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From OCD Symptoms to Sleep Disorders: The Crucial Role of Vitamin B12

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Objective: Vitamin B12 is crucial for neurological functions and linked to various psychiatric disorders. Given its importance, this study explores the impact of vitamin B12 deficiency on sleep quality in Obsessive-Compulsive Disorder (OCD) patients, while also examining folate and homocysteine levels to explore their potential interactions with OCD symptoms and sleep quality.

Methods: This cross-sectional study included 52 patients with OCD and 42 healthy controls. Serum levels of vitamin B12, homocysteine, and folate were measured. The Yale-Brown Obsessive Compulsive Scale (Y-BOCS) and the Pittsburgh Sleep Quality Index (PSQI) were used to evaluate the severity of OCD symptoms and the quality of sleep, respectively. Correlations and mediating effects between these variables were also assessed.

Results: Vitamin B12 levels were significantly lower in OCD patients compared to healthy controls, and scores for sleep disturbances were significantly higher in the OCD group. No significant differences were observed in the levels of folate and homocysteine between the groups. Correlation analysis indicated that lower levels of vitamin B12 were significantly associated with more severe OCD symptoms and poorer sleep quality. Further mediation analysis suggested that low levels of vitamin B12 partially mediated the relationship between OCD symptoms and sleep disturbances.

Conclusion: Lower levels of vitamin B12 not only affect sleep quality but also partially mediate the impact of OCD symptoms on sleep disturbances. Future clinical attention to vitamin B12 deficiency is crucial for further assessing the relationship between OCD symptoms and sleep disorders.

Keywords: obsessive-compulsive disorder, sleep disturbances, vitamin b12, mediating effects

Introduction

Obsessive-Compulsive Disorder (OCD) is a prevalent and debilitating mental disorder.[1] The prevalence of OCD exhibits variation across different countries and sampling times.[2,3] According to Ruscio et al, the lifetime and 12-month prevalence rates of OCD in the United States are 2.3% and 1.2%, respectively.[1] It is characterized by obsessive thoughts (these are distressing and repetitive thoughts, impulses, or intrusive images) and compulsive behaviors (these are excessive actions performed to alleviate the anxiety caused by these obsessions, often ritualistic in nature).[3,4] This disorder can lead to significant functional impairment in various domains such as family, work, and social environments, ultimately reducing the quality of life.[5–8]

Sleep disturbances are prevalent among individuals with OCD and contribute significantly to the disorder's severity and treatment complexity. Research has consistently shown that OCD is associated with poor sleep quality, disruptions in sleep architecture, and altered circadian rhythms.[9–11]

Vitamin B12 is a crucial nutrient essential for the normal functioning of the nervous system, playing a vital role in neurotransmitter synthesis and the maintenance of nerve cells.[12] Vitamin B12 is involved in one-carbon metabolism,

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which is crucial for the methylation processes of neurotransmitters, the synthesis of proteins and neural membrane phospholipids, and is essential for DNA synthesis.[13] The broad neurological implications of vitamin B12 deficiency extend to cognitive decline and an increased risk of other psychiatric disorders, such as schizophrenia.[14,15] In children, deficiencies in vitamins B12 and B9 (folate) are associated with neurological developmental delays and attention deficit hyperactivity disorder, underscoring the importance of these nutrients in brain development.[16] Furthermore, vitamin B12 plays a crucial role in the synthesis of serotonin and dopamine, neurotransmitters that are fundamental to regulating mood and behavior.[17] This function suggests that adequate levels of vitamin B12 can help alleviate anxiety and depressive symptoms associated with OCD, potentially improving sleep quality.[18]

However, research on the specific relationship between vitamin B12 and both OCD and sleep disturbances remains relatively limited. Studies indicate that vitamin B12 deficiency is common among patients with OCD.[19–21] Research by Hermesh et al showed that the frequency of vitamin B12 deficiency in patients with OCD is significantly higher than in healthy controls.[21] Recent studies highlight the roles of folate and homocysteine in OCD, demonstrating their potential as significant biomarkers for the disorder. Türksoy et al reported a strong correlation between these metabolic factors and the severity of OCD symptoms.[22] Similarly, Atmaca et al observed that patients with OCD typically have lower levels of folate and higher levels of homocysteine, further correlating these biochemical changes with symptom severity.[23] This is supported by Balandeh et al, whose systematic review and meta-analysis reinforced the abnormal levels of folate and homocysteine in OCD patients compared to controls.[24] Additionally, Esnafoğlu and Yaman in their study on children and adolescents with OCD, indicated significant variations in vitamin B12, folate, homocysteine, and vitamin D levels,[25] suggesting these nutrients may influence the disorder's development, particularly in young individuals. These findings suggest that metabolic abnormalities in these nutrients may be related to the development and persistence of OCD symptoms.

