

# Characterisation of depression in patients with schizophrenia

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**Background & objectives:** Though number of studies have examined the prevalence of depression at different phases of the schizophrenic illness, the precise nature of depressive symptoms present in different phases of the schizophrenic illness remains unclear. We therefore undertook this study to characterize and compare the profile of depressive symptoms in acute and chronic schizophrenia with those in major depression.

**Methods:** Three groups of patients with (i) an acute schizophrenic episode, (ii) stable schizophrenia and (iii) primary major depression, were compared on demographic variables and on clinical rating scales for depression and the positive and negative syndrome scale (PANSS).

**Results:** The clinical depression seen in acute schizophrenia and primary depression differed significantly from that seen in chronic schizophrenia. This was confirmed by factor analysis which showed that selective subsets of symptoms were more likely to differentiate the three groups clinically. Further, the depression in chronic schizophrenia was less likely to be associated with life events and was best detected by using the Beck depression inventory (BDI).

**Interpretation & conclusions:** Careful analysis of depressive symptoms can differentiate between the three groups - this would also imply that the underlying pathogenetic mechanism for depression in the groups may be different. Our findings support the use of the BDI to identify depressive symptoms in chronic schizophrenia so that appropriate early intervention can be targeted.

**Key words** BDI - depression - psychopathology - schizophrenia

Depressive symptomatology as a feature of schizophrenia has been recognized since Bleuler first introduced the term in 1908<sup>1</sup>. He described depressive symptoms as either directly triggered by the disease process in the acute stages or occurring as secondary symptoms. Bowers and Astrachan (1967)<sup>2</sup> made serial ratings of symptoms and signs in patients admitted with schizophrenia and found a close relationship between depression and psychosis ratings.

Many investigators have examined the prevalence of depression at different phases of the schizophrenic illness. In particular, Knights and Hirsch (1981)<sup>3</sup> found depressive symptoms in nearly two thirds of patients admitted with schizophrenia, and Johnson<sup>4</sup> ascertained that 70 per cent of a sample of 30 subjects with schizophrenia had a depressive episode over a two year period. Depression may occur independently of the symptoms of schizophrenia and several months after

recovery from an acute episode, *i.e.*, post-psychotic depression, in up to 30 per cent of cases<sup>5</sup>. A similar rate of depression was found in the longitudinal study of Birchwood *et al*<sup>6</sup> who found no significant associations between depressive symptomatology and negative schizophrenia symptoms. Tarrier *et al*<sup>7</sup> concluded from their analysis of prodromal symptoms that psychotic relapses can be predicted in 75 per cent of cases on the basis of increasing scores for hallucinations and depressive symptoms in the two months preceding a relapse.

The character of depression in acute schizophrenia was examined by Leff *et al*<sup>8</sup> found that the full spectrum of depressive symptoms was present in varying proportions in their group of drug-free acutely ill schizophrenic patients. In the majority of cases the psychotic and depressive symptoms followed a similar time course.

The precise nature of depressive symptoms present in different phases of the schizophrenic illness is an area of recent interest. We carried out this study with the objective to characterize and compare the profile of depressive phenomena found in acute schizophrenia (first episode or psychotic relapse), in chronic stable schizophrenia (patients free of psychotic symptoms at the time of assessment) and in primary depression, using validated rating scales. We were particularly concerned to identify clinical markers for depression in those with chronic schizophrenia given the strong association between depression and suicidality in this group<sup>9-11</sup>.

### Material & Methods

*Subjects:* Sixty five subjects aged between 18 and 65 yr were included in the study. All were resident in Salford, Greater Manchester (an inner city residential area), UK. Three of them dropped out after initially agreeing to participate. They were consecutive presentations identified either as inpatients or outpatients in the Department of Psychiatry, Hope Hospital, Salford. All had a diagnosis of primary depression (excluding psychotic depression) or schizophrenia (DSM-IV criteria, American Psychiatric Association, 1994) and were seen over a 12 month period.

