Estimating Optimal Treatment Rule in Major Depressive Disorder using Penalized Regression Method

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Abstract

Objectives: Major depressive disorder (MDD) stands as the primary contributor to disability on a global scale. Identifying optimal treatment regimens for patients with MDD using advanced statistical techniques is crucial for improving patient outcomes and reducing the duration of hospitalization.

Methods: We compared treatments including, work therapy (WT; n = 198), WT plus electroconvulsive therapy (WT+ ECT; n = 95), WT plus family therapy (WT+ FT; n = 61), and other psychotherapy (PT; n = 23) in 377 patients with Major Depressive Disorder (MDD). We simultaneously estimated the optimal treatment rule and selected important variables in loss-based framework using penalized regression.

Results: The comparison of treatments show the variable of history of emotional problem and both the education level and the history of emotional problem are important for other three treatments (WT+ECT, WT+FT, PT) and WT+ECT respectively. These optimal treatment rules could decrease duration of hospitalization for 61.3% (231 out of 377) of patients and 74.0% (115 out of 156).

Conclusions: In estimating of optimal treatment rules for patients with Major Depressive Disorder the variables of the history of emotional problems and the education level were estimated as two important variables. Personalized medicine takes into account this individual heterogeneity in individualized characteristics, and optimizes treatment outcomes by identifying important variables into treatment regimens, which could decrease duration of hospitalization.

Keywords: Personalized Medicine; Optimal Treatment Rule; Decision Making; Psychotherapy; Variable Selection; Penalized Regression.

Introduction

Major depressive disorder (MDD) stands as the primary contributor to disability on a global scale, impacting around 350 million individuals across the world as per the World Health Organization's 2012 data. Beyond mood manifestations, patients with MDD encounter limitations in their physical, professional, and social capacities.[1,2] With an estimated 22.8 of the psychiatric diseases burden globally, depressive disorder is accounted the leading cause of disability in the world and often leads to poor quality of life.[3,4]

Identifying optimal treatment regimens for patients with MDD is crucial due to the significant impact it has on the overall outcome and well-being of individuals suffering from this condition. Early and effective treatment plays a vital role in promoting the best outcomes and reducing the risk of relapses associated with MDD.[5] The importance of finding the right treatment early on lies in minimizing the negative consequences of failed treatment attempts, as each unsuccessful trial can compound the impact on the patient.[5] Treatment guidelines emphasize the need for tailored approaches based on the severity of depression, with recommendations for different modalities such as pharmacotherapy, psychotherapy, or a combination of both, depending on the individual's condition.[6] Monitoring treatment efficacy and response is essential, with adjustments or changes in the treatment plan recommended if significant improvement is not observed within a specified time frame.[6]

Electroconvulsive therapy (ECT) is a widely recognized and effective treatment for MDD, particularly for severe, treatment-resistant cases where a rapid response is necessary.[7,8] ECT passes electric currents through the brain to induce a brief cerebral seizure to improve response of mental state. This change in brain chemistry suggests that ECT can reverse symptoms of mental health state, leading to improved clinical outcomes.[9] ECT has been found to be associated with a 28% reduction in the risk of suicide within 12 months and a 42% reduction at 3 months for patients with MDD with psychotic features.The benefits of ECT extend beyond suicide risk reduction, as it has also been linked to reduced all-cause mortality at both 3 and 12 months.[10] However, the response of patients who received ECT is not homogeneous.[9] Studies have identified predictors of ECT response, such as depression severity at baseline and age, which can help guide treatment selection.[11] For instance, remission in older patients has been associated with a 46% reduced risk of suicide, while remission in those aged 65 years and older has been associated with a 70% reduced risk of suicide.[10] Work therapy and family therapy are also important components of MDD treatment. Work therapy, or occupational therapy, can help individuals with MDD develop skills and strategies to manage their symptoms and improve daily functioning.[7] Family therapy, on the other hand, can address the interpersonal relationships and dynamics that may contribute to the development or maintenance of MDD, fostering a supportive environment and improving communication for better treatment outcomes.[7] While ECT, work therapy, and family therapy are valuable treatment options for MDD, it is important to recognize that not all methods may be equally effective for every patient.[12]

