Supplementary Table 1. Clinical and sociodemographic predictors of changes in work productivity

outcomes during acute- and continuation-phases of CO-MED trial.

	Absenteeism		Presenteeism		Work Productivity Loss	
	Estimate	SE	Estimate	SE	Estimate	SE
Acute-phase						
Age	0.09	0.05	0.16	0.08	0.14	0.09
Gender	0.52	1.33	-1.57	2.16	-2.29	2.28
Hispanic ethnicity	-0.15	1.48	2.76	2.49	2.16	2.65
Race[a] black	1.44	1.49	1.26	2.42	0.97	2.54
Race[a] other	1.08	2.07	1.68	3.46	2.64	3.57
Education[b]: 12 – 15 years	-3.62	2.02	**-8.10***	3.32	**-10.49****	3.47
Education[b]: 16 years or more	**-5.44***	2.21	**-8.55***	3.65	**-10.89****	3.81
Depression onset before age 18	1.21	1.18	-0.60	1.94	-0.11	2.02
Suicidal ideation at baseline	0.79	1.24	-1.47	2.04	-2.23	2.13
Anxious depression at baseline	-0.24	1.26	0.07	2.10	0.65	2.19
Bupropion combination[c]	-0.51	1.40	2.52	2.30	1.77	2.41
Venlafaxine combination[c]	0.41	1.38	1.74	2.29	1.45	2.38
Monthly income[d]: $2000 - $4000	0.09	1.35	2.88	2.22	3.40	2.30

Monthly income[d]: > $4000	-2.14	1.63	0.35	2.62	-1.56	2.81
Baseline QIDS-SR	-0.01	0.19	-0.30	0.31	-0.04	0.32
Baseline CPFQ	0.11	0.13	0.12	0.22	0.01	0.23
QIDS-SR (weeks 1-12)	**0.64*****	0.14	**1.73*****	0.18	**1.91*****	0.21
CPFQ (weeks 1-12)	0.01	0.11	**0.79*****	0.13	**0.77*****	0.15
Baseline absenteeism	**0.17*****	0.03				
Baseline presenteeism			**0.27*****	0.03		
Baseline work productivity loss					**0.26*****	0.03
Continuation-phase						
Age	0.04	0.07	-0.02	0.07	-0.04	0.09
Gender	-0.38	1.78	-0.63	1.83	-0.55	2.31
Hispanic ethnicity	1.24	1.93	-0.52	2.10	0.78	2.55
Race[a] black	-3.00	2.20	0.65	2.27	-1.04	2.86
Race[a] other	1.29	2.51	-4.36	2.64	-3.06	3.28
Education[b]: 12 – 15 years	-3.01	2.60	0.86	2.82	2.60	3.42
Education[b]: 16 years or more	-1.01	2.78	0.62	3.05	1.47	3.68
Depression onset before age 18	0.97	1.49	-0.23	1.59	-1.41	1.95
Suicidal ideation at baseline	0.60	1.65	-1.20	1.77	-1.46	2.17

	Est.	SE	Est.	SE	Est.	SE
Anxious depression at baseline	-1.16	1.63	0.73	1.75	-1.08	2.16
Bupropion combination[c]	-2.33	1.77	-0.32	1.86	-1.47	2.31
Venlafaxine combination[c]	-1.62	1.85	-1.16	1.90	-2.68	2.38
Monthly income[d]: $2000 - $4000	-0.95	1.76	-1.49	1.87	-0.16	2.27
Monthly income[d]: > $4000	-1.72	2.00	2.60	2.01	3.20	2.60
Baseline QIDS-SR	-0.40	0.21	-0.30	0.23	-0.49	0.28
Baseline absenteeism	**0.18***	0.04				
Baseline presenteeism			**0.13***	0.03		
Baseline work productivity loss					**0.16***	0.03
Week 12 QIDS-SR	-0.02	0.33	0.05	0.35	0.32	0.43
Week 12 CPFQ	-0.22	0.25	-0.20	0.25	-0.23	0.32
QIDS-SR (weeks 16-28)	**0.77**	0.27	**1.16***	0.28	**1.54***	0.36
CPFQ (weeks 16-28)	**0.70**	0.25	**1.70***	0.26	**1.93***	0.32
Week 12 absenteeism	-0.02	0.05				
Week 12 presenteeism			**0.23***	0.04		
Week 12 work productivity loss					**0.16***	0.04