The participants were categorized into three groups according to presentation:

- (i) Depression in acute schizophrenia (DepASch).
- (ii) Depression in chronic stable schizophrenia (DepChrSch).
- (iii) Primary depression (Dep).

In each group depressive symptoms had been present for at least 14 days prior to assessment. The threshold for inclusion was a score greater than 16 on the Hamilton depression scale<sup>13</sup>. All subjects underwent a physical examination in order to exclude any organic psychosyndromes or concurrent physical illness. Ethical approval was granted by the Salford Ethics Committee. Informed written consent was obtained from each subject before inclusion in the study.

*Assessments:* All subjects were interviewed by a single interviewer. There was a detailed assessment of demographic status, course of the psychiatric illness including total neuroleptic treatment, associated psychotropic treatment and response to treatment, past medical history, family history of psychiatric illness and quantity/pattern of alcohol and drug use. Life events in the previous year were recorded using an adapted Holmes-Rahe Life Stress Inventory<sup>14</sup>.

Psychiatric rating scales administered were the positive and negative syndrome scale (PANSS)<sup>15</sup>, Hamilton depression scale (HDS)<sup>13</sup>, Beck depression inventory (BDI)<sup>16</sup> and the Hamilton anxiety scale (HAS)<sup>17</sup>. Extrapyramidal side effects were rated using the rating scale for extrapyramidal symptoms (ESRS)<sup>18</sup> and the abnormal involuntary movement scale (AIMS)<sup>19</sup>.

*Statistical analysis:* Arithmetic means are given with 95 per cent confidence intervals (CI). Comparisons between the three diagnosis groups were made using one way factor analysis of variance (ANOVA) for normally distributed data, Kruskal-Wallis test for non-normally distributed continuous data and the chi square test for categorical data. In addition, a factor analysis was carried out on the HDS, BDI and HAS scales to investigate the predictive power of individual components, combinations of which were then used in a discriminant function analysis. All analyses were performed using SPSS version 10.5 (Chicago, Illinois, USA 60606).

### Results

*Characteristics of sample:* Subjects with depression in chronic stable schizophrenia (DepChrSch) (42.9 yr, 95% CI 36.3-49.6) and primary depression (Dep) (44.8 yr, 40.9-48.7) tended to be older than those with depression in acute schizophrenia (DepASch) (32.8 yr, 28.1-37.5). There were proportionately more males in the DepChrSch group than the other two groups and a much higher percentage of DepChrSch (67%) and DepASch (43%) were unemployed compared with Dep. (Table

I). Further 52 per cent of DepASch and 44 per cent of DepChrSch were single compared with only 5 per cent of Dep. There was no difference in the number of first degree relatives affected by psychiatric illness nor in the number of smokers between the groups but the DepChrSch group smoked more cigarettes per day (29, 95% CI 24-34 cigarettes/day) as also the DepASch group (22, 16-28 cigarettes/day) compared to the Dep group (17, 12-22 cigarettes/day).

*Illness related variables:* The age of onset of the first episode of illness was highest in Dep at 37.4 (33.0-41.8) years compared with DepASch 26.1 (22.1-30.2) year and DepChrSch 27.8 (23.4-32.1) year. Duration of illness was maximum in DepChrSch as compared with the other two groups (2.9-8.1) year as was total duration of hospitalization in the past. A significantly ( $P<0.001$ ) greater number of relapses had occurred in the DepChrSch subjects compared with the other two groups (Table I).

*Treatment variables and illicit drug use:* Treatment compliance was significantly worse in DepASch group than in the other groups. Oral neuroleptic use was greatest in the DepASch group at 61 per cent whereas depot neuroleptic administration was highest (83%) in the DepChrSch group. There was no significant difference in anticholinergic drug usage between DepChrSch and DepASch groups. As expected, antidepressant usage was maximum in those with Dep

(76%). There was no significant difference in the extent of alcohol or drug problems between the groups (data not shown).

