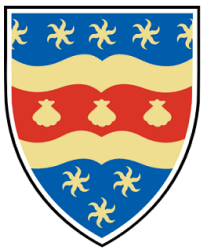

UNIVERSITY OF PLYMOUTH

Analysing Patient-Generated Health Data to Understand Behaviours and Characteristics of Epilepsy Patients

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Thesis submitted to University of Plymouth in partial fulfilment to the requirement for the degree of

MSc Data Science and Business Analytics

School of Computing, Electronics and Mathematics

Faculty of Science and Engineering

September 2021

Abstract

This project aims to analyse patient-generated health data from an epilepsy monitoring application named EpSMON. Using a variety of data analytic techniques, such as logistic regression, this project helps gain insight into epilepsy patients and understand their behaviours and characteristics, particularly women of childbearing age and SUDEP (Sudden Unexpected Death in Epileptic Person) awareness.

Acknowledgements

I would like to thank my project supervisor, Professor Shang-Ming Zhou for his incredible supports throughout the project. Regular meetings as well as his great advice have helped keep the project on track with constant feedback to help me make improvements where there could be. A special thanks goes to Mr Peter Hannon who helped collect data and clarify issues in data fields. I would also like to thank my family and friends for the continued supports they have given to me throughout this study.

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Chapter 1: Introduction and Literature Review

1.1 Introduction

Epilepsy is one of the most common and disabling neurologic conditions that affect millions of people across the world (Vitturi BK et al., 2019), it is caused by excessive, hypersynchronous discharge of neurons in the brain (Stafstrom and Carmant, 2015). Epilepsy can lead to unprovoked seizures that can have a chance of seriously injuring or killing individuals. Epilepsy triggers can vary widely from person to person, but some of the most common triggers include flashing lights, stress, alcohol, and lack of sleep (Epilepsy Action, 2020). In general, the incidence of epilepsy is estimated to be approximately 50 new cases per year per 100,000 population (Hauser and Hersdorffer). One of the biggest risks that can be attributed to epilepsy is Sudden Unexpected Death in Epilepsy (SUDEP), which is when a patient with epilepsy suddenly and unexpectedly dies, who otherwise is healthy. Around 1 in 1000 people with epilepsy die from SUDEP. Around 40% of women with epilepsy of childbearing age account for 0.3-0.7% of recorded pregnancies (Abe K et al, 2014; Vitturi BK et al., 2019). Currently, the best way to prevent SUDEP is to control the individual's seizures (SUDEP, 2021). Similarly, epilepsy medicine can cause a risk in pregnancies in women with epilepsy as these medicines can increase the chance of the baby being born with physical abnormality and harm the baby. Growth figures evidence suggests that if 100 women take valproate medicines during their pregnancy about 10 of the babies will be born with physical birth abnormalities (MHRE, 2021) and is one of the most common neurological disorders to require medical treatment during pregnancy (Vitturi BK et al., 2019; Bollig KJ er al., 2018; Voinescu PE et al, 2017).

1.2 Existing studies

Research efforts have been done to help control and manage risk and communication of SUDEP happening to someone with epilepsy (Shankar, R., Ashby, S., McLean, B. and Newman, C., 2019). For example, a checklist was developed using quality improvement and research methodologies as a tool to aid discussion and evaluation of risk factors for people with epilepsy and how to mitigate risks for them. After 7 years of use of the checklist in Cornwall, feedback from the country shows that 99% of people with epilepsy approve of it (Shankar, R., Ashby, S., McLean, B. and Newman, C., 2019 and that SUDEP death rates are more than halved between 2012 and 2018 (Shankar, R., Ashby, S., McLean, B. and Newman, C., 2019). In 2015, the checklist launched nationally after some of the risk factors were reviewed after its trial run in Cornwall, with an average of 12 new users per month (Shankar, R., Ashby, S., McLean, B. and Newman, C., 2019). Furthermore, a retrospective study was carried out and shows that 25% at most risk having a significant reduction and was adopted by 328 clinicians in the first 18 months (Shankar, R., Ashby, S., McLean, B. and Newman, C., 2019). The Checklist was supported by cycles of design, feedback, and redesign. However, one of the downsides of this study is that the checklist relies on evidence, but in some areas or still, in development or do not have much data surrounding them, moreover, the checklist can produce false positives, showing that something is a risk when it was not. A further issue was that people with epilepsy might be using an older, outdated version of the Checklist, with different risk factors and could put people at risk even more so.

Another research study was carried out to find treatments to prevent SUDEP, it states that the correct antiepileptic treatment regimen around 70% of people with epilepsy can become free of seizures, but around 1/3 of people will continue to have seizures despite taking multiple antiepileptic drugs (Maguire, Jackson, Marson and Nevitt, 2021). Using an electronic database, some studies revealed characteristics of patients with SUDEP comparing with others not related to SUDEP, including changes in anxiety, depression, and quality of life; and several hospital attendances (Maguire, Jackson, Marson and Nevitt, 2021. Among these studies, three of them had a supervisor sharing a room with a patient with epilepsy and using special precaution such as regular checking throughout the night and a listening device to prevent SUDEP, then 2/3 of patients were found alive due to these measures (Maguire, Jackson, Marson and Nevitt, 2020). But the studies also did not report on changes in anxiety, depression, quality of life and number of hospital attendances. Another study examined the effect of giving information to people with epilepsy about SUDEP and whether this could improve the taking of antiepileptic medication and the impact on mood and anxiety. The study followed patients up for six months after being given the information (or not) and did not demonstrate any effect on the taking of medication or mood and anxiety. The effect of giving information and its impact on the risk of SUDEP remains unknown (Maguire, Jackson, Marson, and Nevitt, 2021). The evidence showed that the efficiency of supervision at night prevents SUDEP is very low and further research is needed to identify other treatments.

The research was also carried out to create a seizure-detection system that can be used in long-term in-home situations for early intervention and prevention of seizure-related side effects including SUDEP (Van de Vel et al., 2013). An EEG (electroencephalography) device was attached to the patient's scalp and was used to monitor the body signals to watch for SUDEP. The use of EGG devices allows for early detection of SUDEP and have been identified as one of the key measures for preventing SUDEP (Van de Vel et al., 2013). But the EEG analysis is very labour intensive and is yet to be automated so constant supervision is required when doing it and the availability of such devices are very scarce.

Similar research was carried out to create a digital version of the SUDEP and seizure safety Checklist (Newman, Ashby, McLean, and Shankar, 2019). The researchers aimed to create a digital application to allows people with epilepsy to take digital self-assessments to check their risk of SUDEP and other epileptic-related threats using accessible smartphones. The motive for the development of such was the advance of digital technology in recent years and how accessible smartphones are. This app, named EpSMON (epilepsy self-monitor) has been launched successfully (EpSMON: Epilepsy Self-Monitoring | SUDEP Action, 2021). The development of the EpSMON was done iteratively with support from steering groups and consultants. It has several features, such as 3-month reminders to take a risk assessment and recommendations to see a general practitioner (GP) (Newman, Ashby, McLean and Shankar, 2019). The clinical engagement of the EpSMON was much more positive with multiple awards received for its innovation in the sector Newman, Ashby, McLean, and Shankar, 2019).

The risk of pregnancy in epilepsy can pose a risk in maternal and foetal developments, these risks include spontaneous miscarriage, preterm labour, postpartum haemorrhage (Ozdemir O et al., 2015; Gerard EE, et al., 2016). As well as foetal growth restrictions, development delays and major congenital malformation are often formed within the first 8-10 weeks of pregnancy (Ozdemir O et al., 2015; Gerard EE, et al., 2016; Allotey J et al., 2019). It has also been reported that the risk of mortality in pregnant women with epilepsy can be up to ten times higher than the general population without epilepsy (Abe K et al., 2014; Sibai BM., 2005; Adab N, 2004)

SUDEP has been attributed as the biggest cause of death in maternal women with epilepsy (Kapoor D et al, 2014) with many of their deaths being directly correlating to SUDEP. SUDEP deaths are often related to poor seizure control such as using the wrong medication or not using medication at all that could have controlled or prevented SUDEP. Some women with epilepsy may stop taking their anti-epilepsy drugs (AED's) due to fear it may influence the baby's health (Voinescu PE, 2017; Tomson T, 2019). Allotey J et al, 2019 discovering that up to four in ten women with epilepsy would stop taking their anti-epilepsy drugs during pre-conception or pregnancy due to these concerns. Another reason why SUDEP is such a risk with maternal women is due to how often pregnancies are unplanned (Gerard EE et al., 2016; Tomson T et al., 2019), which can further increase risks as pregnancy can lead to physiologic changes, including hormonal variations, alteration in drug absorption, metabolism and distribution can have an adverse effect on the frequency of seizures (Voinescu PE et al., 2017). The teratogenic risks of anti-epilepsy drugs on pregnant women with epilepsy are unknown to general health practitioners, which could lead to additional risk factors (Voinescu PE et al., 2017; Gerard EE, et al., 2016). Due to all these factors, both women and the healthcare profession are unable to make a truly informed decision about their care and treatment (Voinescu PE et al., 2017).

A report was made by the Maternal and Infant Clinical Outcome Review Program claiming that medication was not properly optimised for women before, during and after pregnancy within most maternal deaths reviewed within the UK (Knight M et al., 2020). Similarly, the high risk of women with epilepsy are not often recognised leading to a lack of support by healthcare workers and can be seen as a factor in epilepsy-related deaths in maternal women (Allotey J et al., 2019), Gerard EE et al., states that a small number of women with epilepsy report having conversations about contraception and pregnancy with their health care providers, additionally a third of women with epilepsy report it never being discussed with them at all (Vazquez B et al., 2007). Research has been carried out that shows that maternal deaths can be minimized by early prepartum consoling, specialist input and support, but these services are not widely offered (Allotey J at al., 2019). These services should start when anti-epilepsy drugs are prescribed to a woman of childbearing to help fully maximise its effectiveness (Gerard EE et al., 2016; Tomson T et al., 2019). Currently, the extent of discussion regarding anti-epilepsy drugs and women of childbearing age in the UK is unknown.

Indeed, digital technologies, such as the EpSMON app, provide an innovative tool to allow epilepsy patients to generate their risk assessment data and record engagements with the GP about their health procedure, diagnosis, and medication events, using accessible smartphones. However, so far, there is a lack of data analysis studies using the EpSMON data to facilitate epilepsy health research. This project is to use a data-driven approach to analyse EpSMON data and help people susceptible to SUDEP and other epileptic problems prepare and lower the chances of it happening as well as the threat of SUDEP and other epilepsy-related issues to women of childbearing age.

1.3 : Aims and objectives including Problem Statement

This project aims to use real-world health data generated by patients themselves via the app EpSMON to investigate and understand the behaviours and characteristics of epilepsy patients. To do these 8 research problems have been identified.

- **Problem 1:** What are the characteristics of childbearing women (16-60) with epilepsy patients who use the EpSMON app?
- **Problem 2:** How do these characteristics vary, if at all, between those who use the EpSMON app regularly and those who do not?
- **Problem 3:** How many EpSMON users report being aware of the increased risks of sudden death?
- **Problem 4:** What relationship, if any, is there between medication changes and risk assessment scores provided by the EpSMON app amongst childbearing women (16-60)?
- **Problem 5:** What relationship, if any, is there between EpSMON risk assessment score, and health-seeking behaviors (such as visiting GP) amongst childbearing women (16-60)?
- **Problem 6:** What was the level of awareness of pregnancy matters at baseline in the women 16 -60
- **Problem 7:** Specifically look at the number of drugs - Antiseizure medication and over all regular medication - Particularly Valproate use ...including changes to its use over time.
- **Problem 8:** What are mental health issues in this group of childbearing women (16-60)?

Chapter 2: Data Description from EpSMON App

The patient data used in this research was taken from the EpSMON App which is a tool that allows users to self-monitor their epilepsy risk in-between visits to the doctor. The app asks you to answer a short assessment which will then produce a risk assessment summarising risks to be aware of and changes from the last risk assessment the user took. Once the assessment is done, the app will give the user a risk score between the ranges of 1 and 20, with 1 being the least at risk and 20 being the most at risk. The data contains 6556 assessments and 4380 different unique users.

The data was received as a .DB file and was recreated in a SQL environment, the data was then exported into the appropriate CSV files where it was then read into R studio and analysed. We will describe baseline characteristics for exposures and outcomes of interest using means, medians, proportions, ORs and rate ratios with appropriate measures of dispersion. We will report on the prevalence of missing data by variable and use two-tailed hypothesis tests with a 5% significance level. Analytical techniques will include descriptive statistics, univariate and multivariate generalised linear mixed models, survival analyses and the use of self-controlled case series for temporary risk factors. Relationships between variables will be clarified before specific analyses.

2.1 EpSMON Data Structure

The assessment table stores the results of the assessments, including the risk score and the recommendations.

Assessment Table	
Column Name	**Description**
Id	Unique assessment ID
UUID	DEFUNCT User ID
User_id	Unique User ID
date_performed	Data assessment was performed (dd/mm/yyyy)
recommendation	Apps recommendation to the user from assessment answers
Medication_categories	Use categories of medication the user is taking
Risk_score	The users risk score
Created_at	The date the assessment was created (dd/mm/yyyy)
Updated_at	The date the assessment was last updated (dd/mm/yyyy)

The assessment_answers table stores the answers that users have given to a specific question on the assessment..

Assessment_answers Table	
Column Name	**Description**
id	Unique question assessment ID
Assessment_id	The assessment id of the question answers belong to
Question_id	Shows the question that the answer belongs to
Answer_given	Boolean value answer to the question
Risk_score	Boolean value that increases the risk score depending on the answer given and the question asked
Language	The language the user completed the question in
Created_at	The date the assessment answer was created (dd/mm/yyyy)
Updated_at	The date the assessment answer was last updated (dd/mm/yyyy)

The assessment_meds table stores the medication a patient declares they use in the assessment..

Assessment_meds Table	
Column Name	**Description**
id	Unique assessment medication ID
Assessment_id	The assessment id where the medication prescription if from
med_id	Shows what medication is being used
dosage	The dosage of medication being used
Dosage_index	The index used for the dosage
dosageKnown	If the user knows what their dosage of medication is
Language	The language the user completed the question in
Created_at	The date the assessment meds was created (dd/mm/yyyy)
Updated_at	The date the assessment meds was last updated (dd/mm/yyyy)

The med_category10n table stores the medical category the medication belongs too

Med_category10n Table	
Column Name	**Description**
id	Unique medication category ID
Med_category_id	The unique medication category id, used for identifying the medication category
Language	The language the user completed the medication category the question in
name	Name of medication category (e.g., Epilepsy)
Created_at	The date the med category was created (dd/mm/yyyy)
Updated_at	The date the med category was last updated (dd/mm/yyyy)

The meds10n table stores each individual medication, along with their respective doses and additional information.

Meds10n Table	
Column Name	**Description**
id	Unique medication ID
Medication_id	The unique medication id, used for identifying the medication
Language_code	The language the user completed the medication in
Medication_name	Name of medication (e.g., Carbamazepine)
Medication_quantity_unit	The measurement the medication uses
Further_information	NULL
Dosage	The dosage of the medication
Dosage_options	The options of dosage available
Dosage_options_short	A shortened version of the dosage options only using integers
Created_at	The date the medication was created (dd/mm/yyyy)
Updated_at	The date the medication was last updated (dd/mm/yyyy)

The oauth_user table is where each unique user is stored with its relevant data.

Outhouses Table	
Column Name	**Description**
id	Users' unique identifier
username	Users' Unique identifier used to link to the users' assessments
password	Users' password (anonymised)
email_address	Users email address (anonymised)
First_name	Users first name (anonymised)
Last_name	Users last name (anonymised)
sex	User's sex (1 = male, 2 = female)
Date_of_birth	User's date of birth (DD/MM/YYYY)
Country_code	Two-character code of the country of the user
Age_of_onset_epilepsy	Users age when they got diagnosed or had their first epileptic attack
Observed_having_convulsive_seizures	User has been observed by another person having convulsive seizures
Seizure_type_known	User knows what type of seizures they have
Seizures_focal	User experiences focal seizure types
Seizures_tonic_clonic	User experience tonic clonic seizure types
Seizures_tonic	User experiences tonic seizure types
Seizures_atonic	User experiences atonic seizure types
Seizures_myclonic	User experiences myoclonic seizure types
Seizures_absence	User experiences absence seizure types
Seizures_non_epilepsy	User experiences non epilepsy related seizures
Seizures_other	User has a seizure not listed here
Created_at	The date the medication was created (dd/mm/yyyy)
Updated_at	The date the medication was last updated (dd/mm/yyyy)

The question_category10n table stores the category that a question in the assessment can belong too.

question_category10n Table	
Column Name	**Description**
id	Unique medication question category ID
category_id	The unique category id, used for identifying the question category
Language	The language the user completed the category
name	Name of category (e.g., Epilepsy)
Created_at	The date the med category was created (dd/mm/yyyy)
Updated_at	The date the med category was last updated (dd/mm/yyyy)

The questions10n table stores the question and the possible answers a user can give to it.

questions10n Table	
Column Name	**Description**
id	Unique question ID
Question_id	The unique question id, used for identifying the question
Language_code	The language the user completed the question in
Question	The question that is asked to the user
Further_information	Additional information regarding the question
Possible_answer_a	Users' choice of answers
Possible_answer_b	Users' choice of answers
Created_at	The date the medication was created (dd/mm/yyyy)
Updated_at	The date the medication was last updated (dd/mm/yyyy)

Chapter 3: Characteristics of Childbearing Women with Epilepsy

3.1 Brief introduction

Childbearing women with epilepsy can be the most at risk of people with epilepsy, this goes both for the woman and the unborn child. Pregnant women with epilepsy are at an increased risk of seizures and complications with an increase in seizure frequency seen in 25%-30% of pregnant women with epilepsy (Yerby, 1992) and adverse pregnancy outcomes and malformation such as dysmorphic features and haemorrhagic disorders (Yerby, 1992). Through looking at the EpSMON data we can see if there are any trends or characteristics of childbearing women with epilepsy and see if there are any trends, this chapter will aim to address the following problems;

Problem 1: What are the characteristics of childbearing women (16-60) with epilepsy patients who use the EpSMON app?

Problem 2: How do these characteristics vary, if at all, between those who use the EpSMON app regularly and those who do not?

32 Methodology

This was done by getting the gender and age of each user from their respected tables into one larger data frame. The users were then split into the age groups 16-20, 21-30,31-40,41-50,51- 59, 60+ and the men were filtered out. By doing this we can see the characteristics of childbearing women and the differences between them in different age groups. They were then made into graphs to give a better visualisation of data. To then see if there were and trends between frequent users of the EpSMON app and infrequent users. Frequent users have been identified as users who have used the app more than once a year or more than three times overall, this is because the application recommends that users take is risk assessment once every 3 months.

3.3 Results

Participants have been split up into different age groups to better understand the characteristics of each age groups individual characteristics.

