#### **ORIGINAL ARTICLE**



# Anxiety Sensitivity as a Predictor of Epilepsy-Related Quality of Life and Illness Severity Among Adult Epilepsy

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#### Abstract

The purpose of the current study was to examine the role of anxiety sensitivity in predicting seizure likelihood and QOL among 49 people with epilepsy (PWE; 63.3% female;  $M_{age} = 48.53$ , SD = 15.91). As hypothesized, after controlling for the effects of negative affectivity and past year seizure presence, greater levels of anxiety sensitivity significantly predicted poorer overall QOL as well as the QOL domains of seizure worry, medication effects, work-driving-social limitations, and cognitive functioning (8.8-22.9% unique variance). Anxiety sensitivity did not significantly predict seizure likelihood or QOL related to emotional well-being and energy difficulties. These findings suggest that PWE who are fearful of arousal-related sensations experience greater functional impairment, but not necessarily more severe epilepsy. Interventions aimed at decreasing anxiety sensitivity may be useful in improving QOL in this population.

**Keywords** Anxiety · Anxiety sensitivity · Epilepsy · Seizures · Quality of life

# Introduction

Epilepsy is the fourth most common neurological disorder, whose main clinical feature is seizures resulting from excessive electrical signaling in the brain (Centers for Disease Control [CDC] 2012; Hesdorffer et al. 2011). Seizures can be classified based on three criteria: (1) where the seizure begins in the brain; (2) level of awareness during a seizure; and (3) other seizure features. Based on seizure onset, seizures are classified as focal (engaging one hemisphere), generalized (i.e., engaging both hemispheres), or unknown onset (Fisher et al. 2017). Importantly, the presence or absence of consciousness during a seizure is one feature that has

considerable impact on functional ability in epilepsy (Blumenfeld 2012). Overall, epilepsy has been strongly associated with substantial impairment among multiple functional domains, including physical, cognitive, social, and emotional well-being.

Physically, epilepsy is associated with a twofold increased risk for heart attack, stroke, and premature death (Chang et al. 2014; Donner 2014; Liedholm and Gudjonsson 1992). People with epilepsy (PWE) also commonly report difficulties with memory, decision-making, and both verbal and nonverbal abilities, such as language acquisition, processing speed, and perceptual ability (Hermann and Seidenberg 2007). Vocationally, PWE report twice as many lost workdays due to their health and are almost six times more likely to qualify for disability than those without epilepsy (Kessler et al. 2012; Thurman et al. 2016). Emotional-well being is also impaired as PWE are also twice as likely to be diagnosed with a psychological disorder compared to those without epilepsy (Kessler et al. 2012). Consistent with numerous types of functional impairment associated with epilepsy, those with the disorder report significantly poorer healthrelated quality of life (OOL) than people without epilepsy (Baker et al. 2005; Gholami et al. 2016; Rajabi et al. 2009). Moreover, among those with epilepsy, individuals who experience more frequent seizures have the poorest QOL (Baker et al. 1997; Devinsky et al. 1999; Leidy et al. 1999).

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In addition to seizure frequency, one of the strongest contributors to poor epilepsy-related QOL is comorbid psychopathology (Boylan et al. 2004; Johnson et al. 2004; Luoni et al. 2011). Comorbid anxiety psychopathology, which occurs in approximately 20-40% of all PWE, is particularly problematic (Beyenburg et al. 2005; Pham et al. 2017; Wiglusz et al. 2018). Common anxiety disorders in epilepsy include panic disorder, generalized anxiety disorder, and specific phobias (Beyenburg et al. 2005; Wiglusz et al. 2018). Anxiety symptoms are stronger predictors of QOL than disease related variables among PWE (Choi-Kwon et al. 2003; Johnson et al. 2004; Kwan et al. 2009), and there is some evidence that anxiety symptoms more strongly predict QOL than depression symptoms (Kwan et al. 2009). Additionally, elevated levels of anxiety symptoms among PWE are associated with greater seizure frequency and shorter time since the last seizure, however, this relationship is mediated by depressive symptoms (Thapar et al. 2009; Kimiskidis et al. 2007).

