

## Supplementary Online Content

Perlis RH, Uher R, Ostacher M, Goldberg JF, Trivedi MH, Rush AJ, Fava M. Association between bipolar spectrum features and treatment outcomes in outpatients with major depressive disorder. *Arch Gen Psychiatry*. 2010;66(12):10.1001/archgenpsychiatry.2010.179.

**eFigure 1.** Proposed structural equation model for association between latent bipolar variable and treatment resistance in major depressive disorder. The figure summarizes the structure assumed in a structural equation model examining association between a latent bipolar variable and failure to remit with multiple treatment trials in major depressive disorder. Both treatment resistance and bipolar liability are assumed to be latent variables which can be estimated based on observed variables (treatment response, for resistance, and bipolar spectrum features, for bipolar liability.) See text for details.

**eFigure 2.** Results of structural equation model for association between latent bipolar variable and treatment resistance in major depressive disorder. The figure superimposes results from fitting a model for the association between latent bipolar variable and treatment resistance in major depressive disorder. Numbers at the bottom (“Loading:”) show loading of individual bipolar spectrum features on the latent bipolar spectrum variable.

**eFigure 3.** Results of structural equation model for association between latent bipolar variable and absence of postbaseline visits. The figure superimposes results from fitting a model for the association between latent bipolar variable and failure to return following baseline study visit. Numbers at the bottom show loading of individual bipolar spectrum features on the latent bipolar spectrum variable.

**eFigure 4.** Results of structural equation model for association between latent bipolar variable and loss to follow-up. The figure superimposes results from fitting a model for the association between latent bipolar variable and loss to follow-up. Numbers at the bottom show loading of individual bipolar spectrum features on the latent bipolar spectrum variable.

**eFigure 5.** Results of structural equation model for association between latent bipolar variable and serious psychiatric adverse events in major depressive disorder. The figure superimposes results from fitting a model for the association between latent bipolar variable and serious psychiatric adverse event. Numbers at the bottom show loading of individual bipolar spectrum features on the latent bipolar spectrum variable.

**eTable 1.** Association between individual bipolar spectrum features and hazard for remission across levels in STAR\*D – alternate model using time-to-event, rather than levels-to-event.

**eTable 2.** PDSQ psychosis screen items endorsed by STAR\*D participants at study entry.

**eTable 3.** Association between potential sociodemographic and clinical confounding variables and remission. These include age, sex, treatment setting (primary versus specialty), ethnicity and race, marital status, payor type, education, depression severity, and comorbid panic disorder, alcohol use disorder, or substance use disorder.

