After >5 ASD
After traditional
Patient (n=41)
Relative (n=63)

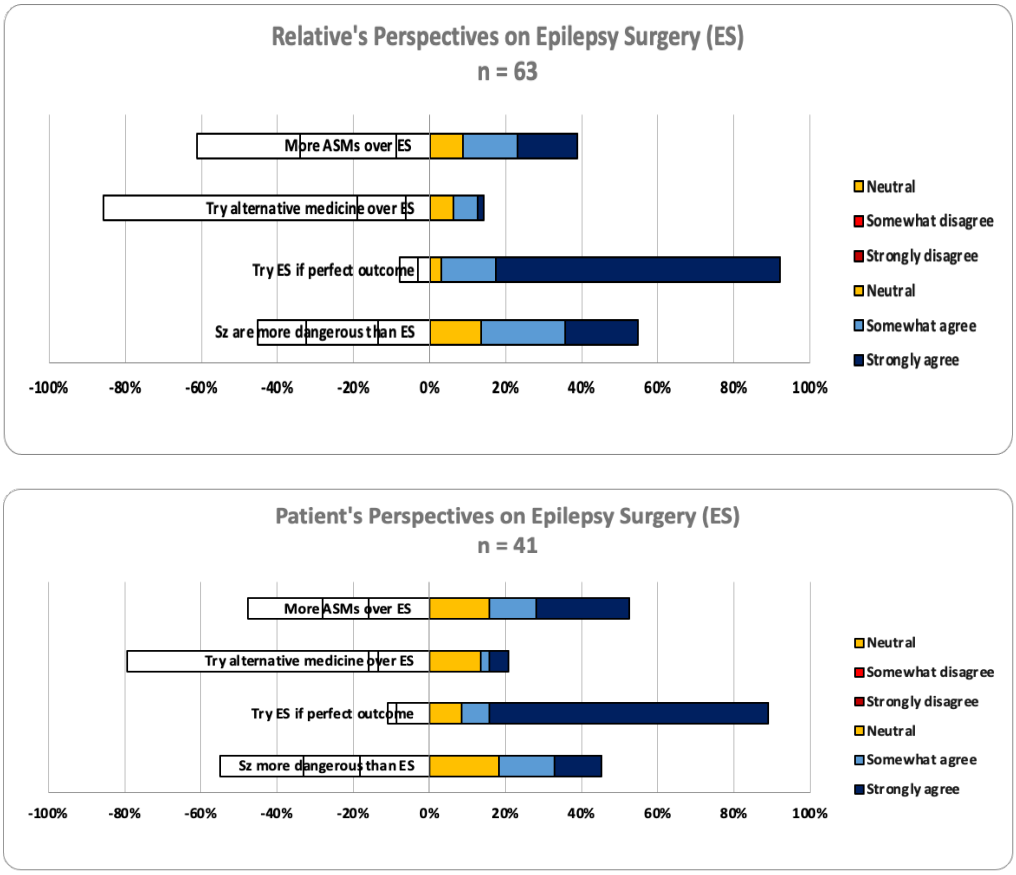


Figure 3: Summary of patients and caregivers responses to study survey

3.3 Interviews of Clinicians Providing Epilepsy Care

Demographics of clinicians interviewed as part of the study are included in Table 8. Twenty-one clinicians were contacted during the study period; the 13 who completed the interviews comprised four attending neurosurgeons, four resident neurosurgeons, two adult neurologists, one pediatric neurologist, one psychiatrist, and one psychiatry clinical officer. The clinical experience of the residents were primarily in-patient care; the other interviewees had significant outpatient clinical practices. The clinicians had been in their respective current clinical

roles at MNRH for 2-16 years (average of 7.46 years). The interviews lasted from 10 minutes to 38 minutes with a mean of 23.33 minutes.

Table 8. Summary of demographics of clinicians completing interviews.

Classification Assignments-Interviewees Demographics

	Gender	Clinical Role	Approximate Years in Clinical Role
P1	Male	Neurosurgery Attending	10
P2	Female	Pediatric Neurologist	7
P3	Male	Neurosurgery Attending	16
P4	Male	Psychiatry Clinical Officer	16
P5	Male	Neurosurgery Resident	4
P6	Female	Neurosurgery Attending	2
P7	Male	Neurosurgery Resident	3
P8	Male	Neurosurgery Attending	2
P9	Male	Adult Neurologist	15
P10	Male	Adult Neurologist	3
P11	Male	Psychiatrist	12
P12	Male	Neurosurgery Resident	3
P13	Male	Neurosurgery Resident	4

After transcribing the interviews, two anchor codes centered on the primary research questions - need for epilepsy surgery and capacity for epilepsy surgery - were created; 29 codes were generated which were subsequently categorized into seven themes addressing the research questions (Figure 4; see Appendix E for codebook and code hierarchy). Distribution of interviewees providing relevant information for each of the anchor codes is provided in Figure 5. Thematic saturation was achieved after nine interviews, as no new themes were identified after the ninth interview. Notably, the four leading references regarding the need for epilepsy surgery were from a psychiatrist, neurosurgery resident, pediatric neurologist, and psychiatry clinical

officer; the four leading references regarding capacity for epilepsy surgery were provided by three neurosurgery attendings and one adult neurologist.

Figure 4. Mind map of generated codes. Parent and daughter codes to the left were anchored on need for epilepsy; parent and daughter codes on right were anchored on capacity for epilepsy surgery.

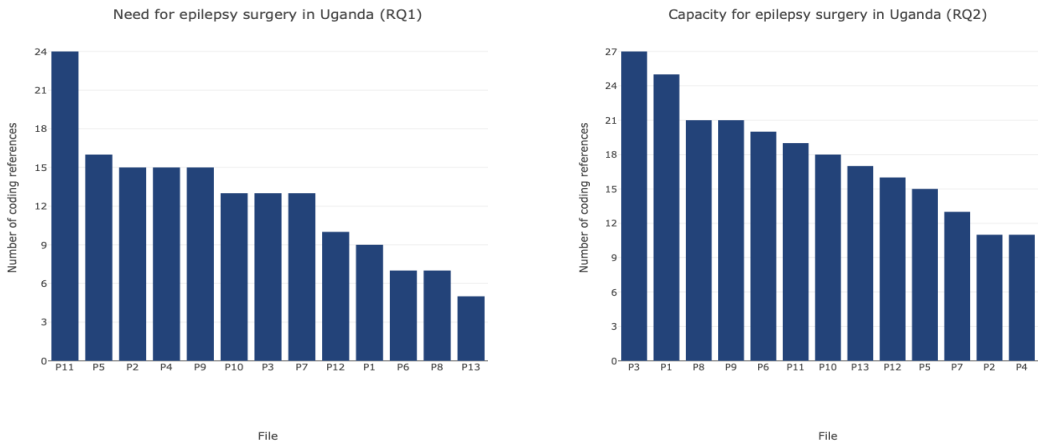


Figure 5. Distribution of coded references among interviewees.

Prevalence of Disease

The interviewees - whether neurologists, neurosurgeons, or psychiatrists - expressed that while the true prevalence of epilepsy in Uganda is not certain, from their clinical experiences it was a common medical condition in their setting. They often encountered patients with epilepsy in their outpatient clinics and occasionally inpatient if patients were in status epilepticus. They noted that the true prevalence of disease cannot be determined simply based on the number of patients with epilepsy they treat because a large portion of Ugandans with epilepsy either do not acknowledge the disease for fear of stigma or, if acknowledged, pursue care with non-medical providers such as traditional healers and clergy due to a prevailing thought that seizures are consequences of evil spiritual activities. Participant 10, an adult neurologist, recalled that there had been a World Health Organization study of country-wide prevalence of epilepsy which estimated “between 2.2 to 6.1 per a hundred thousand but it wasn’t accurate, it was just based on some literature”. In his adult neurology clinic, he thought “[among] neurologic cases, epilepsy contributes a third”.

In pediatric neurology, Participant 2 reported a high prevalence of epilepsy in their visiting patients: “I think the neurology clinic which we run, I think also I can see like over 70% are epilepsy. And we see mainly children who have had uncontrolled seizures, because this is a national referral hospital”. The psychiatric providers shared a similar sentiment.

