THE PRIMARY CARE COMPANION
FOR CNS DISORDERS

Supplementary Material

List of Supplementary Material for the article

1. **Supplementary Material**

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SUPPLEMENTARY MATERIAL

Methods

Data Analysis

Differences in TMB between patients who regularly used sleep aids and those who did not were compared using Satterthwaite t tests for statistical significance and Glass's Δ for effect size due to unequal variance and numbers of patients per group. Chi-square tests compared medication use between patients divided according to whether they reported insomnia and whether they reported a psychiatric comorbidity. ANOVA with $\eta^2_{partial}$ effect size compared levels of TMB between these same groups.

Mediation analyses were conducted in R version 3.5.0 with structural equation modeling, non-parametric bootstrapping, and bias-corrected confidence estimates[46]. These models generate estimates for: the effect of independent variable (IV) on the mediator (M, path *a* in Fig. 1), the effect of the M on the dependent variable (DV, path *b* in Fig. 1), the indirect effect of the IV on DV through M (*a*b*), the direct effect of the IV on DV while controlling for M (*c'* in Fig. 1), and the total effect of IV on DV (*c*, which is equal to a*b* + *c'*). Bootstrapping does not require *a*b* to be normally distributed, and so it can reliably estimate confidence intervals and whether these confidence intervals show an effect significantly different than zero.

Full mediation was defined as a non-significant *c'*: the absence of significant association between the IV (e.g., TMB) and medication use after controlling for M (e.g., ISI) in step 3; partial mediation was defined as both *c'* and *a*b* showing significant associations with medication use. The proportion of mediation (PM) was computed as the ratio of the mediated effect to the total effect (*ab/c*).

Results

The mediation models for TMB-10, ISI, and both OTC sleep and prescription sleep medications are shown in Table 1. The relationship between TMB-10 and OTC medication use was partially mediated by ISI. While there was also partial mediation of the relationship between ISI and OTC medication use by TMB-10, effect sizes were smaller. The relationship between TMB-10 and prescription medication use was fully mediated by ISI. Reverse mediation models showed no significant mediation relationship between M and DV (path *b*) for the full TMB-10 scale.

The mediation models for TMB-10, ISI, and both OTC sleep and prescription sleep medications among patients with self-reported psychiatric diagnoses are shown in Table 2. The relationship between TMB-10 and OTC use was partially mediated by ISI. Reverse mediation models demonstrated that TMB-10 partially mediated the relationship between ISI and OTC use, but with a smaller effect size. The relationship between TMB-10 and prescription medication use was fully mediated by ISI among those reporting psychiatric diagnoses. Reverse mediation analyses showed that TMB-10 did not mediate the relationship between ISI and prescription medication use.

The mediation models for TMB subscales, ISI, and both OTC sleep and prescription sleep medications are shown in Table 3. The relationship between TMB Behavior and OTC medication use was partially mediated by ISI. Reverse mediation analysis models demonstrated that TMB-BX partially mediated the relationship between ISI and OTC use, but with a smaller effect size. The relationship between TMB-SOF and OTC use was partially mediated by ISI. Reverse mediation analysis models demonstrated that TMB Sleep Onset Frustration partially

mediated the relationship between ISI and OTC use, but with a smaller effect size. The relationship between TMB-SMF and OTC use was partially mediated by ISI. Reverse mediation analysis models demonstrated that TMB-SMF partially mediated the relationship between ISI and OTC use, but with a smaller effect size. The relationship between TMB-BX and prescription use was fully mediated by ISI. Reverse mediation analysis models showed no mediation of the relationship between ISI and prescription use by TMB-BX. The relationship between TMB-SOF and prescription use was partially mediated by ISI. Reverse mediation analysis models demonstrated that TMB-SOF partially mediated the relationship between ISI and prescription use, but with a smaller effect size. The relationship between TMB-SMF and prescription use was partially mediated by ISI. Reverse mediation analysis models demonstrated that TMB-SMF partially mediated the relationship between ISI and prescription use, but with a smaller effect size.

The mediation models for TMB subscales, ISI, and both OTC sleep and prescription sleep medications among patients with self-reported psychiatric diagnoses are shown in Table 4. The relationship between TMB-BX and OTC medication use was fully mediated by ISI. Reverse mediation analysis models showed no mediation of the relationship between ISI and OTC use by TMB-BX. The relationship between TMB-SOF and OTC use was partially mediated by ISI. Reverse mediation analysis models demonstrated that TMB-SOF partially mediated the relationship between ISI and OTC use, but with a smaller effect size. The relationship between TMB-SMF and OTC use was partially mediated by ISI. Reverse mediation analysis models demonstrated that TMB-SMF partially mediated the relationship between ISI and OTC use, but with a smaller effect size. There was no mediation of the relationship between TMB-BX and prescription use by ISI. Reverse mediation analysis models showed no mediation of the relationship between ISI and prescription use by TMB-BX. The relationship between TMB-SOF and prescription use was fully mediated by ISI. Reverse mediation analysis models showed that the relationship between ISI and prescription use was not mediated by TMB-SOF. The relationship between TMB-SMF and prescription use was fully mediated by ISI. Reverse mediation analysis models showed that the relationship between ISI and prescription use was not mediated by TMB-SMF.

