

An Evaluation of the Impact of Co-occurring Anxiety
and Substance Use Disorder on Bipolar Disorder
Illness Outcomes in STEP-BD (JAD-2018-1672)

Reviewer Supplement

Use of Current (as Opposed to Lifetime) Co-occurring Diagnoses: Associations between “Substance Use Problems,” “Pathological Anxiety,” and Select, Evaluated Clinical Variables

(only models [$n=4$] in which lifetime Substance Use Problems originally failed to significantly predict a given clinical variable when jointly modeled with Pathological Anxiety were evaluated)

Conclusion: Although 2 of the 4 evaluated models demonstrated different results (i.e., Substance Use Problems significantly predicting the outcome in question), the new-found associations involving Substance Use Problems were small (unlikely to be “clinically” significant) and associated with correspondingly large p-values (i.e., $p=0.023-0.024$) that would not survive correction for multiple comparisons.

STANDARDIZED MODEL RESULTS

INT = Pathological Anxiety
EXT = Substance Use Problems

%anxious

STDYX Standardization

	Estimate	S.E.	Est./S.E.	Two-Tailed P-Value
INT BY				
PHOBIAC	0.606	0.045	13.492	0.000
OCDC	0.529	0.036	14.841	0.000
PTSDC	0.569	0.044	12.850	0.000
GENANXC	0.527	0.034	15.712	0.000
AGC	0.910	0.024	38.269	0.000
PDC	0.879	0.023	38.854	0.000
EXT BY				
ALCDEPC	0.883	0.042	20.810	0.000
ALCABUSC	0.919	0.038	24.053	0.000
DRUGDEPC	0.779	0.039	20.146	0.000
DRUGABC	0.795	0.030	26.854	0.000
ANXDAY ON				
INT	0.466	0.014	33.987	0.000
EXT	0.060	0.026	2.262	0.024
EXT WITH				
INT	0.240	0.038	6.398	0.000
Intercepts				
ANXDAY	1.040	0.031	33.921	0.000
Thresholds				
PHOBIAC\$1	1.006	0.093	10.794	0.000
OCDC\$1	1.399	0.069	20.252	0.000
PTSDC\$1	1.360	0.084	16.198	0.000
ALCDEPC\$1	1.402	0.069	20.309	0.000
ALCABUSC\$1	1.322	0.054	24.594	0.000
DRUGDEPC\$1	1.575	0.062	25.511	0.000
DRUGABC\$1	1.481	0.064	22.967	0.000
GENANXC\$1	0.923	0.080	11.578	0.000
AGC\$1	1.167	0.099	11.844	0.000
PDC\$1	1.203	0.083	14.418	0.000

%depressed

STDYX Standardization

	Estimate	S.E.	Est./S.E.	Two-Tailed P-Value
INT BY				
PHOBIAC	0.613	0.046	13.268	0.000
OCDC	0.521	0.038	13.881	0.000
PTSDC	0.573	0.042	13.785	0.000
GENANXC	0.476	0.033	14.414	0.000
AGC	0.930	0.020	47.004	0.000
PDC	0.887	0.019	45.820	0.000
EXT BY				
ALCDEPC	0.883	0.043	20.711	0.000
ALCABUSC	0.921	0.038	24.244	0.000
DRUGDEPC	0.778	0.039	20.009	0.000
DRUGABC	0.794	0.029	27.227	0.000
DEPDAY ON				
INT	0.348	0.022	16.069	0.000
EXT	0.063	0.028	2.268	0.023
EXT WITH				
INT	0.238	0.037	6.366	0.000
Intercepts				
DEPDAY	1.444	0.053	27.270	0.000
Thresholds				
PHOBIAC\$1	1.005	0.093	10.783	0.000
OCDC\$1	1.396	0.069	20.204	0.000
PTSDC\$1	1.358	0.083	16.267	0.000
ALCDEPC\$1	1.401	0.069	20.252	0.000
ALCABUSC\$1	1.321	0.054	24.550	0.000
DRUGDEPC\$1	1.574	0.061	25.603	0.000
DRUGABC\$1	1.480	0.064	23.031	0.000
GENANXC\$1	0.916	0.079	11.570	0.000
AGC\$1	1.161	0.097	11.923	0.000
PDC\$1	1.195	0.083	14.475	0.000