**eTable 4.** Correlations between putative indicators of latent bipolarity.

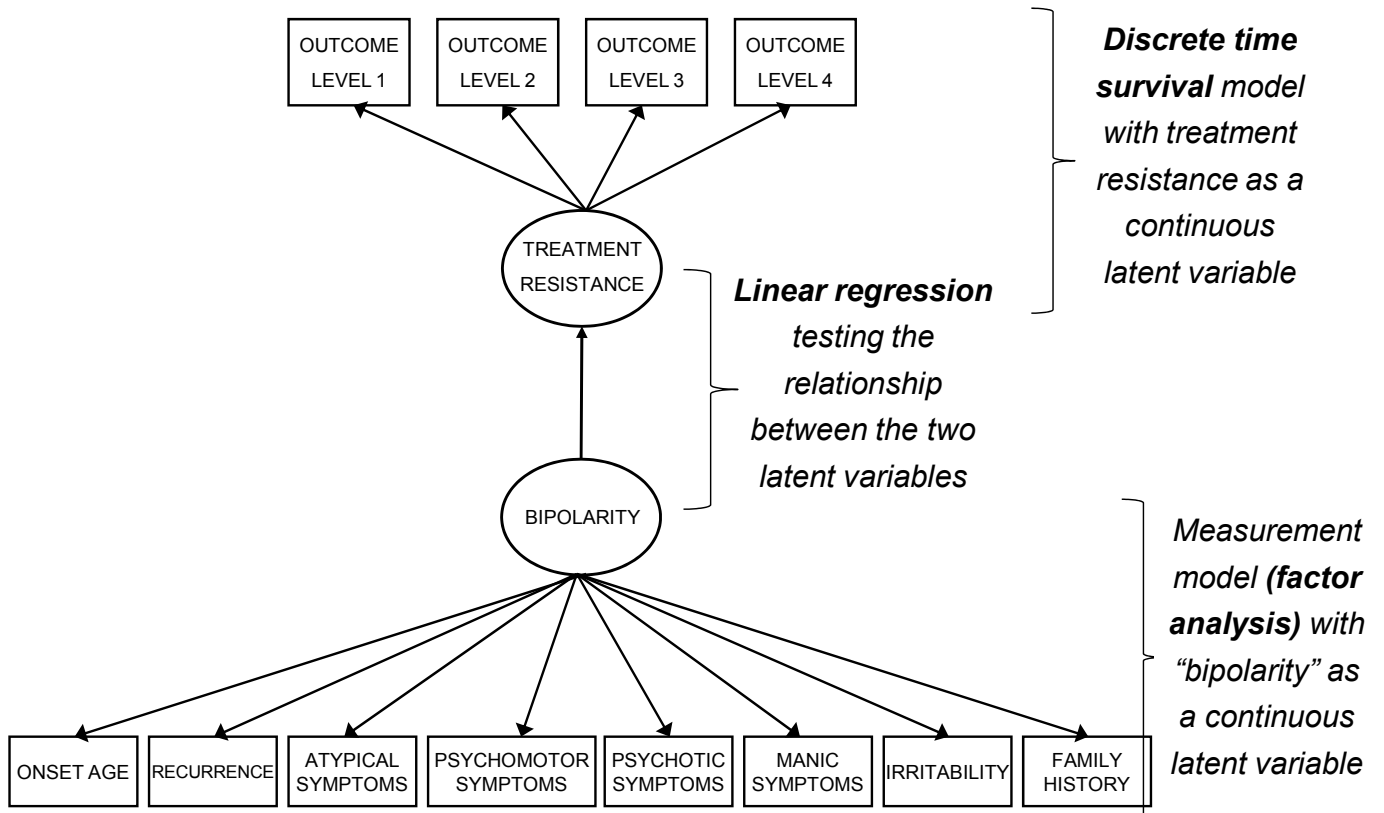
**eTable 5.** Measurement model fit and psychometric indices.

**eTable 6.** Properties of bipolar trait indicators in a measurement model,

**eTable 7.** Association between potential sociodemographic and clinical confounding variables and adverse events.

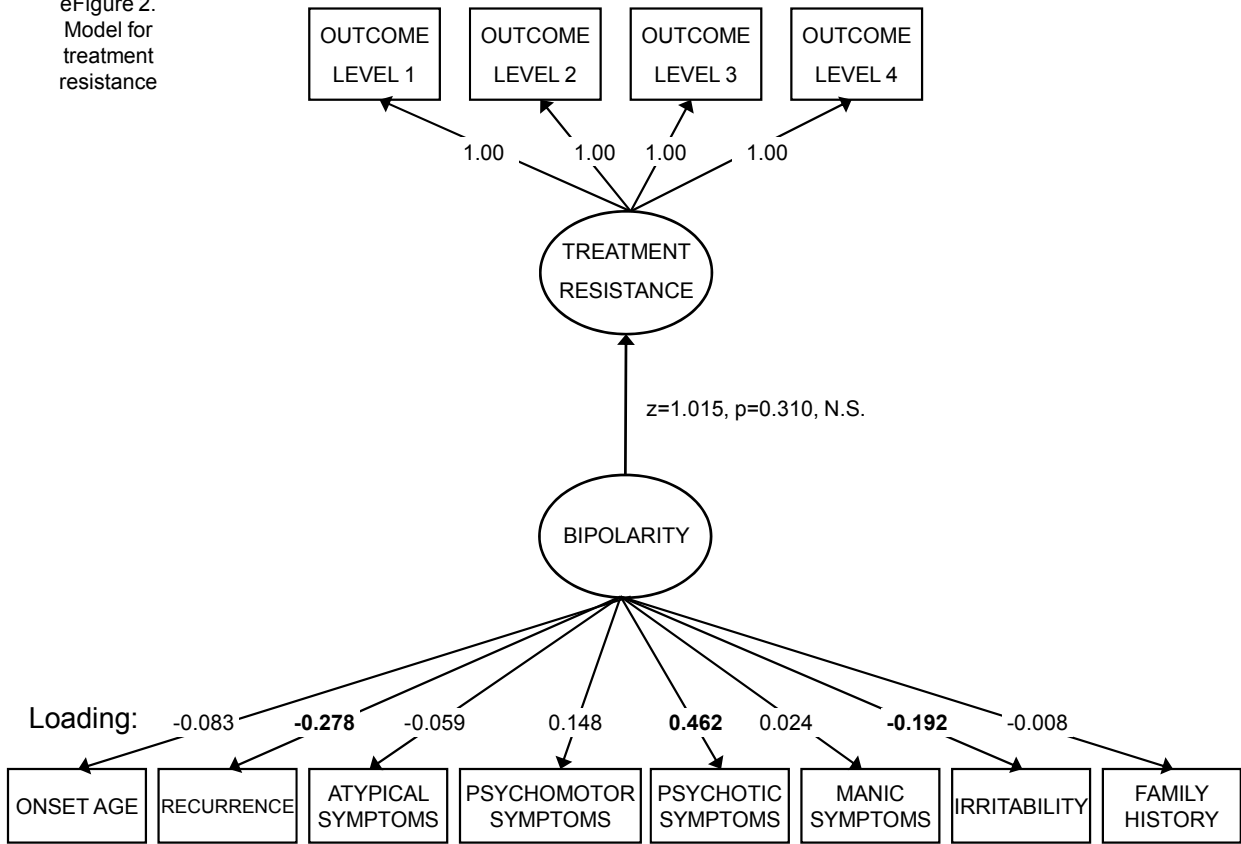
This supplementary material has been provided by the authors to give readers additional information about their work.