One anxiety disorder that is particularly problematic in epilepsy is panic disorder (Johnson et al. 2018). Recent research suggests that panic disorder may the most prevalent of comorbid anxiety disorders in PWE (Wiglusz et al. 2018). However, due to the substantial overlap between panic symptoms and features of ictal fear (i.e., the most frequently reported emotional aura that is common in patients with seizures originating in the temporal lobe; Feichtinger et al. 2001; Kanner 2004), an accurate diagnosis of this anxiety disorder in PWE can be difficult (Johnson et al. 2018). Despite the robust associations between anxiety psychopathology and epilepsy, there has been a dearth of research examining anxiety-related cognitive risk factors and epilepsy. Such work could help not only explicate the anxiety-epilepsy association, but also identify targets for interventions that could improve epilepsy management and QOL. An important construct to examine in this regard was anxiety sensitivity, which is the focus of the present study.

Anxiety sensitivity, commonly known as the fear of anxiety or anxiety-related psychological and physical sensations (McNally 2002; Reiss and McNally 1985), is a relatively stable, cognitive-affective risk factor that leads to increased levels of pre-existing anxiety (McNally 2002). A large body of empirical work indicates that higher levels of anxiety sensitivity are associated with greater risk for anxiety symptoms and with the onset of anxiety diagnoses (McNally 2002; Schmidt et al. 2006; Taylor et al. 2007). In medical conditions other than epilepsy that have anxiety as a common comorbid feature (e.g., asthma, chronic pain, HIV), greater anxiety sensitivity is associated with poorer symptom management and QOL (Admundson et al. 2000; Asmundson and Norton 1995; Avallone et al. 2012; Capron et al. 2012; McLeish et al. 2010). This work suggests that higher levels of anxiety sensitivity may foster greater reactivity to the physiological and cognitive symptoms inherent in multiple medical conditions.

Although there have not yet been studies of anxiety sensitivity in epilepsy, based on existing literature, anxiety sensitivity may be particularly relevant in epilepsy due to the symptomatic overlap between panic attacks and ictal fear. Individuals with epilepsy who are fearful of arousal-related sensations may be particularly fearful of the physiological and cognitive symptoms of epilepsy that are indistinguishable from panic attacks (e.g., nausea, tachycardia, hot flashes, trembling, paresthesia, shortness of breath, sweating, depersonalization, loss of control; Beyenburg et al. 2005; Thompson et al. 2000). Additionally, individuals who are high in anxiety sensitivity may also be fearful of the potential social consequences of having a seizure in front of others, given that over half of individuals with epilepsy report feeling stigmatized by their disease (Baker et al. 1997). We hypothesize that elevated levels of anxiety sensitivity would therefore result in increased stress levels as well as the amplification of pre-existing general and epilepsy-specific anxiety symptoms. These processes could contribute to the documented reduction in overall QOL and increased seizure frequency in those who have both epilepsy and anxiety (Choi-Kwon et al. 2003; Temkin and Davis 1984).

Therefore, the aim of the current study was to provide an initial test of this hypothesis by examining the degree to which anxiety sensitivity serves as a unique predictor of seizure presence in the past year (an index of epilepsy severity) and epilepsy-related QOL. It was hypothesized that, after controlling for the effect of negative affectivity, greater anxiety sensitivity would significantly predict an increased likelihood of having had a seizure in the past year. For epilepsy-related QOL, it was hypothesized that, after controlling for the effects of negative affectivity and the presence of seizures in the past year, greater anxiety sensitivity would be predictive of poorer epilepsy-related QOL in all domains (i.e., seizure worry, overall QOL, emotional well-being, energy/fatigue, medication effects, workdriving-social limitations, cognitive function; Cramer et al. 2005).

# Method

# **Participants**

Participants for the current study were selected from a larger study examining the effects of cigarette smoking on epilepsy severity and QOL. Given the well-established association between cigarette smoking and anxiety sensitivity (Brown et al. 2001; Zvolensky et al. 2006, 2009), the present study purposefully excluded smokers in this initial evaluation of the effects of anxiety sensitivity on epilepsy severity



and QOL. Participants of the present study were 49 nonsmoking adults with epilepsy (63.3% female;  $M_{age} = 48.53$ , SD = 15.91, range 21–76 years). All participants were under the care of epilepsy specialists working at a Comprehensive Epilepsy Center with Level IV certification by the National Association of Epilepsy Centers (Labiner et al. 2010). For inclusion in the study, participants had to be over the age of 18, with a neurologist-confirmed diagnosis of epilepsy, as assessed via medical record review. To ensure that reported seizures were limited to epilepsy, those with a history of non-epileptic seizures diagnosed by a neurologist (assessed via medical record review) were excluded from the current study. In addition, to ensure that participants could provide informed, written consent and complete all study measures, participants were excluded if there was a history of intellectual disability in the medical record or results of the Wide Range Achievement Test-4th Edition (WRAT-4; Wilkinson and Robertson 2006) indicated that they were reading below a 6th grade level.