Although research directly investigating the impact of vitamin B12 on the sleep quality of OCD patients is limited, existing evidence suggests that vitamin B12 plays a significant role in regulating the production of melatonin and circadian rhythms, thus potentially indirectly affecting sleep.[26] Appropriate supplementation of vitamin B12 can help adjust sleep cycles and improve sleep disturbances,[27,28] which may be particularly important in OCD patients, as this group typically experiences higher stress levels,[29] possibly accelerating the depletion of vitamin B12 in the body.

Research findings underscore the potential of vitamin B12, alongside folate and homocysteine, as adjunctive treatments for alleviating OCD symptoms and enhancing sleep quality. This underscores the necessity for further exploration into how these metabolites influence the underlying mechanisms of OCD, particularly through one-carbon metabolism pathways. Therefore, this study aims to comprehensively examine the relationships between vitamin B12, folate, homocysteine levels, OCD symptoms, and sleep quality, while assessing the mediating effects of these nutrients, providing preliminary evidence for encouraging further studies on this topic.

Materials and Methods

Subjects

The study recruited individuals from January 2023 to January 2024 at the psychiatric outpatient clinic of the Mental Health Center at Ningxia Medical University General Hospital and from the local community for the control group. Inclusion Criteria: 1. Age between 18 and 50 years. 2. The diagnosis was based on evaluation by two associate chief psychiatrists, who clinically diagnosed OCD according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5).[4] 3. Experienced OCD symptoms for at least one year. 4. Not received psychiatric medication or psychological therapy in the four weeks prior to joining the study. 5. Achieved a score of ≥16 on the Yale-Brown Obsessive Compulsive Scale (Y-BOCS), or ≥10 if symptoms were limited to obsessive thoughts or behaviors. 6. Scored less than 24 on both the 17-item Hamilton Depression Rating Scale (HAMD) and the Hamilton Anxiety Rating Scale (HAMA). Exclusion Criteria: 1. Diagnosed with schizophrenia, mood disorders, or other psychiatric disorders. 2. Suffering from organic brain disorders or significant physical illnesses. 3. History of alcohol or drug abuse. 4. Conditions that affect vitamin B12 absorption, such as pernicious anemia or gastric diseases.

The control group consisted of healthy volunteers aged 18 to 50, right-handed, and with a minimum of nine years of education. These volunteers had no significant physical illnesses, no personal or direct family history of psychiatric conditions, and were comparable to the patient group in age, gender, and educational level.

This study was authorized by the Ethics Committee of Ningxia Medical University General Hospital, under approval number 2020-231, adhering to the principles of the Declaration of Helsinki. We hereby affirm that all participants involved in the study provided their written informed consent prior to their participation.

Clinical Diagnosis and Assessment

Two psychiatrists, trained for consistency in scale administration, conducted clinical interviews and psychological assessments using the Y-BOCS, HAMD, HAMA and PSQI.

The Y-BOCS[30] is a clinician-administered semi-structured interview designed to quantify the severity of obsessive-compulsive disorder symptoms. This scale is comprised of 10 principal items, rated from 0 (no symptoms) to 4 (extreme symptoms), with a higher total score indicating increased severity. The first five items measure the extent of obsessive thoughts, and the subsequent five assess the intensity of compulsive behaviors. The internal consistency for this sample is notably high, with a Cronbach's alpha of 0.92, affirming its reliability and validity across diverse populations.

