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## Assessment of depression in epilepsy: the utility of common and disease-specific self-report depression measures

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### ABSTRACT

**Objectives:** Depression is common in epilepsy, with rates ranging from 20 to 55% in most samples and reports as high as 70% in patients with intractable epilepsy. However, some contend that depression may be over- and/or under-reported and treated in this population. This may be due to the use of common self-report depression measures that fail to take into account the overlap of disease and depressive symptoms and also the host of side effects associated with antiepileptic medication, which may also be construed as depression.

**Methods:** The present study examined the utility of common self-report depression measures and those designed specifically for the medically ill, including a proposed new measure, to determine which may be more appropriate for use among people with epilepsy.

**Results:** We found that common self-report depression measures are useful for screening depression in epilepsy, particularly with a raised cutoff for one, with sensitivities ranging from .91 to .96. A measure designed for the medically ill obtained the greatest specificity of .91, suggesting its use as a diagnostic tool with a slightly raised cutoff. The positive likelihood ratio of this latter measure was 8.76 with an overall classification accuracy of 88%. **Conclusions:** Assessment of depression in epilepsy can be improved when utilizing self-report measures that better differentiate disease symptoms from neurovegetative symptoms of depression (e.g. fatigue, sleep disturbance). This was demonstrated in the present study. Clinical implications are discussed.

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### KEYWORDS

Epilepsy; depression; assessment; measurement; quality of life; psychological functioning

## Introduction

Depression is common in epilepsy with prevalence rates ranging from 20 to 55% in most samples (Kanner, 2003) and reports as high as 70% in patients whose seizures are refractory to medications (Devinsky, 2003). In general, individuals with epilepsy are thought to have nearly a four- to fivefold higher incidence of depression than the general population (Kanner & Palac, 2000). Depression in epilepsy is known to significantly impact a patient's quality of life, may impede treatment compliance and efficacy, and most importantly, may contribute

to a high suicide risk, which is nearly five to 10 times greater in patients with epilepsy (PWE) than in the general population (Kanner, 2003; Kanner & Palac, 2000). Given the suspected high prevalence, the overall grave impact that depression may have on individuals, and the availability of effective treatments, proper detection of depression among PWE is paramount. However, it has been suggested that depression frequently goes unrecognized and undertreated among PWE (Boylan et al., 2004; Wiegartz, Seidenberg, Woodard, Gidal, & Hermann, 1999). Conversely, others contend that depression may be over-diagnosed in epilepsy, particularly when utilizing self-report screening measures, which are heavily weighted with neurovegetative items such as questions concerning fatigue, sleep disturbances, and appetite changes that may overlap with symptoms related to seizure activity and/or side effects of antiepileptic medications (AEDs; Gilliam et al., 2006).

Possible explanations for the inaccurate detection of depression (either under- or over-diagnosing) by practitioners include: (a) the host of positive and negative effects of AEDs on mood; (b) difficulty in appreciating the difference between normal adjustment to a medical diagnosis and clinical depression, including the so called 'understandability phenomenon' (Blanchard, 1992), which asserts that depressed mood in epilepsy is understandable given the limitations imposed by seizures and the unpredictability of the disease; (c) differences in symptom complaint by patients; and/or (d) failure to consider the overlap of disease symptoms and somatic complaints of depression due to the use of diagnostic criteria and self-report depression screening measures designed for the general, non-medical population. This latter hurdle may be one of the greatest culprits for the inaccurate detection of depression and thus is the focus of the present investigation.

Common and widely used self-report depression screening measures such as the Beck Depression Inventory—Second Edition (BDI-II; Beck, Steer, & Brown, 1996) and the Center for Epidemiological Studies Depression Scale (CES-D; Radloff, 1977) are based on Diagnostic and Statistical Manual for Mental Disorders (DSM) criteria for major depression. Criteria for a major depressive disorder includes the endorsement of five of nine of the following symptoms (with at least one from the first two): depressed mood, loss of interest, sleep changes, appetite changes, fatigue, psychomotor retardation, concentration difficulties, feelings of guilt/worthlessness, and suicidal ideation. Individuals with a medical illness such as epilepsy can easily endorse five out of nine of these symptoms by virtue of their illness and not as a result of experiencing major depression. While these measures have been well validated in the general population, they have not been standardized for use with medical populations. Due to this lack of medical standardization, the BDI-II and CES-D may have limited validity when used in this context, given the significant overlap of neurovegetative symptoms of depression and disease symptoms. Further, a review of nine common self-report depression screening measures used in primary care settings involving the normal population revealed only an average sensitivity of 84% and specificity of 72% (Mulrow et al., 1995). With the report of common depression screening measures yielding a nearly 30% false positive rate (Mulrow et al., 1995), it has been recommended that measures be designed specifically for the medically ill, or even more optimally, for the particular disease of interest.

The Beck Depression Inventory-Primary Care (BDI-PC; Beck, Guth, Steer, & Ball, 1997), for instance, was designed specifically for use in the medically ill. The creation of the BDI-PC entailed adopting an *exclusion approach* in which all neurovegetative symptoms of depression were removed from the full BDI. The BDI-PC consists of only seven items, which are all cognitive-affective in nature and presumed to be most indicative of depression among the

medically ill and relatively free of overlap related to medical illness. Previous investigations have found that a cutoff of 4 on the BDI-PC among a medical sample yielded superb sensitivity of 97% and specificity of 99% (Steer, Cavalieri, Leonard, & Beck, 1999). Other, more disease-specific measures, such as the Neurological Disorders Depression Inventory for Epilepsy (NDDI-E; Gilliam et al., 2006), have been created specifically for use in epilepsy. This measure was created by asking medical professionals with substantial experience in epilepsy to provide phrases that would best represent symptoms of depression that are not also similar to symptoms related to epilepsy and/or side effects of AEDs. A cutoff of 15 on this measure obtained a sensitivity of 81% and specificity of 90% in identifying depressed PWE. As can be seen in this brief review, measures designed specifically for the medically ill or the particular medical population have resulted in improved specificity, which is desirable when utilizing measures to diagnose or screen out disorders that are prevalent in the population, such as depression in epilepsy, and may result in a lower false positive rate.

