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Medication Adherence and Seizure Remission Prediction Model for Patients with Epilepsy at Mbarara Regional Referral Hospital

[1]OWEN OYESIGYE
[1](Faculty of Agriculture Environmental Sciences and Technology, Bishop Stuart University, Mbarara, Uganda.
*Corresponding author: [1]OWEN OYESIGYE

ABSTRACT : Epilepsy is a global burden and accounts for 50 million people worldwide with an estimated 5 million people diagnosed with epilepsy each year. The estimated proportion of the general population with active epilepsy at a given time is between 4 and 10 per 1000 people worldwide. In high-income countries, there are estimated to be 49 per 100000 people diagnosed with epilepsy each year and an estimate of 139 per 100000 people in low- and middle-income countries like Uganda among other sub-Saharan countries, indicating that close to 80% of people with epilepsy live in low- and middle-income countries. The risk of premature death in people with epilepsy is up to 1.6–9.3 times higher than for the general population and three quarters of people with epilepsy living in low-income countries do not get the treatment they need to live a seizure free life due to a number of factors. It is approximated that up to 70% of people living with epilepsy could live seizure- free if properly diagnosed and treated. This study therefore aimed at identifying the factors associated with epileptic seizure attack, examine patients drug adherence patterns using existing patients' records, and formulate a model and its algorithm to predict the likelihood of seizure reoccurrences. The study was retrospective with data from patients' records at Mbarara Regional Referral Hospital. Data analysis was done to investigated patients' drug adherence and the rate of seizure remissions. The dependent variable was the number of seizure/fits attacks per month (seizure attacks per month) which was a count variable, and the best model for predicting and describing the number of seizure attacks was the Poisson regression model. STATA 13.0 was used to analyze the data. The results indicate that there is a 21% reduction in the incidence rate ratio (IRR) of epileptic seizures as visits (or follow up periods) increase compared with patients who had no visits. According to the confidence interval, the reduction could be as much as 24% or as low as 18% (IRR=0.79; 95%CI [0.76-0.82]; p<0.001). The results further indicate that duration of fits among the patients increases the rate of epileptic seizures by 8% (IRR=1.08; 95%CI [1.07-0.1.09]; p<0.001). These results were used to develop a model which can be used to predict the likelihood of seizure reoccurrences among epileptic patients.

Keywords – Epilepsy, Medication adherence, Seizure remission

I. INTRODUCTION

Epilepsy is a chronic neurological disorder of abnormal, recurrent, excessive and self-terminating discharge from neurons that affects the physical, psychological and psychosocial wellbeing of a person (Sibat H., 2011). The degree of epilepsy is the repeated occurrence of two or more unprovoked seizures, whose clinical manifestation consists of sudden and transitory abnormal episodes of motor, sensory, autonomic, or psychic origin. (Shakirullah et al., 2014)

Seizures are results of excessive electrical discharges in a group of neurons in the brain and the behavioral outcome which depends on the brain regions where synchronous firing of a neuronal cell group occurs, (Sibat, 2011). The period between seizures can vary widely and can measure in minutes, hours, days, weeks, months or even years (Hickey, 2003). Epilepsy is one of the most common and widespread neurological disorders globally estimated to be affecting over 65 million people (Ngugi et al., 2010) and it is reported that 80% of people with epilepsy live in the developing world (De Geest & Sabaté, 2019). Worldwide, an estimated five million people are diagnosed with epilepsy every year. Developed countries contribute the smallest percentage of epilepsy with an estimation of 49 per 100000 people diagnosed with epilepsy each year. In developing countries, this figure can be as high as 139 per 100000 people diagnosed (Wo et al., 2017) and it's attributed to the increased risk of endemic conditions such as malaria or neurocysticercosis, the high incidence

of road traffic injuries, birth-related injuries, and variations in medical infrastructure, the availability of preventive health programmes and accessible care (Paschal et al., 2014).

Several studies point clear that epilepsy is not contagious, though many underlying disease mechanisms can lead to epilepsy, the cause of the disease is still unknown however, in about 50% of cases globally it has established that epilepsy is categorized into the following; structural, genetic, infectious, metabolic, immune and unknown for example a severe head injury, brain tumor and brain damage from potential causes(Sánchez et al., 2010). An individual with epilepsy suffers recurrent seizure provoked by acute brain insults or metabolic derangement. Seizures are characterized by a brief period of involuntary shaking. They may be partial, involving only one part of the body or generalized involving the entire body and they may be accompanied by loss of consciousness and lack of bowel or bladder control. Some individuals continue to have frequent seizure with anti-epileptic drugs. However, more than 70% of patients, who are treated, achieve long-term remission or freedom from seizure, usually within 5 years of diagnosis (De-Boer et al., 2008). The majority of people with epilepsy have good prognosis if they receive appropriate treatment (Leonardi & Ustun, 2012).

People with epilepsy often experience changes in their quality of life such as less mobility, as well as the impact on learning, school attendance, employment, relationships, and social interactions however these challenges differ with in people of different age categories that is children, adolescents, and seniors than for adults thus leading to marginalization of the affected people and poor quality of life (Espinso et al., 2018) and these contradict the Sustainable Development Goals (SDGs 1,3 and 4) which talk about ensure healthy lives and promote well-being for all at all ages, End poverty in all its forms everywhere and ensure inclusive and equitable quality education and promote lifelong opportunities for all (WHO, 2019).

According to Alla et al., (2017) indicates that epilepsy may lead to disability and severely reduced quality of life. People with epilepsy can face diminished social support and family function, cognitive challenges, medical and psychiatric comorbidities, and stigmatization. In addition, people with epilepsy also report more difficulty in employment, lower annual incomes, and physical limitations which all don't support the SDGs 1, 3 and 4 (WHO, 2019).

In Africa, many people believe epilepsy is contagious therefore, they are unwilling to help or touch the person who has fallen during seizure and this kind of belief worsens the stigma (Bautista & Rundle-Gonzalez, 2012). Despite a high prevalence of epilepsy in Africa, most people do not receive appropriate treatment. This is due to limited knowledge, poverty, cultural beliefs, stigma, poor health delivery infrastructure, and shortage of trained health care workers (Sibat, 2011). According to (Banerjee & Hauser, 2020) the cultural beliefs have led to discrimination of the epileptic patients which has resulted to the patients have law self-esteem and lack of confidence in themselves. The prevalence of antiepileptic drug non-adherence in sub-Saharan African countries, is significant with about 67% in Nigeria, 54% in Kenya, and 37% in Ethiopia and financial factors were the significant predictors of non-adherence (Modi & Avani, 2011). According to the executive director Epilepsy support association Uganda, the diseases has been fueled by poor access to medical care and lack of awareness about epilepsy. Many of the parents have neglected their children about seeking treatment thinking it can cure on its own (Mugarura, 2017).

This study was therefore aimed at, establishing the relationship between medications adherence, seizure reemissions, the lapse period after seizure remissions and the period an attack takes. This was done at Mbarara Regional Referral Hospital in Psychiatric Ward.

II. PROBLEM STATEMENT

Epilepsy is one of the major psychiatric illnesses affecting people regardless of age, sex, race of people (Gabr, 2015) , and it accounts for 35% of mental illnesses around the world and it is the fourth most common neurological disease. In Uganda alone, the disease accounts for approximately 3.3% of the world epilepsy cases (Shakirullah et al., 2014). Instant seizures can result to sudden unexpected death in epilepsy (SUDEP) and this remains a leading cause of mortality among people with seizure disorders (Devinsky & Sudden., 2011). According to a report from the Epilepsy Support Association Uganda (ESUA), there is an estimated incidence of 156 per 100,000 people each year in Uganda giving more than 55,491 new cases of epilepsy each year (Colebunders et al., 2016).