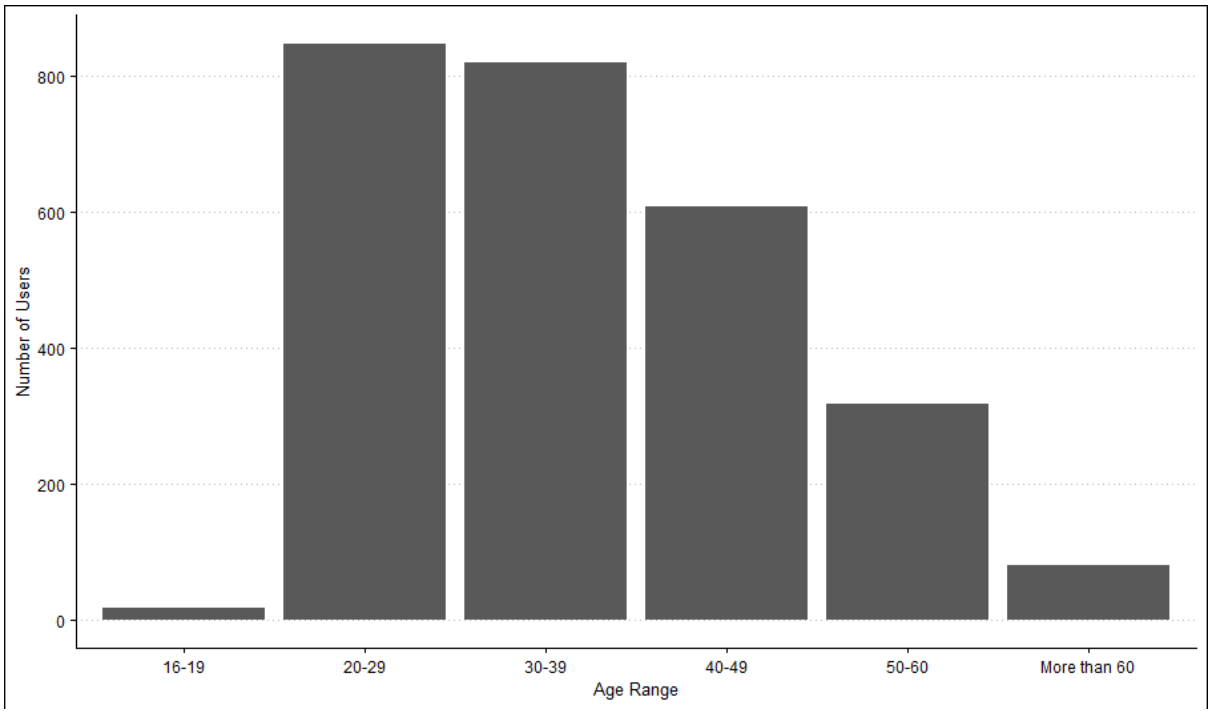


Figure 1: Age Range Of Women Using EpSMON Application

There are not many users between the ages of 16-19 with the most users being 20-29 with the age groups of the participants getting progressively smaller as the age group goes up. The users who use the app the most are between the ages of 20-29.

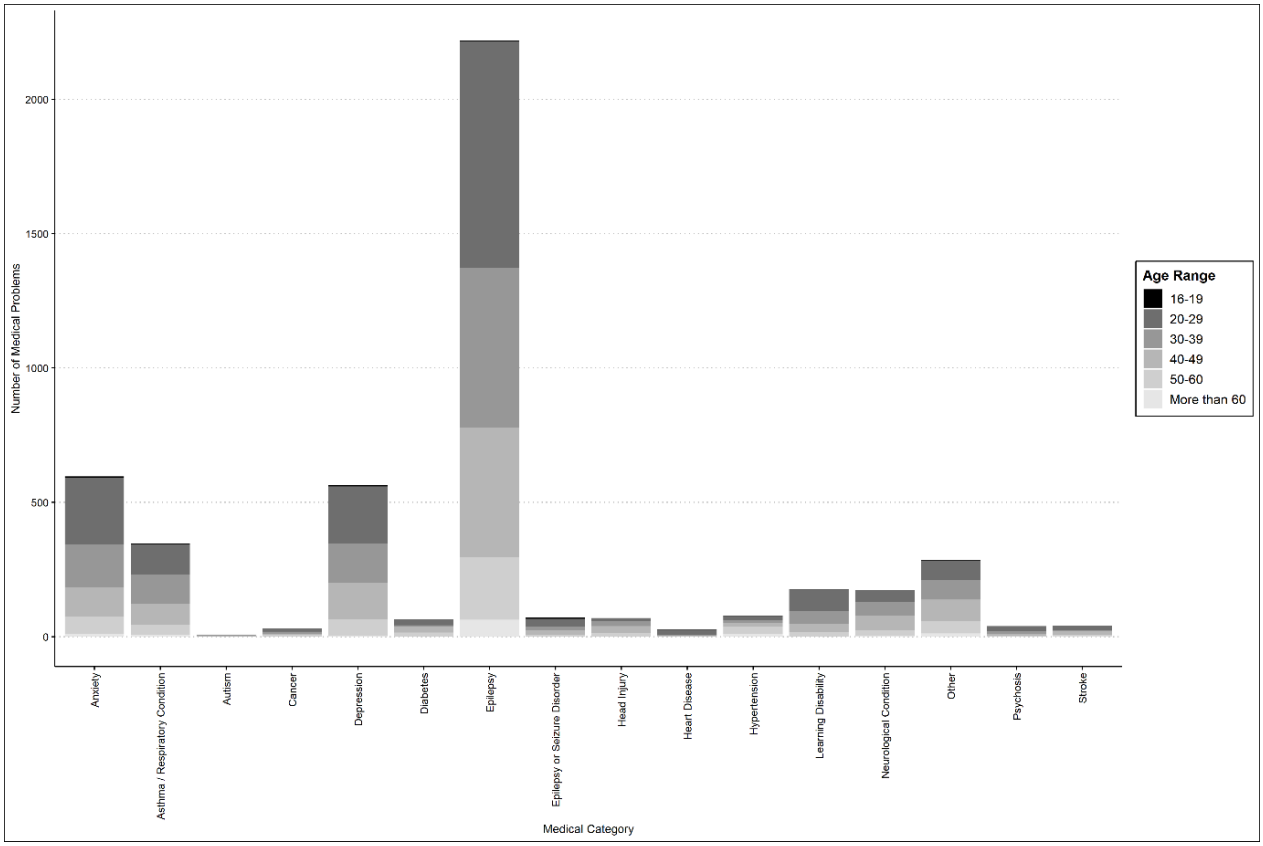


Figure 2: Medical Category of Medication of Women Using the EpSMON Application.

By looking at the medication category of medication participants are prescribed for, epilepsy is the drug most people are prescribed too, with depression and anxiety coming in a close second and third. The age distribution of each medical category is fairly consistent with 20-29 being the most common age group for each medication.

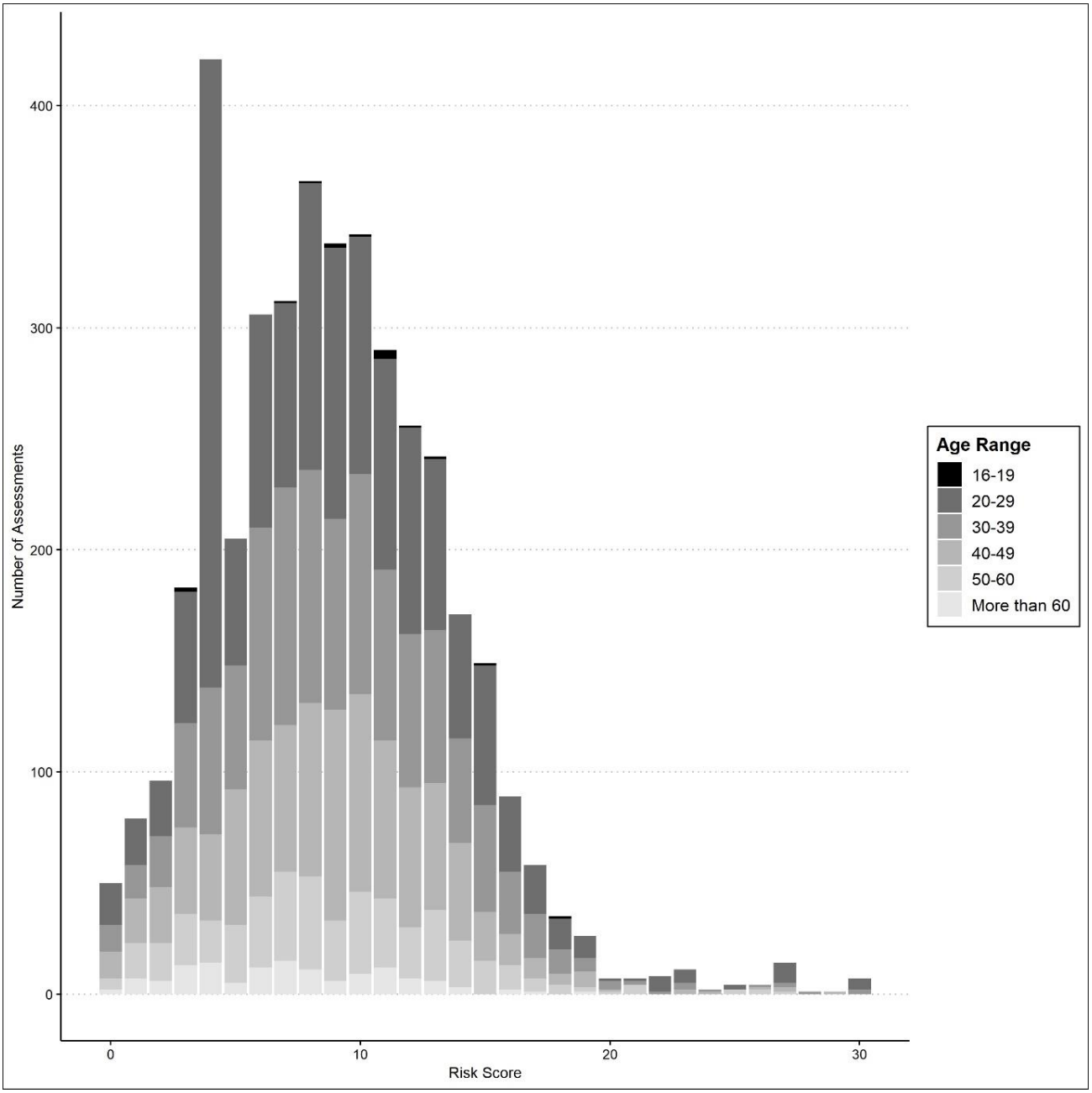
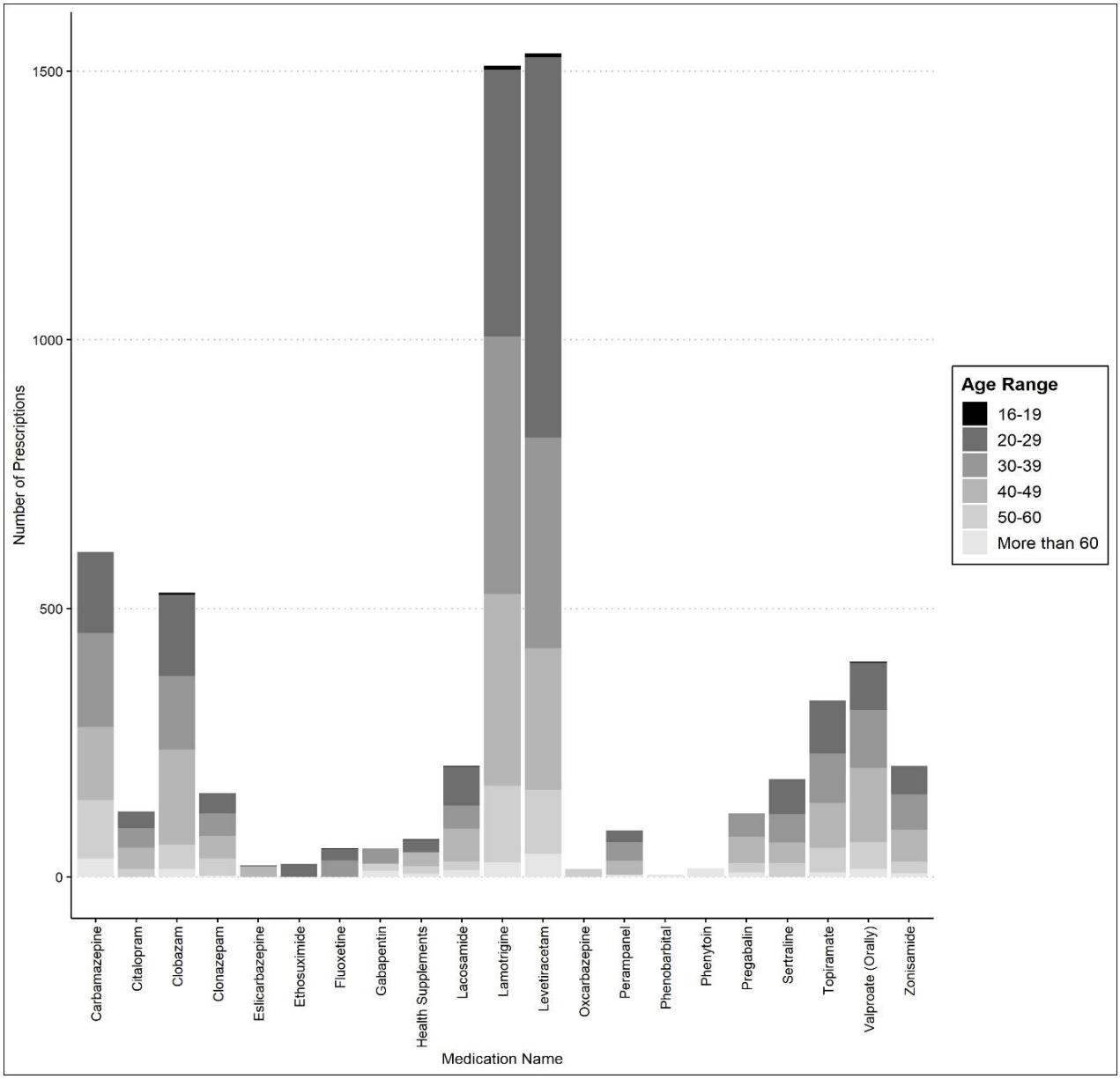


Figure 3: Assessment Risk Scores of Women Using the EpSMON Application

A risk score is a number that is given at the end of an assessment on the EpSMON app, the higher the risk score the more the risk of SUDEP or another epileptic risk. The peak of the distribution is around 9 to 10 with a strong bias towards 5, suggesting that 5 is the most common risk score received from the risk assessments.



The top 15 used medications were used to make a graph of the most used

Figure 4: Medication Prescriptions of Women Using the EpSMON Application

medication. From the graph we can see the most taken medication is Levetiracetam with Lamotrigine coming in a close second, both being used to treat epilepsy. Levetiracetam is an anti-epilepsy medication, this helps stop seizures by slowing down the electrical chemical and signals in the brain to stop and reduce seizures (Levetiracetam: medicine to treat epilepsy, 2021). Similarly, lamotrigine is also used to treat epilepsy (as well as bipolar disorder and depression) and works the same way as lamotrigine, by slowing down the chemical and electrical signals in the brain (Lamotrigine: medicine to treat epilepsy and bipolar disorder, 2021).

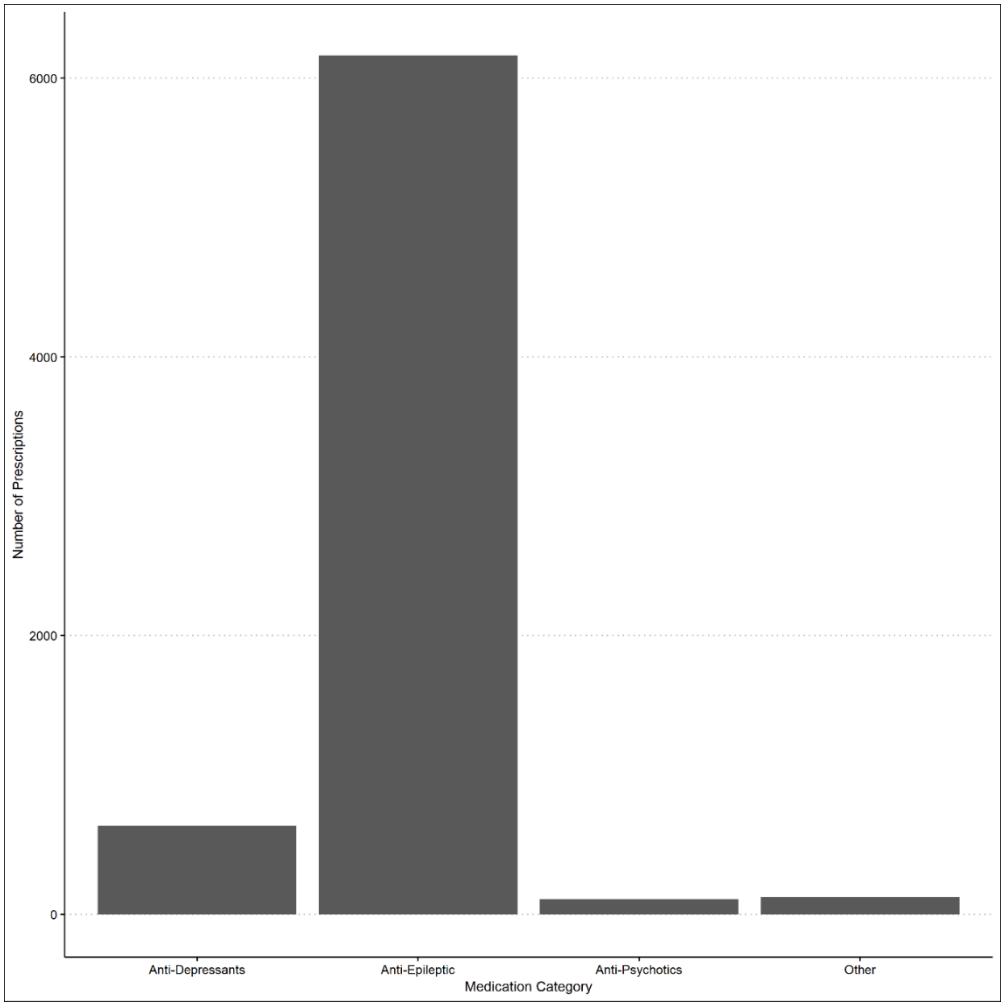


Figure 5: Medication Prescriptions Categories of Women Using the EpSMON Application

Due to a large amount of medication available, the prescriptions were grouped into 4 groups: anti-depressants, anti-epileptic, anti-psychotics and others. The most used medication type by a large margin is anti-epileptic by a significant amount, this would be expected due to the nature of the EpSMON app. The second most prescribed medication are anti-depressants, showing more mental health issues of women with epilepsy.

