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PII: S1059-1311(16)30294-1
DOI: http://dx.doi.org/doi:10.1016/j.seizure.2016.11.026
Reference: YSEIZ 2856

To appear in: *Seizure*

Received date: 5-9-2016
Revised date: 9-11-2016
Accepted date: 30-11-2016

Please cite this article as: Gur-Ozmen Selen, Leibetseder Annette, Cock Hannah R, Agrawal Niruj, von Oertzen Tim J.Screening of anxiety and quality of life in people with epilepsy.*SEIZURE: European Journal of Epilepsy* http://dx.doi.org/10.1016/j.seizure.2016.11.026

SCREENING OF ANXIETY AND QUALITY OF LIFE IN PEOPLE WITH EPILEPSY

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RUNNING TITLE: ANXIETY AND QoL IN EPILEPSY

KEY WORDS: epilepsy; questionnaire; depression; anxiety; human; comorbidity

WORD COUNT: 3299 (text body)

DISCLOSURE: Parts of this study were presented as oral presentation at the EFNS/ENS meeting 2014 in Istanbul.

Dr Gur-Ozmen and Dr Leibetseder have nothing to disclose. Prof. Cock reports personal fees from UCB Pharma Ltd, personal fees from Epilepsy Nurse Specialist Association UK, personal fees from European Medicines Agency, personal fees from Special Products Ltd, personal fees from Eisai Europe Ltd, non-financial support from GSK Ltd, grants from NINDS, NIH USA, outside the submitted work; Dr. von Oertzen reports grants, personal fees and non-financial support from UCB Pharma GmbH, Vienna, personal fees and non-financial support from Eisai Pharma GmbH, Vienna, non-financial support from Medtronic, outside the submitted work;

ABSTRACT

PURPOSE

Up to 60% of people with epilepsy (PwE) have psychiatric comorbidity including anxiety. Anxiety remains under recognized in PwE. This study investigates if screening tools validated for depression could be used to detect anxiety disorders in PWE. Additionally it analyses the effect of anxiety on QoL.

METHODS

261 participants with a confirmed diagnosis of epilepsy were included. Neurological Disorders Depression Inventory for Epilepsy (NDDI-E) and Emotional Thermometers (ET), both validated to screen for depression were used. Hospital Anxiety and Depression Scale-Anxiety (HADS-A) with a cut off for moderate and severe anxiety was used as the reference standard. QoL was measured with EQ5-D. Sensitivity, specificity, positive and negative predictive value and ROC analysis as well as multivariate regression analysis were performed.

RESULTS

Patients with depression (n=46) were excluded as multivariate regression analysis showed that depression was the only significant determinant of having anxiety in the group. Against HADS-A, NDDI-E and ET-7 showed highest level of accuracy in recognizing anxiety with ET7 being the most effective tool. QoL was significantly reduced in PwE and anxiety.

CONCLUSIONS

Our study showed that reliable screening for moderate to severe anxiety in PwE without co-morbid depression is feasible with screening tools for depression. The cut off values for anxiety are different from those for depression in ET7 but very similar in NDDI-E. ET7 can be applied to screen simultaneously for depression and “pure” anxiety. Anxiety reduces significantly QoL. We recommend screening as an initial first step to rule out patients who are unlikely to have anxiety.

Highlights

- Moderate to severe anxiety is a frequent comorbidity in epilepsy, in our cohort prevalence was 26,4%
- Depression was the only significant determinant for anxiety, prevalence of anxiety in non-depressed PwE was 15,8%.
- Screening for anxiety independent from depression can be achieved with the ET7 tool.
- Quality of life was significantly reduced in PwE and anxiety, independent of depression.
- Significant reduction in QoL in PwE and anxiety was not only in subdomains of anxiety/depression, but also pain and activities.

BACKGROUND

Epilepsy is a debilitating disorder not just due to the occurrence of seizures. People with epilepsy (PwE) suffer a range of comorbid conditions which may have a negative impact on quality of life (QoL). QoL of PwE may be affected by several factors. The sudden, often unpredictable occurrence of seizures is a major factor as well as the stigma of the disease[1]. Restrictions on normal activities, resulting in low self-esteem and social rejection are also unfavorable consequences. These factors in this relatively young patient group can themselves contribute to psychiatric disturbances, as well as biological factors. Numerous studies show that the incidence of psychiatric disorders in PwE is significantly higher than in the general population[2-7]. Up to 50 or 60% of patients with chronic epilepsy have at least one mood disorder including depression and anxiety[8]. Prevalence studies on the association between epilepsy and psychiatric disorders have found that epilepsy can precede, co-occur with or follow the diagnosis of a psychiatric disorder[9].

