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Screening of coexisting depression or anxiety disorders among Danish patients with alcohol use disorder in outpatient treatment.

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Abstract

Background

Depression and anxiety are highly prevalent among patients seeking outpatient treatment for alcohol use disorders (AUD) and if depression and anxiety is addressed the prognosis is improved. Screening instruments for depression and anxiety have been validated in populations suffering from drug use disorders, but not in populations suffering from AUD. The aim of this study was to validate four self-administrated screening instruments (*PHQ-9*, *GAD-7*, *Kessler-6*, and *SRQ*) and calculate the optimal cut-off value for identifying depression and anxiety.

Methods

The study included 73 patients with self-reported depression or anxiety during AUD treatment. Each patient filled out the above-mentioned instruments and were subsequently interviewed by trained clinicians blinded to the results of the instruments with Present State Examination to establish a diagnosis of depression or anxiety according to ICD-10. ROC curves were constructed for each instrument and area under the curve (AUC) were calculated using patients with no depression or anxiety as reference. Youden's index was calculated to assess the optimal cut-off for each instrument.

Results

33 (45.2%) were diagnosed with depression or anxiety. The AUC for *PHQ-9*, *GAD-7*, *Kessler-6*, and *SRQ* were 0.767, 0.630, 0.793, and 0.698 respectively. *Kessler-6*, the instruments performing best based on the AUC, identified 27 (82%) of the 33 patients using a cut-off of 10 points.

Conclusion

Kessler-6 seems to be valid and reliable in identifying patients requiring treatment for depression or anxiety among patients seeking treatment for AUD who are reporting depression or anxiety.

Keywords

Alcohol use disorder, depression, anxiety, screening, ROC curves, Youden's index

INTRODUCTION

Depression and anxiety are prevalent with prevalence estimates in the general population of 7.2% for depression (1) and 10.4% for anxiety (2). The prevalence of depression and anxiety is even higher among patients seeking out-patient treatment for alcohol use disorders (AUD): 14% to 75% of the patients enrolled in treatment for AUD are reported to also suffer from depression and 42% to 69% of a co-morbid anxiety disorder (3). This over-representation of depression and anxiety is reported in both studies based on interview data and studies based on register data (4, 5).

Patients suffering from AUD and concurrent depression or anxiety have a poorer prognosis and increased use of health care compared with patients suffering from AUD alone (6, 7).

However, if the mental illness is addressed during treatment, the prognosis for depression as well as for anxiety is improved (7, 8), and thus, during treatment for AUD, the clinician should secure that the patients suffering from co-morbid depression and anxiety are identified and offered relevant treatment.

Although it may be relevant to distinguish between depression and anxiety during a treatment course, there are also many overlaps between the two conditions (9-11). Furthermore, the relevant potential referral of the patients will typically be the same whether it is depression or anxiety that is identified, i.e., referral to specialized psychiatric treatment. Whether or not a referral should take place depends on severity sooner than the type of disorder. It is thus potentially useful to be able to identify patients in treatment for AUD who may have a concurrent depression or anxiety condition and leave the more in-depth assessment to the specialized staff in mental health care, who has the needed expertise available.

Guidelines recommend that all patients seeking treatment for AUD are screened for concurrent depression and anxiety. (12-15). Instruments used for such screening purpose should ideally be both precise, short, and easy to administer, thus helping the clinicians in prioritizing the limited time available to patients that require further assessment and treatment for mental health symptoms. Several screening tools are developed to identify non-psychotic mental illness, but only very few are validated among patients seeking treatment for AUD.

The Norwegian guidelines for assessment and treatment of substance use and co-morbid mental illness review the available screening instruments and recommend the short version of SCL (Symptom Check List) (16) when screening for depression and anxiety. However, it is noted that the evidence is weak since the instrument has not been validated in populations suffering from AUD (15).

In addition to SCL, several short screening instruments are available and validated for the identification of depression and anxiety among patients suffering from substance use disorders: Patient Health Questionnaire depression scale (PHQ-9) (17), The Generalized Anxiety disorder Scale (GAD-7) (18), The Psychological Distress Scale (Kessler-10/6) (19, 20), and The Self Reporting Questionnaire (SRQ) (21). The PHQ-9 and the GAD-7 are specifically developed for identifying depression and anxiety, respectively, while Kessler-6 and SRQ are developed to identify whether the patients suffer from either anxiety or depression (without distinguishing between the two conditions), often referred to as distress. The screening instruments are, however, validated in populations of patients suffering from drug use disorder and not studies in populations of patients suffering from alcohol use disorders.