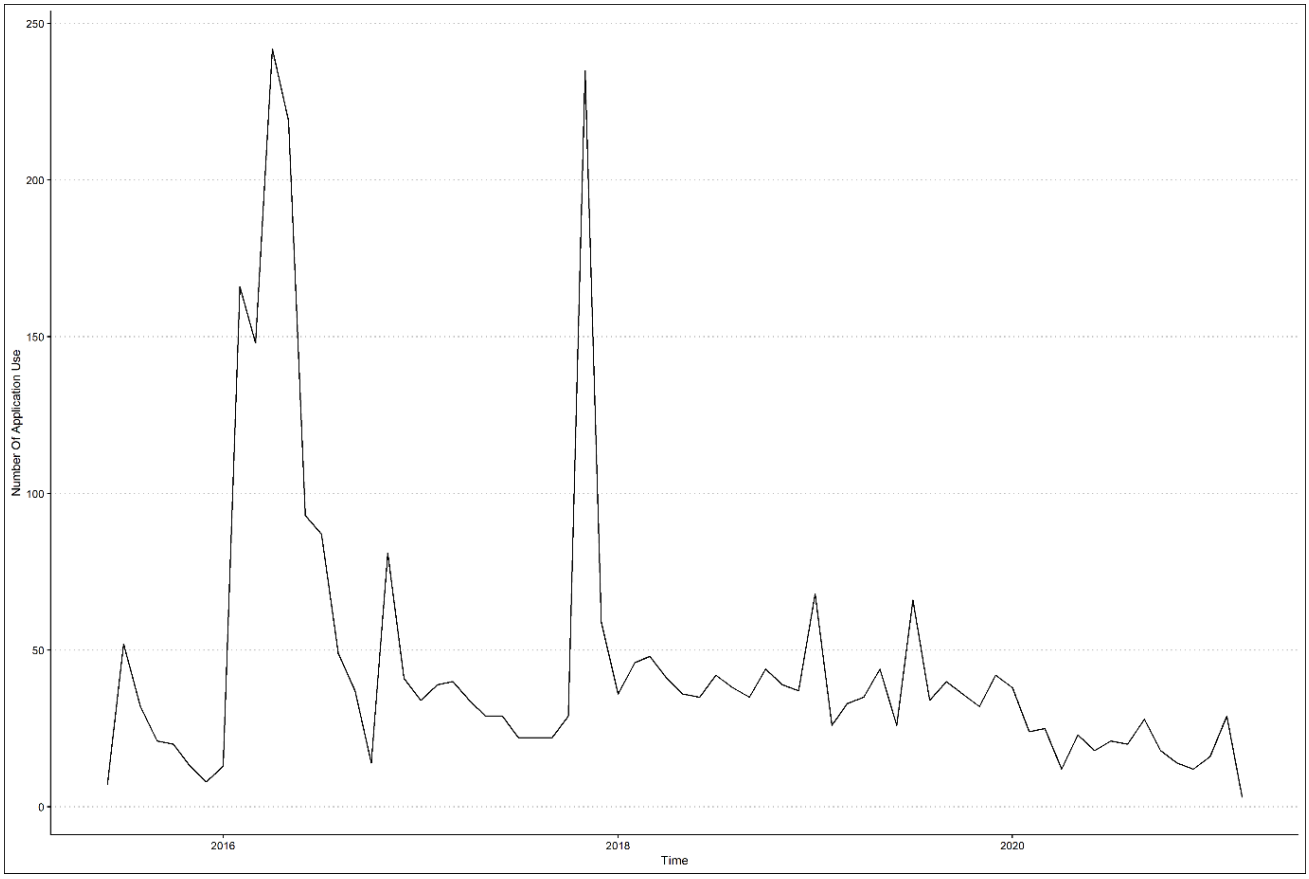


Figure 6: EpSMON Application Usage Over Time

In this graph we can see the application use of EpsMon, there was a huge spike of usage around the release of the application in early 2016 with a sharp decline throughout the year with some resurgence being found after the steep decline. There was a huge boost of use in late 2017 which also saw it drop by almost the same amount in early 2018. The use of the app is very erratic.

Focusing on childbearing women, we can see how the trends differ between frequent childbearing women who use the app and those who do not.

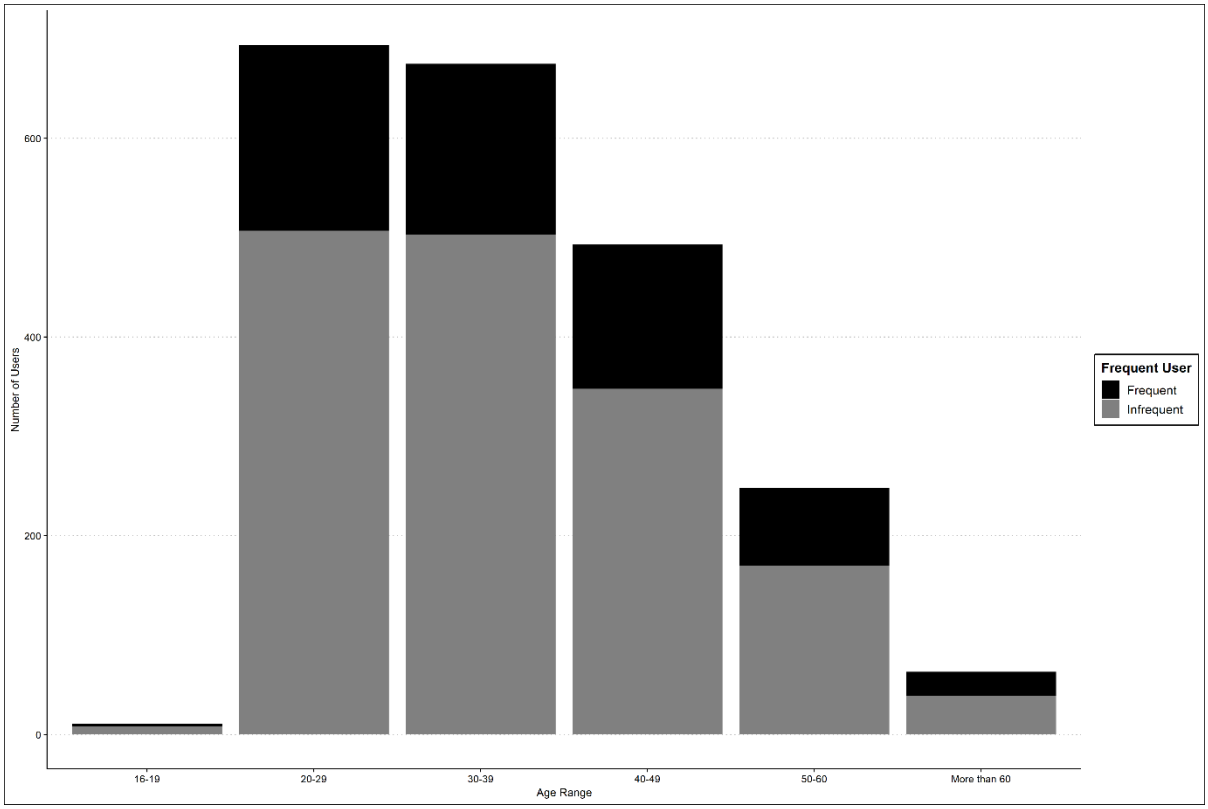


Figure 7: Age Range Of Frequent Female Users of the EpSMON Application

The number of frequent users among the different age ranges are fairly similar across the ranges, with the most being found in 20-29, where the majority of the user's age range lies.

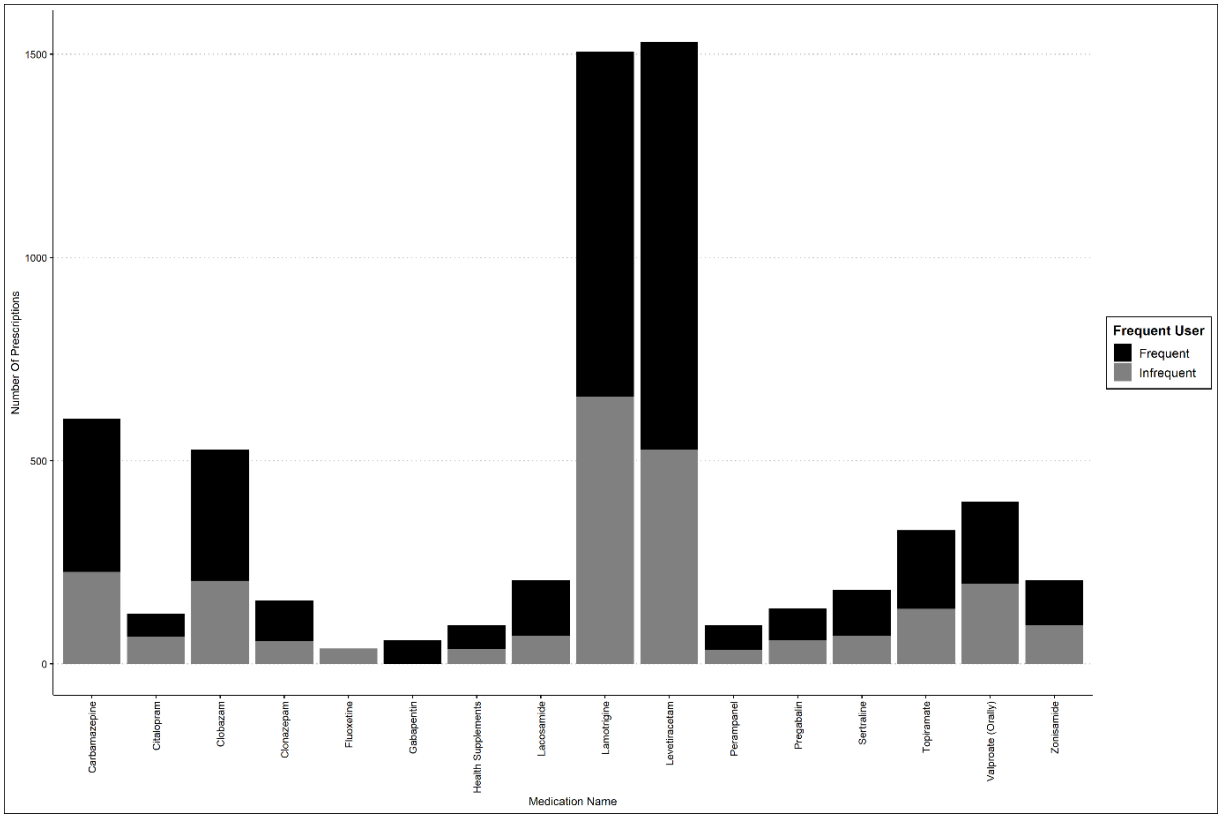


Figure 8: Medication Prescription Of Frequent Female Users of the EpSMON Application

Frequent users are responsible for a large amount of the prescriptions logged on the application, with a large amount of Lamotrigine and Levetireactam being attributed to frequent users. An interesting point of note is that almost all citalopram prescriptions belong to frequent users, citalopram is used to counter depression and anxiety, the use of the app may help them feel more secure. Citalopram is an SSRI (selective serotonin reuptake inhibitor) that can increase the user's mood by release serotonin in the brain (Citalopram: an antidepressant, 2021).

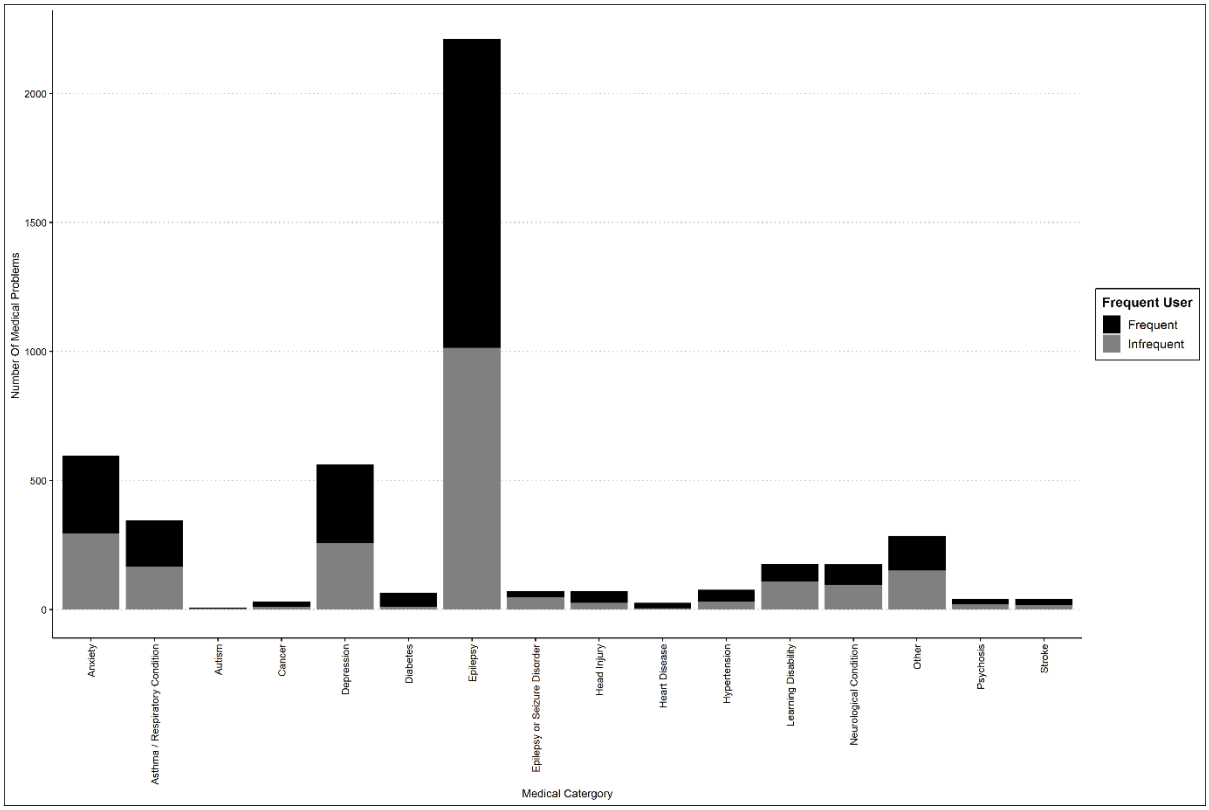


Figure 9: Medication Prescription Category Of Frequent Female Users of the EpSMON Application

The most frequent users of the app take medication for epilepsy, similarly to the previous prescription medical category graph, we can see a large number of frequent users with anxiety and depression.

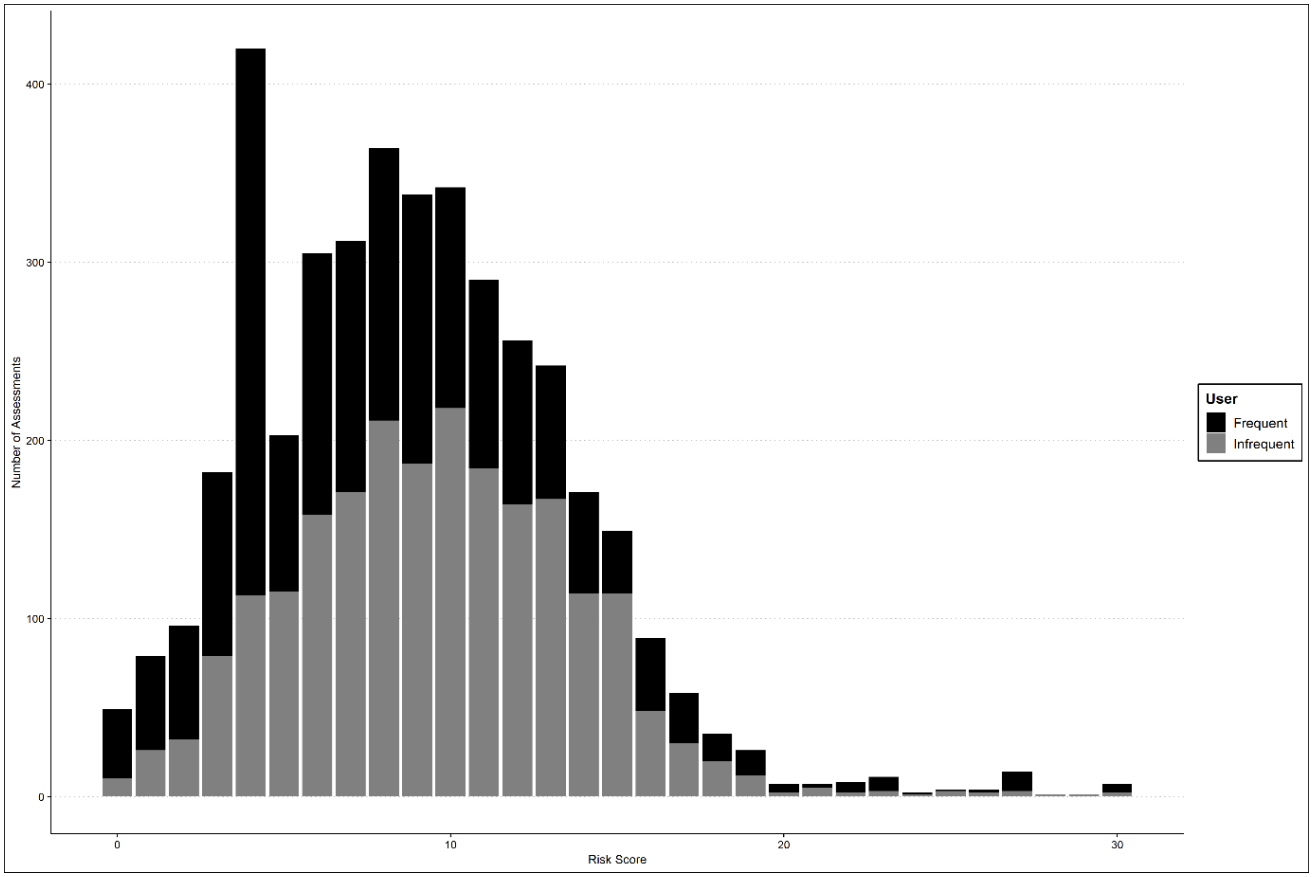


Figure 10:Assessment Risk Score Of Frequent Female Users of the EpSMON Application

With the most common result of the risk score being 5 and the peak of the distribution being around 9 to 10, we can see that an overwhelming majority of it being attributed to frequent users. Overall the lower scores are majority done by frequent users.

Chapter 4: SUDEP Risk and Awareness

4.1 Brief introduction

SUDEP (Sudden Unexpected Death in Epilepsy) is an important concern for those with epilepsy. SUDEP refers to deaths in people with epilepsy that are not caused by injury, drowning or other cases (Devinsky O., 2011). It is suggested that each year there are around 1.16 cases of SUDEP for every 100 people with epilepsy (Thurman DJ et al., 2014). Most SUDEP cases occur during or immediately after a seizure, currently, the exact cause of this is not known and more research into the subject is needed. There are some possible causes for this, one of which being heart rhythm, where a seizure may cause a dangerous heart rhythm or cardiac arrest (Sudden Unexpected Death in Epilepsy (SUDEP), 2021). Another possible cause is the effect a seizure could have on a person's breathing, the seizures can cause pauses in their breathing, if these pauses last too long it can reduce the oxygen in the blood to a life-threatening level. Additionally, to low oxygen levels in the blood, the convulsions from the seizures can cause something to cover or obstruct a person's airway leading to suffocation (Sudden Unexpected Death in Epilepsy (SUDEP), 2021).

One method to reduce the risk of SUDEP is to control and manage seizures, one of the main uses of the EpSMON application is to do just this. By using these applications, people with epilepsy can monitor and track their epilepsy and see how at risk they are. Using the application, we can also find out how are people with epilepsy are of SUDEP and its risks.

This chapter will aim to address the following problems.

Problem 3: How many EpSMON users report being aware of the increased risks of sudden death?

4.2 Methodology

This was done in a similar way to the last aims, using the data from the EpSMON application we can see how many users are aware of SUDEP and its risks. In the risk assessment, question 32 asks "Have you received safety advice and information about SUDEP from your doctor /nurse about epilepsy?". Using this we can find out how much people are aware of SUDEP and if enough awareness is being raised about it by clinicians. Focusing once again on childbearing women, the results were then made into graphs to give a better visualisation of the data.

