

Analysis on the Cessation Effect on Smoking among Patients with MDD with the Combination Treatment of Behavioral Activation and Varenicline

William Qian

November 2024

Introduction

Major Depressive Disorder (MDD) and smoking exhibit a complex relationship, with individuals with MDD being more likely to smoke heavily, demonstrate higher nicotine dependence, and experience more severe withdrawal symptoms during quit attempts. While varenicline is an effective pharmacotherapy for smoking cessation, and Behavioral Activation (BA) has shown promise in treating depression-related symptoms, their combined effectiveness in treating smokers with MDD remains unclear. A previous randomized, placebo-controlled, 2×2 factorial trial comparing BA for smoking cessation (BASC) versus standard behavioral treatment (ST), with and without varenicline, found that BASC did not outperform ST in adult smokers with current or past MDD.

The present study aims to extend these findings by examining baseline variables as potential moderators of treatment effects and evaluating predictors of smoking abstinence, controlling for behavioral treatment and pharmacotherapy. We consider various potential moderators including depression-related factors (anhedonia, current MDD status, depression severity), smoking-related characteristics (nicotine dependence, cigarettes per day, readiness to quit), and demographic variables. Understanding these relationships could help identify which smokers with MDD might benefit most from particular treatment approaches, ultimately leading to more personalized and effective smoking cessation interventions for this high-risk population.

Data

The data contains 300 observations with 25 variables (including 1 id column) collected from a randomized, placebo-controlled, 2×2 factorial trial involving adult smokers with current or past major depressive disorder (MDD). After removing observations with missing values, our final analytical sample consisted of 241 participants.

Variable	Description
abst	Smoking Abstinence
Var	Pharmacotherapy (Varenicline)
BA	Psychotherapy (Behavioral Activation)
age_ps	Age at phone interview
sex_ps	Sex at phone interview
NHW	Non-Hispanic White indicator
Black	Black indicator
Hisp	Hispanic indicator
inc	Income (ordinal categorical, low to high)
edu	Education (ordinal categorical, low to high)
ftcd_score	FTCD score at baseline

Variable	Description
ftcd.5.mins	Smoking within 5 mins of waking up
bdi_score_pq1	BDI score at baseline (a measure of depression)
cpd_ps	Cigarettes per day at baseline phone survey
crv_total_pq1	Cigarette reward value at baseline
hedonsum_n_pq1	Pleasurable Events Scale at baseline – substitute reinforcers
hedonsum_y_pq1	Pleasurable Events Scale at baseline – complementary reinforcers
shaps_score_pq1	Anhedonia
otherdiag	Other lifetime DSM-5 diagnosis
antidepressmed	Taking antidepressant medication at baseline
mde_curr	Current vs past MDD
NMR	Nicotine Metabolism Ratio
Only.Menthol	Exclusive Mentholated Cigarette User
readiness	Baseline readiness to quit smoking

Analysis of the baseline characteristics by treatment groups reveals several notable patterns. When comparing the varenicline and placebo groups, we observe a significant difference in abstinence rates (28% vs 8.4%, $p < 0.001$), indicating varenicline’s potential effectiveness. However, other baseline characteristics were well-balanced between the pharmacotherapy groups, suggesting successful randomization. Similarly, when comparing behavioral activation (BA) and standard treatment groups, most characteristics were balanced, with the exception of antidepressant medication use (35% in BA group vs 19% in standard treatment group, $p = 0.004$).

Table 2: Data Summary Table

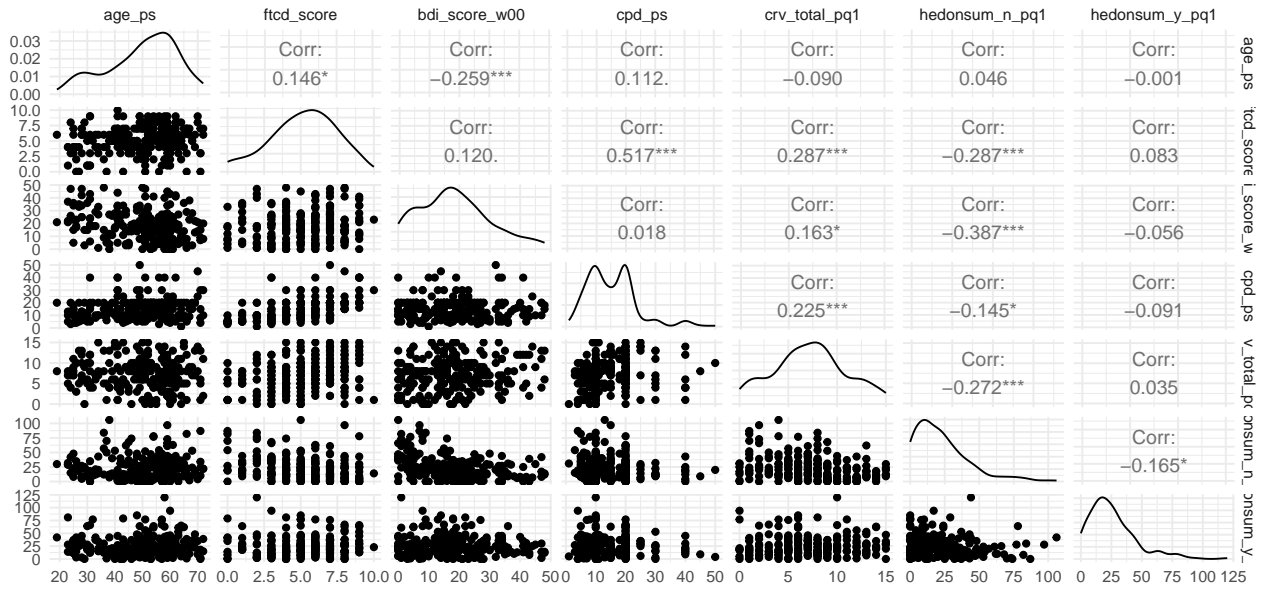
Characteristic	Grouped by Pharmacotherapy Status			Grouped by Psychotherapy Status		
	No Varenicline	Varenicline	p-value	No Psychotherapy	Psychotherapy	p-value
abst			<0.001			0.7
0	98 (92%)	96 (72%)		93 (79%)	101 (81%)	
1	9 (8.4%)	38 (28%)		24 (21%)	23 (19%)	
BA			0.6			
0	54 (50%)	63 (47%)				
1	53 (50%)	71 (53%)				
age_ps	52 (45, 59)	52 (40, 59)	0.4	51 (43, 58)	54 (41, 60)	0.2
sex_ps			0.4			>0.9
1	45 (42%)	63 (47%)		52 (44%)	56 (45%)	
2	62 (58%)	71 (53%)		65 (56%)	68 (55%)	
NHW			0.7			0.5
0	70 (65%)	85 (63%)		78 (67%)	77 (62%)	
1	37 (35%)	49 (37%)		39 (33%)	47 (38%)	
Black			0.2			0.6
0	47 (44%)	70 (52%)		55 (47%)	62 (50%)	
1	60 (56%)	64 (48%)		62 (53%)	62 (50%)	
Hisp			0.7			0.5
0	100 (93%)	127 (95%)		109 (93%)	118 (95%)	
1	7 (6.5%)	7 (5.2%)		8 (6.8%)	6 (4.8%)	
inc			0.6			0.3
1	38 (36%)	47 (35%)		40 (34%)	45 (36%)	
2	25 (23%)	31 (23%)		28 (24%)	28 (23%)	
3	18 (17%)	20 (15%)		21 (18%)	17 (14%)	
4	16 (15%)	15 (11%)		10 (8.5%)	21 (17%)	
5	10 (9.3%)	21 (16%)		18 (15%)	13 (10%)	
edu			0.2			0.6
1	1 (0.9%)	0 (0%)		0 (0%)	1 (0.8%)	
2	3 (2.8%)	9 (6.7%)		4 (3.4%)	8 (6.5%)	
3	29 (27%)	34 (25%)		30 (26%)	33 (27%)	
4	46 (43%)	45 (34%)		48 (41%)	43 (35%)	

Table 2: Data Summary Table (*continued*)

