Assignment 1

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Description of Study

The study was conducted to address controversy around how doctors should manage patients with intrinsic brain tumours. In particular, the study wanted to investigate the effect of radiotherapy and resective surgery, which were believed to be only palliative and not addressing the real cause of the condition. Brain tumours can in some cases cause epileptic seizures and patients presenting with epilepsy in particular usually have a good prognosis. As medical imaging devices developed, it was more likely that people with epileptic symptoms get a brain scan and understanding how these cases should be managed – whether through resective surgery and radiotherapy or merely managing symptoms – had become a problem for neurologists and neurosurgeons.

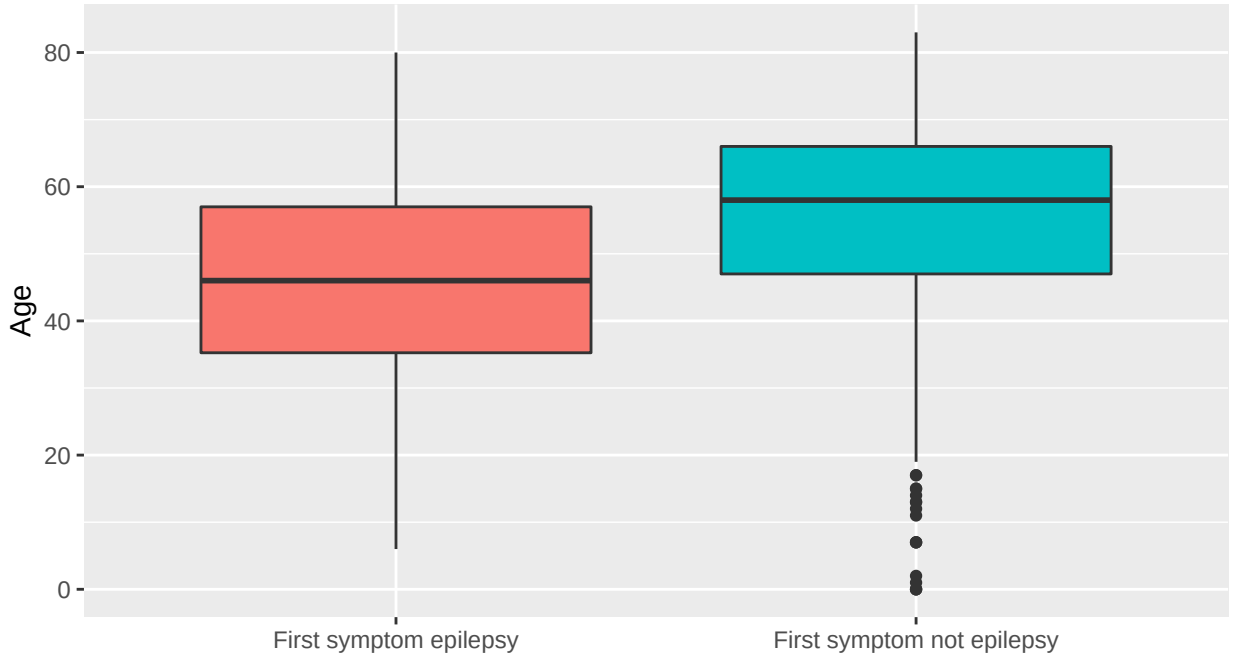
The study was conducted as a retrospective non-randomised study from three databases. The first database contains details from two consultant neurologists and two consultant neurosurgeons between 1978 and 1982. The second database comes from patients presenting to the department of Neurosciences in Walton Hospital, Liverpool between January 1983, and June 1986. The last database comes from patients whose first symptom was epilepsy presenting in the department between 1975 and September 1989. In the study, the group of patients presenting with epilepsy were divided into two groups, those who got early surgery and those who did not. The study looks to find the importance of the presentation of epilepsy in influencing the outcome of patients.

Exploratory Data Analysis

Graphs for intial exploratory data analysis of each person.