Anxiety disorders (AnxD) are the second most prevalent psychiatric disorder in people with epilepsy, mostly commonly a generalized interictal AnxD affecting between 10-25% [8,9,10]. These clinical characteristics were recently confirmed in a study of a specialist neuropsychiatry service for PWE, where 27% suffered from generalized anxiety [11]. AnxD, as other psychiatric comorbidities, are however often under recognized and undertreated in PwE[6], but can significantly affect QoL. In one study, AnxD or major depressive episode (MDE) had a comparable negative impact on quality of life measured with the Quality of Life in Epilepsy Inventory-89 (QOLIE-89) while comorbid occurrence of both mood and anxiety disorders yielded a worse impact[12]. In another study of 154 outpatient adults with epilepsy, presence of anxiety symptoms was the most important factor in explaining a worse QoL[13]. Although it has not yet been systematically demonstrated that the treatment of anxiety

improves QoL in PWE, effective strategies in the general population are well established. As for depression, a first step achieving this in epilepsy must surely be to ensure those who might benefit are more easily identified when attending epilepsy outpatients' clinics. A range of tools have been developed and validated for detection of depression in PwE by ourselves and others[14,15]. In the present paper we investigate whether a range of traditional and visual analogue depression screening tools are also effective in detecting anxiety disorders. Additionally, we investigate QoL in PwE with and without anxiety.

METHODS

Sample

The patients' selection and characteristics are described elsewhere[15]. To summarize, we enrolled consecutive participants at the epilepsy outpatient service at Atkinson Morley Neurosciences Centre in South West London. Subjects were asked to complete selected screening tools for depression and anxiety disorders, including Major Depression Inventory (MDI), Hospital Anxiety and Depression Score (HADS), Neurological Disorders Depression Inventory for Epilepsy (NDDI-E), the Quality of Life Questionnaire (EQ-5D-3L), revised Emotional Thermometers (ET7) prior to or immediately afterwards their clinical consultation. In the present study, we used HADS-A as gold standard to detect anxiety. ICD-10 diagnosis of depression was detected by MDI questionnaire. All examinations and analysis were in accordance with the Declaration of Helsinki (2008). As per Research Ethic Committee (REC) advice, research limited to secondary use of anonymized information previously collected in the course of normal care is excluded from formal REC review.

Inclusion/Exclusion criteria

Epilepsy was diagnosed in all subjects by a neurologist with special interest in epilepsy. The diagnosis and specific epilepsy syndrome were confirmed from reviewing the clinical notes. Incomplete questionnaire samples were excluded from analysis. Our records were examined to ensure that the data of the same individual was not repeatedly entered in the analysis.

Conventional verbal tools

Hospital Anxiety and Depression Scale (HADS)

The HADS was originally designed as a screening tool for depression and anxiety in hospital outpatient clinics[16.] More recently, it was validated in primary care and in the community,

with the advantage of a completion time of 2–5 min[17]. HADS consists of seven questions for depression and seven for anxiety, scored on a 4 item Linkert scale. Score for each subscale (anxiety and depression) can range from 0-21 with HADS scores categorized as follows: normal (0-7), mild (8-10), moderate (11-14), severe (15-21). Scores for the entire scale (emotional distress) range from 0-42, with higher scores indicating more distress. Snaith recommends a cut off of >7 for both HADS-D (the depression subscale) and HADS-A (the anxiety subscale), while combined total scores (HADS-T) can also be used[17].

Definition of HADS-A defined anxiety in this sample

Screening in hospital outpatient clinics for anxiety aims at identifying a clinical relevant anxiety. We therefore decided to choose the cut off for moderate anxiety to differentiate anxiety. Moderate and severe anxiety is more likely to have therapeutic relevance then mild anxiety. Hence, dichotomization of the HADS-A anxiety variable was done as "anxiety positive (+) with cutoff of >10 and anxiety negative (-) with cutoff ≤10".

Neurological Disorders Depression Inventory for Epilepsy (NDDI-E)

This screening tool for depression in PwE consists of six statements about thoughts and feelings in the preceding two weeks that are scored on a 4 item Linkert scale resulting in a minimum score of 6 and maximum of 24. It takes less than 3 min to complete[18]. It was has been validated in a US population (ideal cutoff of >14) and in a UK population (ideal cut off of >15), resulting in 90%/87% specificity and 81%/81% sensitivity against DSM-IV major depression with high NPV of 0.96/0.97 and rather moderate PPV of 0.62/0.51 respectively[14, 15].

Visual analog tool

Revised Emotional Thermometers (ET7)

ET7 is shown in Figure 1. It consists of seven visual analogue scales, which take less than 2 minutes to complete and there is no need to score afterwards. The seven different scales allow individual as well as combined analysis. It has been validated to screen for depression in PwE, resulting in a sensitivity of 85% and specificity of 79%. The NPV was 0.96 and PPV 0.47 for the combined tool[15]. This tool has been used previously with a lower number of scales (ET4, ET5) to detect depression in oncology and cardiology settings against a DSM-IV diagnosis of depression[19, 20].

[Insert Fig 1 here]

EQ-5D-3L:

Quality of Life was measured using 5 questions from EQ-5D and a visual analogue scale (EQ-VAS).