*Clinical rating scales:* Total HDS and BDI scores were significantly greater for both the DepASch and Dep groups compared with DepChrSch with the total scores for DepASch and Dep being similar (Table II). In the case of the BDI the DepChrSch group's total score was much closer to the other two groups than was the case for the HDS. Thus the BDI was more sensitive to depressive symptoms in the DepChrSch group than the HDS.

Multivariate analysis of all the individual scores from the HDS, BDI and HAS showed much lower HDS ratings for the DepChrSch group (Hotellings  $F=7.9$ ,  $P<0.001$ ) and somewhat lower BDI ratings for the DepChrSch group (Hotellings  $F=2.0$ ,  $P=0.009$ ). In the case of the HAS scores were similar in all groups ( $F=1.3$ ,  $p$  NS).

A factor analysis was carried out on the HDS, BDI and HAS in order to ascertain if a smaller number of factors than the individual scale items could still account for the variance seen. From this it was apparent that the HDS items could be combined into subtotal scores corresponding to somatic symptoms of depression (HDS SOM), specifically somatic symptoms, gastrointestinal and somatic symptoms general, insomnia, anorexia, loss of libido and somatic anxiety; psychotic symptoms (HDS P) (depersonalization/ derealization and paranoid symptoms) and anxiety/agitation (HDS ANX)

**Table I.** Demographic data of the subjects in the three groups

	DepASch	DepChrSch	Dep
Number	23	18	21
Age (yr)	32.8 (28.1-37.5)	42.9 (36.3-49.6)	44.8 (40.9-48.7)
Male / female (%) <sup>†</sup>	35/65	72/28	24/76
Unemployed (%) <sup>†</sup>	43	67	9
Single (%) <sup>†</sup>	52	44	5
Age of onset	26.1 (22.1-30.2)	27.8 (23.4-32.1)	37.4 (33.0-41.8)
Duration of illness (yr) *	3.9 (2.1-6.7)	11.6 (7.3-18.2)	5.0 (2.9-8.1)
Duration of hospitalisation (wk)*	6.9 (3.3-13.4)	17.3 (12.2-24.5)	4.0 (2.3-6.5)
No. of relapses*	2.5 (1.6-3.4)	4.3 (3.2-5.5)	1.7 (1.1-2.2)
Treatment compliance(good/poor)	15/8	16/2	17/0
Oral neuroleptic use (%) <sup>†</sup>	61	28	19
Depot neuroleptic use (%) <sup>††</sup>	30	83	0
Anticholinergic use (%) <sup>††</sup>	22	50	0
Antidepressant use (%) <sup>††</sup>	13	22	76

Values are means with 95% confidence intervals

DepASch=depression in acute schizophrenia; DepChrSch=depression in chronic schizophrenia; Dep=primary depression

\* $P<0.001$  (ANOVA)

<sup>†</sup> $P<0.01$ , <sup>††</sup> $P<0.001$  ( $\chi^2$  test)

**Table II.** Comparison of total scores of HDS, BDI, HAS and PANSS (positive and negative subsets and totals)

Total score	DepASch (n=23)	DepChrSch(n=18)	Dep(n=21)
HDS***	32.6 (28.5-36.7)	20.2 (17.0-23.4)	35.0 (31.5-38.4)
BDI***	38.2 (35.0-41.4)	31.7 (29.3-34.0)	39.1 (36.1-42.1)
HAS**	19.3 (14.2-24.5)	13.2 (8.9-17.5)	25.5 (19.9-31.2)
Positive*** subset	23.7 (21.1-26.2)	9.5 (8.1-10.9)	11.2 (9.7-12.8)
Negative* subset	19.9 (16.3-23.6)	15.9 (12.9-19.0)	14.2 (11.2-17.2)
General ***subset	50.0 (44.6-55.3)	35.2 (32.6-37.7)	43.0 (39.9-46.1)
Total score***	93.5 (84.4-102.7)	60.6 (54.9-66.3)	68.5 (62.3-74.6)

Values are given as means with 95% confidence intervals

HDS – Hamilton depression scale, BDI-Beck depression inventory

HS – Hamilton anxiety scale

$P^* < 0.05$ ,  $** < 0.01$ ,  $*** < 0.001$  (ANOVA)

symptoms (anxiety somatic). No such reduction was possible for the BDI and HAS scales.