According to Mugarura, patients diagnosed with epilepsy are given the Anti-Epileptic Drug (AED), but there is still high prevalence of seizure remissions among these patients that have already started on AED drugs (Mugarura, 2017). In this study, the researcher proposes to develop a model for predicting reoccurrence of seizures according to medication adherence records among patients with epilepsy using existing patients' records.

III. LITERATURE REVIEW

Overview of Epilepsy and Seizure

Epilepsy is a central nervous system disorder in which brain activity becomes abnormal, causing seizures or periods of unusual behavior, feelings and sometimes loss of awareness regardless of sex, races, ages and ethnic backgrounds. Everyone can be a victim of epilepsy (Shakirullah, Ali Khan & Nabi, 2014). Seizure is an immediate symptom of epilepsy, it's a sudden uncontrolled electrical disturbance in the brain which results into behavioral changes, feelings, and in levels of unconsciousness (Nissinen et al., 2017). However, these symptoms vary from person to person, where some people with epilepsy simply stare blanky for a few seconds during a seizure, while others repeatedly twitch their arms or legs. (Voll et al., 2015) notes that having a single seizure does not mean having epilepsy. At least two unprovoked are generally required for an epilepsy diagnosis. Treatment with medications or sometimes surgery can control seizures for the majority of people with epilepsy. However, reoccurrence of seizures has been seen in patients who are already on medication and most of these cases have been attributed to non-medication adherence. Therefore, some of these factors to medication non-adherence to the medication are as presented below.

Factors associated with non-adherence to drug among patients with epilepsy

Medication adherence is defined as the extent to which patients take drugs as prescribed by their health care providers (Osterberg & Blaschke, 2005) and when a patient does not coincide with medical or health advice or the drug prescription is known to be non-adherence.

Medication non-adherence is a public health issue estimated to cost $100 billion and contributing to nearly 125,000 deaths each year in the United States (Paschal et al., 2014). The study by Paschal shows that the prevalence of medication non-adherence varies from 8 to 71% and is the cause for 10% of hospital admissions and 23% of admissions to nursing homes (Paschal et al. 2014). While in a study by Kyngäs reported non-adherence between 13% and 93%, with an average rate of 40% and it encompassed all ages and ethnic groups (Kyngäs, 2010). The extensive literature reviews of medication adherence (Johnbull et al., 2011), identified important predictors of medication non-adherence across the numerous regions and some of the key variables identified in these reviews were patient demographics such as age and education, cost of medications, cognitive disabilities, and fear of side effects or dependence on medications; disease characteristics including features of a disease, having psychiatric disorders like depression and anxiety, absence of symptoms, time between taking drug and having an effect; therapeutic regimen characteristics such as regimen complexity, treatment duration, number of medications, and frequency of dosing; and style of interaction with physicians including the duration, frequency, and quality of communication between the patient and physician (Johnbull et al., 2011).

Psychosocial variables such as patient's illness perceptions, beliefs in medications, attitudes towards medications, reasoning made based on the pros and cons of taking medications, constraints of everyday life, and experiences were also identified as significant predictors of medication non-adherence (Sweileh et al., 2011). The patients' beliefs about cause of epilepsy and preference to the treatment modality are important factors influencing epilepsy treatment. Patients' own attitudes towards the treatment are also equally important in ensuring success of treatment and adherence (Bautista & Gonzalez, 2012). Furthermore, failure to adhere through forgetfulness, misunderstanding, or uncertainty about clinician's recommendations, or intentionally due to their own expectations of treatment, side-effects, and lifestyle choice are found to be the reasons for non-adherence (Finsterer & Scorza, 2017).

According to the study conducted by (Bano, 2016) to improve patient drug compliance with anti-convulsant therapy, among 53-hospital outpatient with epilepsy. The patients in the interventional group were subjected to a combination of compliance improving strategies, patient counseling, a special medication container, self-recording of medication intake and seizure and mailed reminders to collect prescription refills and attend clinic appointments, compliance with anticonvulsant therapy (as measured by plasma anticonvulsant levels and prescription refill frequencies), and seizure frequency, were evaluated in each patient prior to intervention and 6 months afterwards (Voll et al., 2015). In a similar study, patient compliance and clinical control improved significantly in the intervention group patients. Seizure frequency was, on average, halved following intervention. Compliance and seizure frequency were unaltered in the control group. Intervention failed to improve clinic appointment keeping (Bautista & Gonzalez, 2012)

It is well established that patients with suboptimal adherence levels are more likely to have seizures that are associated with increased number of hospital admissions and healthcare costs (Jones, et al., 2012). Factors influencing adherence to AEDs are categorized as; patient-, treatment- and health system-related factors and a number of methods have been used to measure therapeutic adherence, including self-report, pill count, appointment attendance, medication refill history, blood or urine drug levels and drug diary (Sweileh, Ihbesheh & Jarar, 2011). There are also some indirect common methods, such as self-reports and patient interviews, that have always been used for measuring medication adherence (Bautista & Gonzalez, 2012). In a study by (Johnbull, Farounbi & Adeleye, 2011) which attempted to fill this information gap and came up with strong recommendation on possible interventions for improving medication adherence behavior among people with

epilepsy revealed that scarcity of published information regarding the prevalence and associated factors of AEDs non-adherence is also said to be one of the factors for increased non-adherence.

Factors associated with drug resistance among patients with epilepsy

There are many factors leading to drug-resistance in patients suffering from epilepsy. Drug-resistance depends on a number of clinical aspects including aetiology, early age at seizure onset, type of epileptic syndrome and seizure, structural brain abnormalities or lesions, or abnormal electroencephalographic findings (French, 2007). Furthermore, drug-resistance can depend on either genetic or acquired factors affecting pharmacokinetics or pharmacodynamics of AEDs (Beck, 2007). Genetic factors may reduce serum drug concentrations either by reducing absorption or by increasing elimination and/or the access of AEDs to the epileptic focus in the central nervous system (CNS) (Regesta & Tanganelli, 2019). While genetic factors may be responsible of changes in AED targets reducing the response to drugs (Sánchez et al., 2010). Resistance to AED is considered as a complex phenomenon that may involve many mechanisms, which occurs across a wide range of seizure types, etiologies and a variety of AEDs (Chin, 2012). The majority of patients with drug-resistant epilepsies are unresponsive right from the beginning of AED treatment, indicating that acquired factors are unlikely to explain this phenomenon while others continue to remain unresponsive to all AEDs, including the newer ones, and even to multiple AED combinations, indicating that they are multidrug resistant right from the beginning (World Health Organization, 2012). Patients with drug-resistant epilepsies, therapeutic serum AED monitoring and optimizing the dosages seldom results in better seizure control, indicating that decreased AED absorption or increased metabolism is unlikely to be a major cause of AED failure in the majority (Johnbull, Farounbi & Adeleye, 2011).

Sweileh et al., (2011) surmises that AED resistance has region-specific expression or function of multidrug efflux transporters at the blood-brain barrier is enhanced, leading to impaired access of AEDs to the central nervous system sites which eventually leads to too low drug concentrations to induce antiepileptic effects at brain sites initiating seizures. However, Sweileh WM, et al., (2011) reveals that AED resistance occur due to changes in the drug targets (receptors) themselves result in reduced AED sensitivity. Sweileh et al., et al further explain that because drug resistance often occurs in a patient to multiple AEDs, if not to all the currently available AEDs simultaneously, the multidrug transporter hypothesis is considered in preference to alterations at specific drug receptor sites to explain the phenomenon of multi-AED resistance. According to a study by (De Geest & Sabaté, 2019) which was aimed at assessing the prevalence and associated factors of antiepileptic drug non-adherence among people with epilepsy, it was found out that poor adherence to antiepileptic drugs is one of many reasons for pharmacological treatment failure and recurrence of seizure and consequently results in poor quality of life, decreased productivity, and seizure related social and economic crisis.