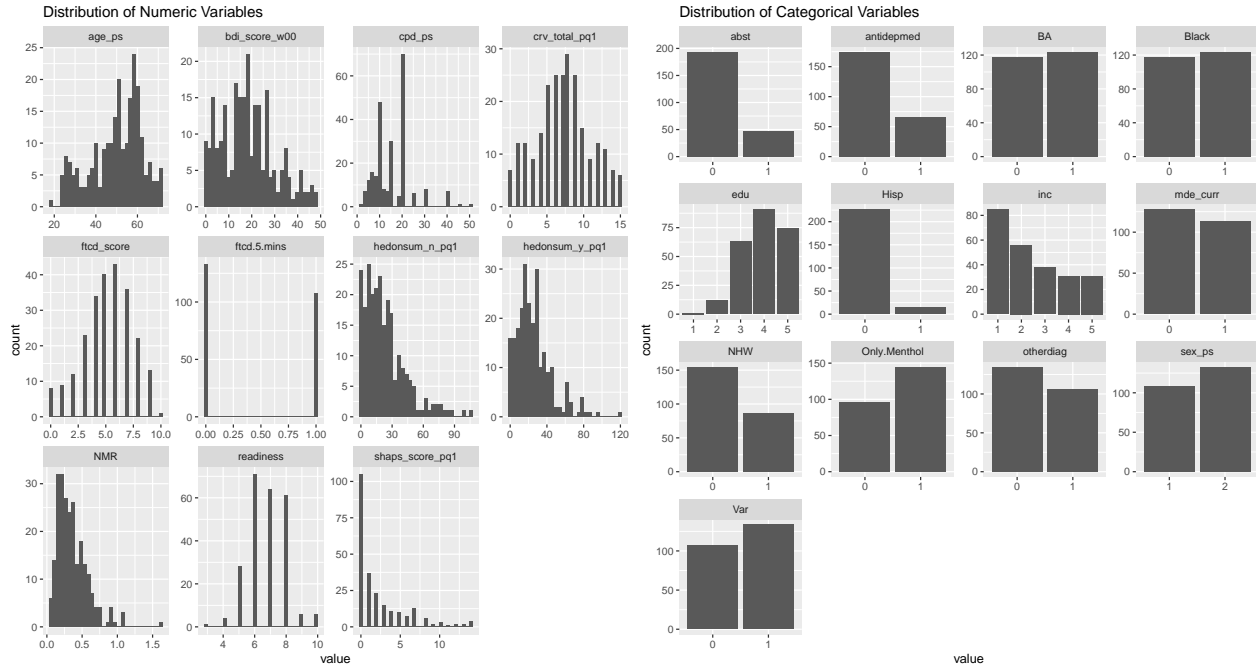
Characteristic	Grouped by Pharmacotherapy Status			Grouped by Psychotherapy Status		
	No Varenicline	Varenicline	p-value	No Psychotherapy	Psychotherapy	p-value
5	28 (26%)	46 (34%)		35 (30%)	39 (31%)	
ftcd_score	6 (4, 7)	5 (4, 7)	0.3	6 (4, 7)	5 (4, 7)	0.4
ftcd.5.mins	51 (48%)	57 (43%)	0.4	57 (49%)	51 (41%)	0.2
bdi_score_w00	18 (9, 27)	18 (9, 24)	0.9	18 (12, 25)	18 (9, 26)	0.6
cpd_ps	15 (10, 20)	15 (10, 20)	0.5	15 (10, 20)	15 (10, 20)	>0.9
crv_total_pq1	7 (5, 9)	7 (5, 10)	0.8	7 (5, 9)	8 (5, 10)	0.4
hedonsum_n_pq1	17 (9, 30)	20 (9, 35)	0.3	18 (9, 32)	20 (9, 31)	>0.9
hedonsum_y_pq1	24 (12, 36)	19 (13, 31)	0.2	21 (13, 35)	22 (12, 33)	>0.9
shaps_score_pq1	1 (0, 4)	1 (0, 3)	>0.9	1 (0, 4)	1 (0, 3)	0.5
otherdiag			0.6			0.7
0	58 (54%)	77 (57%)		64 (55%)	71 (57%)	
1	49 (46%)	57 (43%)		53 (45%)	53 (43%)	
antidepmed			0.3			0.004
0	74 (69%)	101 (75%)		95 (81%)	80 (65%)	
1	33 (31%)	33 (25%)		22 (19%)	44 (35%)	
mde_curr			0.6			0.8
0	59 (55%)	69 (51%)		61 (52%)	67 (54%)	
1	48 (45%)	65 (49%)		56 (48%)	57 (46%)	
NMR	0.32 (0.20, 0.45)	0.31 (0.21, 0.50)	0.8	0.32 (0.20, 0.46)	0.32 (0.22, 0.48)	0.7
Only.Menthol			0.7			>0.9
0	41 (38%)	55 (41%)		47 (40%)	49 (40%)	
1	66 (62%)	79 (59%)		70 (60%)	75 (60%)	
readiness	7.00 (6.00, 8.00)	7.00 (6.00, 8.00)	0.2	7.00 (6.00, 8.00)	7.00 (6.00, 8.00)	0.9
Var						0.6
0				54 (46%)	53 (43%)	
1				63 (54%)	71 (57%)	
¹ n (%); Median (IQR)						
² Pearson's Chi-squared test; Wilcoxon rank sum test; Fisher's exact test						

Examination of correlations among continuous variables revealed several significant relationships. Notably, cigarettes per day (cpd_ps) showed a moderate positive correlation with FTCD score ($r = 0.517$, $p < 0.001$), which is expected as both measure aspects of smoking dependency. The Beck Depression Inventory score (bdi_score_w00) demonstrated negative correlations with both hedonic capacity measures (hedonsum_n_pq1 and hedonsum_y_pq1), suggesting that higher depression levels are associated with reduced pleasure experiences.

Correlation Matrix of Baseline Predictors



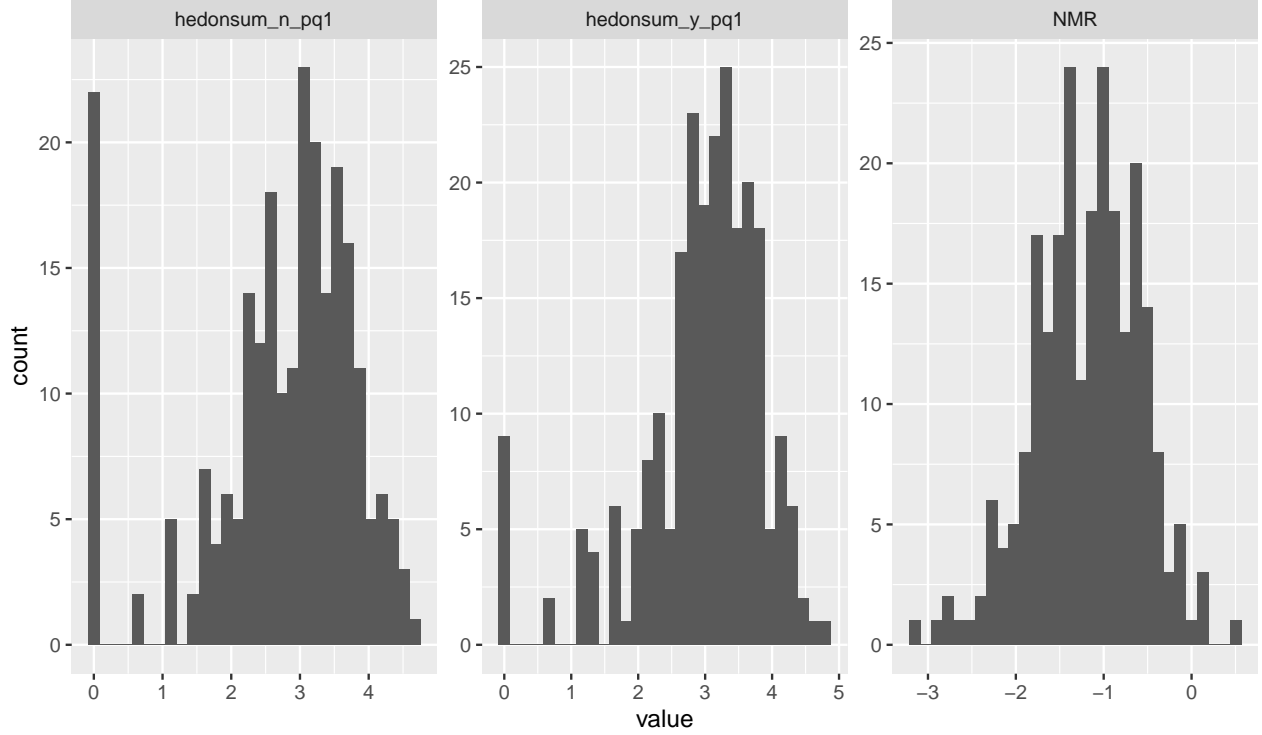
The distribution analysis of numeric variables revealed right-skewed patterns in several measures, particularly hedonsum_n_pq1, hedonsum_y_pq1, and NMR. To address this non-normality, we applied log transformations to these variables. The transformed distributions showed improved symmetry and reduced skewness, making them more suitable for our subsequent analyses. Other numeric variables, including age, FTCD score, and depression measures, showed approximately normal distributions and were kept in their original scale.



```
## TableGrob (1 x 2) "arrange": 2 grobs
##      z      cells      name      grob
## 1 1 (1-1,1-1) arrange gtable[layout]
## 2 2 (1-1,2-2) arrange gtable[layout]
```

This is the distribution of hedonsum_n_pq1, hedonsum_y_pq1, and NMR after log transformation.

Distribution after Log Transformation



Methods

In this study, we employed three regularized regression approaches - LASSO (L1), Ridge (L2), and Elastic Net regularization - to analyze the moderators and predictors of smoking cessation outcomes.

Given our binary outcome of smoking abstinence (y), we used logistic regression with different regularization terms. The basic form of our logistic regression model is:

$$P(y = 1|X) = \frac{1}{1 + e^{-X\beta}}$$

where X represents our predictor variables and β represents the coefficients.

LASSO (L1) Regularization

LASSO (Least Absolute Shrinkage and Selection Operator) adds an L1 penalty term to the log-likelihood function:

$$\hat{\beta}_{LASSO} = \underset{\beta}{\operatorname{argmin}} \{-l(\beta) + \lambda \sum_{j=1}^p |\beta_j|\}$$

where $l(\beta)$ is the log-likelihood and λ is the regularization parameter. The L1 penalty encourages sparsity by shrinking some coefficients exactly to zero, effectively performing variable selection.

Ridge (L2) Regularization

Ridge regression uses an L2 penalty term:

$$\hat{\beta}_{Ridge} = \underset{\beta}{\operatorname{argmin}} \left\{ -l(\beta) + \lambda \sum_{j=1}^p \beta_j^2 \right\}$$

The L2 penalty shrinks coefficients toward zero but rarely sets them exactly to zero. This approach is particularly useful when dealing with correlated predictors.

Elastic Net

Elastic Net combines both L1 and L2 penalties:

$$\hat{\beta}_{ElasticNet} = \underset{\beta}{\operatorname{argmin}} \left\{ -l(\beta) + \lambda \left(\alpha \sum_{j=1}^p |\beta_j| + (1 - \alpha) \sum_{j=1}^p \beta_j^2 \right) \right\}$$

where α controls the mix between L1 and L2 penalties ($\alpha = 1$ gives LASSO, $\alpha = 0$ gives Ridge). This combination allows for both variable selection and handling of correlated predictors.

