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Which is the Optimal Depression Rating Scale to Identify DSM-IV Depression in Schizophrenia?

A Diagnostic Validity Comparison of Five Mood Scales

Twana Abdulrahman Rahim, Zerak Masud Al-Salihy, Mahmood Qasim Mahmood, Asma Subhi Muhyaldin, Alex J Mitchell

ما هو مقياس الكابة المثالي لأيجاد الكابة حسب الدليل (DSM-IV) لدى المصابين بالفصام؟ مقارنة التشخيصي و الأحصائي الرابع الصلاحية التشخيصية لخمس مقاييس المزاج

توانا عبد الرحمن رحيم ، زيرك مسعود الصالحي ، محمود قاسم محمود، أسماء صبحي محي الدين ، أليكس متشل

Abstract

Objectives: To find a brief semi-structured or self-report depression rating scale with the highest accuracy for a diagnosis of DSM-IV defined depression in patients with schizophrenia from Iraqi-Kurdistan. **Methods:** 200 people with schizophrenia living in the Kurdistan Region of Iraq were recruited. The Mini International Neuropsychiatric Interview (MINI) was used to define the presence of schizophrenia; depression was further defined according to DSM-IV criteria. Symptoms of depression were examined using five scales: the Patient Health Questionnaire (PHQ2, PHQ9), Hospital Anxiety and Depression Scale (HADS), the Centre for Epidemiological Studies Depression scale (CES-D) and the Calgary Depression Scale for Schizophrenia (CDSS). Three psychiatrists conducted interviews and rated the Clinical Global Impression (CGI). ROC curve analysis was used to establish the optimal cut-off as well as comparative sensitivity and specificity. **Results:** Eighty (40%) patients had DSM-IV major depression and 97 (48.5%) had major or minor depression; 157 (78.5%) had at least two DSM-IV symptoms of depression. Comparing the five scales for identification of depression showed the optimal methods for detection of major depression (against non-major depression) were the PHQ9 > PHQ2 > CDSS. Against major depression the PHQ9 was the most accurate method with a sensitivity of 93.8% and a specificity of 84.2%. Optimal methods for detection of major or minor depression (against no depression) were the PHQ2 > PHQ9 > CDSS. The PHQ2 had a sensitivity of 85.6% and a specificity of 96.1%. **Conclusion:** Self-report scales, particularly the PHQ2 and PHQ9 appear to perform well against DSM-IV defined depression in schizophrenia. Further validation against non-DSM-IV standards is recommended.

Keywords: Schizophrenia, depression scale, screening diagnostic validity

Declaration of Interest: None

Introduction

Depression in schizophrenia is a common and challenging clinical problem. The prevalence of depression in patients with schizophrenia is reported to range between 7% and 75% depending on the method of assessment.[1-7] Rates for major and minor depression combined are poorly studied, but may reach 59%.[8] Minor depression and sub-syndromal symptoms of depression are increasingly recognized as important.[9] Indeed, symptoms of depression are very common in those with psychoses; identified in 71% in one study which also found that 23% fulfilled the ICD-10 depression criteria.[10] Comorbid depression in schizophrenia is an important clinical factor influencing clinical outcome. Such patients have higher relapse rates than patients without symptoms of depression,[2, 11] extended hospitalization,[12] greater cognitive impairment,[13] poor social functioning,[14,16] an increased risks of suicide,[17,20] and poorer quality of life. [21]

Criteria for Depression in Schizophrenia

There is still uncertainty about how best to define comorbid depression in schizophrenia. In recent operational checklists, depression has been defined as post-psychotic depression (ICD-10) and post-psychotic depressive disorder (DSM-IV). However it is clear that depression occurs not only in the post-psychotic phase, but in phases of schizophrenia.[1,22,24] Lancon et al. (2001) found that 52% had depression in the acute psychotic phase and 38% during more stable periods of the disease.[25] ICD-10 has specific diagnostic criteria for post-schizophrenic depression limiting the diagnosis of depressive episode to the 12 months following the psychotic episode. DSM-IV does not require any specific features for post-psychotic depressive disorder other than to exclude depressive

symptoms that are better accounted for as medication side effects or negative symptoms.[26] DSM-IV also suggests that it occurs only during the residual phase of schizophrenia and is not due to the direct physiological effects of a substance abuse;[26] however, such findings are subject to individual clinician judgment.