STANDARDIZED MODEL RESULTS

INT = Pathological Anxiety
EXT = Substance Use Problems

LIFE-Rift

Rapid Cycling

STDYX Standardization

STDYX Standardization

	Estimate	S.E.	Est./S.E.	Two-Tailed P-Value
INT BY				
PHOBIAC	0.613	0.045	13.730	0.000
OCDC	0.522	0.038	13.723	0.000
PTSDC	0.577	0.039	14.675	0.000
GENANXC	0.467	0.033	14.203	0.000
AGC	0.935	0.020	47.886	0.000
PDC	0.881	0.021	41.630	0.000
EXT BY				
ALCDEPC	0.883	0.043	20.328	0.000
ALCABUSC	0.920	0.039	23.563	0.000
DRUGDEPC	0.780	0.039	19.794	0.000
DRUGABC	0.798	0.030	26.890	0.000

LRTOT ON				
INT	0.366	0.023	15.651	0.000
EXT	0.027	0.023	1.173	0.241

EXT WITH				
INT	0.240	0.040	5.936	0.000

Intercepts				
LRTOT	3.046	0.129	23.598	0.000

Thresholds				
PHOBIAC\$1	1.004	0.094	10.684	0.000
OCDC\$1	1.396	0.069	20.125	0.000
PTSDC\$1	1.358	0.084	16.236	0.000
ALCDEPC\$1	1.401	0.069	20.224	0.000
ALCABUSC\$1	1.321	0.054	24.498	0.000
DRUGDEPC\$1	1.574	0.062	25.581	0.000
DRUGABC\$1	1.480	0.064	22.998	0.000
GENANXC\$1	0.915	0.080	11.404	0.000
AGC\$1	1.160	0.099	11.755	0.000
PDC\$1	1.194	0.084	14.250	0.000

	Estimate	S.E.	Est./S.E.	Two-Tailed P-Value
INT BY				
PHOBIAC	0.606	0.050	12.192	0.000
OCDC	0.521	0.036	14.434	0.000
PTSDC	0.561	0.043	13.148	0.000
GENANXC	0.462	0.037	12.439	0.000
AGC	0.929	0.019	50.098	0.000
PDC	0.888	0.021	41.993	0.000
EXT BY				
ALCDEPC	0.883	0.043	20.667	0.000
ALCABUSC	0.919	0.039	23.318	0.000
DRUGDEPC	0.781	0.039	19.868	0.000
DRUGABC	0.798	0.030	26.668	0.000

RAPIDC ON				
INT	0.311	0.060	5.226	0.000
EXT	0.036	0.039	0.935	0.350

EXT WITH				
INT	0.240	0.040	5.999	0.000

Thresholds				
PHOBIAC\$1	1.003	0.094	10.689	0.000
OCDC\$1	1.396	0.069	20.107	0.000
PTSDC\$1	1.356	0.084	16.112	0.000
ALCDEPC\$1	1.400	0.069	20.220	0.000
ALCABUSC\$1	1.321	0.054	24.467	0.000
DRUGDEPC\$1	1.574	0.062	25.550	0.000
DRUGABC\$1	1.480	0.064	22.957	0.000
GENANXC\$1	0.914	0.080	11.452	0.000
RAPIDC\$1	0.141	0.096	1.476	0.140
AGC\$1	1.158	0.100	11.599	0.000
PDC\$1	1.193	0.085	14.109	0.000

Moderation Analyses: Associations between “Substance Use Problems,” “Pathological Anxiety,” and Evaluated Clinical Variables BY Bipolar Disorder Subtype (I vs. II)

(All models were tested, however only models with statistically significant interactions were included in this report)

Conclusion: Three of the 10 evaluated models demonstrated significant interactions between Bipolar Disorder subtype and self-reported %depressed, %elevated, and %anxious days in the year preceding assessment. Once again, these three moderation effects were small in magnitude and associated with relatively large p-values that would be unlikely to survive control for multiple comparisons. Interpretation of these interactions is also not entirely clear. For example, individuals with Bipolar II Disorder had relatively more depressed days, however, individuals with Bipolar I Disorder had a somewhat stronger association between Pathological Anxiety and %depressed days. Furthermore, given that we did not have a priori hypotheses concerning how associations between Pathological Anxiety, Substance Use Problems, and clinical variables would be moderated by Bipolar subtype, we do not feel comfortable attempting to interpret these findings.