> Epilepsy might be the number one reason why patients visit our clinic. If it's not number one, then it’s a very [close] second to mood disorders. So yeah, we see patients with epilepsy, most of them come as outpatients. Elsewhere where I give one day of my private practice time, I also get to see some patients with epilepsy.
>
> - Participant 11, psychiatrist

The estimate of prevalence from the perspective of neurosurgical providers differed. Attending neurosurgeons who had significant outpatient clinic time reported that they had a large number of patients with seizures reporting to their clinics. However, the residents who spent most of their time providing service inpatient cared for fewer patients with idiopathic epilepsy.

> It's not common to have epilepsy patients come to our clinic … We see them once in a while, especially when it's their first time maybe to have seizures or if they have had seizures, breakthrough seizures and then they come to us in status.
>
> - Participant 7, neurosurgery resident

Although the neurologists and neurosurgeons reported that they encounter a significant number of patients with seizures refractory to medications, the psychiatric providers suggested that it was rare for their patients to have seizures refractory to medications. Regarding prevalence of refractory epilepsy, Participant 11 (psychiatrist) disputed the frequently quoted data from the literature that 30% of patients with epilepsy have disease refractory to medications. He noted,

> Although I agree with you that, you know, there are some patients that just generally don't get better despite you know the several epileptics you may have tried. I don't know if the figures are that high in my clinical experience. Perhaps, maybe a lot less. In fact, I love working with patients with epilepsy, in part because they actually do get better…. So in my clinical practice that number is very small. In fact, I think if I were to be honest, I think I have two patients. In the last 10 years I've been practicing, I've had two patients who really nothing just seemed to work.

That was different from report from the pediatric neurologist, Participant 2:

> We've not really followed it [estimate of medication refractory epilepsy (MRE)] up and I can't really attest to that [report in literature that 30% of patients have MRE] because we've not had a follow up study to see how many…. We get a lot of intractable seizures, especially those who have Lennox Gastaut syndrome, some who have Landau Kleffner, those quite difficult syndromes in children. We do get them who have intractable seizures.

State of medical management

Participants from all three disciplines - Neurology, Neurosurgery, and Psychiatry - repeatedly discussed that the basis of managing patients with epilepsy is anti-epilepsy drugs (AEDs), which within the public health sector are provided by the government. There is, however, no established algorithm that drives medical diagnostic work up of epilepsy among patients presenting with concern for seizures. Among the psychiatry providers, diagnosis of epilepsy is primarily driven by reported accounts of seizure episodes, more so than on investigations with EEG.

> Here, we tend not to rely too much on the EEG. We tend to rely on eyewitness accounts because sometimes you know the eyewitness account tells you one thing that sounds like epilepsy and the EEG comes up totally normal. So most clinicians here want to talk to somebody who has seen what happened and then couple that with the history that you have taken to make your diagnosis.
>
> - Participant 11, psychiatrist

The neurosurgeons seemed to count more on investigative tools.

> We initially check up … with a CT. The CT is not diagnostic enough to show us anything and the patient is still having seizure disorders, we start them on anticonvulsants- that's the medicine- but we tell them to do an MRI. And so if MRI still doesn't show us much, we think that maybe it's a seizure disorder.
>
> - Participant 5, neurosurgery resident

Participant 11 summarized the dogma he learned for managing patients with epilepsy:

> Find the right antiepileptic drug: start small, go slow until you manage half the seizures…. If you're able to do that, then that antiepileptic is effective. So then what you need to do is just titrate the dose until you can find a maintenance dose for the [patient].

The most commonly administered AEDs were carbamazepine and valproic acid; reports on the clinical practice of using others AEDs such as phenytoin were conflicting. Participant 11,

for instance, reported that phenytoin was rarely used in Kampala: “We have relegated phenytoin to the lower health centers. In fact, you may hardly find phenytoin in most Kampala health centers, but it's very much common at health center 2 and health center 3. So you get phenytoin there and phenobarb, those kind of drugs at that level”. But Participant 7 from neurosurgery reported that “the common drug[s] here we have [are] carbamazepine and phenytoin, so we have to go up to a maximum dose of either drugs, or even go up for stronger anti-seizures like sodium valproate, levetiracetam, lacosamide, even in combination”. The clinicians were aware that some of these AEDs require routine lab work to check serum levels of the medications, but that was not a common practice even at the highest level of care.

> There are others like carbamazepine and sodium valproate, for which, you know, in the teaching we are supposed to run the blood works, in practice that doesn't really happen. Most clinicians are quite comfortable with the therapeutic index of carbamazepine and valproate. So we don't tend to do the blood work as aggressively as we do it for lithium [a medication often used in treating bipolar disease].
>
> - Participant 11, psychiatrist

Only one interviewee voluntarily spoke about adherence to medications. Many of the patients he had managed in his clinic struggled to adhere to the prescribed AEDs.

> Adherence was a big issue. More than 60% of the patients had adherence issues. There are many reasons why adherence is difficult. One is that it's [the medications are] expensive so people just run out of money…. There are perceptions about the medicine limits that you have to take for a long period of time; people don’t like that so they quit. Anti-epilepsy medicine is strong so when they start feeling drowsy … they feel slowed down [and] they just quit. There are a few who get side effects and feel that the world has ended so they don't want to take anymore.
>
> - Participant 3, neurosurgery attending

Although not specifically included in the semi-structured interviews, a few interviewees voluntarily discussed challenges with obtaining AEDs. In Uganda, the government provides AEDs to the clinics which then avail these medications to patients free-of-charge. The clinicians suggested that while stock-out on AEDs was a bigger challenge in the past, it is less

common now; the Uganda Epilepsy Society had succeeded in advocating for some AEDs to be included in the national drug register.

> Incidentally, all the anticonvulsants are free except in a situation where the drugs are out of stock. [During stock out] I give [the patient] a prescription and they go and buy it from a private pharmacy outside the hospital. But most times we have them [ie. the AEDs] available.
>
> - Participant 4, Psychiatry clinical officer

> We're also part of the International League Against Epilepsy under the Uganda Epilepsy Society and we're advocating for availability of the basic drugs from the Ministry [of Health]. We presented some document to the Ministry … [that] came out of the World Health Organization that having available epilepsy drugs is … among the rights [of patients]. Right now, at least we are having less stock outs as before. So at least the basic first line drugs are available. They are not as prior.
>
> - Participant 10, Adult neurologist

Management of refractory epilepsy

Patients with epilepsy refractory to medications are managed by trying different AEDs at higher doses, often in combination. Interviewees described the current practice in managing patients with refractory disease as follows:

> To do different combinations or increase the doses to the maximum or keep on adding on different combinations that we are able to control.
>
> - Participant 10, adult neurologist

> [They] keep trying. We try with one medication, then two, if we're not succeeding then add three.
>
> - Participant 2, pediatric neurologist

> We really end up with a large amount of medicine to control the seizure".
>
> - Participant 3, attending neurosurgeon

> I for one, I don't know whether it is the right practice, what normal[ly] I do, because I've seen a number of them despite of the the anticonvulsant, they continue to get the attacks [ie. seizure episodes]. So I've been combining the anticonvulsants which has [yielded] good results. For example, if this person has been initiated on phenobarbitone in a peripheral health facility, on arrival here I'm going to introduce a more superior one [AED] and then first continue with the Phenobarbitone before tapering it down.
>
> - Participant 4, psychiatry clinical officer

On occasion, a patient with refractory epilepsy may be referred to facilities outside the country for further management which may include surgery.