There are issues to consider when contemplating whether to implement screening programs for depression and anxiety in treatment for AUD. Screening should only be carried out, if useful treatments are available, and the screening does not incur unreasonable costs to the clinic or distress to the patient. Secondly, the timing of screening. When patients stop drinking, withdrawal symptoms can occur. During the withdrawal phase, a patient may experience transient anxiety symptoms, melancholy, sleep problems, and restlessness. (22). Screening during withdrawal phase may therefore result in many false positive screenings and subsequently further unnecessary diagnostic procedures. Screening instruments consist typically of several items contrived to identify a latent structure, e.g. a mental health problem as anxiety or depression, with high probability. As different psychiatric symptoms often are represented in several mental health illnesses, it is important to validate screening instruments in each target population where the instrument is considered used. Thus, demonstrating that the instrument more likely identifies patients who truly need treatment, less likely miss patients who need an intervention, and reduce waste of resources.

The aim of this study was to validate the above-mentioned screening instruments aimed at identifying depression and anxiety, since they can be implemented by non-specialist staff in a busy clinical routine and are easy to administer, as the patients fill them out themselves:

1. To investigate the validity of the screening instruments PHQ-9, GAD-7, Kessler-6, and SRQ among patients, suffering from alcohol use disorder seeking outpatient treatment in a publicly funded Danish out-patient treatment specialized in treatment of AUD
2. To calculate sensitivity and specificity and decide optimal cut-off values for screening to identify patients with anxiety or depression.

METHODS

Setting

The study was performed as a cross-sectional study at the outpatient treatment center for alcohol use disorder in the Municipality Odense, Denmark, between 29th of April, 2020 and 31st of May, 2021. Initially, as a patient seeks treatment, pharmacotherapy for withdrawal symptoms is offered if needed. Then, when stable, an assessment interview is performed to get an overview of the patient's problems and profile. Based on the assessment, a treatment strategy is allocated to the patient (23). The assessment interviews are performed by means of Addiction Severity Index, 5th edition (ASI-5) (24). The ASI explores seven areas: 1) medical status, 2) employment/ support status, 3) alcohol use, 4) other drug use, 5) legal problems, 6) family and social situation, and 7) mental health. For each of the seven areas, a composite score can be calculated with a value between 0 and 1; 0 indicates no problems at all in this area, and 1 the most severe problems. Thus, the closer to zero the composite score is, the better the functioning in this area during the last month.

When exploring mental health status during the assessment interview, the therapists ask the patient if they have experienced severe depression or anxiety during the last month prior to treatment start. The question was phrased "In the last 30 days, have you had a significant period of time (that was not a direct result of alcohol use) in which you have experienced severe depression or severe anxiety or tension?". It is particularly stressed that the patient should disregard depressive thoughts and symptoms, or symptoms of anxiety caused by the drinking. During treatment, the status of the seven areas is evaluated every three months using the follow-up version of the ASI, using the composite scores.

Screening instruments

Patient Health Questionnaire-9 (PHQ-9)

PHQ-9 is a nine-items screening questionnaire for depression (Kroenke et al., 2010). Each item is rated on a four-point Likert scale from 0 to 3. The sum score can range from 0 (no problem noted at any of the items) to 27 (daily or almost daily problems noted at all items). In a meta-analysis, it was shown that a cut-off score of 10 or above gave the best balance between sensitivity and specificity for the identification of depression (25).

Generalized Anxiety Disorder-7 (GAD-7)

The GAD-7 is a seven-item questionnaire designed to screen for anxiety, and like the PHQ-9, each item is rated on a four-point Likert scale, and the sum score can range from 0 (no problem noted at any of the items) to 21 (daily or almost daily problems noted at all items). Spitzer et al reported a cut-

off score of 10 or above represents the optimal cut-point for the identification of moderate to severe general anxiety (18). GAD-7 was primarily developed for generalized anxiety screening but has also proven to be able to screen for panic anxiety, social anxiety, and post-traumatic stress syndrome (26). Based on a meta-analysis, the cut-off for precision for identifying all anxiety disorders was the same for all scores between 7 and 10, and therefore not possible to recommend a specific cut-off value (27).

Kessler-6

The Kessler-6 (19) consists of six items concerning anxiety/depression during the last month. Each item is rated on a Likert scale from 0 (no problem at any time) to 4 (a problem all the time) (28). Kessler-6 is validated in relation to diagnostic interviews, and a cut-off score of 13 is recommended to identify patients with moderate to severe anxiety/depression (29).