Tests of Between-Subjects Effects

Dependent Variable: DEPRESSED_DAYS_YR

BPMIC	32629.949	1	32629.949	39.456	.000
INT_L	95664.432	1	95664.432	115.676	.000
EXT_L	238.678	1	238.678	.289	.591
BPMIC * INT_L	3730.734	1	3730.734	4.511	.034
BPMIC * EXT_L	1590.903	1	1590.903	1.924	.166

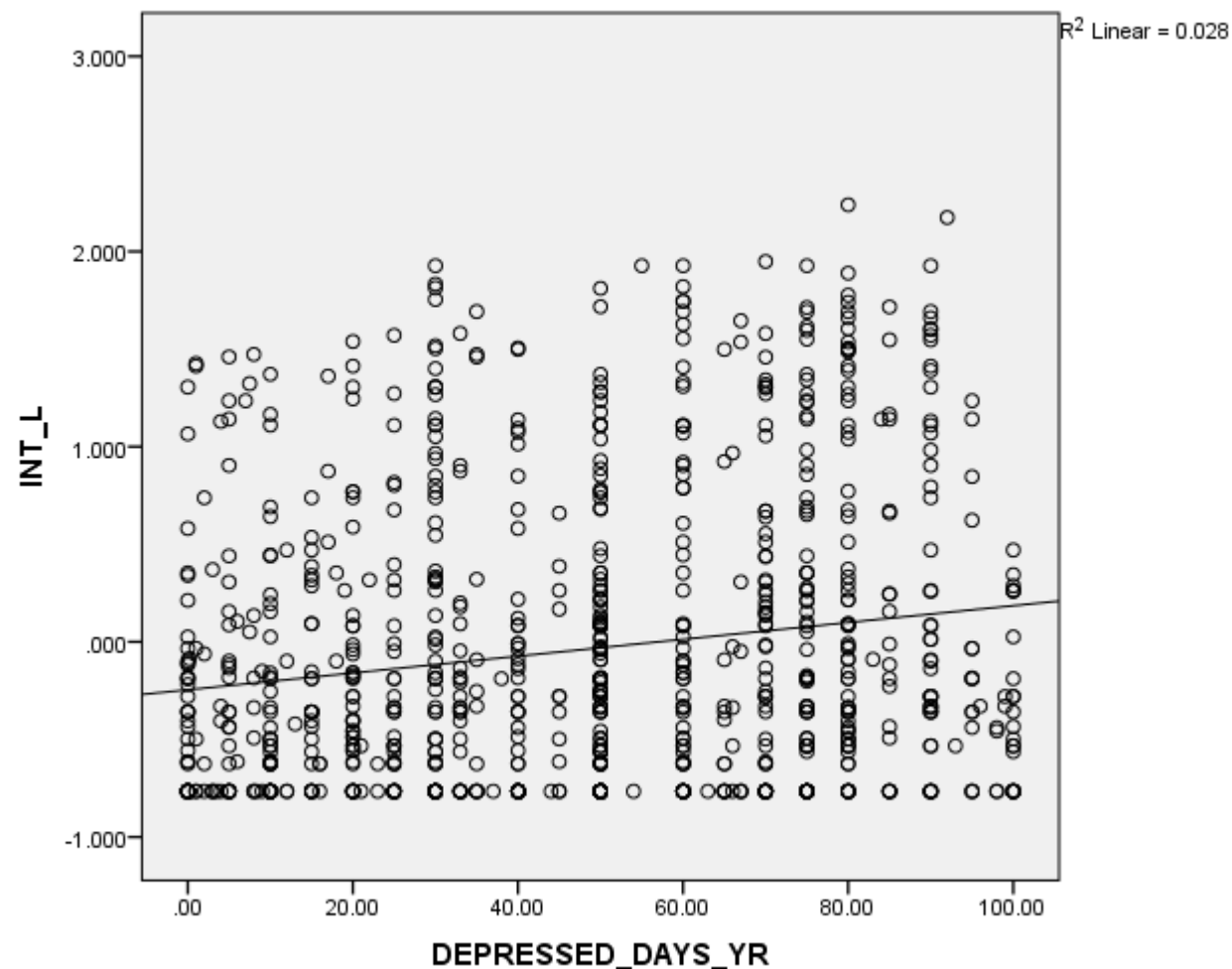
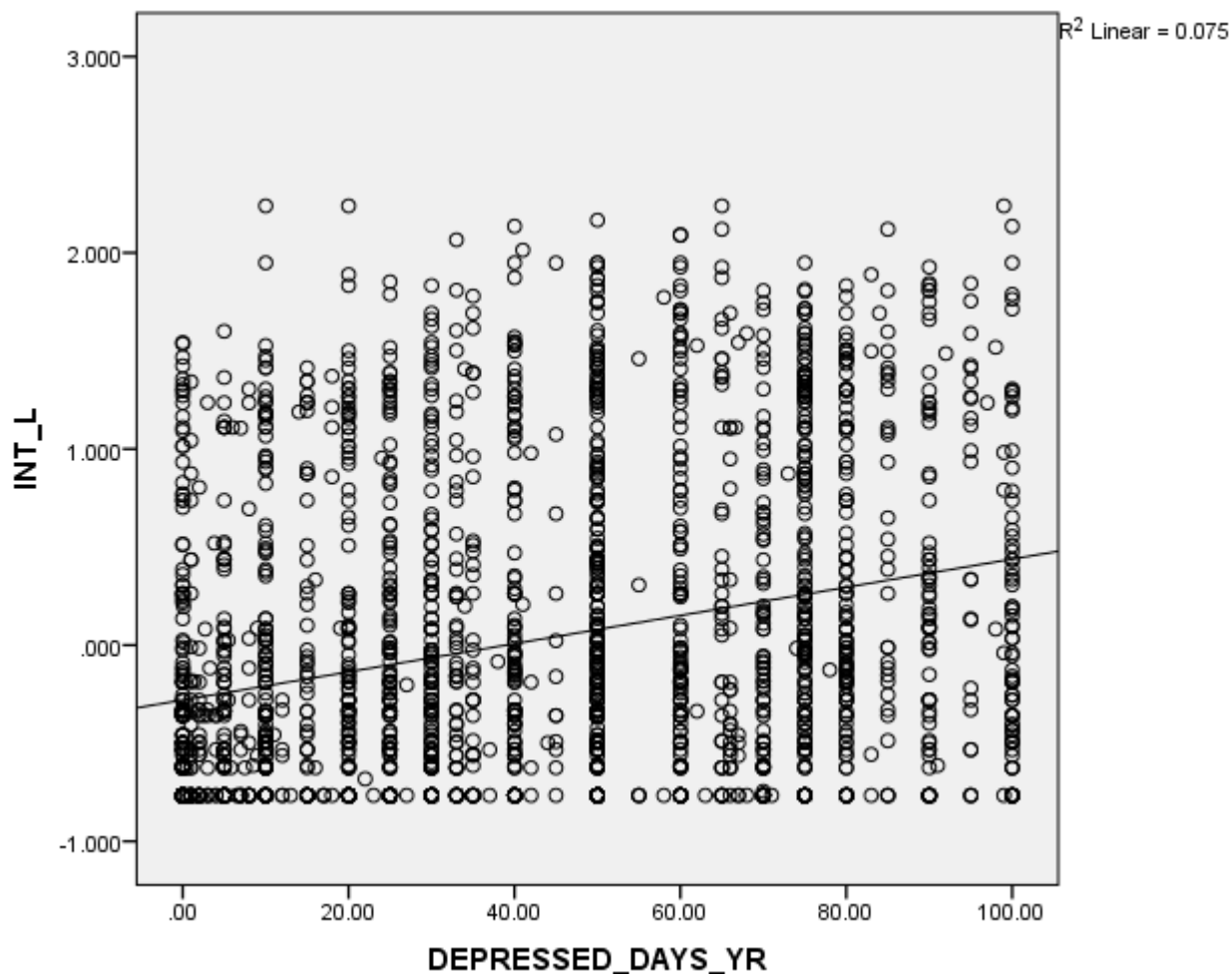
Dependent Variable: DEPRESSED_DAYS_YR