To date, few investigators have examined or compared the utility of common and disease-specific depression screening measures in epilepsy. One investigation by Jones et al. (2005) evaluated the validity of the BDI-II and CES-D in a sample of PWE and found that both measures were adequate screening tools of depression in their sample. In particular, Receiver Operating Characteristic (ROC) analyses suggested that the optimal cutoff of 11 on the BDI-II had a sensitivity of 96% and a specificity of 80%, and the optimal cutoff of 14 on the CES-D resulted in comparable sensitivity and specificity (96 and 81%, respectively). While these measures demonstrated a great level of sensitivity, their specificity remains less than ideal. Gilliam et al. (2006) later compared the NDDI-E to the BDI-II and CES-D and found that in comparison to its predecessors, the odds ratio for predicting depression was higher in the NDDI-E (41.2) as compared to the BDI-II (33.5) and CES-D (35.2), though they did overlap (Gilliam et al., 2006). However, the improvement in specificity of the NDDI-E (90%) in comparison to the BDI-II and CES-D (80 and 81%, respectively) was noteworthy. These authors contended that the NDDI-E was more accurate in assessing depression in epilepsy than measures such as the BDI-II, which include symptoms likely influenced by side effects of medication (e.g. sleep disturbance) resulting in an inflated sensitivity at the expense of specificity.

A more recent investigation also found the NDDI-E to be slightly more specific than the BDI-II. In particular, when evaluating the NDDI-E and the BDI-II, Rampling et al. (2012) found that a cutoff of 15 on both measures yielded a sensitivity of 90 and 94% and a specificity of 83 and 79%, respectively. Given their nearly identical performance, the authors concluded that both measures were adequate for screening given their high sensitivity. They recommend the use of the NDDI-E given its ease in administration, but it should be noted that they failed to find a significant improvement in specificity with the NDDI-E as was found by Gilliam et al. (2006) previously.

The primary objective of the present investigation is to determine whether a new disease-specific measure that accounts for the influence of medication side effects and seizure activity per patient's report (a modified version of the Beck Depression Inventory [BDI]; Beck & Steer, 1987) or a more general measure designed for medical samples (BDI-PC) has greater utility than the BDI-II and CES-D in differentiating epilepsy patients with and without comorbid depression. The modified version of the BDI, hereinafter referred to as the Epilepsy-Specific BDI (EPI-BDI), allows participants to rate the extent to which their seizures and/or medication side effects contribute to their endorsement of depressive symptoms. This *best*

*estimate* approach, in which judgment is used to assess the extent to which disease symptoms influence patients' reports, allows for the inclusion of all symptoms of depression (including neurovegetative) when assessing depression in the medically ill, and is recommended when there is a possibility of 'masked depression' in which pain and other physical complaints are presenting features of depression (Rodin & Voshart, 1986) rather than simply symptoms of the medical illness or medication side effects. The inclusion of such items is believed to be important as it allows for those with 'masked depression' to still be identified and is a significant advantage over the BDI-PC in which these items are removed a priori. We chose the BDI as the measure to modify in hopes that it could be easily compared to the BDI-II and BDI-PC, which have also been well validated for use in the general population and medically ill population, respectively.

Strober and Arnett (2015) previously developed a similar disease-specific measure, the Multiple Sclerosis-Specific Beck Depression Inventory (MS-BDI), which was guided by a 'trunk and branch' model that best differentiated depressed and non-depressed individuals with MS (Strober & Arnett, 2010). This new measure (MS-BDI) was subsequently compared to a common self-report measure and measures designed specifically for use among the medically ill and found to outperform these measures as a diagnostic tool. More specifically, when compared to the BDI-II, BDI-PC, and the Chicago Multiscale Depression Inventory (CMDI), a measure designed for use in MS, the MS-BDI was found to have the greatest specificity of 96%, a positive likelihood ratio of 16.97, and a 93% classification accuracy. The authors concluded that the MS-BDI was the best measure for determining the presence of depression, showing the importance in having measures that are disease-specific and based on a best estimate approach in order to gain the most accurate prevalence rates of depression within clinical populations.

In the present study, we hypothesize that the BDI-II and CES-D would obtain adequate to superb sensitivity, but at a cost of specificity in PWE given the hurdles discussed above, such as the overlap of neurovegetative symptoms in depression and epilepsy. When further comparing these commonly used measures to measures designed specifically for the medically ill and/or which take into account disease overlap and side effects of AEDs (BDI-PC and EPI-BDI, respectively), it is hypothesized that the latter measures will obtain greater specificity than both the BDI-II and CES-D as they are likely to be capturing 'true' depression and will result in less false positives as they are rid of the overlap of neurovegetative items. It is further hypothesized that the EPI-BDI will perform better (as per ROC analyses) than the BDI-PC in accurately identifying clinically depressed patients. This is based on the EPI-BDI allowing for the inclusion of *all* items (i.e. neurovegetative symptoms) and only removing items when patients reported they did not contribute to their depressive symptoms but were only related to their epilepsy. Finally, as suggested by others, it is hypothesized that the derived prevalence rate of depression using the BDI-II would be the highest, while the BDI-PC and EPI-BDI would have the lowest prevalence rates and be most akin to the derived prevalence rate using the gold standard of a structured clinical interview.

## Methods

### Participants

PWE were recruited through the adult Epilepsy Monitoring Unit (EMU), the Epilepsy Outpatient Clinic and the Neuropsychology Section at the Cleveland Clinic. Inclusion criteria

were: (1) age 18 or older; (2) history of epilepsy confirmed by medical record review; (3) fluency in English; (4) reading level at sixth grade level or higher; (5) no history of developmental disorder; and (6) no prior neurosurgical intervention. Patients were provided with information about the study, including that the study examines the prevalence of depression in epilepsy and overlap of depressive symptoms with symptoms related to epilepsy and medication side effects, in an informed consent form consistent with the guidelines set forth by the Institutional Review Board of the Cleveland Clinic in accordance with the Helsinki Declaration.

## Measures

The Reading subtest of the Wide Range Achievement Test—Fourth Edition (WRAT-4 Reading; Wilkinson & Robertson, 2006) was administered to all potential participants in order to assess their general reading ability. Individuals were only included in the study if their raw score was greater than or equal to 48, which is equivalent to a sixth grade reading level. Participants subsequently completed the BDI-II, CES-D, BDI-PC, and EPI-BDI. Given the novelty of the EPI-BDI, a full description of the creation and modification is provided.

The EPI-BDI takes into account clinical observations and prior research in epilepsy by adding follow-up questions to certain BDI items thought to be confounded with symptoms of epilepsy and/or medication side effects (e.g. concentration difficulties). To determine which items may be confounded by symptoms related to epilepsy and/or side effects of AEDs, a survey was completed by epileptologists at the Cleveland Clinic Epilepsy Center. The survey consisted of the 21 symptoms on the BDI and respondents were asked to rate on a Likert scale of 1–5, how much they believed each particular symptom could be influenced by seizures or AED effects. Any item that was rated 3 or higher (i.e. moderately to highly likely to be influenced) was chosen to have follow-up questions. Past research and clinical experience of the authors, LS and RB also contributed to the decision as to which items may be influenced. These questions were intended to ascertain if and how much a patient's endorsement of particular BDI items may be due to his or her medical condition, medications and/or depression. In particular, this epilepsy-specific modification of the BDI contains follow-up questions to the following items hypothesized to be related to the experience of epilepsy and/or medication side effects: sadness, discouragement/pessimism, sense of failure, satisfaction in activities, disappointment, self-criticism, self-appraisal, suicidal ideation, irritability, loss of interest, indecision, work difficulty, sleep disturbance, fatigue, appetite changes, weight changes, somatic preoccupation, and sexual dysfunction.