For psychiatric disorders, there is no single best treatment for all patients. Therefore, patients with MDD may benefit from multiple treatments, including psychological therapies. A person with certain characteristics may experience improved outcomes, while others may have worse adverse events.[12-15] Each individual with MDD may respond differently to these interventions based on their unique characteristics, preferences, and needs.[12] Therefore, finding the optimal method among ECT, work therapy, and family therapy or combination of these, is crucial to ensure that patients receive the most benefit from personalized treatment. Personalizing the treatment approach for each patient with MDD can lead to better outcomes and improved overall well-being. By considering individual’s characteristics, healthcare providers can tailor the treatment plan to meet the specific needs of each patient. For some patients, ECT may be the most effective option, especially in cases of severe, treatment-resistant depression where a rapid response is necessary. Work therapy can be particularly beneficial for individuals struggling with daily functioning and occupational challenges due to their depression. Family therapy, on the other hand, can address interpersonal dynamics and provide a supportive environment for those whose relationships play a significant role in their mental health state. By carefully assessing each patient's unique circumstances and preferences, healthcare providers can collaborate with patients to determine the most suitable treatment approach. This personalized approach can maximize the benefits of treatment, improve patient engagement and adherence, and ultimately lead to better outcomes for individuals with MDD. It is essential to prioritize individualized care and strive to find the optimal method among ECT, work therapy, and family therapy to ensure that patients receive the most effective and personalized treatment for their specific needs.[4,9,16-20]

In the few past decades, personalized medicine has received much attention, playing a main role in making optimal treatment rule.[12] Finding the optimal treatment rule for each patient based on their characteristics is the best way to obtain an effective treatment option that increase the probability of successful treatments and subsequently improves the outcomes for patients.[4,21] Improving treatment outcomes including, reducing the duration of recovery after treatment sessions and number of hospitalizations, can improve physical health and quality of life as an outcome for psychiatric disorders.[22-27] To date, no study has been conducted to determine the optimal treatment regimen for patients with MDD incorporating and regarding work therapy, family therapy, ECT, or their combinations. Therefore, this study aimed to utilize health record data to identify and characterize which patients may derive the most benefit from these treatments to improve patient outcomes and to reduce the duration of hospitalization.

Methods

The primary data were collected from a retrospective cohort study (nonrandomized) of 1005 individuals with major depressive disorder (MDD) who were hospitalized. Existing data are part of primary data and we used them as secondary data. The eligible patients were those who were admitted for the treatment of depression. The information of 377 patients whose treatment assignments were made according to routine clinical practice was extracted. The other patients were excluded of study. Diagnosis of MDD was conducted through a clinical interview by a psychiatrist based on the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5).[22].[8]

The study individuals were treated with four different treatment groups:

- Work therapy (WT): 198 subjects (52.52%)
- Work therapy + electroconvulsive therapy (WT + ECT): 95 subjects (25.2%)
- Work therapy + family therapy (WT + FT): 61 subjects (16.18%)
- Other psychotherapy treatments (PT): 23 subjects (6.1%)

The distribution of treatment groups is shown in Table 1 and Table 2.

