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## A systematic review of instruments to measure depressive symptoms in patients with schizophrenia

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# Journal of Affective Disorders



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Review

# A systematic review of instruments to measure depressive symptoms in patients with schizophrenia

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#### ABSTRACT

Background: Depressive symptoms require accurate recognition and monitoring in clinical practice of patients with schizophrenia. Depression instruments developed for use in depressed patients may not discriminate depressive symptoms from negative psychotic symptoms. Objective: We reviewed depression instruments on their reliability and validity in patients with schizophrenia.

Methodology: A systematic literature search was carried out in three electronic databases. Psychometric properties were extracted for those instruments of which reliability, divergent, concurrent and predictive validity were reported in one or more publications.

Results: Forty-eight publications described the reliability and validity of six depression instruments in patients with schizophrenia. The only self-report was the Beck Depression Inventory (BDI). The Brief Psychiatric Rating Scale-Depression subscale (BPRS-D), Positive and Negative Syndrome Scale-Depression subscale (PANSS-D), Hamilton Rating Scale for Depression (HAMD), Montgomery Asberg Depression Rating Scale (MADRS) and Calgary Depression Scale for Schizophrenia (CDSS) were clinician rated. All instruments were reliable for the measurement of depressive symptoms in patients with schizophrenia. The CDSS most accurately differentiated depressive symptoms from other symptoms of schizophrenia (divergent validity), correlated well with other depression instruments (concurrent validity), and was least likely to miss cases of depression or misdiagnose depression (predictive validity).

Conclusions: We would recommend to use the CDSS for the measurement of depressive symptoms in research and in daily clinical practice of patients with schizophrenia. A valid selfreport instrument is to be developed for the use in clinical practice.

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#### 1. Introduction

Depressive symptoms are highly prevalent (25%) in patients with schizophrenia (Buckley et al., 2008; Siris and Bench, 2003). These comorbid depressive symptoms are associated with a higher burden of disease and more frequent relapses (Conley et al., 2007; Tollefson et al., 1999). Schizophrenia is a lifelong psychiatric disorder and depressive symptoms may occur through all phases of illness: during acute psychosis (Häfner, 2000; Leff et al., 1988) as well as after remission of psychosis (Birchwood et al., 2000). Recent literature suggests that depressive symptoms may also be understood as a dimension within the schizophrenia concept and that individual symptom profiles should guide treatment (Van Os and Kapur, 2009). Furthermore, the upcoming fifth edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) advocates to measure psychopathology in terms of quantitative dimensions, instead of solely as discontinuous categories (http://www. dsm5.org). Adequate screening and monitoring of depressive symptoms is required to guide appropriate treatment (Bressan et al., 2003; Lako et al., 2011; Schennach-Wolff et al., 2011).

Measurement instruments can be helpful for screening and for monitoring of symptomatic changes (Möller, 2009). The assessment of depressive symptoms is complicated in patients with psychotic disorders, as they resemble "classic" symptoms of schizophrenia, such as negative symptoms and extrapyramidal symptoms (EPS) (Barnes and McPhillips, 1995; Harrow et al., 1994; Siris and Bench, 2003; Van Putten and May, 1978). Particularly drug-induced parkinsonism may resemble a depressed state (Norman and Malla, 1991). It is doubtful whether instruments, primarily developed for use among depressed patients, are able to selectively discriminate depressive symptoms from other symptom dimensions in schizophrenia (divergent validity) (Allan and Martin, 2009; Fitzgerald et al., 2002). Currently there is no overview of available depression instruments and their psychometric properties in patients with schizophrenia.

This systematic review provides an overview of instruments that can be used for the screening on depressive symptoms (further referred to as "depression instruments"). Instruments are compared regarding their divergent validity and other psychometric properties in this patient population. This review may help in choosing a suitable instrument for the measurement of depressive symptoms in research as well as in daily clinical practice of patients with schizophrenia.

#### 2. Methods

#### 2.1. Search procedure

As a first step, titles and abstracts were screened on relevance for the defined topic and, if appropriate, the full paper was examined. Inclusion criteria were: 1) studies assessing psychometric properties of instruments measuring depressive symptoms in a population of patients with schizophrenia or non-affective psychotic disorders, 2) the availability of a validated English translation of the depression instrument and 3) publication in English, German, French or Dutch language. Unidimensional depression instruments (measuring a single dimension, in this case depressive symptoms), as well as multidimensions providing a subscale for depressive symptoms, were included. We refer to the depression subscale of a multidimensional instrument by the addition of [-D] to the abbreviation of the instrument, for example BPRS-D. We excluded studies describing diagnostic instruments and instruments designed to measure related symptoms, such as anxiety or suicidality.

The following search terms were entered in the online databases PubMed, Embase and PsychINFO: (("depression" or "depressive symptoms") and ("schizophrenia" or "psychosis" or "psychotic") and ("instrument" or "rating scale" or "scale" or "questionnaire" or "interview") and ("psychometric" or "reliability" or "validation" or "validity" or "reproducibility")). The search was carried out in May 2010. All retrieved studies were checked for cross-references.

#### 2.2. General information

General information about the most recent version of each instrument was collected from (original) validation studies and the Handbook of Psychiatric Measures. In order to quantify the recent use of the selected instruments in research, we counted the number of studies published between May 2005 and May 2010. The composition of each depression instrument was explored as follows. Each item of an instrument was categorized under one the nine diagnostic criteria for a Major Depressive Episode (MDE), defined by the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) (American Psychiatric Association, 1994). Remaining items were categorized under three additional symptom dimensions: "delusional ideas," "other vital symptoms" and "anxiety." Four of the nine diagnostic criteria for MDE show overlap with symptom dimensions of schizophrenia, in particular negative symptoms and extrapyramidal symptoms. For each instrument, the number of potentially overlapping items was divided by the total number of items. This illustrated the instruments' ability to discriminate depressive symptoms from other symptom dimensions of schizophrenia.

Psychometric properties were extracted for those instruments of which reliability, divergent, concurrent and predictive validity were reported in one or more publications. In the next paragraphs we explain these psychometric properties.