After completing each of these items, patients are asked to rate the extent to which they believe each endorsed symptom reflects epilepsy and/or medication effects. Patients rate the contribution on a five-point Likert scale ranging from '1 – Not at All' to '5 – Completely.' For example, if a patient was to endorse a '2' on sleep changes on the BDI, the patient is then asked to rate on a Likert scale of 1–5, the extent that their endorsement is due to or influenced by their seizures/epilepsy or medication side effects, with '1' being 'Not at All' and '5' being 'Completely.' A copy of the EPI-BDI can be found in Appendix 1.

The EPI-BDI-M (EPI-BDI Minus Symptoms and Side Effects Contribution) was subsequently created by removing any items of the EPI-BDI that patients rated as more related to epilepsy and/or medication side effects than depression in order to provide a purer representation of depression in epilepsy. Data reduction of the EPI-BDI to the EPI-BDI-M was conducted in

the following manner: If a participant rated the contribution of epilepsy and/or medication side effects as 1 (Not at All) or 2 (A Little), the item was considered to be unaffected in a significant way by disease processes or medication. However, if a participant rated the contribution of epilepsy or medication side effects from 3 (Moderately) to 5 (Completely), endorsement of that item was interpreted as suggesting that the symptom was either typical (Moderate) or excessive (Quite a Bit, Completely) and was considered more representative of disease processes or medication side effects than depression. These items were subsequently not included in the new measure of depression (EPI-BDI-M). A prorated score was derived for each individual utilizing the following formula: Prorated Score = Score of Valid Items \* (21/Number of Valid Items). A prorated score was needed due to the process of exempting certain questions being individualized.

### **Procedures**

Participants first underwent a structured clinical psychiatric interview with the Mini International Neuropsychiatric Interview (M.I.N.I.; Sheehan et al., 1998) in order to obtain a current diagnosis, and then completed the BDI-II, BDI-PC, CES-D, and EPI-BDI in said order at their study visit. The M.I.N.I. follows DSM-IV and ICD-10 criteria for psychiatric disorders, encompassing 17 Axis I disorders. This instrument has acceptably high validation and reliability scores when compared to the Structured Clinical Interview for DSM-IV (SCID; First, Spitzer, Gibbon, & Williams, 1995), yet is easier to administer and requires less time, making it much less cumbersome for the patient. The M.I.N.I. was administered by the principal investigator (LS), who was blind to the participants' responses on the self-report depression questionnaires at the time the interview was conducted. Structured clinical interviews, such as the M.I.N.I., are considered the gold standard for the assessment of clinical depression (Davison, McCabe, & Mellor, 2009). Patients who met criteria for any of the following diagnoses as determined by the M.I.N.I. were classified as 'depressed': major depressive episode ( $n = 5$ ), major depressive disorder ( $n = 5$ ), dysthymia ( $n = 8$ ), adjustment disorder with depressed mood ( $n = 2$ ), and/or double depression ( $n = 3$ ). Patients who did not meet criteria for any of these diagnoses based on M.I.N.I. interview were classified as 'non-depressed.'

### **Analyses**

Independent t-tests and chi-square analyses were first conducted to examine group differences on demographic and seizure variables. Pearson correlation coefficients were then obtained in order to examine the relationship between the proposed epilepsy-specific measure (EPI-BDI-M) and the BDI-II, CES-D, and BDI-PC to assure its concurrent validity with pre-existing measures. Then, independent t-tests were conducted to determine differences in depression scores between the depressed and non-depressed groups on all depression measures. Finally, ROC analyses were conducted to examine the sensitivity and specificity of Jones et al.'s (2005) and Steer et al.'s (1999) previously suggested cutoffs (11 for the BDI-II, 14 for the CES-D, and 4 for the BDI-PC), used among PWE and primary care settings, respectively. Inspection of the ROC curves also assisted in the determination of the optimal cutoff for each measure in this epilepsy sample. Once the cutoff was identified, sensitivity, specificity, negative predictive value (NPV), positive predictive value (PPV), and likelihood ratios were calculated for each measure and summarized in an algorithmic table designed in



accordance with Steiner's (2003) publication regarding the utility of diagnostic and screening tools (DeFife, 2004). For reference, the area under the curve (AUC) indicates, generally, how good the test is. An AUC of .90–1.0 is indicative of an excellent test, while an AUC of .80–.90 is good, and .70–.80 is considered fair. Sensitivity is the proportion of patients with disease who test positive, while the specificity is the proportion of patients without disease who test negative. Together, these are attributes of the test and describe how well the test discriminates between patients with and without disease. In general, a sensitivity is more important for 'ruling out' a diagnosis and a cutoff of .90 is considered optimal. Specificity is more involved with 'ruling in' a diagnosis and should also be high, but the balance of specificity and sensitivity are important and it has been suggested that a specificity of .60 with a sensitivity of .80 is appropriate for 'ruling in' a diagnosis (Lincoln, Nicholl, & Flannaghan, 2003). The predictive values can be considered slightly more relevant in that they identify the 'true positives' and 'true negatives.' The PPV is the proportion of individuals with a positive test who in fact have the disease, while NPV is the proportion of individuals who have a negative test and who do not have the disease. Thus, these indices are similar to sensitivity and specificity, respectively, but the difference is the predictive values are reliant on the incidence of the disease in the population of question. Ideally, the closer to 100%, the greater the test is performing. Finally, the PLR is an overall index that takes into account the sensitivity and specificity and indicates the likelihood that a positive test would result in the individual having the disease. In general, a PLR of 1–2 indicates an unlikely chance that the individual has the condition. A PLR of 2–5 indicates a small chance; 5–10 suggests a moderate chance, and a PLR > 10 indicates a large chance and almost conclusive that the condition is present.

All statistical analyses were conducted using SPSS 21.0 computer software in conjunction with the algorithmic table described above.