The PSQI[31] was used to assess sleep quality over the past month. This self-assessment questionnaire covers seven dimensions, including subjective sleep quality, sleep latency, duration, habitual efficiency, disturbances, use of sleep medication, and daytime dysfunction. Each item is scored from 0 to 3, with a total score ranging from 0 to 21. Confirmatory factor analysis confirmed good construct validity, and the reliability coefficient of the Chinese version ranged from 0.80 to 0.82.

The HAMD[32] utilized to evaluate the level of depressive symptoms among OCD patients, consists of 17 items. Each item on this scale helps identify the severity of depression, with scores ranging from 0 (no depression) to a possible maximum that highlights the acute severity of symptoms. Higher aggregate scores correlate with more severe depressive states.

The HAMA[33] serves to assess anxiety levels, comprising 14 items scored between 0 and 4. This scale measures the severity of anxiety symptoms, where increasing scores indicate more severe anxiety. It is widely applied in clinical settings to evaluate anxiety in patients with OCD and other anxiety-related disorders.

Vitamin B12, Homocysteine and Folate Testing

All participants were required to fast for over 8 hours prior to venous blood collection. The collected whole blood samples were placed into serum separator tubes and stored at 4°C overnight. Subsequently, the samples were centrifuged at 1000×g for 20 minutes. The supernatant was then stored at −80°C until analysis. Analyses of homocysteine, vitamin B12, and folate levels were performed at Beijing Jihua Biotechnology Service Co., Ltd., using test kits purchased from Jianglai Biology. The manufacturer-provided coefficients of variation for these assays are 7.4% for vitamin B12, 9.8% for folate, and 8.5% for homocysteine.

Data Analysis

Data were processed using SPSS version 26.0,[34] the normality of all quantitative variables was assessed. Descriptive statistics (mean, standard deviation, frequency, and percentage) were used to quantify quantitative and categorical study variables and outcomes. The Student's *t*-test, which was two-tailed, was applied to independent samples to compare the means of quantitative outcome variables across different categories of study variables where appropriate. Non-parametric tests were used for variables with non-normal distributions. Covariate adjustments were made using Analysis of Covariance (ANCOVA). A correlation analysis was conducted between the severity of OCD symptoms and levels of vitamin B12, folate, and homocysteine in the OCD group, with sex, age, and education level as covariates.

To evaluate potential common method bias, Harman's single-factor test was utilized. An exploratory factor analysis (EFA) of all variables, conducted without factor rotation, revealed that the largest single factor explained only 28% of the total variance, significantly below the critical threshold of 50%. This indicates the absence of significant common method bias, thus ensuring the internal validity and reliability of the study results.

Mediation effects were assessed using Model 4 of the PROCESS macro in SPSS. All models were assessed using 5000 bootstrap samples for correction; effects were considered statistically significant if the 95% confidence intervals did not include zero. Two-tailed p-value of <0.05 was defined as statistically significant for group differences.

Results

Demographic Data

This study conducted clinical assessments on 128 patients with OCD, of which 16 were excluded due to a HAMD score greater than 24, 12 were excluded for a HAMAscore above 24, and 6 were discarded due to incomplete assessments. Ultimately, 52 OCD patients were included (29 males and 23 females) with an average age of 27.61 ± 9.59 years. The control group consisted of 42 healthy individuals (24 males and 18 females) with an average age of 29.70 ± 8.27 years. There were no significant differences in gender or age between the two groups (p=0.576 and p=0.308, respectively).

In the OCD group, the average HAMA score was 17.59 ± 3.28, compared to 13.51 ± 2.42 in the control group, which was not statistically significant (t=6.195, p<0.001). The average HAMD score in the OCD patients was 16.65 ± 4.13, while in the control group, it was 13.86 ± 2.69, also showing no significant difference (t=3.493, p<0.001). However, the average PSQI score was significantly higher in OCD patients at 13.66 ± 4.27 compared to 4.84 ± 2.02 in the control group (t=11.456, p<0.001).

Comparisons of folate, vitamin B12, and homocysteine levels between the two groups revealed that only the vitamin B12 levels were significantly lower in OCD patients compared to the controls (t=1.997, p=0.049). No significant differences were found in folate (t=−0.451, p=0.65) or homocysteine levels (t=1.001, p=0.32) between the groups (Table 1 and Figure 1).