* p Value < 0.05, ** p Value <0.005, *** p Value <0.0001 Work productivity loss is percent overall work impairment (absenteeism or presenteeism), presenteeism is percent impairment while working due to health, and absenteeism is percent of time missed from work due to general health. Est. is estimate, SE

is standard error. Comparison group for a) race is white, b) education is less than high school, c) treatment arm is selective serotonin reuptake inhibitor (SSRI) monotherapy with Escitalopram plus placebo, and d) monthly income is less than $2000. Bupropion combination refers to sustained-release bupropion plus escitalopram combination, Venlafaxine combination refers to extended-release venlafaxine plus mirtazapine, and QIDS-SR is Quick Inventory of Depressive Symptomatology Self-Report.

Supplementary Table 2. Model development of changes in work productivity loss with 6 weeks of

treatment

Number of Groups	Order of Polynomials	Bayesian information criteria (BIC)	Akaike information criteria (AIC)
2	1, 1	-5157	-5146
	2, 2	-5154	-5139
	2, 1	-5152	-5139
	3, 3	-5150	-5131
	4, 4	-5156	-5133
	1, 0	-5162	-5152
3	1, 1, 1	-5135	-5118
	2, 2, 2	-5138	-5116
	2, 0, 1	-5134	-5117
	3, 3, 3	-5136	-5108
Final model	3, 1, 3	-5132	-5107
	4, 4, 4	-5145	-5111
	1, 0, 0	-5141	-5128
	3, 3, 4	-5139	-5109

	3, 3, 2	-5136	-5109
	3, 2, 3	-5135	-5108
4	1, 1, 1, 1	-5132	-5109
	1, 0, 1, 0	-5127	-5108
	2, 2, 2, 2	-5135	-5105
	0, 1, 1, 0	-5127	-5108
	3, 3, 3, 3	-5143	-5105
	0, 3, 1, 0	-5125	-5102
	4, 4, 4, 4	-5152	-5107
	0, 4, 4, 4	-5141	-5103
	0, 1, 4, 4	-5138	-5106
	0, 1, 3, 4	-5136	-5107
	0, 1, 3, 2	-5131	-5105
	0, 1, 3, 1	-5129	-5104
	0, 1, 3, 0	-5126	-5103
	0, 2, 3, 0	-5126	-5099
	1, 3, 3, 0	-5129	-5104

	2, 3, 3, 0	-5132	-5102
	1, 3, 3, 1	-5132	-5102
5	1, 1, 1, 1, 1	-5136	-5107
	2, 2, 2, 2, 2	-5140	-5102

Supplementary Table 3. Maximum likelihood estimates of 3 class 3-degree censored normal model (3, 1, 3) of trajectories of work productivity change during the first 6 weeks of Combining Medications to Enhance Depression Outcomes (CO-MED) trial

Group	Parameter	Estimate	Standard Error	T for H0: Parameter=0	Prob > |T|
1	Intercept	23.61134	4.51033	5.235	0.0000
	Linear	-55.46913	11.57674	-4.791	0.0000
	Quadratic	19.13004	4.71155	4.060	0.0001
	Cubic	-1.84798	0.50903	-3.630	0.0003
2	Intercept	32.22176	3.85415	8.360	0.0000
	Linear	-1.58918	0.68581	-2.317	0.0206
3	Intercept	80.18164	4.71225	17.016	0.0000
	Linear	-22.14253	6.84666	-3.234	0.0013
	Quadratic	7.72452	2.96803	2.603	0.0094
	Cubic	-0.77318	0.32950	-2.347	0.0191
	Sigma	29.64576	0.78880	37.584	0.0000
Bayesian Information Criterion (BIC)= -5132; Akaike Information Criterion (AIC)= -5107					

Supplementary Table 4. Differences in baseline clinical and sociodemographic variables amongst the three groups identified by trajectories of changes in work productivity loss during the first 6 weeks of Combining Medications to Enhance Depression Outcomes (CO-MED) trial