Table 1: Variables and Treatment Characteristics

Variables		**Treatments**				
		WT	**WT+ECT**	**WT+FT**	**PT**	**Total**
H. Recurrence	No	142 (53.8)	57 (21.6)	48 (18.2)	17 (6.4)	264 (100)
	Yes	56 (49.6)	38 (33.6)	13 (11.5)	6 (5.3)	113 (100)
Gender	Male	86 (46.0)	52 (27.8)	42 (22.5)	7 (3.7)	187 (100)
	Female	112 (59.0)	43 (22.6)	19 (10.0)	16 (8.4)	190 (100)
H. Medication Adherence	No	112 (53.3)	51 (24.3)	35 (16.7)	12 (5.7)	210 (100)
	Yes	86 (51.5)	44 (26.3)	26 (15.6)	11 (6.6)	167 (100)
Living status	Parents	45 (47.4)	22 (23.1)	23 (24.2)	5 (5.3)	95 (100)
	Others	153 (54.2)	73 (25.9)	38 (13.5)	18 (6.4)	282 (100)
Number of children	No	46 (46.5)	28 (28.3)	20 (20.2)	5 (5.0)	99 (100)
	Yes	152 (54.7)	67 (24.1)	41 (14.7)	18 (6.5)	278 (100)
Marital status	Single	38 (48.1)	19 (24.1)	17 (21.5)	5 (6.3)	79 (100)
	Married	160 (53.7)	76 (25.5)	44 (14.8)	18 (6.0)	298 (100)
Education level	No	132 (52.6)	59 (23.5)	45 (17.9)	15 (6.0)	251 (100)
	Yes	66 (52.4)	36 (28.6)	16 (12.7)	8 (6.3)	126 (100)
Occupation	unemployed	141 (54.0)	66 (25.3)	35 (13.4)	19 (7.3)	261 (100)
	employed	57 (49.1)	29 (25.0)	26 (22.4)	4 (3.5)	116 (100)
Type of Residence	Urban	141 (52.2)	61 (22.6)	50 (18.5)	18 (6.7)	270 (100)
	Rural	57 (53.2)	34 (31.8)	11 (10.3)	5 (4.7)	107 (100)
H. Psychiatric Illness	No	149 (52.1)	65 (22.7)	52 (18.2)	20 (7.0)	286 (100)
	Yes	49 (53.8)	30 (33.0)	9 (9.9)	3 (3.3)	91 (100)
H. Suicide	No	150 (54.3)	60 (21.7)	49 (17.8)	17 (6.2)	276 (100)
	Yes	48 (47.5)	35 (34.7)	12 (11.9)	6 (5.9)	101 (100)
H. Medical Disorders	No	96 (47.8)	59 (29.3)	34 (16.9)	12 (6.0)	201 (100)
	Yes	102 (58.0)	36 (20.5)	27 (15.3)	11 (6.2)	176 (100)
H. Emotional Problem	No	77 (52.7)	29 (19.9)	32 (21.9)	8 (5.5)	146 (100)
	Yes	121 (52.4)	66 (28.6)	29 (12.5)	15 (6.5)	231 (100)

H. Smoking	No	113 (56.0)	54 (26.7)	20 (9.9)	15 (7.4)	202 (100)
	Yes	85 (48.6)	41 (23.4)	41 (23.4)	8 (4.6)	175 (100)
Clearance. Type	Personal	45 (53.6)	22 (26.2)	12 (14.3)	5 (5.9)	84 (100)
	Doctor	153 (52.2)	73 (24.9)	49 (16.7)	18 (6.2)	293 (100)

H: History
WT+ECT indicates work therapy plus Electroconvulsive therapy
WT+ FT indicates work therapy plus family therapy
PT indicates other psychotherapy treatments

Table 2: Variable**s** and Treatment Characteristics.

Variables		**Treatments**				
		WT (n=198)	**WT+ECT (n= 95)**	**WT+FT (n=61)**	**PT (n=23)**	**Total (n=377)**
Age (years)	Mean ± SD	40.28 ± 1.39	38.47 ± 1.32	39.88 ± 1.26	37.6 ± 1.28	39.6 ± 1.34
Recurrent Number	Mean ± SD	0.72 ± 3.01	0.99 ± 1.79	0.33 ± 0.83	0.48 ± 0.99	0.71 ± 2.4
Duration of Disorder (years)	Mean ± SD	7.43 ± 8.35	7.26 ± 7.53	5.53 ± 5.9	6.25 ± 6.3	7 ± 7.68
Population (log)	Mean ± SD	4.66 ± 1.13	4.47 ± 1.25	4.87 ±0.99	4.69 ± 1.06	4.65 ± 1.14
Duration of Hospitalization *	Mean ± SD	14.51±7.35	10.6±5.24	9.92 ± 4.73	12.32 ± 3.87	11.58 ± 5.96

We included 19 baseline covariates, of which four were continuous: number of recurrences, age (years), duration of disorder (years), and population of the residential area (log population). The remaining 15 covariates were dichotomous: history of recurrence, gender, history of medical disorder, living status, number of children, marital status, education level, occupation, type of residence, history of psychiatric illnesses/mental disorders in family members, history of suicide attempt, history of medication adherence, history of emotional problem including death/disease of a family member or relatives, history of smoking, and clearance type. All continuous covariates were standardized, and dummy code values for dichotomous variables were set to 1 and 0.