4.3 Results

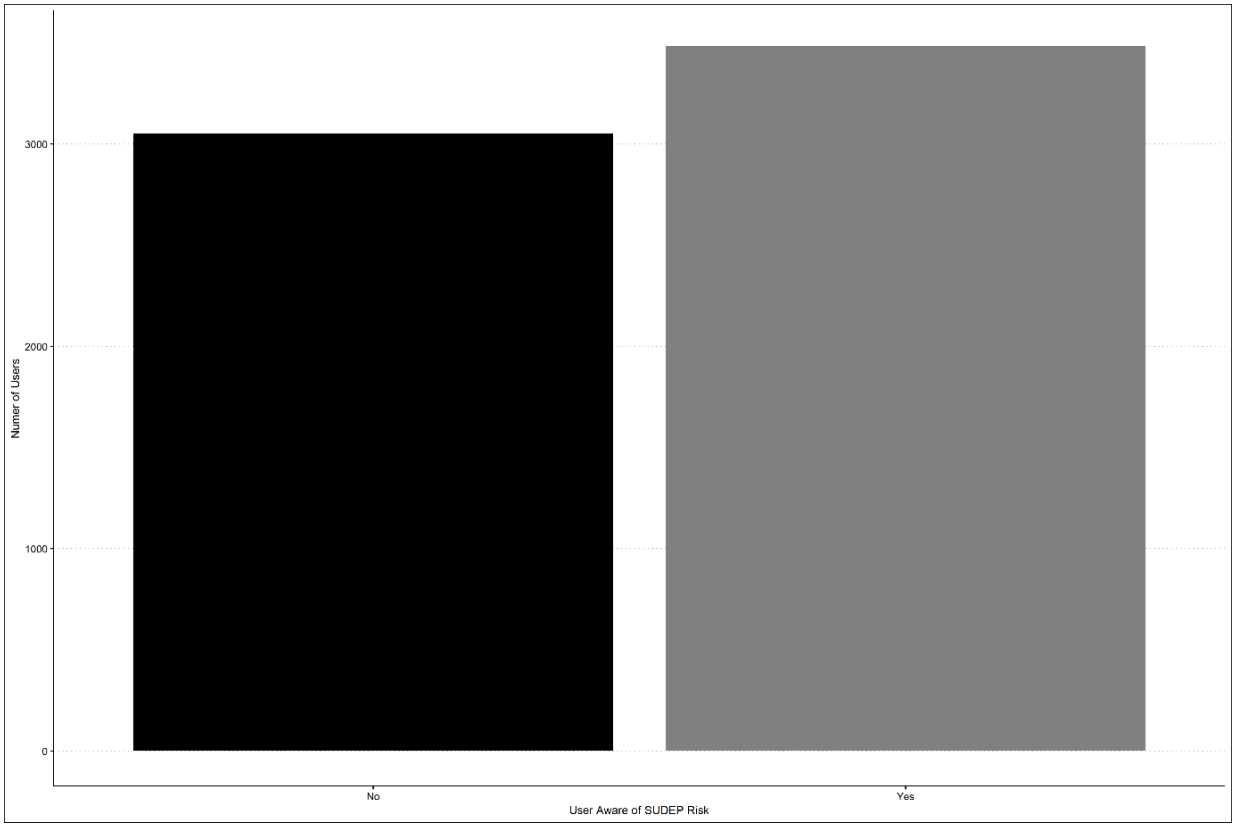


Figure 11: EpSMon Application Users Aware of SUDEP Risk

From this graph, we can see that most users are aware of the risks of SUDEP (Sudden Unexpected Death in Epileptic Person), but an alarming number of users are unaware of the risks. If people with epilepsy are aware of these risks' seizure management practices can be used to reduce the risks of death.

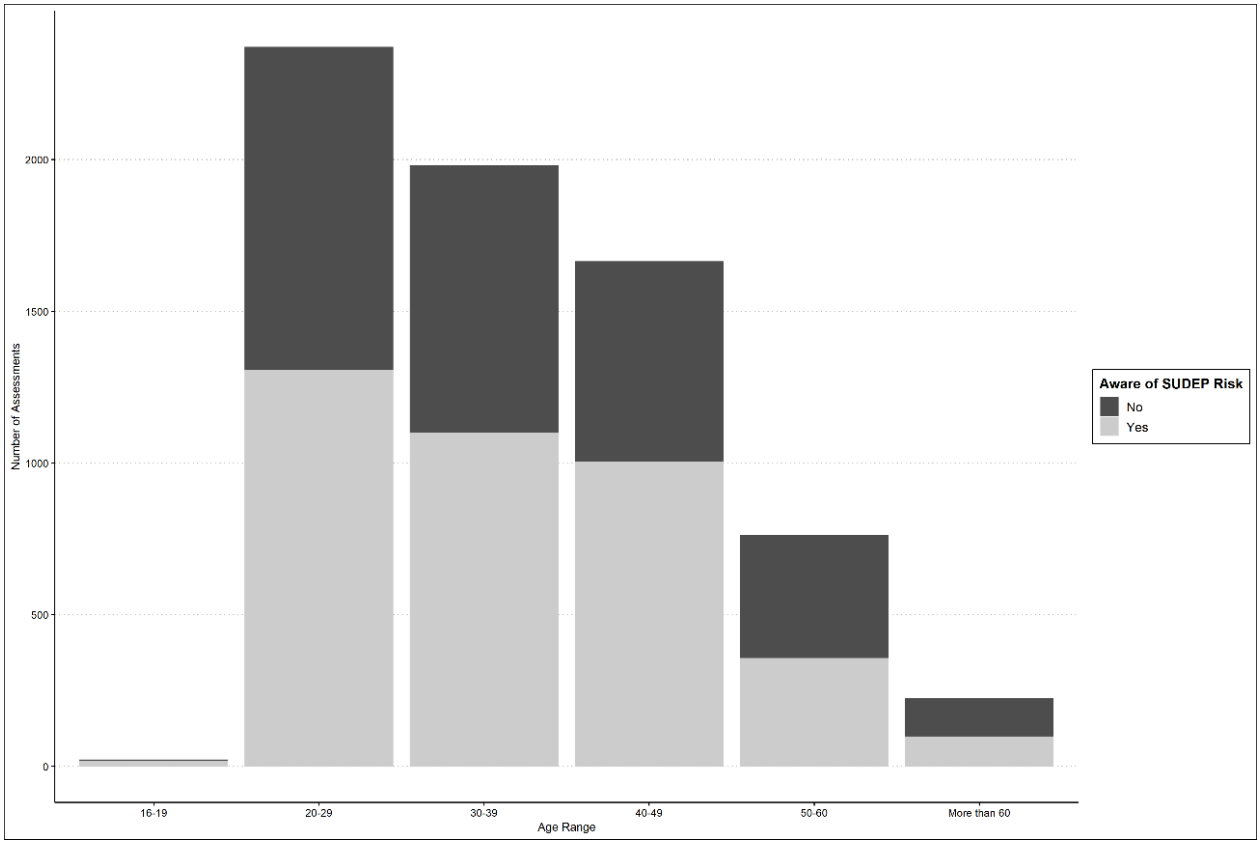


Figure 12: SUDEP Awareness of EpSMon App Users by Age Group

From this graph, we can see that the awareness of SUDEP is evenly split across all age ranges with no bias towards one. Meaning that people of all ages are not aware of the risks of SUDEP as they should be and not just a few age ranges.

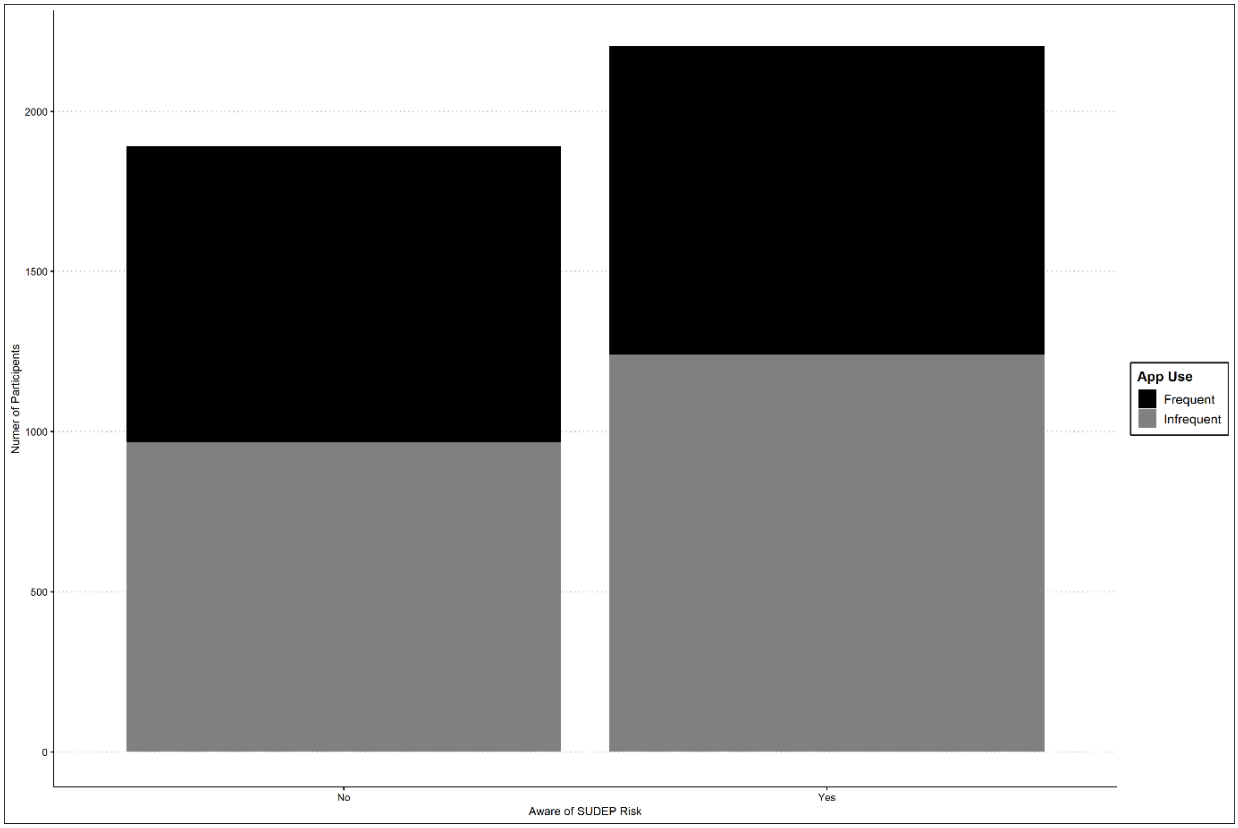


Figure 13: Frequent Users of EpSMon Application SUDEP Awareness

Both the frequent users and age range of users do not show any discernable difference on whether users are aware of SUDEP risks or not.

Chapter 5: Medication and Health Seeking Behaviours Risks of Childbearing Women with Epilepsy

5.1 Brief introduction

Certain drugs and health-seeking behaviours can have a positive and negative impact on the health of people with epilepsy an example of this is anti-seizure medication (such as valproate) and those taking multiple types have an even higher risk of birth defects (Seizures, Medications and Pregnancy, 2021). On average 6.1% of women with epilepsy who take anti-seizure medication are at risk of giving birth to a baby with birth defects (Meador and Loring, 2015). Through using the data we can find out what drugs and health-seeking behaviours have an effect on the risk of people with epilepsy. Such as if visiting GP's more often or certain medication such as lamotrigine reduces the risks of epilepsy. By seeing the medication use over time we can see if there are any trends in the epilepsy medication users are using and see if one type of medication has fallen out of favour for another.

This chapter will aim to address the following problems.

Problem 4: What relationship, if any, is there between medication changes and risk assessment scores provided by the EpSMON app amongst childbearing women (16-60)?

Problem 5: What relationship, if any, is there between EpSMON risk assessment score, and health-seeking behaviours (such as visiting GP) amongst childbearing women (16-60)?

Problem 7: Specifically look at the number of drugs - Antiseizure medication and overall regular medication - Particularly Valproate use ...including changes to its use over time.

5.2 Methodology

For this the total risk score of each user would be added up and split into two categories, if the user had less than 20 total risk score then it would be count as a low-risk score and if it was 20 or above it would count as a high-risk score.

To see if there is any relationship between medication changes and risk assessment scores, logistic regression was used to see if there is any relationship between the medication and the total risk score of users who use that medication. Medications with 3 or fewer users were dropped from the logistic regression due to them being unreliable due to a strong bias.

$$\hat{Y} = \beta 0 + \beta 1X$$

Figure 14: GLM Equation

Using the coefficients from the linear regression we can convert the logits into odds ratio to tell us the odds of if the user taking medication to their total risk score. This will make the results much more readable than only using GLM. The higher the odds ratio (OR) the more likely a user with a high-risk score would take the medication.

Logistic regression and odds ratios are also used to find relationships between health-seeking behaviours and risk scores, additionally, Pearson correlation tests are used, this test shows the correlation between two variables.

Using the date users inputted their prescriptions we can see the use of drugs each month over time, turning these into graphs shows use the use of them over time, specifically focusing on anti-epilepsy drugs.

5.3 Results

The first logistic regression run includes all of the medications that have 3 or more user's using them as using medication with less were unreliable due to strong bias.

term	estimate	std.error	statistic	p.value
(Intercept)	-2.46508	0.14228	-17.3255	3.02E-67
`Amitriptyline Hydrocloride`	1.275616	0.477909	2.669163	0.007604
Aripiprazole	0.60752	0.973419	0.624109	0.532556
Carbamazepine	0.638164	0.158431	4.02802	5.62E-05
Citalopram	0.09495	0.277765	0.341836	0.732475
Clobazam	0.544408	0.150249	3.623379	0.000291
Clonazepam	0.788265	0.242237	3.254103	0.001138
Doxepin	1.723051	1.499224	1.149295	0.250434
Duloxetine	1.556029	0.556838	2.794404	0.0052
Escitalopram	0.713441	0.656351	1.086981	0.277045
Eslicarbazepine	0.452332	0.484732	0.93316	0.350737
Ethosuximide	0.165895	0.499155	0.332352	0.739624
Fluoxetine	0.617527	0.332421	1.857666	0.063217
Gabapentin	0.284565	0.340837	0.834901	0.403773
`Health Supplements`	0.956558	0.280047	3.415706	0.000636
Lacosamide	0.414921	0.234768	1.767364	0.077167
Lamotrigine	0.46391	0.128703	3.604492	0.000313
Levetiracetam	0.655148	0.125876	5.2047	1.94E-07
Lofepramine	2.444957	1.294941	1.888084	0.059015
Mirtazapine	0.259179	0.374307	0.692424	0.488671
Nortriptyline	2.624319	1.220583	2.150055	0.031551
Olanzapine	-0.24785	1.372635	-0.18056	0.85671
Other	0.853486	0.893799	0.954896	0.33963
Oxcarbazepine	0.423109	0.420997	1.005016	0.314889
Perampanel	0.82954	0.301349	2.752754	0.00591
Phenobarbital	0.917828	0.483044	1.900093	0.057421
Phenytoin	0.438223	0.363501	1.205563	0.227986
Pregabalin	0.393887	0.26586	1.481559	0.138458
Primidone	-0.15183	0.689105	-0.22034	0.82561
Quetiapine	0.130653	0.685724	0.190534	0.848891
Retigabine	0.113058	1.827945	0.06185	0.950682
Rufinamide	-0.51576	0.82597	-0.62443	0.532348
Sertraline	0.832282	0.225005	3.69895	0.000216
Tiagabine	1.883814	1.417329	1.329129	0.183805
Topiramate	0.418353	0.187427	2.232083	0.025609
Valproate	0.297848	0.179534	1.659002	0.097115
Venlafaxine	0.979937	0.416653	2.351926	0.018677
Vigabatrin	-2.16809	1.481552	-1.46339	0.14336
Zonisamide	0.171604	0.234517	0.731734	0.464331

Figure 15: All Medication Logistic Regression Coefficients

	OR	2.50%	97.50%
(Intercept)	0.085002	0.064316	0.112341
`Amitriptyline Hydrocloride`	3.580906	1.403448	9.136701
Aripiprazole	1.835872	0.272437	12.37139
Carbamazepine	1.893002	1.387696	2.582308
Citalopram	1.099604	0.637973	1.895268
Clobazam	1.723588	1.283931	2.313799
Clonazepam	2.199576	1.36819	3.536158
Doxepin	5.601596	0.296599	105.7922
Duloxetine	4.739961	1.591453	14.11743
Escitalopram	2.041002	0.563841	7.388054
Eslicarbazepine	1.571974	0.607912	4.064899
Ethosuximide	1.180449	0.443778	3.139996
Fluoxetine	1.854336	0.966566	3.557507
Gabapentin	1.329184	0.681498	2.592422
`Health Supplements`	2.602723	1.50332	4.506137
Lacosamide	1.514251	0.955791	2.399016
Lamotrigine	1.590279	1.235723	2.046566
Levetiracetam	1.925427	1.504461	2.464183
Lofepramine	11.53006	0.911121	145.9107
Mirtazapine	1.295865	0.622228	2.698797
Nortriptyline	13.79518	1.261147	150.9
Olanzapine	0.780478	0.052963	11.50138
Other	2.347816	0.40725	13.53528
Oxcarbazepine	1.526701	0.66896	3.484236
Perampanel	2.292263	1.26986	4.137836
Phenobarbital	2.503847	0.971494	6.453204
Phenytoin	1.549951	0.760161	3.160316
Pregabalin	1.482733	0.880567	2.496684
Primidone	0.859131	0.222583	3.316094
Quetiapine	1.139573	0.297203	4.369497
Retigabine	1.119697	0.031128	40.27636
Rufinamide	0.597049	0.118289	3.013539
Sertraline	2.298558	1.478873	3.572565
Tiagabine	6.578546	0.408975	105.8188
Topiramate	1.519457	1.052326	2.19395
Valproate	1.346957	0.947401	1.915021
Venlafaxine	2.664287	1.177404	6.02888
Vigabatrin	0.114396	0.006271	2.086935
Zonisamide	1.187208	0.749731	1.879959

Figure 16: All Medication Logistic Regression Odds Ratio

The higher the odds ratio (OR) is the more likely a user with a high-risk score would take the medication. Looking at the odd ratios we can see that the medication that users with the highest risk score will most likely take is lofepramine (Nortriptyline Oral: Uses, Side Effects, Interactions, Pictures, Warnings & Dosing - WebMD, 2021) and nortriptyline (Excellence, 2021), both of which are used to treat depression. Another two medications of note are tiagabine and doxepin, tiagabine is an anti-convulsive medication used to treat partial seizures in epilepsy (Tiagabine: Uses, Interactions, Mechanism of Action | DrugBank Online, 2021). Doxepin is a tricyclic antidepressant that increases the number of natural substances in the brain that is needed for a mental balance, it is also used to treat insomnia (Drugs, 2021). Looking at the valproates we can see that the user would also likely use this medication, valproate is used to treat epilepsy by preventing seizures.

The medication was then split into different categories to see if there were any relationships with a certain type of drug.

term	estimate	std.error	statistic	p.value
(Intercept)	-2.79986	0.427009	-6.5569	5.49E-11
`Anti-Depressants`	0.795979	0.136546	5.829378	5.56E-09
`Anti-Epileptic`	1.277339	0.422858	3.020729	0.002522
`Anti-Psychotics`	0.491461	0.42486	1.156759	0.247371

Figure 17: Medication Type Logistic Regression Coefficients

	OR	2.50%	97.50%
(Intercept)	0.060819	0.026337	0.140446
`Anti-Depressants`	2.216609	1.696137	2.896792
`Anti-Epileptic`	3.587083	1.566044	8.216349
`Anti-Psychotics`	1.634703	0.710881	3.759071

Figure 18: Medication Type Logistic Regression Odds Ratio

From looking at the odd ratio we can see that users will be more likely to take anti-epileptic medication over the rest, though this would be no surprise as most of the users on the app would have epilepsy and would therefore be taking anti-epileptic drugs, we can see that odd ratio for anti-depressants is also quite high, meaning that people with epilepsy may have underlying mental health issues.