Scales to measure depression in schizophrenia

Various methods have been utilized to help clinicians assess depression in patients with schizophrenia. Examples of self-report scales include the Beck Depression Inventory (BDI)[27] and the Hospital Anxiety and Depression Scale (HADS).[28] Observer rated scales have also been used such as the Hamilton Rating Scale for Depression (HAM-D).[29] None of these instruments were specifically developed for this population and like all tools may theoretically be influenced by other clinical factors, such as negative psychotic symptoms and extrapyramidal symptoms (EPS). For example, the HAM-D has been shown to be influenced by negative symptoms and EPS in schizophrenia, according to most, (Craig et al., 1985; Goldman et al., 1992; Collins et al., 1996; Kontaxakis et al., 2000; Yazaji et al., 2002)[30,34] but not all studies.[35] In 1990, Addington and colleagues developed a customized scale, the Calgary Depression Scale for Schizophrenia (CDSS), based on items selected from the HAM-D and the Present State Examination,[36] which had reasonable ability to distinguish between depression, negative symptoms and EPS.[37] The CDSS has a unique format with eight semi-structured questions rated on a four-point scale and one purely observer based item (item nine). The CDSS has been shown to be a reliable, valid, and specific measure of depression in patients with schizophrenia.[37]A limitation of many scales, however, is that they are too lengthy or impractical for routine clinical use. Recently a number of short self-report instruments have been extensively validated in primary care and hospital settings. Examples include the two and nine item Patient Health Questionnaire and the seven item HADS-Depression subscale.

Given these developments in screening for depression, our aim was to find the optimal tool with the highest accuracy in comparison to DSM-IV defined major depression and DSM-IV defined major or minor depression.

Methods

Sample and patients

Recruitment involved a non-probability, purposive sample of schizophrenic patients who visited both inpatient and outpatient clinics in the psychiatric unit of the largest teaching hospital and two health centres that provided out-patient psychiatry services in Erbil between the period of April 2009 and March 2010. The process was undertaken by three trained psychiatrists among the authors.

Patients with schizophrenia were identified with the Mini International Neuropsychiatric Interview (MINI). Within this group, we used DSM-IV criteria for major depression and minor depression without assumptions of causation or phase of illness. We wished to clarify which scales most accurately identified the presence of depression as comorbidity, regardless of opinions about the origin of the depressive symptoms. We did not require the exclusion of cases who were not in the residual phase of schizophrenia. None of the patients had a history of drug use at the time of interview.

Tools

The following scales were used: CES-D; PHQ9; HADSD and CDSS. The CES-D scale (Radloff 1977) is a 20item self-report scale designed to measure depressive symptoms in the general population.[38] It was found to have a high internal consistency and adequate test-retest repeatability when tested in household interview surveys and in psychiatric settings. The PHQ-9 is the nine item depression scale of the Patient Health Questionnaire[39] based directly on the diagnostic criteria for major depressive disorder in the DSM-IV. It is viewed as a potentially valuable tool for assisting primary care clinicians in diagnosing depression as well as selecting and monitoring treatment. The HADS-D is the depression subscale of the HADS, a 14 item self-report scale[28] which has been extensively used by hospital and primary care patients with and without somatic symptoms. It has equally good sensitivity and specificity as other commonly used self-rating screening instruments.[40] As mentioned above the CDSS has been evaluated widely in patients with schizophrenia.[41] All questionnaires applied in the present study were translated into Kurdish since all participants were Kurds. These were then back translated into English by a linguistic expert who was blind to the original English versions. Validities of translated versions were confirmed by a team of ten experts in the field before distributing them to participants.

Analysis

ROC curve analysis was used for each scale against an interview standard diagnosis of depression based on the MINI. In addition, we calculated the optimal sensitivity, specificity and Positive Predictive Value (PPV) and Negative Predictive Value (NPV).

Results

Eighty (40%) patients had DSM-IV major depression and 97 (48.5%) had major or minor depression; 157 (78.5%) had at least two DSM-IV symptoms of depression.