EQ5D is a descriptive system, which records the current health status and the subjective perception of quality of life. It is a form of questionnaire divided into 5 dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression). The intensity of disability in each range should be stated as none (0), moderate (1), severe (2). Furthermore, it records the patients' self-rated health on a vertical visual analogue scale (EQ-VAS). It is ranged from 0 (the worst possible health status) to 100 (the best possible health status)[21].

Statistical Analysis

Accuracy measures

There are various measures that incorporate both sensitivity and specificity to describe the validity of screening or diagnostic tests. These include positive and negative predictive values (PPVs and NPVs), the area under receiver operating characteristic (ROC) curves, positive utility index (UI+), negative utility index (UI). Clinical utility measures the clinical value of a screening test by combining its ability to identify cases and to discriminate non-cases. UI+ is calculated as sensitivity×positive predictive value while UI is calculated as specificity×negative predictive value. UI+ shows how well the tool identifies a diagnosis when present and UI shows how well the tool excludes a diagnosis when absent[20].

ROC curve analysis was performed to create area under the curve (AUC) scores for the various tools against the diagnosis of anxiety. This analysis was used to calculate the optimal cutoff scores for maximizing sensitivity and specificity of the tools. PPVs, NPVs, UI+ and UI- were calculated. Further measures of diagnostic accuracy were recorded including Youden J (sensitivity + specificity) -1).

Performance of the tests was taken as follows: <0.2 poor, 0.2–0.4 fair, 0.4–0.6 moderate, 0.6–0.8 good, >0.8 very good. Conventionally AUC scores >0.8 are said to be good and >0.9 excellent.

Reliability measures

Internal consistency was reported using the Cronbach alpha (CA) estimate using standardized variables. CA estimates the proportion of variance in the test scores that can be attributed to true score variance. So it is used to estimate the proportion of variance that is systematic or consistent in a set of test scores. It can range from 00.0 (if no variance is consistent) to 1.00 (if all variance is consistent) with all values between 00.0 and 1.00 also being possible. Scores are interpreted as follows: ≥0.7 = reasonable, ≥0.8 = good, ≥0.9 = excellent reliability.

Relationship measures

The relationships between the dependent and independent variables were analyzed using the non-parametric chi-square test (when both variables were categorical), Student's T-test (when one variable was categorical and the other one was continuous) and Mann-Whitney-U (when the distribution was not homogenous in T-test).

The correlation between anxiety and quality of life was analyzed by using a standardized regression coefficient. Graphical illustration was accomplished by scatter plots.

Further the effect of anxiety on quality of life was demonstrated separately for each domain of EQ-5D.

Multivariable analysis is a statistical tool for determining the unique contributions of various factors to a single event or outcome[22]. It is an accepted statistical method for assessing association between an antecedent characteristic (risk factor) and a quantal outcome (probability of disease occurrence), statistically adjusting for potential confounding effects of other covariates[23].

We performed a multivariate analysis to show the significant determinants of having HADS-A defined anxiety in the sample.

RESULTS

Descriptive statistics and demographics of the study population are given in Table 1.

[Insert Table 1 here]

In our sample of 261 patients, the prevalence of depression (Dep) was 17.6% (n=46) and anxiety (Anx) was 26.4% (n=69). There was a higher proportion of women in PwE with anxiety as compared to PwE without anxiety but this wasn't stastically significant.
Of the 46 patients with depression 76% (n=35) had moderate or severe anxiety according to HADS-A. There was a significant overlap noted between anxiety and depression with over half of PwE with anxiety also showing depression. Hence, prevalence of anxiety in the non-depressed group was 15.8% (34 out of 215).

Multivariate analysis

Multivariate regression analysis showed "presence of depression" according to "ICD-10 defined depression" was the only variable having a statistically significant effect on the presence of HADS-A anxiety (table 2).

[Insert Table 2 here]

Correlation of anxiety and QoL

In view of this relationship, the correlation of anxiety (ET-A as well as HADS-A) and quality of life (EQ-VAS) was analyzed with all patients including those with depression (n=261) and in a group excluding all patients with depression (n=215).

Simple regression showed for both samples a statistically significant negative correlation between EQ-VAS score and HADS-A/ET-A. The lower the EQ-VAS was stated, the higher was the scoring for HADS-A and ET-A ($p <= 0{,}001$). Scatter plots for the two groups are demonstrated side by side in Figure 2.

[Insert Figure 2 here]

The EQ-5D-3L was only fulfilled by 258 patients (Anx- n=191, Anx+ n=67). It was found that a larger proportion of patients with anxiety rated themselves more impaired in various domaines of EQ-5D QoL-Scale than patients without anxiety.

The same could be stated after exclusion of patients with depression. Based on all patients (n=258) a statistical significance was stated in EQ (Anx/Dep), EQ (Pain) and EQ (Activities). After extracting depressed patients EQ (Anx/Dep) showed a statistical significance only. Figure 3 shows the impairment of quality of life by EQ-5D domains compared in three groups, PwE with depression, PwE without depression but anxiety, and PwE without depression and without anxiety.