#### 2.3. Reliability

Reliability is generally estimated by internal consistency, inter-rater and test-retest reliability. Internal consistency reflects the coherence between items within an instrument. Corresponding Cronbach's alpha values of 0.60-0.70 are considered acceptable and values of > 0.70 as good (Cicchetti, 1994). Good inter-rater and test-retest reliability is reflected by little variation between the scores by different raters and, respectively, by repeated measurements; these are commonly expressed by intra-class coefficients (ICC) > 0.70.

#### 2.4. Divergent validity

Divergent (or discriminant) validity refers to the extent that different symptom dimensions are unrelated to each other. Here, an instrument designed to measure depressive symptoms, should not measure negative symptoms, EPS or anxiety as well. Divergent validity is commonly expressed by the Pearson's product moment correlation (PPMC) between scores on a depression instrument and scores on an instrument measuring another symptom dimension. Absent correlation with negative symptoms or EPS indicates good divergent validity. Nevertheless weak correlations (<0.30) are acceptable, as depressive symptoms tend to occur together with negative symptoms and EPS (Kulhara et al., 1989; Van Putten and May, 1978).

Divergent validity can also be evaluated on the stability of the underlying factor structure of a particular instrument across different samples. For multidimensional instruments, principal component factor analysis (PCA) should identify depressive symptoms as a separate factor from psychotic symptom dimensions. In addition, the content of this depression factor should remain stable by confirmatory factor analysis in different samples. PCA of unidimensional instruments in a population with schizophrenia should identify factors describing depressive symptom dimensions, but no psychotic symptom dimensions.

#### 2.5. Concurrent validity

Concurrent (or convergent) validity refers to the extent that common symptom dimensions are in fact related. Concurrent validity is high when the scores on two instruments measuring the same symptom dimension correlate well (PPMC). Based on the mean correlation of each possible comparison between two instruments, we calculated a pooled mean correlation over all comparisons for each instrument.

#### 2.6. Predictive validity

Predictive validity represents the accuracy of an instrument to correctly detect a case (here of depression). Included were publications using a validated diagnostic interview such as the Structured Clinical Interview for DSM-IV (First et al., 1995) as gold standard to identify positive cases of depression. Good predictive validity is reflected by high sensitivity (not likely to miss cases of depression) combined with high specificity (not likely to misdiagnose depression) at the optimal cut-off value, i.e. the best balance between sensitivity and specificity determined by area under the receiver operating curve methods (Hanley and McNeil, 1983).

#### 3. Results

#### 3.1. Inclusion of studies

The systematic search generated a total of 2642 articles, of which 57 publications were eligible for further evaluation (Fig. 1). For six depression instruments complete information on psychometric properties in a population with schizophrenia or psychotic disorders was described in forty-nine publications. These included two multidimensional instruments: the Brief Psychiatric Rating Scale, Expanded Version (BPRS) (Lukoff et al., 1986; Overall et al., 1972) and the Positive And Negative Syndrome Scale (PANSS) (Kay et al., 1987), and four unidimensional instruments: the Hamilton Rating Scale for Depression (HAMD) (Hamilton, 1960), Montgomery Asberg Depression Rating Scale (MADRS) (Montgomery, 1979), Calgary Depression Scale for Schizophrenia (CDSS) (Addington et al., 1993) and Beck Depression Inventory-II (BDI) (Beck et al., 1996). The remaining 8 publications

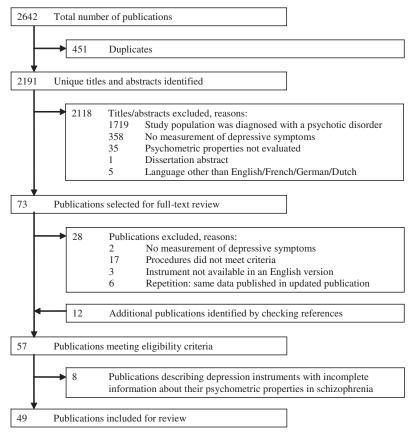


Fig. 1. Flow diagram of publications identified in databases PsychINFO, Medline and PubMed with keywords for schizophrenia, depressive symptoms and psychometrics.

described depression instruments with incomplete information about their psychometric properties in schizophrenia. For example, no information was available on reliability or divergent validity in schizophrenia for the Brief Symptom Inventory (BSI) (Derogatis and Spencer, 1982) and Center for Epidemiologic Studies Depression Scale (CES-D) (Radloff, 1977).

#### 3.2. General characteristics

General characteristics of the six reviewed depression instruments are described in Table 1. Only one instrument was based on self-report. Unidimensional instruments required on average 10 minutes less time to be completed than multidimensional instruments. The number of items per depression instrument varied between 4 and 21. A quantitative investigation of the use of these depression instruments over the past five years showed that the CDSS was most frequently used in research in this period, closely followed by the PANSS-D and the HAMD.

Table 2 illustrates the composition of the depression instruments in the context of schizophrenia. The depressive symptoms covered by the CDSS had minimal overlap with

Table 1	
General characteristics	of reviewed instruments.

	Symptom dimensions	Mode	Training	Duration (minutes)	Time-frame	Number of items	Likert scale	Recent use
BPRS	Multidimensional	Clin.r.	++	25-40	2 weeks	24	7	3
PANSS	Multidimensional	Clin.r.	+++	30-40	1 week	30	7	6
HAMD	Unidimensional	Clin.r.	+	20	3 days	17	5	5
MADRS	Unidimensional	Clin.r.	+	15	1 week	10	4	1
CDSS	Unidimensional	Clin.r.	++	15-20	2 weeks	9	4	6
BDI	Unidimensional	Self-r.	n.a.	10	2 weeks	21	4	4

BPRS = Brief Psychiatric Rating Scale; PANSS = Positive and Negative Syndrome Scale; HAMD = Hamilton Rating Scale for Depression; MADRS = Montgomery Asberg Depression Rating Scale; CDSS = Calgary Depression Scale for Schizophrenia; BDI = Beck Depression Inventory. Clin.r. = clinician rated; Self-r. = selfrated. The amount of training needed to standardize raters varied between + (reading the instructions and/or a single consensus training), ++ (a short training session, followed by  $\geq$  3 times of practice) and +++ (more than one day of training); n.a. = not applicable. Recent use was expressed by the number of publications reporting the use of an instrument for the measurement of depressive symptoms in patients with schizophrenia between 2005 and 2010.