The factors obtained by factor analysis were included in a step-wise discriminant analysis which showed that the three patient groups could be successfully discriminated from each other (Fig. 1, Table III). The functions shown on the graph are linear combinations of the best group of predictors as selected by the step-wise discriminant function analysis. The functions of the discriminant analysis are such that all the subjects in one group will have high values of the function whereas all the subjects in the other group will have low values. Function 1 which discriminates DepASch from DepChrSch is dominated by the PANSS positive symptom score [canonical discriminant function coefficient (C) = -1.224] (more negative in DepASch). Function 2 which discriminates DepChrSch from Dep is dominated by the HDSSOM subscale score (C=0.727) (greater in Dep), number of relapses (C=-0.445) (more negative in DepChrSch) and sex (C=-0.309) (DepChrSch predominantly male).

For positive and negative syndrome scale ratings (Table II), in the DepASch group there were significantly higher ratings for anxiety ( $P=0.02$ ) and tension ( $P=0.01$ ) than in the DepChrSch group. The highest positive subset scores occurred in the DepASch group (Table II) which also rated higher than the DepChrSch group. General

subset scores were highest in DepASch as was the total score for psychopathology as a whole. Examination for association between depressive symptomatology and PANSS positive, negative and general subscales for the DepChrSch group indicated a significant association between the BDI total and negative symptoms Spearman's  $\rho=0.55$ ,  $P=0.02$  (but not with positive or general symptoms) and between the HDS total and PANSS general symptoms ( $\rho = 0.53$ ,  $P=0.02$ ).

Side effects of neuroleptic agents were quantified using the extrapyramidal symptom rating scale (ESRS)<sup>18</sup> and abnormal involuntary movement scale (AIMS)<sup>19</sup>. There was no significant relationship between total score on either the ESRS or the AIMS and severity of depression as measured by HDS or BDI, for any of the groups studied (as measured by Spearman correlation).

Life events in the previous year were rated using the Holmes-Rahe life stress inventory (Fig. 2). Total scores for life events (given as means with 95 per cent confidence intervals) were significantly greater for Dep [305 (239-371)] than for DepASch [196 (136-256)] which was greater than DepChrSch [99 (58-141)] ( $F=12.3$ ,  $P<0.001$ ).

The independent life event score was much higher for Dep [72 (51-94)] than for DepASch [29 (10-47)] or DepChrSch [28 (9-47)] ( $F=7.3$ ,  $P=0.001$ ) for which scores were similar. Dependent life event ratings were significantly higher for DepASch [67 (45-89)] and Dep [95 (64-126)] than for DepChrSch [32 (14-47)] ( $F=6.53$ ,  $P=0.003$ ) as were semi-independent life events DepASch [85 (55-115)], Dep [104 (72-136)] vs DepChrSch [28 (12-44)] ( $F=7.9$ ,  $P<0.001$ ). Thus the depression seen in chronic schizophrenia was least likely to be associated with life events.