Model Implementation

We implemented these models using the `glmnet` package in R, with cross-validation to select the optimal λ value. For the Elastic Net model, we set $\alpha = 0.5$ to give equal weight to L1 and L2 penalties. The models were evaluated using AUC and accuracy metrics on both training and test sets, with the data split in a 50:50 ratio to ensure robust validation of our findings.

Regression Analysis

Basic Models

We first implemented two fundamental regularized regression models (Ridge and LASSO regression without interaction terms) to examine the relationship between smoking abstinence and our predictors.

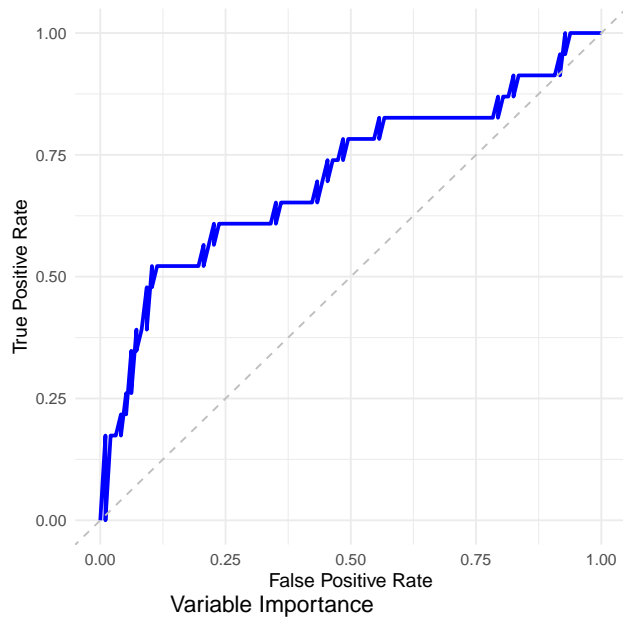
Lasso Regression

The LASSO regression with $\lambda = 0.033$ can be expressed as:

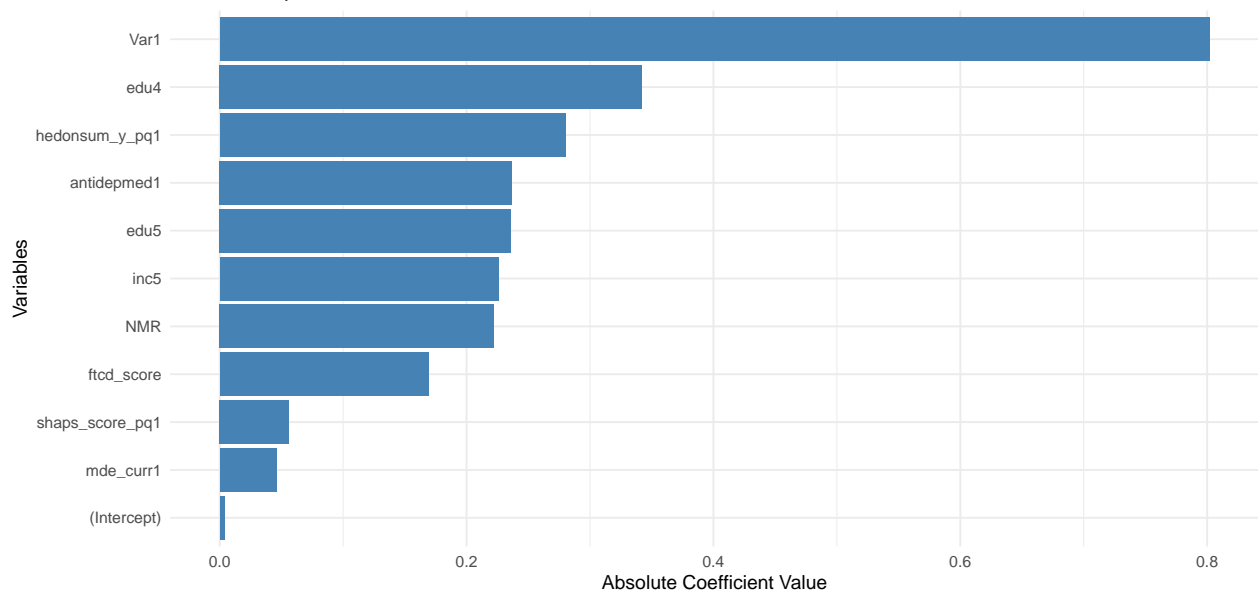
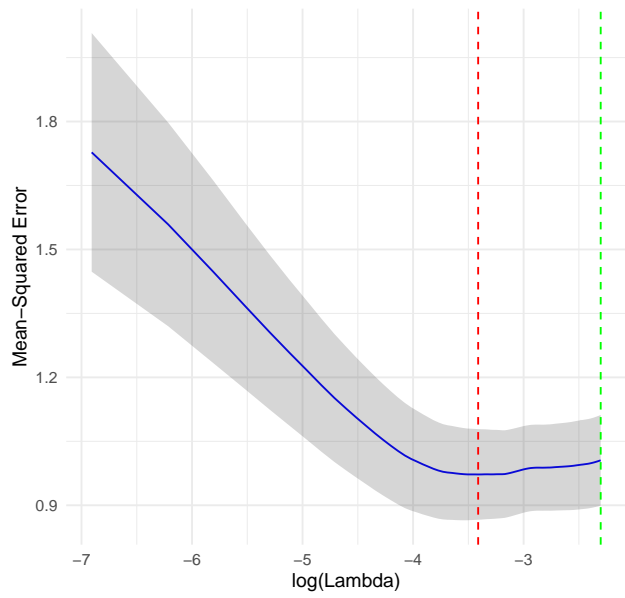
$$\begin{aligned} \logit(P(abst = 1)) = & \beta_0 + \beta_1 \times Var + \beta_2 \times inc5 + \beta_3 \times edu4 + \beta_4 \times edu5 \\ & + \beta_5 \times ftcd_score + \beta_6 \times hedonsum_y_pq1 + \beta_7 \times shaps_score_pq1 \\ & + \beta_8 \times mde_curr1 + \beta_9 \times antidepressmed1 + \beta_{10} \times \log(NMR) \\ = & 0.004 + 0.802 \times Var + 0.226 \times inc5 - 0.342 \times edu4 + 0.236 \times edu5 \\ & - 0.169 \times ftcd_score - 0.280 \times hedonsum_y_pq1 - 0.056 \times shaps_score_pq1 \\ & - 0.046 \times mde_curr1 + 0.237 \times antidepressmed1 + 0.222 \times \log(NMR) \end{aligned}$$

The LASSO model achieved an AUC of 0.841 on the training set and 0.705 on the test set. Through its variable selection property, LASSO identified 10 key predictors. As shown in the variable importance plot, Varenicline treatment showed the strongest positive effect (coefficient = 0.802) on abstinence probability, followed by high income level (inc5: 0.226) and antidepressant medication use (0.237). Education levels showed mixed effects, with edu4 showing a negative association (-0.342) while edu5 showed a positive association (0.236). Clinical measures including `ftcd_score` (-0.169) and `hedonsum_y_pq1` (-0.280) showed moderate negative associations with abstinence.

A ROC Curve (AUC = 0.705)



B Cross-validation Results



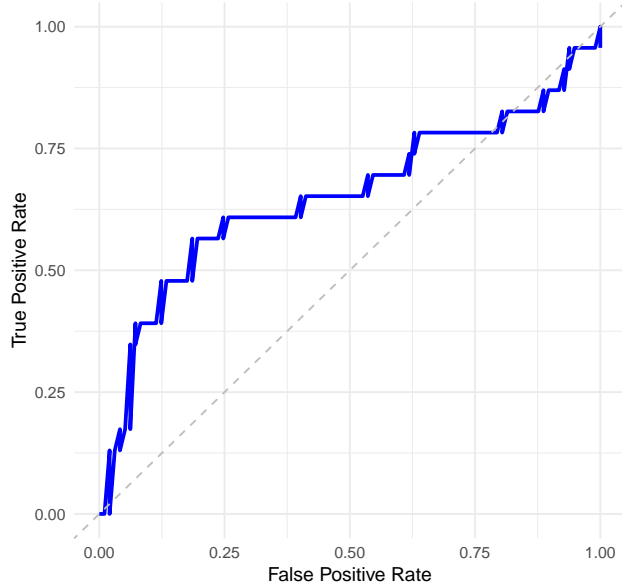
Ridge Regression

The Ridge regression with $\lambda = 0.100$ can be expressed as:

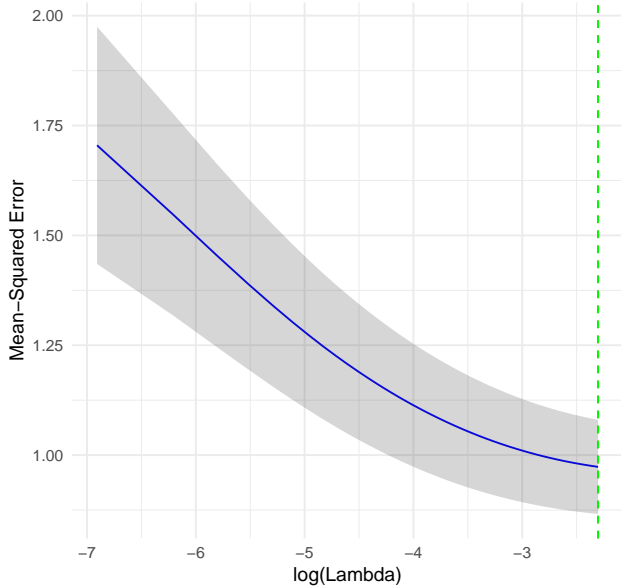
$$\begin{aligned}
\text{logit}(P(\text{abst} = 1)) = & \beta_0 + \beta_1 \times \text{Var} + \beta_2 \times \text{BA} + \beta_3 \times \text{age_ps} + \beta_4 \times \text{sex_ps2} \\
& + \beta_5 \times \text{NHW1} + \beta_6 \times \text{Black1} + \beta_7 \times \text{Hispl} \\
& + \beta_8 \times \text{inc2} + \beta_9 \times \text{inc3} + \beta_{10} \times \text{inc4} + \beta_{11} \times \text{inc5} \\
& + \beta_{12} \times \text{edu2} + \beta_{13} \times \text{edu3} + \beta_{14} \times \text{edu4} + \beta_{15} \times \text{edu5} \\
& + \beta_{16} \times \text{ftcd_score} + \beta_{17} \times \text{ftcd.5.mins} + \beta_{18} \times \text{bdi_score_w00} \\
& + \beta_{19} \times \text{cpd_ps} + \beta_{20} \times \text{crv_total_pq1} + \beta_{21} \times \log(\text{hedonsum_n_pq1}) \\
& + \beta_{22} \times \log(\text{hedonsum_y_pq1}) + \beta_{23} \times \text{shaps_score_pq1} + \beta_{24} \times \text{otherdiag1} \\
& + \beta_{25} \times \text{antidepmed1} + \beta_{26} \times \text{mde_curr1} + \beta_{27} \times \log(\text{NMR}) \\
& + \beta_{28} \times \text{Only.Mentholl} + \beta_{29} \times \text{readiness} \\
= & -0.382 + 0.740 \times \text{Var} - 0.106 \times \text{BA} + 0.007 \times \text{age_ps} + 0.017 \times \text{sex_ps2} \\
& + 0.022 \times \text{NHW1} + 0.009 \times \text{Black1} + 0.534 \times \text{Hispl} \\
& + 0.131 \times \text{inc2} + 0.141 \times \text{inc3} - 0.069 \times \text{inc4} + 0.470 \times \text{inc5} \\
& - 0.176 \times \text{edu2} + 0.146 \times \text{edu3} - 0.461 \times \text{edu4} + 0.459 \times \text{edu5} \\
& - 0.139 \times \text{ftcd_score} + 0.007 \times \text{ftcd.5.mins} + 0.002 \times \text{bdi_score_w00} \\
& + 0.003 \times \text{cpd_ps} - 0.024 \times \text{crv_total_pq1} + 0.127 \times \log(\text{hedonsum_n_pq1}) \\
& - 0.336 \times \log(\text{hedonsum_y_pq1}) - 0.062 \times \text{shaps_score_pq1} + 0.036 \times \text{otherdiag1} \\
& + 0.480 \times \text{antidepmed1} - 0.299 \times \text{mde_curr1} + 0.372 \times \log(\text{NMR}) \\
& + 0.377 \times \text{Only.Mentholl} - 0.061 \times \text{readiness}
\end{aligned}$$

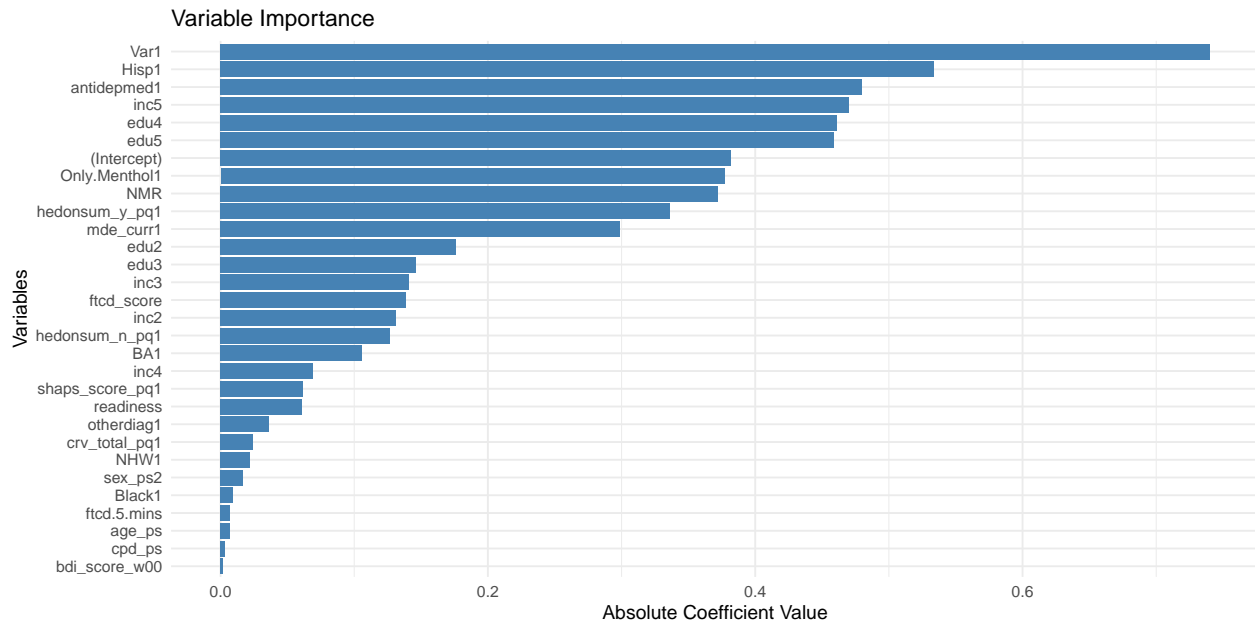
The Ridge model achieved a higher training AUC of 0.878 with a test AUC of 0.651. While retaining all variables, the variable importance plot reveals similar patterns to LASSO, with Varenicline treatment (0.740) and antidepressant medication use (0.480) showing the strongest positive associations with abstinence probability. Notably, Hispanic ethnicity also showed a strong positive association (0.534). Among clinical predictors, nicotine metabolism ratio (NMR: 0.372) and menthol cigarette use (0.377) showed moderate positive associations, while depression-related measures generally showed negative associations with abstinence probability.

A ROC Curve (AUC = 0.651)



B Cross-validation Results





The comparison of the Ridge model and the Lasso model is shown below. The table of coefficients are also included.

Table 3: Comparison of Basic Ridge and Lasso Regression Models

Variable	Ridge Regression Model	Lasso Regression Model
(Intercept)	-0.382	0.004
Var1	0.740	0.802
BA1	-0.106	Eliminated
age_ps	0.007	Eliminated
sex_ps2	0.017	Eliminated
NHW1	0.022	Eliminated
Black1	0.009	Eliminated
Hisp1	0.534	Eliminated
inc2	0.131	Eliminated
inc3	0.141	Eliminated
inc4	-0.069	Eliminated
inc5	0.470	0.226
edu2	-0.176	Eliminated
edu3	0.146	Eliminated
edu4	-0.461	-0.342
edu5	0.459	0.236
ftcd_score	-0.139	-0.169
ftcd.5.mins	0.007	Eliminated
bdi_score_w00	0.002	Eliminated
cpd_ps	0.003	Eliminated
crv_total_pq1	-0.024	Eliminated
hedonsum_n_pq1	0.127	Eliminated
hedonsum_y_pq1	-0.336	-0.28
shaps_score_pq1	-0.062	-0.056
otherdiag1	0.036	Eliminated
antidepmed1	0.480	0.237
mde_curr1	-0.299	-0.046
NMR	0.372	0.222
Only.Menthol1	0.377	Eliminated
readiness	-0.061	Eliminated

Table 4: Results of Basic Ridge and Lasso Regression Models

Metric	Ridge Regression Model	Lasso Regression Model
AUC (Train)	0.878	0.841
AUC (Test)	0.651	0.705
Accuracy (Train)	0.835	0.818
Accuracy (Test)	0.800	0.808
Lambda Min	0.100	0.033

Model with Interaction Terms

Our investigation of interaction effects progressed through two stages, each guided by specific theoretical considerations.