[Insert Figure 3 here]

Performance of screening tools

We have used ROC curve analysis to identify the optimal cutoff for anxiety for each tool in this sample. Equally patients with depression (n=46) were excluded for the evaluation of using depression screening tools for detection of anxiety.

For the conventional verbal tool, the NDDI-E, the optimal cutoff for our sample was 14 versus 15. For the visual analogue scales, the ET7, we compared the results for the five individual thermometers: distress (DT), anger (AngT), depression (DepT), anxiety (AnxT), and need for help (HelpT) as well as sum scores for both the ET4 (excluding the HelpT) and the ET7 tool. Overall, ET4 had an optimal cutoff of 12 vs 13 and ET7 of 21 vs 22. The optimal cut offs for the subscales of both tools are shown in detail in Table 3.

[Insert Table 3 here]

Reliability

The overall reliability of both, the ET7 and NDDI-E was good, although the former was slightly superior to the latter (α =0.894, 95% lower confidence limit [CL] 0.871 vs α =0.836, 95% lower confidence limit [CL] 0.799).

DISCUSSION

We showed with a multivariate logistic regression analysis that ICD-10 defined depression was the only statistically significant factor affecting the presence of AnxD. In fact it is highlighting the complex overlap between the two conditions. Our sample showed that moderate to severe anxiety was more prevalent than depression. Three quarters of PWE who had depression also had anxiety whereas only half of PWE who had anxiety had co-morbid depression. This means not only is anxiety more common overall, there are more PWE who have "pure" anxiety than "pure" depression highlighting importance of recognition of anxiety in PWE.

Moreover our findings demonstrate that the presence of anxiety, according to HADS-A and ET-A, is associated with a significant impairment of QoL. Equally the influence of anxiety could be shown after excluding the patients with depression, which implies anxiety as an independent factor on QoL.

As NDDI-E and ET7 are validated for screening depression, cut offs for anxiety were identified in a sample without depression to avoid confounding effects. After excluding patients with depression we focused in the analysis on the non-depressed sample (n=215). 34 (15.8%) patients had anxiety according to HADS-A (cutoff >10). Gaitatzis et al[9] had found that prevalence of anxiety disorders in PwE was 10-25% and our sample's percentage was consistent with the literature. A Canadian population-based study showed a lifetime prevalence of any AnxD in PwE of 22.8% (vs 11% in non-epilepsy subjects). AnxD and DD tend to occur together with a high frequency, and, in the Canadian study, a lifetime prevalence of 34.2% was found for comorbid AnxD and DD in PwE (vs 19.6% in non-epilepsy subjects)[6]. Again, our findings are in line with previously reported data. Whereas anxiety in the healthy population is more prevalent in women, previous studies in PwE showed that there

is no such difference[22,24] . Although in our study slightly more women were screened positive for anxiety, the difference was not statistically significant, which is in line with the previously reported findings.

We defined having anxiety as "positive" grouping moderate and severe anxiety together (HADS-A >10=anxiety(+)) while we took the mild anxiety group into the "anxiety negative" ones. This was to differentiate the group who would likely require treatment for anxiety. The most accurate scales by ROC area were NDDI-E and ET7 and the Anxiety Thermometer (AnxT) as single item (Table-3). ET7 showed a slightly superior reliability. Cut off values for detecting anxiety were very close to those detecting depression in NDDI-E (14 vs 15 for anxiety and 15 vs 16 for depression) and identical in AnxT (5 vs 6 for anxiety and 5 vs 6 for depression). In contrast ET7 showed a clear distinction for cut off levels detecting anxiety (21 vs 22) and depression (28 vs 29) i.e. a score between 22 and 28 identifies PwE who may suffer "pure" anxiety but not depression.

In the present study QoL is measured by a different scale than in previous studies[12, 24, 25], but yields the same conclusions showing the effect of anxiety on QoL in PWE is robust. Interestingly, after removing all depressed patients, PwE and anxiety showed no more physical complains in the QoL domains but low QoL in view of depression/anxiety. This is in line with our previous observation that PwE and depression report more somatic symptoms [27, 28] .

Similar to depression, anxiety is often missed as comorbidity in PwE [12]. Given that anxiety and depression in PwE respond well to pharmacological treatments or cognitive behavioral therapy and that anxiety in PwE significantly worsens QoL and health care costs, neurologists are urged to start identifying and treating this comorbidity [12, 26.]

Screening tools can support the clinician in daily practice to identify a condition, in the present study comorbidity of anxiety in PwE. The ideal tool should reliably identify the condition as a ‘‘rule-in’’ or ‘‘case-finding’’ tool. Alternatively screening tools can support by identifying subjects who are not suffering from the condition, i.e. working as a “rule-out” tool. In the present study the screening tools didn’t perform well in a ‘case finding role’, but several items performed well as a “rule out” tool due to the high negative predictive value and specificity. In this role, the most effective tool was the ET7 having NPV= 0.964, specificity = 0.757, ROC area = 0.882. Using these accuracy levels and a point prevalence of HADS-A anxiety of 15.8%, ET7 would help exclude anxiety in 64 of 85 non-anxiety patients with 3 PwE with anxiety being missed (false negative), and correctly identify 12 of 15 cases with anxiety with 21 false positives. The high number of false positives reflects the relatively low PPV of approximately 0.4. We have to stress at this point that screening tools do not diagnose and treatment should never be started purely on the basis of a positive result on screening. This illustrates rather the usefulness of this screening tool, guiding the clinician to a group of patients where further questions about potential AnxD should be applied. Post screening clinical enquiry to clarify the diagnosis or referral to an appropriate professional such as a neuropsychiatrist would be recommended.