> If it's a case that we can't handle, we can refer [the patient] to neighboring Kenya, I think that's the closest and cheapest. Kenya. India is also a little cheap. Those are the common two destinations: Nairobi and India. Because of the closeness to the country and also the cost.
>
> - Participant 7, neurosurgery resident

Only one interviewee suggested that he had referred patients with refractory epilepsy to an in-country facility for possible surgical management:

> So usually [I] call the people in CURE Hospital [a private children's hospital in Uganda] then put them in contact with the patient, and they take it from there. Some of their surgeries are free, especially for children. So they kind of hold [surgical] camps … and they do the surgeries".
>
> - Participant 9, adult neurologist

Generally, the psychiatrists and neurologists would not refer patients with refractory epilepsy to the neurosurgeons at MNRH, unless there was a structural pathology on brain imaging that necessitated neurosurgical evaluation. This was in part because there was no clearly recognized algorithm in managing patients which called for surgical referral. Interviewees summarized the current practice thus,

> I mean, there's no algorithm saying that, you know, when you reach point X, that's when you refer to the surgeon. It doesn't exist. It is just to the discretion of the child neurologist or other neurologists who say, well, let me … consult my colleague and see [if] there is anything that can be done.
>
> - Participant 2, pediatric neurologist

> [We] almost never [refer epilepsy patients to neurosurgeons at MNRH]. I would [more readily] send to the neurologist, perhaps than to the neurosurgeon. Here we imagine [that] if I send to the neurosurgeons … I've got to have some scans that show that there's something worth it, managing surgically.… So you probably see a clot in the brain or something like that or some tumor or mass.
>
> - Participant 11, psychiatrist

<u>Priority of epilepsy surgery</u>

While they all appreciated the potential benefits of epilepsy surgery, the interviewees varied in their perspective on prioritizing epilepsy surgery (Figure 6). Clinicians noted that epilepsy surgery would augment their treatment options for patients, especially since medications are sometimes limited either in options or in availability.

> Over 10 years after residency, I'm back here [using] the same drugs … [this] makes a surgical option actually a very appetizing proposition too". From his perspective, epilepsy surgery would not only improve outcomes for patients but also improve quality of lives of families with patients with MRE: to him, with epilepsy surgery "the quality of life is improving not just for the patient but for the family as well… [as you can] move people from completely moribund state to the state where they actually function.
>
> - Participant 1, neurosurgery attending

Other interviewees agreed on the potential benefits of epilepsy surgery in improving patients' clinical outcomes and socioeconomic involvement, and in combating stigma around the disease.

> If Neurosurgery is able to help the remain[der] of the patients who are not able to be helped with the drugs, then that will go a long way to improve the livelihood [of] these individuals - be it children developing, be it the young generation that is productive to the country…. I think that neurosurgery has a big role in the management and helping [of] these patients [with refractory epilepsy]".
>
> - Participant 12, neurosurgery resident

> I think the role of surgery would play a big role. We know that surgery is one of the treatment modalities for epilepsy, especially the intractable seizures. And based on the fact that [the] majority of our patients still get breakthrough seizures, I think surgery would be really welcome.
>
> - Participant 9, adult neurologist

In spite of noting the potential benefits of epilepsy, some interviewees from neurosurgery thought epilepsy surgery should fall lower in the priorities of their clinical teams as there are more pressing needs.

> I have a range of anticonvulsants that I can play around with the doses and the combinations and if the patient is adherent, at least they can have some months or years until maybe they need surgery if it's intractable. So if I have a list of three it will be my number three.
>
> - Participant 7, neurosurgery resident

> I think epilepsy is not [on] the list, but it should be listed also. Honestly, I think it's low on the list, maybe the last on the list. If we talk about functional, in general, yes, but it's specific. It will be low, very low on the list.
>
> - Participant 8, neurosurgery attending

In many regards, these providers considered that the burden of traumatic brain injury and brain tumors made those pathologies higher priorities. Interviewees outside Neurosurgery, generally, thought epilepsy surgery should be of higher priority.

> I think surgery because we know that for patients, if you're able to localize the lesion and you resect it, 100% [of the time] you bring the seizures under control. And we have candidates, a substantial number of candidates who would really benefit from surgery. If I were to rank, I think it comes …. maybe number 1 [or] number 2".
>
> - Participant 9, adult neurologist

> It's pertinent. I mean it's been way behind schedule. I mean something long overdue. Because from the experience I've seen in Western countries, this is something where you could really map and see where there's a lesion and then be able to intervene.
>
> - Participant 2, pediatric neurologist

<u>Comprehensive epilepsy care</u>

In Uganda, epilepsy care is provided through Psychiatry, Neurology and Neurosurgery; much of that is due to the evolution of the disciplines over the decades.

> I think from the start, I think we really had one or two neurologists previously within the country. If you put that in context with the burden of epilepsy within the country, then you would say 90 or 95% of the epilepsy patients would not interface with the neurologist. And the next available specialty, which kind of approximates what the neurologist [does is] psychiatry. And I think at that time, the person who was interested in epilepsy … was a psychiatrist, and he was the one who was doing quite some research and care. So that's how [the] majority of the patients with epilepsy ended up with psychiatry…. We are trying first of all to bridge the two disciplines, especially in epilepsy care. So we work with psychiatrists. We know that actually [the] majority of the patients are not seen by psychiatrists; they are seen by the psychiatrist clinical officers.
>
> - Participant 9, adult neurologist

The psychiatrists carry a different version of this evolution of care.

> It seems in Uganda, neurologists kind of slowly started to let go of epilepsy to the psychiatrist. They started to send the entire disorder to psychiatry, I think mostly because epilepsy in our setting doesn't come just as a neurological problem. It comes with a lot of

> psychosocial issues as well, issues of stigma, issues of comorbidities. And most of the comorbidities tended to be comorbidities of distress, so mostly psychiatric comorbidities and they were … at a loss of what to do: … what am I going to do about the hallucinations? What am I going to do about the mental retardation, the learning disability, and things like that. And I think that's kind of how it started.
>
> - Participant 11, psychiatrist

To move epilepsy care in Uganda to the realm of actively incorporating surgery as a treatment option, interviewees expressed a need to develop a comprehensive practice, a collaboration between clinicians from different disciplines to develop an algorithm to care for patients.

> I think it needs joint effort between the neurologists and surgeons, we need to sit and then come up with a structural algorithm…. Probably [get] the people who work in these various district hospitals, … have a meeting, bring everyone on board, you sit and structure what it is that needs to be done…. We come as a team and decide this is the way we shall be processing… [so we] have a clear algorithm in terms of how the patient is going to be trapped [ie. channeled through care to appropriate services].
>
> - Participant 2, pediatric neurologist

<u>Barriers to implementing epilepsy surgery</u>

When asked about anticipated barriers to implementing an epilepsy surgery program within the public sector of the Ugandan health system, interviewees made comments surrounding infrastructure, cost, clinical personnel, training, and public's perception. Regarding infrastructure, the participants noted that EEG, CT, and MRI are available and accessible within Kampala, the latter two within MNRH.

> We just acquired an EEG lab, although I think we have one EEG machine which was donated by … UCSF. We don't have a video lab where you can be able to monitor somebody who has had seizures or epilepsy…. Currently our CT scan is down. We do have a CT scan, but I don't think it's able to do the number of patients that we have to efficiently handle the volume because it's one CT scan running for all of the hospital…. In Mulago [National Referral Hospital] we don't have an MRI; it's very absent.
>
> - Participant 10, adult neurologist

> CTs can be done in house or out of hospital. But there's a season when most of them are done in house. And then of course, when the machines are down, then they have to be outsourced…. Rarely do we do video EEGs…. Stereotactic EEGs, those don't happen….

> Even if we had it, the MRI machine is not functional and I'm not so sure if they [the radiologists] know exactly what we'll be looking for yet". More advanced studies like PET and SPECT scans are being introduced to Mulago in the near future, according to Participant 9: "as they set up a PET scan here on the hill, then we should be able to access it in case surgery is ready.
>
> - Participant 6, neurosurgery attending

For many patients receiving care at MNRH, cost can prove a significant challenge in accessing the available infrastructure, and interviewees believed that would be a potential barrier to investigating patients for epilepsy surgical candidacy.

> The problem is the bulk of our patients, economically, they're not doing well. So an MRI is like 750 upwards? 750,000 Shillings, that's what? $200? It's around $200.00…. So you find that most of the population will think 700,000 [Shillings] is a lot of money. So they get [a] negative attitude … when you tell them to do an MRI. So it's not that easy.
>
> - Participant 12, neurosurgery resident

> It's money. It's an out-of-pocket money and I think you realize that [in] our nation… whatever we make … [is what we] eat so we don't have a particular health insurance, and therefore not everyone can even put out 750,000 shillings [for an MRI] which comes to about $200…. And then for a CT, CT's range will be probably $50, … there are families that can't afford that.
>
> - Participant 6, neurosurgery attending

> It's an expensive disease or sickness where you have to do [a] series of imaging, but the images are expensive. So it's quite uncomfortable or quite disturbing to the patient that they have to do, say, a series of images to check the progression of disease. But these images are really expensive. The cost of the CT is expensive already to the patients, but the cost of an MRI is like three times.
>
> - Participant 13, neurosurgery resident

To some interviewees the cost associated with these investigative assessments may not be worth it as there are no surgical interventions routinely performed to treat pathologies that may be diagnosed on those studies.