Performance of the PHQ2

Against major depression the PHQ2 was very accurate with a sensitivity of 86.3% and a specificity of 85%. Overall accuracy was 85.5% with an AUC of 0.921. Against major or minor depression the PHQ2 was the most accurate method with a sensitivity of 85.6% and a specificity of 96.1% and an overall accuracy of 91.0%. It achieved excellent accuracy for both rule-in and rule-out of depression in schizophrenia.

Performance of the PHQ9

Against major depression the PHQ9 was the most accurate method with a sensitivity of 93.8% and a specificity of 84.2%. Overall accuracy was 88% with an AUC of 0.957. It had the best case-finding and best screening properties. Against major or minor depression the PHQ9 was the second most accurate method with good sensitivity and specificity (80.4% and 84.5%, respectively). The optimal cut-off point was >=14.

Performance of the CES-D

Against major depression the CESD was modestly accurate with better rule-out than rule-in properties. It achieved a low sensitivity of 67.5%, but with a specificity of 86.7%. Overall accuracy was 79.0% with an AUC of 0.845. Against major or minor depression the CESD was modestly accurate with a good sensitivity of 81.4%, but with a specificity of only 64.1%. Overall accuracy was 72.5% with an AUC of 0.804. The optimal cut-off point was >=24.

Performance of the HADS

Against major depression the HADS-D was not particularly accurate and although sensitivity was 95%, specificity was only 35%. Overall accuracy was 59.0% with an AUC of 0.525. It was neither good in casefinding nor in screening for depression in schizophrenia. Similarly against major or minor depression the HADSD was not accurate with a low specificity of only 29.1%. Overall accuracy was 60.5% (AUC 0.505).

Performance of the CDSS

Against major depression the CDSS was fairly accurate particularly in rule-out (screening). It had a sensitivity of 68.8% and a specificity of 89.2%. Overall accuracy was 81% with an AUC of 0.822. Against major or minor depression the CDSS was modestly accurate with a sensitivity and specificity of 76.3% and 79.6% respectively. Overall accuracy was 78% with an AUC of 0.824. The optimal cut-off point was calculated as >=6, although a higher threshold of >=9 was suggested for the diagnosis of major depression alone.

Discussion

We aimed to find a brief semi-structured or self-report depression rating scale with high accuracy in the diagnosis of DSM-IV defined depression in patients with schizophrenia from Kurdistan Region of Iraq. We used a broad DSM-IV definition of major depression as well as major or minor depression (combined) without assumption of causality. This has the advantage of highlighting depression comorbidity in any form that might occur. Using this method we found a high rate of comorbidity in the present sample; indeed, 78.5% had at least two DSM-IV symptoms of depression; 48.5% qualified as having either major or minor depression, and 40% had DSM-IV major depression. Thus minor depression alone was relatively uncommon, seen in only 8.5%.

Comparing five well known scales for the identification of depression showed that the optimal methods for detection of major depression (against non-major depression) were the PHQ9 > PHQ2 > CDSS. The optimal methods for detection of major or minor depression (against no depression) were the PHQ2 > PHQ9 > CDSS. Looking in more detail, rule-in and ruleout accuracy was consistently good or excellent for PHQ9 and PHQ2, but no other scales achieved this level of performance. The HASD-D was the only scale that was rated as qualitatively poor, especially in a rule-out capacity. The superior performance of the PHQ might be expected when the criterion reference under study is DSM-IV defined depression as the PHQ9 asks the same questions required by DSM-IV

for a diagnosis. Definitions of both major and minor depressions require that one of two core symptoms (low mood or loss of interest) are present. It would be interesting to define depression according to ICD-10 criteria and repeat the study. It would also be interesting to use a strict definition of post-psychotic depression and see if performance of the scales differs. Our study appears to be the first to examine the PHQ and the CESD in the context of depression in schizophrenia. The superior performance of the PHQ is attractive particularly given the brevity of the PHQ2. However, this requires confirmation ideally against ICD-10 criteria. If one excludes the PHQ because of symptom overlap with DSM-IV criteria then it appears that the CDSS is the next best scale.