## Results

Seventy-six patients met criteria for the study and agreed to participate. Participants were primarily Caucasian (92%) and consisted of 45 women and 31 men. Mean age of all participants was 38.88 ( $SD = 12.82$ ), and mean level of education was 13.46 ( $SD = 2.18$ ). The average age at seizure onset was 18.47 ( $SD = 12.80$ ) with an average duration of epilepsy of 20.41 years ( $SD = 13.88$ ). Participants were divided into two groups based on results of the M.I.N.I. structured clinical interview. Twenty-three participants (30%) were classified as 'depressed' and 53 were found to be 'non-depressed.' A summary of demographic and seizure characteristics of the two groups is provided in Table 1. There were no significant differences between the non-depressed and depressed groups on any of the demographic or seizure variables.

Fourteen participants (18%) were diagnosed with generalized epilepsy and the rest with focal epilepsy. Among those with well-lateralized focal epilepsy, 35 (46%) participants were found to have seizures originating from the left hemisphere and 24 (31%) were found to have seizures originating from the right. Three participants were presumed to have bilateral involvement. With regard to seizure localization, 34 participants were diagnosed with temporal lobe epilepsy and 22 were considered extratemporal. Six individuals experienced seizures that were not sufficiently localizable.

Initial examination of the EPI-BDI found that depressed and non-depressed PWE attributed their endorsement of items on the BDI to their seizures or medications at nearly



**Table 1.** Participant demographics, seizure characteristics, and depression diagnosis.

	Depressed ( <i>n</i> = 23) Mean ( <i>SD</i> ), Frequency, or <i>N</i>	Non-depressed ( <i>n</i> = 53) Mean ( <i>SD</i> ) or Frequency	<i>t</i> or $\chi^2$ value	<i>p</i>
Age	38.04 (10.77)	39.25 (13.69)	.410	.683
Gender	17 Female/6 Male	28 Female/26 Male	2.95	.086
Ethnicity	22 C/1 EM	48 C/5 EM	.571	.450
Education	13.87 (1.98)	13.28 (2.25)	-1.08	.283
WRAT-4 reading	59.96 (6.28)	59.02 (5.85)	-.628	.532
Seizure characteristics				
Age at seizure onset	18.67 (11.47)	18.39 (13.44)	-.087	.931
Duration of epilepsy	19.38 (12.84)	20.86 (14.41)	.425	.672
Side of seizure*	10 Left/9 Right	25 Left/15 Right	.520	.471
Seizure focus†	10T,4F,1P,1M,1PL	24T,5F,1P,7M,2PL	.037‡	.848
Depression diagnosis				
MDD single episode	5	–	–	–
MDD recurrent	5	–	–	–
Dysthymia	8	–	–	–
Adjustment disorder	2	–	–	–
Double depression	3	–	–	–

Note: C = Caucasian, EM = Ethnic Minority; WRAT-4 = Wide Range Achievement Test-Fourth Edition raw score.

\* = Of the non-depressed group: 10 = generalized epilepsy, 3 = bilateral involvement. Of the depressed group: 4 = generalized epilepsy; †T = Temporal, F = Frontal, P = Parietal, M = Multilobar, PL = Periorolandic. Of the non-depressed group, 4 were not localizable, of the depressed group 2 were not localizable.

‡Temporal versus extratemporal.

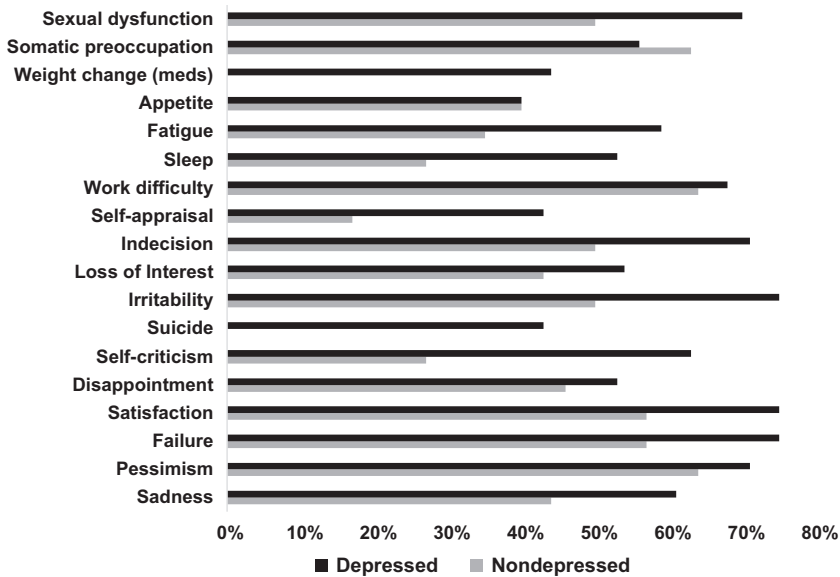
comparable rates (See Figure 1). When these items were removed to create the EPI-BDI-M, the range of 'valid' items ranged from 0 to 21, with a median of 19.

Examination of the relationship between the EPI-BDI-M and existing self-report depression screening measures found the EPI-BDI-M to be highly correlated with the two common self-report depression screening measures (BDI-II and CES-D) ( $r = .70$ ,  $p < .001$  and  $r = .71$ ,  $p < .001$ , respectively) and the BDI-PC ( $r = .74$ ,  $p < .001$ ). The correlations among the other measures ( $r = .84$  to  $.88$ ,  $p < .001$ ) were all significantly higher than the correlation with the EPI-BDI ( $p$ 's  $< .05$ ), suggesting that while they are all strongly related, the EPI-BDI also demonstrates some divergent validity from the commonly used measures (See Table 2).

Comparisons of depressed and non-depressed groups on all depression screening measures revealed significantly greater endorsement of depressive symptoms among the depressed group as compared to the non-depressed group across all measures (see Table 3).

ROC analyses suggested that the BDI-II, CES-D, and BDI-PC all have excellent test accuracy with areas under the curve (AUCs) ranging from .92 to .96. The EPI-BDI-M was found to have good test accuracy (AUC = .83). Initial examination of the previously recommended cutoffs by Jones et al. (2005) (14 for the CES-D and 11 for the BDI-II) found the CES-D to have a perfect sensitivity of 100%, accurately identifying all 23 depressed participants. However, this came with a great sacrifice in specificity (77%). Their previously recommended cutoff of 11 on the BDI-II resulted in a sensitivity of 91% and specificity of 70%. The BDI-PC obtained a sensitivity of 91% and a specificity of 74% when utilizing the previously suggested cutoff of 4.