> When someone has done an MRI, you feel like they have done a lot. They have passed through all the basic [assessments]. They have done a CT, you have sent them for an MRI, and they are already poor. We don't want them to spend more [money on] tests when even after identifying the lesion, what you're going to do is to actually just tell them [to] still [take] the medicine for life. Because if you take surgery, it's not done in Uganda, so after spending all that money on diagnosis, you're going to tell them the same.… We don't want to spend patients' money when you're not going to do much.
>
> - Participant 5, neurosurgery resident

Another barrier identified by the interviewees is having personnel in the requisite disciplines trained to care for epilepsy surgical candidates.

> We still don't have a good school of neurology here…. Everyone needs to go outside [of Uganda] and train and then come back or do additional training, but most of them are graduating and then they add training like postgraduate training as neurologists.
>
> - Participant 8, neurosurgery attending

There is need to train intensivists who have special interest in neurosurgical patients: "[In the ICU] they have only … one intensivist … the rest are anesthesiologists who usually have their duties somewhere else who come just to help out" (Participant 12, neurosurgery resident). The participants identified that there is need to train radiologists and technicians specialized in implementing investigative assessments. "[We also need] rehabilitative therapy, physiotherapy and all that to help these patients improve. And then also we need more radiologists" (Participant 10, adult neurologist).

While the attending neurosurgeons were familiar with epilepsy surgery procedures from either prior experiences in Uganda or outside of the country, they may need further training in doing select procedures if an epilepsy surgery program is to be implemented.

> You need to have a team that is dedicated to epilepsy, and that team needs training and others who are trained to actually look after them, and some technicians as well…. Also [the neurosurgeons need to] pick up the experience because I don't think [there is] anybody …. at the moment that we have [in the department who] has been involved in epilepsy surgery, so that's the other thing.
>
> - Participant 1, neurosurgery attending, participated in the 2007 pilot epilepsy surgery program at the CURE Hospital

To garner the interest of patients and their caregivers in subscribing to an epilepsy surgery program, one would have to overcome persisting public perceptions about brain surgery.

> I think our patients still have fear for brain surgery, and to me I think that many patients that we operate on … [if] they [had] been conscious, they would actually refuse because we have very many who come in conscious but then they are hesitant to have the surgery…. Out of 10 [patients], you can have one who does in fact have the surgery done…. They

believe once you open someone's brain, you're not going to leave them the same. Yes, you're going to have issues.

- Participant 7, neurosurgery resident

The way to combat these perceptions will be to demonstrate to the public with real patient stories that epilepsy surgery can be done in Uganda and can be very effective.

Most of the people think that these surgeries can only happen in India or Nairobi, so the system actually has to know that this can be offered [locally]. As long as the system knows that the basic minimum can be offered then the others can come through. And then of course I think we need to know success stories. But these are just because if I have no success story, then I don't think [a] mom will allow me to touch a child".

- Participant 6, neurosurgery attending

Make people aware that the service is available, because if you're not going to make people aware then who will … refer them? And then when there are success stories post them, let people know that this actually works, and then probably the stigma and all these other things might, you know, be reduced a bit if they know that it's done.

- Participant 2, pediatric neurologist

Non-clinical factors

In addition to the clinical factors, the interviewees pointed out strong social factors that need to be considered in any effort to implement an epilepsy surgery program in Uganda. Most notable among these factors is the stigma surrounding epilepsy.

The stigma owes a lot to the low health literacy, but also to the explanatory models of the disease. So depending on how people you know define or explain what causes it, they will seek treatments elsewhere. So again, that tells you also that maybe in spite of the stigma, they are still seeking help except it's just not in the formal health centers. So they're probably going to traditional healers, spiritualists, and diviners and things like that, which is true for basically 85% of mental health conditions. The first start in that setting is informal health care and then come to the, you know, formal health care as a last resort.

- Participant 11, psychiatrist

For us growing up, we thought of epilepsy as a spiritual thing. We thought about [it] as a spiritual thing. So actually to come out to tell someone you have epilepsy, you should say it softly, first of all. You should say it after knowing the environment you're speaking it from, and you should have first prepared your patient to tell them they have epilepsy…. Because for us, when you ask in the local language, epilepsy and seizures are the same thing. So when you ask someone if they have epilepsy, the first thing they tell you is no. Yes, first thing they say is no but when you go on to really ask you will find out this is a person who has been having epilepsy… [for] many years.

- Participant 12, neurosurgery resident

Another nonclinical factor to consider is advocacy, which was most discussed by Participant 8, who argued that clinicians taking care of epilepsy patients must also advocate for the needed services such as an epilepsy surgery program.

> We don't do anything to tell the government that we don't have this service and we need this service. So the government will not just come and think 'oh, let me give you this service." It should come from the user and the user should request, but before requesting you need to know yourself that I can do it [epilepsy surgery] or I can go and train for it then I can do it…. So the barrier is knowledge and attitude from the experts…. Maybe somebody [should] advocate [for the program, then] the government [can] send someone [for training] and provide [the] equipment…. But if you're [an] expert who is not communicating to the government the need, who is not giving the government the plan to make [the program] … I don't believe the government will come and say, 'hey here, we need epilepsy surgery'.
>
> I still believe there's no action if there is no advocacy, because we all assume everything is fine until someone raises their voice, then it becomes a problem. And the voice come[s] with evidence. This is data, this may be from the expert. They will give the voice.
>
> - Participant 8, neurosurgery attending

4. Discussion

As demonstrated in the systematic literature review, in spite of the need for surgical treatment of refractory epilepsy across Africa, there have been very few reported attempts to implement epilepsy surgical programs on the continent.[20] There is growing evidence that the morbidity and mortality associated with idiopathic epilepsy in Africa is markedly higher than reported in the global population.[8,42] In Uganda, an earlier pilot program had been very effective in achieving seizure control among patients with refractory temporal lobe epilepsy, but was not sustained.[28,29] This study thus explored the need for and capacity to implement an epilepsy surgery program in Uganda, particularly within the public health sector, providing insights on the apparent need for surgical options for treating refractory epilepsy and actionable steps to develop the presently available capacity for a surgical program.

In Uganda, epilepsy care is provided largely by clinicians in Psychiatry and Neurology, and to a lesser extent Neurosurgery. This evolution in practice has been driven by historical factors inclusive of human resource capacity, with markedly fewer neurologists than psychiatrists as well as public perception of the illness, which is impacted by the many psychiatric comorbidities often associated with epilepsy.[43] The World Health Organization references epilepsy as a neurologic condition, but many initiatives (such as the Mental Health Gap Action Programme, mhGAP 2.0) classify epilepsy as a mental disorder.[44] In this study, clinicians from both Psychiatry and Neurology noted that epilepsy was likely the leading reason for patient visits to their clinics. As acknowledged in the interviews, any estimate of prevalence of epilepsy in Uganda is likely to be an underestimate. Almost half of PWE first seek care with traditional and religious healers because of prevailing beliefs that seizures are of spiritual etiology, which delays presentation to biomedical care by an average of two years.[7,45] Indeed, among the 41 PWE who completed this study's surveys, there was, on average a four year delay between onset of seizures

and first presentation to biomedical clinicians, suggesting a delay in seeking and receiving definitive medical treatment. University of Colorado neurologist, Dr. Joseph Pelinnen, has described a 3-tier framework to delay in treating epilepsy, with the first tier being a delay in diagnosis that is often related to social, educational, technological, and geographical barriers, among others.[46] These barriers are conceivably more pronounced in resource limited settings. In Central Uganda, one qualitative study identified limited knowledge about epilepsy among PWE and their caregivers, lack of family support, poor health care access, among others, were the leading barriers to seeking epilepsy care.[47]

From the retrospective chart review, 49% of patients with epilepsy seen at the Bosa Clinic during the period reviewed had been managed on 2 or more AEDs over the course of their disease but none had been referred for surgical evaluation. The clinical outcomes of these patients were difficult to decipher as medical records did not consistently contain specific information on the frequency, duration, semiology, or severity of seizures at follow-up visits. Per guidelines for managing refractory epilepsy, some of these patients who continued to have seizures despite trying multiple AEDs, may be referred for surgical evaluation.[12] However, this recommendation to refer patients for evaluation for surgical candidacy is significantly constrained in low resource settings such as Uganda for multiple reasons, including the unavailability of an epilepsy surgery program and challenges with determining patients with medication refractory epilepsy. Concerning the former, interviewees in this study expressed that not having an active epilepsy surgery program at MNRH dis-incentivizes referring patients to neurosurgery. Indeed the neurosurgeons acknowledged that they refer patients with idiopathic epilepsy to psychiatry and neurology so that those patients can continue medical treatment since surgery is not an option locally.