**Table III.** Predicted group membership from discriminant function analysis

Count	Predicted group membership			Total
	DepASch	DepChrSch	Dep	
DepASch	22	0	1	23
DepChrSch	0	16	2	18
Dep	0	1	20	21

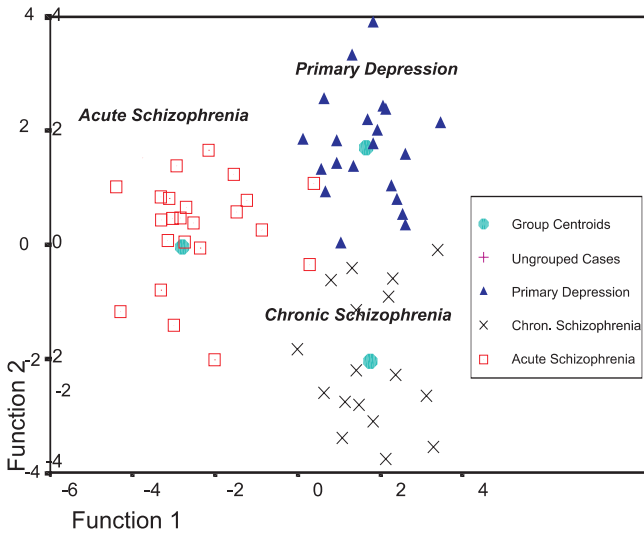


Fig. 1. Plot of discriminant functions and group centroids.

**Discussion**

Depression is common among patients with schizophrenia<sup>20,21</sup>. We have identified the BDI as a measure which has validity for identifying depressive symptoms in stable chronic schizophrenia in whom depressive symptoms are an identifiable risk factor for suicide.

The BDI was able to detect depressive symptoms in stable chronic schizophrenia. In other words, the nature of symptoms in stable chronic schizophrenia is predominantly subjective in nature whereas in acute schizophrenia the symptom profile includes the classical biological symptoms of depression as rated by the HDS. This accords with Siris’s<sup>5</sup> view that the major difference between depression and negative symptoms is ‘blue mood’, a valuable indicator of depression that differentiates it from symptoms such as anhedonia, alogia, affective flattening and apathy, providing a clear rationale for distinguishing negative symptoms of schizophrenia from depression.

Zisook *et al*<sup>23</sup> confirmed the high prevalence of depressive symptoms in middle-aged and older persons with schizophrenia and schizoaffective disorder examined in the “Citalopram Augmentation in Older Adults with Psychoses” study. The most prevalent symptoms cut across the several domains of symptoms, namely psychological, somatic, psychomotor and functional. In a subset of 107 patients in the ABC schizophrenia study all but one of these experienced one to ten episodes of depressed mood between index