Both screening tools are simple to apply and take only 2-3 minutes to complete. The visual analogue scales are easier to score for the clinician and may be less dependent on language skills particularly in a multicultural setting or in people with learning disability. However, the latter statement is an assumption our sample size was too small to support this statistically. Our data support ET7 as the only tool which allows to screen for depression and independently for “pure” anxiety in PwE.

Limitations

As mentioned in our previous study on screening for depression, our subject population may not have a true representation of the demographic spread of the clinic population because of the number of exclusions we were forced to make on the grounds of poor English language skills, in particular among the middle aged and elderly Asian population. We attempted to include consecutive attendees, but some refusals and exclusions may have compromised our findings, and we do not have data of those who were excluded [15]. However the data represents a routine clinical practice and hence has high clinical applicability.

We have used HADS-A to be a gold standard a likelihood of the diagnosis of anxiety in this sample. However, HADS-A was originally designed to be used as a screening instrument for use with outpatients attending medical clinics [16]. Future replication of this work with a more robust gold standard of anxiety such as structured clinical interviews would be recommended.

CONCLUSION

Anxiety is an important health problem in epilepsy patients and it has attainable and simple means of detection and treatment.

Our intention was to validate if the depression screening tools for use in epilepsy outpatients are identifying anxiety as well. As the screening tools are designed to be given to patients prior to the clinic appointment, results should be available at the consultation. Our results indicate that ET7 allows screening for depression and “pure” anxiety independently. Furthermore we have shown that anxiety has a significant impact on QoL measure with the EQ-5D-3L independent of depression.

ACKNOWLEDGEMENT

The authors would like to thank Alex Mitchell who holds the copyright on the revised Emotional Thermometers (ET7) but has made it freely available (royalty-free) for noncommercial and clinical use. The authors appreciate the permission by EuroQol Research Foundation for using the EQ-5D-3L in this study. The authors are also grateful to Marie Synnott-Wells, epilepsy nurse specialist at Atkinson Morley Neuroscience Centre, St George's Hospital, London, who supported the clinical application of the screening tool with great patients.

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Tables and Figure legends

Table1. Characteristics of the patients data and it's relation to anxiety (HADS-A)

	All cases **N=261**	**Anxiety (+) according to HADS-A (>10) N=69**	**Anxiety (-) according to HADS-A (≤10) N=192**	**P value**
Age,mean,(standard deviation)	39,8 (15,2)	39,9 (14,3)	39,8 (15,6)	0,74
Gender,female, n (%)	153 (58,6%)	44 (63,7%)	109 (56,7%)	0,31
Epilepsy type: Focal, n (%)	159 (60,9%)	44 (63,7%)	115 (59,8%)	0,57
Epilepsy type: Generalised, n (%)	86 (32,9%)	21 (30,4%)	65 (33,8%)	0,60
Epilepsy type: Unclassified, n (%)	16 (6,1%)	4 (5,7%)	12 (6,25%)	0,89
Depression (+) (MDI-ICD-10) , n (%)	46 (17,6%)	35 (50,7%)	11 (5,7%)	<0,001

***p≤0.05,** statistically significant

Table 2. The parameters of the multivariate logistic regression model for anxiety (+) and levels of significance

	B	SE	Wald	df	Sig	Exp(B)	95% CI for Exp(B) lower	95% CI for Exp(B) upper
Depression (+) (MDI-ICD-10)	2,830	0,393	51,850	1	0,000	16,939	7,841	36,590
Constant	-1,672	0,187	80,032	1	0,000	0,188		

***p≤0.05,** statistically significant

Table 3. Accuracy and utility of tools to identify HADS-A defined anxiety episode (>10=anxiety(+)) in epilepsy patients (n=215) without depression according to MDI ICD-10. Scores for the complete screening tools are marked in grey. ET4 includes of the first four mentioned subscales.