#### Table 2

Composition of instruments evaluating depressive symptoms in schizophrenia.

Symptom dimensions	Symptoms	MDE criteria	BPRS-D	PANSS-D	HAMD	MADRS	CDSS	BDI
Depressive symptoms	Depressed mood <sup>a</sup>	1	1	1	1	3	4	4
	Changed appetite or weight	1	-	-	2	1	-	1
	Sleeping problems	1	-	-	3	1	1	1
	Worthlessness <sup>b</sup>	1	-	-	-	-	2	4
	Suicidal ideation	1	1	-	1	1	1	1
Negative symptoms	Loss of interest or pleasure	1	-	-	-	1	-	2
	Fatigue/lack of initiative or motivation	1	-	-	1	1	-	2
	Indecisiveness/lack of concentration	1	-	-	-	1	-	2
EPS	Psychomotor agitation or retardation	1	-	-	2	-	-	1
Other	Delusional ideas <sup>c</sup>	-	3	2	3	-	1	2
	Other vital symptoms <sup>d</sup>	-	-	-	2	-	-	1
	Anxiety/tension <sup>e</sup>	-	1	2	2	1	-	-
	Items identifying symptoms in non-depressive dimensions	4	4	4	10	4	1	10
	Total number of items of the (sub)scale <sup>f</sup>	9	6	5	17	10	9	21
	% of items identifying non-depressive dimensions	44%	67%	80%	59%	40%	11%	48%

Depressive symptoms (dimensions) potentially overlapping with psychotic symptoms. a) Appeared or perceived depressed mood, including hopelessness, crying, pessimism, irritability and diurnal variation of mood. b) Including self-blame and non-delusional feelings of guilt. c) Including paranoid symptoms, hypochondriacal delusions, feeling criticized by others, poor insight and delusional feelings of guilt or punishment. d) Including loss of libido and somatization. e) Including obsessional and compulsory symptoms. f) Depression subscale of the BPRS as defined by Dingemans et al. (1995); depression subscale of the PANSS as defined by Kay et al. (2000).

other symptom dimensions of schizophrenia. In contrast, about three quarter of the items of the PANSS-D and BPRS-D showed overlap with anxiety and positive symptoms. The

HAMD contained many items on delusional symptoms. Almost half of the items of the MADRS and BDI could also be interpreted as negative symptoms.

#### Table 3

Aspects of reliability and validity of depression instruments in schizophrenia.

a. Reliabilit	у									
	In	ternal consiste	ency	Inter-rat	er		Test-r	etest	References	
BPRS-D	0.0	0.67		0.74			0.72		(1,2)	
PANSS-D	0.3	77		0.80			-		(3,4)	
HAMD	0.3	75 (0.73-0.77)	)	0.94 (0.9	0.94 (0.93–0.95)		0.75 (	0.65-0.80)	(1,2,5-7)	
MADRS	0.9			0.81			0.71		(3,7,8)	
CDSS	0.8	82 (0.76-0.88)		0.86 (0.7	3-0.98)		0.83 (	0.69-0.93)	(1,5-7,9-18)	
BDI	0.9	0.90 (0.88–0.91)		n.a.			-		(1,19)	
b. Divergen	nt validity									
	Ne	egative sympto	oms	Reference	es		EPS		References	
BPRS-D	0.0	00 (-0.11-0.1	0)	(2,20,21	)		0.14 (	0.07-0.21)	(22,23)	
PANSS-D	0.	19 (-0.11-0.4	1)	(3,15,21			0.07 (	0.01-0.20)	(22,24–26)	
HAM-D	0.	18 (0.02-0.45)	1	(2,15,21	23,24,26-3	31)	0.40 (	0.02-0.79)	(14,22-24,26)	
MADRS	0.3	36 (0.12-0.51)	)	(3,15,23	25)		0.52 (	0.16-0.86)	(14,23,25)	
CDSS	0.	0.10(-0.24-0.54)		(9,11-15	(9,11-15,21,23,24,26,27,32,33) 0.			0.07-0.42)	(9,11,13,14,22-24,26,32,33	
BDI	· · · · · · · · · · · · · · · · · · ·		(19,26,31,34)			0.23		(26)		
c. Concurre	ent validity									
	BPRS-D	PANSS-D	HAMD	MADRS	CDSS	BDI	Pooled mean	References		
BPRS-D		0.23	0.66	0.66	0.79	0.64	0.60 (0.17-0.87)	(1,2,5,21,23,28,3	5,36)	
PANSS-D			0.62	0.72	0.66	0.49	0.54 (0.17-0.87)	(3,7,9,11,13,15,19,21,24–27,36)		
HAMD				0.80	0.74	0.57	0.68 (0.26-0.90)	(1,2,5,7,8,11,13-15,21,23,24,26-28,30,31		
MADRS					0.81	-	0.75 (0.56-0.90)	(3,7,8,11,14,15,23,25)		
CDSS						0.83	0.77 (0.26-0.90)	(1,7,9,11-15,21,2	23,24,26,27,37)	
BDI	DI					0.63 (0.44–0.90)	(1,5,12,19,26,30,	31,34,35)		
d. Predictiv	e validity									
		Sensiti	vity		Spee	cificity		Cut-off value	References	
BPRS-D		-			_			-	_	
PANSS-D		78% (7	(4-81%)		85%	(79-90%)		≥5; ≥10 (1		
HAMD		79% (6	67–91%)		83%	(81-84%)		≥12 (15,26)		
MADRS		81%			81%			≥11 (15)		
CDSS		88% (6	57-100%)	88% (74–97%)				$\geq 5; \geq 6; \geq 9$ (1,9,11,15,26)		
CD33										

#### 3.3. Reliability

The internal consistency of the BPRS-D was acceptable and good for the remaining instruments in schizophrenia (Table 3a). The inter-rater and test-retest reliability was good for all instruments, especially the inter-rater reliability of the HAMD.