Supplemental Results

Mediation models for TMB-10, ISI, and OTC and prescription sleep medications among patients who met study criteria for chronic insomnia disorder are shown in Table S1. There was no mediation of the relationship between TMB-10 and OTC use by ISI. There was no mediation of the relationship between ISI and OTC use by TMB-10. There was no mediation of the relationship between TMB-10 and prescription use by ISI. There was no mediation of the relationship between ISI and prescription use by TMB-10.

Mediation models for TMB subscales, ISI, and OTC sleep medications among patients who met study criteria for chronic insomnia disorder are shown in Table S2. There was no mediation of the relationship between TMB-BX and OTC use by ISI. There was no mediation of the relationship between ISI and OTC use by TMB-BX. The relationship between TMB-SOF and OTC use was partially mediated by ISI. There was no mediation of the relationship between ISI and OTC use by TMB-SOF. There was no mediation of the relationship between TMB-SMF and OTC use by ISI. There was no mediation of the relationship between ISI and OTC use by TMB-SMF.

Mediation models for TMB subscales, ISI, and prescription sleep medications among patients who met study criteria for chronic insomnia disorder are shown in Table S3. There was no mediation of the relationship between TMB-BX and OTC prescription use by ISI. There was no mediation of the relationship between ISI and prescription use by TMB-BX. The relationship between TMB-SOF and prescription use was fully mediated by ISI. There was no mediation of the relationship between ISI and prescription use by TMB-SOF. There was no mediation of the relationship between TMB-SMF and prescription use by ISI. There was no mediation of the relationship between ISI and prescription use by TMB-SMF.

	TMB mediated by ISI					ISI mediated by TMB				
Effect	Estimate	SE	p	95% CI	PM	Estimate	SE	p	95% CI	PM
Full TMB-10 Scale and OTC medication										
a	0.075	0.010	<.001	0.055, 0.093		0.487	0.063	<.001	0.361, 0.606	
b	0.038	0.014	0.008	0.009, 0.067		0.007	0.006	0.230	-0.005, 0.019	
c'	0.007	0.006	0.224	-0.005, 0.020		0.038	0.015	0.012	0.012, 0.068	
a x b	0.003	0.001	0.013	0.001, 0.005		0.004	0.003	0.243	-0.002, 0.010	
c	0.010	0.006	0.085	-0.002, 0.022	NS	0.041	0.015	0.006	0.016, 0.074	NS
Full TMB-10 Scale and Prescription Medication										
a	0.070	0.010	<.001	0.055, 0.095		0.487	0.066	<.001	0.364, 0.616	
b	0.133	0.016	<.001	0.099, 0.162		-0.005	0.006	0.442	-0.017, 0.008	
c'	-0.005	0.006	0.438	-0.017, 0.008		0.133	0.016	<.001	0.102, 0.165	
a x b	0.010	0.002	<.001	0.007, 0.014		-0.002	0.003	0.452	-0.009, 0.004	
c	0.005	0.006	0.438	-0.007, 0.018	NS	0.130	0.016	<.001	0.100, 0.163	NS

Table S1. Mediation models of sleep medication use among participants meeting study criteria for chronic insomnia disorder.
This table reports mediation analyses that examine the relationship between ISI and TMB with regard to medication use in the subset of the sample meeting study criteria for chronic insomnia disorder. The left half of the table reports analyses in which TMB is the independent variable (IV) and ISI is the mediator (M); in the right half, ISI is the IV and TMB is the mediator. Regular use of OTC sleep medication is the dependent variable (DV) in the top half of the table; prescription sleep medication use is the DV in the bottom half. a: path from IV to M; b: path from M to DV, c': direct path from IV to DV; a x b: indirect path from IV to DV through M; c: direct path from IV to DV after controlling for indirect effect (a x b); SE: standard error; p: p value; 95% CI: 95% confidence interval of estimate; PM: proportion mediated (ratio of indirect path a x b to direct path c).