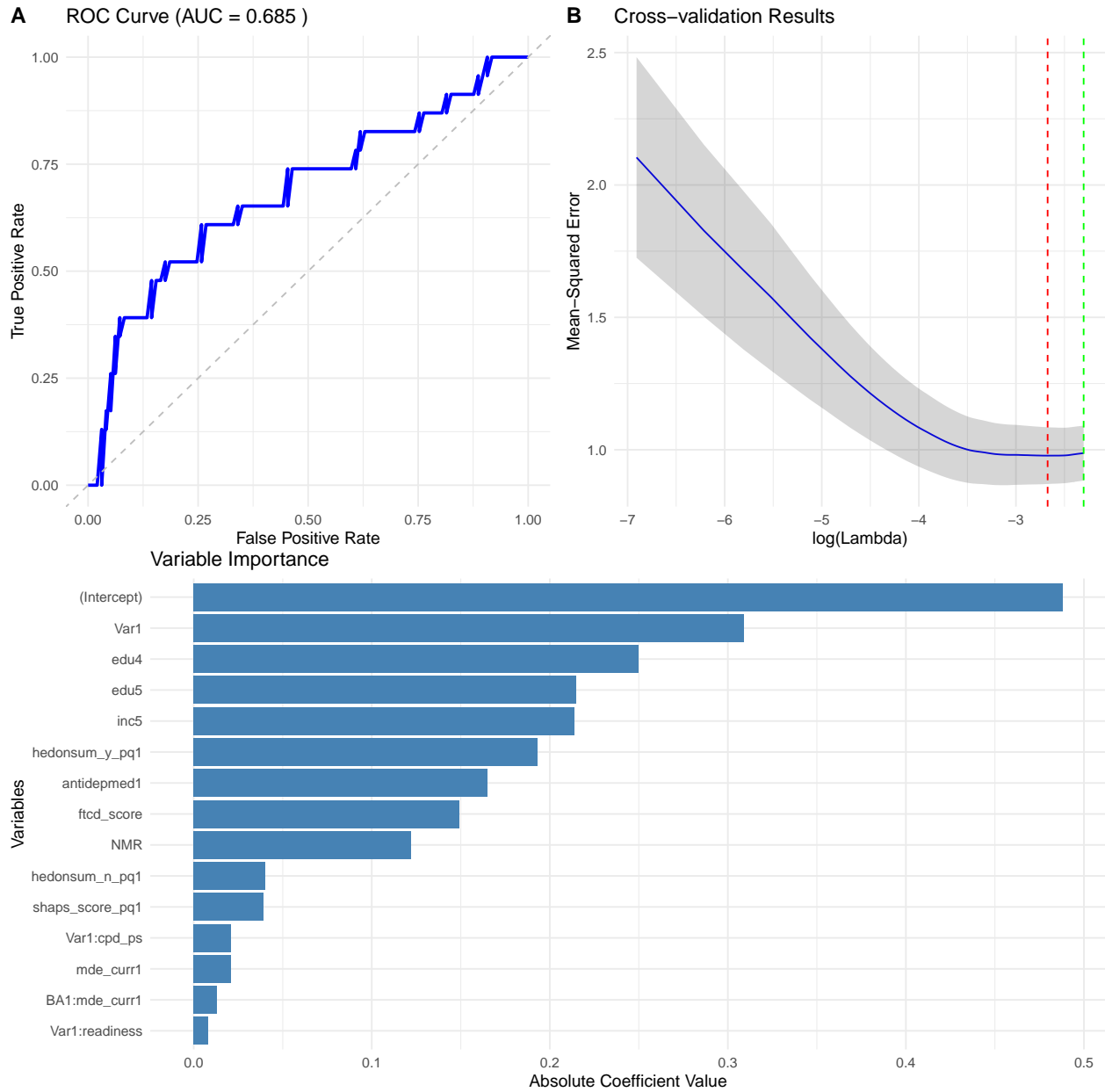
Basic Interaction Model

In the basic interaction model, we focused on treatment-specific interactions that directly address our primary research questions about treatment effectiveness. For BA, we concentrated on its interaction with depression-related variables (*mde_curr*, *bdi_score_w00*, *shaps_score_pq1*) because BA was specifically designed to address depression symptoms, particularly anhedonia. The interaction between BA and current MDD status was included to test whether BA’s effectiveness differs between current and past MDD patients. For Varenicline, we included interactions with smoking-related characteristics (*ftcd_score*, *cpd_ps*) and readiness to quit, as previous research suggests that pharmacotherapy effectiveness may vary with baseline smoking intensity and motivation levels.

The elastic net model with $\alpha = 0.5$ and $\lambda = 0.069$ can be expressed as:

$$\begin{aligned}
\text{logit}(P(\text{abst} = 1)) = & \beta_0 + \beta_1 \times \text{Var} + \beta_2 \times \text{BA} + \beta_3 \times \text{ftcd_score} \\
& + \beta_4 \times \text{antidepmed1} + \beta_5 \times \text{hedonsum_n_pq1} + \beta_6 \times \text{hedonsum_y_pq1} \\
& + \beta_7 \times \text{shaps_score_pq1} + \beta_8 \times \text{mde_curr1} + \beta_9 \times \text{NMR} \\
& + \beta_{10} \times (\text{BA} \times \text{mde_curr1}) + \beta_{11} \times (\text{Var} \times \text{cpd_ps}) + \beta_{12} \times (\text{Var} \times \text{readiness}) \\
= & -0.488 + 0.309 \times \text{Var} + 0.215 \times \text{edu5} - 0.250 \times \text{edu4} \\
& + 0.165 \times \text{antidepmed1} - 0.149 \times \text{ftcd_score} + 0.040 \times \text{hedonsum_n_pq1} \\
& - 0.193 \times \text{hedonsum_y_pq1} - 0.039 \times \text{shaps_score_pq1} - 0.021 \times \text{mde_curr1} \\
& + 0.122 \times \text{NMR} - 0.013 \times (\text{BA} \times \text{mde_curr1}) + 0.021 \times (\text{Var} \times \text{cpd_ps}) \\
& + 0.008 \times (\text{Var} \times \text{readiness})
\end{aligned}$$

This initial interaction model achieved an AUC of 0.685 on the test set. The variable importance plot reveals that while Varenicline maintained its strong main effect (0.309), its effectiveness appeared to vary with baseline smoking characteristics. The positive interaction with cigarettes per day (0.021) suggests that Varenicline might be particularly effective for heavier smokers. The interaction between BA and current MDD status (-0.013) indicates a potentially reduced treatment effect for current MDD patients, highlighting the complexity of treating this subgroup.



Advanced Interaction Model

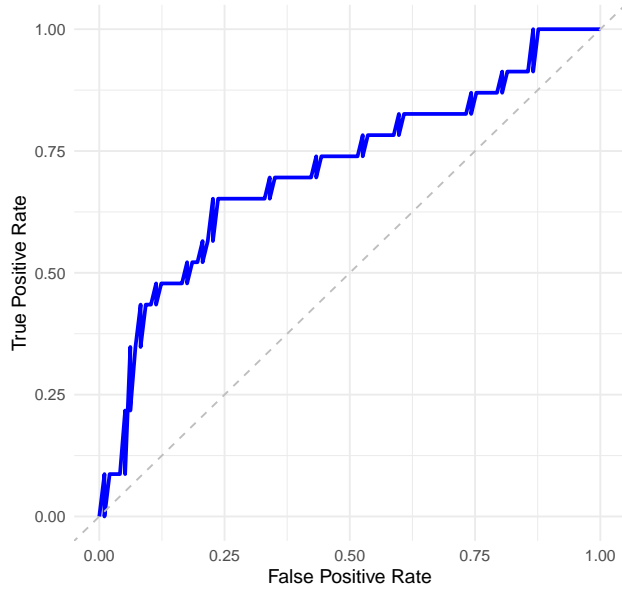
In the advanced interaction model, we expanded our investigation to include a broader set of theoretically meaningful interactions based on three key mechanisms. First, we considered interactions between depression symptoms ($bdi_score_w00 \times shaps_score_pq1$) because the combination of high depression severity and anhedonia might create a particularly challenging scenario for smoking cessation. Second, we examined how smoking behavior characteristics might interact with quit motivation ($ftcd_score \times readiness$), hypothesizing that high nicotine dependence might diminish the positive effect of quit motivation. Third, we investigated socioeconomic interactions ($edu \times readiness$, $inc \times antidepmed$) because education might influence how motivation translates to success, and medication effectiveness might vary by socioeconomic status due to differences in access to resources and support systems.

The advanced interaction model with $\alpha = 0.5$ and $\lambda = 0.071$ can be expressed as:

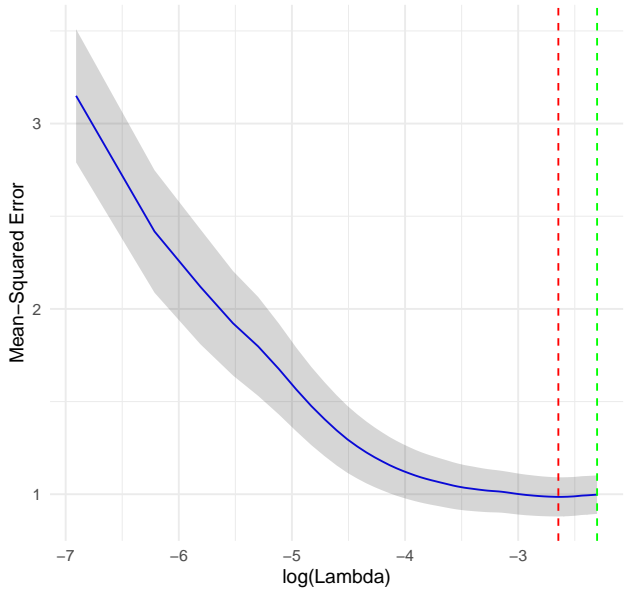
$$\begin{aligned}
\text{logit}(P(\text{abst} = 1)) = & \beta_0 + \beta_1 \times \text{Var} + \beta_2 \times \text{inc5} + \beta_3 \times \text{edu4} + \beta_4 \times \text{edu5} \\
& + \beta_5 \times \text{ftcd_score} + \beta_6 \times \text{hedonsum_n_pq1} + \beta_7 \times \text{hedonsum_y_pq1} \\
& + \beta_8 \times \text{shaps_score_pq1} + \beta_9 \times \text{antidepmed1} + \beta_{10} \times \text{NMR} \\
& + \beta_{11} \times (\text{Var} \times \text{cpd_ps}) + \beta_{12} \times (\text{Var} \times \text{readiness}) \\
& + \beta_{13} \times (\text{bdi_score_w00} \times \text{shaps_score_pq1}) + \beta_{14} \times (\text{ftcd_score} \times \text{readiness}) \\
& + \beta_{15} \times (\text{edu4} \times \text{readiness}) + \beta_{16} \times (\text{inc3} \times \text{antidepmed1}) \\
= & -0.430 + 0.242 \times \text{Var} + 0.244 \times \text{inc5} - 0.206 \times \text{edu4} + 0.138 \times \text{edu5} \\
& - 0.097 \times \text{ftcd_score} + 0.046 \times \text{hedonsum_n_pq1} - 0.156 \times \text{hedonsum_y_pq1} \\
& - 0.033 \times \text{shaps_score_pq1} + 0.015 \times \text{antidepmed1} + 0.149 \times \text{NMR} \\
& + 0.019 \times (\text{Var} \times \text{cpd_ps}) + 0.017 \times (\text{Var} \times \text{readiness}) \\
& + 0.000 \times (\text{bdi_score_w00} \times \text{shaps_score_pq1}) - 0.011 \times (\text{ftcd_score} \times \text{readiness}) \\
& - 0.014 \times (\text{edu4} \times \text{readiness}) + 1.204 \times (\text{inc3} \times \text{antidepmed1})
\end{aligned}$$

This advanced model achieved the highest test set AUC of 0.711, suggesting that incorporating comprehensive interaction terms improved predictive performance. The variable importance plot revealed several noteworthy patterns. The most striking finding was the strong interaction between middle income level and antidepressant medication use (1.204), indicating substantial treatment effect heterogeneity across socioeconomic groups. Treatment-related interactions showed modest but meaningful effects, with Varenicline's effectiveness increasing with higher cigarettes per day (0.019) and readiness to quit (0.017). The model also captured important behavioral interactions, showing that higher nicotine dependence slightly reduced the benefit of quit readiness (-0.011), and that education level modified the effect of quit readiness (-0.014). Interestingly, the hypothesized interaction between depression severity and anhedonia showed minimal effect (0.000), suggesting that these symptoms might influence smoking cessation independently rather than synergistically.