Self-Reporting Questionnaire (SRQ)

The SRQ (World Health Organization, 1994) consists of 20 items related to depression and anxiety symptoms. A "yes" to an item is equivalent to 1 point and a "no" to 0 points on the item. The total score is the sum across items. Cut-off scores between 7 and 10 are reported to have almost the same precision (21, 30).

Study procedure

The inclusion criteria were as follows: The therapists in the alcohol treatment center offered patients participation in the present study if, at any time during the treatment course, they reported suffering from severe depression or anxiety during the last month, based on the items in the ASI, and at the same time reported not having been drinking alcohol at all or drinking below the maximum limits recommended by the Danish Health Authorities during the last four weeks (at the time of the study it was 14 standard units/week for men and 7 standard units/week for women, and for both sexes never drinking 5 or more units during a day).

Patients already in pharmacological treatment for anxiety or depression; but still reported severe depression or anxiety symptoms, were also offered participation in the study. Exclusion criteria were: use of other substances, psychotic symptoms, and severe cognitive problems.

Patients fulfilling the inclusion criteria above, and not fulfilling the exclusion criteria were informed about the study both verbally and in writing. If they accepted participation, they were asked to fill out the four screening questionnaires. The patients were presented with the four screening instruments in the same order as they are presented above (PHQ-9 – GAD-7 – Kessler-6 – SRQ).

Within a maximum of two weeks after filling out the questionnaires, the patients participated in a diagnostic interview conducted by experienced clinicians, who were blinded to the results of the screening instruments. The diagnostic interview was carried out in accordance with *The Present State Examination (PSE)* (31) and thus functioned as a “Golden standard.”

For decades the PSE has been one of the most frequently used diagnostic instruments in mental health (32). The PSE is a semi-structured interview designed to be conducted by trained clinicians aimed at offering an objective evaluation of the patient’s psychiatric symptoms that, according to ICD-10 criteria (33), can be grouped as moderate/severe anxiety or moderate/severe depression, and a group of no/mild/ anxiety or no/mild depression. The severity was assessed by the trained clinicians conducting the PSE interview. Severity of anxiety was based on the number of symptoms presented by the patients and the impact on their self-reported level of functioning. The severity of depression was based on the number of symptoms as outlined in ICD-10. In the present study, the interview lasted 1.5 hours and was performed by either a clinical psychologist (5 years of experience) or one of two psychiatrists (30 years and 14 years of experience, respectively).

After the diagnostic interview, the patient had the possibility of discussing the results of the diagnostic interview with the interviewer and relevant interventions, e.g., referral to the patient’s general practitioner or a psychiatric department, depending on the severity of symptoms, were initiated if the patient was diagnosed with moderate/severe depression or anxiety.

Data analysis

PHQ-9 was evaluated in relation to depression, GAD-7 in relation to anxiety, while Kessler- 6 and SRQ were assessed regarding whether one of the two conditions were present. Following this comparison, it was possible to compare the scoring values from each instrument with the presence of moderate/severe anxiety and depression diagnosis and construct Receiver Operating Characteristic (ROC) curves (34). The reference group was individuals without anxiety and depression.

The ROC- curves were used together with the area below the curves to determine the cut-off score with the optimal sensitivity and specificity for prediction of diagnose of moderate/severe anxiety or depression. The area below the curves (AUC) can be interpreted as follows: No informative value (AUC = 0.5), low accuracy ($0.5 < \text{AUC} \leq 0.7$), moderate accuracy ($0.7 < \text{AUC} \leq 0.9$), high accuracy ($0.9 < \text{AUC} < 1$) Perfect accuracy (AUC = 1) (35). The AUCs were compared using Stata’s function “roccomp”, which has implemented the method described by DeLong, DeLong and Clarke-Pearson (36). Youden’s index was calculated to assess the optimal cut-point for each instrument (37).

A description of patient characteristics according to the seven problem areas in ASI was performed. Wilcoxon rank test and Pearson's chi-square test were used when comparing no/mild anxiety/depression with moderate anxiety/depression, and the significant level was set to $p < 0.05$.

Ethical considerations

The study was accepted by the National Data Security Authorities (nr. 19/406). The Scientific Ethical Committee decided that the study did not need approval (nr. 20182000-164). The participating patients gave their consent to participate after having received information both verbally and in writing and was given the opportunity to ask questions and receive all the information that they felt they needed before accepting to participate.