eFigure 1.  
Proposed  
model



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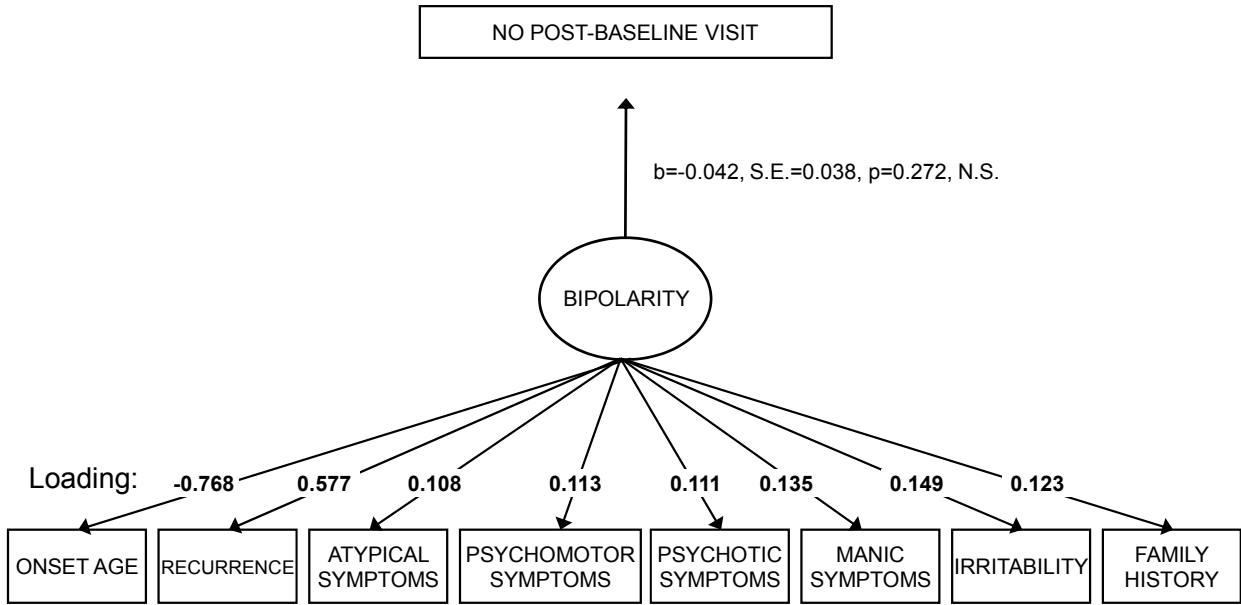
eFigure 2.  
Model for  
treatment  
resistance