Analysis of Main Variables Correlation

Within the OCD group, Spearman correlation analysis was conducted. The results showed a statistically significant negative correlation between vitamin B12 levels and clinical symptoms of OCD ($r = -0.647$, $p < 0.001$), as well as with sleep quality scores ($r = -0.418$, $p < 0.001$). Additionally, vitamin B12 levels were significantly positively correlated with folate levels ($r = 0.33$, $p < 0.05$). There was a significant positive correlation between the severity of OCD symptoms and sleep disturbances ($r = 0.543$, $p < 0.001$). No significant correlations were observed between levels of homocysteine and folate with OCD symptoms or sleep quality (Table 2).

Table 1 Comparison of Demographic Data Between the OCD Group and the Control Group (M+SD)

	OCD (N=52)	HC (N=42)	t/χ^2	*P*-value
Age (Year)	29/23	24/18	0.562	0.576
Gender (Male/Female)	27.61±9.59	29.70±8.27	1.025	0.308
Education (Year)	15.70±5.29	16.08±5.31	1.316	0.752
Y-BOCS	21.70±5.18	3.49±4.03	18.773	<0.001**
HAMA	17.59±3.28	13.51±2.42	6.195	<0.001**
HAMD	16.65±4.13	13.86±2.69	3.493	<0.001**
PQSI	13.66±4.27	4.84±2.02	11.456	<0.001**
VB12 (pg/mL)	416.05±107.25	466.37±122.75	1.997	0.049*
Folate (pg/mL)	26.19±8.20	27.29±13.94	−0.451	0.653
HCY (pg/mL)	15.80±3.52	14.87±5.32	1.001	0.319

Notes: The values are presented as mean; *Indicates statistical significance at p<0.05; **Indicates statistical significance at p <0.01.

Abbreviations: SD, standard deviation; OCD, obsessive-compulsive disorder; HC, Healthy controls; HAMD, Hamilton rating scale for Depression; HAMA, Hamilton rating scale for Anxiety; Y-BOCS, Yale-Brown obsessive-compulsive scale; PQSI, Pittsburgh Sleep Quality Index; HCY, Homocysteine; VB12, VitaminB12.

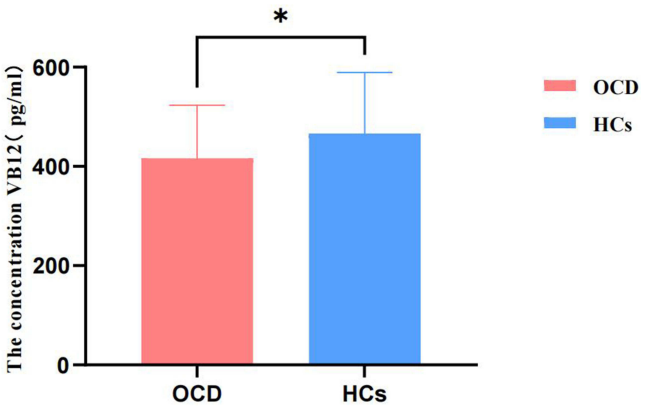

Figure 1 Statistical difference of vB12 between OCD and HCs.
Note: *p<0.05.
Abbreviations: OCD, Obsessive-Compulsive Disorder; HCs, Healthy Controls.

Mediation Effect Analysis

Further correlation analysis confirmed significant interrelationships among OCD symptoms, vitamin B12 levels, and sleep quality, fulfilling the prerequisites for testing mediation effects. Mediation Effect Analysis explored the mediating role of vitamin B12 in the relationship between OCD symptoms and sleep quality. Path coefficients among these three variables are displayed in Figure 2.

As illustrated in Table 3, the Bootstrap 95% confidence intervals for the mediation effect of vitamin B12 on the relationship between OCD symptoms and sleep quality do not include zero. This indicates that OCD symptoms not only have a direct effect on sleep quality but also exert a partial mediating effect through vitamin B12. Specifically, the direct effect (0.471) and the mediating effect (0.127) account for 78.76% and 21.23% of the total effect (0.598), respectively. This highlights the significant role that vitamin B12 plays in modulating the impact of OCD symptoms on sleep quality.

