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Title: Estimating Penetrance of C9orf72 Repeated Expansion for Family Members of ALS Patients

Summary:
The Data Studio Workshop brings together a biomedical investigator with a group of experts for an in-depth session to solicit advice about statistical and study design issues that arise while planning or conducting a research project. This week, the investigator(s) will discuss the following project with the group.

Amyotrophic lateral sclerosis (ALS) is a rare neurodegenerative disorder. It leads to loss of motor neurons which causes severe muscle weakness. Patients usually die, on average, within three to five years after first symptom onset. The cause of ALS is largely unknown, but is believed to be a combination of genetic and environmental risk factors. In approximately 10% of the patients with ALS, a familial form of ALS can be identified where multiple family members are affected. The most common genetic mutation is a repeat expansion of the C9orf72 gene. It is found in 5–10% of the patients with ALS.

A key clinical question is how to counsel offspring and family members of patients who are known to be C9orf72 carriers. To date, there are only a few studies that have looked at the penetrance of C9orf72. Penetrance is defined as the probability for an individual to develop ALS if the same carries the gene. We have collected data on first-degree family members of patients with ALS who are known to be C9orf72 carriers. We would like to estimate the penetrance of C9orf72 and have used a binomial model.

Questions:
The statistical challenges are:

1. Inheritance pattern is known, but genetic status of the first-degree family members is unknown.

2. Some first-degree family members are still at risk to develop ALS, but are censored.

3. Clustering of familial data

4. Selection bias
Zoom Meeting Information

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