BPMIC	Mean	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
.00	41.313 ^a	.637	40.063	42.562
1.00	48.235 ^a	.943	46.386	50.084

a. Covariates appearing in the model are evaluated at the following values: INT_L = -.00270, EXT_L = -.00294.

BPI

BPII



Tests of Between-Subjects Effects

Dependent Variable: ELEVATED_DAYS_YR

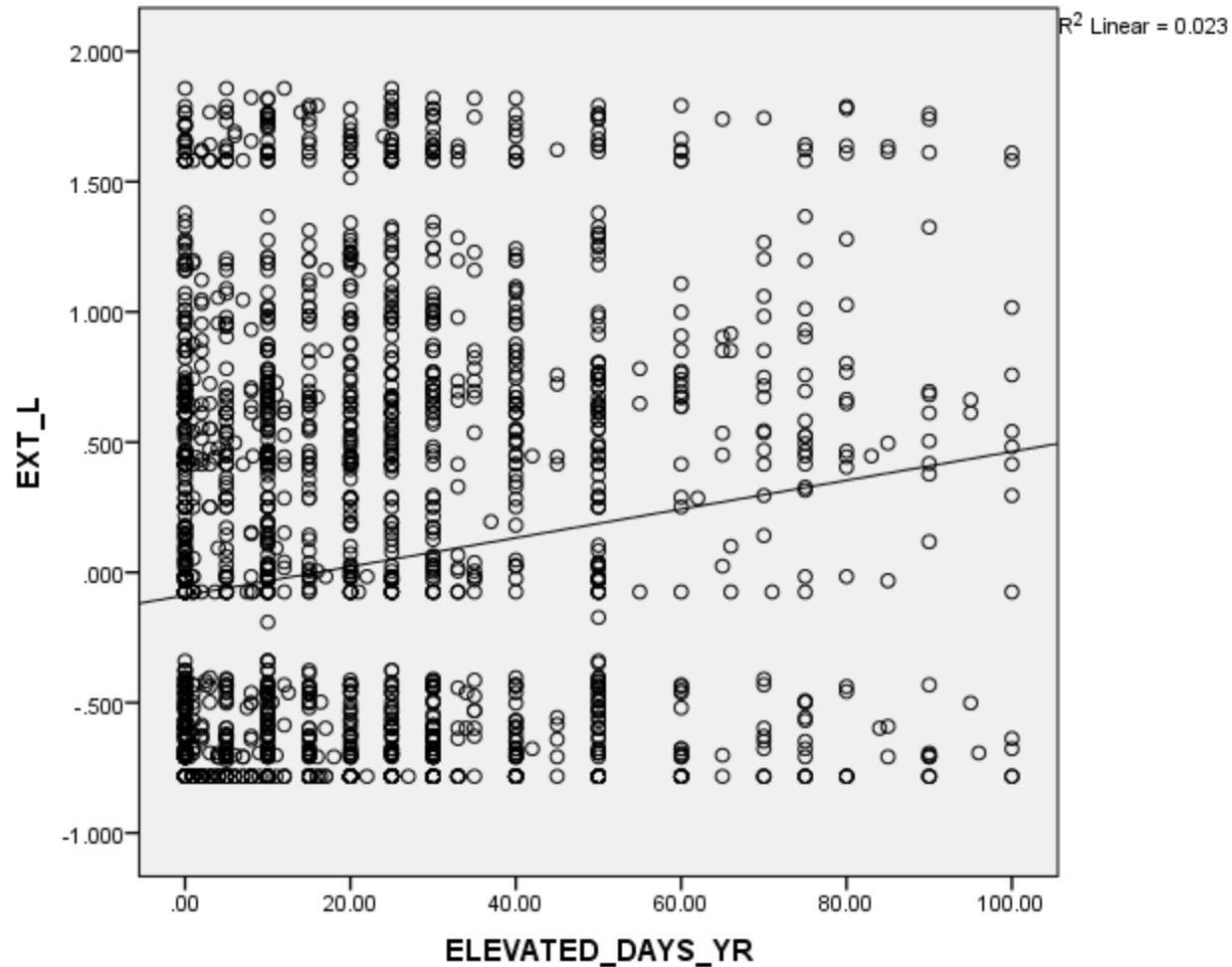
Source	Type III Sum of Squares	df	Mean Square	F	Sig.
BPMIC	5268.095	1	5268.095	12.198	.000
INT_L	2677.468	1	2677.468	6.200	.013
EXT_L	3444.616	1	3444.616	7.976	.005
BPMIC * INT_L	1662.244	1	1662.244	3.849	.050
BPMIC * EXT_L	2659.058	1	2659.058	6.157	.013