	Robust Early Improvement		Minimal Change		High-Impairment Slight Reduction		Test statistic*		p-Value
Continuous variables	Mean	SD	Mean	SD	Mean	SD	F value	df	
Age in years	42.9	12.7	40.9	13.0	39.5	11.5	1.5	2	0.23
Monthly income in USD	3281.0	4557.1	3911.4	8420.8	2827.2	2734.4	0.76	2	0.47
QIDS-SR	13.5	4.0	14.5	4.1	17.1	3.4	18.3	2	<0.001
Categorical variables	n	%	n	%	n	%	χ^2	df	
Sex							1.02	2	0.60
Male	18	18.8	54	56.3	24	25			
Female	54	23.0	119	50.6	62	26.4			
Race							3.73	6	0.71
White	58	25.4	39	17.1	93	40.8			
Black	18	24	13	17.3	26	34.7			
Other	8	28.6	4	14.3	13	46.4			
Education							6.27	4	0.18

							χ^2	df	p
<12 years	5	15.2	15	45.5	13	39.4			
12 -15 years	42	24.7	83	48.8	45	26.5			
>15 years	23	19.8	68	58.6	25	21.6			
Treatment Arm							4.49	4	0.34
Bupropion Combination	23	19.3	68	57.1	28	23.5			
SSRI Monotherapy	20	20.2	55	55.6	24	24.2			
Venlafaxine Combination	29	25.7	50	44.3	34	30.1			
	N	Y	N	Y	N	Y			
Hispanic (N/Y)	56	16	144	29	66	20	1.92	2	0.38
Anxious features (N/Y)	25	47	49	124	18	67	3.59	2	0.17
Suicidal ideation, (N/Y)	33	39	73	100	29	57	2.68	2	0.26
Onset of depression before age 18 (N/Y)	37	35	98	75	42	43	1.39	2	0.50

χ^2 is chi-square, SD is standard deviation, df is degrees of freedom, n is number, N is no or absent, Y is yes or present, Bupropion combination is sustained-release bupropion plus escitalopram, SSRI monotherapy is escitalopram plus placebo, Venlafaxine combination is extended-release venlafaxine plus mirtazapine, and QIDS-SR is Quick Inventory of Depressive Symptomatology Self-Report.

Supplementary Table 5. Prediction of short and longer-term remission outcomes in univariates and

multivariate analyses

	Remission at 3 months		Remission at 7 months	
	Odds Ratio	95% CI	Odds Ratio	95% CI
Univariate analysis				
Trajectory Group				
Robust early improvement vs. minimal change	3.09	1.45, 6.58	2.87	1.22, 6.76
Robust early improvment vs. high-impairment slight reduction	7.69	3.17, 18.52	7.14	2.65, 19.23
Treatment-arm				
Bupropion vs. Venlafaxine Combinations	0.84	0.44, 1.62	0.77	0.38, 1.55
SSRI monotherapy vs. Venlafaxine Combination	0.62	0.32, 1.20	0.89	0.43, 1.84
Race				
White vs. Others	1.09	0.43, 2.77	1.74	0.69, 4.39
Black vs. Others	0.74	0.25, 2.19	1.10	0.36, 3.35
Education				
>15 years vs. <12 years	0.77	0.27, 1.17	0.84	0.29, 2.49
> 15 years vs. 12-15 years	091	0.52, 1.59	1.12	0.60, 2.07
Income				
<$2000/month vs. >$4000/month	1.39	0.70, 2.70	1.14	0.56, 2.35
$2000-$4000/month vs. >$4000/month	1.31	0.61, 2.78	1.36	0.61, 3.05
Remission at Week 6	14.41	6.14, 33.80	6.12	2.78, 13.48
Male Gender	1.05	0.59, 1.88	0.65	0.35, 1.23
Onset of depression before age 18	0.86	0.51, 1.47	1.08	0.60, 1.93

Hispanic ethnicity	1.57	0.79, 3.06	3.79	1.58, 9.09
Presence of anxious features	0.90	0.50, 1.62	1.44	0.76, 2.72
Presence of suicidal ideations	0.50	0.29, 0.87	0.46	0.25, 0.84
Baseline depression severity	0.88	0.82, 0.84	0.91	0.84, 0.99
Baseline CPFQ score	0.92	0.87, 0.97	0.94	0.89, 1.0
Multivariate analysis with backwards elimination				
Trajectory Group				
Robust early improvement vs. minimal change	2.67	1.02, 6.94	2.15	0.75, 6.13
Robust early improvement vs. high-impairment slight reduction	5.35	1.81, 15.87	5.03	1.53, 16.39
Remission at Week 6	13.60	5.37, 34.45	6.51	2.62, 16.17
Hispanic ethnicity			3.86	1.43, 10.42