A ROC Curve (AUC = 0.711)



B Cross-validation Results



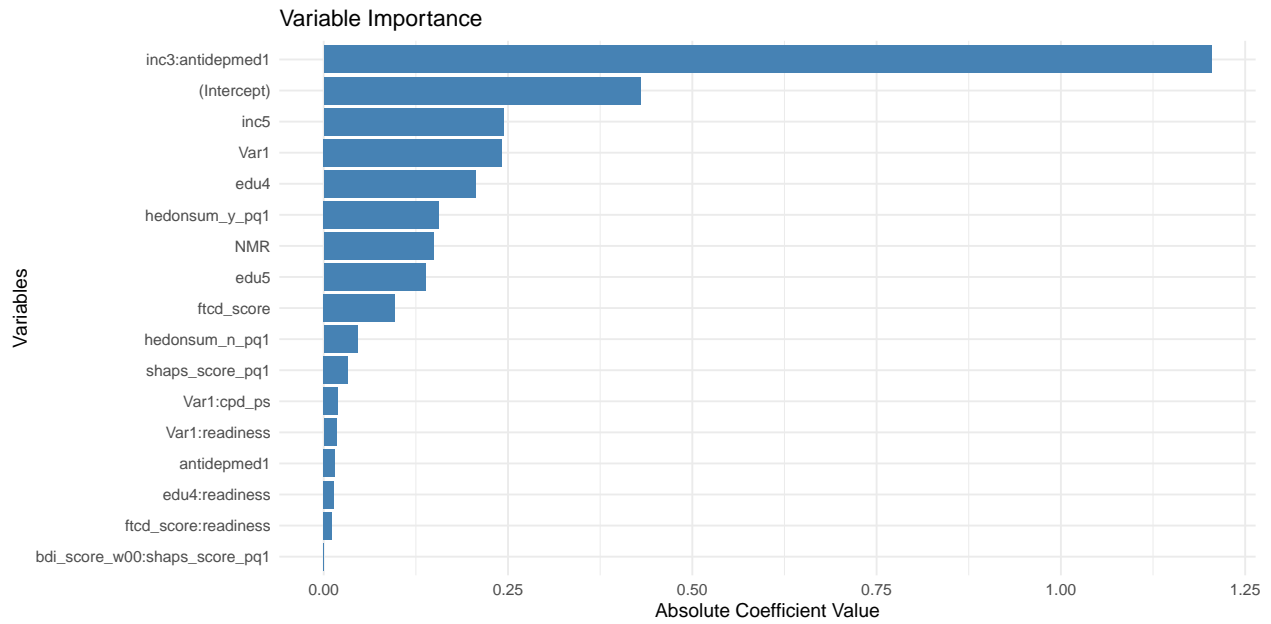


Table 5: Comparison of Models with Interaction Terms

Variable	Model with Basic Interaction Term	Model with Advanced Interaction Terms
(Intercept)	-0.488	-0.43
BA1	Eliminated	Eliminated
Var1	0.309	0.242
age_ps	Eliminated	Eliminated
sex_ps2	Eliminated	Eliminated
NHW1	Eliminated	Eliminated
Black1	Eliminated	Eliminated
Hisp1	Eliminated	Eliminated
inc2	Eliminated	Eliminated
inc3	Eliminated	Eliminated
inc4	Eliminated	Eliminated
inc5	0.214	0.244
edu2	Eliminated	Eliminated
edu3	Eliminated	Eliminated
edu4	-0.25	-0.206
edu5	0.215	0.138
bdi_score_w00	Eliminated	Eliminated
cpd_ps	Eliminated	Eliminated
ftcd_score	-0.149	-0.097
ftcd.5.mins	Eliminated	Eliminated
shaps_score_pq1	-0.039	-0.033
mde_curr1	-0.021	Eliminated
crv_total_pq1	Eliminated	Eliminated
hedonsum_n_pq1	0.04	0.046
hedonsum_y_pq1	-0.193	-0.156
otherdiag1	Eliminated	Eliminated
antidepmed1	0.165	0.015
NMR	0.122	0.149
Only.Menthol1	Eliminated	Eliminated
readiness	Eliminated	Eliminated
BA1:shaps_score_pq1	Eliminated	Eliminated
BA1:mde_curr1	-0.013	Eliminated
BA1:bdi_score_w00	Eliminated	Eliminated
Var1:ftcd_score	Eliminated	Eliminated

Table 5: Comparison of Models with Interaction Terms (*continued*)

Variable	Model with Basic Interaction Term	Model with Advanced Interaction Terms
Var1:cpd_ps	0.021	0.019
Var1:readiness	0.008	0.017
BA1:Black1	NA	Eliminated
BA1:NHW1	NA	Eliminated
Var1:Black1	NA	Eliminated
Var1:NHW1	NA	Eliminated
bdi_score_w00:shaps_score_pq1	NA	0
shaps_score_pq1:mde_curr1	NA	Eliminated
cpd_ps:ftcd_score	NA	Eliminated
ftcd_score:readiness	NA	-0.011
inc2:antidepmed1	NA	Eliminated
inc3:antidepmed1	NA	1.204
inc4:antidepmed1	NA	Eliminated
inc5:antidepmed1	NA	Eliminated
edu2:readiness	NA	Eliminated
edu3:readiness	NA	Eliminated
edu4:readiness	NA	-0.014
edu5:readiness	NA	Eliminated
ftcd_score:Only.Menthol1	NA	Eliminated
NMR:Only.Menthol1	NA	Eliminated

Table 6: Results of Models with Interaction Terms

Metric	Model with Basic Interaction Term	Model with Advanced Interaction Terms
AUC (Train)	0.845	0.854
AUC (Test)	0.685	0.711
Accuracy (Train)	0.802	0.802
Accuracy (Test)	0.800	0.808
Lambda Min	0.069	0.071

Discussion

In this study, we employed a series of regularized regression models to investigate the effectiveness of behavioral activation and varenicline for smoking cessation among individuals with current or past MDD. Through progressively complex modeling approaches, from basic LASSO and Ridge regression to interaction models, we gained several key insights about treatment effects and their moderators.

Our models consistently demonstrated good predictive performance, with test AUC values ranging from 0.651 to 0.711. The advanced interaction model achieved the highest predictive accuracy, suggesting the importance of considering treatment effect heterogeneity. However, the relatively small gap between training and test performance (AUC difference < 0.15) indicates that our models avoided severe overfitting, likely due to the effective regularization strategies employed.

Regarding treatment effectiveness, varenicline emerged as a consistently strong predictor of smoking cessation across all models. The basic LASSO model identified a substantial positive effect (coefficient = 0.802), which remained robust even after accounting for various interactions. In contrast, behavioral activation showed more modest and variable effects. The lack of a strong main effect for BA in our models aligns with the previous trial findings where BASC did not outperform standard behavioral treatment.

Importantly, our interaction models revealed significant treatment effect heterogeneity across different patient subgroups. For varenicline, the effectiveness appeared enhanced among heavier smokers (Var \times cpd_ps: 0.019) and those with higher readiness to quit (Var \times readiness: 0.017). These findings suggest that varenicline might be particularly beneficial for more severely dependent smokers who are motivated to quit. For BA,

the negative interaction with current MDD status ($BA \times mde_curr$: -0.013) indicates potentially reduced effectiveness among currently depressed patients, highlighting the challenges of treating this subgroup.

The advanced interaction model uncovered important socioeconomic dimensions of treatment response. The strong positive interaction between middle income level and antidepressant medication use ($inc3 \times antidepm$: 1.204) suggests that the effectiveness of depression treatment might be significantly moderated by socioeconomic status. Additionally, the negative interaction between education level and quit readiness ($edu4 \times readiness$: -0.014) implies that the translation of motivation into successful cessation might vary across educational backgrounds.

Several limitations of our study should be noted. First, our analysis was constrained by the relatively small sample size ($n=241$ after removing missing values), which might have limited our ability to detect smaller interaction effects. Second, the 50-50 train-test split, while ensuring robust validation, reduced the data available for model training. Third, the binary nature of our outcome measure (7-day point prevalence abstinence) might not fully capture the complexity of smoking cessation trajectories. Fourth, our models did not account for potential time-varying effects of treatments or the dynamic nature of depression symptoms during the quit attempt.

Future research should consider several directions. Larger sample sizes would enable more precise estimation of interaction effects and potentially reveal additional treatment effect moderators. Incorporating longitudinal measures of both smoking behavior and depression symptoms could provide insights into the temporal dynamics of treatment effects. Finally, more sophisticated modeling approaches, such as Bayesian methods or machine learning techniques, might better capture the complex relationships between patient characteristics and treatment outcomes.

Despite these limitations, our findings have important clinical implications. The consistent effectiveness of varenicline, particularly among heavier smokers, supports its use as a first-line treatment. However, the variable effects of behavioral activation and the important role of socioeconomic factors suggest the need for more personalized treatment approaches. Clinicians should consider both clinical and socioeconomic factors when tailoring smoking cessation interventions for patients with MDD.