Dependent Variable: ELEVATED_DAYS_YR

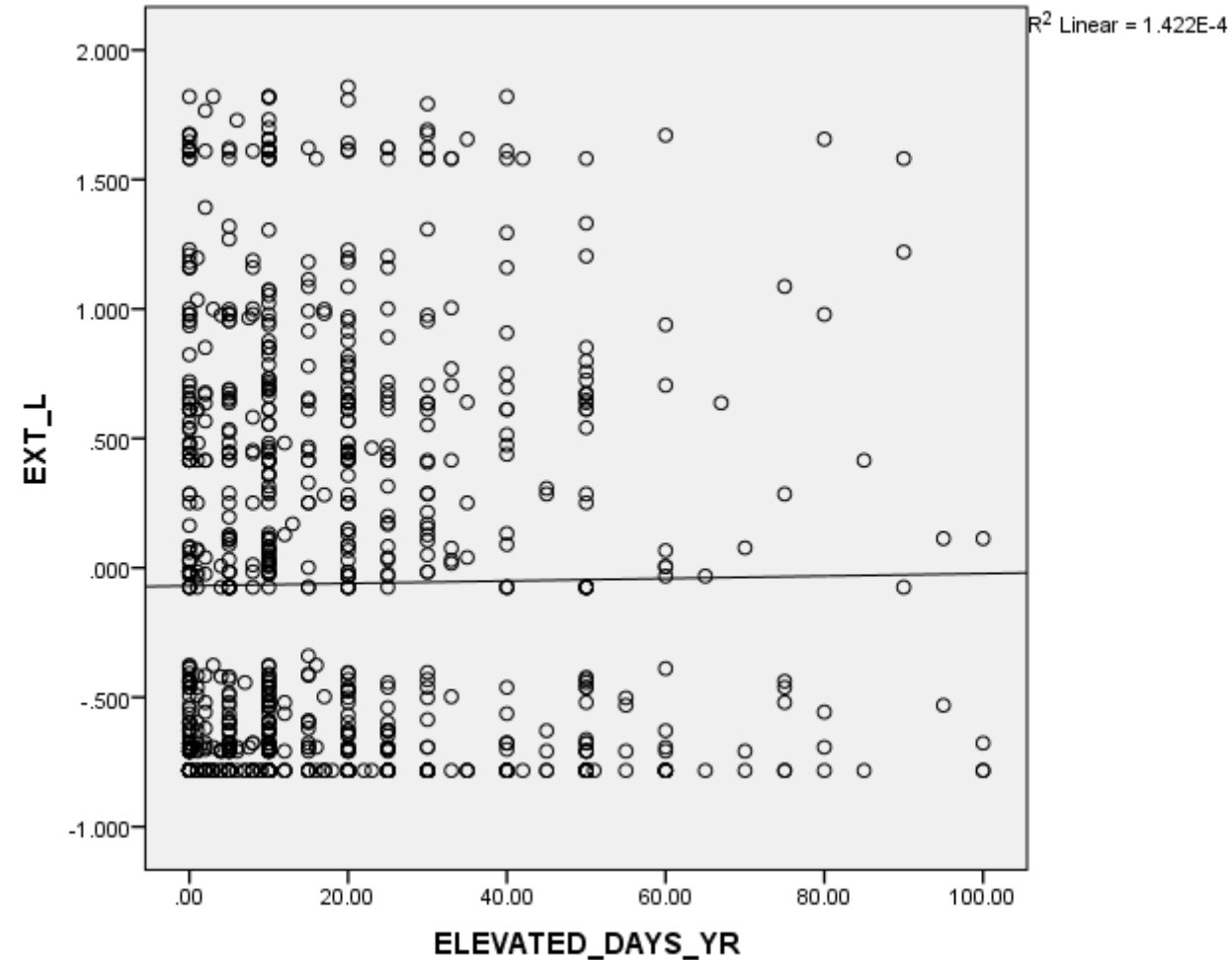
BPMIC	Mean	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
.00	20.227 ^a	.461	19.323	21.132
1.00	17.453 ^a	.685	16.110	18.795

a. Covariates appearing in the model are evaluated at the following values: INT_L = -.00304, EXT_L = -.00134.