Previous studies involving the CDSS have largely compared it with PANS positive and negatives symptom profile, but rarely against any gold standard for depression.[34,36,42,43] These have generally demonstrated that the CDSS is able to distinguish depression from negative psychotic symptoms and EPS, but there has been inconsistent relationship between the CDSS and positive symptoms in schizophrenia[44,46] Further, in our view it is the ability of a scale to identify the core concept of depression that is important rather than its relationship with possible confounding factors. In this regard, Addington et al. (1994) found that a score above six points on the CDSS may best separate patients with schizophrenia and depression from those with schizophrenia alonel.[37] However, in the present study we found a cut-off point of 8v9 was optimal. Bressan et al. (1998) found that cut-off values of 4v5 were recommended in order to detect minor depression in schizophrenia patients,[45] which was similar to our optimal threshold of 5v6. To date, only a handful of head-to-head comparisons of depression scales in schizophrenia have been conducted and none have considered the advantages of self-report or semistructured scales without requiring observer judgment. Lancon et al. (2000)[43] examined 95 patients with schizophrenia according to DSM-III-R criteria and the CDSS, Hamilton Depression Rating Scale (HDRS), Montgomery and Asberg Rating Scale (MADRS), and Widlocher Psychomotor Retardation Scale (ERD). There was no criterion standard in this study, but the authors did find high inter-correlations with other depressionrating scales. Kim et al. (2006) studied 84 inpatients meeting the DSM-IV criteria for schizophrenia using four scales: CDSS, BDI, HAM-D and PANSS[46]. The areas under the Receiver Operating Characteristic (ROC) curves using DSMIV major depression as the criterion was 0.94, 0.89, 0.90, and 0.81, respectively for the CDSS, HAM-D, PANSS-D, and BDI. Liu et al. (2009) studied 101 inpatients meeting the DSM-IV criteria for schizophrenia and DSM-IV major depression criteria. They examined the CDSS, MADRS, HAM-D and PANSS-D. The areas under the receiver operating characteristic curves of the CDSS, HAM-D, MARDS, and PANTSS-D were 0.954, 0.881, 0.828, and 0.897, respectively.[47] Thus, two smaller previous studies have examined the CDSS and found higher AUC than that documented here (0.822).

We acknowledge several limitations to the present study. We could not differentiate co-morbid depression with schizophrenia from 'post-psychotic' depression. This shortage in our study might be due to our being bound by the MINI when diagnosing schizophrenia, through which there is no obvious place to differentiate the 'psychotic' from 'post-psychotic' phases. Furthermore, we did not measure phase of illness or positive or negative symptoms in schizophrenia; therefore, no analysis of these subgroups was possible. We acknowledge that tools may perform differently in these subgroups. As previously mentioned we kept an intentionally broad definition of depression without assumption of aetiology or other restrictions. This could be seen as both a study strength and study weakness. A fundamental question not addressed here is whether the symptom profile of DSM-IV is ideal for diagnosing depression in the context of psychosis. This is a difficult question to address and re-defining the criterion standard requires a fundamental objective measure tightly associated with comorbid depression in schizophrenia. To our knowledge, no study has attempted this although some studies have begun to examine if symptoms of depression may differ in schizophrenia with comorbid depression from the classical primary depression.[48] Moreover, questionnaires applied in the present study were designed primarily for cultures with high-income societies that possibly differ from the Iraqi-Kurdish society. Cross-culturally validated questionnaires might fail to assess possible different phenomenological expressions of disorders. Nevertheless, we found this method the most feasible means of assessment until a future culturally-specific way of assessment can be delivered.

In conclusion, in a sample of 200 individuals with schizophrenia, we found a high prevalence of broadly defined DSM-IV depression and very high rates of symptoms of depression. Comparing five well-known scales for the identification of depression demonstrated that the optimal methods for detection of depression (against non-major depression) were self-report, namely the PHQ9 and PHQ2. We suggest further validation of these findings should be attempted against ICD-10 criteria and in different phases of schizophrenia.