Each medication in its category was then looked at to see the relationship of the drugs in that category.

term	estimate	std.error	statistic	p.value
(Intercept)	-2.25297	0.142016	-15.8642	1.12E-56
Carbamazepine	0.645942	0.154903	4.169973	3.05E-05
Clobazam	0.580807	0.146309	3.969726	7.2E-05
Clonazepam	0.843915	0.231831	3.640221	0.000272
Eslicarbazepine	0.424553	0.460372	0.922196	0.356426
Ethosuximide	0.010942	0.494734	0.022118	0.982354
Gabapentin	0.471032	0.324595	1.451137	0.146742
Lacosamide	0.352688	0.229697	1.53545	0.124673
Lamotrigine	0.418008	0.128502	3.252941	0.001142
Levetiracetam	0.592277	0.125312	4.726434	2.28E-06
Oxcarbazepine	0.366972	0.410171	0.894679	0.370959
Perampanel	0.853094	0.293879	2.902871	0.003698
Phenobarbital	0.804099	0.472347	1.702348	0.08869
Phenytoin	0.337458	0.356294	0.947132	0.343572
Pregabalin	0.63416	0.255786	2.47926	0.013166
Primidone	0.235923	0.623462	0.378408	0.705127
Retigabine	1.151559	1.655559	0.695571	0.486698
Rufinamide	-0.68231	0.816084	-0.83608	0.403109
Tiagabine	1.540111	1.447996	1.063616	0.287503
Topiramate	0.438752	0.183227	2.394584	0.016639
Valproate	0.298122	0.175479	1.698903	0.089337
Vigabatrin	-1.62362	1.056582	-1.53667	0.124373
Zonisamide	0.247433	0.224498	1.102159	0.270393

Figure 19: Anti-Epilepsy Medication Logistic Regression Coefficients

	OR	2.50%	97.50%
(Intercept)	0.105086	0.079554	0.138813
Carbamazepine	1.907783	1.408235	2.584537
Clobazam	1.78748	1.341846	2.381111
Clonazepam	2.325453	1.476294	3.663043
Eslicarbazepine	1.528907	0.620172	3.769207
Ethosuximide	1.011003	0.383384	2.666065
Gabapentin	1.601646	0.847756	3.025954
Lacosamide	1.422887	0.907094	2.231973
Lamotrigine	1.518933	1.18075	1.953977
Levetiracetam	1.8081	1.414351	2.311468
Oxcarbazepine	1.443357	0.646004	3.224869
Perampanel	2.346897	1.3193	4.174885
Phenobarbital	2.234682	0.885428	5.63999
Phenytoin	1.401381	0.697072	2.817309
Pregabalin	1.885437	1.142054	3.1127
Primidone	1.266077	0.373051	4.296864
Retigabine	3.16312	0.123282	81.15777
Rufinamide	0.505446	0.102099	2.502227
Tiagabine	4.665108	0.273102	79.68888
Topiramate	1.550771	1.082891	2.220805
Valproate	1.347327	0.955223	1.900383
Vigabatrin	0.197183	0.02486	1.563991
Zonisamide	1.280733	0.824832	1.988622

Figure 20: Anti-Epilepsy Medication Logistic Regression Odds Ratio

From looking at the odd ratio we can see those users with high-risk scores or more likely to take Tiagabine, with the second-highest odds ratio being Perampanel. The medication with the lowest odds ratio is Vigabatrin with 0.19, suggesting that people with lower risk scores take them.

term	estimate	std.error	statistic	p.value
(Intercept)	-2.29065	0.510699	-4.48533	7.28E-06
Agomelatine	-14.2754	2399.545	-0.00595	0.995253
`Amitriptyline Hydrocloride`	1.573611	0.582851	2.69985	0.006937
Citalopram	0.90947	0.532596	1.707616	0.087708
`Clomipramine Hydrocloride`	-21.439	4156.134	-0.00516	0.995884
`Dosulepin Hydrocloride`	15.42987	2399.545	0.00643	0.994869
Duloxetine	1.853241	0.716347	2.587071	0.00968
Escitalopram	1.055413	0.735867	1.434244	0.151503
Fluoxetine	1.423321	0.535094	2.659946	0.007815
`Imipramine Hydrocloride`	16.87922	2399.545	0.007034	0.994387
Isocarboxazid	17.4334	2399.545	0.007265	0.994203
Lithium	2.290653	1.5036	1.523445	0.127647
Lofepramine	2.9838	1.326956	2.248604	0.024538
`Minaserin Hydrocloride`	-34.3518	4488.378	-0.00765	0.993893
Mirtazapine	0.819368	0.486799	1.683175	0.092341
Moclobemide	1.597505	1.326956	1.203887	0.228633
Nortriptyline	1.977502	1.274077	1.552106	0.120637
Paroxetine	1.762946	1.541568	1.143606	0.252787
Phenelzine	16.3896	2399.545	0.00683	0.99455
Reboxetine	NA	NA	NA	NA
Sertraline	1.557648	0.523218	2.977052	0.00291
`Trazodone Hydrocloride`	16.94684	1694.724	0.01	0.992021
Trimipramine	18.85672	2399.545	0.007858	0.99373
Venlafaxine	1.797308	0.604481	2.97331	0.002946

Figure 21: Anti-Depressant Medication Logistic Regression Coefficients

	OR	2.50%	97.50%
(Intercept)	0.1012	0.037194	0.275353
Agomelatine	6.31E-07	0	Inf
`Amitriptyline Hydrocloride`	4.824035	1.53917	15.11939
Citalopram	2.483006	0.874241	7.052201
`Clomipramine Hydrocloride`	4.89E-10	0	Inf
`Dosulepin Hydrocloride`	5024664	0	Inf
Duloxetine	6.380466	1.567099	25.97816
Escitalopram	2.873162	0.679186	12.15434
Fluoxetine	4.150883	1.454346	11.84713
`Imipramine Hydrocloride`	21406787	0	Inf
Isocarboxazid	37258847	0	Inf
Lithium	9.881383	0.518742	188.2281
Lofepramine	19.76277	1.466697	266.2902
`Minaserin Hydrocloride`	1.21E-15	0	Inf
Mirtazapine	2.269066	0.873942	5.891306
Moclobemide	4.940692	0.366674	66.57254
Nortriptyline	7.224676	0.594733	87.76359
Paroxetine	5.829586	0.284088	119.6251
Phenelzine	13119399	0	Inf
Reboxetine	NA	NA	NA
Sertraline	4.747643	1.702605	13.23861
`Trazodone Hydrocloride`	22904524	0	Inf
Trimipramine	1.55E+08	0	Inf
Venlafaxine	6.033383	1.845126	19.72857

Figure 22: Anti-Depressant Medication Logistic Regression Odds Ratio

From the odd ratio, we can see that epilepsy users are likely to use anti-depressants, another note on how epilepsy patients are struggling with their mental health. People with a high-risk score using drugs such as duloxetine, nortriptyline and citalopram.

term	estimate	std.error	statistic	p.value
(Intercept)	29.3491	9313.248	0.003151	0.997486
Amisulpride	186.2831	58161.22	0.003203	0.997444
Aripiprazole	-29.7546	9313.248	-0.00319	0.997451
Benperidol	NA	NA	NA	NA
Clozapine	-48.9152	14226.22	-0.00344	0.997257
Flupentixol	-9.78303	14226.22	-0.00069	0.999451
Haloperidol	-9.78303	9313.248	-0.00105	0.999162
Levomepromazine	NA	NA	NA	NA
`Lurasidone Hydrochloride`	NA	NA	NA	NA
Olanzapine	-29.3491	9313.248	-0.00315	0.997486
Paliperidone	NA	NA	NA	NA
Pericyazine	NA	NA	NA	NA
Perphenazine	NA	NA	NA	NA
Pimozide	NA	NA	NA	NA
Prochlorperazine	NA	NA	NA	NA
`Promazine Hydrocloride`	20.12568	10754.01	0.001871	0.998507
Quetiapine	-29.9087	9313.248	-0.00321	0.997438
Risperidone	-9.78303	9313.248	-0.00105	0.999162
Sulpiride	-48.9152	12023.35	-0.00407	0.996754
Trifluoperazine	NA	NA	NA	NA
Zuclopenthixol	NA	NA	NA	NA
`Zuclopenthixol Acetate`	NA	NA	NA	NA

Figure 23: Anti-Psychotics Medication Logistic Regression Coefficients

	OR	2.50%	97.50%
(Intercept)	5.57E+12	0	Inf
Amisulpride	7.97E+80	0	Inf
Aripiprazole	1.2E-13	0	Inf
Benperidol	NA	NA	NA
Clozapine	5.71E-22	0	Inf
Flupentixol	5.64E-05	0	Inf
Haloperidol	5.64E-05	0	Inf
Levomepromazine	NA	NA	NA
`Lurasidone Hydrochloride`	NA	NA	NA
Olanzapine	1.79E-13	0	Inf
Paliperidone	NA	NA	NA
Pericyazine	NA	NA	NA
Perphenazine	NA	NA	NA
Pimozide	NA	NA	NA
Prochlorperazine	NA	NA	NA
`Promazine Hydrocloride`	5.5E+08	0	Inf
Quetiapine	1.03E-13	0	Inf
Risperidone	5.64E-05	0	Inf
Sulpiride	5.71E-22	0	Inf
Trifluoperazine	NA	NA	NA
Zuclopenthixol	NA	NA	NA
`Zuclopenthixol Acetate`	NA	NA	NA

Figure 24: Anti-Psychotics Medication Logistic Odds Ratio

Looking at the results from these tests, we can see that there is no real correlation between risk scores and anti-psychotic medication. This could be due to there not being enough data available in the dataset to look at the risk effects of anti-psychotics

To analyze the relationship between the risk score and health-seeking behaviours generalized logistic regression and Pearson correlation tests were carried out between answers given in the risk score assessment and the total risk score.

The following assessment questions were used concerning this problem:

Q8- Have you had any injuries/ED/999/emergency services calls after a seizure?

```
        Pearson's product-moment correlation

data:  p_q8_merge2_factor$answer_given and p_q8_merge2_factor$total_risk_score
t = 4.1163, df = 4069, p-value = 0.00003927
alternative hypothesis: true correlation is not equal to 0
95 percent confidence interval:
 0.03374235 0.09492778
sample estimates:
       cor
0.06439559
```

Figure 25: Question 8 Pearson Test

Looking at the output of a Pearson correlation test, we can see with a correlation of 0.06 is a positive meaning there is a positive correlation between if users call emergency services after a seizure and risk score. With a p-value of 0.00003927 we can reject null hypothesis as there is a positive correlation between risk score and if participants contact emergency services after a seizure.

term	estimate	std.error	statistic	p.value
(Intercept)	-0.22253	0.05263	-4.22814	2.356350E-05
q8	0.269298	0.065604	4.104872	4.045389E-05

Figure 26: Question 8 Logistic Coefficients

	OR	2.50%	97.50%
(Intercept)	0.800493	0.722035	0.887475
q8	1.309045	1.151097	1.488665

Figure 27: Question 8 Logistic Odds Ratio

From the odds ratio (OR) we can see there is an increased occurrence of events, suggesting that participants who contact emergency services are 1.309 likely to have a lower risk score.

Q21- Have you had contact with health services to help you with a mental health problem?

```
        Pearson's product-moment correlation

data:  p_q21_merge_bin_factor$answer_given and p_q21_merge_bin_factor$total_risk_score
t = -3.1571, df = 4069, p-value = 0.001605
alternative hypothesis: true correlation is not equal to 0
95 percent confidence interval:
 -0.08003137 -0.01874140
sample estimates:
        cor
-0.04943292
```

Figure 28: Question 21 Pearson Test

Looking at the output of a Pearson correlation test, we can see with a correlation of -0.49 is a negative meaning there is a negative correlation between if users have had contact with health services with a mental health problem and risk score. With a p-value of 0.001605 we can reject null hypothesis as there is a positive correlation between risk score and if participants contact emergency services after a seizure.

term	estimate	std.error	statistic	p.value
(Intercept)	0.116454	0.06136	1.897877	0.057712
q21	-0.22505	0.071415	-3.15125	0.001626

Figure 29: Question 21 Logistic Coefficients

	OR	2.50%	97.50%
(Intercept)	1.123506	0.996198	1.267084
q21	0.798479	0.694184	0.918443

Figure 30: Question 21 Logistic Odds Ratio

From the odds ratio (OR) we can see there is an increased occurrence of events, suggesting that participants who contact health services for their mental health problems are 0.8 likely to have a lower risk score.

Q30 -Has there been contact with your epilepsy nurse/neurologist for a planned next review of your epilepsy?

```
        Pearson's product-moment correlation

data:  p_q30_merge_bin_factor$answer_given and p_q30_merge_bin_factor$total_risk_score
t = 5.6361, df = 4069, p-value = 0.00000001857
alternative hypothesis: true correlation is not equal to 0
95 percent confidence interval:
 0.05744894 0.11841341
sample estimates:
      cor
0.08801359
```

Figure 31: Question 30 Pearson Test

Looking at the output of a Pearson correlation test, we can see with a correlation of 0.08 is a positive meaning there is a positive correlation between if users have had contact with health specialists to plan their next epilepsy review and risk score. With a p-value of 0.00000001857 we can reject null hypothesis as there is a positive correlation between risk score and if participants contact health specialists for their next epilepsy review.

term	estimate	std.error	statistic	p.value
(Intercept)	-0.22512	0.044431	-5.06671	4.05E-07
q30	0.353078	0.062955	5.608379	2.04E-08

Figure 32:Question 30 Logistic Coefficients

	OR	2.50%	97.50%
(Intercept)	0.798422	0.731835	0.871068
q30	1.423442	1.258207	1.610377

Figure 33: Question 30 Logistic Odds Ratio

From the odds ratio (OR) we can see there is an increased occurrence of events, suggesting that participants who contact health service for their next planned review of epilepsy are 1.423442 likely to have a lower risk score.

Q31 - Have you received safety advice and information about SUDEP from your doctor /nurse about epilepsy?

```
        Pearson's product-moment correlation

data:  p_q31_merge_bin_factor$answer_given and p_q31_merge_bin_factor$total_risk_score
t = 6.8133, df = 4069, p-value = 0.00000000001094
alternative hypothesis: true correlation is not equal to 0
95 percent confidence interval:
 0.07573384 0.13648141
sample estimates:
      cor
0.1062067
```

Figure 34: Question 31 Pearson Test

Looking at the output of a Pearson correlation test, we can see with a correlation of 0.106 is a positive meaning there is a positive meaning correlation between if users have had SUDEP safety advice from a medical specialist and risk score. With a p-value of 0.0000000001094, we can reject null hypothesis as there is a positive correlation between risk score and if participants have received SUDEP safety advice from medical specialists.

term	estimate	std.error	statistic	p.value
(Intercept)	-0.19985	0.038533	-5.18662	2.1414E-07
q31	0.45305	0.067048	6.757133	1.4075E-11

Figure 35: Question 31 Logistic Coefficients

	OR	2.50%	97.50%
(Intercept)	0.81885	0.759286	0.83087
q31	1.573103	1.379387	1.794024

Figure 36: Question 32 Logistic Odds Ratio

From the odds ratio (OR) we can see there is an increased occurrence of events, suggesting that participants who contact health services for their next planned review of epilepsy are 1.5 likely to have a lower risk score. *Using the user's data from the risk assessments, we can see what medication the user is prescribed at that time, due to a large amount of medication available and how inconsistent the number of users are for each, the graphs will only represent anti-epilepsy medication.*

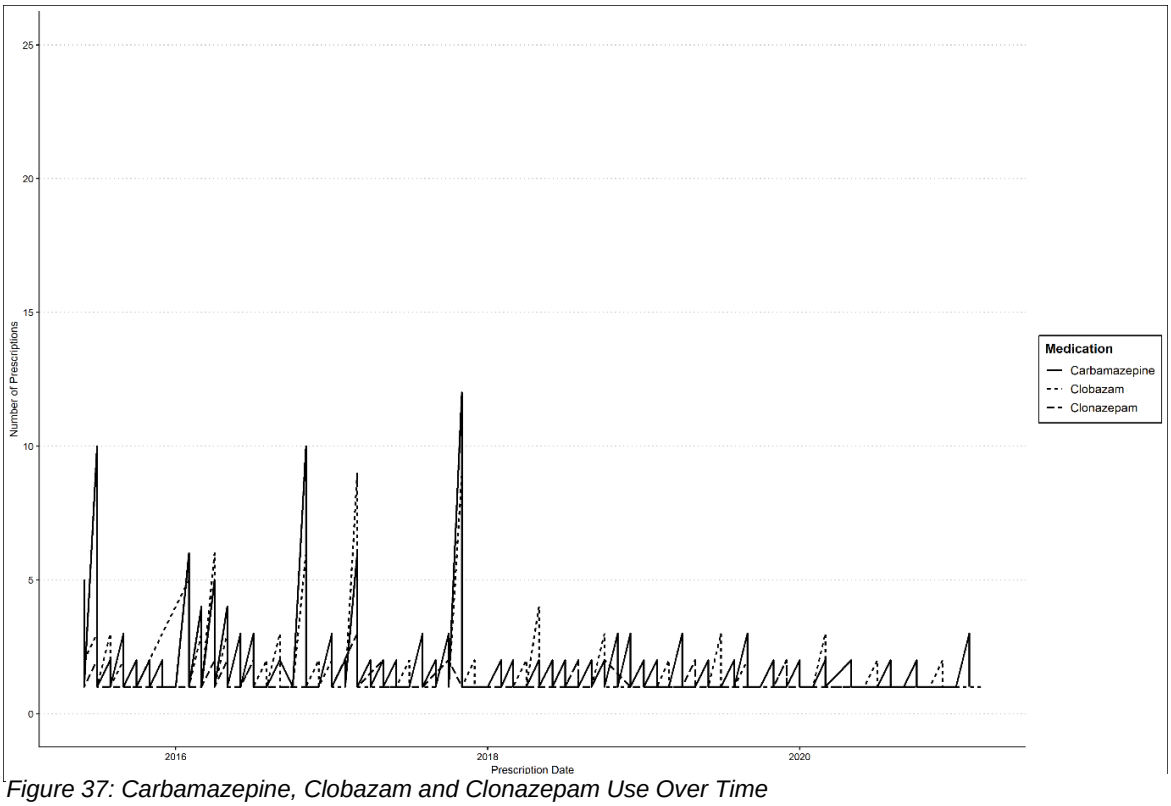


Figure 37: Carbamazepine, Clobazam and Clonazepam Use Over Time

From this graph, we can see a higher use of Carbamazepine as well as Clobazam, following a similar tread as each other with Carbamazepine being used more overall.

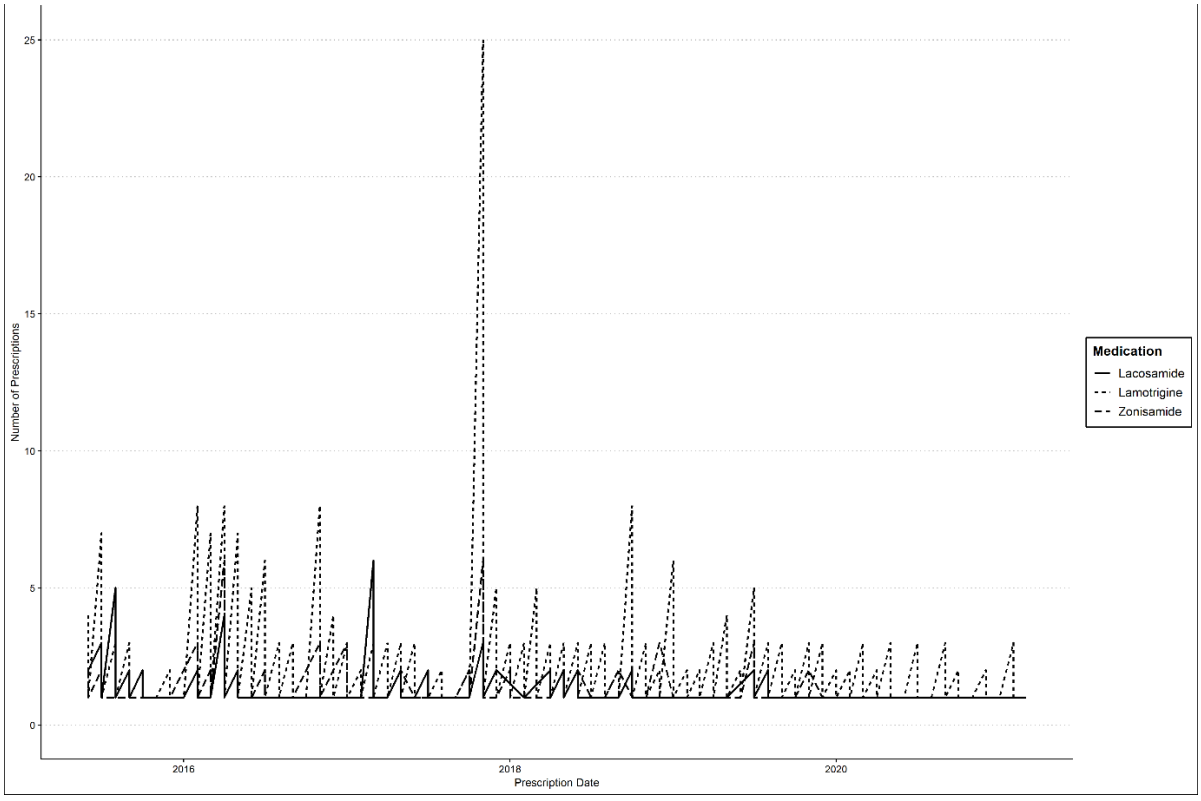


Figure 38: Lacosamide, Lamotrigine and Zosamide Use Over Time

There is a high amount and steady use of Lamotrigine, we can also see the use of Lacosamide being used semi-frequently between 2015 and 2018 but starts to lose usage.