Discussion

This study aimed to assess the symptoms of OCD and sleep quality using the Y-BOCS and the PSQI, while also exploring the potential correlation between these factors and vitamin B12, folate and homocysteine levels. Our findings indicate that vitamin B12 levels in OCD patients are significantly lower than those in the normal population, and these lower levels of vitamin B12 are significantly correlated with both OCD symptoms and poor sleep quality. Further analysis revealed that vitamin B12 partially mediates the relationship between OCD symptoms and sleep quality.

Current research on levels of folate, vitamin B12, and homocysteine in patients with OCD remains limited. Our study adds important data by demonstrating a significant reduction in vitamin B12 levels in OCD patients compared to a control group, with these lower levels correlating with more severe OCD symptoms. These findings are consistent with those of Hermesh et al, who found that vitamin B12 deficiency is more common in OCD patients than in the control group.[21] This suggests that vitamin B12 deficiency may be a marker for OCD symptoms and predict more severe

Table 2 The Correlation Between the Main Variables

	M	SD	1	2	3	4	5
1. Y-BOCS	21.74	5.18					
2. PQSI	12.07	3.67	0.543**	1			
3. VB12 (pg/mL)	367.45	66.47	−0.647**	−0.418**	1		
4. Folate(pg/mL)	26.12	12.30	−0.91	−0.029	0.333*	1	
5. HCY (pg/mL)	16.51	4.51	0.044	−0.137	−0.182	0.045	1

Notes: The values are presented as mean standard deviation, or percentage. *Indicates statistical significance at p <0.05.**Indicates statistical significance at p <0.01.
Abbreviations: SD, standard deviation; Y-BOCS, Yale-Brown obsessive-compulsive scale; PQSI, PittsburghSleep Quality Index; HCY, Homocysteine; VB12, VitaminB12.

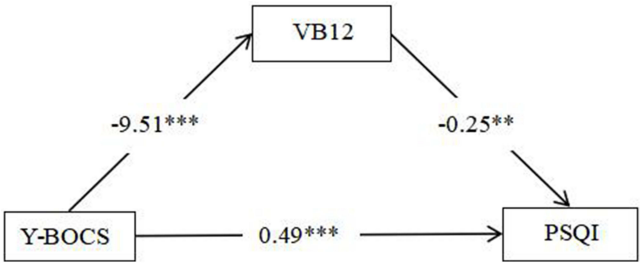

Figure 2 Path coefficient of VB12 between OCS and sleep quality variables.
Notes: **Indicates statistical significance at p <0.01; ***Indicates statistical significance at p <0.001.
Abbreviations: OCS, obsessive-compulsive symptoms; Y-BOCS, Yale-Brown obsessive compulsive scale; PSQI, Pittsburgh Sleep Quality Index; VB12, VitaminB12.

manifestations of the disorder. Additionally, case reports by Sharma and Biswas describe a middle-aged male presenting with OCD symptoms who had low serum levels of vitamin B12 and a family history of vitamin B12 deficiency.[19] These comprehensive evaluations suggest that one-carbon metabolism, which includes vitamin B12, folate, and homocysteine, may be implicated in the etiology of OCD. One-carbon metabolism is crucial for the methylation processes of neurotransmitters, the synthesis of proteins and neural membrane phospholipids, and is essential for DNA synthesis.[13] These metabolic pathways may play a central role in the development of neuropsychiatric symptoms.[35] Deficiencies in folate and vitamin B12 can reduce methylation reactions, leading to decreased neurotransmitter levels and consequently affecting intracellular biochemical pathways.[13] However, our study did not find significant differences in folate and homocysteine levels between the two groups. Hermesh et al suggest that this might indicate that vitamin B12 deficiency is a characteristic feature of patients with OCD.[21] Atmaca et al noted that folate levels in these patients were significantly negatively correlated with YBOCS scores, whereas homocysteine levels were positively correlated with both the duration of the disease and Y-BOCS scores.[23]

In our study, levels of folate and homocysteine did not show significant correlations with the total Y-BOCS scores or sleep quality ratings; only vitamin B12 demonstrated a statistically significant negative correlation with both. Notably, the patients in our study were treatment-naïve individuals presenting with OCD for the first time, potentially representing an early stage of disease progression in which biochemical markers, such as folate and homocysteine, may not yet display significant differences from those in controls. Additionally, first-episode, untreated patients may exhibit variations in genetic makeup, lifestyle, or nutritional status compared to long-term patients or other cohorts, factors that could influence baseline folate and homocysteine levels. Another possible reason is that our study excluded patients with anxiety and depression scores above 24, while some studies have found a relationship between high homocysteine levels and mood disorders, particularly depressive states.[36–38] This might explain the lack of statistically significant differences in serum homocysteine levels between the patient group and the normal control group observed in our study.