Drug adherence and seizures reemissions prediction models

Prediction models estimate the risk (absolute probability) of the presence or absence of an outcome or disease in individuals based on their clinical and non-clinical characteristics (Grobbee DE, 2009). Depending on the amount of time until outcome assessment, predictions can be outcome or disease present at this moment or predictive (outcome occurs within a specified time frame). During diagnostic practice, doctors always incorporate information from history-taking, clinical examination, laboratory tests or imaging test results to judge and determine whether or not a suspected patient is adhering/revering. In essence, prediction model development mimics this diagnostic by combining all this patient information which is summarized as predictors of the outcome, in a statistical multivariable model (Nissinen et al., 2017).

Prediction model provides an estimated probability that allows for risk analysis for individuals. Hence, it can guide physicians in deciding upon further diagnostic tests or treatments. For example, patients with a high probability of having a disease might be suitable candidates for further testing, while in low probability patients, it might be more effective to refrain from further testing. For instance, the combination of the Wells PE rule and a negative D-dimer test can safely rule out PE in about 40% of all patients suspected of having PE. These patients can be refrained from further testing, thus improving efficiency of the diagnostic process (Lucassen & Weert et al., 2011). The outcome of a prediction model has to be chosen as such that it reflects a clinically significant and patient relevant health state, for example, death yes or no, or absence or presence of (recurrent) pulmonary embolism (Lucassen & Weert et al., 2011). A clear and comprehensive predefined outcome definition limits the potential of bias. This includes a proper protocol on standardized (blinded or independent) outcome assessment. In case of prognostic prediction research, a clear-defined follow-up period is needed in which the outcome development is assessed. For example, the PESI score, developed to identify PE patients with a low risk of short-term mortality in whom outpatient treatment may be safe, used 30 days of follow-up to assess the outcome PE recurrence or mortality during that period (Eichinger et al., 2010).

According to (Beck, 2007), complete remission was defined as achieving a 5-year seizure-free and 5-year medication-free period. Any subsequent seizure for any reason was considered a relapse. Complete

remission at last contact was defined based on the date of last seizure and date seizure medications were completely stopped. Therefore, seizure remission is the time lag between two successive seizure attacks. The study by (Rikir, Grisar & Sadzot, 2010) examined seizure outcomes over an extended period of time. He created three additional indicators for the seizure outcomes occurring between 2 and 5 years: relapse after first remission, failure of a second medication (late pharmaco-resistance), and attainment of a first 1-year remission (late remission). In a similar study, the analysis of relapse following complete remission was based on calculating the person-years from attaining complete remission to date of relapse or of last contact if no relapse. Poisson regression was used to determine the rates of relapse during the first 5 years, second 5 years, and >10 years after achieving complete remission. The 'rule-of-three' was used to calculate upper confidence limits for 0-numerator results (Hendriksen et al., 2013).

Bivariate comparisons were performed with t-tests and chi-square tests as appropriate to the data. Proportional hazards models were used to identify independent predictors of complete remission at last contact and only considered first only those factors that were ascertainable at baseline. The non-syndromic group was used as the comparison against each other epilepsy type group that was tested. They later added 2-year seizure outcomes to that model and reassessed contributions of the original baseline variables. Finally, the 5-year seizure outcome variables were added. Sequential models were created for the full group and separately for participants with complicated and uncomplicated presentations. Logistic regression was used to determine the sensitivity and specificity and overall predictive value of the three sequential models and to determine the area under the curve, a metric of predictive accuracy, for each model (Shams & Barakat, 2010).

The decision to stop medications was to greatly influenced by the same prognostic factors under study (e.g. family history, early seizure history, etc.), models of complete remission were compared at last contact to those for 5-year and for 10-year remission at last contact regardless of medication (Zullig et al., 2017). The study concluded that Antiepileptic Drugs (AEDs) are effective in the treatment of epilepsy, but poor adherence to medication is major problem to sustained remission and functional restoration resulted in treatment failure and seizure recurrence (Unni, 2008). Even though around 70% of people who had epilepsy supposed to be seizure-free with optimum AED treatment, many people with epilepsy did not take their antiepileptic drugs appropriately and the mortality rate in non-adherent patients was more than threefold higher than that of adherent one (Samsonsen, & Reimers, et al., 2014). The consequence of AEDs non-adherence behavior has been associated with poor seizure control, increased morbidity and mortality along with increased time of hospitalization, worsened patient outcome, poor quality of life, and increased health care cost (Prince, et al., 2009). Additionally, AEDs non-adherence will also lead to increase burden of inpatient and emergency department services; moreover, it also affects the family members socially, economically, and psychologically (World Health Organization, 2012; Sweileh et al., 2011).

In another interventional / experimental study by (Lois, et al., 2006) which aimed at predicting risk of seizure recurrence after a single seizure and early epilepsy, patients were randomly assigned either immediate treatment with an antiepileptic drug or delayed treatment after a time when the clinician and patient agreed treatment was necessary. Information about past seizures and neurological and family history, in addition to demographic information and findings of neurological examination, was gathered at baseline.

Lois, et al., (2006) found out that number of seizures of all types at presentation, presence of a neurological disorder, and an abnormal electroencephalogram (EEG) were significant factors in indicating future seizures. Follow-up information was obtained at 3 months, 6 months, 1 year, and successively at yearly intervals after randomization. The test sample was used to develop a prognostic model for the interval from randomization to first seizure based on Cox regression stratified by treatment allocation. Stepwise regression was used to assess the predictive value of baseline covariates of interest with exclusion at $p \geq 0.1$ and inclusion at $p \leq 0.05$.

An abnormal EEG was defined as specific focal or generalized epileptiform or slow wave abnormality. This definition excluded non-specific abnormality. Missing values of covariates were imputed using the mean of remaining observations in the sample (mode for categorical variables). Transformation of continuous variables was assessed with Martingale residuals. Sensitivity analyses were done for only those individuals with complete covariate data, and for only those with an EEG in the interval from 9 months pre-randomization to 3 months post-randomization (excludes 7% of the test sample with no EEG data and 5% with an EEG outside of this interval). The proportion of individuals who had a further seizure was similar among those with an EEG in and outside of the time period (48%), but was lower in those with missing EEG data (33%). Application of a shrinkage factors to the regression coefficients was also considered, to compensate for over-fitting in the validation sample.

A prognostic index was defined as the linear predictor resulting from the final model. The predictive value of this prognostic index is assessed by calculation of a separation statistic, D, which indicates the predictive ability of the index. An optimism-adjusted version of the statistic, Dadj, was used to correct for bias when fitting the model and estimating the separation statistic on the same dataset. Risk group classifications

were assigned by use of terciles of the prognostic index distribution obtained from the model, and probabilities of seizure recurrence by 1, 3, and 5 years then calculated for each of these groups. The prognostic index constructed from the test sample was then applied to the validation sample, enabling assignment of each individual to a specific risk group. The predicted risk (as observed in the test sample) of seizure recurrence in each of these groups was compared with the observed seizure recurrence in the validation sample. Kaplan-Meier plots were used to assess the differences across risk groups in both the test (predicted risk) and validation (observed risk) samples. The predictive accuracy of the prognostic index in the validation sample was also assessed more formally by use of a censoring adjusted Brier score.