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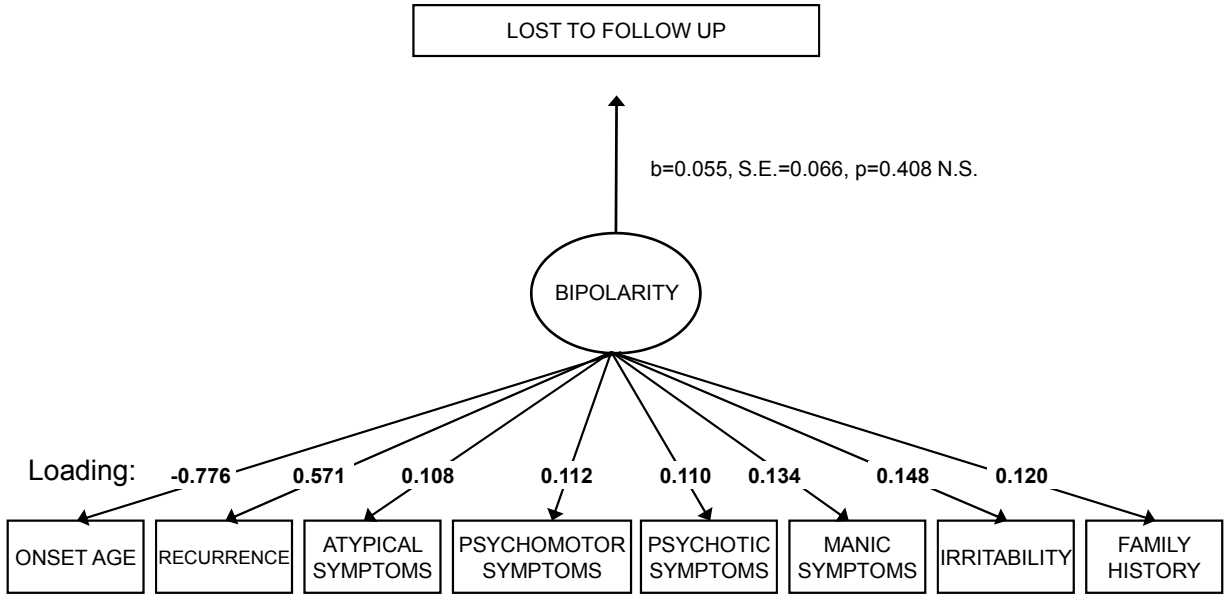
eFigure 3. Model for no post-baseline visit



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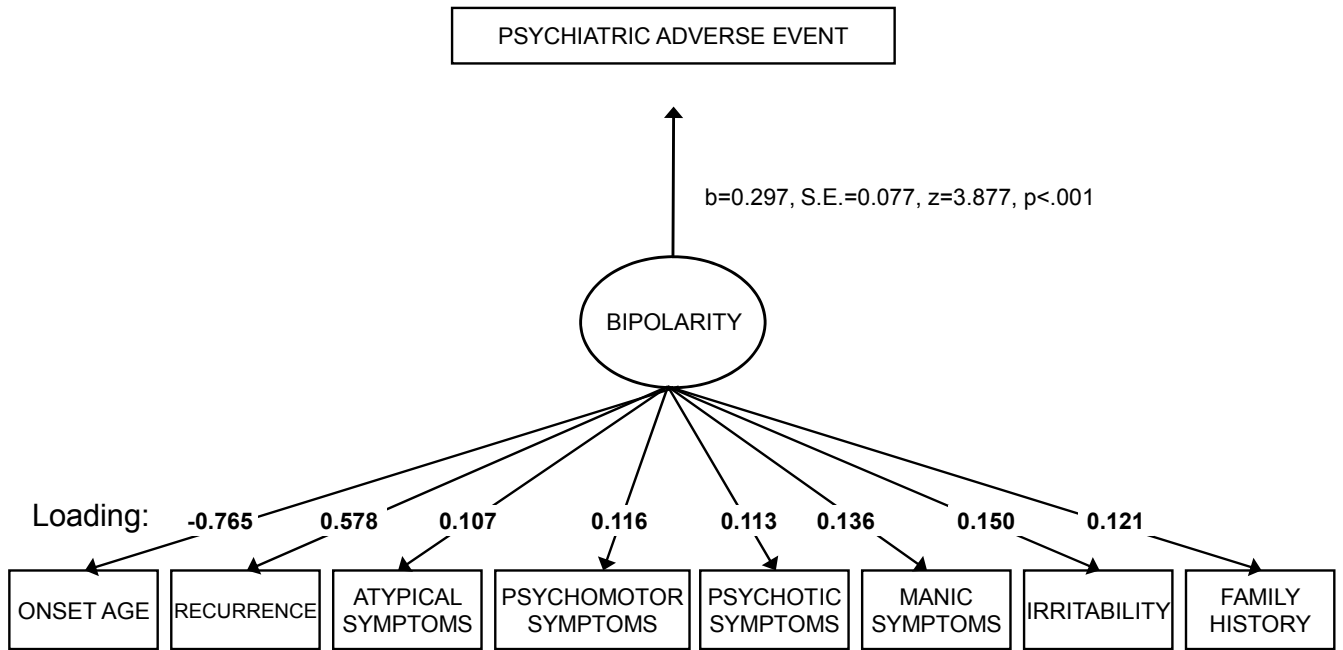
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eFigure 4. Model for loss to follow-up