Further inspection of the ROC curves obtained in this sample suggested optimal cutoffs of 15 for the BDI-II, 18 for the CES-D, and 6 for the BDI-PC. This resulted in an improved specificity of the BDI-II (70 to 83%) with some cost to sensitivity (91 to 83%). The CES-D showed similar patterns of increased specificity (77 to 85%) with little cost to sensitivity (100 to 96%). Raising the cutoff of the BDI-PC to 6 also resulted in a significant improvement in specificity (74 to 91%) with some cost to its sensitivity (91 to 83%). Given its novelty, there



**Figure 1.** Percentage of attribution to seizures for endorsed items on the EPI-BDI among depressed and non-depressed people with epilepsy.

**Table 2.** Pearson correlations between various depression screening measures.

	BDI-II	CES-D	BDI-PC
1. EPI-BDI-M	.70*	.71*	.74*
2. BDI-II	–	.84*	.85*
3. CES-D	–	–	.88*
4. BDI-PC	–	–	–

Note: EPI-BDI-M = Epilepsy-Specific Beck Depression Inventory Minus Symptom and Side Effects Contribution; BDI-II = Beck Depression Inventory – Second Edition; CES-D = Center for Epidemiological Studies-Depression; BDI-PC = Beck Depression Inventory-Primary Care.

\* $p < .001$ .

**Table 3.** Differences between depressed and non-depressed patients with epilepsy (PWE) on depression measures.

Measure	Depressed ( $n = 23$ )		Non-depressed ( $n = 53$ )		$t$	$p$
	Mean ( $SD$ )	Range	Mean ( $SD$ )	Range		
EPI-BDI-M	14.26 (8.99)	0–35	5.19 (5.72)	0–23	–4.46	<.001
BDI-II	25.09 (11.03)	6–47	7.87 (6.68)	0–24	–6.95	<.001
CES-D	32.74 (9.86)	15–54	9.77 (8.40)	0–35	–10.39	<.001
BDI-PC	7.70 (3.39)	1–15	1.83 (2.50)	0–8	–8.40	<.001

Note: EPI-BDI-M = Epilepsy-Specific Beck Depression Inventory Minus Symptom and Side Effects Contribution; BDI-II = Beck Depression Inventory-Second Edition; CES-D = Center for Epidemiological Studies-Depression; BDI-PC = Beck Depression Inventory-Primary Care.

were no existing cutoffs for the EPI-BDI-M. Inspection of the ROC curve suggested an optimal cutoff of 11 in the current sample, resulting in a sensitivity of 74% and a specificity of 85% (see Table 4).

**Table 4.** Sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), positive likelihood ratios (PLR), and overall correct classification (OCC) using the various self-report depression screening measures.

Measure	AUC	Cutoff	Sensitivity	Specificity	PPV	NPV	PLR	OCC, %
BDI-II	.92	11	.91	.70	.57	.95	3.02	76
BDI-II	.92	15	.83	.83	.68	.92	4.87	83
CES-D	.96	14	1.0	.77	.66	1.0	4.42	84
CES-D	.96	18	.96	.85	.73	.98	6.34	88
BDI-PC	.92	4	.91	.74	.60	.95	3.46	80
BDI-PC	.92	6	.83	.91	.79	.92	8.76	88
EPI-BDI-M	.83	11	.74	.85	.68	.88	4.90	82

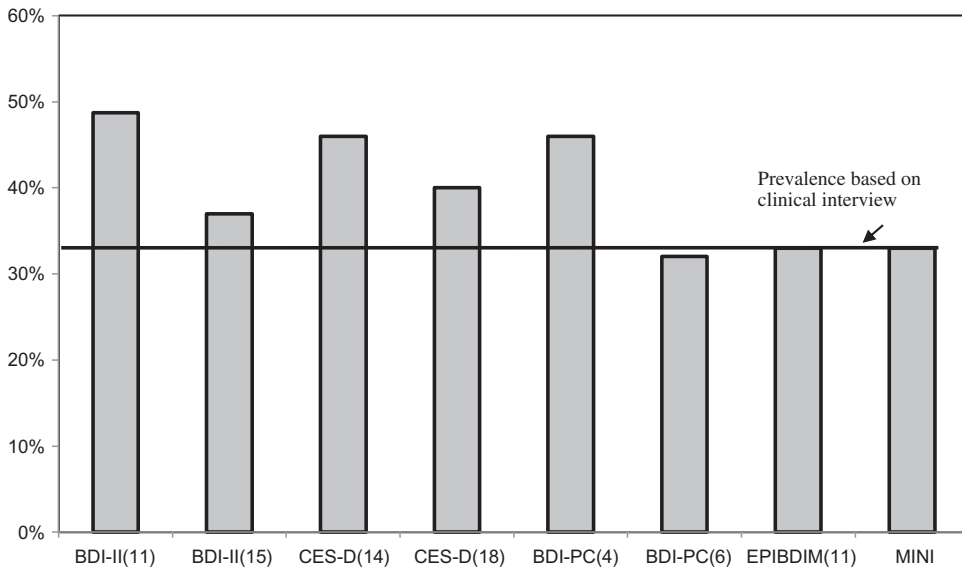
Note: BDI-II = Beck Depression Inventory-Second Edition; CES-D = Center for Epidemiological Studies- Depression; BDI-PC = Beck Depression Inventory-Primary Care; EPI-BDI-M = Epilepsy-Specific Beck Depression Inventory Minus Symptom and Side Effects Contribution.

Finally, to further examine the characteristics of the EPI-BDI-M and BDI-PC and assess whether these measures generate more accurate depression prevalence rates, comparisons were made between the prevalence rates resulting from use of the EPI-BDI-M and BDI-PC contrasted with prevalence rates resulting from use of the BDI-II and CES-D. Each measure's prevalence rates were then compared to the 30% prevalence rate gained by the clinical interview administered to this sample (See Figure 2). Comparable prevalence rates were found for the BDI-II and CES-D when utilizing the optimal cutoffs of 15 and 18 with rates of 37 and 40%, respectively. Higher prevalence rates were found with the previously recommended cutoffs of 11 on the BDI-II (49%), 14 on the CES-D (46%), and 4 on the BDI-PC (46%). Compared to the prevalence based on a clinical interview in this sample (30%), these cutoffs would suggest a nearly 20% higher rate of depression in this sample. Again, the use of the BDI-II, CES-D, and BDI-PC may result in an inaccurate and inflated picture of the prevalence of depression among PWE. Consistent with expectations, the EPI-BDI-M obtained a prevalence rate akin to that obtained with a clinical interview (33%). The suggested optimal cutoff of 6 on the BDI-PC also resulted in a prevalence of 32%, which is a closer approximation to the clinical interview as well.