A prognostic index was calculated, on the basis of model 1, as the sum of the covariate values for a particular patient, weighted by the corresponding estimated regression coefficients. So, for an individual with two seizures, an abnormal EEG, and no neurological disorder, the prognostic index is: (loge2×loge1.56)+(1×loge1.54)+(0×loge1.35) = (loge2×0.44)+(1×0.43)+(0×0.30) = 0.74

Since the two variables added at the forward stepwise regression phase were both of borderline significance (model 2), it was decided to omit these from the final prognostic index for simplicity. The separation statistic Dadj was 0.77 (95% CI 0.36–0.90). Since the confidence interval excludes zero, this suggests that the prognostic index has acceptable ability to discriminate between patients' risks of seizure recurrence. The D statistic can also be used to provide guidance on the largest number of prognostic groups that would (with 90% power) maintain significant separation. For our prognostic model, the maximum number of groups likely to maintain reasonable separation is three. 10 Tertiles of the continuous prognostic index described correspond to values of <0.30, <0.50, and ≥0.50 i.e., group 1 (low risk) includes individuals with a prognostic index of <0.30, group 2 (medium risk) includes individuals with a prognostic index of 0 · 30–0 · 49, and group 3 (high risk) includes individuals with a prognostic index of ≥0.50. Table 3 shows the probabilities of a further seizure by 1, 3, and 5 years in each of these risk groups.

No significant difference is observed between treatments for low-risk individuals (Log-rank test $\chi 2=1.7$, p=0.2), but there is an indication of improvement with immediate antiepileptic-drug treatment for medium-risk and high-risk individuals (7.0, p=0.008; 21.9, p<0.0005, respectively; overall likelihood ratio test for interaction between risk group and treatment 13.27, p=0.001). Predictive accuracy of the prognostic model in the validation sample was examined by plotting observed proportions of individuals with seizure recurrence within six groups of predicted seizure recurrence (bandwidths 0.2, 0.1, 0.1, 0.1, 0.1, and 0.4) based on the continuous prognostic model 1 at 1 and 3years post-randomization. These plots suggest that some shrinkage remains despite adjustment for this, with observed proportions experiencing seizure recurrence less extreme than predicted at very high and very low predicted proportions of seizure recurrence.

The censoring adjusted Brier score suggests a degree of success of the model, with a score of 0.23 at 1 year, 0.24 at 3 years, and 0.25 at 5 years (the Brier score ranges from 0 to 1, with a large score indicating poorer predictive accuracy of the model). Use of the prognostic index in practice requires some simplification; it is useful to rewrite the final model using integer values. This is derived from the continuous prognostic index obtained from model 1.

Evaluation of seizure measurement / seizure severity

According to, (Joyce & Jacqueline, 2001) the basic unit of measurement in epilepsy is the frequency of seizures. Events have been reported in ordinal scales as the number of seizures, or in cardinal scales as few, many, fewer, or more seizures. Additionally, data have been transformed into percentage change from a baseline frequency or a rate based on frequency per specified time period (e.g., number of seizures per month). The standard end point in clinical trials has been the proportion of patients whose seizure frequency decreased by ≥50% from baseline. Other interpretations include the number of patients whose seizure frequency or rate decreased or reached a specified range (e.g., ≥50%, 100%), as well as the number of months with no seizures.

According to (Unni, 2008) the new rating system was developed for the Veterans Affairs (VA) co-cooperative study to compare AED monotherapy for newly treated patients (Cramer et al., 2003). The system assessed the frequency of events in partial seizures (secondarily generalized tonic-colonic, complex partial, simple partial) as well as by severity. The VA seizure frequency and severity scale (VA Scale) was completed by the clinician based on specific questions about seizure components performed by examination and interview (Cramer et al., 2003). Seeking a simplification of the VA scale, the Chalfont Seizure severity scale was in 1990 (Cramer & Jacqueline, 2001). It was updated and renamed the National Hospital Seizure Severity Scale (NHS3) (O'Donoghue et al., 1996), these scales were used for assessment of institutionalized patients. Generalized statements about frequency and duration as well as impairments caused by the typical events define six levels.

The next approach to seizure severity was a departure from traditional instead toward patient-based assessment of severity (Duncan & Sander, 1991). The Liverpool severity questionnaire was developed with trials support from Burrouhg-Welcome for use in clinical trials of lamotrigine (LTG). It was designed to evaluate both severity in children by asking parents to complete a questionnaire (Carpay & Arts, 1996). The parent-based

Hague Seizure severity scale (HASS) was based largely on the Liverpool Scale with the adoption of parent response.

Although the developers of each new instrument used different approaches to assess seizure severity, some basic components of seizures are assessed in all the scales (Joyce & Jacqueline, 2001). The approach to data collection is by interview of the adult patients and an observer (VA, NHS3, Hazard), the patient alone (Liverpool), or the parent of a child with seizures (Hague). The inclusion of an observer is standard clinical practice because it is often difficult for patients to describe their seizures. Reasons include poor memory and lack of awareness of the relationship of events (e.g., olfactory aura as a sensory component of a seizure) (Duncan & Sander, 1991). Patients can recall associated precipitating factors that they relate to seizure occurrence (e.g., missed medication and illness only). Rather than attempting to document all clinical details of seizures, as can be done during inpatient closed-circuit television monitoring, on out-patient self-report system such as a seizure severity scale should be based on information collected from multiple sources (Baker et al., 1998).

In a study by Kaddumukasa and his team, about the association of seizure severity with the quality of life in people living with epilepsy in Kampala Uganda, seizure frequency was arbitrary determined as the number of seizures reported by the PLWE or caregiver over a period of one year. The patients or immediate caregivers provided the seizure frequency information retrospectively, which was categorized to facilitate some statistical analyses: no seizures 1 year, one – nine seizures a year, having 10 – 20 seizures in a year and having more than 20 seizures in a year (Kaddumukasa et al., 2019). Relatedly parents / caretakers were also used to record seizure details of the patients and the key information recorded was; Age of the patient, Number of fit/seizures, Duration of the seizures, treatment and lapse/ missed days but did not record seizure severity. Therefore, for this study, the ordinal scales (basic unit of measurement of epilepsy is the frequency number of seizures) will be adopted to measure the severity of the seizures by scaling the number of seizures per month as; <0 = recovery, 1 – 3 few and 3 - 5 as many / alert which will give warning to the clinician or caretakers and > 5 will be acute which means immediate attention

Discussion

In the first model by Rikir et al. (2010) which examined seizure outcomes over an extended period of time and used logistic regression to determine the sensitivity and specificity and overall predictive value of the three sequential models and to determine the area under the curve, a metric of predictive accuracy, for each model.

Poisson regression was used to determine the rates of relapse at different time intervals. The basic factors that were considered in the model were only family history and early seizure history. This model did not consider some factors like number of fits, duration of fits, treatment and lapse days which are paramount in predicting the re-occurrence of seizures among epileptic patients.

In the second model by (Lois et al., 2006), the follow-up information was obtained at 3 months, 6 months, 1 year, information about past seizures and family history, in addition to demographic information and findings of neurological examination, was gathered at baseline. More so Electro encephalogram (EEG) and CT scan data were also collected where available. This was the information used in developing the model while neglecting the drug adherence patterns, duration of the seizure and the period between the last seizures which are key in determining the likelihood of seizure reoccurrences in patients with epilepsy.

In conclusion therefore, the models that were reviewed in this study used information like family history and early seizure history, Electro encephalogram (EEG) and CT scan data were the information used to develop the models for predicting seizure remissions thus indicating some key information which would be available for the model was left out including drug adherence patterns, duration of the seizure and the period between the last seizures which the proposed model intends to look at.

IV. METHODOLOGY

Introduction

In this research, Cross Industry Standard Process for Data Mining (CRISP-DM) approach was used which involves Study definition, Data understanding, data presentation, modeling, evaluation and deployment (Shearer, 2000) as seen in Figure 3.1 below. However, the study did not do the deployment since it was not part of the study.