Fig 1. ROC Curve of five depression scales against DSM-IV major depression in schizophrenia

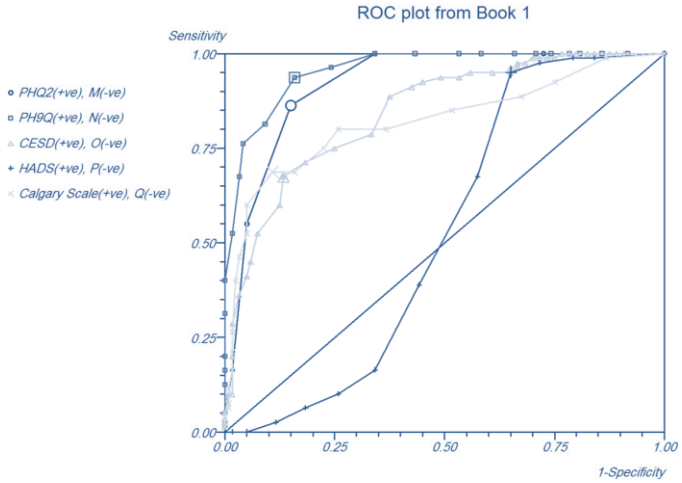

Fig 2. ROC Curve of 5 Depression Scales against DSM-IV major or minor depression in schizophrenia

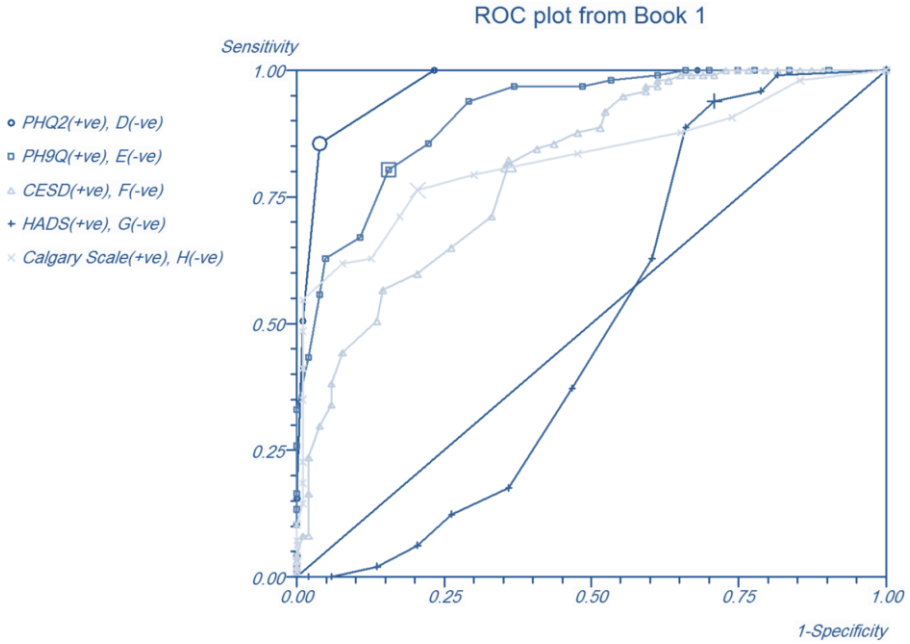

Table 1: Demographics of the sample

	Mean (SD)
Age	31.8 (10.5)
Male	148 (74%)
Unemployed	18 (9%)
Education (secondary or higher)	88 (44%)
Married	23 (11.5%)
Single	137 (68.5%)

Table 2: Correlation matrix for self-report scales

	PHQ2	**PH9Q**	**CESD**	**HADS**	**CDSS**
PHQ2	1				
PH9Q	0.760582	1			

	PHQ2	PH9Q	CESD	HADS	CDSS
CESD	0.563995	0.86176	1		
HADS	-0.01439	0.280424	0.454264	1	
CDSS	0.766872	0.734336	0.641409	0.068959	1