There are multiple challenges to determining which patients on multiple AEDs truly have epilepsy refractory to medications. As Participant 3 noted in the interviews, a large portion of patients (in his case, more than half) had significant challenges to adhering to AEDs due to not tolerating side effects, among other factors. In one study involving patients with epilepsy receiving care at the pediatric neurology clinic in MNRH, nearly 60% had subtherapeutic levels of AEDs, implying that AEDs were underdosed and/or patients did not adhere to prescribed dosages and timing. [23] Clearly, continuing to have seizures in spite of multiple AEDs because of non-adherence to the medications or underdosage of the medications does not render a patient's disease to be medication refractory. These impacts on medication efficacy can be related to patient non-adherence, possibly related to suboptimal understanding of the medication regimen, quality of medications, or interruption of steady availability of the AEDs due to "stock outs". These factors add layers to this challenge in determining which patients on multiple AEDs truly have refractory epilepsy. Interviewees in this study suggested that AED stock-outs are much less common now, in part because the Uganda Epilepsy Society had successfully advocated for some AEDs to be included in the nation's drug registry. In considering a future epilepsy surgery program, one would note that the threat of AED stock-outs and the limitations in available AED options only make it more difficult to determine if a patient with continued debilitating seizures would have improved with different and/or consistent supply of AEDs, or if that patient should proceed to surgical evaluation. In addition to concerns over "stock outs", Uganda' complex health supply chain system of medications, as reviewed by Lugada et al., faces many challenges, notably including unavailability and/or lack of adoption of some medications at lower tiers of the health system.[48] As discussed later in this thesis, these challenges would have to be addressed prior to implementing an epilepsy surgery program.

While interviewees uniformly noted a need to develop an epilepsy surgery program in Uganda - likely MNRH, since it's the premier national referral hospital - they differed on prioritization of such effort. The nonsurgical clinicians expressed that implementing an epilepsy surgery program would be a top priority and may be overdue. Interestingly, some of the neurosurgical providers thought differently. They suggested that efforts to advance neurosurgical care at MNRH should focus on the burdens of traumatic brain injuries and brain tumors, arguing that they already have multiple options of AEDs that can be used in treating patients with epilepsy. Notably, some of the interviews from neurosurgery, particularly the residents, had much less experience caring for patients with idiopathic epilepsy since those patients did not present to their clinics often, and if they did were frequently referred to psychiatry or neurology instead.

Epilepsy surgery hinges on the ability to use various investigative tools - patient's history, EEG, brain imaging, among others - to identify foci from which seizures may be emanating. This study demonstrates that tools such as EEG, CT and MRI are available and accessible within MNRH. Patients can readily obtain EEGs at multiple sites around Kampala, and on a limited basis at MNRH if scheduled ahead of time. Similarly, patients can obtain CT of the brain at MNRH, but the one CT machine services all patients who seek care at the more than 1500 bed hospital. There were mixed reports on availability of MRI at MNRH: while some interviewees suggested that it was not available, others noted that there was an MRI machine but it had not been put to function as of the time of this study. One interviewee reported that PET/SPECT scanning would be available shortly as those resources are being introduced for oncologic care but would also be available for other medical use. Cost of obtaining these investigations was a frequently reported barrier as many of the patients who seek care at MNRH are of relatively lower socioeconomic status. This may even be truer of patients with epilepsy; from the study surveys we learned that, compared to caregivers, patients were less likely to have

secondary or tertiary education (61% vs 81%; p = 0.007) and less likely to be self employed or have full time employment positions (44% vs 77%, p = 0.003, Table 7). This apparent relationship between living with epilepsy and having lower socioeconomic status is, at least in part, due to stigma and uncertainty around the disease which make it challenging for patients to enter relationships, plan for the future, or even commit to educational and/or career pursuits.

Beyond the availability and affordability of investigative tools for an epilepsy surgery program were frequently reported concerns about personnel and their respective training to provide such care. Radiologists and intensivists at MNRH are trained broadly in their clinical discipline but are not sub-specialized to care for epilepsy and/or neurosurgical patients. Postgraduate training in Neurology usually requires traveling outside Uganda after one has completed training in Medicine. The neurosurgery attendings who were interviewed had varied experiences with epilepsy surgery: one was involved in the 2007 pilot program at CURE, others had observed epilepsy surgeries performed in foreign countries. The neurosurgery residents, however, noted that their experience with epilepsy surgery was limited to didactics and reading from textbooks in preparation for their examinations with the College of Surgeons of East, Central and Southern Africa (COSECSA).

A paramount factor to consider in implementing an epilepsy surgery program, as gathered from the interviews, are social elements such as stigma surrounding the seizures and the public's perceptions about neurosurgical procedures. An insight gathered from this study is that a successful epilepsy surgery program would be a compelling response to the stigma around the disease as it would validate the anatomic and biomedical bases of the disease. From surveying patients with epilepsy and caregivers, our study demonstrated patients' goals to be free of their seizures, have more predictability to their lives, be able to engage in daily activities such as driving, and commit to relationships or employment. Patients (80.6%) and their families (89%)

were willing to pursue surgical treatment to treat epilepsy if the procedures could be done safely and with high likelihood of achieving seizure freedom. Their biggest concerns in considering surgical treatment surrounded the risk of perioperative complications and the cost of care. Thus, if an epilepsy surgery program could be implemented with a demonstrable record of being highly effective in controlling seizures, being associated with limited complications, and being affordable, many patients and their relatives would be willing to consider surgery as a treatment option for their disease, even if it is after trying traditional healing methods and multiple AEDs.

4.1 Study strengths and limitations

This present study brings to fore insights regarding the need to develop an epilepsy surgery program in Uganda, and by extension across Africa, where very few attempts have been made to advance epilepsy surgery in spite of a significant burden of the disease. It makes a compelling case using data acquired from retrospective chart review, interviews of clinicians across multiple disciplines, and surveys of patients and caregivers to patients with epilepsy. Moreover, the study evaluates the current infrastructure and human resource capacity for implementing an epilepsy surgery program. In so doing, it identifies barriers that can be duly addressed in a future attempt to reintroduce epilepsy surgery to Uganda in a sustainable fashion.

The study has some limitations. It was conducted at only one facility and only in the outpatient setting at the Psychiatric Clinic and Child Neurology Clinic; MNRH is the premier national referral hospital in Uganda and likely attracts only a subset of patients that do not represent the entirety of the population who suffer from epilepsy. From conversations with others who are familiar with epilepsy care in Uganda, the lower tier health centers and mental health hospitals such as the Butabika National Referral Mental Hospital serve larger populations of patients with epilepsy. Further, only 13 clinicians were interviewed as part of the study; this limitation was in part due to an ongoing strike among clinicians in the public health sector that

coincided with the study period. As previously mentioned, no new themes were identified after the first 9 interviews were analyzed, suggesting sufficient thematic saturation among the cohort of 13 interviewees. Regarding the retrospective review of patients' charts, we could not gather data on clinical outcomes because they were not consistently documented in the medical records, with providers often writing hard-to-interpret comments such as "doing well", "no more attacks", "continues to have attacks", but without specificity about the frequency, duration, type, or severity of seizures. Interpretable data on patients' outcomes would have been very helpful in estimating the prevalence of medication refractory epilepsy.