Our study also found that vitamin B12 partially mediates the relationship between obsessive-compulsive symptoms and sleep disturbances. This suggests that vitamin B12 levels not only directly impact sleep quality but also play a transmitting or amplifying role between OCD symptoms and sleep disorders. Specifically, a deficiency in vitamin B12 may exacerbate the neurochemical dysregulation associated with OCD, further affecting the sleep quality of patients. Existing research indicates that there is an independent inverse relationship between adult serum vitamin B12 levels and sleep duration.[39] In a cross-sectional study involving 63 children with familial Mediterranean fever, the relationship between serum vitamin B12 levels and sleep was assessed using the PSQI. The study found that children with lower

Table 3 Mediation Effect Analysis

	Effect	SE	LLCI	ULCI	Effect Size
Total effect	0.598	0.0214	0.4553	0.542	
Direct effect	0.471	0.0248	0.2073	0.3078	78.76%
Indirect effect	0.127	0.0405	0.1913	0.3429	21.23%

serum vitamin B12 levels also had lower sleep efficiency.[40] Additional research confirms that vitamin B12 plays a crucial role in the synthesis of melatonin.[26] Melatonin is a key hormone involved in regulating the sleep-wake cycle, and vitamin B12 participates as a cofactor in the methionine cycle, contributing to its synthesis.[41] Therefore, insufficient levels of vitamin B12 may lead to reduced production of melatonin, thereby disrupting normal sleep patterns and potentially causing sleep disturbances such as insomnia. Furthermore, vitamin B12 supports the methylation of neurotransmitters involved in mood and cognitive function, which are often dysregulated in OCD.[17] A deficiency in vitamin B12 may lead to a decrease in the synthesis of these critical neurotransmitters, exacerbating the neurochemical dysregulation associated with OCD.[22] This, in turn, can worsen OCD symptoms and further impact sleep quality, creating a complex interplay between these factors.

Certainly, this study has its limitations. The limited sample size may impact the generalizability and statistical significance of the results. Larger scale studies could provide more robust conclusions. Additionally, the use of a cross-sectional design prevents the determination of causality. Future longitudinal studies are needed to better understand the dynamic relationships between vitamin B12 levels, OCD symptoms, and sleep quality. Furthermore, this study excluded patients who had received treatment for OCD, so the results may not apply to the treated OCD patient population. The impact of medication on vitamin B12 levels and its relationship with OCD symptoms and sleep quality requires further investigation. It should also be noted that vitamin B12 levels can be influenced by diet and lifestyle habits. This study did not assess participants' dietary and lifestyle habits in detail, which could potentially affect the results.

Conclusion

In summary, the results of this study underscore the significant role of vitamin B12 in patients with Obsessive-Compulsive Disorder (OCD), particularly in terms of its potential mechanisms in regulating sleep quality. Our findings demonstrate that vitamin B12 levels in OCD patients are significantly lower than those in healthy controls and are significantly correlated with the severity of OCD symptoms and sleep disturbances. Moreover, vitamin B12 partially mediates the pathway through which OCD symptoms affect sleep quality, further validating its critical role in mental health and neurological function. However, as this is a cross-sectional study, causality cannot be established. Nonetheless, these findings might encourage further research on this topic. Future studies could expand the sample size and take into account participants' dietary patterns for a more detailed investigation of this phenomenon, but these findings provide a direction for future research.

Abbreviations

OCD, Obsessive-compulsive disorder; Y-BCOS, Yale-Brown Obsessive Compulsive Scale; HAMD, Hamilton Depression Rating Scale; HAMA, Hamilton Anxiety Rating Scale; PSQI, Pittsburgh Sleep Quality Index.

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Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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