Participants in this study had a wide range of epilepsy, with 57.1% of participants reporting experiencing seizures in the past year (46.9% with seizure with loss of consciousness and 10.2% with only seizures without loss of consciousness). The vast majority (93.8%) of participants had a longstanding epilepsy diagnosis (i.e., diagnosed≥5 years), refractory (i.e., uncontrolled) epilepsy status (81.6%), were taking multiple anti-epileptic drugs (67.3%) at the time of the study, and were medication compliant (81.6%). 93.9% of the sample self-identified as Caucasian and 6.1% as African American. No participants endorsed Hispanic ethnicity. Approximately 16.7% percent of the sample had a high school degree, 20.8% had completed some college education, 18.8% had a 2-year college degree, 29.2% had a 4-year college degree, and 14.6% had completed some graduate school or had a graduate degree.

# Measures

# Wide Range Achievement Test-4th Edition (WRAT-4)

The WRAT-4 (Wilkinson and Robertson 2006) assesses an individual's ability to read individual words. Participants read a series of increasingly difficult words aloud and are scored on the number of words that are pronounced correctly. The WRAT-4 was used to ensure that participants had sufficient reading ability to complete the self-report instruments.

#### Positive Affect Negative Affect Schedule (PANAS)

The PANAS is a self-report measure used to assess an individual's overall mood (Watson et al. 1988). This measure has consistently demonstrated good reliability and validity and

is commonly used in psychological research (Watson et al. 1988). In the current study, only the negative affect subscale (PANAS-NA; Watson et al. 1988) was used to assess ones overall experience of multiple negative affective states. Internal consistency for the PANAS-NA in the current sample was good ( $\alpha$  = .83).

#### **Epilepsy History**

Information about participants' epilepsy, including whether or not they had experienced a seizure in the past 12 months, was collected from participants' electronic medical records.

# Quality of Life in Epilepsy (QOLIE-31)

The QOLIE-31 (Cramer et al. 2005) is a 31-item self-report measure that assesses epilepsy-related QOL. Participants are asked to rate the effect their seizures have on various aspects of their lives on a six-point Likert-type scale assessing the duration of impairment  $(1 = all \ of \ the \ time \ to \ 6 = none \ of \ the$ time) and a four-point Likert-type scale assessing degree of impairment  $(1 = ves \ a \ great \ deal \ to \ 4 = no, \ not \ at \ all)$ . The QOLIE-31 comprises seven subscales grouped into two factors: Emotional/Psychological Effects and Medical/ Social Effects (Cramer et al. 2005). Emotional/Psychological Effects consists of the subscales of (1) seizure worry (e.g., "How fearful are you of having a seizure during the next month") (Cramer et al. 2005, p. 87); (2) overall QOL (e.g., "How has your quality of life been during the past 4 weeks") (Cramer et al. 2005, p. 86); (3) emotional well-being (e.g., "How much of the time during the past 4 weeks have you felt downhearted and blue") (Cramer et al. 2005, p. 86); and (4) energy/fatigue (e.g., "How much of the time during the past 4 weeks did you feel tired") (Cramer et al. 2005). Medical/ Social Effects consists of the following subscales: (1) medication effects (e.g., "How worried are you that medications you are taking will be bad for you if taken for a long time") (Cramer et al. 2005, p. 87); (2) work-driving-social limitations (e.g., "How worried are you about embarrassment or other social problems resulting from having a seizure during the next month") (Cramer et al. 2005, p. 87); and (3) cognitive function (e.g., "During the past 4 weeks have you had any trouble with your memory") (Cramer et al. 2005, p. 86). Lower scores on the QOLIE-31 indicate poorer epilepsyrelated QOL. The QOLIE-31 shows good construct and discriminant validity, and the subscales show good internal consistency and test-retest reliability (Cramer et al. 2005). Internal consistency for the QOLIE-31 (Cramer et al. 2005) subscales in the current sample was acceptable for the medication effects subscale ( $\alpha = .78$ ), good for the seizure worry, overall QOL, emotional well-being, and social function subscales (range .80-.88), and excellent for the energy/fatigue subscale ( $\alpha = .90$ ).