#### 3.4. Divergent validity

The MADRS correlated with negative symptoms and the HAMD with EPS, whereas the other reviewed instruments neither showed substantial correlation with negative nor extrapyramidal symptom dimensions (Table 3b). The following instruments were used for the rating of negative and extrapyramidal symptoms: Affective Flattening Scale (AFS) (Andreasen, 1979), Scale for the Assessment of Negative Symptoms (SANS) (Andreasen, 1982), negative subscale of the PANSS (Kay et al., 1987), negative subscale of the BPRS (Lukoff et al., 1986; Overall et al., 1972), Psychomotor Retardation Scale (Widlocher, 1983), and Rating Scale for Extrapyramidal Side Effects (Simpson and Angus, 1970).

The underlying factor structure of the multidimensional instruments (BPRS and PANSS) generally consisted of one factor for depression and two to four other factors. The depression factor was comprised of the three items "depression," "guilt" and "anxiety" (Lykouras et al., 2000; McMahon et al., 2002), but additional items loading on the depression factor were "tension" (Lindenmayer et al., 1995; Van Der Gaag et al., 2006; White et al., 1997; Wolthaus et al., 2000), "somatic concern" (Eisenberg et al., 2009; El Yazaji et al., 2002; Lee et al., 2003; Loas et al., 1997) and "suicidality" (Kopelowicz et al., 2008; Ruggeri et al., 2005), or other combinations including "self neglect" (Dingemans et al., 1995) or "motor retardation" (Alves et al., 2005). Inspection of the factor structure of the MADRS and the CDSS did not lead to separate factors for negative symptoms (Lee et al., 2003; Maggini and Raballo, 2006; Wolthaus et al., 2000). The BDI consisted of three factors, including one for "psychosomatic symptoms" (Chemerinski et al., 2008). Of note, no publications reported the factor structure of the HAMD in patients with schizophrenia.

#### 3.5. Concurrent validity

The concurrent validity of the depression instruments in schizophrenia is described in Table 3c. Concurrent validity has been assessed for almost every possible combination of

#### Notes to Table 3:

- 1. Addington et al. (1993)
- 2. Craig et al. (1985)
- 3. Wolthaus et al. (2000)
- 4. Haro et al. (2003)
- 5. Baynes et al. (2000)
- 6. Addington et al. (1996)
- 7. Bernard et al. (1998)
- 8. Lee et al. (2003)
- 9. Bressan et al. (1998)
- 10. Schuetze et al. (2001)
- 11. Sarro et al. (2004)
- 12. Schwartz-Stav et al. (2006)
- 13. Xiao et al. (2009)
- 14. Reine et al. (2000)
- 15. Liu et al. (2009)
- 16. Müller et al. (1999)
- 17. Kontaxakis et al. (2000a)
- 18. Kaneda et al. (2000)
- 19. Chemerinski et al. (2008)
- 20. Kuck et al. (1992)
- 21. Kontaxakis et al. (2000b)
- 22. Kontaxakis et al. (2002)
- 23. Lançon et al. (2000)
- 24. Collins et al. (1996)
- 25. Fitzgerald et al. (2002)
- 26. Kim et al. (2006)
- 27. El Yazaji et al. (2002)
- 28. Goldman et al. (1992)
- 29. Kitamura and Suga (1991)
- 30. Markou (1996)
- 31. Norman et al. (1998)
- 32. Addington et al. (1994) 33. Müller (2002)
- 34. Möser et al. (2006) 35. Huppert et al. (2002)
- 36. Lindenmayer et al. (1992)
- 37. Müller et al. (2006)

a) Reliability was expressed by mean Cronbach's alpha and ICC values; n.a. = not applicable. b) Mean correlation ( $R^2$ ) with either a negative symptom scale or extra-pyramidal symptoms rating scale. c) Average correlation for each comparison of two depression instruments and the pooled mean correlation indices for each instrument. d) Mean sensitivity and specificity values at the optimal cut-off point. References:

the six instruments. The HAMD was most frequently investigated (by 19 comparative studies), followed by the CDSS, PANSS-D, BDI, BPRS-D and MADRS. The highest concurrent validity indices were found for the CDSS and MADRS.

#### 3.6. Predictive validity

Four studies evaluated whether the six depression instruments adequately predicted the presence of MDE in patients with schizophrenia. Table 3d illustrates that the highest ranges for sensitivity and specificity were found for the CDSS. Of note, the optimal cut-off values obtained for the CDSS and PANSS-D varied widely between studies.

#### 4. Discussion

#### 4.1. Summary of results

We identified five clinician-rated instruments and only one self-report with tested reliability and validity for the measurement of depressive symptoms in patients with schizophrenia.

#### 4.2. Reliability

The reliability of the reviewed depression instruments was good in populations with schizophrenia and comparable to populations with depressed patients or healthy subjects (Müller et al., 2005; Rush et al., 2008). In other words, patients with schizophrenia can reliably be assessed on the presence of depressive symptoms by interview or self-report.

#### 4.3. Validity

The instruments differed in their accuracy to distinguish depressive symptoms from other symptoms of schizophrenia (divergent validity). Correlation studies and factor analysis showed that the CDSS measures nearly no other symptoms of schizophrenia. Inspection of the items of the CDSS supported that the overlap with negative symptoms or EPS was minimal compared to the other depression instruments. The high divergent validity of the CDSS is in line with the fact that this instrument has especially been developed for this population (Addington et al., 1993). For example, "lack of interest" was not included, as this is both a symptom of depression and part of the negative symptoms of schizophrenia (Kulhara et al., 1989; Montgomery, 1979; Romney and Candido, 2001). Divergent validity of the other (older) instruments may be hampered as they are based on several items about anxiety or somatic concern (Snaith, 1993), albeit anxiety-like symptoms do not belong to the current DSM-IV diagnostic criteria for depression.

This wide variation of symptom dimensions covered by the reviewed instruments may explain the modest intercorrelations between most depression instruments. The low concurrent validity between instruments may even be overestimated by the halo-effect. Ideally raters are not influenced by knowledge of the subject's scores on other instruments (Nisbett and DeCamp Wilson, 1977). However, in some studies multiple instruments for depressive symptoms were rated by a single rater (Lançon et al., 2000), or the distribution of tasks among raters was unclear (El Yazaji et al., 2002; Kim et al., 2006).

The sensitivity and specificity to detect cases of depression in schizophrenia was highest for the CDSS, even though the CDSS did not cover all diagnostic criteria for depression as outlined above. Among the relatively scarce reports of predictive validity we noticed inconsistencies in the reported cut-off values for the PANSS-D and CDSS. Nevertheless we were able to compare the instruments on their predictive validity as we included only those studies with standardized procedures to obtain the optimal cut-off value (area under the curve methods).