		Directional accuracy				Overall accuracy				
Test	**Optimal cutoff**	**SN**	**SP**	**PPV**	**NPV**	**ROC area (95% CI)**	**Youden**	**Fraction correct**	**Clinical utility İndex (+)**	**Clinical utility İndex (-)**
NNDI-E	14 vs 15	0.735	0.862	0.500	**0.945**	0.874 (0.806-0.941)	0.**597**	0.841	0.367	0.814
NDDI-E Q1	2 vs 3	0.824	0.630	0.294	**0.950**	0.778 (0.695-0.861)	0.454	0.660	0.242	0.598
NDDI-E Q2	2 vs 3	0.676	0.812	0.403	**0.930**	0.782 (0.698-0.866)	0.488	0.790	0.272	0.755
NDDI-E Q3	2 vs 3	0.588	0.702	0.270	**0.900**	0.701 (0.605-0.797)	0.290	0.683	0.158	0.631
NDDI-E Q4	1 vs 2	0.647	0.867	0.478	**0.928**	0.765 (0.664-0.866)	0.514	0.832	0.309	0.849
NDDI-E	3 vs 4	0.500	0.917	0.531	**0.967**	0.783	0.417	0.902	0.265	0.886

Q5						(0.699-0.867)				
NDDI-E	2 vs 3	0.676	0.751	0.338	**0.925**	0.768	0.427	0.739	0.228	0.694
Q6						(0.680-0.855)				
ET7	21 vs 22	0.853	0.757	0.397	**0.964**	0.882	0.610	0.772	0.338	0.729
						(0.827-0.938)				
ET4	12 vs 13	0.882	0.685	0.344	**0.968**	0.866	0.567	0.716	0.303	0.663
						(0.809-0.923)				
DistT	2 vs 3	0.824	0.652	0.307	**0.951**	0.800	0.476	0.679	0.252	0.620
						(0.727-0.872)				
AnxT	5 vs 6	0.765	0.862	0.509	**0.951**	0.866	0.627	0.846	0.389	0.819
						(0.803-0.929)				
DepT	2 vs 3	0.853	0.691	0.337	**0.961**	0.826	0.544	0.711	0.287	0.664
						(0.753-0.900)				
AngT	3 vs 4	0.765	0.713	0.320	**0.940**	0.779	0.478	0.706	0.244	0.670
						(0.693-0.864)				
DurT	4 vs 5	0.735	0.757	0.362	**0.938**	0.796	0.492	0.753	0.266	0.710
						(0.719-0.874)				
BurT	1 vs 2	0.853	0.740	0.381	**0.964**	0.843	0.593	0.758	0.324	0.713
						(0.766-0.920)				
HelpT	1 vs 2	0.824	0.696	0.337	**0.954**	0.779	0.536	0.716	0.277	0.663
						(0.715-0.883)				

SN, sensitivity; SP, specificity; PPV, positive predictive value; NPV, negative predictive value; TP, true positive; TN, true negative; FP, false positive; FN, false negative.

Fraction correct (overall accuracy) = TP + TN/TP + TN + FP + FN

***p≤0.05,** statistically significant

Figure 1. Revised Emotional Thermometers (ET7). The following instruction was given: *In the first four columns, please mark the number (0-10) that best describes how much emotional upset you have been experiencing in the **past two weeks**, including today. In the next three columns please indicate how much impact this has had on you, how long you have been experiencing these emotional problems and how much you need help for these.*

Figure 2. Simple regression showed negative correlation of QoL and Anxiety in both groups – anxiety with (left) and without (right) depression. Upper chart for comparison to HADS score, lower chart comparing to emotional thermometer anxiety.

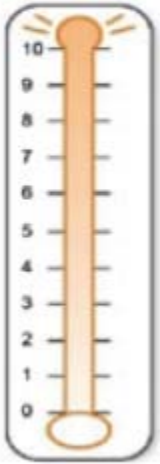
Figure 3: Impairment of QoL according to the EQ-5D domains in PwE. It shows the results of PwE with depression and anxiety (blue) compared with PwE with anxiety but no depression (orange) and PwE with neither depression nor anxiety. Activities and pain are statistically significant relevant for reduction of QoL as is feeling of anxiety and depression in PwE with anxiety independent from depression.

statistically significant *$p \leq 0.05$, ** $p \leq 0{,}01$, *** $p \leq 0{,}001$