	TMB mediated by ISI					ISI mediated by TMB				
Effect	Estimate	SE	p	95% CI	PM	Estimate	SE	p	95% CI	PM
TMB Behavior and OTC medication										
A	0.102	0.022	<.001	0.058, 0.147		0.135	0.029	<.001	0.078, 0.192	
B	0.041	0.014	0.004	0.013, 0.069		0.004	0.013	0.738	-0.019, 0.030	
c'	0.004	0.012	0.726	-0.021, 0.027		0.041	0.014	0.005	0.011, 0.066	
a x b	0.004	0.002	0.019	0.001, 0.008		0.001	0.002	0.743	-0.003, 0.004	
C	0.008	0.012	0.485	-0.016, 0.031	NS	0.041	0.014	0.004	0.012, 0.068	NS
TMB Sleep Onset Frustration and OTC medication										
A	0.279	0.032	<.001	0.219, 0.342		0.183	0.020	<.001	0.145, 0.222	
B	0.034	0.015	0.020	0.005, 0.064		0.037	0.018	0.044	-0.001, 0.072	
c'	0.037	0.018	0.039	0.004, 0.074		0.034	0.014	0.016	0.004, 0.063	
a x b	0.010	0.004	0.025	0.002, 0.019		0.007	0.003	0.052	0.000, 0.014	
C	0.047	0.018	0.008	0.014, 0.082	0.21	0.041	0.014	0.003	0.010, 0.067	NS
TMB Sleep Maintenance Frustration and OTC medication										
a	0.252	0.031	<.001	0.186, 0.312		0.170	0.022	<.001	0.123, 0.210	
b	0.037	0.015	0.013	0.007, 0.067		0.025	0.018	0.158	-0.011, 0.061	
c'	0.025	0.019	0.174	-0.011, 0.062		0.037	0.015	0.012	0.007, 0.065	
a x b	0.009	0.004	0.018	0.002, 0.018		0.004	0.003	0.176	-0.002, 0.011	
c	0.035	0.018	0.061	-0.002, 0.070	NS	0.041	0.014	0.004	0.012, 0.070	NS

Table S2. Mediation models of sleep medication use among participants meeting study criteria for chronic insomnia disorder. This table reports mediation analyses that examine the relationship between ISI and TMB with regard to medication use in the subset of the sample meeting study criteria for chronic insomnia disorder. The left half of the table reports analyses in which TMB is the independent variable (IV) and ISI is the mediator (M); in the right half, ISI is the IV and TMB is the mediator. Regular use of OTC sleep medication is the dependent variable (DV). The table is further divided according to what aspect of TMB is being examined: behavior, sleep onset frustration, or sleep maintenance frustration. a: path from IV to M; b: path from M to DV, c': direct path from IV to DV; a x b: indirect path from IV to DV through M; c: direct path from IV to DV after controlling for indirect effect (a x b); SE: standard error; p: p value; 95% CI: 95% confidence interval of estimate; PM: proportion mediated (ratio of indirect path a x b to direct path c).

	TMB mediated by ISI					ISI mediated by TMB				
Effect	Estimate	SE	p	95% CI	PM	Estimate	SE	p	95% CI	PM
TMB Behavior and Prescription Medication										
A	0.102	0.022	<.001	0.058, 0.145		0.135	0.029	<.001	0.075, 0.187	
B	0.134	0.016	<.001	0.103, 0.164		-0.027	0.014	0.06	-0.054, 0.001	
c'	-0.024	0.014	0.06	-0.055, -0.001		0.134	0.016	<.001	0.102, 0.163	
a x b	0.014	0.003	<.001	0.008, 0.021		-0.004	0.002	0.086	-0.009, 0.000	
C	-0.013	0.014	0.363	-0.041, 0.014	*NS*	0.130	0.016	<.001	0.100, 0.160	*NS*
TMB Sleep Onset Frustration and Prescription Medication										
A	0.279	0.032	<.001	0.219, 0.344		0.183	0.020	<.001	0.139, 0.221	
B	0.128	0.016	<.001	0.098, 0.160		0.012	0.020	0.544	-0.026, 0.050	
c'	0.012	0.021	0.588	-0.032, 0.048		0.128	0.016	<.001	0.096, 0.160	
a x b	0.036	0.006	<.001	0.025, 0.050		0.002	0.004	0.547	-0.005, 0.010	
C	0.048	0.020	<.001	0.006, 0.085	0.75	0.130	0.016	<.001	0.099, 0.161	*NS*
TMB Sleep Maintenance Frustration and Prescription Medication										
a	0.252	0.030	<.001	0.192, 0.313		0.170	0.020	<.001	0.132, 0.208	
b	0.131	0.016	<.001	0.098, 0.165		-0.006	0.019	0.747	-0.041, 0.031	
c'	-0.006	0.021	0.768	-0.046, 0.036		0.131	0.016	<.001	0.099, 0.166	
a x b	0.033	0.006	<.001	0.022, 0.046		-0.001	0.003	0.749	-0.007, 0.005	
c	0.027	0.020	0.189	-0.012, 0.069	*NS*	0.130	0.016	<.001	0.099, 0.166	*NS*

Table S3. Mediation models of sleep medication use among participants meeting study criteria for chronic insomnia disorder. This table reports mediation analyses that examine the relationship between ISI and TMB with regard to medication use in the subset of the sample meeting study criteria for chronic insomnia disorder. The left half of the table reports analyses in which TMB is the independent variable (IV) and ISI is the mediator (M); in the right half, ISI is the IV and TMB is the mediator. Regular use of prescription sleep medication is the dependent variable (DV). The table is further divided according to what aspect of TMB is being examined: behavior, sleep onset frustration, or sleep maintenance frustration. a: path from IV to M; b: path from M to DV, c': direct path from IV to DV; a x b: indirect path from IV to DV through M; c: direct path from IV to DV after controlling for indirect effect (a x b); SE: standard error; p: p value; 95% CI: 95% confidence interval of estimate; PM: proportion mediated (ratio of indirect path a x b to direct path c).