4.2 Implications for policy and practice

This study identifies opportunities to improve both practice and policy surrounding care for epilepsy patients in Uganda. One is the need to improve adherence to guidelines for managing patients presenting with seizures. The 2016 Uganda Clinical Guidelines from the Ministry of Health contains a guide for diagnosing and managing patients with clinical concern for epilepsy; this was never referenced by the interviewees in this study, which may suggest that clinicians do not routinely adhere to this guideline.[49] As demonstrated in the interviews, patients come under the care of psychiatrists, neurologists, neurosurgeons, psychiatric clinical officers, general practitioners, among others. Interviewees noted that there is no algorithm or workflow used among these disciplines, except for an algorithm used in the emergency setting for patients presenting in status epilepticus. With improved adherence to a guideline or algorithm for epilepsy care, patients can be more confident of receiving suitable treatment regardless of which medical discipline they seek care from. Further, such an algorithm would make it clearer when clinicians should consider EEGs, obtain brain imaging, refer to other consultants such as neurosurgeons, obtain serum levels of AEDs, among others. Lastly, it would serve as a basis for building

teamwork among the various clinicians in an attempt to make epilepsy care at MNRH comprehensive - a suitable response to one of the needs identified by the interviewees.

A second practice implication is the opportunity to provide continued medical education on managing patients with epilepsy. Globally, there is currently a wide array of AEDs available, including newer medications that carry much more tolerable side effects profiles. From this study, it is apparent that less tolerated AEDs such as phenytoin are still commonly used in Uganda. Continued education on newer alternatives and the role of surgical evaluation in medication refractory epilepsy could improve the current practice, notwithstanding the need to address the cost and availability of these newer AEDs in Uganda.[22,50] Another practice implication involves documentation of medical encounters. For more reliable charting and future research, clinicians can adopt systematic ways and/or templates for maintaining patients records and documenting seizure outcomes. Within the public health sector, the government provides AEDs for Ugandans living with epilepsy. From this study, it appears there is opportunity for the government to expand the assortment of AEDs available, especially to include newer AEDs which have more tolerable side effect profiles. Development of international collaboration between local clinicians and international colleagues would provide a platform for exposure to the various facets of an epilepsy surgery program.

A third practice implication gets at the heart of determining medication refractory epilepsy (MRE). We learned from this study that nearly half of patients attending the Bosa Clinic for epilepsy were on multiple AEDs, similar to findings in prior studies.[22,23] However, this observation does not suggest that these patients have MRE. First, there was no standardized way of documenting seizure outcomes in the patients' clinical charts. A practice change that requires clinicians to document frequency of seizures, semiology of seizures, and functional impact of ongoing seizures is necessary to determine which patients have adequate seizure control with

AEDs. The current practice of often subjective statements such as “doing well”, “no more attacks” would make it a challenge to determine which patients have poor seizure control on their combination of AEDs. Two, our interviewees noted that they do not frequently check serum level of AEDs; one prior study found that 59.7% of PWE attending the pediatric neurology clinic at MNRH had subtherapeutic levels of their AEDs. [23] To introduce an epilepsy surgery program at MNRH, or within the public health sector in Uganda, it is imperative to adopt a practice of routinely monitoring serum levels of AEDs, particularly for patients who continue to have seizures and/or have been prescribed multiple AEDs since they may not truly have MRE and can be managed by adequate titration of their AEDs.

4.3 Implications for further work

In light of DGNN’s ongoing efforts to improve neurosurgical care in Uganda, there are multiple opportunities for next steps identified by this study (summarized in Table 9). One next step would be educating clinicians on current practice guidelines for diagnosing and managing epilepsy. With the advent of virtual platforms for education, DGNN can host virtual sessions with local Ugandan clinicians for continued education through journal clubs and academic conferences. There are reports in the literature of this method being used successfully to train clinicians in LMICs in caring for patients with neurologic conditions.[51,52] Similarly, locally driven training efforts have been shown to be effective in improving clinicians’ knowledge of epilepsy, its management and its psychological effects on PWE.[50] These courses could be the basis for bringing clinicians from various disciplines together to collaborate in developing an algorithm for evaluating and managing patients presenting to MNRH with epilepsy. Eventually, dedicating some of DGNN’s surgical camps in Uganda to epilepsy surgery would: 1) serve as pilot programs to demonstrate effectiveness of epilepsy surgery in the setting, 2) provide opportunities for

Ugandan and DGNN clinicians to collaborate, and 3) provide training to Ugandan neurosurgical residents as a means to sustain an epilepsy surgery program in Uganda.

Table 9. Summary of next steps in developing an epilepsy surgery program at MNRH

Establishing reliable clinical documentation
Promoting adherence to established clinical guidelines in diagnosing and treating epilepsy
Ensuring subspecialty expertise and multidisciplinary care
Improving access to neurodiagnostics
Advocacy for augmenting in-country epilepsy care

5. Conclusion

Using qualitative and quantitative methods, this study demonstrates that there is a need for a surgical program for treating epilepsy in Uganda, in light of growing evidence in the literature that surgical treatment can be highly effective in controlling seizures among patients with otherwise refractory epilepsy [11,13,28]. While advanced imaging such as PET and SPECT scans are not available at MNRH at the time of this study, EEGs, CT, and MRI are available and accessible. In many cases of epilepsy, these currently available tools are sufficient to identify surgically treatable seizure foci. Pilot surgical camps for treating patients with medication refractory epilepsy would provide preliminary information on patients outcomes which would be effective tools to garner the government's and public's support of an epilepsy surgery program within the public health sector in Uganda.

Appendix A

Interview Guide

Interviews in this study will cover similar topics but will do so organically. Interview questions may not be phrased in the same way in each interview and may not progress in the same order. This interview guide contains questions that cover the key topics discussed during each interview. Interviewees may ask follow-up questions that cover unanticipated topics. Emergent topics will be included at the researcher's discretion and may be incorporated into future interviews if they are relevant to the study.

Introduction

Hello, my name is _____. Today, I want to talk to you about your perspectives on surgery as a treatment modality for intractable seizures as part of this research study. I will ask questions about your perspective on epilepsy surgery, what resources are currently available for performing epilepsy surgery here at MNRH, and what barriers exist in accessing or utilizing these resources. Your responses are valuable, so please feel free to share whatever you think is important. We will be recording this discussion, and the microphone will be taping the session, so we do not miss any important information. Do you have any questions before we begin?

Demographic Information

I would like to start by gathering some demographic information about you

How old are you?

What is your role in the hospital?

Do you work full-time or part-time?
If part-time: Do you have any other jobs

Do you work directly with patients with epilepsy in your job?
If no: who do you interact with daily in your job?

How long have you been working in your current job capacity/position?
Prior to your current position, were you in a job position that involved working with patients with epilepsy?

In-depth Interview Guide

Question	Focus of Question Related to Methods or study Aims	Probes
Part 1- First, I want to get a general sense of your experiences treating epilepsy here at the hospital. Answer these questions as fully as possible, and if you're unsure about a question, please don't hesitate to ask for clarification.		
If any, what is your role in caring for epilepsy patients?	To characterize the interview study sample	
In your estimate, what proportion of the patients you directly work with have epilepsy?	To get a better understanding of the participant's background with treating the disease	
In your estimate, what proportion of the patients you take care of have debilitating seizures in spite of medical treatments tried?	To get a better understanding of the participant's personal experiences with medication-refractory epilepsy	
Do you or the hospital (if you know) have a workflow on what tiers of treatment options should be tried for patients with epilepsy? If yes, what is the workflow?	To understand the individual provider's (and hospital's) algorithm(s) for determining which treatments patients receive	How have your training and career so far informed this workflow in your practice?
Part 2- We will now discuss the possibility of surgery as a treatment option for epilepsy		
In your practice, does surgery come up as an option for treating patients with intractable seizures? If yes, what is your threshold (ie. the number of medications, duration of	To understand individual providers' perception of what counts as medication-refractory epilepsy	How consistently have you applied this threshold in taking care of patients? What are the reasons for varying that threshold for different patients?

medication trials, etc) for considering surgery?		
If you ever thought a patient could benefit from surgery for treating epilepsy, what would be your next steps? Any labs/scans obtained? Any referrals made?	To understand an individual provider's possible workflow for surgical candidacy evaluation.	What information are you hoping the lab/scan would tell you, and how does that influence your next step in caring for the patient?
To the best of your knowledge, what percentage of patients with intractable seizures are likely to have marked improvement after surgery?	To evaluate providers' perceptions of outcomes of epilepsy surgery	In your view, what chance of improvement in seizures would you consider to be reasonable for one to recommend a patient for surgery for epilepsy?
Have you had any previous experiences of recommending (or observing another physician recommend) surgery for a patient with epilepsy? How did the physician go about it and/or the patient and family take it?	To assess patient responses to surgery for epilepsy through the physician's lens	How were those interactions? How did the patients and/or their caregivers respond?
What do you think are the risks of surgery for intractable epilepsy?	To evaluate knowledge of surgical risks	Do any of these risks seem reasonably acceptable in your opinion?