## Anxiety Sensitivity Index-3 (ASI-3)

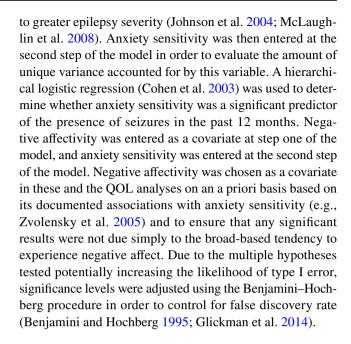
The ASI-3 (Taylor et al. 2007) is an 18-item self-report measure that assesses the degree to which individuals fear the negative physical, social, and psychological consequences associated with anxiety symptoms. The ASI-3 is the most psychometrically sound measure of anxiety sensitivity currently available (Taylor et al. 2007). Internal consistency for the ASI-3 in the current study was excellent ( $\alpha$ =.94).

#### **Procedure**

Participants were recruited from patients arriving for outpatient appointments at the university-based Gardner Neuroscience Institute. Prior to the clinic appointments, trained research assistants screened potential participants for initial inclusion and exclusion criteria (i.e., older than 18, physician diagnosis of epilepsy, no history of non-epileptic seizures or intellectual disability) based on information from their electronic medical records. Those patients meeting initial eligibility criteria were invited to participate in the study by a trained research assistant upon arrival for their regularly scheduled appointment. After providing written, informed consent, participants completed the WRAT-4 to confirm their reading level. They were then given options to either complete the packet of questionnaires in the office or to complete them at home and return them by mail. Upon receipt of the completed questionnaires, participants were given (or mailed) a \$25 gift card as compensation for their time and effort (return rate = 77.8%). After receiving the completed questionnaire packets, participants' electronic medical records were then reviewed to obtain information about the presence of seizures in the past 12 months.

# **Data Analytic Plan**

The relationship between all study variables was first examined using zero-order correlational analyses. Then, a series of hierarchical multiple regression analyses were completed to examine the effect of anxiety sensitivity on epilepsy-related QOL and epilepsy severity (Cohen et al. 2003). To test the hypothesis that anxiety sensitivity negatively impacted all domains of epilepsy-related QOL, separate models were constructed for predicting each of the QOLIE-31 subscales (i.e., seizure worry, overall QOL, emotional well-being, energy/fatigue, medication effects, workdriving social limitations, and cognitive function; Cramer et al. 2005). In each model, negative affectivity and seizure presence in the past year were entered simultaneously as covariates in step one. Presence of seizures was chosen as an a priori covariate based on previous research demonstrating that seizure frequency is associated with poorer QOL in order to ensure that any significant results are not due simply



# Results

Associations between all study variables are presented in Table 1. Greater negative affectivity was significantly associated with higher anxiety sensitivity (r = .51, p < .01) and poorer QOL across all measured domains (range - .39 to -.68). Presence of seizures in the past 12 months was correlated with poorer overall QOL, greater seizure worry, and greater work-driving-social limitations (range -.34 to -.42), but not emotional well-being, energy/fatigue, medication effects, and cognitive limitations. Higher levels of anxiety sensitivity were significantly correlated with poorer QOL across all domains except energy/fatigue (range - .42 to -.69). Anxiety sensitivity was not significantly correlated with the presence of seizures in the past year. All of the QOL domains were significantly correlated with one another (range .38-.67) except for a non-significant association between emotional well-being and medication effects.

Results of the logistic regression analysis examining the predictive role of anxiety sensitivity on seizure presence revealed that neither step nor step two of the model were significant predictors. Negative affectivity did not significantly predict seizure presence at step one (OR .98, p = .72, 95% CI .88–1.09), nor did anxiety sensitivity at step two (OR 2.08, p = .11, 95% CI .98–1.09).