Emotional Upset

1. Distress

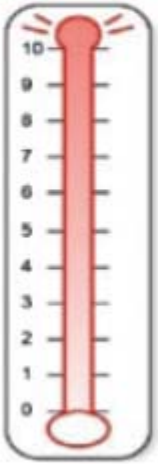
10 = Extreme



0 = None

2. Anxiety

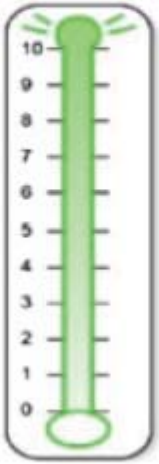
10 = Extreme



0 = None

3. Depression

10 = Extreme



0 = None

4. Anger

10 = Extreme

0 = None

Emotional Impact

5. Duration

10 = 10+ months

0 = Just today

6. Burden

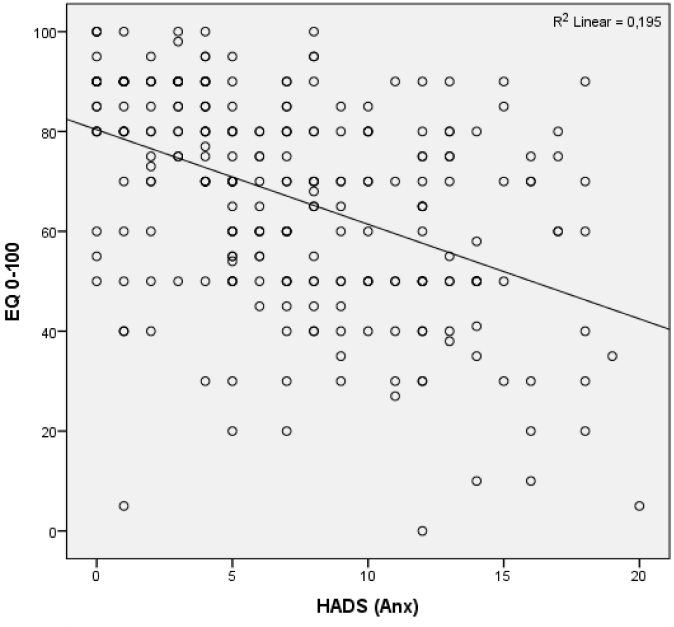
10 = Cannot function at all

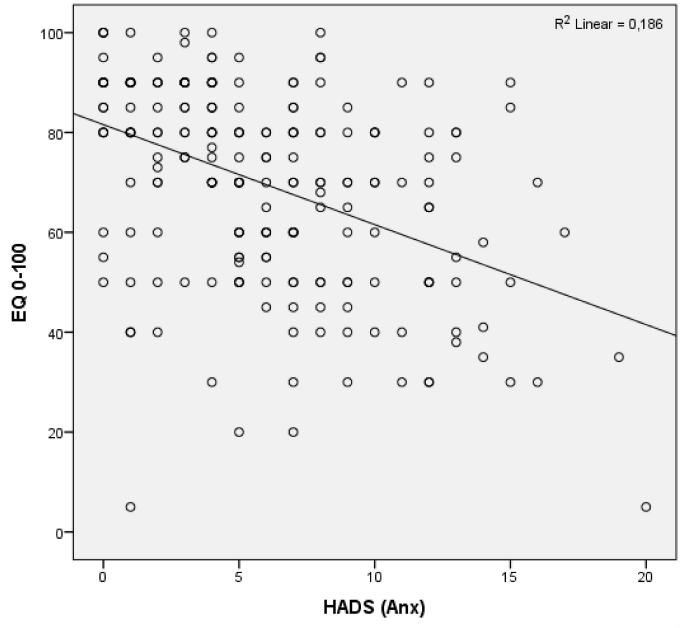
0 = No Effect on me

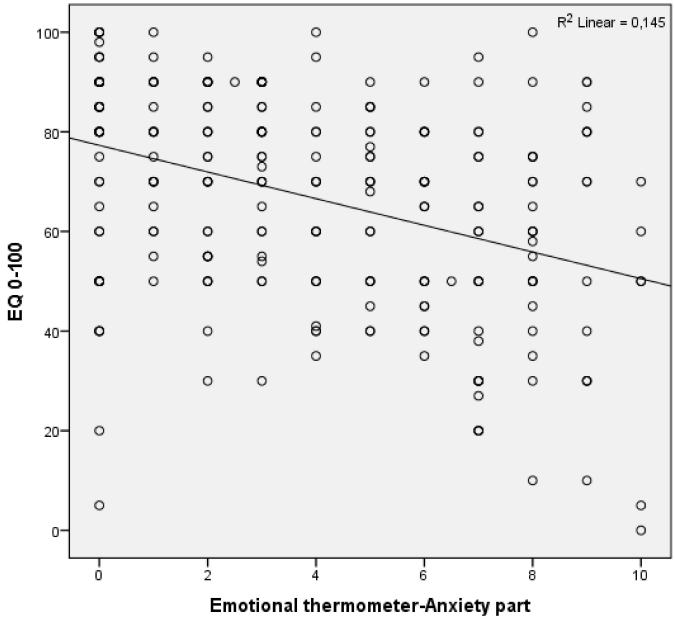