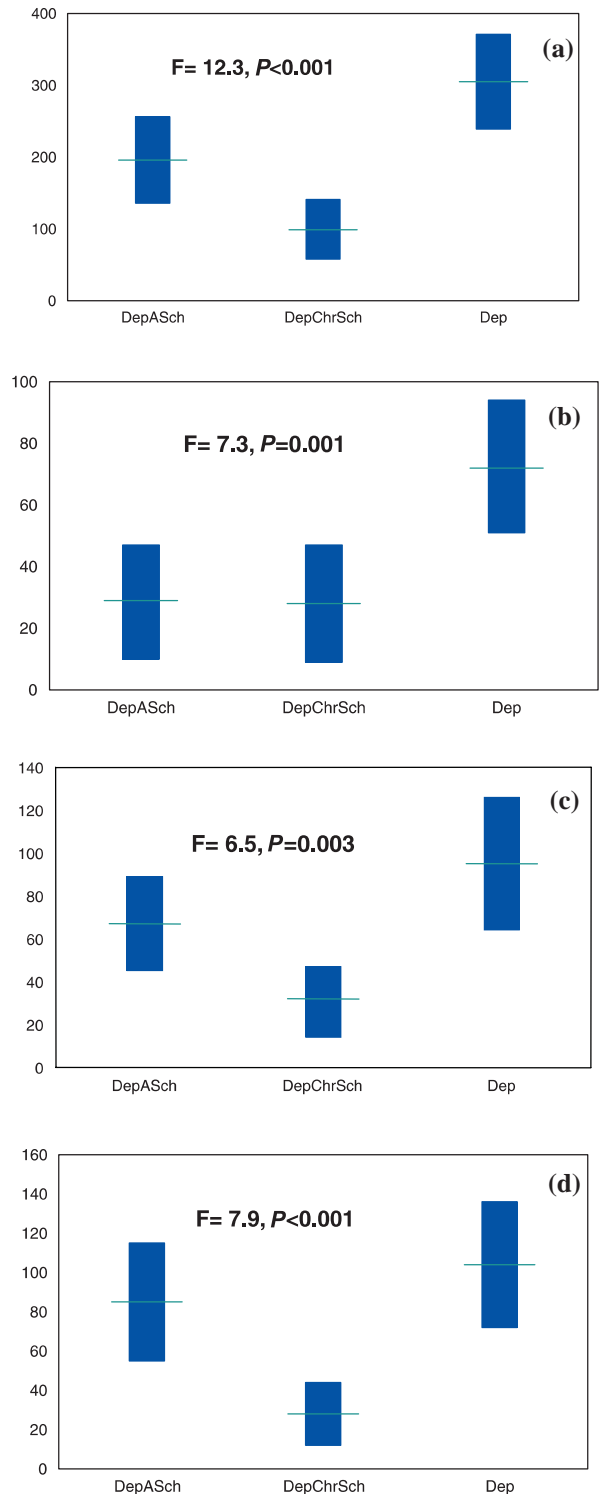


Fig. 2. (a) Holmes-Rahe total life event inventory scores (means and 95% CI) by diagnosis group, (b) Holmes-Rahe independent life event inventory scores (means and 95% CI) by diagnosis group, (c) Holmes-Rahe dependent life event inventory scores (means and 95% CI) by diagnosis group, (d) Holmes-Rahe semi-dependent life event inventory scores (means and 95% CI) by diagnosis group.

assessment and long-term follow up. Further in any month of the observation period, 30-35 per cent of patients presented at least one symptom of the depressive core syndrome<sup>24</sup>.

An important finding is that the rating of all life events dependent and semi-independent in the year preceding the onset of depression was much lower for the DepChrSch group than for either DepASch or Dep. This suggests that the onset of affective symptoms in the DepChrSch group is much more an intrinsic feature of the illness process itself than the consequence of external life events. Depression in the context of acute and chronic schizophrenia was equally less likely than primary depression to be associated with independent life events than primary depression.

The sensitivity of the BDI to DepChrSch contrasted with the much lower HDS scores for this group compared to the DepASch and Dep groups. This is likely a consequence of the distinction between the type of phenomena detected by the BDI, which addresses the subjective/self-reported experience of depression and the HDS which addresses the more biological/objective features of depression. Thus patients with primary depression and depression in acute schizophrenia both feel depressed and display the objective features of depression whereas those with depression in stable schizophrenia feel equally depressed but do not manifest the typical biological symptoms and signs. The finding of the full range of depressive symptoms in acute schizophrenia leading to high total HDS and BDI scores is in accordance with the observations of Leff *et al*<sup>8</sup>, who found that the full range of depressive symptoms was present in varying proportions in their group of drug-free patients with acute schizophrenia.

The importance of identifying such individuals was highlighted by the study of Harrow *et al*<sup>25</sup>, in which of the 75 patients with schizophrenia and schizoaffective disorder, 30 per cent showed full depressive syndromes during the follow up year, and by the report of a positive benefit of olanzapine in treating depressive symptoms in schizophrenia<sup>26</sup>. It is relevant to point out that depression following acute psychosis may be a psychological response (demoralisation) to an apparently uncontrollable life event (the psychosis) and its attendant disabilities<sup>27,28</sup>.