#### 4.4. Practical considerations

Practical issues such as time investment may also be important when choosing an instrument, apart from the psychometric aspects discussed above. The amount of training and time to complete the interview of the CDSS was comparable to the HAMD and MADRS. In contrast, the multidimensional instruments BPRS and PANSS may need more time and training to complete the interview, although an advantage may be that besides depressive symptoms, other psychotic symptoms can be evaluated at the same time.

#### 4.5. Future research

An important finding was the lack of self-report instruments for the measurement of depressive symptoms in this population. The concurrent and predictive validity of the only reviewed self-report here BDI was rather poor. Especially for routine outcome monitoring of depressive symptoms in clinical practice, self-report may save time and costs compared to a clinical interview. Although filling out questionnaires may be difficult for patients with considerable cognitive problems (Addington et al., 1993; Müller et al., 2006; Norholm and Bech, 2006) and observable signs of depression could be missed by self-report (Möller, 2009), self-report may provide more independent information on the patients' experience of depression in schizophrenia than interview-based assessments (Lindenmayer et al., 1992). The literature search identified several other self-report questionnaires for depressive symptoms, such as the CES-D and the BSI (a short version of the Symptom Checklist-90). Evaluation of the composition of the BSI showed that only one of the six items of the depression subscale had potential overlap with negative symptoms [data not shown]. Future research is needed to develop and validate a selfreport comparable to the CDSS with respect to reliability and validity in schizophrenia.

#### 4.6. Recommendations and conclusions

In most of the reviewed studies the CDSS outperformed other depression instruments in terms of reliability and validity in patients with schizophrenia. Nevertheless the other depression instruments are still applied in schizophrenia research (Freudenreich et al., 2008; Heald et al., 2008; Möser et al., 2006; Saarni et al., 2010; Schennach-Wolff et al., 2010). This is in accordance to a survey under psychiatrists demonstrating the popularity of the HAMD, BDI and BPRS-D in daily practice (Siris et al., 2001). The current review may aid clinicians and researchers to choose a well-validated instrument that selectively measures the symptoms of interest.

In summary, the CDSS was most reliable and valid for the measurement of depressive symptoms of schizophrenia. We recommend to use the CDSS in research as well as in daily clinical practice. Patients with a high score should be re-assessed using a diagnostic interview. As self-report is more expedient for the use in routine clinical practice, further research is needed to develop a self-reporting instrument with psychometric properties comparable to the CDSS.

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#### **Conflict of interest**

The authors have not transmitted any conflicts of interest.

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#### References

- Addington, D., Addington, J., Maticka-Tyndale, E., 1993. Assessing depression in schizophrenia: the Calgary Depression Scale. The British Journal of Psychiatry. Supplement 39–44.
- Addington, D., Addington, J., Maticka-Tyndale, E., 1994. Specificity of the Calgary Depression Scale for schizophrenics. Schizophrenia Research 11, 239–244.
- Addington, D., Addington, J., Atkinson, M., 1996. A psychometric comparison of the Calgary Depression Scale for Schizophrenia and the Hamilton Depression Rating Scale. Schizophrenia Research 19, 205–212.
- Allan, R., Martin, C.R., 2009. Can the Hospital Anxiety and Depression Scale be used in patients with schizophrenia? Journal of Evaluation in Clinical Practice 15, 134–141.
- Alves, T.M., Pereira, J.C., Elkis, H., 2005. The psychopathological factors of refractory schizophrenia. Revista Brasileira de Psiquiatria 27, 108–112.
- American Psychiatric Association, 1994. Diagnostic and Statistical Manual of Mental Disorders, 4th ed. American Psychiatric Association, Washington, DC.
- Andreasen, N.C., 1979. Affective flattening and the criteria for schizophrenia. The American Journal of Psychiatry 136, 944–947.
- Andreasen, N.C., 1982. Negative symptoms in schizophrenia. Definition and reliability. Archives of General Psychiatry 39, 784–788.
- Barnes, T.R., MCPhillips, M.A., 1995. How to distinguish between the neurolepticinduced deficit syndrome, depression and disease-related negative symptoms in schizophrenia. International Clinical Psychopharmacology 10 (Suppl 3), 115–121.
- Baynes, D., Mulholland, C., Cooper, S.J., Montgomery, R.C., MacFlynn, G., Lynch, G., Kelly, C., King, D.J., 2000. Depressive symptoms in stable chronic schizophrenia: prevalence and relationship to psychopathology and treatment. Schizophrenia Research 45, 47–56.
- Beck, A.T., Steer, R.A., Ball, R., Ranieri, W., 1996. Comparison of Beck Depression Inventories -IA and -II in psychiatric outpatients. Journal of Personality Assessment 67, 588–597.
- Bernard, D., Lancon, C., Auquier, P., Reine, G., Addington, D., 1998. Calgary Depression Scale for Schizophrenia: a study of the validity of a Frenchlanguage version in a population of schizophrenic patients. Acta Psychiatrica Scandinavica 97, 36–41.
- Birchwood, M., Iqbal, Z., Chadwick, P., Trower, P., 2000. Cognitive approach to depression and suicidal thinking in psychosis. 1. Ontogeny of postpsychotic depression. The British Journal of Psychiatry 177, 516–521.