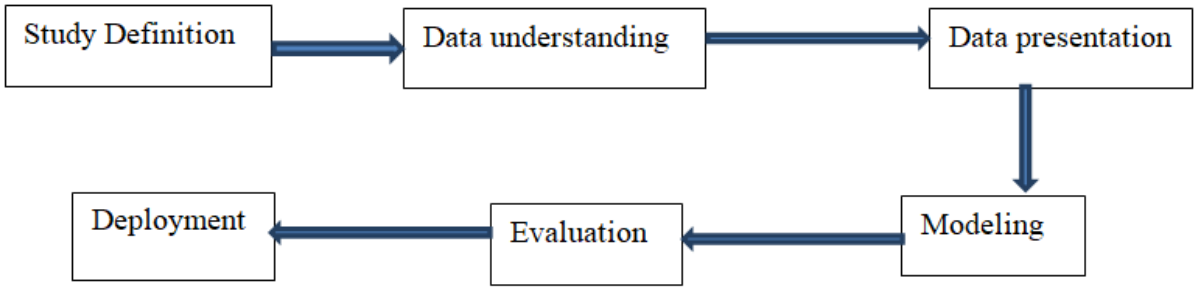


Figure 3.1: Cross Industry Standard Process for Data Mining Methodology (Shearer,2000)

Study Design

This was a retrospective study. It looked back and examined exposures to suspected risk or protection factors in relation to an outcome that is established at the start of the study. The study examined the already existing records from the psychiatric department. This study was only interested in data concerning epileptic patients' drug adherence and seizure remissions that were captured for the past five years.

Sampling techniques

In this study, the researcher used simple random sampling techniques to select the patients' records to use for the study. Since data already existed, only extraction and sorting were done to remain with the information that was only needed for the study.

Sample size determination

The actual sample was calculated using the statistical formula by Yamane (1967):

$$n = \frac{N}{1+ N(e)^2}$$

Where; n = sample; N = Population size; and e = Level of significance which is 0.05. But the level of precision was adjusted to 0.07 for the researcher to get a manageable size.

The actual calculation of the sample was as follows:

$$n = \frac{984}{1+ 984\ (0.07 \times 0.07)}$$

$$n = 169$$

Therefore, the total sample size was only 169 patients' records.

Data collection

In the study, secondary data was used and this included the already existing patients' records at the hospital which was used in the developing of the model. The medical records were accessed for detailed information and the baseline demographic variables included in this analysis were age (in years); lapse days (days) duration of fits (minutes).

The researcher used research assistants for the successful study. The researcher hired research assistants from the people who work in the psychiatry department and those that work in the records department because the researcher was not a medical expert. Therefore, these people helped him to get the required information since they had a medical background and they were working in this field for a good time, therefore they were of great importance in retrieving the needed information and sorting it to give meaning to the researcher.

Data analysis

This involved processing of the data which was done at three levels using Statistics/Data Analysis (STATA) version 13. Univariate analysis encompasses the descriptive summary for each variable. To study characteristics of patients, techniques for summarizing data for continuous variables were used and these included: Mean, variance and standard deviation while the frequencies and percentages were used for categorical variables.

Bivariate Analysis at the second level to test any possible associations between each of the independent variables (treat, visits, age, lapsedays and duration of fits) and the dependent variable (seizure occurrence). Statistical significance of the relationships was determined for the P-value (P=0.05) and all significant variables at this level were considered at multivariate level analysis. This was done using Poisson regression because the level of measurement of the dependent/outcome variable was count. The appropriate model was given as: $\ln(\lambda) = \alpha + \beta X + uj$,

where λ is the rate at which the seizure occurs

X - exposure variables

α is the baseline corresponding to X=0

β is a parameter of the effect of a unit change in X on the log rate (Poisson reg)

i = 1,2,3, …

Multivariable analysis was the third level of analysis which was performed to assess which factor associated with seizure remissions more than the other. The outcome variable was count data obtained from a longitudinal and therefore the suitable model to analyze this kind of outcome variable is the Poisson regression model. The Poisson regression analysis was used because it attempts to control possible confounding effect of independent/exposure variables on each other and thus finds the independent association for each exposure variable with the outcome variable.

The model is given by;

$\log_e(\lambda) = \alpha_j + \beta_j \times_I$,

where α is the baseline corresponding to X=0

λ is the rate at which the seizure occurs

X - exposure variables

β is a parameter of the effect of a unit change in X on the log rate (Poisson reg)

Variables with a p-value of ≤ 0.05 were considered to be important in explaining the outcome of interest. Independent variables that were not significant at bivariate level were not considered at this level of analysis.

Objective One: To investigate patients' drug adherence patterns and seizure remissions

The predictive variables that were considered include those factors associated with medication non-adherence among patients with epilepsy. Literature review has been done on the factors associated with non-adherence from other related studies. These factors were correlated with the socio-economic, personal among other factors from the secondary data available.

Medication adherence was measured using a well-documented Medication Possession Ratio (MPR). The MPR is measured as an average over a patient's entire observation period by dividing the total of the daily supply of medication by the number of days in the observation period (Manjunath et al., 2011). In this retrospective study, MPR was got from the patients records which have been taken for the past five years. Patients' clinical visits were used as the MPR. It was assumed that patients return to the clinic on the appointment date indicates that he / she is adhering to his medication. Therefore, the lapse days between the appointed date of return to the clinic and the actual dates were used to measure the medication non-adherence /missed medication.

Objective Two: To develop a model for predicting the likelihood of seizure reoccurrences using existing patients' records

In the theoretical background of probability models, count data usually have Poisson distribution. Several modifications (extensions) to the Poisson model have been proposed for different reasons which may include; (1) repeated measures of the outcome variable, (2) the occurrence of over-dispersion (the variability of the data is larger than the mean), and (3) the occurrence of excess zeros.

Poisson regression – Poisson regression is often used for modeling count data. Poisson regression has a number of extensions useful for count models. Zero-inflated regression models attempt to account for excess zeros. In other words, two kinds of zeros are thought to exist in the data, "true zeros" and "excess zeros". Zero-inflated models estimate two equations simultaneously, one for the count model and one for the excess zeros.

The model was developed basing on different variables among which included baseline demographic variables included in this analysis are age (in years); lapse days (days) duration of fits (minutes). Adherence (visits) was measured as a continuous variable representing monthly follow-up visits to the hospital. The variable visits start with the value 1 for the first follow-up visit, 2 for the second visit, and so on. The dependent variable: count variable- The number of seizure/fits attacks per month (seizure attacks per month)

After the development of the model, a web-based application was designed which can be used by the medical personnel at Mbarara Regional Referral Hospital – Psychiatric department to predict the likelihood of seizure reoccurrences among the epileptic patients.

Objective Three: To test and evaluate the accuracy of the model in predicting seizure reoccurrences among patients with epilepsy

The predictive model was tested and evaluated basing on test statistics for goodness of fit of seizure attacks. The better and appropriate easy test statistic to use for Poisson model include Power-Divergence and chi-square tests.

Cressie and Read (1984 & 1988) incorporated the Pearson's X^2 and Deviance goodness of fit (G^2) statistics into a family of "Power-Divergence (PD) Statistics" (PD_λ, $R \in \lambda$) for testing and evaluating Poisson regression models. In this family, each member PD_λ is the sum of deviance between the observed and expected counts.