Age distribution of people depending on first symptom

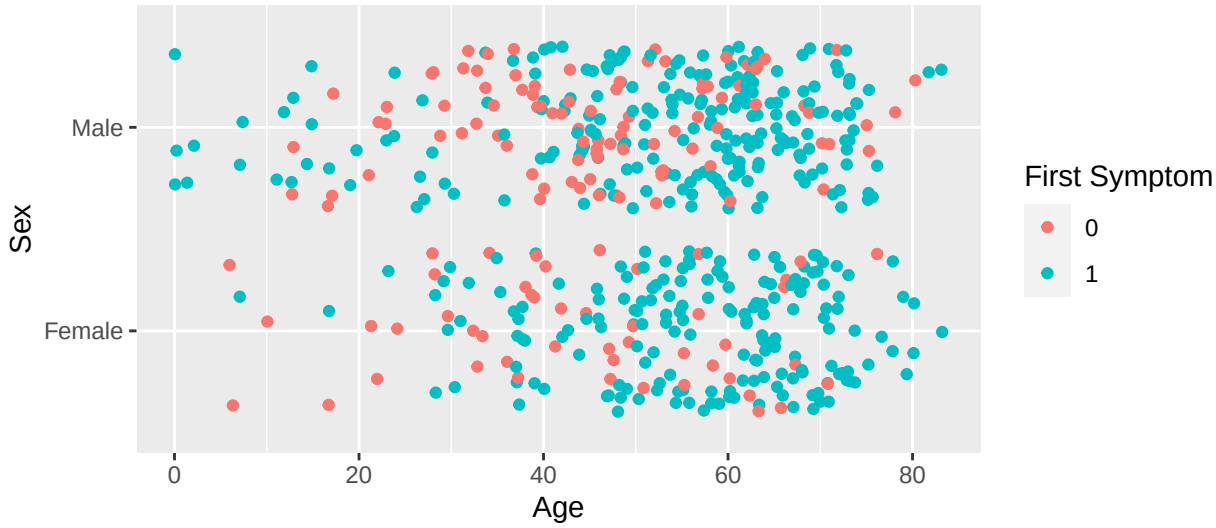
1806359



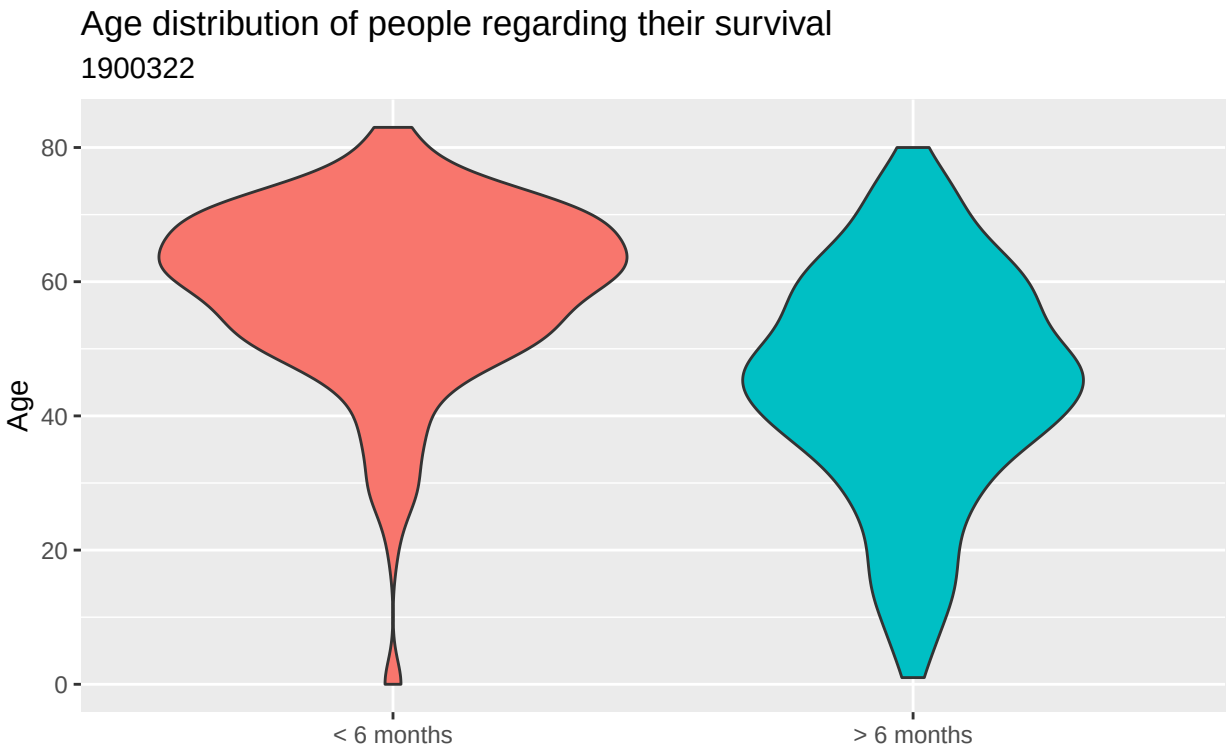
People whose first symptom was epilepsy were generally younger than those who did not have epilepsy as their first symptom

Are gender and age associated with higher chances of epilepsy as a first symptom?

1921225



Where 0 = Epilepsy and 1 = Not Epilepsy
From the above graph, the following can be noticed:
1. Females are more likely to experience epilepsy as the first symptom in the 20−50 age group.
2. Younger males are also likely to experience epilepsy as the first symptom.
3. It is quite evident that both males and females in the 50−80 age group are less likely to experience epilepsy as the first symptom.



People who survive longer than 6 months tens to be younger than those who die before 6 months. People dying before 6 months are definitely skewed towards the elder, highlighting their vulnerability.

Odds Ratio Calculation

The two by two table is given below.

	Survived more than 6 months	Survived less 6 months
Surgery	182	190
No Surgery	67	95

The associated odds ratio is 1.358.

Logistic Regression model for effect of surgery

To choose which variables need to be included in our model, we will start by creating a model using all the variables, and a null model.