## Discussion

The purpose of the present investigation was to determine whether screening measures designed for the general population, the medically ill, or PWE are superior for use in detecting depression in PWE. It has previously been suggested that common self-report depression screening measures, particularly those more heavily weighted with neurovegetative symptoms of depression such as the BDI-II, may result in inaccurate reports of depression, particularly a high false positive rate and subsequent inflated prevalence rates. Conversely, those designed specifically for the medically ill, which remove confounding neurovegetative items, may miss important depression-related symptoms such as seen in 'masked depression.' Thus, the new measure developed within, which excludes items only based on patient report was hypothesized to yield better specificity and overall accuracy at differentiating depressed versus non-depressed PWE as compared to existing measures.

As expected, the proposed EPI-BDI-M was found to obtain greater specificity (85%) than previously proposed cutoffs of the BDI-II and CES-D (70 and 77%, respectively). It also obtained a higher specificity than the previous cutoff of 4 on the BDI-PC. The prevalence



**Figure 2.** Varying derived prevalence rates depending on the utilized measure, cutoff, and structured clinical interview.

Note: BDI-II = Beck Depression Inventory-Second Edition; CES-D = Center for Epidemiological Studies-Depression; BDI-PC = Beck Depression Inventory-Primary Care; EPI-BDI-M = Epilepsy-Specific Beck Depression Inventory Minus Symptom and Side Effects Contribution. Numbers in parentheses are respective cutoffs.

rate derived from this measure was also most akin to the rate derived from a clinical interview, suggesting some merit to utilizing follow-up questions on a self-report measure; similar to what is done through a clinical interview. However, while the measure demonstrated an improved specificity, it came at a sacrifice to its sensitivity, which is not seen with a raised cutoff of 6 on the BDI-PC, which has superb specificity and good sensitivity. Findings of the EPI-BDI in this sample suggests that there is need for improvement with this measure if it is to be utilized with PWE.

With regard to the commonly used measures (BDI-II and CES-D), study findings suggest that they are both adequate screening tools for depression in epilepsy given their high level of sensitivity. However, our findings failed to replicate those of Jones et al. (2005). More specifically, we found a lower sensitivity (91%) with the BDI-II using a cutoff of 11, than that found in the Jones et al. study (96%). As anticipated, the specificity the BDI-II and CES-D (based on Jones et al. recommended cutoffs) was less than ideal, likely a result of the inclusion of neurovegetative symptoms. Inspection of the ROC curve of the BDI-II suggested that raising the cutoff to 15 resulted in a decline in sensitivity (91 to 83%) but a vast improvement in specificity (70 to 83%). A higher cutoff on the BDI-II (13) has previously been suggested for use in other neurological samples, including multiple sclerosis (Sullivan, Weinschenker, Mikail, & Bishop, 1995).

We found that while the suggested cutoff of 14 on the CES-D had superb sensitivity, accurately identifying all 23 depressed participants, a cutoff of 18 resulted in greater specificity with little sacrifice to sensitivity (sensitivity = 96%, specificity = 85%) and a positive likelihood ratio (PLR) of 6.34. A score of >16 on the CES-D has long been considered the cutoff indicative of clinically meaningful depression, but higher cutoffs ranging from 20 to

27 have been recommended for use among the medically ill (Schein & Koenig, 1997; Schulberg et al., 1985). Given the ease of administration for this measure and minimal cost (the CES-D is in the public domain), the CES-D is a likely candidate as a quick and simple depression screening tool in epilepsy. However, it should be noted that, similar to the findings of Jones et al. (2005), use of either the BDI-II or CES-D still results in an approximate 15% false positive rate.

Rather unexpectedly, the BDI-PC performed adequately as both a screening tool and diagnostic aide, depending on the cutoff used. In particular, using the previously recommended cutoff of 4, the BDI-PC performed comparably to the BDI-II, with a sensitivity of 91% and a less than ideal specificity of 74%. Raising the cutoff to 6 resulted in a decrease in sensitivity (83%) but attained the highest level of specificity (91%) and PLR (8.76) among all measures, suggesting that the BDI-PC can be useful in assisting in the diagnosis of depression in PWE.

Overall, study findings suggest that the BDI-II and CES-D may have varying utility among PWE. In choosing to use a self-report depression measure, one must first identify the main objective for using the measure. For instance, for screening purposes, in which one wants to detect if an individual exhibits any of the attribute under question (i.e. depression), sensitivity is more important than specificity. This is particularly true when there are potentially severe consequences for missing a diagnosis, such as suicide. However, when it is suspected that an individual has the attribute (e.g. when there is a high prevalence of the disorder) and one is trying to determine or confirm a diagnosis, specificity is more important (Streiner, 2003). The latter is particularly important for practitioners when treatment decisions are being determined by such tests. False positives may result in ineffective, wrongly prescribed treatment. For the purposes of detecting depression in PWE, the distinction should be on what is acceptable for screening and what is advisable for diagnosis. Again, it is suggested by some that a sensitivity greater than 80% and specificity greater than 60% is acceptable for diagnosis while a sensitivity of 90% is acceptable for screening (Lincoln et al., 2003). However, others suggest that both a high sensitivity and specificity is warranted when differentiating depressed and non-depressed individuals (Weintraub, Oehlberg, Katz, & Stern, 2006).

Based on our findings, it would appear that a cutoff of 18 on the CES-D and a cutoff of 4 on the BDI-PC are best for screening for depression in epilepsy, given their sensitivities being above 90%. When one speculates that depression is present and would like to utilize a self-report measure with greater specificity to assist in diagnosis, using a cutoff of 6 on the BDI-PC appears to be optimal.

With regard to the development of the proposed 'disease specific' measure, the EPI-BDI, in this study, our findings support the contention that measures designed for the population of interest are likely to result in improved specificity, such as was seen with the NDDI-E (Gilliam et al., 2006). However, the EPI-BDI-M failed to perform as well as the BDI-PC. This may be the result of the BDI-PC having more rigorous validation, for one. But, it should be noted that the BDI-PC still required a raise in its cutoff to obtain its high specificity. The previously established cutoff of 4 resulted in a specificity of 74%, which was well below the specificity of the EPI-BDI on 85%. Further validation and studies employing the EPI-BDI may result in an improvement as to what is the optimal cutoff for this measure. Additionally, the format of the BDI-PC is brief and succinct and may have greater face validity than the EPI-BDI, which required the individual to make attributions for potentially 21 items and may have induced some degree of questionnaire fatigue, particularly given the fact that this measure was administered last.