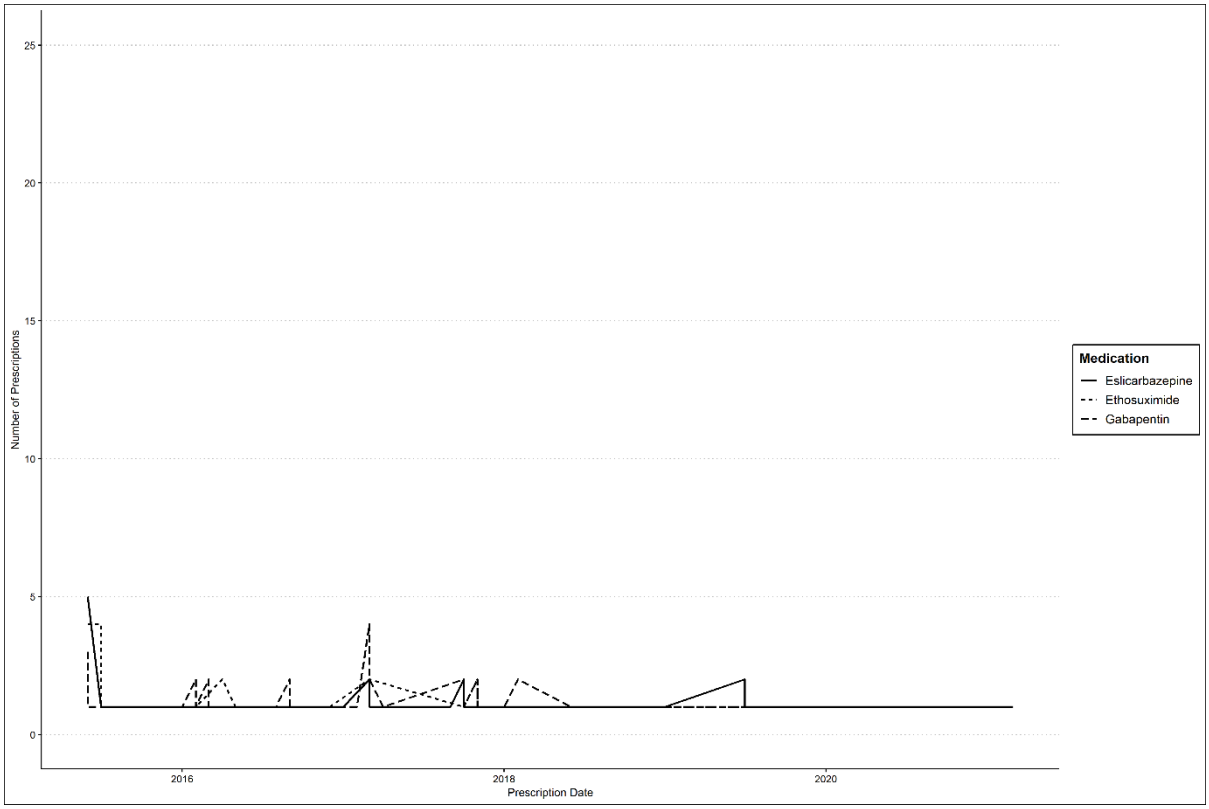


Figure 37: Eslicarbazepine, Ethosuximide and Gabapentin Use Over Time

There is not much use of Eslicarbazepine and Gabapentin, there is also limited use of Ethosuximide.

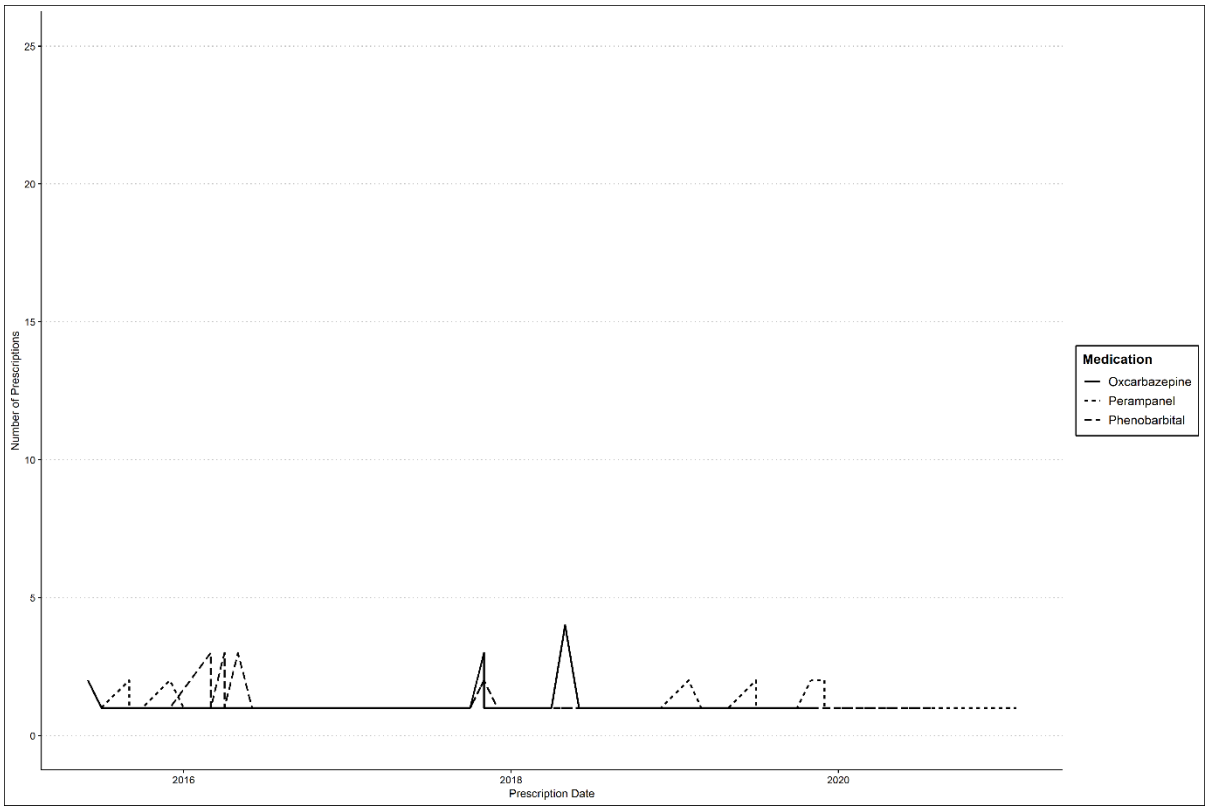


Figure 38: Oxcarbazepine, Phenobarbital and Perampanel Use Over Time

There is not much use of Oxcarbazepine, Phenobarbital or Perampanel.

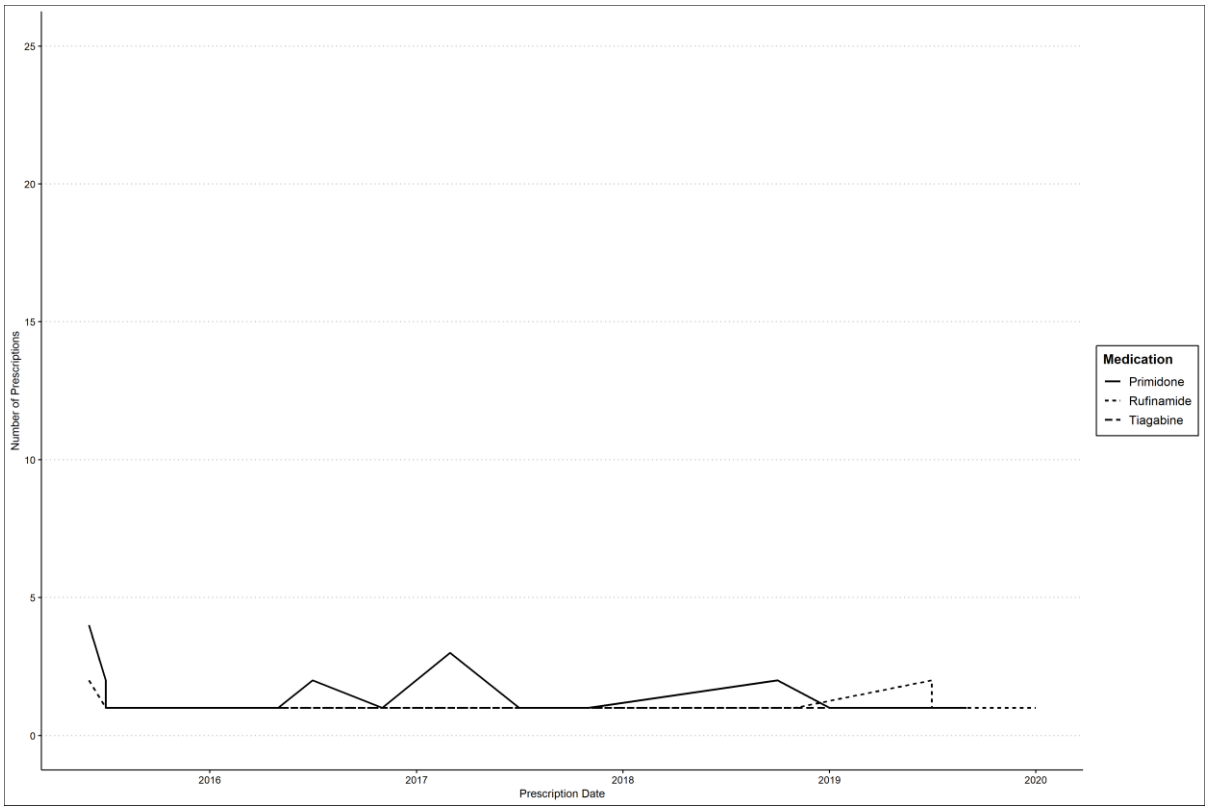


Figure 39: Primidone, Rufinamide and Tiagabine Use Over Time

There is not much use of Rufinamide and Tiagabine, but we can see some consistent use of Primidone over the years.

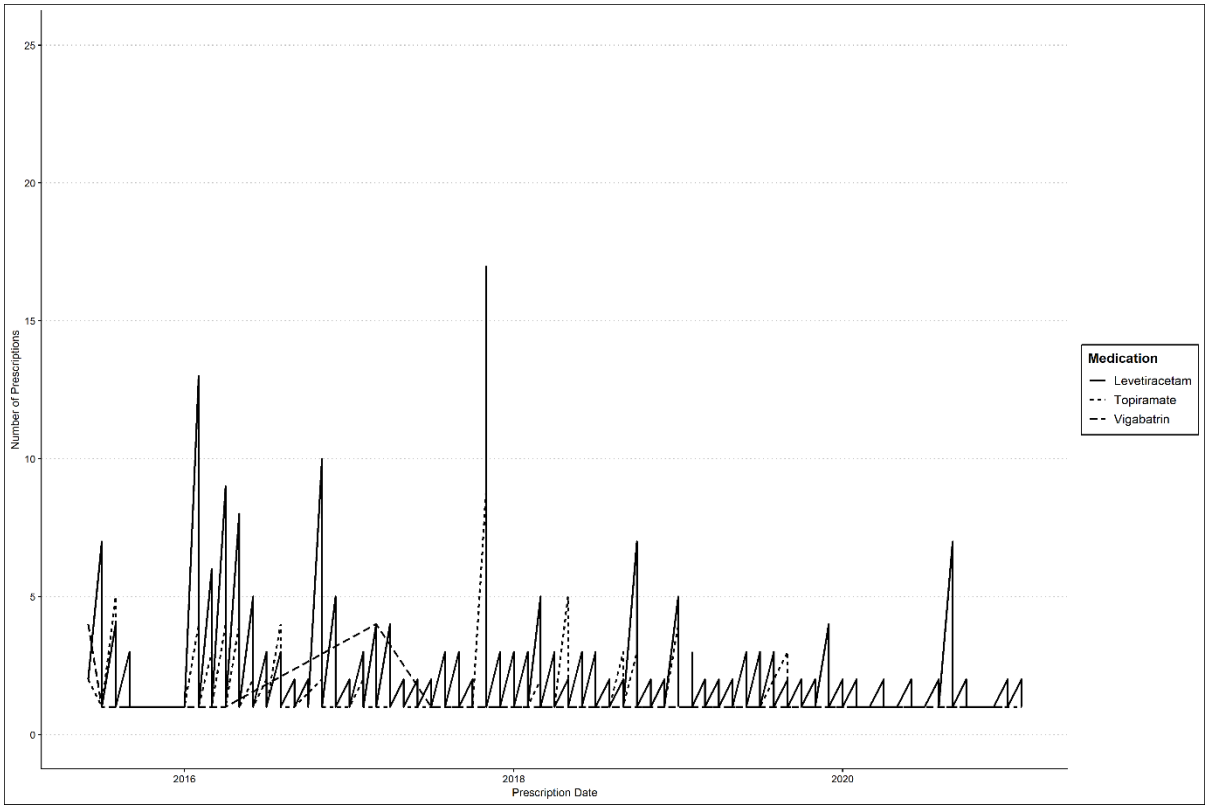


Figure 40: Levetiracetam, Topiramate and Vigabatrin Use Over Time

We can see some frequent use of topiramate, with vigabatrin being used between 2016 and 2017 before dropping substantially. We can see a high amount of levetiracetam prescriptions being used, this is a drug used for anti-epilepsy treatment. Overall we can see consistent high and consistent use of Topiramate and Topiramate.

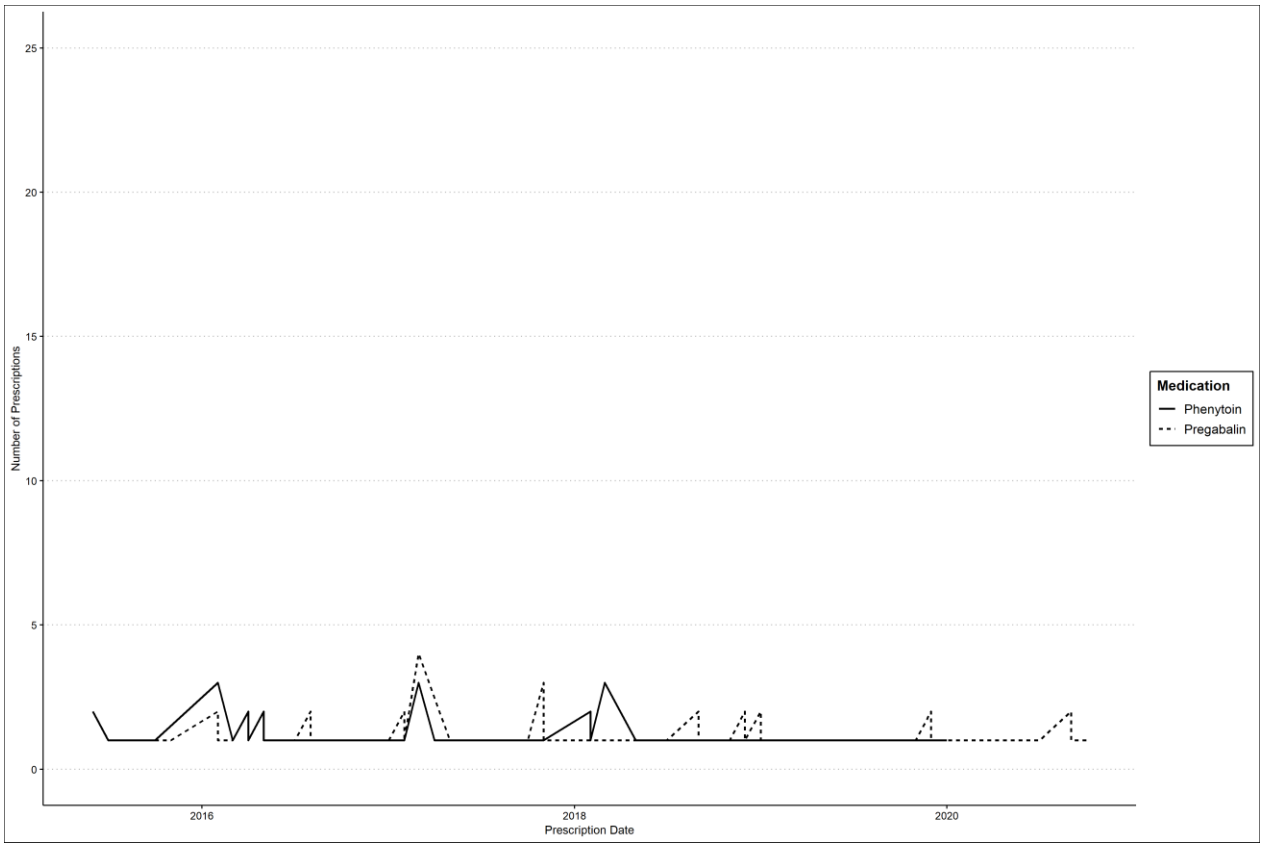


Figure 41: Phenytoin and Pregabalin Use Over Time

There is around an equal amount of phenytoin and pregabalin being used, though they are not used much.