BPI



BPII



Tests of Between-Subjects Effects

Dependent Variable: ANXIETY_DAYS_YR

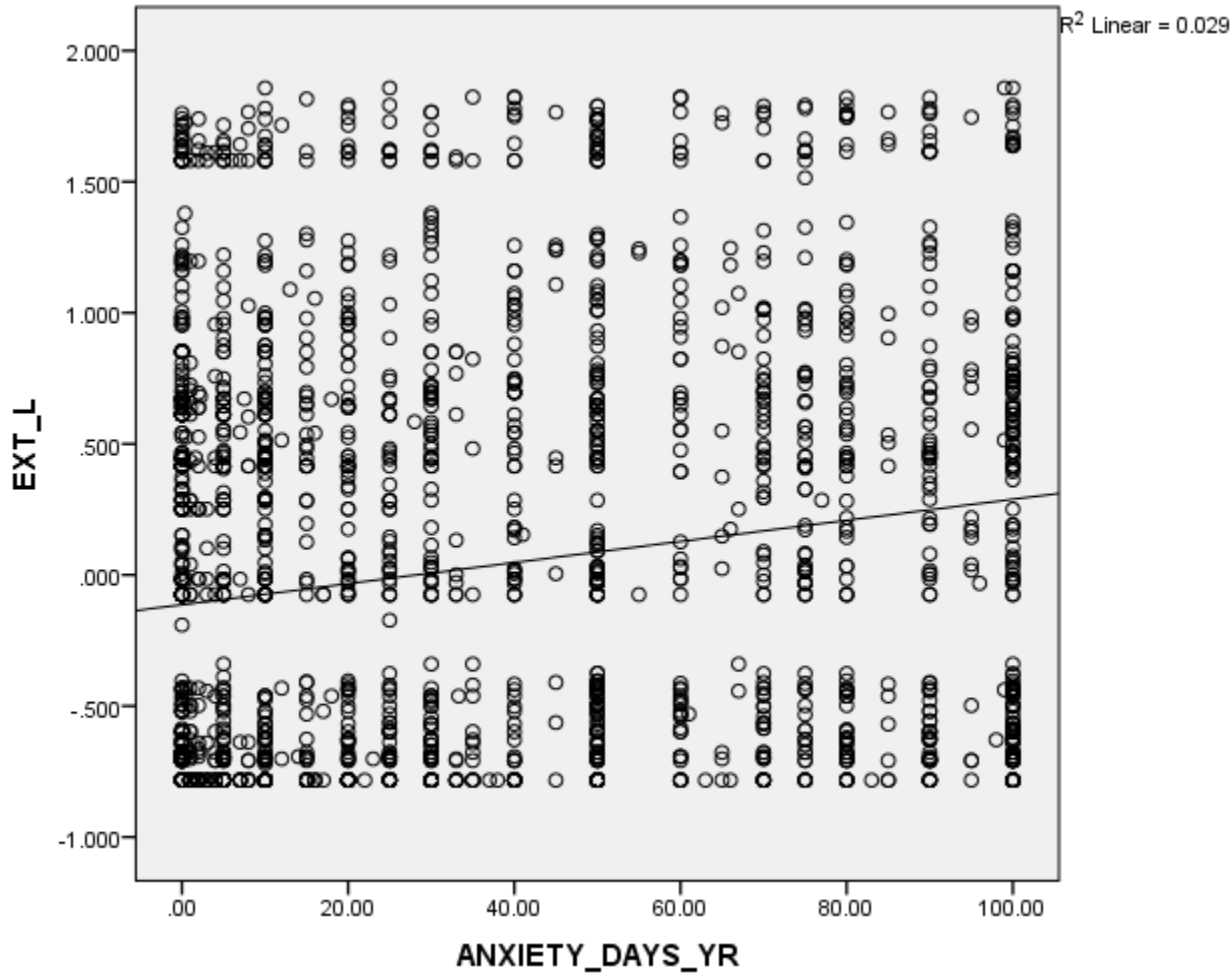
Source	Type III Sum of Squares	df	Mean Square	F	Sig.
BPIVIC	5617.856	1	5617.856	5.601	.018
INT_L	278960.017	1	278960.017	278.100	.000
EXT_L	2189.044	1	2189.044	2.182	.140
BPIVIC * INT_L	354.582	1	354.582	.353	.552
BPIVIC * EXT_L	4467.310	1	4467.310	4.454	.035

Dependent Variable: ANXIETY_DAYS_YR

BPIVIC	Mean	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
.00	33.993 ^a	.707	32.607	35.379
1.00	36.880 ^a	1.043	34.835	38.925

a. Covariates appearing in the model are evaluated at the following values: INT_L = -.00127, EXT_L = -.00097.

BPI



BPII