Conley *et al*<sup>29</sup> in a multi-site prospective, naturalistic, observational study found that at enrollment 39.4 per cent patients were depressed. Across the three year study the depressed cohort was significantly more likely than the

non-depressed to use relapse related mental health services, to be a safety concern, to have substance-misuse related problems and to report poorer life satisfaction emphasizing the importance of treating the non psychotic dimensions of schizophrenia. Pharmacogenic theories have suggested that the depression observed in psychosis may be simply a drug-induced akinetic dysphoria<sup>30</sup>. However, we found no significant relationship between total score on either the extrapyramidal symptom rating scale (ESRS) or the abnormal involuntary movement scale (AIMS) and severity of depression as measured by HDS or BDI, for any of the groups studied.

A limitation of the study, given that the DepChrSch group consisted of a high proportion of chronic and multiple-relapse cases living within a socio-economically depressed inner-city area, is lack of generalizability to other demographic groups. Also the study was cross-sectional. However, the robustness of the findings is supported by the use of only one interviewer and by the concordance of our findings with other studies in this area.

Seen in the context of the findings of Mortensen and Juel<sup>11</sup> that suicide accounted for 50 per cent of deaths in men and 35 per cent of deaths in women with schizophrenia, the importance of identifying depressive symptomatology in patients with schizophrenia in long-term follow up cannot be understated. We propose the BDI as a sensitive screening instrument for identifying depressive symptoms in patients who do not show active psychotic features; in these individuals supportive measures and cognitive therapy may be appropriately targeted with or without adjunctive antidepressant treatment. The Calgary depression scale has been well validated as a sensitive instrument for detecting depression in acute schizophrenia with active psychosis<sup>31,32</sup>. Importantly, it has been reported to be able to differentiate between depressive, negative and extrapyramidal symptoms. All items in the Calgary scale were covered in the ratings carried in this study.

In conclusion, this study showed that there were qualitative differences between the presentation of depression in acute and chronic schizophrenia. It appears that patients with chronic schizophrenia experience predominantly subjective symptoms whereas those who experience depression in acute schizophrenia are much more akin to primary major depression in their presentation. We identified the BDI as a screening tool for identifying depressive symptoms in stable chronic schizophrenia, so that these individuals can be targeted with appropriate interventions.