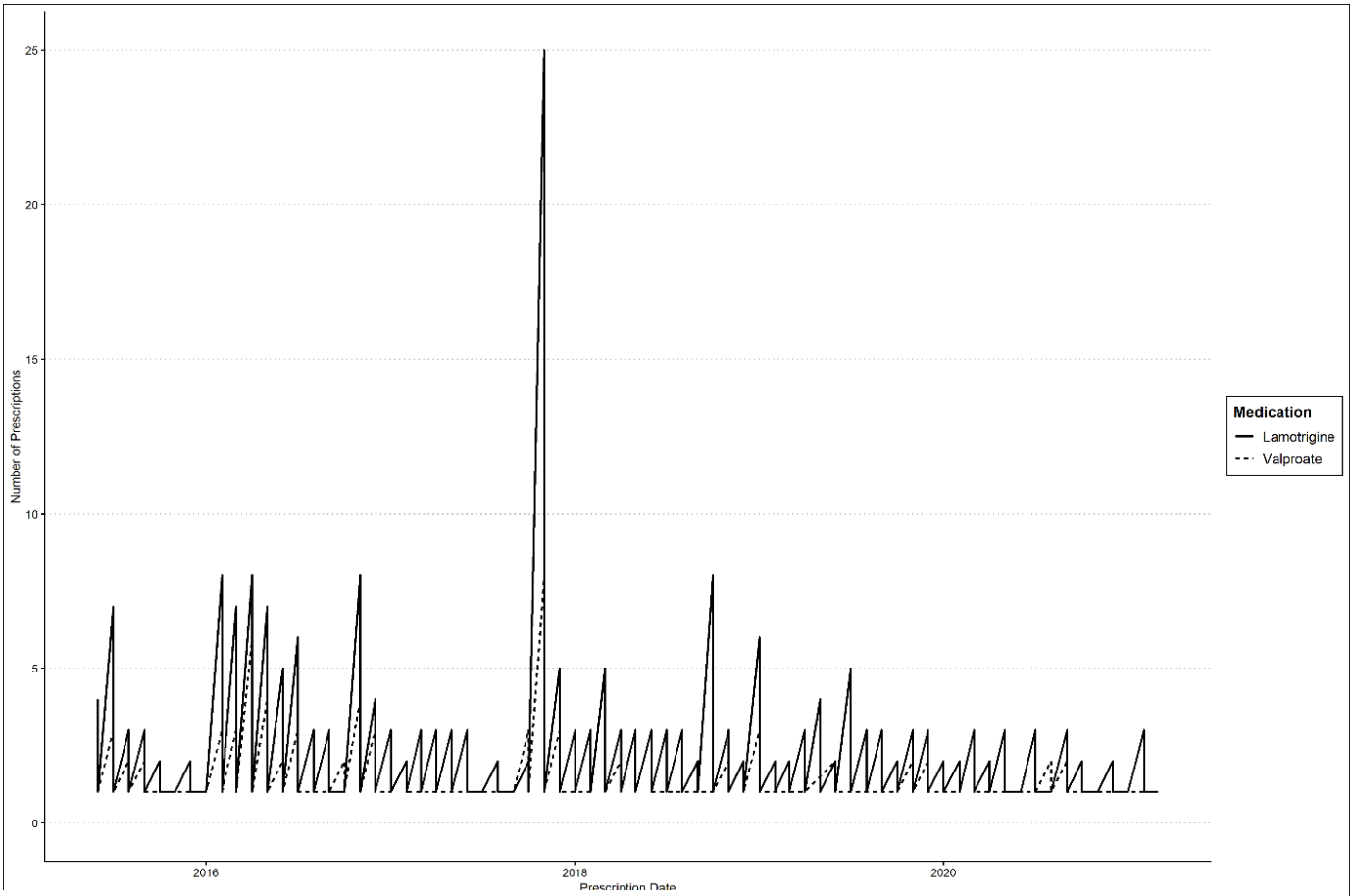


Figure 42: Lamotrigine and Valproate Use Over Time

Regarding Valproate, we can see it being used more consistently than others and it is following a similar trend as lamotrigine but on a smaller scale. Valproate is a medication used to treat epilepsy, this is done by slowing down chemical and electrical activity in the brain to reduce the chance of seizures. Valproate use during pregnancy can cause birth defects and problems with the child's development and learning, such as malformation of the limbs, heart, kidney, urinary tract, and sexual organs as well as spina bifida (Sodium valproate medicines pregnancy risks | Epilepsy Action, 2021). Lamotrigine is also a drug used to treat epilepsy and it's the most used anti-epilepsy drug from these graphs.

Chapter 6: Mental Health and Pregnancy Risks of Childbearing Women with Epilepsy

6.1 Brief introduction

Pregnancy of epileptic people come with their risks compared to non-epileptic people, as epileptic people not on anti-epilepsy still have a 2.2% chance of babies born with birth defects, which cannot always be prevented or predicted. Seizures themselves are a greater risk as they can harm the baby. Seizures can lead to miscarriages, premature labour, physical trauma from falls and also lower the baby's heart rate to a critical condition (Seizures, Medications and Pregnancy, 2021).

Using the data we can see how many epileptic people are aware of pregnancy matters tied to epilepsy, to see how weak informed they are on the risks, by knowing the risks they could lower them with countermeasures. We can also see what kind of mental health issues childbearing women are having and what are the most common.

This chapter will aim to address the following problems;

Problem 6: What was the level of awareness of pregnancy matters at baseline in the women 16 -60

Problem 8: What are mental health issues in this group of childbearing women (16-60)?

6.2 Methodology

To find out the level of awareness of pregnancy risks and mental health of childbearing women, some of the assessment questions can be used. Looking at the results of one of the questions on the risk assessment, we can see if users are aware of pregnancy risks. Question 15 of the risk assessments states "Are you a female of child-bearing age who has not had preconception counselling or an annual review? (information on contraception, pregnancy & managing your medication and epilepsy risks)". Using the data from the question allows us to see how many childbearing women are aware of the risks. The data was transformed into graphs to better visualize the data. The same method was used for the mental health of childbearing women but using questions: 17,18,19,20,21,23

6.3 Results

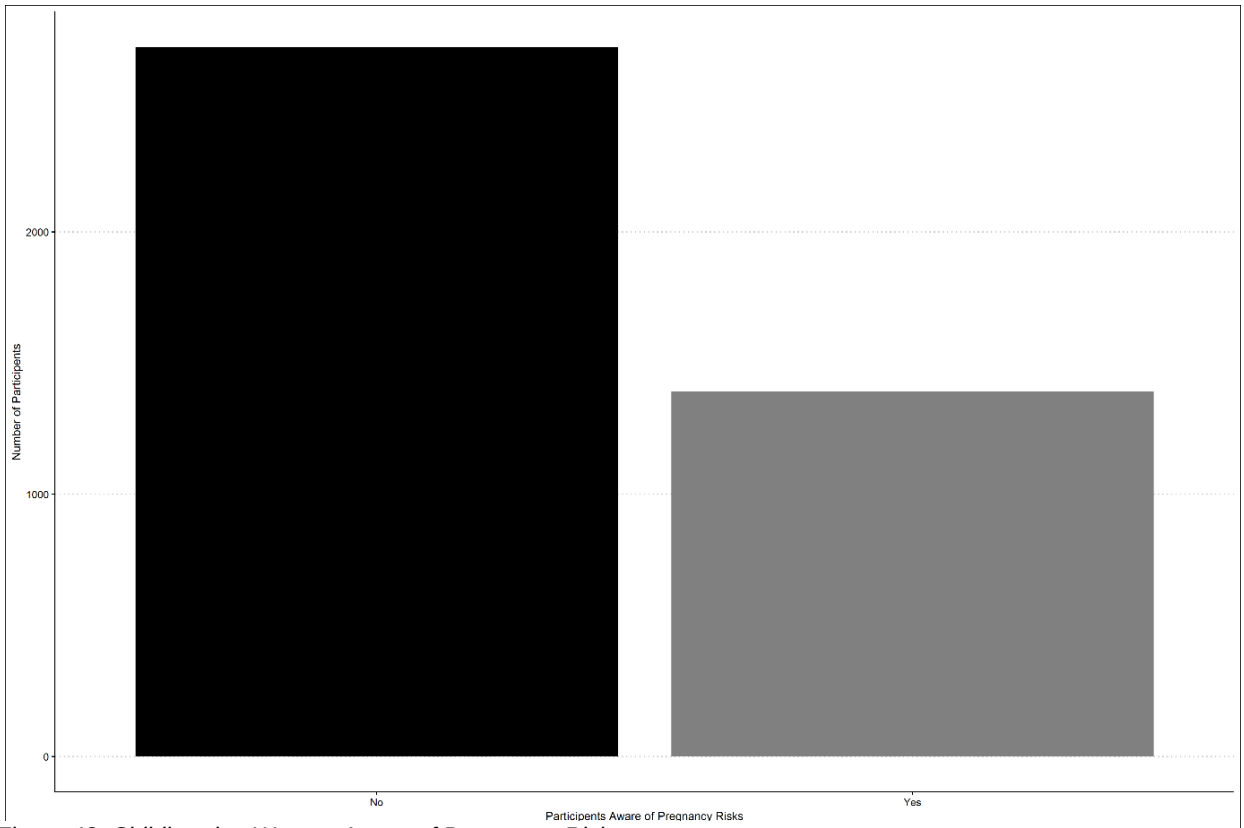


Figure 43: Childbearing Women Aware of Pregnancy Risks

The outcome of Question 15 of the risk assessment - “Are you a female of child-bearing age who has not had preconception counselling or an annual review? (information on contraception, pregnancy & managing your medication and epilepsy risks)”.

From this graph, we can see that an alarming number of women are not aware of the pregnancy risks associated with epilepsy, with the majority of them.

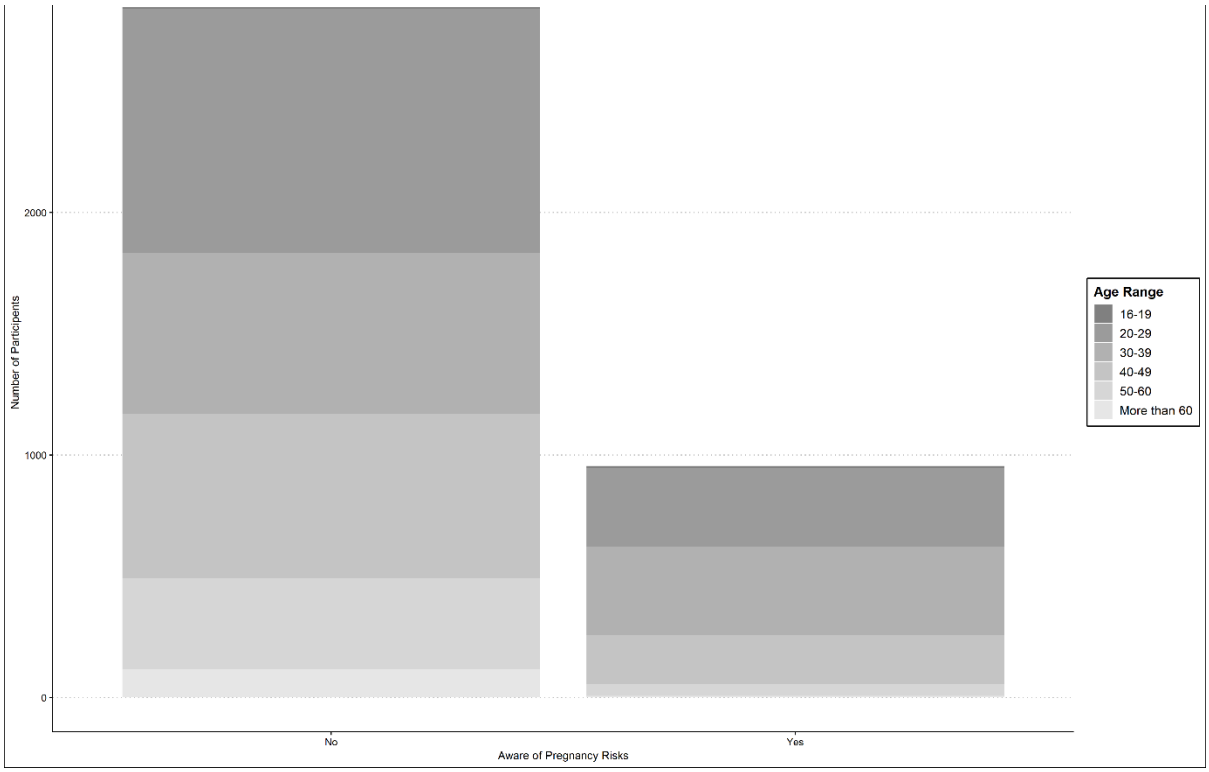


Figure 44: Childbearing Women Aware of Pregnancy Risks by Age

Though there is not much difference of knowledge among the different age groups, it seems the younger 20-29 age range seems to be less aware

Using a variety of questions from the risk assessment we can see trends in the mental health of childbearing women.

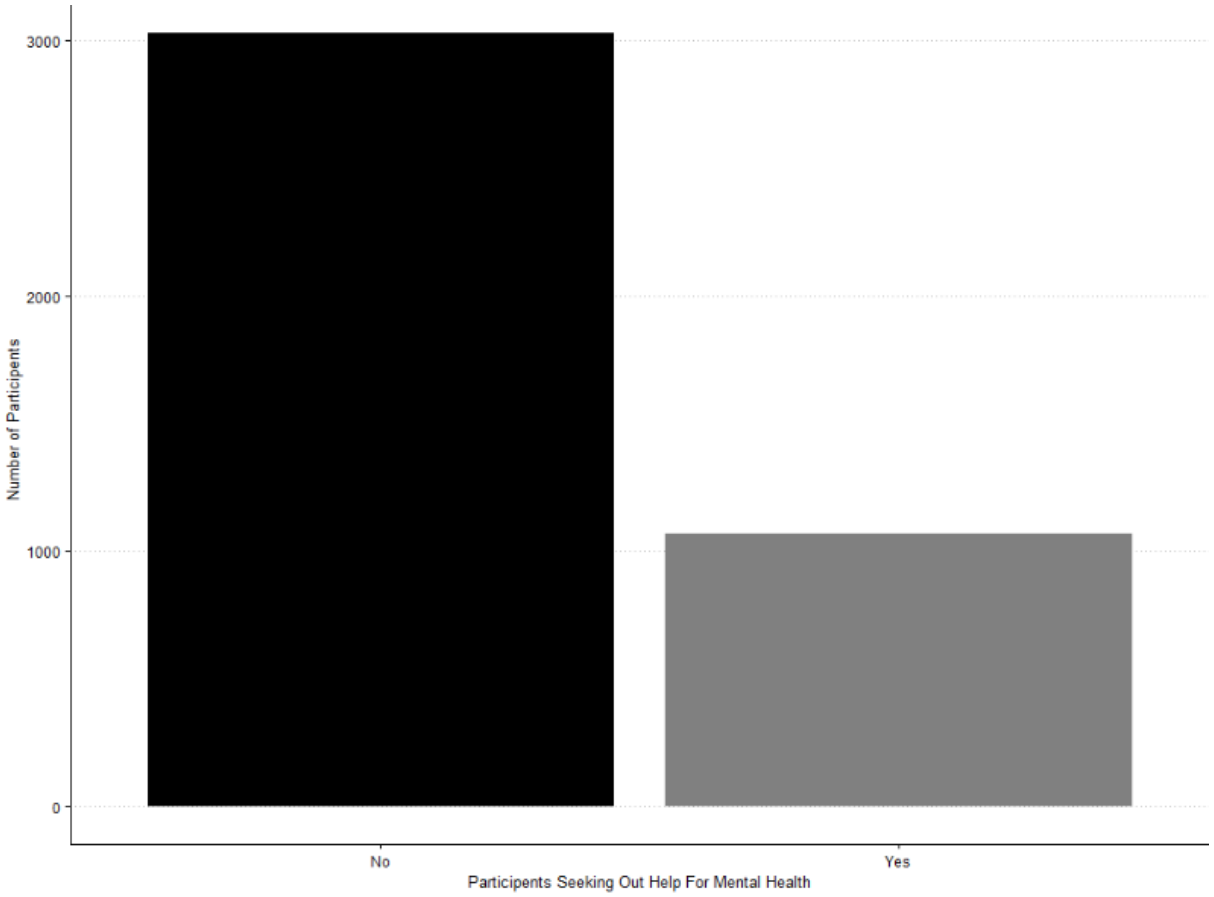


Figure 45: Childbearing Women Seeking Help with Mental Health

The outcome of Question 21 of the risk assessment – “Have you had contact with health services to help you with a mental health problem?”

An overwhelming majority of women are not seeking out help for their mental health, 73% of women are not seeking our help for their mental health

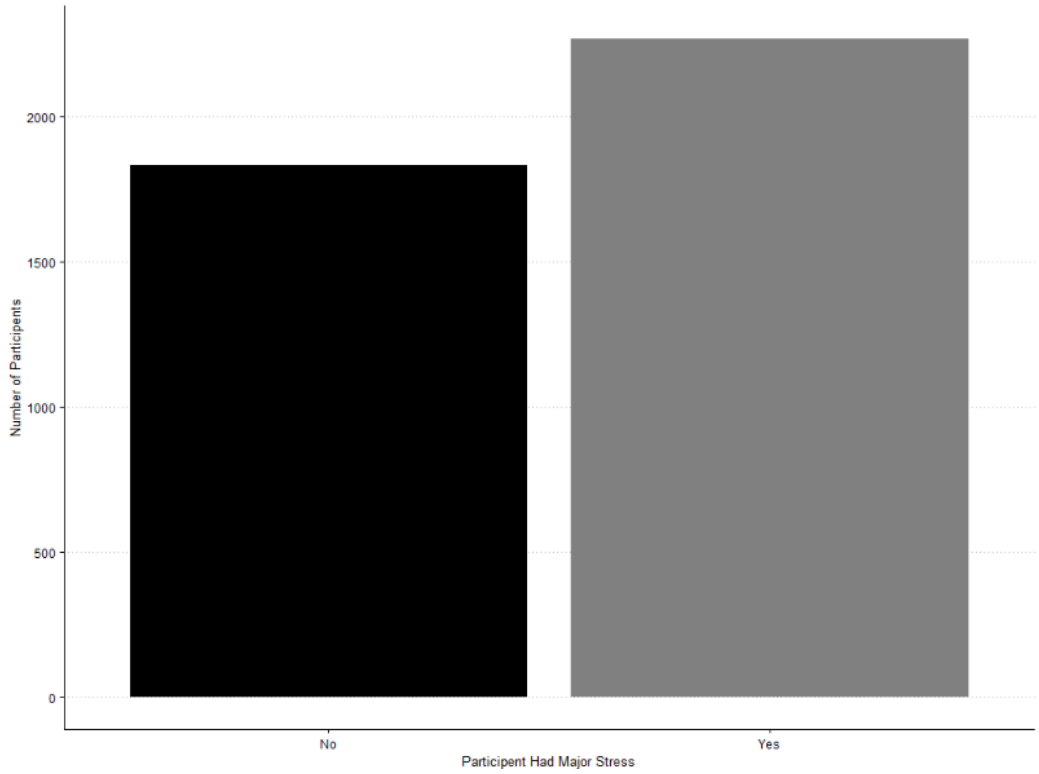


Figure 46: Childbearing Women Had Major Stress Recently

The outcome of Question 23 of the risk assessment – "*Have you had any major changes or stresses in your life, job or family situation (such as increased work or job loss, bereavement, a new partner or a baby or a relationship breakdown)?"

From this graph, we can see 55% of childbearing women have been affected by major stress whereas 45% of women do not.

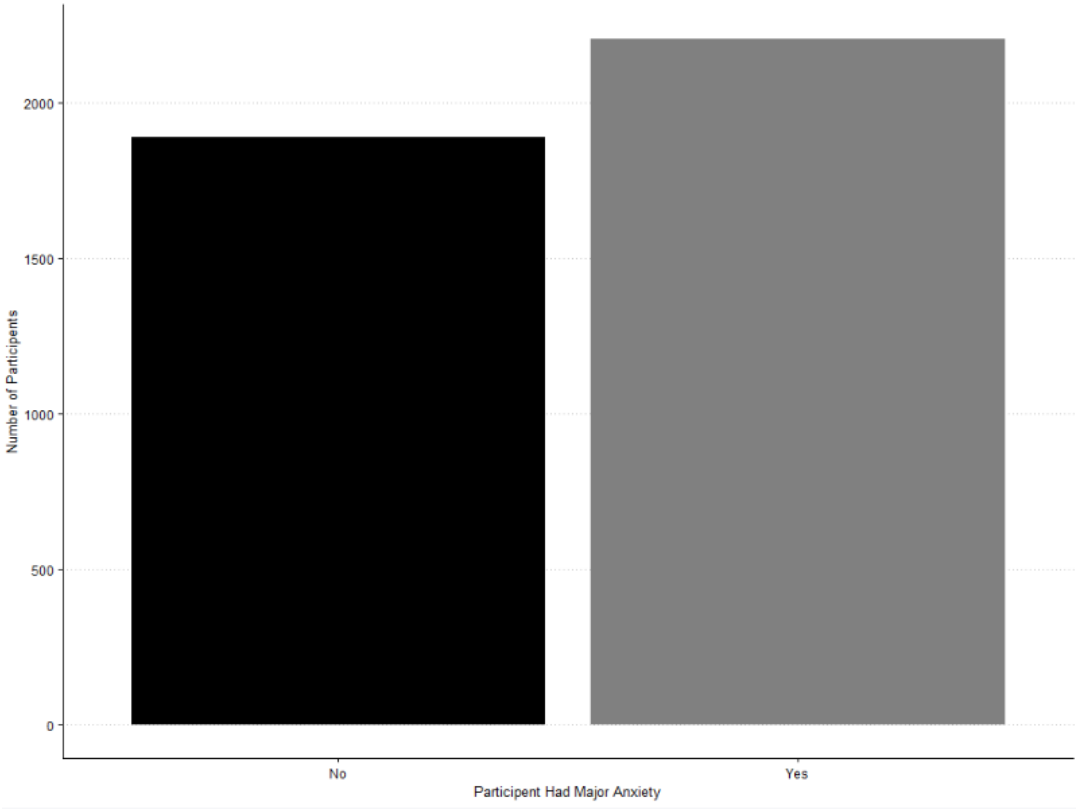


Figure 47: Childbearing Women Had Major Anxiety

The outcome of Question 19 – “Have you been experiencing any major anxiety or feelings of panic?”