Consider a data set, consisting of n subjects from a clinical trial or observational study. The observed data include baseline patient characteristics, before treatment, denotes by vector of X and the assigned treatment denotes by $A = \{0,1\}$. Let Y be the observed outcome of interest where we assume that higher values are preferred. Our goal is to obtain an optimal treatment rule which maximizes the expected outcome Y, i.e., $E(Y(g(X)))$ In this context, a treatment regime, g, is defined as a mapping from X into a treatment would be assigned to an individual based on the observed covariates. For example, a patient with X=x is recommended treatment 1 if g(x)=1 and so one.

We first define the concept of potential outcomes. Let Y(a) denote the potential outcome value under treatment a. We define Y(a) is the potential results that could be seen under treatment assignments if a patient receive treatment 1 or 0. Let G denote a class of treatment regimens of interested and $g \in G$ an arbitrary treatment regime. We define the potential outcome under g, denoted $Y(g) = Y(1).I(g(X) = 1) + Y(0).I(g(X) = 0)$.

Under exchangeability assumption the potential outcomes of patients who receive the treatment should be identical on average with those of patients who do not receive the treatment. That is, this assumption assumes that there are no unmeasured confounders that may influence the outcome except for the treatment itself. Under consistency assumption, the actual value of Y is not influenced by the treatment allocation of other patients.

These assumptions are true in a randomized study but unverifiable assumptions in a nonrandomized study. Rubin proposed that in both randomized and nonrandomized studies, investigator should control important variables that may causally affect Y either by matching or adjustment or both.

Under the above conditions, it can be shown that the expectation of the potential outcome where E_x (.) is the marginal distribution of X, is

$$E(Y(a)) = E_X[E(Y \mid X, A = a)].$$

In the class of all treatment regimens $g^{opt} \in G$ it can be shown that

$$E(Y(g)) = E_X[E(Y \mid X, A = 1)g(X) + E(Y \mid A = 0, X)\{1 - g(X)\}] \text{ (28).(22).}$$

In our current regression model, we consider the linear form for the interaction effect, where. $E(Y \mid X, A) = \gamma X + A(\beta(X))$, $\beta = (\beta_1, ..., \beta_{p+1})$. The main object is to estimate the interaction function βX but not the baseline function γX .[28]

Let, Y_i denotes the observed outcome of interested, X_i denotes the observed variables of individual; $A_i \in \{0,1\}$ denotes the observed of assigned treatment to individual and $\pi(x_i)$ denotes the propensity score. In a multiple regression model, loss functions are typically used to estimate parameters using least squares methods.[29] We use least square method to minimize the following loss function. The minimizers are denoted as $(\tilde{\gamma}, \tilde{\beta})$

$$\mathrm{L}_{n,}(\beta, \gamma) = \frac{1}{n}\sum_{i=1}^{n}\left[Y_i - \gamma X_i - \beta X_i \ \{A_i - \pi(X_i)\}\right]^2$$

Given the observations $(Y_i \ , X_i \ , A_i, e_i)$, new observations are constructed, $(Y_{i\,new}, X_{i\,new}, A_i, e_i)$, for each individual. Where $Y_{i\,new}$ denotes the subtraction between Y_i and values of baseline mean function of covariates, i.e., $Y_{i.new} = Y_i - \tilde{\gamma} X_i$, $X_{i\,new}$ denotes the multiplication of X_i to $\{A_i - \pi(x_i)\}$, i.e., $X_{i.new} = X_i * \{A_i - \pi(x_i)\}$, A_i denotes two available treatments $A = \{0,1\}$ and e_i denotes propensity scores for treatment, $\pi(X_i) = p(A_i = 1 \mid X_i = x_i)$ [28,30] which obtain with a logistic regression model based on all of covariates, X.[31]

$$\pi_i(x; b) = \frac{e^{b_0 + b_1 x_1 + \ldots + b_k x}}{1 + e^{b_0 + b_1 x_1 + \ldots + b_k x}} \text{ (28, 32).}$$