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eFigure 5. Model for psychiatric adverse event



**eTable 1.** Association between individual bipolar spectrum features and hazard for remission across levels in STAR\*D (alternate model using time-to-event, rather than levels-to-event).

Feature	crude			adjusted		
	HR	95% CI	*	HR	95% CI	*
Family history - bipolar	0.99	0.85-1.15		0.98	0.84-1.14	
Episode duration ≤ 3 mo	1.20	1.09-1.33	*	1.21	1.09-1.34	*
3 or more prior episodes	0.92	0.84-1.01		0.92	0.83-1.01	
Onset before age 25	1.00	0.92-1.09		0.97	0.88-1.07	
Atypical depression (DSM-IV)	0.78	0.69-0.88	*	0.79	0.70-0.90	*
Manic-like symptoms (1+)	1.01	0.93-1.11		1.03	0.94-1.12	
Manic-like symptoms (2+)	1.10	0.99-1.22		1.12	1.01-1.25	*
Manic-like symptoms (3+)	1.22	1.06-1.39	*	1.25	1.09-1.44	*
Psychosis-like symptoms (1+)	0.77	0.69-0.85	*	0.81	0.73-0.90	*
Psychosis-like symptoms (2+)	0.68	0.58-0.79	*	0.74	0.63-0.86	*
Psychosis-like symptoms (3+)	0.76	0.60-0.97	*	0.87	0.68-1.11	
Bipolar spectrum illness <sup>^</sup>	0.92	0.82-1.02		0.91	0.81-1.01	
IDS~: irritability	0.88	0.83-0.93	*	0.87	0.82-0.91	*
IDS: slowing	0.80	0.74-0.86	*	0.81	0.75-0.88	*
IDS: agitation	0.83	0.79-0.89	*	0.84	0.79-0.89	*
IDS: hypersomnia	0.93	0.88-0.97	*	0.91	0.86-0.96	*
IDS: increased appetite	0.89	0.85-0.94	*	0.90	0.85-0.94	*
Onset age (years)	1.00	1.00-1.00		1.00	1.00-1.01	
PDSQ~ mania-like score	1.04	1.00-1.07	*	1.04	1.01-1.08	*
PDSQ psychosis-like score	0.86	0.81-0.91	*	0.89	0.84-0.94	*

<sup>^</sup> Bipolar spectrum defined by Ghaemi and Goodwin criteria; see text for details

~ IDS: Inventory of Depressive Symptoms; PDSQ: Psychiatric Diagnostic Screening Questionnaire

\* 95% CI excludes 1 (i.e., p<0.05)



**eTable 2. PDSQ psychosis-like screen items endorsed by STAR\*D participants (n=3,999)^**

Item	n	%
Told things that happened were your imagination	501	12.5
Convinced others were spying	827	20.7
Someone was plotting to harm you	278	7.0
Special powers	102	2.6
Controlled by outside force	128	3.2
Seeing or hearing things	228	5.7

^ Refers to patient-reported symptoms in the 2 weeks prior to study entry; see text for details.  
PDSQ, Psychiatric Diagnosis Screening Questionnaire

**eTable 3. Sociodemographic and clinical features examined for association with remission hazard**

Feature	HR	95% CI
Ham-D total score	0.95	0.94-0.96
Male gender	0.98	0.90-1.07
Age (in decades)	0.98	0.95-1.01
Primary care (versus specialty) site	1.04	0.95-1.14
White (vs non)	1.37	1.22-1.54
Hispanic (vs non)	0.99	0.87-1.13
Married (current)	1.16	1.06-1.27
Public insurance	0.79	0.70-0.90
Did not graduate high school	0.84	0.73-0.96
Panic disorder (by PDSQ)	0.70	0.63-0.77
Substance use disorder (by PDSQ)	0.88	0.75-1.02
Alcohol use disorder (by PDSQ)	1.01	0.91-1.11

\* 95% CI excludes 1 (i.e.,  $p < 0.05$ )