Next, we will be talking about what resources are actually available for considering people for surgery

Are there any resources you have to help you localize where a patient's seizures may be originating from? EEG, brain imaging?	To assess needed resources	How often do you use these resources? Are there any other resources that you wished MNRH had?
Do you ever run into challenges assessing any of the aforementioned resources to help you care for your patients?	To assess perceived or observed barriers to accessing presurgical evaluation tools	How have these barriers changed over time? Are there ways you have learned to navigate these challenges?
In your opinion, how important is it that patients who receive care for epilepsy at MNRH have surgery as a safe and accessible option if their seizures are intractable to medications?	To determine providers' perspectives on the urgency of meeting the epilepsy surgery need	

Finally, do you have any questions or anything else you'd like to add?

Thank you for taking the time to speak with us today.

Appendix B

Patient Survey

Study ID: Date of completion:

Questions to know you

How old are you today? _____

Please select your highest level of education

- No education
- Primary education
- Secondary education (high school, technical school)
- Tertiary education (college, university, polytechnic)

Please select your current employment status

- Not employed
- Self-employed
- Employed part-time
- Employed full time

Questions about your seizures

How old were you when you first had a seizure? _____

How old were you when you first saw a neurologist for epilepsy? _____

As best as you can estimate, how often do you have seizures in a month? _____

How many anti-seizure medications have you tried over time? _____

Which seizure medications are you currently taking?

_____

_____

How long have you gone without a seizure on your current anti-seizure medications? _____ days/weeks/months/years

What side effects, if any, do you have with your current anti-seizure medications?

_____

_____

Questions about your opinions on epilepsy surgery

Did you know that brain surgery is sometimes an option for treating epilepsy?

- Yes
- No

Which of these sources has made you aware of surgery as a possible treatment option for epilepsy? Please check all that apply.

- Family/friends
- Community health worker
- General practitioner/family medicine physician/internist
- Neurologist
- Epilepsy support group
- Internet
- I know someone who had brain surgery for epilepsy
- Other: please specify _____

Which of these sources would you trust the most to discuss with you if brain surgery was an option for treating seizures? Please select only one.

- Family/friends
- Community health worker
- General practitioner/family medicine physician/internist
- Neurologist
- Neurosurgeon

In your opinion, which of these can occur to someone who has seizures? Select all that apply.

- Injury during seizure
- A seizure that takes a long time to break and requires being hospitalized
- Difficulty keeping a job and/or doing well in school
- Side effects from anti-seizure medications
- Feeling discriminated against by others in society (also called “stigma”)
- Difficulty starting and/or maintaining relationships
- Not being allowed to drive or operate heavy machines
- Sudden unexpected death

In your opinion, which of these can be negative effects of brain surgery for epilepsy? Select all that apply.

- Memory loss
- Change in personality
- Difficulty seeing
- Difficulty speaking
- Loss of function of arm/leg on one side of the body
- Death

Given the risks you may associate with brain surgery, in your opinion, when should epilepsy surgery be considered?

- As a first resort
- After trying traditional treatments (herbs, concoctions, etc)
- After trying one medication prescribed by the neurologist

- After trying 2-5 medications prescribed by the neurologist
- After trying more than 5 medications prescribed by the neurologist
- Only as a last resort

In general, continuing to have seizures in spite of trying multiple medications is more dangerous than having surgery to treat seizures.

- Strongly disagree
- Disagree
- Neutral
- Agree
- Strongly agree

If one of your doctors suggested that you consider having surgery to treat your seizures, what would be your first reaction? Select only one option.

- Refusal
- Suspicious
- Discouraged
- Curious
- Interested

If you were to consider surgery as a possible treatment for epilepsy, which person's opinion would matter most to you? Select only one option.

- Family/friends
- General practitioner/family medicine physician/internist
- Neurologist
- Neurosurgeon

If you were considering surgery as a treatment for epilepsy, which of these would you be worried about? Please select all that apply.

- How to pay for the care received (transportation, surgery, hospitalization, etc)
- How my friends/family will see me or feel about me
- Developing a complication from the surgery

- Other, please specify: _____

What are your most important goals in the treatment of your epilepsy?

- To have less frequent and/or fewer debilitating seizures
- To never have a seizure again
- To stop taking anti-seizure medications
- To be allowed to drive and operate heavy machines
- To take part in activities and hobbies without the uncertainty of having a seizure
- To be able to plan for the future
- To have improved memory and concentrations
- To be able to hold a job
- To be able to start and/or maintain a relationship
- Other, please specify _____

I would rather try more anti-seizure medications than ever consider having surgery for epilepsy.

- Strongly disagree
- Disagree
- Neutral
- Agree
- Strongly agree

I would rather try alternative medicine (ie. herbal medicine, traditional healers) than ever consider having surgery for epilepsy.

- Strongly disagree
- Disagree
- Neutral
- Agree
- Strongly agree

Would you be willing to undergo surgery to treat your seizures if you were guaranteed that you will no longer have seizures after the surgery and will have no complications or brain injury?

- Strongly disagree
- Disagree
- Neutral
- Agree
- Strongly agree

Has your knowledge and/or perception of surgery as a treatment option for epilepsy changed after completing this questionnaire?

- Yes, I am more curious or interested in epilepsy surgery
- No

Appendix C

Caregiver Survey

Study ID: Date of completion:

Questions to know you

How old are you today? _____

What is your relationship to the patient with epilepsy?

- Parent
- Grandparent
- Aunt/uncle
- Neighbor
- Other, please specify _____

How long have you known the patient with epilepsy? _____ days/weeks/months/years

Please select your highest level of education

- No education
- Primary education
- Secondary education (high school, technical school)
- Tertiary education (college, university, polytechnic)

Please select your current employment status

- Not employed
- Self-employed
- Employed part-time
- Employed full time

Questions about your opinions on epilepsy surgery

Did you know that brain surgery is sometimes an option for treating epilepsy?

- Yes
- No

Which of these sources has made you aware of surgery as a possible treatment option for epilepsy? Please check all that apply.

- Family/friends
- Community health worker
- General practitioner/family medicine physician/internist
- Neurologist
- Epilepsy support group
- Internet
- I know someone who had brain surgery for epilepsy
- Other: please specify _____

Which of these sources would you trust the most to discuss with you if brain surgery was an option for treating your relative's epilepsy? Please select only one.

- Family/friends
- Community health worker
- General practitioner/family medicine physician/internist
- Neurologist
- Neurosurgeon

In your opinion, which of these can occur to someone who has seizures? Select all that apply.

- Injury during seizure
- A seizure that takes a long time to break and requires being hospitalized
- Difficulty keeping a job and/or doing well in school
- Side effects from anti-seizure medications
- Feeling discriminated against by others in society (also called "stigma")
- Difficulty starting and/or maintaining relationships

- Not being allowed to drive or operate heavy machines
- Sudden unexpected death

In your opinion, which of these can be negative effects of brain surgery for epilepsy? Select all that apply.

- Memory loss
- Change in personality
- Difficulty seeing
- Difficulty speaking
- Loss of function of arm/leg on one side of the body
- Death

Given the risks you may associate with brain surgery, in your opinion, when should epilepsy surgery be considered?

- As a first resort
- After trying traditional treatments (herbs, concoctions, etc)
- After trying one medication prescribed by the neurologist
- After trying 2-5 medications prescribed by the neurologist
- After trying more than 5 medications prescribed by the neurologist
- Only as a last resort

In general, continuing to have seizures in spite of trying multiple medications is more dangerous than having surgery to treat seizures.