Therefore, the most common test statistics are Pearson's X^2 and the scaled deviance (G^2). For a Poisson model, the variance is equal to the mean.

i) $$PD = \frac{2}{\lambda(\lambda+1)} \sum_{i=1}^{1} \sum_{j=1}^{j} O_{ij} \left\{ \left(\frac{O_{ij}}{E_{ij}} \right)^{\lambda} - 1 \right\}$$

ii) $G^2(u;n) = \sum_{i-1}^{n} 2\left[y_i \log\left(\frac{y_i}{u_i}\right) - (y_i - u_i)\right]$

Therefore, the power-divergence family was used for model checking and evaluation.

i) $PD = \frac{2}{\lambda(\lambda+1)} \sum_{i=1}^{1} \sum_{j=1}^{j} O_{ij} \left\{\left(\frac{O_{ij}}{E_{ij}}\right)^{\lambda} - 1\right\}$

Where by: O= observed data and E = expected data

Note: λ is real valued parameter that is chosen by the user (rate at which seizures reoccurrence)

The cases λ=0 & λ= -1 are defined as the limits λ -> 0 and λ-> -1; respectively

The power of divergence family consists of the statistics evaluated for all choices of λ in the interval -∞< λ<∞.

Research procedure and Ethical considerations

The researcher got permission from the MUST Research Ethics Committee (REC) after certifying the research proposal and granting permission to go to the field. After the researcher getting permission from the REC, the researcher sought approval from Mbarara Regional Referral Hospital Director who approved the research proposal from data collection from the Psychiatric Clinic/ department.

V. DATA ANALYSIS AND PRESENTATION

Results Descriptive and investigative analyses

A sample of 1610 individuals was obtained from patients' records stratified by those that were on medication and those not yet started the treatment. The sample was used to develop a predictive model of seizure recurrence based on Poisson regression stratified by treatment apportionment.

The outcome variable: The number of fits/seizure attacks per follow-up periods ranged from 0 to 30. The average number of fits in each of the follow-up periods ranges from 0.2 to 5.3, and it was substantially smaller than the variance (0.58 to 27.04), which indicated that there exists over-dispersion in the data set. Taking the data set all together, the variance (9.16) was 7.05 times higher than the mean (1.3), which is a clear implication of the existence of over-dispersion.

The distribution of the data was highly positively skewed (skewness=4.02), with a high spike on the left and a long tail on the right. The median age for participants obtained from patients' records was 9 years; Interquartile range [6 – 16].

Values ranged from 0 to 30, but about 94% of the counts were between 0 and 4. Generally, there were about 61.5% zeros (Fig. 1), indicating excess zeros in the data. Thus, appropriate procedures for overdispersion and excess zeros were catered for in the analysis models.

Table 1: Descriptive Statistics for outcome variable (Number of fits/seizures per follow-up)

Follow-up periods	Mean No. of fits	Variance	Min	Max
1	5.3	27.04	0	30
2	1.2	9.09	0	22
3	1.5	9.12	0	20
4	1.2	7.84	0	18
5	1.1	9.92	0	24
6	0.7	3.5	0	14
7	0.6	2.46	0	14
8	0.3	058	0	4
9	0.3	1.22	0	12
10	0.2	0.61	0	6
Overall	1.3	9.16	0	30

Table 2: Frequency distribution of number of fits

Seizure Categories	Frequency (F)	Percent (%)
no seizure	1,086	67.5
1+ seizures	522	32.5
Total	**1,608**	**100**

Findings in table above, majority 1086 (67.5%) had no fits during follow-up while 522 (32.5%) of epileptic patients had at least one seizure during follow-up.

Objective One: Examining patients drug adherence patterns using existing patients' records

Medication adherence was measured using Medication Possession Ratio (MPR). This was got from the patients records which had been taken for the past five years. It was assumed that patients return to the clinic on the appointment date indicates that he / she was adhering to his medication.

Relationships between levels of fits and treatment

Table 3: Cross tabulation for treatment and Category of fits

No. of fits	Not on treatment	On Treatment
no fits	938 (86.37)	148 (13.63)
1or more fits	420 (80.46)	102 (19.54)
Total	1,358 (84.45)	250 (15.55)
	$X^2 = 9.39$ P = 0.002	

Overall, 250(16%) of the patients were on treatment. Of these 102(20%) had experienced one or more seizure attacks and 148(14%) had not experience any seizure attacks.
According to the findings in table 4.3, Pearsons' Chi-square=9.39; P=0.002 indicate that treatment has a significant relationship with the number of fits.

Relationship between the number of fits and medication

Results shows that patients on treatment or medication, the log odds of their seizure attack change on average by 1.7% but not statistically significant. The result indicates that there is a positive association between treatment and epileptic seizure recurrence and therefore treatment or medication is protective (Coef. =0.017).

Table 4 Poisson regression output for the relationship between the number of fits and medication

Parameter	Coef.	95%CI	p-value
Treat	0.017	-0.29 - 0.33	0.916

Objective Two: To develop a model for predicting the likelihood of seizure reoccurrences using existing patients' records

Results in display in the table 4.5 indicate that there is a 14% reduction in the incidence rate of epileptic seizures in the treated group compared with un treated group. According to the confidence interval, the reduction could be as low as 37% or there could be a much as an 18% increase.

Results further show that age was positively associated with the number of fits/seizure attacks. Specifically, when the age of the patient increased by one year, the frequency of seizure attacks on average will be 0.99, holding all other factors (variables) constant. Explicitly, the age of patients is positively associated with number of seizure attacks (IRR=0.99; 95%CI (0.98-1.01); P=0.252). This implies that increasing age reduces seizure attacks by 1%. Furthermore, the results show that the significant visits (IRR=0.79) indicate that, as the follow-up times increased regularly, the number of seizure attacks decreased almost by 21%. The significant duration of fits (IRR=1.083 with P-value <0.001) revealed that increased duration of fits among patients increases the seizure re-occurrence by 8.3%. However, factors such as treat, age and lapse days were not statistically significant with the number of fits experienced by the epileptic patients.
The significant factors were considered as potentially predictive factors and then used for further analysis in the final model.

Table 5: Model 1 Forward stepwise regression (stratified by treatment) investigating the relationship between treatment and number of fits/seizures

Variables	IRR	Std. Err.	[95% Conf. Interval]	P-Value
Treat	0.863	0.138	0.63 - 1.18	0.356
Visits	0.79	0.018	0.75 - 0.83	0.000
Age	0.99	0.008	0.98 – 1.01	0.252
Lapse days	0.999	0.0008	0.99 - 1.001	0.468
Duration of fits	1.083	0.0071	1.07 - 1.097	0.000

Model II: Multivariable level (final model)

Forward stepwise regression was then undertaken to establish the importance of the significant variables in bivariate analysis at p≤0·05) and this resulted in the identification of two predictive factors (follow up visits and duration of fits).

Table 6: Results of forward stepwise Poisson regression model of number of fits in relation to age, visits and duration of fits.

Variables	IRR	Std. Err.	[95% Conf. Interval]	P-Value
Treat	1.15	0.158	0.89 1.52	0.277
Age	0.99	.0078	0.976 1.006	0.246
Visits	0.79	0.015	0.76 -0 .82	0.000

Duration of fits	1.08	0.0056	1.072 - 1.094	0.000

The results indicate that there is a 21% reduction in the incidence rate of epileptic seizures as visits (follow up periods) increase compared with patients who had no visits and is statistically significant (P<0.001). According to the confidence interval, the reduction could be as low as 24% or there could be a much as an 18% increase (IRR=0.79; 95%CI [0.76-0.82]; p<0.001).

The results further indicate that duration of fits among the patients increases the rate of epileptic seizures by 8% (IRR=1.08; 95%CI [1.07-0.1.09]; p<0.001) and according to confidence interval an increase could be as much as 7% or there could be a much as a 9% increase.

The study results show that at Multivariate level, treat and age were not statistically significant (P>0.05), thus not considered as predictive factors for the recurrence of fits. Results indicate that the incidence ratio of the occurrence of seizures increase at only 15% and reduced at 1% respectively.