References

1. Hitsman, Brian, George D. Papandonatos, Jacqueline K. Gollan, Mark D. Huffman, Raymond Niaura, David C. Mohr, Anna K. Veluz-Wilkins, et al. "Efficacy and Safety of Combination Behavioral Activation for Smoking Cessation and Varenicline for Treating Tobacco Dependence among Individuals with Current or Past Major Depressive Disorder: A 2×2 Factorial, Randomized, Placebo-controlled Trial." *Addiction* 118, no. 9 (September 2023): 1710–25. <https://doi.org/10.1111/add.16209>.

Code Appendix

```
knitr::opts_chunk$set(echo = FALSE)
knitr::opts_chunk$set(message = FALSE)
knitr::opts_chunk$set(warning = FALSE)
library(mice, warn.conflicts = FALSE)
library(naniar)
library(ggplot2)
library(dplyr)
library(readr)
library(tidyr)
library(readxl)
library(ggpubr)
library(gtsummary)
library(GGally)
library(ggcorrplot)
library(knitr)
library(kableExtra)
library(lubridate)
library(patchwork)
library(introdataviz)
library(glmnet)
library(gt)
library(L0Learn)
library(gridExtra)
library(purrr)
library(pROC)
library(caret)

# Load the data
data <- read.csv("../Data/project2.csv")
data

# Transform data type
data$abst <- as.factor(data$abst)
data$Var <- as.factor(data$Var)
data$BA <- as.factor(data$BA)
data$sex_ps <- as.factor(data$sex_ps)
data$NHW <- as.factor(data$NHW)
data$Black <- as.factor(data$Black)
data$Hispanic <- as.factor(data$Hispanic)
data$inc <- as.factor(data$inc)
data$edu <- as.factor(data$edu)
data$otherdiag <- as.factor(data$otherdiag)
data$antidepmed <- as.factor(data$antidepmed)
data$mde_curr <- as.factor(data$mde_curr)
data$Only.Menthol <- as.factor(data$Only.Menthol)
data$readiness <- as.numeric(data$readiness)

dim(data)

summary(data)

data <- na.omit(data)
```



```

summary(data)
dim(data)

summary_var1 <- tbl_summary(data %>% select(-id), by = Var, type = list(readiness ~ "continuous")) %>%
  add_p() %>%
  modify_header(stat_1 = "**No Varenicline**", stat_2 = "**Varenicline**")
summary_var2 <- tbl_summary(data %>% select(-id), by = BA, type = list(readiness ~ "continuous")) %>%
  add_p() %>%
  modify_header(stat_1 = "**No Psychotherapy**", stat_2 = "**Psychotherapy**")

tbl_merge(
  tbls = list(summary_var1, summary_var2),
  tab_spanner = c("**Grouped by Pharmacotherapy Status**", "**Grouped by Psychotherapy Status**")
) %>%
  as_kable_extra(booktabs = TRUE,
  caption = "Data Summary Table",
  longtable = TRUE, linesep = "") %>%
  kableExtra::kable_styling(font_size = 8, latex_options = c("repeat_header", "HOLD_position"))

continuous_vars <- data[, c("age_ps", "ftcd_score", "bdi_score_w00", "cpd_ps", "crv_total_pq1", "hedonsum_n_pq1", "hedonsum_y_pq1")]
corr_plot <- ggpairs(continuous_vars, title = "Correlation Matrix of Baseline Predictors") +
  theme_minimal()

ggsave("../Figures/corr_plot.png", plot = corr_plot, dpi = 300)
corr_plot

dist_numeric <- data %>%
  select(-id) %>%
  keep(is.numeric) %>%
  gather() %>%
  ggplot(aes(value)) +
    facet_wrap(~ key, scales = "free") +
    geom_histogram() +
    ggtitle("Distribution of Numeric Variables")

dist_cat <- data %>%
  select(-id) %>%
  keep(is.factor) %>%
  gather(key = "key", value = "value") %>%
  ggplot(aes(x = value)) +
    facet_wrap(~ key, scales = "free") +
    geom_bar() +
    ggtitle("Distribution of Categorical Variables")

dist_plot <- gridExtra::grid.arrange(dist_numeric, dist_cat, ncol = 2)

ggsave("../Figures/dist_plot.png", plot = dist_plot, dpi = 300)
dist_plot

data$hedonsum_n_pq1 <- log(data$hedonsum_n_pq1 + 1)
data$hedonsum_y_pq1 <- log(data$hedonsum_y_pq1 + 1)
data$NMR <- log(data$NMR)

```

```

dist_after_log <- data %>%
  select(c(hedonsum_n_pq1, hedonsum_y_pq1, NMR)) %>%
  gather() %>%
  ggplot(aes(value)) +
    facet_wrap(~ key, scales = "free") +
    geom_histogram() +
    ggtitle("Distribution after Log Transformation")

ggsave("../Figures/dist_after_log.png", plot = dist_after_log, dpi = 300)
dist_after_log

# Split the data
set.seed(123)

train_index <- createDataPartition(data$abst, p = 0.5, list = FALSE)

train_data <- data[train_index, ] %>% select(-id)
test_data <- data[-train_index, ] %>% select(-id)

X_train <- model.matrix(abst ~ ., data = train_data)[, -1]
Y_train <- factor(train_data$abst)

X_test <- model.matrix(abst ~ ., data = test_data)[, -1]
Y_test <- factor(test_data$abst)
model_fit <- function(X_train, Y_train, X_test, Y_test, alpha, lambda_seq = seq(0.001, 0.1, length.out = 100)) {
  set.seed(123)
  cv_model <- cv.glmnet(X_train, Y_train, alpha = alpha, family = "binomial", lambda = lambda_seq)
  best_lambda <- cv_model$lambda.min
  lasso_coef <- coef(cv_model, s = best_lambda)

  # Get predictions for both train and test sets
  train_pred <- predict(cv_model, newx = X_train, s = best_lambda, type = "response")
  test_pred <- predict(cv_model, newx = X_test, s = best_lambda, type = "response")

  # Convert predictions to binary using 0.5 threshold
  train_pred_binary <- ifelse(train_pred > 0.5, 1, 0)
  test_pred_binary <- ifelse(test_pred > 0.5, 1, 0)

  # ROC and AUC
  train_roc <- roc(Y_train, as.numeric(train_pred))
  test_roc <- roc(Y_test, as.numeric(test_pred))

  # Calculate metrics
  metrics <- data.frame(
    Metric = c(
      "AUC (Train)",
      "AUC (Test)",
      "Accuracy (Train)",
      "Accuracy (Test)",
      "Lambda Min"
    ),
    Value = c(
      auc(train_roc),

```

```

    auc(test_roc),
    mean(train_pred_binary == Y_train),
    mean(test_pred_binary == Y_test),
    cv_model$lambda.min
  )
) %>%
  mutate(Value = round(Value, 3))

# Create ROC curve data
roc_df <- data.frame(
  FPR = 1 - test_roc$specificities,
  TPR = test_roc$sensitivities
)

# Create ROC plot using ggplot2
roc_plot <- ggplot(roc_df, aes(x = FPR, y = TPR)) +
  geom_line(color = "blue", size = 1) +
  geom_abline(slope = 1, intercept = 0, linetype = "dashed", color = "gray") +
  labs(
    title = paste("ROC Curve (AUC =", round(auc(test_roc), 3), ")"),
    x = "False Positive Rate",
    y = "True Positive Rate"
  ) +
  theme_minimal()

# Create CV plot data
cv_df <- data.frame(
  lambda = log(cv_model$lambda),
  mean = cv_model$cvm,
  upper = cv_model$cvup,
  lower = cv_model$cvlo
)

# Create CV plot using ggplot2
cv_plot <- ggplot(cv_df, aes(x = lambda)) +
  geom_line(aes(y = mean), color = "blue") +
  geom_ribbon(aes(ymin = lower, ymax = upper), alpha = 0.2) +
  geom_vline(xintercept = log(cv_model$lambda.min), linetype = "dashed", color = "red") +
  geom_vline(xintercept = log(cv_model$lambda.1se), linetype = "dashed", color = "green") +
  labs(
    title = "Cross-validation Results",
    x = "log(Lambda)",
    y = "Mean-Squared Error"
  ) +
  theme_minimal()

# Combine plots
combined_plot <- ggarrange(roc_plot, cv_plot,
  ncol = 2,
  labels = c("A", "B"))

# Create coefficient dataframe
coef_df <- data.frame(

```

```

    Variable = rownames(lasso_coef),
    Coefficient = as.vector(lasso_coef)
  ) %>%
  mutate(Coefficient = ifelse(Coefficient == 0, "Eliminated", round(Coefficient, 3)))

  return(list(
    combined_plot = combined_plot,
    coef_df = coef_df,
    metrics = metrics
  ))
}

plot_variable_importance <- function(coef_df) {
  # Calculate variable importance by taking absolute values of non-eliminated coefficients
  var_importance <- coef_df %>%
    filter(Coefficient != "Eliminated") %>%
    mutate(
      Coefficient = as.numeric(Coefficient),
      Importance = abs(Coefficient)
    ) %>%
    arrange(desc(Importance))

  # Create bar plot of variable importance
  importance_plot <- ggplot(var_importance, aes(x = reorder(Variable, Importance), y = Importance)) +
    geom_bar(stat = "identity", fill = "steelblue") +
    coord_flip() + # Flip coordinates for horizontal bars
    theme_minimal() + # Use minimal theme for clean look
    labs(title = "Variable Importance",
         x = "Variables",
         y = "Absolute Coefficient Value")

  # Return both plot and processed data
  return(list(
    plot = importance_plot,
    importance_df = var_importance
  ))
}

lambda_seq <- seq(0.001, 0.1, length.out = 100)
lasso_model <- model_fit(X_train, Y_train, X_test, Y_test, alpha = 1, lambda_seq = lambda_seq)

print(lasso_model$combined_plot)
plot_variable_importance(lasso_model$coef_df)$plot

ggsave("../Figures/lasso_model.png", plot = lasso_model$combined_plot, dpi = 300)
ggsave("../Figures/lasso_variable_importance.png", plot = plot_variable_importance(lasso_model$coef_df))

lambda_seq <- seq(0.001, 0.1, length.out = 100)
ridge_model <- model_fit(X_train, Y_train, X_test, Y_test, alpha = 0, lambda_seq = lambda_seq)

print(ridge_model$combined_plot)
plot_variable_importance(ridge_model$coef_df)$plot

ggsave("../Figures/ridge_model.png", plot = ridge_model$combined_plot, dpi = 300)