- Strongly disagree
- Disagree
- Neutral
- Agree
- Strongly agree

If one of your relative's doctors suggested that your relative consider having surgery to treat his/her epilepsy, what would be your first reaction? Select only one option.

- Refusal

- Suspicious
- Discouraged
- Curious
- Interested

If you and your relative were to consider surgery as a possible treatment for epilepsy, which person's opinion would matter most to you? Select only one option.

- Family/friends
- General practitioner/family medicine physician/internist
- Neurologist
- Neurosurgeon

If you and your relative were considering surgery as a treatment for epilepsy, which of these would you be worried about? Please select all that apply.

- How to pay for the care received (transportation, surgery, hospitalization, etc)
- How friends/family will see or feel about my relative
- Developing a complication from the surgery
- Other, please specify: _____

What are your most important goals in treating your relative's epilepsy? (check all that apply):

- To have less frequent and/or fewer debilitating seizures
- To never have a seizure again
- To stop taking anti-seizure medications
- To be allowed to drive and operate heavy machines
- To take part in activities and hobbies without the uncertainty of having a seizure
- To be able to plan for the future
- To have improved memory and concentrations
- To be able to hold a job
- To be able to start and/or maintain a relationship
- Other, please specify _____

I would rather have my relative try more anti-seizure medications than ever consider having surgery for epilepsy.

- Strongly disagree
- Disagree
- Neutral
- Agree
- Strongly agree

I would rather have my relative try alternative medicine (ie. herbal medicine, traditional healers) than ever consider having surgery for epilepsy.

- Strongly disagree
- Disagree
- Neutral
- Agree
- Strongly agree

Would you encourage your relative to undergo surgery to treat his/her seizures if he/she was guaranteed that he/she will no longer have seizures after the surgery and will have no complications or brain injury?

- Strongly disagree
- Disagree
- Neutral
- Agree
- Strongly agree

Has your knowledge and/or perception of surgery as a treatment option for epilepsy changed after completing this questionnaire?

- Yes, I am more curious or interested in epilepsy surgery for my relative
- No

Appendix D

Chart Data Collection Guide

Demographic information

- Age as of December 31, 2021
- Gender
- City/town of residence

Epilepsy history

- Primary neurological diagnosis
- Age of onset of seizures
- Frequency of seizures- approximate number of seizures per month
- Semiology of seizures
- Concurrent medical conditions

Treatment history

- Current medication(s) and duration of trial (include any available information on when patient was started on a medication, when medication was changed and reason for the change
- Past medications and duration of each trial (estimated based on when medication was started and when it was changed, if information available in charts)
- Any previous cranial neurosurgical procedure related to epilepsy (date and type of procedure)

Surgical candidacy consideration

- EEG monitoring (date(s), duration of monitoring, if video included, localization findings)
- Past cranial imaging (CT, MRI, PET, SPECT)
- Any previous neuropsychiatric evaluation
- Any documented recommendation for surgery as treatment of epilepsy

Appendix E

Codebook

Name	Description	No. of Participants	References
Capacity for epilepsy surgery in Uganda	Covers interview questions regarding: - Training and education of clinicians to manage patients with refractory epilepsy - Resources for investigating epilepsy patients for surgical candidacy	13	200
Barriers to implementing epilepsy surgery	Any reported barriers - present or anticipated - that may be encountered in implementing an epilepsy surgery program	13	124
Infrastructure	Availability, limitation, or lack thereof, of infrastructure (EEG, CT, MRI, ICU beds, etc) to assess patients for epilepsy surgery candidacy or manage them postoperatively	13	57
Public's perception and attitude toward epilepsy surgery	From the interviewees' perspective, what is or will be the attitude of the public to surgery as treatment for epilepsy	6	14
Advertising epilepsy surgery to the public	Comments on how to get the news of epilepsy surgery to the public to garner their patronage	4	6

Education on risks of uncontrolled seizures	Education of patients and public on what can happen if patients live with uncontrolled seizures	1	1
Training of personnel for epilepsy care	Comments on availability of trained health care workers to assess and/or manage potential candidates for epilepsy surgery	13	51
Teaching around epilepsy surgery	Comments on didactic teaching on epilepsy surgery that interviewees receive(d) during their respective training	7	17
Comprehensive epilepsy care	Comments on holistic approach to managing patients with epilepsy	4	9
Collaboration between clinicians	Comments on teamwork approach to managing epilepsy patients	3	5
Cost as hindrance to epilepsy care in Uganda	Covers anything finances related with respect to any aspect of epilepsy care	11	25
Government and administration support	Any comments on role of government or hospital administration in pursuing epilepsy surgery	6	14
Demonstrating need for epilepsy surgery in country	Need to have data/evidence that epilepsy surgery is needed as a service in Uganda	1	3

Lack of advocacy to secure epilepsy services	Comments on advocacy, if any, to pursue epilepsy surgery at MNRH	1	2
Lack of dedicated epilepsy practice	Comments on not having a clinical service dedicated to managing epilepsy patients	4	9
Need for international collaboration	Any comments on prior or anticipated need to have support from international partners to pursue epilepsy surgery at MNRH	6	7
Post-treatment support	Availability, or lack thereof, of social system to support patients with epilepsy	2	2
Prior experience with epilepsy surgery in Uganda	Any reports from interviewees on epilepsy surgery being done in Uganda, regardless of whether or not the interviewee was personally involved	4	10
Need for epilepsy surgery in Uganda	Covers interview questions regarding: - Clinical practice patterns on how epilepsy patients receive care - Workflow or algorithm for managing epilepsy patients - Prevalence of patients with refractory epilepsy - Practice patterns for managing patients with refractory epilepsy - Priority of epilepsy surgery in current clinical needs	13	142

Impact of refractory epilepsy on patients and families	Perceived or reported risks to patients and their families if patients continue to live with seizures refractory to medications	2	2
Management of patients with refractory epilepsy	Covers comments on how patients are treated if their seizures are refractory to medications (formally defined as 2 or more anti-seizure meds)	11	36
Referral to neurosurgeons at Mulago	Referrals of patients from neurologists or psychiatrists to neurosurgeons at MNRH for epilepsy refractory to medications	5	8
Referral to other hospitals or countries	Any referrals of patients made to hospitals other than MNRH or countries outside Uganda to receive (surgical) care for epilepsy	5	8
Medications for treating epilepsy in Uganda	Covers comments on options and/or availability of anti-seizure medications for patients receiving care for epilepsy	7	12
Neurosurgical management of patients with seizures	Covers accounts from neurosurgical providers on their workflow in assessing and treating patients who present to their care with seizures	7	29
Potential benefit of epilepsy surgery	Interviewees perspectives on how epilepsy surgery may benefit their patients	8	10

Prevalence of patients with seizures	Interviewees report on how commonly they see patients with epilepsy in their clinical practice	10	20
Prevalence of refractory epilepsy	Interviewees report on how common patients with epilepsy refractory to medications are in their respective clinical practices	4	5
Priority of epilepsy surgery	Interviewees' perspective on where epilepsy surgery falls within their perceived clinical needs of their health center	8	13
Workflow of managing patients with epilepsy	Treatment algorithm or practice guideline on how to manage patients presenting what seizures	8	15
Diagnosing epilepsy	Practice guideline or typical practice in working up patient to make a diagnosis of epilepsy	5	7
Other findings	Covers codes not directly relevant to the need and/or capacity for epilepsy surgery in Uganda	13	54
Dynamic of neurology, neurosurgery and psychiatry	Clinical relationship between Neurology, Neurosurgery, and Psychiatry as it pertains to providing care for patients with epilepsy	8	18
Who manages patients with seizures	Clinical department(s) that primarily take care of patients presenting with seizures	2	3

Health system disparities	Differences in care received by patients with epilepsy based on which tier of health system they attend, public vs private care, economic status, etc.	2	5
High prevalence of trauma, tumors, and NTDs	Burden of other neurologic conditions, beside epilepsy, that constitute the practice of neurosurgeons	5	9
Demands of other clinical practice in trauma, tumor, NTDs, etc		1	1
Nonadherence to epilepsy treatment	Patients not continuing with recommended treatment(s) for their epilepsy	1	2
Social factors influencing epilepsy care	Sociocultural factors that impact seeking, receiving or continuing care for epilepsy	10	20

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