The variables to consider are:

1. fclsi - Focal Signs (α_1)
2. fclsy - Focal symptoms (α_2)
3. mtlsy - Mental Symptoms (α_3)
4. ctcyst - CT scan for cyst (α_4)

5. ctenh - CT scan for enhancement (α_5)
6. ctcalc - CT scan for calcification (α_6)
7. first - Whether or not epilepsy was the first symptom (α_7)
8. age - Age in years (α_8)
9. radio - Radiotherapy (α_9)
10. dursym - Duration of Symptoms (α_{10})
11. nonrsurg - Non-resective surgery (α_{11})
12. resurg - Resective surgery (α_{12})
13. survived6mnths - Survived longer than 6 months after diagnosis (γ)

Full model: $logit(\gamma) = \alpha_0 + \sum_{p=1}^{12} \beta_i \alpha_i$

Null model: $logit(\gamma) = \alpha_0$

We will look at doing two stepwise regressions, one with the resective and non-resective surgeries separate and another with them combined under the variable `surgery`.

After running the step model in both cases the variables that remained were: focal signs, mental symptoms, CT scan for cyst, CT scan for calcification, whether the first symptom was epilepsy, age, radiotherapy and duration of symptoms. In both models surgery was also kept whether or not it was combined under one variable.

The odds ratios, confidence intervals and p-values for the coefficients were then calculated for both models as can be seen in the table below.

Step models for resective and non-resective surgery combined and separate

Predictors	*Odds Ratios*	*CI*	*p*
(Intercept)	47.78	14.63 – 169.03	**<0.001**
fclsi	0.47	0.29 – 0.77	**0.003**
mtlsy	0.55	0.34 – 0.88	**0.012**
ctcyst	2.15	1.31 – 3.54	**0.003**
ctcalc	2.90	1.22 – 7.31	**0.019**
first	0.57	0.32 – 1.00	**0.050**
age	0.96	0.94 – 0.97	**<0.001**
radio	0.29	0.18 – 0.45	**<0.001**
dursym	1.47	0.93 – 2.33	0.099
nonrsurg	0.53	0.31 – 0.90	**0.020**
resurg	2.46	1.02 – 6.20	**0.048**
Observations	534		

Predictors	*Odds Ratios*	*CI*	*p*
(Intercept)	54.64	17.29 – 186.98	**<0.001**
fclsi	0.45	0.28 – 0.72	**0.001**
mtlsy	0.53	0.33 – 0.84	**0.007**
ctcyst	2.02	1.24 – 3.30	**0.005**
ctcalc	3.01	1.30 – 7.43	**0.013**
first	0.55	0.32 – 0.97	**0.039**
age	0.96	0.94 – 0.97	**<0.001**
radio	0.30	0.19 – 0.46	**<0.001**
dursym	1.46	0.93 – 2.30	0.102
surgery	0.64	0.38 – 1.08	0.096
Observations	534		

Step model selection gives the same predictors for both models except for the surgery variables which was combined

On comparing the two models the AIC of surgery combined is 548.18 and that of surgery not combined is 535.24 suggesting that separating the types of surgery provides us with a better model. This is the model that wil be used for the rest of this paper.

Conclusions

According to the original study, selection bias had an important influence on the findings. Although it is hard to claim that we have proved anything, it is interesting to see that from our model, we have a better understanding of the effects of resective and non-resective surgery on the survival of the individual.

On investigating the odds ratio of our final model, it is evident that an individual receiving resective surgery has a much high chance of surviving than an individual receiving non-resective surgery. Interestingly, a person receiving non-resective surgery, our model suggests, is more likely to die before 6 months than a person receiving no surgery at all. The same applies to radiotherapy, which was thought as one of the most effective treatments for intrinsic brain tumours, where the estimated odds ratio of 0.29 suggests people are 3 times more likely to die before 6 months following radiotherapy.

At the diagnosis stage, CT scan for cysts or calcifications acts as a key role, with odds ratio greater than 2. If the patient is provided with a chance of high-resolution CT scan rather than a simple diagnosis, they are twice as likely to survive. But as mentioned above, sometimes is reporting bias from patients, which puts forward higher requirements for the doctors.

The longer the duration of symptoms the more likely the individual is to survive 6 months, nonetheless the p-value for this is high and the confidence interval includes 1, which suggests the estimate is not good. Finally, not having epileptic seizures as the first symptom also seems to result in an estimated odds ratio of 0.57 which increases the probability of not surviving. Consequently, having an epileptic seizure as a first symptom makes it more likely to at least survive 6 months.

Limitations

If we had more variables that provided us with other information, such as other underlying health conditions, patient family history etc it could provide useful information on how an individual may/may not suffer from a brain tumour.

Since the original study was analysed using survival analysis methods another limitation is some of the data provided was censored. In our case, some individuals may have survived the duration of the study but might have passed away after with the cause of death being related to a brain tumour.

Finally, the study does not come from random data and hence there is selection bias. Performing a randomized control trial could provide better quality data to accurately understand the effects of surgery and epilepsy on the survival of intrinsic brain tumours.

Appendix

1806359 - Putting all the assignment together on R Markdown - Q1 - Q2 - Q3 - Q4

1900322 - Q1 - Q2 - Q5

11921225 - Q2 - Q4 - Q5