- Bressan, R.A., Chaves, A.C., Shirakawa, I., de Mari, J., 1998. Validity study of the Brazilian version of the Calgary Depression Scale for Schizophrenia. Schizophrenia Research 32, 41–49.
- Bressan, R.A., Chaves, A.C., Pilowsky, L.S., Shirakawa, I., Mari, J.J., 2003. Depressive episodes in stable schizophrenia: critical evaluation of the DSM-IV and ICD-10 diagnostic criteria. Psychiatry Research 117, 47–56.
- Buckley, P.F., Miller, B.J., Lehrer, D.S., Castle, D.J., 2008. Psychiatric comorbidities and schizophrenia. Schizophrenia Bulletin 35, 383–402.
- Chemerinski, E., Bowie, C., Anderson, H., Harvey, P.D., 2008. Depression in schizophrenia: methodological artifact or distinct feature of the illness? The Journal of Neuropsychiatry and Clinical Neurosciences 20, 431–440.
- Cicchetti, D.V., 1994. Multiple comparison methods: establishing guidelines for their valid application in neuropsychological research. Journal of Clinical and Experimental Neuropsychology 16, 155–161.
- Collins, A.A., Remington, G., Coulter, K., Birkett, K., 1996. Depression in schizophrenia: a comparison of three measures. Schizophrenia Research 20, 205–209.
- Conley, R.R., Ascher-Svanum, H., Zhu, B., Faries, D.E., Kinon, B.J., 2007. The burden of depressive symptoms in the long-term treatment of patients with schizophrenia. Schizophrenia Research 90, 186–197.
- Craig, T.J., Richardson, M.A., Pass, R., Bregman, Z., 1985. Measurement of mood and affect in schizophrenic inpatients. The American Journal of Psychiatry 142, 1272–1277.
- Derogatis, L.R., Spencer, P.M., 1982. The Brief Symptom Inventory (BSI) Administration Scoring and Procedures Manual-I. In: Riderwood, M.D. (Ed.), Clinical Psychometric Research.
- Dingemans, P.M., Linszen, D.H., Lenior, M.E., Smeets, R.M., 1995. Component structure of the expanded Brief Psychiatric Rating Scale (BPRS-E). Psychopharmacology 122, 263–267.
- Eisenberg, D.P., Aniskin, D.B., White, L., Stein, J.A., Harvey, P.D., Galynker, I.I., 2009. Structural differences within negative and depressive syndrome dimensions in schizophrenia, organic brain disease, and major depression: a confirmatory factor analysis of the positive and negative syndrome scale. Psychopathology 42, 242–248.
- El Yazaji, M., Battas, O., Agoub, M., Moussaoui, D., Gutknecht, C., Dalery, J., d'Amato, T., Saoud, M., 2002. Validity of the depressive dimension extracted from principal component analysis of the PANSS in drug-free patients with schizophrenia. Schizophrenia Research 56, 121–127.
- First, M.B., Spitzer, R.L., Gibbon, M., Williams, J.B.W., 1995. The Structured Clinical Interview for DSM-III-R personality disorders (SCID-II), part I: description. Journal of Personality Disorders 9.
- Fitzgerald, P.B., Rolfe, T.J., Brewer, K., Filia, K., Collins, J., Filia, S., Adams, A., de Castella, A., Davey, P., Kulkarni, J., 2002. Depressive, positive, negative and parkinsonian symptoms in schizophrenia. Aust. N.Z.J Psychiatry 36, 340–346.
- Freudenreich, O., Tranulis, C., Cather, C., Henderson, D.C., Evins, A.E., Goff, D.C., 2008. Depressive symptoms in schizophrenia outpatients—prevalence and clinical correlates. Clinical Schizophrenia & Related Psychoses 2, 127–135.
- Goldman, R.S., Tandon, R., Liberzon, I., Greden, J.F., 1992. Measurement of depression and negative symptoms in schizophrenia. Psychopathology 25, 49–56.
- Häfner, H., 2000. Onset and early course as determinants of the further course of schizophrenia. Acta Psychiatrica Scandinavica 102, 44–48.
- Hamilton, M., 1960. A rating scale for depression. Journal of Neurology, Neurosurgery, and Psychiatry 23, 56–62.
- Hanley, J.A., McNeil, B.J., 1983. A method of comparing the areas under receiver operating characteristic curves derived from the same cases. Radiology 148, 839–843.
- Haro, J.M., Kamath, S.A., Ochoa, S., Novick, D., Rele, K., Fargas, A., Rodriguez, M.J., Rele, R., Orta, J., Kharbeng, A., Araya, S., Gervin, M., Alonso, J., Mavreas, V., Lavrentzou, E., Liontos, N., Gregor, K., Jones, P.B., 2003. The Clinical Global Impression—Schizophrenia scale: a simple instrument to measure the diversity of symptoms present in schizophrenia. Acta Psychiatrica Scandinavica. Supplementum 16–23.
- Harrow, M., Yonan, C.A., Sands, J.R., Marengo, J., 1994. Depression in schizophrenia: are neuroleptics, akinesia, or anhedonia involved? Schizophrenia Bulletin 20, 327–338.
- Heald, A., Morris, J., Soni, S.D., 2008. Characterisation of depression in patients with schizophrenia. Indian Journal of Medical Research 127, 544–550.
- Huppert, J.D., Smith, T.E., Apfeldorf, W.J., 2002. Use of self-report measures of anxiety and depression in outpatients with schizophrenia: reliability and validity. Journal of Psychopathology and Behavioral Assessment 24, 275–283.
- Kaneda, Y., Fujii, A., Ohmori, T., 2000. Psychometric properties of the Japanese version of the Calgary Depression Scale for Schizophrenics. The Journal of Nervous and Mental Disease 188, 237–239.
- Kay, S.R., Fiszbein, A., Opler, L.A., 1987. The positive and negative syndrome scale (PANSS) for schizophrenia. Schizophrenia Bulletin 13, 261–276.