Basing on statistically significant predictive factors at the final model, Therefore, the developed predictive model is as follows

$\log(\lambda) = \alpha_j + \beta_1 *$follow up period/visits $+ \beta_2 *$duration of fits

λ is the rate at which the seizure occurs.

α_j is the constant or the log rate at which the seizure occurs when there are none follow up visits and none duration of fits

The regression coefficients (the betas ie β_1 & β_2) are estimated as those values that optimize the ability of the model to predict the outcomes in the epileptic patient cohort. This is called "fitting the rate model," and was achieved using Poisson regression.

Prediction model

nooffits	Coef.	Std. Err.	P>|z|	P-Value	[95% Conf.	Interval]
visits	-.2327201	.019427	-11.98	0.000	-.2707964	-.1946438
durationoffits	.0808031	.0051713	15.63	0.000	.0706676	.0909387
_cons	.7596665	.1043896	7.28	0.000	.5550666	.9642665

(Standard errors scaled using square root of Pearson X2-based dispersion)

To predict the rate of seizure, the fitted risk model was used to calculate a rate score for each patient. For example, using the estimated regression coefficients for the prediction model, that is:

- $\beta_1 = -0.23$
- $\beta_2 = 0.081$
- Intercept = 0.76

Therefore; the prediction model would be as follows;

$\log_e(\lambda) = \alpha + \beta_1 *$ visits $+ \beta_2 *$durationoffits

$\log_e(\lambda) = 0.76 - 0.23 *$follow up period/visits $+ 0.081 *$duration of fits

Assuming, the rate at which the seizure occurs for an epileptic patient with two follow up visits and spends 8 minutes (duration of fits) during the attack, would then be calculated as:

$\log_e(\lambda) = 0.76 - 0.23 * 2 + 0.081 * 8 = 0.948$

⇨ $(\lambda) = \exp(0.948) = 2.580$

Therefore, the predicted rate at which the seizure reoccurrences for this epileptic patient would be 2.6 times.

A web-based application which can be used to do this prediction was developed. Database was designed using phpMyAdmin which was used to capture the constants and stored them. Visual studio is the text editor with good languages like Hypertext Markup language and Cascading style sheet which were used for graphic user interface design (***appendix 3)*** and Hypertext Preprocessor (php) for back-end design.

Figure 1 shows a sample code for the model designed showing how the researcher calculated the likelihood of seizure reoccurrences depending on the patients' medication adherence (clinical visits) and the durations of seizures which were used to make the predictions.

```
17      <title><?php echo APPNAME;?></title>
18  </head>
19  <body>
20      <div class="container">
21          <div style="margin-top:50px" class="mainbox col-md-6 col-md-offset-3 col-sm-8 col-sm-offset-2">
22              <?php
23                  if (isset($_POST["Predict"])){
24                      $Visit = $_POST["Visit"];
25                      $Fit   = $_POST["Fit"];
26                      $A1 = $Rows["Const"]+($Rows["Visit"]*$Visit)+($Rows["Duration"]*$Fit);
27                      $A2 = pow($Rows["NLog"],$A1);
28                  }
29              ?>
30              <div id="printableArea">
31                  <div class="panel panel-<?php echo Color();?>">
32                      <div class="panel-heading">
33                          <div class="panel-title text-center"><b><?php echo $Msg;?></b></div>
34                      </div>
35                      <div class="panel-body">
36                          <form class="form-horizontal" method="POST" action="">
37                              <div class="form-group">
38                                  <label for="Visit" class="col-md-4 control-label">No. of Visits:</label>
39                                  <div class="col-md-8">
40                                      <input type="number" class="form-control" id="Visit" name="Visit" value="<?php if(isset
41                                  </div>
42                              </div>
43                              <div class="form-group">
44                                  <label for="Fit" class="col-md-4 control-label">Duration of Fits: <br><small>(In minutes)</
45                                  <div class="col-md-8">
46                                      <input type="number" class="form-control" id="Fit" name="Fit" value="<?php if(isset($_P
47                                  </div>
48                              </div>
```

Figure 4.2: Seizure reoccurrences prediction model

Algorithm steps

Step 1: Start

Step 2: Enter number of visits

Step 3: Enter patient's duration of fits

Step 4: Compute the counts $\log_e(\lambda)$

$\log_e(\lambda) = \alpha + \beta_1 * X + \beta_2 * Y$

Step 5: Compute the log λ for the number of visits and duration of fits

$\log_e(\lambda) = \alpha + \beta_1 *$ visits $+ \beta_2 *$durationoffits

$$\lambda = e^{(\alpha + \beta 1 * \text{visits} + \beta 2 * \text{durationoffits})}$$

Step 6: If (λ < 1 print Recovery with Green Background, λ > 1<=5 print Moderate with Orange background, λ < 5 print High Risk with Red background)

Step 7: Repeat step 1 to step 6 for each patient

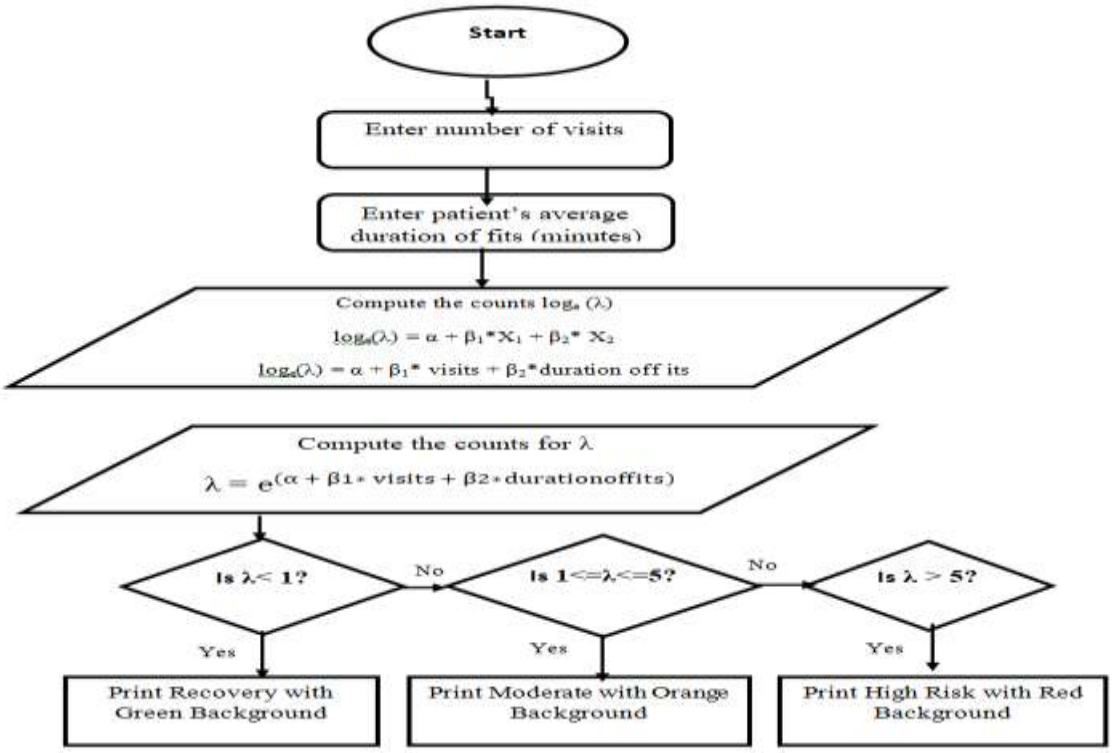
Step 8: Print results

The ordinal scales (basic unit of measurement of epilepsy is the frequency number of seizures) will be adopted to measure the severity of the seizures by scaling the number of seizures per month as; <1 recovery, 1 <= 5 as moderate which will give warning to the clinician or caretakers and > 5 will be acute or high risk which means immediate attention

```php
<?php
function Color(){
    global $λ2;
    global $Msg;
    if (isset($λ2) && round($λ2, 2) < 1) {
        echo "success";
        $Msg = "Alert level: Recovery";
    } elseif (isset($λ2) && round($λ2, 2) >= 1 && round($λ2, 2) <= 5) {
        echo "warning";
        $Msg = "Alert level: Moderate";
    }
    /**elseif (isset($λ2) && round($λ2, 2) > 3 && round($λ2, 2) <= 5) {
        echo "warning";
        $Msg = "Alert level: Warning/Alert";
    }
    **/ elseif (isset($λ2) && round($λ2, 2) > 5) {
        echo "danger";
        $Msg = "Alert level: High Risk";
    } else {
        echo "default";
        $Msg = APPNAME;

    }
}
?>
```

Figure showing Seizure count alert code



Prediction of the likelihood of seizure reoccurrences using the developed application.