7. Need Help

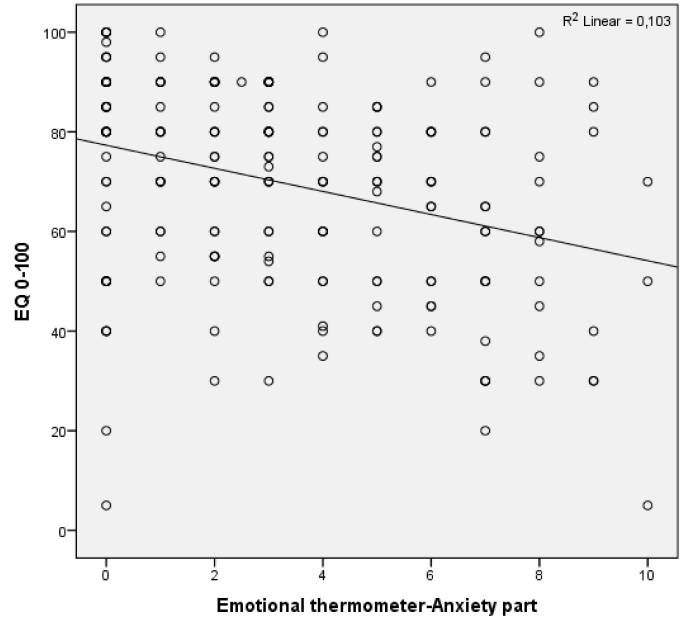
10 = Desperately

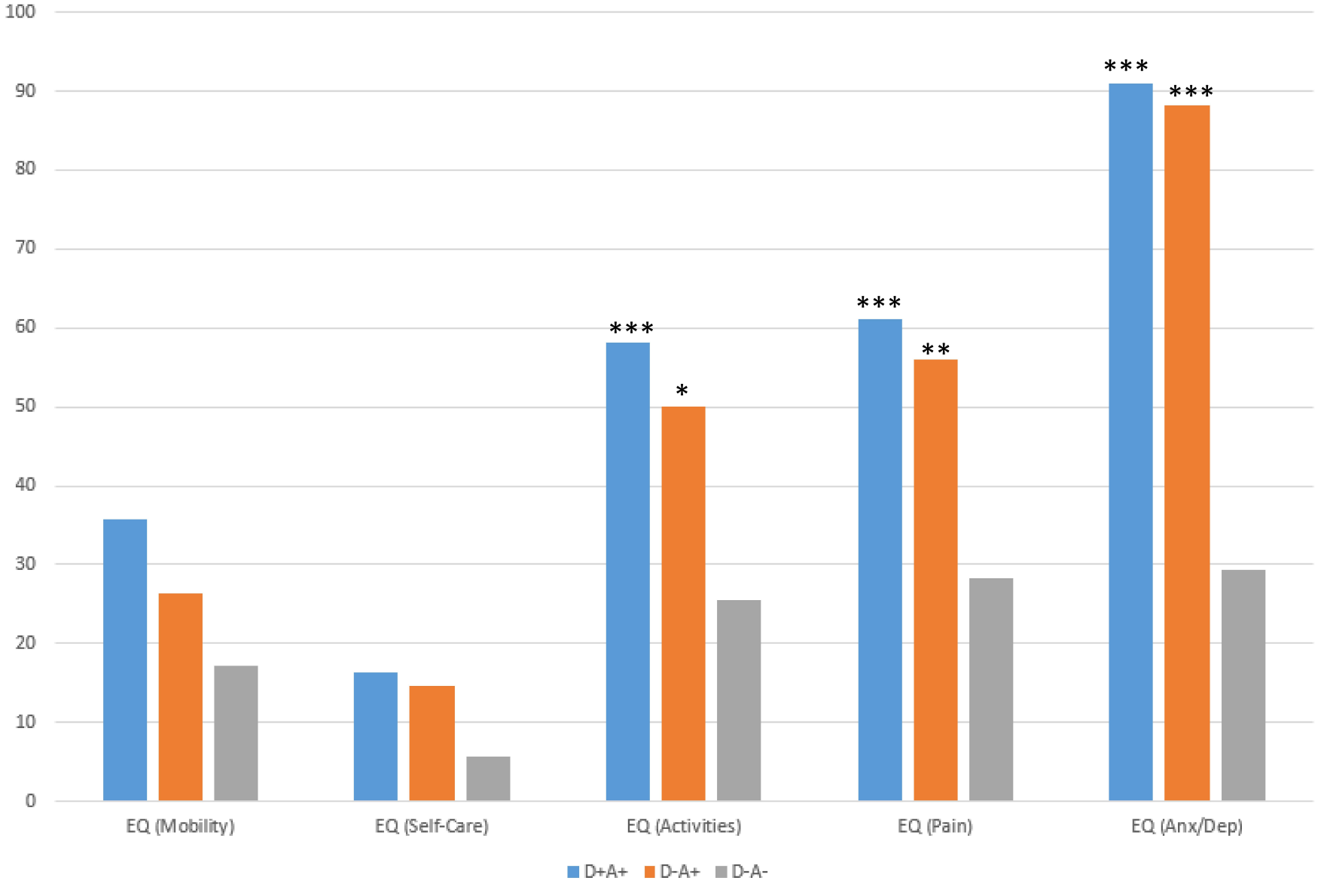
0 = Can manage myself


R² Linear = 0,195
EQ 0-100
HADS (Anx)


R² Linear = 0,186
EQ 0-100
HADS (Anx)


R² Linear = 0,145
EQ 0-100
Emotional thermometer-Anxiety part


R² Linear = 0,103
EQ 0-100
Emotional thermometer-Anxiety part


100
90
80
70
60
50
40
30
20
10
0
***
***
***
*
***
**
EQ (Mobility)
EQ (Self-Care)
EQ (Activities)
EQ (Pain)
EQ (Anx/Dep)
D+A+
D-A+
D-A-