Table 3: Summary of accuracy of scales

Test	Optimal Cut	AUC	Sensitivity	Specificity	PPV	NPV	Clinical Utility (+)	Clinical Utility (-)	Overall Correct
Major Depression									
PHQ2 (2 items)		0.921	86.3%	85.0%	79.3%	90.3%	0.684 [good]	0.767 [good]	85.5%
PHQ9 (9 items)	13v14	0.957	93.8%	84.2%	79.8%	95.3%	0.748 [good]	0.802 [good]	88%
CES-D (20 items)	27v28	0.845	67.5%	86.7%	77.1%	80.0%	0.521 [average]	0.693 [good]	79%
HADS-D (7 items)	3v4	0.525	95.0%	35.0%	49.4%	91.3%	0.469 [poor]	0.320 [poor]	59%
CDSS (9 items)	8v9	0.822	68.8%	89.2%	80.9%	81.1%	0.556 [average]	0.723 [good]	81%
Major or minor									
PHQ2 (2 items)		0.970	85.6%	96.1%	95.4%	87.6%	0.816 [excellent]	0.842 [excellent]	91%
PHQ9 (9 items)	13v14	0.913	80.4%	84.5%	83.0%	82.1%	0.667 [good]	0.693 [good]	82.5%
CES-D (20 items)	23v24	0.804	81.4%	64.1%	68.1%	78.6%	0.555 [average]	0.503 [average]	72.5%
HADS-D (7 items)		0.505	93.8%	29.1%	55.5%	83.3%	0.521 [average]	0.243 [poor]	60.5%
CDSS (9 items)	5v6	0.824	76.3%	79.6%	77.9%	78.1%	0.594 [average]	0.622 [average]	78%

AUC- Area under receiver operator characteristic curve. PPV – Positive predictive value. NPV - Negative predictive value. UI - Clinical utility index. The positive utility index (UI+ = sensitivity x PPV) measures rule-in value and the negative utility index (UI - specificity x NPV) measures rule-out value. The following qualitative grades of diagnostic accuracy have been applied to the clinical utility index were >= 0.81: excellent, >=0.64: good and >=0.49: average <0.49 = poor.[49]

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الملخص

الأهداف: هدفت هذه الدراسة لايجاد مقياس شبه منظم مختصر أو مقياس تسجيل- ذاتي ذو دقة عالية لتشخيص الكآبة حسب مقياس الدليل التشخيصي و الأحصائي الرابع (DSM-IV) لدى مرضى الفصام. الطرق: تمت دراسة 200 مريض مصاب بالفصام في أقليم كوردستان العراق. تم الاعتماد على مقياس (ميني) لتشخيص الفصام والكآبة بالإضافة الى الرجوع لمقياس الدليل التشخيصي و الأحصائي الرابع(DSM-IV) لتشخيص الكآبة. تم تقييم أعراض الكآبة من خلال خمس مقاييس معروفة Patient Health Questionnaire (PHQ-2)):و (Hospital Anxiety and Depression Scale -9) (PHQ)، و (Calgary Depression Scale for Schizophrenia (CDSS)). التقييم تم بواسطة ثلاث أطباء نفسانين والذين قاسوا ايضا انطباعهم السريري العام .(CGI) حللت النتائج مستخدمين (ROC curve) لتأسيس نقطة الفرق المثالي لتشخيص الكآبة، مع مقارنة الحساسية والنوعية الأحصائيتين بين المقاييس الخمسة. النتائج: 80(40%) من مرضى الفصام كانوا يعانون من الكآبة العظمى حسب (DSM-IV) و 97 (48.5%) من المرضى كانوا يعانون من الكآبة بشكل عام. 157 (78.5%) من المرضى كانوا يشكون من عرضين من أعراض الكآبة على أقل تقدير. عند مقارنة المقاييس الخمس، أظهرت الدراسة بأن المقياس المثالي لتمييز الكآبة العظمى من بقية انواع الكآبة هو كالتالي- .PHQ9>PHQ-2>CDSS :لتميز الكآبة العظمى، PHQ-9كان الأدق مع حساسية أحصائية (93.8%) و نوعية أحصائية (84.2%). أما بانسبة الى أيجاد الكآبة بشكل عام، فقد كان أداء المقاييس المثالية كالتالي .PHQ-2>PHQ-9>CDSS : امتاز PHQ-2 بحساسية و نوعية أحصائيتين (85.6%) و (96.1%) على التوالي. الأستنتاجات: تتميز مقاييس التسجيل-الذاتي، بشكل محدد مقياسا 2- PHQ و PHQ-9 بأداء جيد لتشخيص الكآبة حسب (DSM-IV) لدى المصابين بالفصام. هذه النتائج تدعو الى تأكيد مصداقياتها عند قياس الكآبة بمقاييس أخرى غير.(DSM-IV) .

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