Finally, the standard quadratic form of loss function is formed as $\mathrm{L}_{n,}(\tilde{\gamma}, \beta) = \frac{1}{n}\sum_{i=1}^{n}\left[Y_{i.new} - \beta X_{i.new}\right]^2$

The minimizers is denoted as $(\hat{\beta})$.

To estimate the optimal treatment rule, we need to estimate the treatment and treatment-covariates interaction effects βX . Certainly, coefficients of these important variables, X, must be non-zero. The loss function makes it possible to achieve shrinkage penalties of coefficients for variable selection.[32] This penalty term forces the model to select a small number of predictors, which are the most important variables in the model. In this process, the coefficients of the model are estimated by minimizing the loss function as an objective function.[33]

To select important prescriptive variables, we solve equation i.e., $\min_{\beta} \mathrm{L}_{n,}(\beta,\tilde{\gamma}) + \lambda_n \sum_{i=1}^{p+1} w_j \left|\beta_j\right|$ where λ and w_j are tuning parameter and shrinkage penalty respectively. We use adaptive lasso penalty $w_j = \frac{1}{|\tilde{\beta}_j|}$ j=1,..,p+1.[34] The adaptive lasso penalty shrinks the coefficients towards zero, with larger coefficients being shrunk more than smaller coefficients.[33]

An optimal treatment rule depends on the treatment and prescriptive variables effects, $\beta^T \tilde{X}$. So that it is easy to show that the optimal treatment regime which patients receive with covariate X=x is $g^{opt}(X) = I(\hat{\beta}X > 0)$.[15,28,31,32,35-37]

For example, in the model $E(Y \mid X, A) = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + A(\beta_3 + \beta_4 X_1 + \beta_5 X_2)$, the mean optimal rule is $I(\beta_3 + \beta_4 X_1 + \beta_5 X_2 > 0)$. Therefore, the variables with non-zero beta coefficients are named important variables.[13,28,32,38]

Results

Table 1 and Table 2 present the distribution of patient variables (mean ± sd) in four treatment groups and negative duration of hospitalization. The response variable considered was the duration of hospitalization.[1,4,12,13,39,40]

We assumed that there was heterogeneity in the outcome of treatments. The comparison of four treatment groups showed that the difference between the mean negative duration of patient's hospitalization is significant (df=3, F=12.09, p-value<0.01), and there was heterogeneity between the treatment groups (df1=3, df2= 373, p-value<=0.04). It is necessary to identify the source of heterogeneity. Individual heterogeneity should be specified in their characteristics. We first created a new dataset of matched groups based on propensity score predictions and the actual treatment for each individual.

Analysis I: that compares the effectiveness of work therapy (WT) (A=1) to the combination of the other three treatments (A=0) in 377 patients, of whom 198 (52.5%) received WT(A=1) and 179 (47.5%) received the other three treatments (A=0). Analysis II: that compares WT+ECT (A=1) to WT+FT (A=0) in 156 patients, of whom 95 (61.0%) received WT+ECT (A=1) and 61 (39.0%) received WT+FT (A=0).

To estimate the optimal treatment rule, we need to show how variables affect the determination of the optimal treatment (Table 3). For both constant and linear models in Analysis I, the estimated coefficients using adaptive LASSO penalty are given. One important covariate, history of emotional problems including death/disease of a family member or relative (h.emotional), was selected. Patients with h.emotional=1 were more likely to receive the other three treatments (A= 0), which is reflected in the negative b*c value (Table 3). This shows that the other three treatments for all patients with h.emotional=1, is an optimal treatment rule. Based on the results, 61.3% of patients should receive the other three treatments (A=0), whereas only 47.5% of patients were assigned.