Results

A total of 73 participants reported having experienced severe anxiety or depression during the ASI interview. According to PHQ-9, 32 had a positive test for depression (17 (53.1%) were false positive), according to GAD-7, 32 had a positive test for anxiety (22 (34.4%) were false positive), according to Kessler-6, 41 had a positive test for depression or anxiety (14 (34.1%) were false positive), and according to SRQ, 49 had a positive test for depression or anxiety (20 (40.8%) were false positive). Based on the diagnostic PSE-interview, 33 patients (45.2%) were diagnosed with moderate anxiety or depression, and none with severe depression or severe anxiety, including 13 patients (39.4%) in treatment for their mental health illnesses (Table 1). A total of 20 patients (27.4 %) were diagnosed with moderate depression; three of these patients were also diagnosed with moderate anxiety symptoms. Four patients (5.5%) were diagnosed with subclinical depression symptoms.

(Place table 1 approx. here)

Sixteen patients (21.9%) were diagnosed with moderate anxiety and seven (9.5%) with mild anxiety. The moderate anxiety disorders included social phobia (seven patients), panic disorder (three patients) and generalized anxiety (six patients). The patients diagnosed with depression or anxiety scored significantly higher on the ASI-composite score for mental health problems, compared to patients without anxiety/depression, indicating a higher level of mental health problems ($p = 0.009$).

The AUC for PHQ-9 (moderate depression) was 0.767, and the AUC for GAD-7 (moderate anxiety) was 0.630, (Figure 1). Table 2 shows the sensitivity and specificity for PHQ-9 and GAD-7.

Youden's index showed that a cut-off score of 14 or above on the PHQ-9 led to the best balance between sensitivity (0.74) and specificity (0.68) when identifying patients suffering from moderate

depression. A GAD-7 score of 10 or above led to the best balance between sensitivity (0.66) and specificity (0.62).

(Place figure 1 and table 2 approx. here)

The AUC for Kessler-6 and SRQ (moderate anxiety/depression) was 0.793 and 0.698, respectively; the difference between the two was significant ($P=0.042$) (Figure 2).

(Place figure 2 approx. here)

The sensitivity and specificity for the Kessler-6 and SRQ are presented in table 3. Youden's index indicates that a cut-off score of 10 or above for the Kessler-6 scale leads to the best balance between sensitivity (0.82) and specificity (0.65) when identifying patients with anxiety/depression. The optimal score at the SRQ-scale is eight, corresponding to a sensitivity of 0.89, a specificity of 0.50.

(Place table 3 approx. here)

Relying solely on information from the ASI-interview questionnaire to identify patients relevant for further assessment, all 73 patients should be further assessed to identify the 33 patients with depression or anxiety disorder (45%). Kessler-6 performed best of the four instruments. Implementation of the Kessler-6 scale would lead to 41 patients of the 73 (56%) testing positive; patients, who should thus be further assessed. Among those, 14 patients would not suffer from moderate anxiety/depression. Among the 33 patients diagnosed with anxiety or depression according to ICD-10 would lead to 27 the 33 patients in the study (82%) being correctly identified as suffering from anxiety/depression, while 6 of the patients (18%) would not be recognized (false negative).

Discussion

The present study is the first to examine screening instruments for the identification of depression or anxiety of a clinically meaningful severity, e.g. severity deeming referral to further treatment, among patients in outpatient treatment for alcohol use disorders.

PHQ-9

The cut-off score for PHQ-9 of 14 based on the optimal sensitivity (0.74) and specificity (0.68) in the present study was somewhat higher than found in other studies performed in the field of addiction. The scale was tested on 103 out-patients suffering from drug use disorder, most of them using multiple substances and receiving substitution treatment at the time of the study. A total of 77 patients

(74.7%) were diagnosed with depression. A PHQ-9 score of 12 and above was found to have the optimal sensitivity (0.81) and specificity (0.75) to identify clinically meaningful depression (38).

GAD-7

In our study, the AUC of the GAD-7 scale (0.630) was less precise than found in other studies. A meta-analysis including GAD-7 demonstrated that AUC for anxiety was between 0.65 to 0.72 (27). In a study of 103 patients suffering from substance use disorders (both alcohol and illegal drugs) and seeking outpatient treatment, AUC was found to be 0.88 for the identification of anxiety, and for a score of 9 or above, the sensitivity was found to be 0.80 and specificity 0.86 (39). In the present study, the cut-off was 10 with sensitivity of 0.66 and specificity of 0.62. It should be noted that most of the patients in the Delgadillo study (94%) were currently using drugs and/or alcohol compared to the patients in the present study where participants solely had an AUD, were not drinking above recommended guidelines (if drinking at all) and were excluded if any other substance abuse disorder.