PDSQ, Psychiatric Diagnosis Screening Questionnaire

**eTable 4: Correlations between putative indicators of latent bipolarity.** The non-parametric Spearman's rank correlation coefficients are given.

		yonage	recc	atyp	psymot	psych	man	iirtb	bip
Age of onset (younger)	yonage								
Recurrence	recc	0.48							
Atypical symptoms	atyp	0.10	0.04						
Psychomotor symptoms	psymot	0.04	0.05	-0.02					
Psychotic-like symptoms	psych	0.05	0.01	0.00	0.22				
Manic-like symptoms	man	0.07	0.03	0.00	0.11	0.22			
Irritability	iirtb	0.08	0.02	0.03	0.20	0.15	0.09		
Family history of bipolar	bip	0.09	0.06	0.02	0.05	0.03	0.02	0.02	

**eTable 5: Measurement model fit and psychometric indices.**

Index/Criterion	value
Cronbach alpha	0.14
Covariance explained	0.74
CFI	0.54
TLI	0.39
RMSEA	0.09
WRMR	3.54
AIC	89644.08
BIC	89776.47
BICadj	89709.74

CFI, comparative fit index; TLI, Tucker-Lewis index; RMSEA, root mean square error of approximation; WRMR, weighted root mean square residual

AIC, Akaike's information criterion; BIC, Bayesian information criterion; BICadj, Bayesian information criterion (adjusted)

**eTable 6: Properties of bipolar trait indicators in a measurement model.** Inter-item covariance is the standardized average covariance with all other items. Item-rest correlation (also termed adjusted item-total correlation) is the correlation with a scale constructed with all items except the item under examination. Common factor loading is the standardized factor loading from a one-factor confirmatory factor analysis model.

	Inter-item covariance	Item-rest correlation	Common factor loading	Percentage covariance explained by common factor	Percentage variance explained by common factor (R <sup>2</sup> )
Age of onset (younger)	0.04	0.28	0.78	0.59	0.28
Recurrence	0.28	0.41	0.57	0.56	0.18
Atypical symptoms	0.62	0.08	0.11	0.62	0.02
Psychomotor symptoms	0.65	0.07	0.11	0.80	0.31
Psychotic-like symptoms	0.68	0.07	0.14	0.80	0.37
Manic-like symptoms	0.67	0.10	0.16	0.85	0.20
Irritability	0.63	0.12	0.15	0.88	0.27
Family history of bipolar	0.69	0.09	0.23	0.78	0.06
Total	0.53	0.14	0.28	0.74	0.21

**eTable 7.** Sociodemographic and clinical features examined for association with odds of adverse outcomes

Feature	Early discontinuation			Loss to follow-up			Adverse event		
	OR	95% CI		OR	95% CI	*	OR	95% CI	*
Ham-D total score	1.01	0.99-1.03		1.07	1.05-1.10	*	1.13	1.09-1.18	*
Male gender	0.81	0.65-1.02		0.93	0.73-1.18		1.44	0.93-2.22	
Age (in decades)	0.99	0.98-0.99	*	0.98	0.97-0.99	*	0.97	0.96-0.99	*
Primary care (versus specialty) site	1.41	1.14-1.75	*	1.41	1.11-1.77	*	0.68	0.42-1.09	
White (vs non)	0.67	0.52-0.85	*	0.59	0.46-0.76	*	0.78	0.47-1.28	
Hispanic (vs non)	1.28	0.95-1.73		1.45	1.06-1.99	*	1.44	0.81-2.58	
Married	0.82	0.64-1.03		0.64	0.49-0.83	*	1.00	0.63-1.58	
Public insurance	1.84	1.45-2.35	*	1.39	1.05-1.84	*	1.33	0.78-2.25	
Did not graduate high school	1.98	1.51-2.59	*	1.59	1.16-2.17	*	1.12	0.59-2.12	
Panic disorder (by PDSQ)	1.62	1.30-2.01	*	1.93	1.52-2.43	*	2.15	1.40-3.32	*
Substance use disorder (by PDSQ)	1.47	1.08-2.02	*	1.40	0.99-1.98		2.45	1.44-4.17	*
Alcohol use disorder (by PDSQ)	0.90	0.70-1.17		1.29	1.00-1.68		1.29	0.80-2.09	

Ham-D, Hamilton Rating Scale of Depression Severity

PDSQ, Psychiatric Diagnosis Screening Questionnaire

\* 95% CI excludes 1 (i.e.,  $p < 0.05$ )