Results of the hierarchical linear regression analyses are presented in Table 2. Step one of each of these analyses was significant for each QOL domain, accounting for 15.1–51.7% unique variance. Negative affectivity was a significant predictor at step one in all models. Seizure presence in step one was only a significant predictor of overall QOL, seizure worry, emotional well-being, and work/driving/social



**Table 1** Descriptive statistics and zero-order correlations among all study variables

	1	2	3	4	5	6	7	8	9	10	M	SD	Observed range
1. Negative affectivity	_	07	.51**	47**	49**	68**	40**	39**	51**	58**	17.49	5.46	10–31
2. Seizure presence	_	_	.22	42**	39*	20	22	.06	34*	11	-	-	_
3. Anxiety sensitivity	_	_	_	68**	64**	42**	28	51**	69**	50**	10.23	11.69	0-61
4. Seizure worry	_	-	-	_	.58**	.38*	.42**	.45**	.67**	.62**	68.44	27.38	0-100
5. Quality of life	_	-	-	_	-	.65**	.53**	.56**	.67**	.62**	73.53	17.62	27-100
6. Well-being	_	_	_	_	_	_	.53**	.26	.43**	.52**	71.72	15.60	40-100
7. Energy/fatigue	_	_	_	_	_	_	-	.44**	.48**	.55**	52.72	21.28	10-100
8. Medication effects	_	_	_	_	_	_	-	_	.53**	.44**	61.81	27.16	0-100
9. Limitations	_	_	-	_	_	_	_	_	_	.46**	70.09	30.38	0-100
10. Cognitive function	_	-	-	_	-	_	_	_	_	-	65.28	22.99	12-100

Negative affectivity: Positive Affect Negative Affect Schedule—Negative Affect subscale (Watson et al. 1988); seizure presence: presence of seizures in the past 12 months coded as 0=no, 1=yes; anxiety sensitivity=Anxiety Sensitivity Index-3 (Taylor et al. 2007); seizure worry: Quality of Life in Epilepsy—Seizure Worry subscale (Cramer et al. 2005); quality of Life: Quality of Life in Epilepsy—overall quality of life subscale (Cramer et al. 2005); well-being: Quality of Life in Epilepsy—Emotional Well-Being subscale (Cramer et al. 2005); energy/fatigue: Quality of Life in Epilepsy—Medication Effects subscale (Cramer et al. 2005); limitations: Quality of Life in Epilepsy—Work-Driving-Social Limitations subscale (Cramer et al. 2005); cognitive function: Quality of Life in Epilepsy—Cognitive Function subscale (Cramer et al. 2005)

p < .05, \*\*p < .01

limitations. At step two, anxiety sensitivity was a significant predictor of overall QOL, seizure worry, medication effects, work-driving-social limitations, and cognitive functioning, accounting for 8.8–22.9% unique variance. Anxiety sensitivity was not a significant predictor of quality of emotional well-being or energy/fatigue.

All results remained unchanged after adjusting significance levels using the Benjamini–Hochberg procedure (adjusted significance levels are available from author by request; Benjamini and Hochberg 1995).

# Discussion

The current study examined the association between anxiety sensitivity and epilepsy severity and QOL among individuals with a wide variety of epilepsy types treated in an outpatient clinic. As hypothesized, greater anxiety sensitivity predicted poorer self-reported QOL in terms of QOLIE-31 (Cramer et al. 2005) subscales of seizure worry, overall QOL, medication effects, work-driving-social limitations, and cognitive functioning. It should be noted that these significant effects were above and beyond the variance accounted for by negative affectivity and seizure presence in the past year. Contrary to the hypothesis, anxiety sensitivity did not significantly predict the presence of seizures in the past year or functional limitations with emotional well-being and fatigue beyond the unique effects of negative affectivity and seizure presence.

This finding suggests that a fear of arousal-related sensations is related to decreased QOL and greater functional

impairment, but is not related to the likelihood of experiencing a seizure in the past year. Seizures can involve multiple arousal-related sensations, including nausea, tachycardia, hot flashes, trembling, paresthesia, shortness of breath, sweating, depersonalization, and loss of control (Beyenburg et al. 2005; Kanner 2004; Thompson et al. 2000). For individuals who are high in anxiety sensitivity and fear such sensations, it would likely fuel worry about seizures and could contribute to greater functional limitations due to avoidance of activities or situations that might trigger a seizure or produce such arousal-related sensations. Elevated levels of anxiety sensitivity may also impair cognitive function, because attentional processes are diverted towards anxiety and anxiety-related intrusive thoughts. Taken together, it appears that greater anxiety sensitivity does not result in greater seizure likelihood, but rather exacerbates the negative impact of the disease.