Kessler-6

The Kessler-6 scale is previously evaluated among 71 individuals suffering from AUD and receiving acute treatment. It was found that a score of 10 or above resulted in the best balance between sensitivity and specificity when identifying anxiety and depression (40). The cut-off score in our study was similar (cut-off = 10). Similarly, our study corresponded to the findings of a study performed among a group of patients seeking treatment for substance use disorders, including AUD, with an AUC equal to 0.84 (slightly higher compared to the AUC of 0.793 in the present study), and an optimal cut-off score for anxiety and depression again at 10 points (20).

Our study indicates that the implementation of the Kessler-6 in a daily routine would lead to most of the patients being correctly identified as suffering from anxiety or depression, while less than one in five would not be recognized (i.e., being false-negative).

SRQ

The SRQ scale has been investigated in an Australian study of patients receiving outpatient treatment for substance misuse (41). The study found that an SRQ score of 4 and above identified patients with substance use who also suffered from depression and anxiety symptoms with a sensitivity of 0.81 and a specificity of 0.84, compared to 0.89 and 0.50, respectively, in the present study. The cut-off was

much higher in our study (cut-off = 8), but comparable to other studies reviewed by Harpham et al. (30).

ASI

You could argue that ASI is used as screening instrument, and indeed, participants were asked if they experienced severe depression or anxiety. However, as the ASI is based on one question only and is examining the patients' own general experience and feeling of depression or anxiety, almost half of all patients seeking treatment (45%) would be false positive and be referred to further examination. Thus, in our view, not suitable for more specific screening.

To summarize, we found different sensitivities, specificities, and cut-off values compared to other studies. We think this is mainly because of study populations, as other studies have had broader inclusion criteria, thus including patients with both AUD and/or other substance use disorders or allowing inclusion of patients in the withdrawal phase.

Limitations

When interpreting the results of the four instruments, it must be noted that the order of the instruments was fixed (PHQ-9 – GAD-7 – Kessler-6 – SRQ). All four instruments have been validated separately in other settings, but when presenting all four instruments sequentially to the same patient it may introduce some cognitive bias. That is, the wording of an item in one instrument may influence the completion of a similar item in another instrument, “anchoring” when making decisions (42).

The severity of anxiety was not assessed by a validated scale but based on the clinicians conducting the PSE interview, and this may have introduced some bias.

Finally, when evaluating the four screening instruments included in this study, it must be noted that only patients reporting an experience of depression or anxiety were examined further with the instruments and we have no data on patients not reporting severe depression or anxiety, thus it is a selected group, and this must be viewed as a limitation.

Our study indicates that the implementation of the Kessler-6 in a daily routine would lead to most of the patients being correctly identified as suffering from anxiety or depression, while less than one in five would not be recognized (i.e., being false-negative). The Kessler-6 does not differentiate between the two diagnoses. However, since it is a screening only, the patients who screen positive may be

referred to a full diagnostic evaluation, where it will be clarified if the patients are suffering from anxiety, depression, or both.

Conclusion

Our study indicates that the Kessler-6 scale with a cut-off score of 10 or above can be used for screening for anxiety/depression among patients suffering from AUD and seeking outpatient treatment. The scale is short and easy for patients to administer and, thus, timesaving for the staff. The Kessler-6 does not differentiate between anxiety and depression. However, since it is a screening only, the patients who screen positive should be referred to a full diagnostic evaluation, where it will be clarified if the patients are suffering from anxiety or depression to a degree deeming treatment. Since this is the first time the screening instrument have been tested in homogeneous treatment-seeking groups, suffering from AUD (albeit currently abstinent or consuming alcohol within recommended limits), the screening instrument should be tested further in similar studies to ensure that the findings are consistent.

Data Availability

The data that support the findings of this study are available from the corresponding author, KA, upon reasonable request.

Conflict of interest/Disclosure statement

None of the authors has any conflict of interest.