- Kay, S.R., Opler, L.A., Fiszbein, A., 2000. Positive and Negative Syndrome Scale (PANSS). Multi-Health Systems, Toronto.
- Kim, S.W., Kim, S.J., Yoon, B.H., Kim, J.M., Shin, I.S., Hwang, M.Y., Yoon, J.S., 2006. Diagnostic validity of assessment scales for depression in patients with schizophrenia. Psychiatry Research 144, 57–63.
- Kitamura, T., Suga, R., 1991. Depressive and negative symptoms in major psychiatric disorders. Comprehensive Psychiatry 32, 88–94.
- Kontaxakis, V.P., Havaki-Kontaxaki, B.J., Margariti, M.M., Stamouli, S.S., Kollias, C.T., Angelopoulos, E.K., Christodoulou, G.N., 2000a. The Greek version of the calgary depression scale for schizophrenia. Psychiatry Research 94, 163–171.
- Kontaxakis, V.P., Havaki-Kontaxaki, B.J., Stamouli, S.S., Margariti, M.M., Collias, C.T., Christodoulou, G.N., 2000b. Comparison of four scales measuring depression in schizophrenic inpatients. European Psychiatry 15, 274–277.
- Kontaxakis, V.P., Havaki-Kontaxaki, B.J., Stamouli, S.S., Margariti, M.M., Kollias, C.T., Christodoulou, G.N., 2002. Depression measures and motor sideeffects in patients with acute schizophrenia. Schizophrenia Research 56, 197–198.
- Kopelowicz, A., Ventura, J., Liberman, R.P., Mintz, J., 2008. Consistency of Brief Psychiatric Rating Scale factor structure across a broad spectrum of schizophrenia patients. Psychopathology 41, 77–84.
- Kuck, J., Zisook, S., Moranville, J.T., Heaton, R.K., Braff, D.L., 1992. Negative symptomatology in schizophrenic outpatients. The Journal of Nervous and Mental Disease 180, 510–515.
- Kulhara, P., Avasthi, A., Chadda, R., Chandiramani, K., Mattoo, S.K., Kota, S.K., Joseph, S., 1989. Negative and depressive symptoms in schizophrenia. The British Journal of Psychiatry 154, 207–211.
- Lako, I.M., Taxis, K., Bruggeman, R., Knegtering, H., Burger, H., Wiersma, D., Slooff, C.J., 2011. The course of depressive symptoms and prescribing patterns of antidepressants in schizophrenia in a one-year follow-up study. European Psychiatry. doi:10.1016/j.eurpsy.2010.10.007.
- Lançon, C., Auquier, P., Reine, G., Bernard, D., Toumi, M., 2000. Study of the concurrent validity of the Calgary Depression Scale for Schizophrenics (CDSS). Journal of Affective Disorders 58, 107–115.
- Lee, K.H., Harris, A.W., Loughland, C.M., Williams, L.M., 2003. The five symptom dimensions and depression in schizophrenia. Psychopathology 36, 226–233.
- Leff, J., Tress, K., Edwards, B., 1988. The clinical course of depressive symptoms in schizophrenia. Schizophrenia Research 1, 25–30.
- Lindenmayer, J.P., Kay, S.R., Plutchik, R., 1992. Multivantaged assessment of depression in schizophrenia. Psychiatry Research 42, 199–207.
- Lindenmayer, J.P., Grochowski, S., Hyman, R.B., 1995. Five factor model of schizophrenia: replication across samples. Schizophrenia Research 14, 229–234.
- Liu, H., Zhang, H., Xiao, W., Liu, Q., Fu, P., Chen, J., Wang, G., Yang, F., Wang, G., Wang, X., Li, L., 2009. Scales for evaluating depressive symptoms in Chinese patients with schizophrenia. The Journal of Nervous and Mental Disease 197, 140–142.
- Loas, G., Noisette, C., Legrand, A., Delahousse, J., 1997. A four-dimensional model of chronic schizophrenia based on the factorial structure of the Positive and Negative Syndrome Scale (PANSS). A study of a group of 153 chronic schizophrenic patients and comparison with the factorial structure of the BPRS. Encephale 23, 10–18.
- Lukoff, D., Liberman, R.P., Nuechterlein, K.H., 1986. Symptom monitoring in the rehabilitation of schizophrenic patients. Schizophrenia Bulletin 12, 578–602.
- Lykouras, L., Oulis, P., Psarros, K., Daskalopoulou, E., Botsis, A., Christodoulou, G.N., Stefanis, C., 2000. Five-factor model of schizophrenic psychopathology: how valid is it? European Archives of Psychiatry and Clinical Neuroscience 250, 93–100.
- Maggini, C., Raballo, A., 2006. Exploring depression in schizophrenia. European Psychiatry 21, 227–232.
- Markou, P., 1996. Depression in schizophrenia: a descriptive study. The Australian and New Zealand Journal of Psychiatry 30, 354–357.
- McMahon, R.P., Kelly, D.L., Kreyenbuhl, J., Kirkpatrick, B., Love, R.C., Conley, R.R., 2002. Novel factor-based symptom scores in treatment resistant schizophrenia: implications for clinical trials. Neuropsychopharmacology 26, 537–545.
- Möller, H.J., 2009. Standardised rating scales in psychiatry: methodological basis, their possibilities and limitations and descriptions of important rating scales. The World Journal of Biological Psychiatry 10, 6–26.
- Montgomery, S.M., 1979. Depressive symptoms in acute schizophrenia. Progress in Neuro-Psychopharmacology 3, 429–433.
- Möser, C., Krieg, J.C., Zihl, J., Lautenbacher, S., 2006. Attention and memory deficits in schizophrenia: the role of symptoms of depression. Cognitive and Behavioral Neurology 19, 150–156.
- Müller, M.J., 2002. Overlap between emotional blunting, depression, and extrapyramidal symptoms in schizophrenia. Schizophrenia Research 57, 307.
- Müller, M.J., Marx-Dannigkeit, P., Schlosser, R., Wetzel, H., Addington, D., Benkert, O., 1999. The Calgary Depression Rating Scale for Schizophrenia:

development and interrater reliability of a German version (CDSS-G). Journal of Psychiatric Research 33, 433–443.