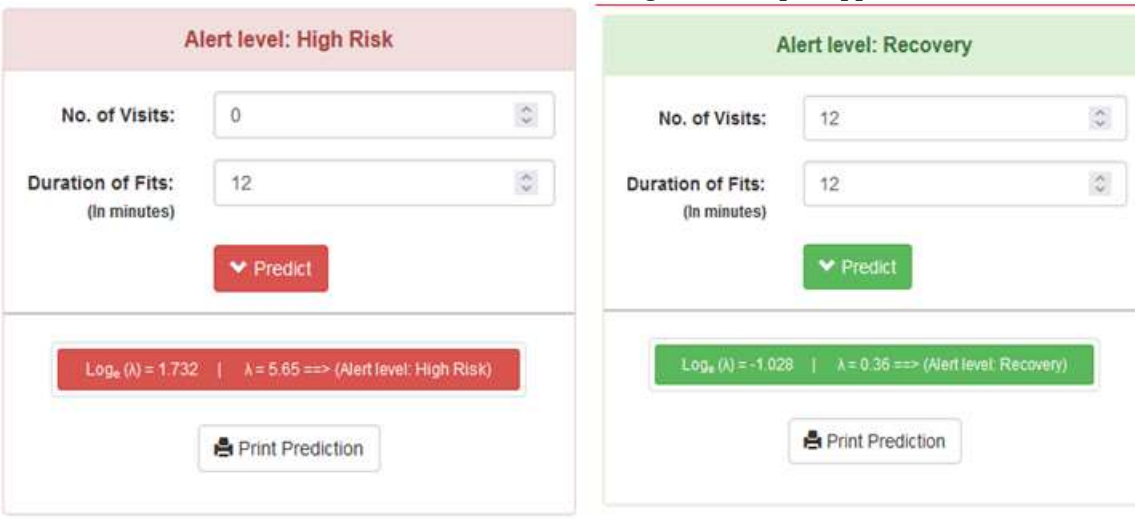


Figure 4. Second Prediction showing medication non-adherence
Figure 4.3: First Prediction showing medication adherence

Figures 4 and 5 above are the outputs of the developed application which can be used to predict the likelihood of seizure re-occurrence among epileptic patients. Fig 4 shows a patient with seizures taking an average of 12 minutes to come back to his/her normal senses and does not adhere to his/her medication which show that he is at a high risk of death.

Fig 5 indicates that if a patient receives seizures with an average of 12 minutes and receives medication for atleast 12 times, he/she will be less likely to get any attack indicating recovery.

Objective Three: To test and evaluate the accuracy of the model

The predictive model was tested and evaluated basing on test statistics for goodness of fit of seizure attacks using the Power-Divergence and chi-square tests and the results were as shown in table 4.5 below.

Table 7: Results of Goodness of Fit (GOF) tests for the Poisson model

Goodness-of-fit	Coef.	P-Value
Pearson's X^2	15768.36	0.0000
Log likelihood ratio	5546.98	0.0000
Cressie-Read (2/3)	10148.04	0.0000

The p-values of the tests based on Pearson's X^2 (P<0.0001), the Cressie–Read statistic(P<0.0001), and the likelihood-ratio statistic (P<0.0001) suggest that the null hypothesis of the data not fitting the model is rejected. Hence the results indicate that the data in the sample, best fits the model.

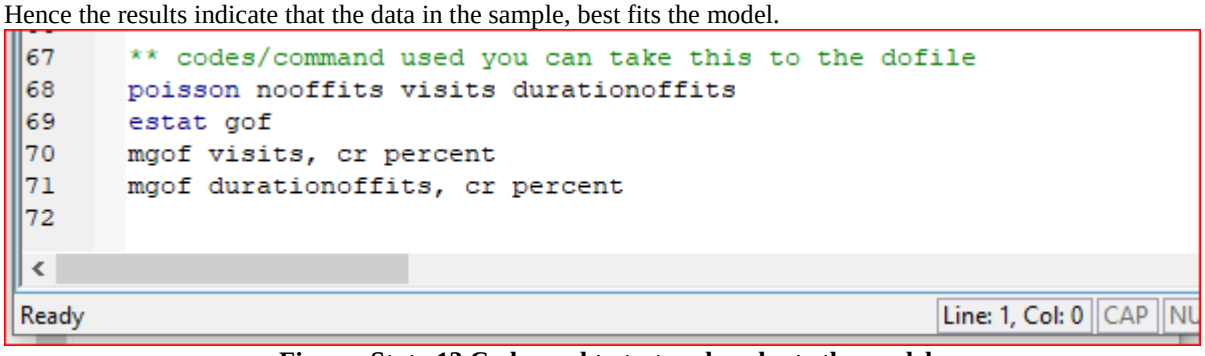


Figure: Stata 13 Code used to test and evaluate the model

VI. DISCUSSION, CONCLUSION AND RECOMMENDANTION

Discussion

The results of the study are in accordance with the objectives and findings: age showed to be associated with a recurrence of seizure, although in the multivariable model the level of statistical significance was not reached (P = 0.247). Age also plays an important role in the susceptibility of epilepsy seizures; the rate of recurrence of seizure declines with growing older but not statistically significant.

In general, the model indicates that incident rate ratio of seizure recurrence increases with duration of fits a patient encounter and reduces with the number of follow up visits/follow up periods made. The other predictor of follow up visits/follow up periods. The researcher considered the first ten months of patients' visits. An increase in follow up visits, decreases the incident rate ratio of epileptic seizures. The result is consistent with some literature reviewed by Johnbull, (2011). Furthermore, it is well established that patients with suboptimal adherence levels are more likely to have seizures that are associated with increased number of hospital admissions and healthcare costs (Jones & Butler, 2012).

The findings indicate that the duration of the epilepsy seizures last increases the incidence rate ratio of epilepsy seizure relapse. Most seizures last from 30 seconds to two minutes. A seizure that lasts longer than five minutes is a medical emergency.

Conclusion

The study established that a reduction in follow up visits increases the incidence rate ratio for epilepsy seizures. Meaning that longer follow-up gives the treating physician more time to adjust the drug(s) and formulate a plan that is appropriate for patients with difficult to treat seizures. Poorer drug adherence might result in more seizures; this should be highlighted for patients in every single visit. The study also revealed that the duration of the epilepsy fits last increases the incidence rate ratio of epilepsy seizure relapse.

Recommendations

The study findings of this study have implications for public health. Basing on significant results (follow up visits and duration of fits), the following recommendations were made:

Patients should do be advised to have frequent visits to the hospital for reviews, treatment, drug refills, and counselling.

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Corresponding author: Oyesigye Owen
[1](Faculty of Agriculture Environmental Sciences and Technology, Bishop Stuart University, Mbarara, Uganda)