Table 3: Estimated coefficients for interaction using the linear model.

Variables	Analysis I				Analysis II			
	Beta (b)	**Se**	**Input Value ©**	**b*c**	**Beta (b)**	**Se**	**Input Value ©**	**b*c**
H. Recurrence	0	-	-	-	0	-	-	-
Gender	0	-	-	-	0	-	-	-
H. Medication Adherence	0	-	-	-	0	-	-	-
Living status	0	-	-	-	0	-	-	-
Number of children	0	-	-	-	0		-	-
Marital status	0	-	-	-	0	-	-	-

Education level	0	-	-	-	4.02		1	4.02
Occupation	0	-	-	-	0	-	-	-
Type of Residence	0	-	-	-	0	-	-	-
H. Psychiatric Illness	0	-	-	-	0	-	-	-
H. Suicide	0	-	-	-	0	-	-	-
H. Medical Disorders	0	-	-	-	0	-	-	-
H. Emotional Problem	-2.22	0.66	1	-2.22	3.68	0.94	1	3.68
H. Smoking	0	-	-	-	0	-	-	-
Clearance. Type	0	-	-	-	0	-	-	-
			Sum b*c	-2.22			Sum b*c	7.7

H: History

Optimal treatment rules estimated from the Combining Treatments to Enhance mean duration of hospitalization. A treatment rule depends on the coefficients of prescriptive variables in interaction linear model. In analysis I, the negative coefficient implies a benefit from the other three treatments (treatment A=0). If linear combination is less than zero. In analysis II, the positive coefficients imply a benefit from the WT+ECT (treatment A=1) if linear combination is greater than zero.

For the linear model in Analysis II, the estimated coefficients using adaptive LASSO estimation are given. Two important covariates were selected: h.emotional and education level (edu). Table 3 shows how variables affect the determination of the treatment. Patients with h.emotional=1 and edu=1, h.emotional=0 and edu=1, or h.emotional=1 and edu=0 should receive WT+ECT (A=1), which is reflected in the positive b*c values (Table 3). This show that the WT+ECT for all patients with h.emotional=1 and edu=1, h.emotional=0 and edu=1, or h.emotional=1 and edu=0 is an optimal treatment rule. Of the 156 patients, 115 (74.0%) should receive treatment 1, whereas only 95 (61.0%) of patients were assigned to treatment 1.

For the constant model in Analysis II, the adaptive LASSO selects no important covariates, suggesting that WT+ECT (A=1) and WT+FT (A=0) are equally good for all patients in this study (Table 4).

Table 4: Estimated coefficients for interaction using the constant model.

Variables	Analysis I				Analysis II			
	Beta (b)	**Se**	**Input Value (c)**	**b*c**	**Beta (b)**	**Se**	**Input Value (c)**	**b*c**
H. Recurrence	0	-	-	-	0	-	-	-
Gender	0	-	-	-	0	-	-	-
H. Medication Adherence	0	-	-	-	0	-	-	-
Living status	0	-	-	-	0	-	-	-
Number of children	0	-	-	-	0	-	-	-
Marital status	0	-	-	-	0	-	-	-
Education level	0	-	-	-	0	-	-	-
Occupation	0	-	-	-	0	-	-	-
Type of Residence	0	-	-	-	0	-	-	-
H. Psychiatric Illness	0	-	-	-	0	-	-	-
H. Suicide	0	-	-	-	0	-	-	-
H. Medical Disorders	0	-	-	-	0	-	-	-
H. Emotional Problem	-2.51	0.68	1	-2.51	0	-	-	-
H. Smoking	0	-	-	-	0	-	-	-
Clearance. Type	0	-	-	-	0	-	-	-
			Sum b*c	-2.51			Sum b*c	-

H: History

Optimal treatment rules estimated from the Combining Treatments to Enhance mean duration of hospitalization. A treatment rule depends on the coefficients of predictor variables in interaction constant model. In analysis I, the negative coefficient implies a benefit from the other three treatments including of WT+ECT, WT+FT, PT (treatment A=0) if linear combination is less than zero. In analysis II, there are no important covariates, suggesting that WT+ECT and WT+FT are equally good for all patients.