Further investigations pertaining to the development and validation of the EPI-BDI-M or similar disease-specific measures are warranted. Nonetheless, findings lend further support to the development of disease-specific measures, as they identify rates of depression similar to when using a structured clinical interview, while not overestimating rates as seen in the BDI-II and CES-D. Until such 'disease specific' measures are validated in larger samples, it is recommended that the raised cutoffs of 18 and 15 for the CES-D and BDI-II, respectively, be used when screening for depression in epilepsy. The use of the BDI-PC is encouraged to assist in diagnostic determinations, with a cutoff of 6. Of course, we acknowledge and recommend the use of a clinical interview when making final diagnostic and treatment decisions, as such decisions should not be based solely on self-report questionnaires. In doing so, practitioners are advised to adopt a *best estimate* approach in their assessment as was utilized in the EPI-BDI-M. Thorough follow-up of symptom endorsement will not only result in more accurate diagnoses but will provide practitioners with invaluable information as to the causes of the symptoms, better informing treatment. For example, if sleep problems are endorsed but are more related to ones' seizures or medications, pharmacological intervention or adjustments may be warranted and this is different than prescribing cognitive behavioral therapy to someone who is experiencing rumination as part of their depression, resulting in insomnia. Accurate delineation of the underlying cause of the endorsed symptom is likely to result in more targeted and effective treatment. Finally, while this investigation provides valuable information and recommendations to guide the assessment of depression among PWE, there are a few limitations. For one, the relatively small sample size, particularly with regard to our depressed sample. In examining the psychometric properties of any new measure or the properties of existing measures, a large sample is ideal with the construct of interest present in half the sample. Additionally, this was a fairly homogenous, Caucasian, Midwestern sample consisting of individuals whose seizure were intractable to medication, which may not be the most generalizable. Subsequent investigations using larger, heterogeneous sample sizes are warranted. In particular, future investigations in both clinical- and community-based samples are needed. Specifically, a comparison between the EPI-BDI-M to the NDDI-E, another depression questionnaire specific for epilepsy, is warranted. Despite these limitations, our investigation provides clinicians and researchers a better understanding and appreciation of the intricacies involved in assessing depression among PWE. Future work is needed to expand upon these comparative findings to provide convergent validity so that these depression measures can be used with confidence in clinical settings.

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No potential conflict of interest was reported by the authors.

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## Appendix 1. EPILEPSY-SPECIFIC BECK DEPRESSION INVENTORY (EPI-BDI)

**DIRECTIONS:** On this questionnaire are groups of statements. Please read each group of statements carefully. Then pick out the one statement in each group that best describes the way you have been feeling the **PAST WEEK. INCLUDING TODAY!** Circle the number beside the statement you picked. If several statements in the group seem to apply equally well, circle each one.

**Be sure to read all the statements in each group before making your choice.**

**Following some of the numbered statements below are follow-up questions that relate to the immediately preceding numbered question. These statements generally ask you to estimate the extent to which symptoms of epilepsy and side effects of medications contribute to your answer to the numbered question. Please answer these to the best of your ability.**

- 1    0 I do not feel sad.  
       1 I feel sad.  
       2 I am sad all the time and I can't snap out of it.  
       3 I am so sad or unhappy that I can't stand it.

**If you rated yourself "1" or higher on question # 1 above, please answer the following questions:**

**On a scale of 1–5, please rate how much of your sad mood has been influenced by your seizures/epilepsy.**

Not at All	A Little	Moderately	Quite a bit	Completely
1	2	3	4	5

**On a scale of 1–5, please rate how much of your sad mood has been influenced by your seizure medications.**

Not at All	A Little	Moderately	Quite a bit	Completely
1	2	3	4	5

- 2    0 I am not particularly discouraged about the future.  
       1 I feel discouraged about the future.  
       2 I feel I have nothing to look forward to.  
       3 I feel that the future is hopeless and that things cannot improve.

**If you rated yourself "1" or higher on question # 2 above, on a scale of 1–5, please rate how much your view of the future has been influenced by your seizures/epilepsy.**

Not at All	A Little	Moderately	Quite a bit	Completely
1	2	3	4	5

- 3
- 0 I do not feel like a failure.
  - 1 I feel I have failed more than the average person.
  - 2 As I look back on my life, all I can see is a lot of failures.
  - 3 I feel I am a complete failure as a person.

**If you rated yourself "1" or higher on question # 3 above, on a scale of 1–5, please rate how much your sense of failure is influenced by the limitations placed on you by your seizures/epilepsy.**

Not at All	A Little	Moderately	Quite a bit	Completely
1	2	3	4	5

- 4
- 0 I get as much satisfaction out of things as I used to.
  - 1 I don't enjoy things the way I used to.
  - 2 I don't get real satisfaction out of anything anymore.
  - 3 I am dissatisfied or bored with everything.

**If you rated yourself "1" or higher on question # 4 above, on a scale of 1–5, how much have your seizures prevented you from enjoying what you do?**

Not at All	A Little	Moderately	Quite a bit	Completely
1	2	3	4	5

- 5
- 0 I don't feel particularly guilty.
  - 1 I feel guilty a good part of the time.
  - 2 I feel quite guilty most of the time.
  - 3 I feel guilty all of the time.

- 6
- 0 I don't feel I am being punished.
  - 1 I feel I may be punished.
  - 2 I expect to be punished.
  - 3 I feel I am being punished.

- 7
- 0 I don't feel disappointed in myself.
  - 1 I am disappointed in myself.
  - 2 I am disgusted with myself.
  - 3 I hate myself.

**If you rated yourself "1" or higher on question # 7 above, on a scale of 1–5, how much of your perception of being disappointed with yourself is influenced by the limitations placed on you because of your seizures/epilepsy?**

Not at All	A Little	Moderately	Quite a bit	Completely
1	2	3	4	5

- 8
- 0 I don't feel I am any worse than anybody else.
  - 1 I am critical of myself for my weaknesses or mistakes.
  - 2 I blame myself all the time for my faults.
  - 3 I blame myself for everything bad that happens.

**If you rated yourself "1" or higher on question # 8 above, on a scale of 1–5, how much of your self-criticism is influenced by the limitations placed on you because of your seizures/epilepsy?**

Not at All	A Little	Moderately	Quite a bit	Completely
1	2	3	4	5

- 9
- 0 I don't have thoughts of killing myself.
  - 1 I have thoughts of killing myself, but I would not carry them out.
  - 2 I would like to kill myself.
  - 3 I would kill myself if I had the chance.

**If you rated yourself "1" or higher on question # 9 above, on a scale of 1–5, please rate how much your seizures/epilepsy influence your feelings or thoughts of suicide**

Not at All 1	A Little 2	Moderately 3	Quite a bit 4	Completely 5
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- 10 0 I don't cry any more than usual.  
1 I cry more now than I used to.  
2 I cry all the time now.  
3 I used to be able to cry, but now I can't cry even though I want to.