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## References

- Bleuler M. *Die Prognose der Dementia Praecox*. (Schizophreniegroppe). *Allgemeine Zeitschrift* 1908; 65 : 436-64.
- Bowers MB, Astrachan BM. Depression in acute schizophrenic psychosis. *Am J Psychiatry* 1967; 134 : 14-20.
- Knights A, Hirsch SR. Revealed depression and drug treatment for Schizophrenia. *Arch Gen Psychiatry* 1981; 38 : 806-11.
- Johnson DAW. Studies of depressive symptoms in schizophrenia. *Br J Psychiatry* 1981; 139 : 89-101.
- Siris SG. Depression and schizophrenia. In: Hirsch SR, Weinberger DR, editors, *Schizophrenia*, Oxford: Blackwell; 1995. p. 128-45.
- Birchwood M, Iqbal Z, Chadwick P, Trower P. Cognitive approach to depression and suicidal thinking in psychosis. 1. Ontogeny of post-psychotic depression. *Br J Psychiatry* 2000; 177 : 516-21.
- Tarrier N, Barrowclough C, Bamrah JS. Prodromal signs of relapse in schizophrenia. *Soc Psychiatry Psychiatr Epidemiol* 1991; 26 : 157-61.
- Leff J, Tress K, Edwards B. The clinical course of depressive symptoms in schizophrenia. *Schizophr Res* 1988; 1 : 25-30.
- Drake RE, Gates C, Cotton PG, Whitaker A. Suicide among schizophrenics: who is at risk? *J Nerv Ment Dis* 1984; 172 : 613-7.
- Roy A. Depression, attempted suicide and suicide in patients with chronic schizophrenia. *Psychiatr Clin North Am* 1986; 9 : 193-206.
- Mortensen PB, Juel K. Mortality and causes of death in first admitted schizophrenic patients. *Br J Psychiatry* 1993; 163 : 183-9.
- Diagnostic and statistical manual of mental disorders*, 4<sup>th</sup> ed. Washington DC: American Psychiatric Association; 1994.
- Hamilton M. Development of a rating scale for primary depressive illness. *Br J Soc Clin Psychology* 1967; 6 : 278-96.
- Holmes T, Rahe RH. The social adjustment rating scale. *J Psychomatic Res* 1967; 11 : 213-8.
- Kay SR, Fiszbein A, Opler LA. The Positive and Negative Syndrome Scale (PANSS) for Schizophrenia. *Schizophrenia Bull* 1987; 13 : 261-76.
- Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. *Arch Gen Psychiatry* 1961; 4 : 561-71.
- Hamilton M. The assessment of anxiety states by rating. *Br J Med Psychol* 1959; 32 : 321-7.
- Chouinard G, Ross-Chouinard A, Annable L, Jones BD. Extrapyramidal symptom rating scale. *Can J Neurol Sci* 1980; 7 : 233.
- Simpson GM, Angus JWS. A rating scale for extrapyramidal side effects. *Acta Psychiatr Scand* 1970; 212 (Suppl) : 11-19.
- Barnes TRE, Curson DA, Liddle PF, Patel M. The nature and prevalence of depression in chronic schizophrenic inpatients. *Br J Psychiatry* 1989; 154 : 486-91.
- Kulhara P, Avasthi A, Chadda R, Chandiramani K, Mattoo SK, Kota SK, et al. Negative and depressive symptoms in schizophrenia. *Br J Psychiatry* 1989; 154 : 207-11.
- Prasad AJ. Attempted suicide in hospitalised schizophrenics. *Acta Psychiatr Scand* 1986; 74 : 41-2.
- Zisook S, Nyer M, Kasckow J, Golshan S, Lehman D, Montross L. Depressive symptom patterns in patients with chronic schizophrenia and subsyndromal depression. *Schizophrenia Res* 2006; 86 : 226-33.
- Heiden W, Könnecke R, Maurer K, Ropeter D, Häfner H. Depression in the long term course of schizophrenia. *Eur Arch Psychiatry Clin Neuro* 2005; 255 : 174-84.
- Harrow M, Yonan CA, Sands JR, Marengo J. Depression in schizophrenia: are neuroleptics, akinesia or anhedonia involved. *Schizophrenia Bull* 1994; 20 : 327-38.
- Tollefson D, Sanger TM, Lu Y, Thieme ME. Depressive symptoms and signs in schizophrenia. A prospective blinded trial of Olanzapine and Haloperidol. *Arch Gen Psychiatry* 1998; 55 : 250-8.
- Birchwood M J, Mason R, MacMillan F, Healy J. Depression, demoralisation and control over psychotic illness: a comparison of depressed and non-depressed patients with a chronic psychosis. *Psychological Med* 1993; 23 : 387-95.
- Rooke O, Birchwood M. Loss, humiliation and entrapment as appraisals of schizophrenic illness: a prospective study of depressed and non-depressed patients. *Br J Psychology* 1998; 37 : 259-68.
- Conley RR, Ascher-Svanum H, Zhu B, Faries DE, Kinon BJ. The burden of depressive symptoms in the long-term treatment of patients with schizophrenia. *Schizophrenia Res* 2007; 9 : 186-97.
- Van Putten T, May P. 'Akinetic depression' in schizophrenia. *Arch Gen Psychiatry* 1978; 35 : 1101-7.
- Addington D, Addington J, Maticka-Tyndale E. Assessing depression in schizophrenia. *Br J Psychiatry* 1993; 163 (Suppl 22) : 39-44.
- Collins AA, Remington G, Coulter K, Birkett K. Depression in schizophrenia: a comparison of three measures. *Schizophrenia Res* 1996; 20 : 205-9.

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