Discussion

With a penalized regression-based estimation approach, we obtained optimal treatment rules focusing on variable selection.[41] Our results show that two important variables including emotional problem and education level, have a main role in estimating the optimal treatment in MDD patients. In a cluster analysis study, researchers identified, subgroup of psychiatric patients who received ECT based on their characteristics. They showed that patients who received ECT were not homogeneous. They found three important variables. Older unemployed females with MDD disorder, received fewer ECT sessions. Our findings are consistent with this study and our results confirm.[9]

Based on the results of our study in patients with MDD, two important variables are identified and the combination of three other treatments, including WT+ECT, WT+FT and PT were estimated as the optimal treatments for all patients with emotional problems and in contrast, WT alone, is not an optimal treatment. In addition, WT+ECT was identified as an optimal treatment for all patients, except, uneducated patients with no emotional problems. In similar studies in patients with schizophrenia, it has been shown that employment may have positive effects on the cognitive function of patients[42] and neurocognitive enhancement therapy plus work therapy (WT) may modify performance on neuropsychological tests, not WT alone. Our result is consistent with the results of this study.[18]

We concluded that the combination of ECT and WT for patients with the mentioned characteristics can reduce the duration of hospitalization and is an optimal treatment in MDD patients. Based on published reviewed works, ECT is an efficient short-term treatment for reducing depression regardless of which patients are candidates for this treatment. Different treatment approaches may be recommended for MDD for different subsets of patients, regardless of their characteristics and treatment efficacy. However, findings of our study are consistent with this study.[16]

In our study, we identified two important variables which, included the history of emotional problems and education level. Also, we found that a combination of treatments may be an optimal treatment rather than mono-treatment alone. In an investigation by Sies and colleagues in MDD, an optimal treatment rule achieved using the combination of medication was found to enhance depression outcomes based on a conjunction of patients' pretreatment characteristics. In this RCT dataset, the efficacy of two combination treatments was compared to the efficacy of a mono-treatment. They indicate that panic disorder problem and age are two important variables. With the weighted linear treatment regime, patients with panic disorder and patients younger than 28.5 years old should receive the combination treatment, whereas patients without panic disorder who are at least 28.5 years old should receive the mono-treatment.[13,43] These results confirm our findings.

Most studies have considered the quality of effectiveness of different therapy methods, such as psychotherapy, cognitive therapy, and medication, while the combination of different therapies appears to be necessary. Research has shown that although ECT is highly efficient treatment in protecting against relapse among MDD therapies, it needs to be augmented with depression-specific psychotherapy.[17] Additionally, based on the evidence, work therapy alone does not affect MDD patients. The results of these studies confirm our findings.

Another multivariate approach to treatment selection is the Personalized Advantage Index (PAI). This approach was used to predict post-treatment scores for each of used treatments. In this study with using a regression model, Personalized Advantage Index of patients was calculated as an outcome. Based on the results, optimal treatment was predicted for 60% of the patients compared to others (PAI>=3). In this approach, in addition to estimating individualized treatment, it estimates the predicted advantage of an indicated treatment over the none-indicated treatment.[13] In another study, using Personalized Advantage Index method, patients receiving optimal treatment had fewer post-treatment symptoms of depression compared when they received suboptimal treatment.[39]

In this approach DeRubeis et al. and Friedl et al. identified important variables to determine the optimal treatment rules. These variables predicted differential response to treatment. They showed that important variables that can predict differential response should be included in the regression model. They identified the treatment predicted to produce the better outcome for each patient using the personalized advantage index (PAI).[12]

Conclusions

In estimating of optimal treatment rules for patients with Major Depressive Disorder the variables of the history of emotional problems and the educated level of patients were estimated as two important variables. Personalized medicine takes into account this individual heterogeneity in individualized characteristics, and optimizes treatment outcomes by identifying important variables into treatment regimens, which could decrease duration of hospitalization.

Conflict of Interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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