- Müller, M.J., Brening, H., Gensch, C., Klinga, J., Kienzle, B., Muller, K.M., 2005. The Calgary Depression Rating Scale for schizophrenia in a healthy control group: psychometric properties and reference values. Journal of Affective Disorders 88, 69–74.
- Müller, M.J., Müller, K.M., Fellgiebel, A., 2006. Detection of depression in acute schizophrenia: sensitivity and specificity of 2 standard observer rating scales. Canadian Journal of Psychiatry 51, 387–392.
- Nisbett, R.E., DeCamp Wilson, T., 1977. The halo effect: evidence for unconscious alteration of judgments. Journal of Personality and Social Psychology 35, 250–256.
- Norholm, V., Bech, P., 2006. Quality of life in schizophrenic patients: association with depressive symptoms. Nordic Journal of Psychiatry 60, 32–37.
- Norman, R.M., Malla, A.K., 1991. Dysphoric mood and symptomatology in schizophrenia. Psychological Medicine 21, 897–903.
- Norman, R.M., Malla, A.K., Cortese, L., Diaz, F., 1998. Aspects of dysphoria and symptoms of schizophrenia. Psychological Medicine 28, 1433–1441.
- Overall, J.E., Henry, B.W., Markett, J.R., 1972. Validity of an empirically derived phenomenological typology. Journal of Psychiatric Research 9, 87–99.
- Radloff, L.S., 1977. The CES-D scale: a self-report depression scale for research in the general population. Applied Psychology Measurement 1, 385–401.
- Reine, G., Bernard, D., Auquier, P., Le Fur, B., Lançon, C., 2000. Psychometric properties of French version of the Calgary depression scale for schizophrenics (CDSS). Encephale 26, 52–61.
- Romney, D.M., Candido, C.L., 2001. Anhedonia in depression and schizophrenia: a reexamination. The Journal of Nervous and Mental Disease 189, 735–740.
- Ruggeri, M., Koeter, M., Schene, A., Bonetto, C., Vazquez-Barquero, J.L., Becker, T., Knapp, M., Knudsen, H.C., Tansella, M., Thornicroft, G., 2005. Factor solution of the BPRS-expanded version in schizophrenic outpatients living in five European countries. Schizophrenia Research 75, 107–117.
- Rush, A.J., First, M.B., Blacker, D., 2008. Handbook of Psychiatric Measures, 2nd ed. American Psychiatric Publishing Inc, Washington, DC.
- Saarni, S.I., Viertio, S., Perala, J., Koskinen, S., Lonnqvist, J., Suvisaari, J., 2010. Quality of life of people with schizophrenia, bipolar disorder and other psychotic disorders. The British Journal of Psychiatry 197, 386–394.
- Sarro, S., Duenas, R.M., Ramirez, N., Arranz, B., Martinez, R., Sanchez, J.M., Gonzalez, J.M., Salo, L., Miralles, L., San, L., 2004. Cross-cultural adaptation and validation of the Spanish version of the Calgary Depression Scale for Schizophrenia. Schizophrenia Research 68, 349–356.
- Schennach-Wolff, R., Jager, M., Seemuller, F., Obermeier, M., Schmauss, M., Laux, G., Pfeiffer, H., Naber, D., Schmidt, L.G., Gaebel, W., Klosterkotter, J., Heuser, I., Maier, W., Lemke, M.R., Ruther, E., Klingberg, S., Gastpar, M., Moller, H.J., Riedel, M., 2010. Outcome of suicidal patients with schizophrenia: results from a naturalistic study. Acta Psychiatrica Scandinavica 121, 359–370.
- Schennach-Wolff, R., Obermeier, M., Seemuller, F., Jager, M., Messer, T., Laux, G., Pfeiffer, H., Naber, D., Schmidt, L.G., Gaebel, W., Klosterkotter, J., Heuser, I., Maier, W., Lemke, M.R., Ruther, E., Klingberg, S., Gastpar, M., Moller, H.J., Riedel, M., 2011. Evaluating depressive symptoms and their impact on outcome in schizophrenia applying the Calgary Depression Scale. Acta Psychiatrica Scandinavica 123, 228–238.
- Schuetze, T., Norholm, V., Raabaek Olsen, L., Hougaard, H., Ekstrom, M., Wagn, P., Bech, P., 2001. Reliability and validity of the Danish version of the Calgary Depression Scale for Schizophrenia. Nordic Journal of Psychiatry 55, 119–122.
- Schwartz-Stav, O., Apter, A., Zalsman, G., 2006. Depression, suicidal behavior and insight in adolescents with schizophrenia. European Child & Adolescent Psychiatry 15, 352–359.
- Simpson, G.M., Angus, J.W., 1970. A rating scale for extrapyramidal side effects. Acta Psychiatrica Scandinavica. Supplementum 212, 11–19.
- Siris, S.G., Bench, C., 2003. Depression and schizophrenia. In: Hirsch, S.R., Weinberger, D. (Eds.), Schizophrenia. Blackwell, Oxford, UK, pp. 140–167.
- Siris, S.G., Addington, D., Azorin, J.M., Falloon, I.R., Gerlach, J., Hirsch, S.R., 2001. Depression in schizophrenia: recognition and management in the USA. Schizophrenia Research 47, 185–197.
- Snaith, P., 1993. What do depression rating scales measure? The British Journal of Psychiatry 163, 293–298.
- Tollefson, G.D., Andersen, S.W., Tran, P.V., 1999. The course of depressive symptoms in predicting relapse in schizophrenia: a double-blind, randomized comparison of olanzapine and risperidone. Biological Psychiatry 46, 365–373.
- Van Der Gaag, M., Hoffman, T., Remijsen, M., Hijman, R., De Haan, L., Van Meijel, B., Van Harten, P.N., Valmaggia, L., De Hert, M., Cuijpers, A., Wiersma, D., 2006. The five-factor model of the Positive and Negative Syndrome Scale II: a ten-fold cross-validation of a revised model. Schizophrenia Research 85, 280–287.

Van Os, J., Kapur, S., 2009. Schizophrenia. Lancet 374, 635-645.

- Van Putten, T., May, R.P., 1978. "Akinetic depression" in schizophrenia. Archives of General Psychiatry 35, 1101–1107.
- White, L., Harvey, P.D., Opler, L., Lindenmayer, J.P., 1997. Empirical assessment of the factorial structure of clinical symptoms in schizophrenia. A multisite, multimodel evaluation of the factorial structure of the Positive and Negative Syndrome Scale. The PANSS Study Group. Psychopathology 30, 263–274.
- Widlocher, D.J., 1983. Psychomotor retardation: clinical, theoretical, and psychometric aspects. The Psychiatric Clinics of North America 6, 27–40.
- Wolthaus, J.E., Dingemans, P.M., Schene, A.H., Linszen, D.H., Knegtering, H., Holthausen, E.A., Cahn, W., Hijman, R., 2000. Component structure of the positive and negative syndrome scale (PANSS) in patients with recent-onset schizophrenia and spectrum disorders. Psychopharmacology 150, 399–403.
- Xiao, W., Liu, H., Zhang, H., Liu, Q., Fu, P., Chen, J., Wang, X., Wang, G., Li, L., Shu, L., 2009. Reliability and validity of the Chinese version of the Calgary Depression Scale for Schizophrenia. The Australian and New Zealand Journal of Psychiatry 43, 548–553.