```

```

ggsave("../Figures/ridge_variable_importance.png", plot = plot_variable_importance(ridge_model$coef_df))

combined_table <- full_join(ridge_model$coef_df, lasso_model$coef_df, by = "Variable") %>%
  kable(
    col.names = c("Variable", "Ridge Regression Model", "Lasso Regression Model"),
    caption = "Comparison of Basic Ridge and Lasso Regression Models"
  ) %>%
  kable_styling(bootstrap_options = c("striped", "hover"),
                full_width = FALSE, font_size = 8, latex_options = c("repeat_header", "HOLD_position"))
column_spec(1, bold = TRUE)

combined_table

combined_result <- full_join(ridge_model$metrics, lasso_model$metrics, by = "Metric") %>%
  kable(
    col.names = c("Metric", "Ridge Regression Model", "Lasso Regression Model"),
    caption = "Results of Basic Ridge and Lasso Regression Models"
  ) %>%
  kable_styling(bootstrap_options = c("striped", "hover"),
                full_width = FALSE, font_size = 8, latex_options = c("repeat_header", "HOLD_position"))
column_spec(1, bold = TRUE)

combined_result
X_train_interactions <- model.matrix(
  ~ BA + Var +
  # Demographic variables
  age_ps + sex_ps + NHW + Black + Hisp + inc + edu +
  # Clinical and smoking-related variables
  bdi_score_w00 + cpd_ps + ftcd_score + ftcd.5.mins +
  shaps_score_pq1 + mde_curr + crv_total_pq1 +
  hedonsum_n_pq1 + hedonsum_y_pq1 +
  otherdiag + antidepmed + NMR + Only.Menthol + readiness +
  # BA interaction terms
  BA:shaps_score_pq1 + # BA * anhedonia
  BA:mde_curr + # BA * current depression status
  BA:bdi_score_w00 + # BA * depression severity
  # Varenicline interaction terms
  Var:ftcd_score + # Varenicline * nicotine dependence
  Var:cpd_ps + # Varenicline * cigarettes per day
  Var:readiness, # Varenicline * readiness to quit
  data = train_data %>% select(-abst))[, -1]

X_test_interactions <- model.matrix(
  ~ BA + Var +
  # Demographic variables
  age_ps + sex_ps + NHW + Black + Hisp + inc + edu +
  # Clinical and smoking-related variables
  bdi_score_w00 + cpd_ps + ftcd_score + ftcd.5.mins +
  shaps_score_pq1 + mde_curr + crv_total_pq1 +
  hedonsum_n_pq1 + hedonsum_y_pq1 +
  otherdiag + antidepmed + NMR + Only.Menthol + readiness +
  # BA interaction terms
  BA:shaps_score_pq1 + # BA * anhedonia

```

```

BA:mde_curr +          # BA * current depression status
BA:bdi_score_w00 +      # BA * depression severity
# Varenicline interaction terms
Var:ftcd_score +        # Varenicline * nicotine dependence
Var:cpd_ps +            # Varenicline * cigarettes per day
Var:readiness,          # Varenicline * readiness to quit
data = test_data %>% select(-abst))[, -1]
lambda_seq <- seq(0.001, 0.1, length.out = 100)
basic_interaction_model <- model_fit(X_train_interactions, Y_train, X_test_interactions, Y_test, alpha = 0.05)

print(basic_interaction_model$combined_plot)
plot_variable_importance(basic_interaction_model$coef_df)$plot

ggsave("../Figures/basic_interaction_model.png", plot = basic_interaction_model$combined_plot, dpi = 300)
ggsave("../Figures/basic_interaction_variable_importance.png", plot = plot_variable_importance(basic_interaction_model$coef_df))

# Create model matrix with extended interaction terms
X_train_interactions <- model.matrix(
  ~ BA + Var +
  # Demographic variables
  age_ps + sex_ps + NHW + Black + Hisp + inc + edu +
  # Clinical and smoking-related variables
  bdi_score_w00 + cpd_ps + ftcd_score + ftcd.5.mins +
  shaps_score_pq1 + mde_curr + crv_total_pq1 +
  hedonsum_n_pq1 + hedonsum_y_pq1 +
  otherdiag + antidepmed + NMR + Only.Menthol + readiness +
  # BA interaction terms
  BA:shaps_score_pq1 + # BA * anhedonia
  BA:mde_curr +        # BA * current depression status
  BA:bdi_score_w00 +   # BA * depression severity
  BA:Black +           # BA * race (Black)
  BA:NHW +             # BA * race (Non-Hispanic White)
  # Varenicline interaction terms
  Var:ftcd_score +     # Varenicline * nicotine dependence
  Var:cpd_ps +         # Varenicline * cigarettes per day
  Var:readiness +      # Varenicline * readiness to quit
  Var:Black +          # Varenicline * race (Black)
  Var:NHW +            # Varenicline * race (Non-Hispanic White)
  # Depression symptom interactions
  bdi_score_w00:shaps_score_pq1 + # Depression severity * anhedonia
  mde_curr:shaps_score_pq1 +      # Current depression status * anhedonia
  # Smoking behavior interactions
  ftcd_score:cpd_ps +             # Nicotine dependence * cigarettes per day
  ftcd_score:readiness +         # Nicotine dependence * readiness to quit
  # Socioeconomic status interactions
  antidepmed:inc +               # Antidepressant medication * income
  edu:readiness +               # Education * readiness to quit
  # Menthol cigarette interactions
  Only.Menthol:ftcd_score +      # Menthol use * nicotine dependence
  Only.Menthol:NMR,             # Menthol use * nicotine metabolism ratio
data = train_data %>% select(-abst))[, -1]

X_test_interactions <- model.matrix(

```

```

~ BA + Var +
# Demographic variables
age_ps + sex_ps + NHW + Black + Hisp + inc + edu +
# Clinical and smoking-related variables
bdi_score_w00 + cpd_ps + ftc_d_score + ftc_d.5.mins +
shaps_score_pq1 + mde_curr + crv_total_pq1 +
hedonsum_n_pq1 + hedonsum_y_pq1 +
otherdiag + antidepmed + NMR + Only.Menthol + readiness +
# BA interaction terms
BA:shaps_score_pq1 + # BA * anhedonia
BA:mde_curr + # BA * current depression status
BA:bdi_score_w00 + # BA * depression severity
BA:Black + # BA * race (Black)
BA:NHW + # BA * race (Non-Hispanic White)
# Varenicline interaction terms
Var:ftcd_score + # Varenicline * nicotine dependence
Var:cpd_ps + # Varenicline * cigarettes per day
Var:readiness + # Varenicline * readiness to quit
Var:Black + # Varenicline * race (Black)
Var:NHW + # Varenicline * race (Non-Hispanic White)
# Depression symptom interactions
bdi_score_w00:shaps_score_pq1 + # Depression severity * anhedonia
mde_curr:shaps_score_pq1 + # Current depression status * anhedonia
# Smoking behavior interactions
ftcd_score:cpd_ps + # Nicotine dependence * cigarettes per day
ftcd_score:readiness + # Nicotine dependence * readiness to quit
# Socioeconomic status interactions
antidepmed:inc + # Antidepressant medication * income
edu:readiness + # Education * readiness to quit
# Menthol cigarette interactions
Only.Menthol:ftcd_score + # Menthol use * nicotine dependence
Only.Menthol:NMR, # Menthol use * nicotine metabolism ratio
data = test_data %>% select(-abst))[, -1]
lambda_seq <- seq(0.001, 0.1, length.out = 100)
advanced_interaction_model <- model_fit(X_train_interactions, Y_train, X_test_interactions, Y_test, alphas = lambda_seq)

print(advanced_interaction_model$combined_plot)
plot_variable_importance(advanced_interaction_model$coef_df)$plot

ggsave("../Figures/advanced_interaction_model.png", plot = advanced_interaction_model$combined_plot, dpi = 300)
ggsave("../Figures/advanced_interaction_variable_importance.png", plot = plot_variable_importance(advanced_interaction_model$coef_df), dpi = 300)

combined_table <- full_join(basic_interaction_model$coef_df, advanced_interaction_model$coef_df, by = "Variable")
kable(
  col.names = c("Variable", "Model with Basic Interaction Term", "Model with Advanced Interaction Term"),
  caption = "Comparison of Models with Interaction Terms"
) %>%
kable_styling(bootstrap_options = c("striped", "hover"),
  full_width = FALSE, font_size = 8, latex_options = c("repeat_header", "HOLD_position"))
column_spec(1, bold = TRUE) # Make Variable column bold

combined_table

```

```

combined_result <- full_join(basic_interaction_model$metrics, advanced_interaction_model$metrics, by =
  kable(
    col.names = c("Metric", "Model with Basic Interaction Term", "Model with Advanced Interaction Terms"),
    caption = "Results of Models with Interaction Terms"
  ) %>%
  kable_styling(bootstrap_options = c("striped", "hover"),
    full_width = FALSE, font_size = 8, latex_options = c("repeat_header", "HOLD_position"))
  column_spec(1, bold = TRUE) # Make Metric column bold
combined_result

```