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Figure 1. ROC curves for PHQ-9 moderate depression disorders (n=20) and GAD-7 moderate anxiety disorders (n=16)

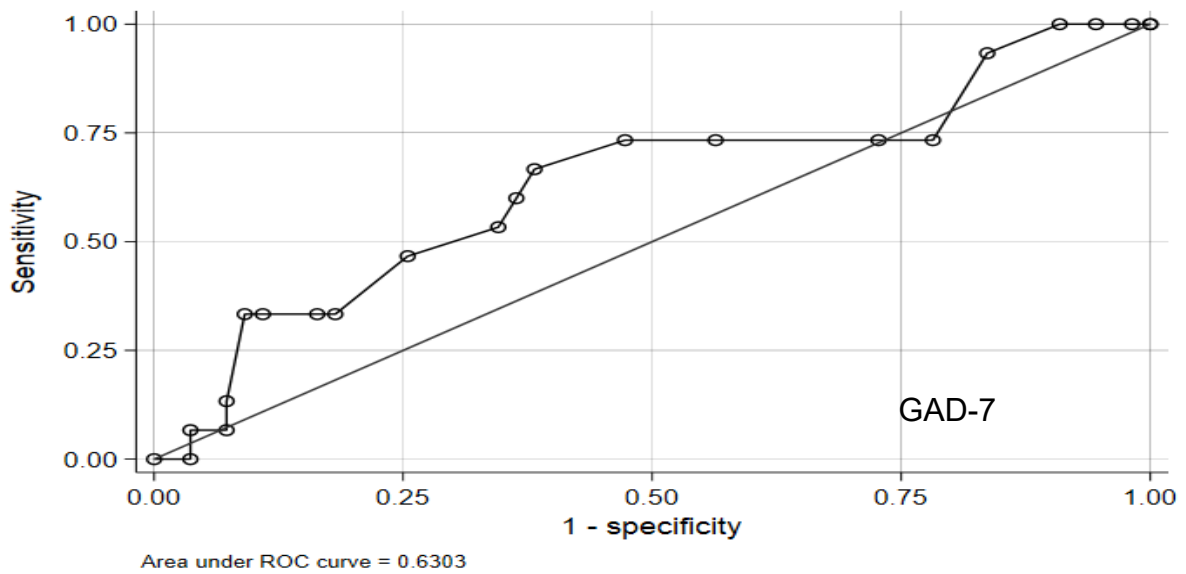
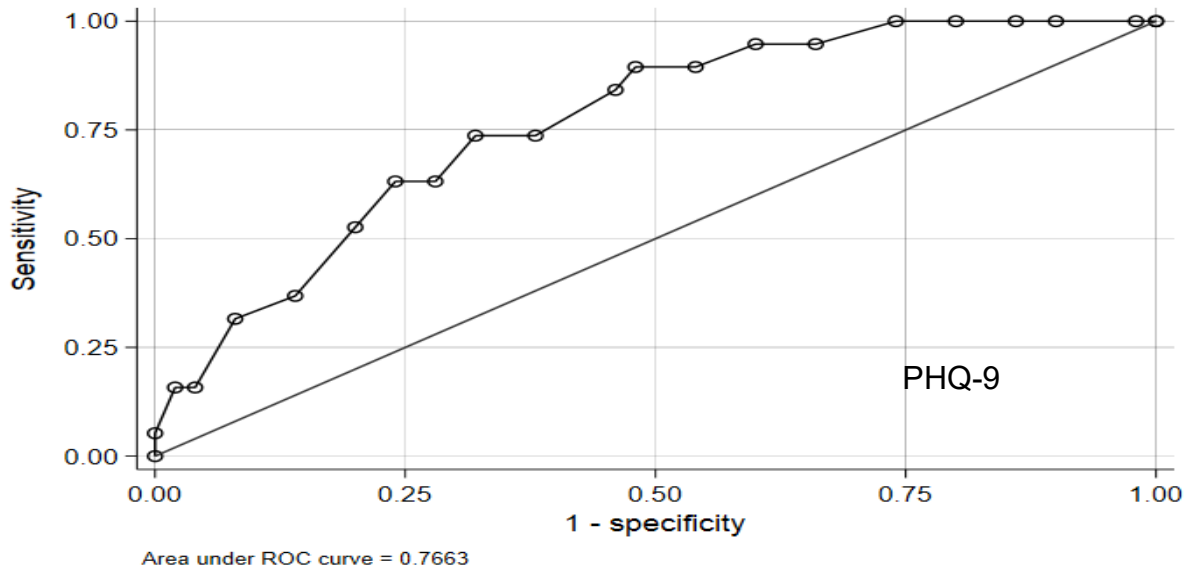
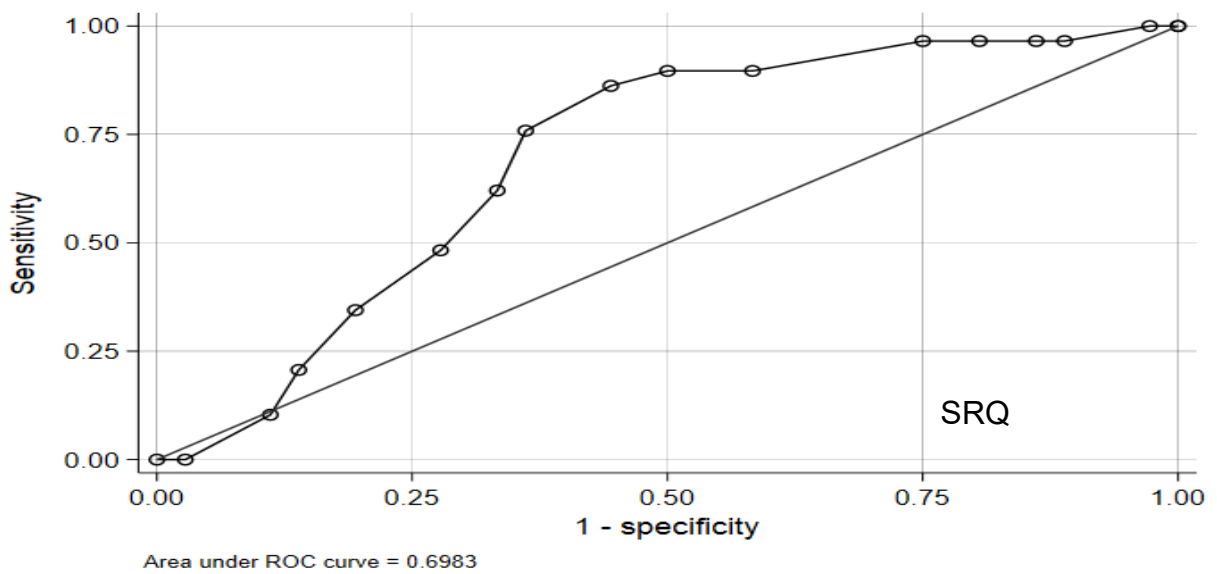
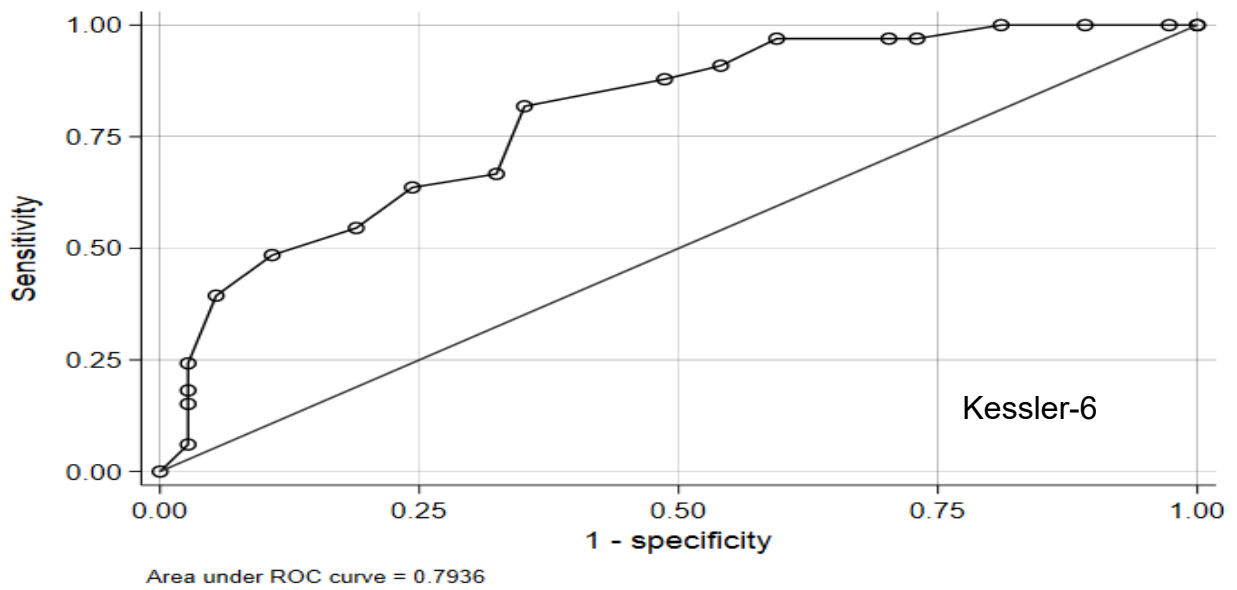


