Choosing a Second-generation Antidepressant using Demographic Characteristics and Clinical Symptoms of Depression

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Background

Depression is the sixth most costly health condition in the United States and the single largest contributor of non-fatal health loss in the world.[1] Depression that does not respond to its first trial of antidepressant treatment causes increased healthcare utilization, impaired productivity, poorer quality of life, and increased suicide rates.[2,3] Thus, choosing an effective starting antidepressant has the potential to decrease morbidity, mortality, and the overall economic burden of depression.

Second-generation antidepressants are considered first-line pharmacological therapy for depression. Since all second-generation antidepressants have comparable efficacies,[4,5] current clinical guidelines call for a trial-and-error approach to prescribing antidepressants.[6]

The fact that most patients need to try multiple antidepressants before finding an effective regimen suggests disparate efficacies between antidepressants at the individual level despite comparable efficacies at the population level.

Purpose

This study used a secondary analysis of the Collaborative Psychiatric Epidemiology Survey (CPES) to create a model that uses demographic characteristics and clinical symptoms to predict the efficacy of different second-generation antidepressants. Such a model can provide physicians with a tool to more effectively tailor their choice of antidepressants to each patient, ultimately increasing quality of life and functional status while decreasing the overall cost of depression to society.

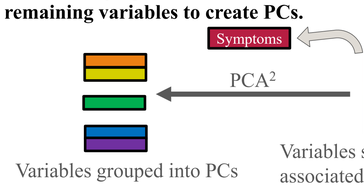
Methods

1. Obtain study sample, and use chi-square tests to screen for variables significantly associated with drug efficacy.

2. Use the entire study sample for subsequent analyses on symptom associations. Randomly allocate 50% of the subjects from the study sample to a training cohort and the remaining 50% to a testing cohort. Use the training cohort for subsequent analyses on model creation.

Symptom Associations

3. Remove symptoms. Run PCA on remaining variables to create PCs.

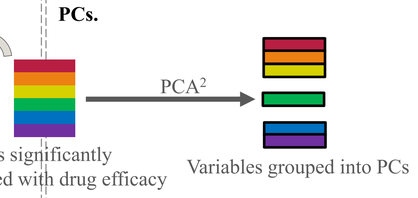


4. Run a regression analysis with PCs and clinical symptoms.

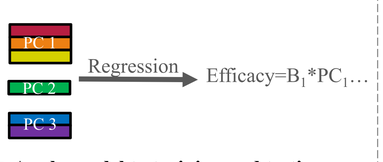
5. Analyze odds ratios to understand associations between clinical symptoms and drug efficacy.

Model Creation

3. Run PCA on all variables to create PCs.



4. Run a regression analysis with PCs to create a model.



5. Apply model to training and testing cohorts to test for accuracy and internal validity, respectively.

6. Repeat steps 1-5 for all seven drugs of interest.

Figure 1. Methods for statistical analyses.
[1]Includes fluoxetine, sertraline, citalopram, paroxetine, venlafaxine, bupropion, and trazodone. Each drug was analyzed separately. [2]PCA=Principal Component Analysis

Results

The seven drugs studied were fluoxetine, sertraline, citalopram, paroxetine, venlafaxine, bupropion, and trazodone. The demographic characteristics associated with the efficacy of each drug are shown in Table 1.

Table 1

Demographic Characteristics Associated with the Effectiveness of Each Drug

	Sex	Age	Income to Needs Ratio	Marital Status	Employment Status
Fluoxetine	x				
Sertraline		x	x	x	x
Citalopram		x	x		x
Paroxetine		x			
Venlafaxine		x			
Bupropion			x		
Trazodone		x	x		

Symptoms were grouped into four categories: mood, anxiety, fatigue, and appetite. The odds ratio of a drug being ineffective given a one point increase in each symptom group's score is shown in Table 2. The efficacy of bupropion was not associated with the presence or severity of any clinical symptoms. Regression results for trazodone were not included because of a small sample size.