The non-significant findings for energy/fatigue may be due to the nature of this QOL domain; low energy states may not be aversive, because they do not involve physiological arousal. Interestingly, anxiety sensitivity did not predict emotional well-being. These non-significant results may be due to our use of negative affectivity as a covariate. The items for the emotional well-being subscale of the QOLIE-31 conceptually overlap with negative affectivity (e.g., "have you been a nervous person") (Cramer et al. 2005, p. 86), and the shared variance between negative affectivity and the emotional well-being subscale is nearly 50%. Given our small sample size, there simply may not have been enough power, given these strong associations,



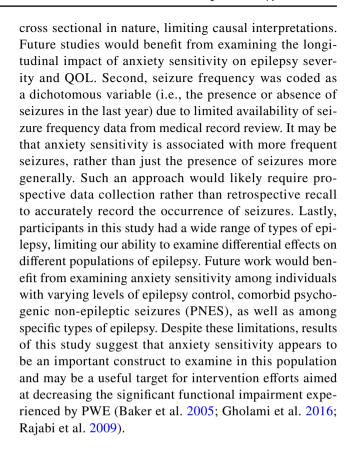
Table 2 Anxiety sensitivity predicting epilepsy-related QOL

	4 E2		0	2	
	$\Delta R^2$	<i>t</i>	β	$sr^2$	<i>p</i>
Criterion variable: seizure	e worry				
Step 1	.41				.00**
Negative affectivity		-3.75	47	.22	.00**
Seizures		-3.66	46	.21	.00**
Step 2	.23				.00**
Anxiety sensitivity		-4.84	58	.23	.00**
Criterion variable: quality	y of life				
Step 1	.41				.00**
Negative affectivity		-3.80	53	.28	.00**
Seizures		-2.66	37	.14	.01*
Step 2	.09				.03*
Anxiety sensitivity		-2.27	36	.09	.03*
Criterion variable: emotion	onal wel	l-being			
Step 1	.52				.00**
Negative affectivity		-5.64	66	.34	.00**
Seizures		-2.34	27	.08	.03*
Step 2	.00				.61
Anxiety sensitivity		61	07	.00	.61
Criterion variable: energy	//fatigue				
Step 1	.23				.01*
Negative affectivity		-2.80	40	.16	.02*
Seizures		-1.99	28	.08	.10
Step 2	.00				.94
Anxiety sensitivity		01	08	.00	.94
Criterion variable: medic	ation eff	ects			
Step 1	.15				.04*
Negative affectivity		-2.58	38	.14	.01*
Seizures		.38	06	.00	.71
Step 2	.16				.006**
Anxiety sensitivity		-2.93	48	.16	.006**
Criterion variable: work-o	driving-	social limit	tations		
Step 1	.40				.00**
Negative affectivity		-4.35	56	.31	.00**
Seizures		-2.62	33	.11	.00**
Step 2	.15				.00**
Anxiety sensitivity		-3.39	46	.15	.00**
Criterion variable: cognit	ive func	tion			
Step 1	.35				.00**
Negative affectivity		-4.37	58	.33	.00**
Seizures		-1.19	16	.02	.24
Step 2	.11				.01**
Anxiety sensitivity		-2.67	40	.11	.01**

 $\beta$  = standardized beta weight;  $sr^2$  = squared semi-partial correlation \*p < .05, \*\*p < .01

for anxiety sensitivity to uniquely predict emotional wellbeing above and beyond negative affectivity.

The current findings do need to be considered in the context of the study's limitations. First, this study was



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# **Compliance with Ethical Standards**

Conflict of Interest Adrienne L. Johnson, Alison C. McLeish, Talya Alsaid-Habia, Paula K. Shear, and Michael Privitera declare that they have no conflict of interest.

**Informed Consent** The Institutional Review Board of the study site approved all aspects of this study prior to data collection.

**Animal Rights** No animal studies were carried out by the authors for this article.

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