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Predicting Who Will Develop Treatment Resistant Depression after Being Newly Diagnosed With Depression

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Abstract

A large percentage of people with are treated for depression end up becoming treatment resistant. In this work we used the OHDSI PatientLevelPrediction package to develop a model using observational data to predict, at the point of first dispensing of an antidepressant in newly depressed patients, who will develop resistance to treatment within a year. The model performed moderately at being able to discriminate those who develop TRD and those who do not within a year of treatment with an AUC of 0.66. This model could then be used at the point of anti-depressant dispensing to identify high risk patients that could be monitored or offered alternative treatments. In future work more advanced machine learning techniques should be implemented to investigate whether the discrimination can be improved.

Introduction

No treatment for major depressive disorder is uniformly effective, and subsequent interventions are often needed. Patients who do not respond to antidepressants have treatment resistant depression (TRD). If one could predict whether a patient who is being diagnosed with depression for the first time would develop TRD, health care providers could monitor these patients more closely or implement treatments in different ways. We sought to identify factors that predict who develops TRD in a real-world setting using claims databases.

Methods

We used the OHDSI PatientLevelPrediction package[1] to develop a regularized logistic regression model for the problem of: in a target population of newly diagnosed depressed people with therapeutic treatment, who will develop the outcome of TRD within a year of the start of depression diagnosis. The model was develop in a US claims database and internally validated. The target population was defined as adult subjects with depression with a first dispensing of an antidepressant. They were also required to be in the database for at least a year before the index date (date of the antidepressant dispensing), and have the first depression diagnosis within 60 days of the index date. We excluded subjects with pre-existing mania, dementia and psychosis. The outcome was subjects who developed TRD, defined as having dispensings for at least 3 distinct antidepressants or 1 antidepressant and 1 antipsychotic within a year after the index date. Model covariates were age, gender, all medical conditions, medications dispensed, and procedures one year before the index date. We excluded covariates that only occurred for less than 20 people. Because of the large number of covariates, we used lasso regularized logistic regression. To create and validate the model, the database was randomly split into a train set (75%) used to "learn" the model parameters, and test set (25%) used to internally validate the model on unseen data. The model hyper-parameters were chosen using 10-fold cross validation on the test set. To assess the discriminate performance of the predicting model, we calculated area under the curve (AUC).

Results

Out of 230,801 patients in the target population, 10.4% developed TRD within one year. The AUC was 0.66. It was

found that TRD patients at baseline were younger, 10.87% were between 18 to 19 years old versus 7.64% in the no TRD group, RR=1.42, (95% CI 1.37-1.48). TRD patients were more likely to have a diagnosed anxiety disorder at baseline than non-TRD patients, RR=1.38, (95% CI 1.35-1.14). Fatigue, had the highest risk ratio, RR= 3.68, (95% CI 3.18-4.25). TRD patients also had diagnosed substance use disorders, psychiatric conditions, insomnia and pain more often at baseline than non-TRD patients.

Conclusion

Ten percent of the subjects newly diagnosed and treated for depression developed TRD within a year. They were younger and suffered more frequently from fatigue, substance use disorders, anxiety, psychiatric conditions, insomnia and pain than non-TRD patients. The discriminate performance of the model was modest and in future work it would be useful the test more advance machine learning techniques such as deep learning with the aim of developing models with higher discriminative ability.

References

1. Jenna Reps, Martijn J. Schuemie, Marc A. Suchard, Patrick B. Ryan and Peter R. Rijnbeek (2017). PatientLevelPrediction: Package for patient level prediction using data in the OMOP Common Data Model. R package version 1.2.1.