From the graph, we can see 53% of childbearing women are affected by major stress compared to 47% of women who are not.

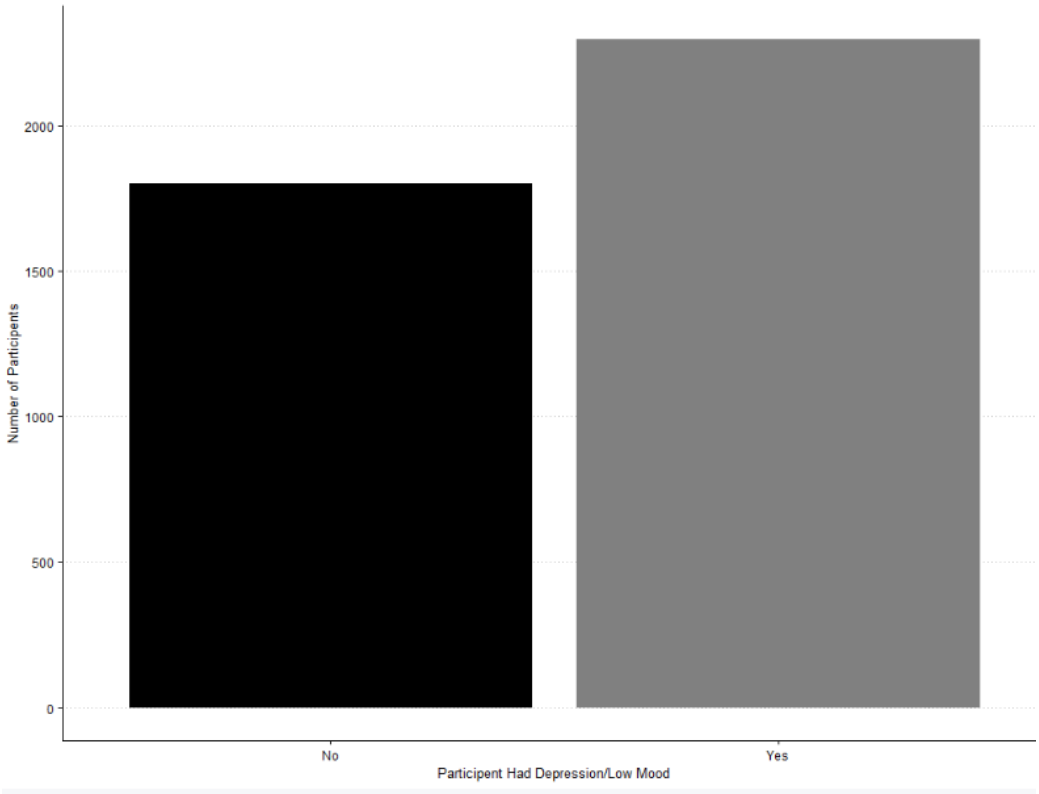


Figure 48: Childbearing Women Had Major Depression/Low Mood

The outcome of Question 20 - “Have you experienced any feelings of depression or periods of low mood or extreme sadness?”

From the graph, we can see that 56% of childbearing women have depression or low mood compared to 46% of women who do not.

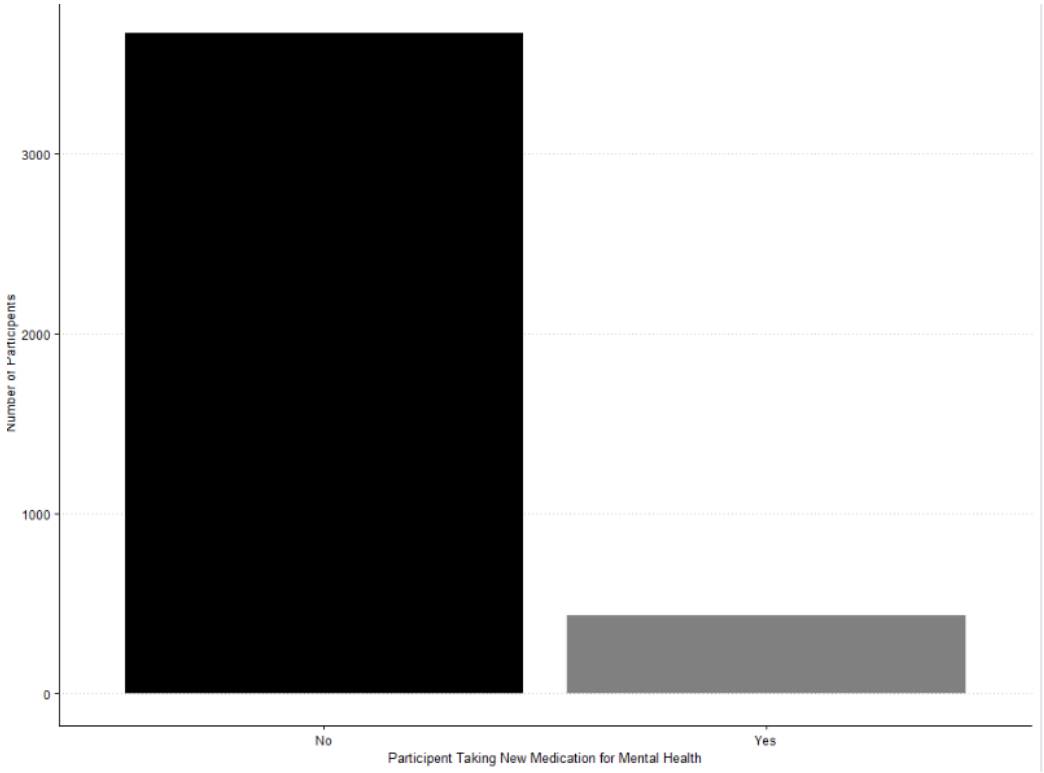


Figure 49: Childbearing Women Taking New Medication For Mental Health

The outcome of Question 17 – “Have you commenced any new long term medication for something other than your epilepsy?”

Most childbearing women (89%) are not taking a new medication for their mental health, this could be due to them not getting help for their mental health or have already been taking their medication for a while

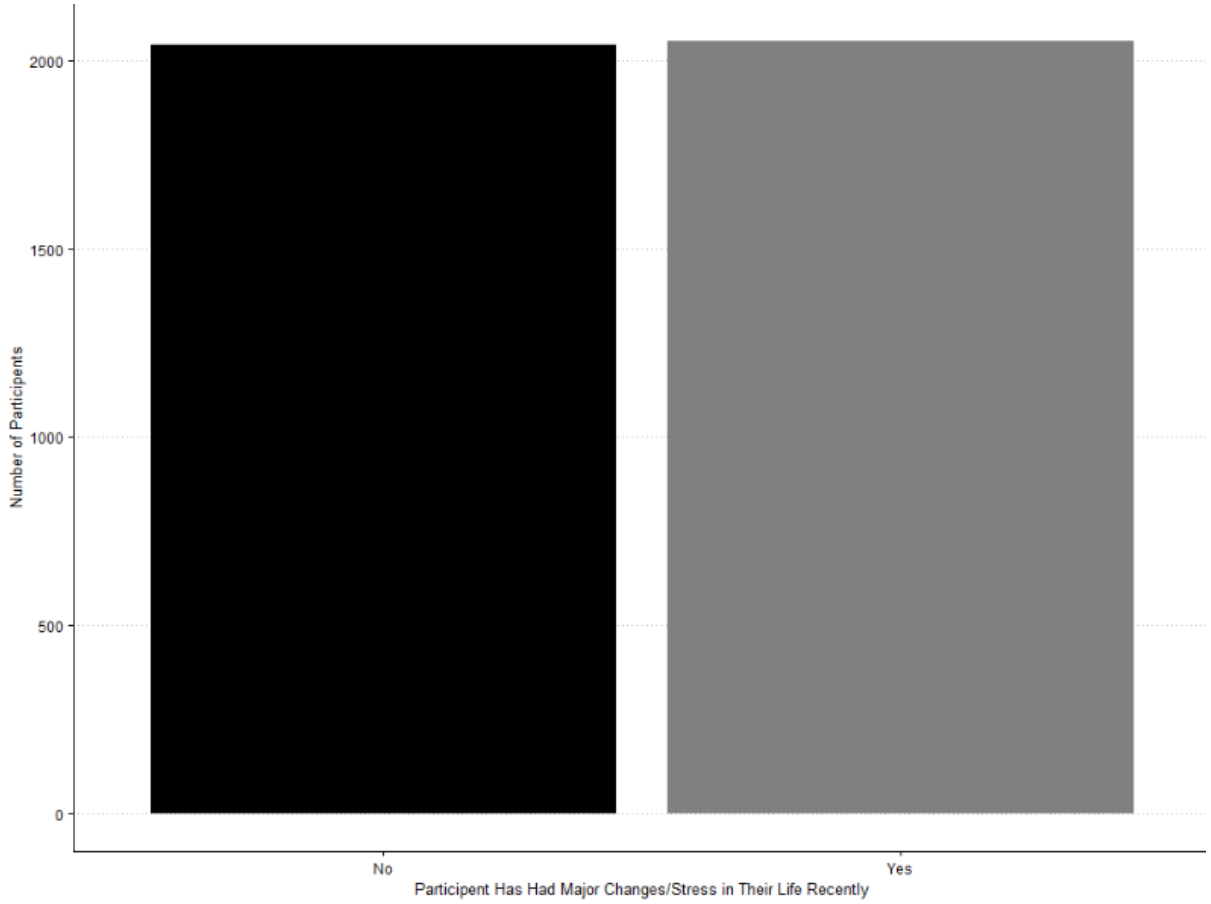


Figure 50: Childbearing Women Had Major Changes/Stress In Their Life Recently

The outcome of Question 23: -“Have you had any major changes or stresses in your life, job or family situation (such as increased work or job loss, bereavement, new partner or a baby or a relationship breakdown)?”

An almost split of childbearing women have (50%) or have not (50%) had a major change in their life, this graph shows how little control women have over what happens in their life and how quickly their mental health can change.

From these graphs, we can see that childbearing women are not focusing on their mental health as much as they should.

Chapter 7: Discussions

The discussion we are split into 8 sections to aim to address the respective problems.

Problem 1: What are the characteristics of childbearing women (16-60) with epilepsy patients who use the EpSMON app?

From looking at the data we can see the age range of the people who use the app the most are between the ages of 20-29 with 30-39 closing in close behind with the number of users steadily decreasing as the age range goes up. The most prescribed medication category for users of the EpSMON app is by a large proportion of around 2400 users is Epilepsy which is expected due to the purpose of the app. The next highest two categories being depression (around 550) and anxiety (around 525), meaning people with epilepsy also deal with mental health issues and is a problem for a lot of them.

The most common risk score for users of the app is 5 of around 440 assessments, with over half of it being attributed to the age range 20-29 with the second highest being 9. Besides the strong bias towards the 5, there is a normal distribution of risk score with the peak of it being around 9. Similarly, the distribution of ages is spread out very evenly besides the risk score of 5.

The most used medication is Levetracetam with Lamotrigine following very closely behind, these are both anti-epilepsy medications, the third most prescribed medication is carbamazepine and clobazam close behind.

Problem 2: How do these characteristics vary, if at all, between those who use the EpSMON app regularly and those who do not?

The most frequent users can be found in the 20-29 age bracket with a similar spread of frequent and infrequent in the rest of the age groups. Frequent users are responsible for more than half of the prescriptions, this is due to them doing the assessments more often, the same trend can be seen with the medication categories.

Around 75% of biased risk scores 5 are due to frequent users, meaning frequent users are more frequently getting this score. Frequent users also seem to have a lower risk score overall compared to infrequent users.

Problem 3: How many EpSMON users report being aware of the increased risks of sudden death?

From the data we can see that a majority of users (around 3400) are not aware of the risks of SUDEP, this is very dangerous as if the person with epilepsy doesn't know about the risks they cannot attempt to mitigate the risks. The awareness is spread pretty evenly throughout the age ranges with no clear bias towards one age group, a similar thing can be seen between frequent and infrequent user awareness.

Problem 4: What relationship, if any, is there between medication changes and risk assessment scores provided by the EpSMON app amongst childbearing women (16-60)?

From looking at the coefficients and odds ratio, we can see that users with high-risk scores are more likely to take certain drugs. Looking specifically at anti-epilepsy medication, the medication that has the highest odds ratio is Tiagabine (4.6), meaning users with a high-risk score would be more likely to use this. Another medication of note that can be tied to high-risk score usage is Retigabine, Perampanel, Phenobarbital and Clonazepam. With Vigabatrin having the lowest odds ratio of 0.19. Valproate has one of 1.3. From this, we can gather what users with high-risk scores are more likely to take.

Problem 5: What relationship, if any, is there between EpSMON risk assessment score, and health-seeking behaviours (such as visiting GP) amongst childbearing women (16-60)?

From the test ran we can see there is a positive correlation between users risk scores and the following health-seeking behaviours, meaning users who do these things usually have a lower risk score than those who don't:

- Have you had any injuries/ED/999/emergency services calls after a seizure?
- Have you had contact with health services to help you with a mental health problem?
- Has there been contact with your epilepsy nurse/neurologist for a planned next review of your epilepsy?
- Have you received safety advice and information about SUDEP from your doctor /nurse about epilepsy?

Based on the tests and data, performing these actions can help reduce the risk score.

Problem 6: What was the level of awareness of pregnancy matters at baseline in the women 16 – 60

The data shows that an overwhelming amount of users (around 66%) are unaware of the pregnancy risks associated with epilepsy (including both epilepsy risks and medication risks such as valproate). This is a very dangerous amount of number and could have serious ramifications unless addressed. If people with epilepsy are unaware of the pregnancy risks they cannot mitigate the risks.

Problem 7: Specifically look at the number of drugs - Antiseizure medication and overall regular medication - Particularly Valproate use ...including changes to its use over time.

The most consistently used anti-epilepsy medication without much change over time are:

- Carbamazepine
- Lamotrigine
- Levetiracetam
- Lamotrigine

We can see valproate follows a similar trend as the rest of these medications but on a much smaller scale. Due to the use of the app and input of the data being very erratic, the data peaks on certain dates and declines very rapidly making the data inconsistent. Some medications such as Phenytoin and Oxcarbazepine see very little use over time while other medications like the stated above see a very high and frequent amount of use over time.

Problem 8: What are mental health issues in this group of childbearing women (16-60)?

From the graphs and data, we can see that anxiety and depression is a big problem for people with epilepsy as around 60% of participants suffer from them, this can be seen more with the second and third highest medication category used after anti-epilepsy medication are anti-depression and anti-anxiety medication. Additionally, an

overwhelming majority of people with epilepsy are not seeking help for their mental health issues, this is one of the biggest findings of the analysis, that people with epilepsy are suffering and not seeking help for their mental health. Similarly, half the users have recently had major stress in their life which again can have a huge effect on their mental health.

Limitations

The biggest limitation with this project was the amount of data was available in the EpSMON data set, as it is reliant on public downloads and uses from a mobile app store its data amount is reliant on how much people discover and download the application. With a richer and fuller dataset, the results would become more reliable and properly represent childbearing women. Similarly, not everyone doing the assessment on the application may be truthful with their answers meaning some results may not be as accurate, due to the length of the assessment users may have caused boredom in the user causing them to press any answer to get through it. The use of a broader and diverse dataset would allow for a better representation of the aims of the project. Another limitation is that this data does not represent people with epilepsy as a whole, rather a small pocket of individuals who have found the EpSMON App.

Chapter 8: Conclusions

In conclusion, from this analysis, we can find out behaviours and characteristics of epilepsy patients using the EpSMON application. One of the main findings is that more frequent users of the EpSMON application on average have a lower risk score than those who do not use it as frequently. Another finding was that not enough people with epilepsy are aware of the risks of SUDEP nor the risks of pregnancy in epileptic women, these both should be addressed, and health professionals should talk to their epileptic patients about these risks. Though, having contact and visiting health specialists regularly has been found to minimise the risk score of people with epilepsy. One of the biggest findings in the analysis amount of people with epilepsy who are suffering from mental health problems and the amount of the seeking help for their problems. Regarding medication, some have ties to high-risk levels such as Tiagabine and Retigabine, while others such as Vigabatrin and Rufinamide do not. This analysis has found some valuable information regarding the characteristics of people with epilepsy and hopefully using this, improvements can be made to increase the awareness of mental health, pregnancy and SUDEP awareness issues in childbearing women with epilepsy.

Publication

Shang-Ming Zhou, Rebecca Baines, Elis Roberts, Peter Hannon, Samantha Ashby, Arunangsu Chatterjee, Arjune Sen, Richard Laugharne, Rohit Shankar, “Analysing Patient-Generated Data to Understand Behaviours and Characteristics of Childbearing Women with Epilepsy,” to be submitted to Lancet Digital Health, 2021

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Appendix

Appendix A: EpSMON Risk Assessment Questions

id	question
1	Have you experienced increased seizure frequency?
2	Have you experienced a Generalised Seizure or Generalised Tonic-Clonic Seizure? (i.e. loss of consciousness during a convulsion, sometimes called 'grand-malâ€™)
3	Have you experienced a seizure during sleep?
4	Do your seizures sometimes include convulsions that last longer than 5 minutes?
5	Do your seizures sometimes cluster i.e happen closely one after another during one day or over a couple of days?
6	Have you experienced any increase in the number or frequency of your seizures?
7	Have you experienced/perceived a deterioration in the seizures you normally experience?
8	Have you had any injuries/ED/999/emergency services calls after a seizure?
9	Do you use emergency/rescue medication? (eg: midazolam, diazepam, clobazam, clonazepam or lorazepam)
10	If you use rescue medication has this use increased?
11	Do you use rescue medication (e.g. midazolam)?
12	Do you take more than two different anti-epilepsy medications daily?
13	Have you experienced any noticeable disturbance in sleep (e.g. unaccounted injuries, bruises, wetting the bed etc.)?
14	Have you had any new physical health condition diagnosed?
15	Are you a female of child-bearing age who has not had preconception counselling or an annual review? (information on contraception, pregnancy & managing your medication and epilepsy risks)
16	Have you experienced any major change to your body such as a change in weight?
17	*Have you commenced any new long term medication for something other than your epilepsy?
18	*Have you had any major stress or experienced increased pressure at work or in your personal life?
19	*Have you been experiencing any major anxiety or feelings of panic?
20	*Have you experienced any feelings of depression or periods of low mood or extreme sadness?
21	*Have you had contact with health services to help you with a mental health problem?
22	Have you commenced any new medication for anxiety or depression?
23	*Have you had any major changes or stresses in your life, job or family situation (such as increased work or job loss, bereavement, new partner or a baby or a relationship breakdown)?
24	Do you find yourself needing alcohol daily or binge drinking?
25	Has there been an increase in alcohol intake?
26	Do you find yourself needing recreational drugs?
27	Has there been any new or increased recreational drug use?
28	Do you have any of the following problems with your epilepsy medication: - You forget to take it on time - Youâ€™re not always able to collect your prescription - The medication tastes bad or is hard to take - Youâ€™re not sure the medication is helping your epilepsy - You donâ€™t like the side-affects you get from the medication - You need more information & support to take your medication regularly & as prescribed by your health professional.

29	Have you made or are you planning changes to your living or sleeping arrangements such as moving from home to college?
30	Has there been contact with your GP for a planned next review of your epilepsy?
31	Has there been contact with your epilepsy nurse/neurologist for a planned next review of your epilepsy?
32	Have you received safety advice and information about SUDEP from your doctor /nurse about epilepsy?