Table 2

Multivariable Logistic Regression Results

	OR	95% Confidence Interval Lower	95% Confidence Interval Upper	p-value
Fluoxetine				
Mood Score	2.117	0.994	4.507	0.052
Anxiety Score	**4.014**	**1.527**	**10.554**	**0.007**
Fatigue Score	1.893	0.232	15.442	0.531
Appetite Score	1.138	0.171	7.557	0.887
Sertraline				
Mood Score	0.514	0.164	1.606	0.238
Fatigue Score	**30.957**	**1.914**	**500.723**	**0.018**
Insomnia Score	0.944	0.166	5.382	0.946
Appetite Score	7.102	0.904	55.766	0.061
Citalopram				
Mood Score	1.733	0.849	3.540	0.111
Appetite Score	0.256	0.037	1.781	0.141
Paroxetine				
Mood Score	**2.831**	**1.017**	**7.879**	**0.047**
Anxiety Score	2.021	0.286	14.296	0.457
Fatigue Score	0.891	0.336	2.362	0.804
Venlafaxine				
Mood Score	**1.876**	**1.041**	**3.379**	**0.039**
Insomnia Score	2.463	0.522	11.621	0.212
Appetite Score	2.435	0.400	14.841	0.282

OR=Odds Ratio
Statistically significant values are bolded

Accuracy was tested using the training cohort, and internal validity was tested using the testing cohort. Together, these models have a mean accuracy of 84% and a mean internal validity of 62% (see Figure 2).

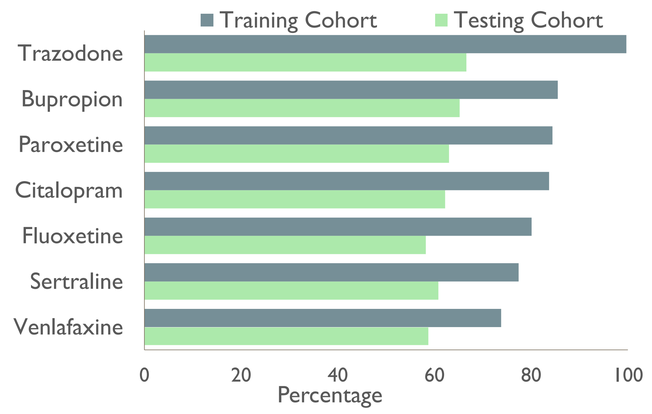


Figure 2. Percentage of cases correctly classified by the model for the training and testing cohorts.

Results (continued)

The models were used to predict the efficacy of each of the seven drugs for two hypothetical patients. Sertraline has the greatest odds of being effective for Patient A. Venlafaxine has the greatest odds of being effective for Patient B (see Figure 3).

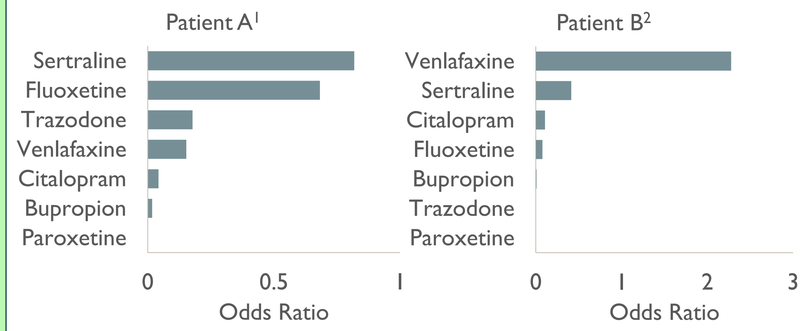


Figure 3. Example of a prediction of drug efficacy for two hypothetical individuals. [1]Patient A is a 24 year old female with moderate depression and few socioeconomic risk factors. [2]Patient B is a 40 year old female with moderate to severe depression and many socioeconomic risk factors.

Discussion

Our models provide an opportunity to individualize each patient's choice of antidepressants. Similarly, pharmacogenomics (i.e., the use of genetic data to guide treatment decisions) has been increasingly used as a way to individualize and optimize the choice of second-generation antidepressants.[7] This requires a DNA sample that is processed in a laboratory, a process that costs roughly $2000.[8] In contrast, demographic characteristics and clinical symptoms are readily accessible information, so the cost of obtaining and utilizing the information needed for our model is minimal. This provides another option for patients seeking individualized treatment but cannot afford pharmacogenomic-guided treatment or live in an area without the necessary laboratory equipment.

Currently, choosing between second-generation antidepressants is mostly trial-and-error, and fewer than 50% of patients respond to their first antidepressant.[9] With a mean accuracy of 84% and a mean internal validity of 62%, the use of our models could provide a modest improvement to the status quo. This could subsequently decrease the morbidity, mortality, and overall cost to society associated with depression.

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