- 11 0 I am no more irritated now than I ever am.  
1 I get annoyed or irritated more easily than I used to.  
2 I feel irritated all the time now.  
3 I don't get irritated at all by the things that used to irritate me.

**If you rated yourself "1" or higher above on question # 11 above, please answer the following two questions:**

**On a scale of 1–5, to what extent does your seizures/epilepsy contribute to your increased irritation?**

Not at All 1	A Little 2	Moderately 3	Quite a bit 4	Completely 5
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**On a scale of 1–5, to what extent do your medications contribute to your increased irritation?**

Not at All 1	A Little 2	Moderately 3	Quite a bit 4	Completely 5
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- 12 0 I have not lost interest in other people.  
1 I am less interested in other people than I used to be.  
2 I have lost most of my interest in other people.  
3 I have lost all of my interest in other people.

**If you rated yourself "1" or higher on question #12 above, please answer the following questions to how they may pertain to your reduced interest in others:**

**On a scale 1–5, please rate how much your seizures/epilepsy influences your interest in other people.**

Not at All 1	A Little 2	Moderately 3	Quite a bit 4	Completely 5
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**On a scale 1–5, please rate how much your seizures/epilepsy limits your social activity.**

Not at All 1	A Little 2	Moderately 3	Quite a bit 4	Completely 5
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**On a scale of 1–5, please rate how much you take your seizures/epilepsy into account when making plans with others.**

Not at All 1	A Little 2	Moderately 3	Quite a bit 4	Completely 5
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- 13 0 I make decisions about as well as I ever could.  
1 I put off making decisions more than I used to.  
2 I have greater difficulty in making decisions than before.  
3 I can't make decisions at all anymore.

**If you rated yourself "1" or higher on question #13 above, please answer the following two questions:**

**On a scale of 1–5, to what extent does your seizures/epilepsy contribute to your difficulty in making decisions?**

Not at All 1	A Little 2	Moderately 3	Quite a bit 4	Completely 5
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**On a scale of 1–5, to what extent do your medications contribute to your difficulty in making decisions?**

Not at All 1	A Little 2	Moderately 3	Quite a bit 4	Completely 5
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- 14 0 I don't feel I look any worse than I used to.  
 1 I am worried that I am looking old or unattractive.  
 2 I feel that there are permanent changes in my appearance that make me look unattractive.  
 3 I believe that I look ugly.

**If you rated yourself "1" or higher on question #14 above, on a scale of 1–5, how much of your appraisal of yourself has been influenced by your seizures/epilepsy?**

Not at All 1	A Little 2	Moderately 3	Quite a bit 4	Completely 5
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- 15 0 I can work or do things about as well as before.  
 1 It takes an extra effort to get started at doing something.  
 2 I have to push myself very hard to do anything.  
 3 I can't do work at all.

**If you rated yourself "1" or higher on question #15 above, please answer the following two questions: On a scale of 1–5, to what extent does your seizures/epilepsy contribute to your work difficulty?**

Not at All 1	A Little 2	Moderately 3	Quite a bit 4	Completely 5
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**On a scale of 1–5, to what extent do your medications contribute to your work difficulty?**

Not at All 1	A Little 2	Moderately 3	Quite a bit 4	Completely 5
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- 16 0 I can sleep as well as usual.  
 1 I don't sleep as well as I used to.  
 2 I wake up 1-2 hours earlier than usual and find it hard to get back to sleep  
 3 I wake up several hours earlier than I used to and cannot get back to sleep

**If you rated yourself "1" or higher on question #16 above, please answer the following two questions: On a scale of 1–5, to what extent does your seizures/epilepsy contribute to your sleep problems?**

Not at All 1	A Little 2	Moderately 3	Quite a bit 4	Completely 5
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**On a scale of 1–5, to what extent do your medications contribute to your sleep problems?**

Not at All 1	A Little 2	Moderately 3	Quite a bit 4	Completely 5
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- 17 0 I don't get more tired than usual.  
 1 I get tired more easily than I used to.  
 2 I get tired from doing almost anything.  
 3 I am too tired to do anything.

**If you rated yourself "1" or higher above on question #17, please answer the following two questions: On a scale of 1–5, to what extent does your seizures/epilepsy contribute to your tiredness or fatigue?**

Not at All 1	A Little 2	Moderately 3	Quite a bit 4	Completely 5
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**On a scale of 1–5, to what extent do your medications contribute to your tiredness or fatigue?**

Not at All 1	A Little 2	Moderately 3	Quite a bit 4	Completely 5
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- 18 0 My appetite is no worse than usual.  
1 My appetite is not as good as it used to be.  
2 My appetite is much worse now.  
3 I have no appetite at all anymore.

***If you rated yourself "1" or higher on question #18 above, please answer the following two questions:***  
**On a scale of 1–5, to what extent does your seizures/epilepsy contribute to your change in appetite?**

Not at All 1	A Little 2	Moderately 3	Quite a bit 4	Completely 5
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**On a scale of 1–5, to what extent do your medications contribute to your change in appetite?**

Not at All 1	A Little 2	Moderately 3	Quite a bit 4	Completely 5
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- 19 0 I haven't lost much weight, if any, lately.  
1 I have lost more than 5 pounds.  
2 I have lost more than 10 pounds.  
3 I have lost more than 15 pounds.

***If you rated yourself "1" or higher on question #19 above, on a scale of 1–5, to what extent do your medications contribute to your weight change?***

Not at All 1	A Little 2	Moderately 3	Quite a bit 4	Completely 5
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- 20 0 I am no more worried about my health than usual.  
1 I am worried about physical problems such as aches and pains; or upset stomach; or constipation.  
2 I am very worried about physical problems and it's hard to think of much else.  
3 I am so worried about my physical problems that I cannot think about anything else.

***If you rated yourself "1" or higher on question # 20 above, on a scale of 1–5, how much of your concern for your health is due the symptoms mentioned above that you can attribute solely to your epilepsy?***

Not at All 1	A Little 2	Moderately 3	Quite a bit 4	Completely 5
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- 21 0 I have not noticed any recent change in my interest in sex.  
1 I am less interested in sex than I used to be.  
2 I am much less interested in sex now.  
3 I have lost interest in sex completely.

***If you rated yourself "1" or higher on question # 21 above, please answer the following two questions:***  
**On a scale of 1–5, to what extent does your seizures/epilepsy contribute to your sexual functioning/interest?**

Not at All 1	A Little 2	Moderately 3	Quite a bit 4	Completely 5
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**On a scale of 1–5, to what extent do your medications contribute to your sexual functioning/interest?**

Not at All 1	A Little 2	Moderately 3	Quite a bit 4	Completely 5
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