Figure 2. ROC curves for Kessler-6 and SRQ in screening for mixed moderate anxiety and depressive disorders (n=33)



AUC: Kessler -6 versus SRQ, P=0.0419

Table 1. Baseline characteristic

Sociodemographic	Mild or no anxiety/depression (n=40)	Moderate Anxiety/depression (n=33)	Sig.
Female %(n) ²	40 % (16)	24.2 % (8)	0.154
Age (Mean (sd)) ¹	49.0 (14.0)	48.9 (13.4)	0.859
Marital status (Living together) % (n) ²	42.5% (17)	42.4% (14)	0.995
Somatic health			
ASI-Composite score ^a Mean (sd) ¹	0.271 (0.34)	0.268 (0.34)	0.472
Employment			
ASI-Composite score ^a Mean (sd) ¹	0.227 (0.30)	0.321 (0.37)	0.423
Alcohol related			
Alcohol debut – Age (Mean (sd)) ¹	15.5 (3.3)	15.2 (2.2)	0.834
Abuse debut – Age Mean (sd) ¹	28.8 (11.7)	30.8 (13.1)	0.564
ASI-Composite score ^a Mean (sd) ¹	0.695 (0.22)	0.651 (0.20)	0.250
Drug related			
ASI-Composite score ^a Mean (sd) ¹	0.020 (0.06)	0.024 (0.06)	0.519
Legal problems			
ASI-Composite score ^a Mean (sd) ¹	0.025 (0.09)	0.018 (0.07)	0.867
Family, social			
ASI-Composite score ^a Mean (sd) ¹	0.120 (0.23)	0.106 (0.24)	0.606
Mental health			
Days with problems within the last 30 days Mean (sd) ¹	8.4 (11.7)	21 (11.8)	0.000
ASI-Composite score ^a Mean (sd) ¹	0.234 (0.20)	0.355 (0.16)	0.009
Use of medicine for mental health problems during the last 30 days (yes) %(n)	30.0% (19)	39.4% (13)	0.400

¹Wilcoxon ranksum²Peasons chi-square

a) Based on Addiction Severity Index – composite score. Scores vary from 0 (no problem) to 1 (extreme problem) in preceding 30 days.

Table 2. Selected scales' score for identifying patient with moderate anxiety or depression disorders: Area under the curve (AUC), sensitivity, specificity and Youden's index at different cut-off scores.

Scales	AUC	Cut-off	Youden's index %	Sensitivity % (95 % CL)	Specificity % (95 % CL)
GAD-7	0.630	≥ 8	0.26	0.73 (0.48-0.89)	0.53 (0.38-0.65)
		≥ 9	0.28*	0.66 (0.42-0.85)	0.62 (0.49-0.73)
		≥ 10	0.23	0.60 (0.35-0.80)	0.63 (0.50-0.75)
		≥ 11	0.18	0.53 (0.30-0.75)	0.65 (0.52-0.76)
PHQ-9	0.767	≥ 11	0.41	0.89 (0.68-0.97)	0.52 (0.39-0.65)
		≥ 12	0.38	0.84 (0.62-0.94)	0.54 (0.40-0.67)
		≥ 13	0.36	0.74 (0.51-0.88)	0.62 (0.48-0.74)
		≥ 14	0.42*	0.74 (0.51-0.88)	0.68 (0.54-0,79)

*) cut-off score with maximum Youden index (i.e., best trade-off between sensitivity and specificity)

Table 3. Selected scales score for identifying patient with mixed moderate anxiety and depression disorders: Area under the curve (AUC), sensitivity, specificity and Youden's index at different cut-off scores.

Scales	AUC	Cut-off	Youden's index %	Sensitivity % (95 CL)	Specificity % (95 CL)
SRQ	0.698	≥ 7	0.32	0.90 (0.73-0.96)	0.42 (0.27-0.58)
		≥ 8	0.46*	0.89 (0.73-0.96)	0.50 (0.34-0.66)
		≥ 9	0.42	0.86 (0.69-0.94)	0.56 (0.39-0.70)
		≥ 10	0.40	0.76 (0.57-0.87)	0.64 (0.47-0.77)
Kessler-6	0.793	≥ 9	0.39	0.87 (0.72-0.95)	0.51 (0.33-0.63)
		≥ 10	0.45*	0.82 (0.66-0.91)	0.65 (0.45-0.73)
		≥ 11	0.34	0.67 (0.50-0.80)	0.67 (0.48-0.76)
		≥ 12	0.40	0.64 (0.47-0.78)	0.76 (0.55-0.82)

*) cut-off score with maximum Youden index (i.e., best trade-off between sensitivity and specificity)