

PROGNOSTIC VARIABLES IN SCHIZOPHRENIA*

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SUMMARY

This study examined the relationship between measures of outcome and socio-demographic and diagnostic variables in schizophrenia. Product moment co-efficient of correlation and stepwise multiple regression were the main statistical techniques of analyses. The results of the study indicate that DSM-III diagnosis of schizophrenia, duration of illness, and Present State Examination-PSE Syndrome of non-specific psychosis are important predictors of outcome. CATEGO and Research Diagnostic Criteria-RDC diagnosis of Schizophrenia, and Schneiderian First Rank Symptoms were found to be poor predictors of outcome. Socio-demographic and clinical variables like gender of the patient, place of origin, impersistence at work, poor premorbid work record, hospitalization at the time of admittance into the study, loss of interest, affective flattening and incoherent speech were found to have prognostic implications.

Kraepelin (1919) and Bleuler (1950) in their writings about schizophrenia emphasized poor prognosis of this disorder. Subsequent workers like Langfeldt (1937, 1939), Kleist (1960) and Leonhard (1961) continued to conceptualize "true" schizophrenia as having poor prognosis and maintained that the notion of recovery was untenable with diagnosis of schizophrenia. Several investigators over the past 3 decades have endeavoured to elucidate the nature of prognosis in schizophrenia and identification of variables with which prognosis of schizophrenia could be predicted (Pope and Lipinski, 1978; Cloaingner et al., 1985; McGlashan, 1986).

In the late 60's and early 70's, realization grew that operational or semantic definitions for all psychiatric diagnostic categories in general and schizophrenia in particular more so for research purposes, must be provided (Cooper et al, 1972). Pioneering work of Feighner and his colleagues (1972) culminated in

the publication of operational criteria for 15 diagnostic categories. Ensuing years witnessed publication of a number of such operationalized schema of diagnosis for research in psychiatry, especially in relation to schizophrenia (Wing et al., 1974; Spitzer et al., 1978; American Psychiatric Association, 1980).

These operationalized definitions ushered in a new era of research pertaining to the diagnosis and prognosis of this disorder (Brockington et al., 1978; Kendell & Brockington, 1980; Helzer et al., 1981, 1983) and have highlighted that diagnosis of schizophrenia according to DSM-III (American Psychiatric Association, 1980) or Feighner et al (1972) is the most potent predictor of outcome. A shift towards deployment of multivariate techniques of statistical analysis as opposed to traditional univariate methods of analysis data is also discernible (McGlashan 1986; Endicott et al., 1986).

From our country, research data pertaining to prediction of outcome in

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schizophrenia is rather sparse. Reports of the International Pilot Study of Schizophrenia-IPSS of the World Health Organization (1973, 1979) and the works of investigators like Kulhara and Wig (1978), Verghese *et al.* (1985), Rajkumar *et al.* (1986), Sethi *et al.* (1987) and Kulhara and Chandiramani (1988) are some of the substantial investigations conducted in our country in relation to the course and outcome of schizophrenia. The present work was undertaken with the following aims :

- a. to study the relationship between various sociodemographic and clinical variables as prognostic indicators and outcome measures in schizophrenia.
- b. to develop through multivariate analyses a composite set of variables which predict outcome best.

Material and Method

The details of the setting of the study, procedures adopted for patient selection and categorizing them into various test definitions of schizophrenia have been described elsewhere (Kulhara *et al.*, 1986; Kulhara & Chandiramani, 1988). A brief description, however, is as follows

Patient Selection : Consultant colleagues in the department were requested to refer to the research team patients with a clinical diagnosis of schizophrenia. Consultant's diagnosis which conformed to ICD-9 (World Health Organisation, 1978) criteria for the diagnosis of schizophrenia was taken as the index diagnosis. The patients were reassessed and diagnosis of schizophrenia according to following definitions and criteria was formulated :

1. CATOGO Class S+ (Wing *et al.*, 1974).
2. First Rank Symptoms-FRS (Schneider, 1959)

3. Research Diagnostic Criteria-RDC (Spitzer *et al.*, 1978)
4. Criteria of Feighner *et al.* (1972).
5. DSM-III (American Psychiatric Association, 1980)

Outcome Measures : The patients were followed-up for a period ranging from 18 months to 30 months. At the end of the follow-up period outcome in the following areas was assessed using operationalized criteria as described by us earlier (Kulhara & Chandiramani, 1988) :

- a. Global clinical outcome
- b. Course of the disorder
- c. Work outcome
- d. Severity of illness at follow-up.

Assessment Tools : For assessing the clinical status and the outcome at the end of follow-up, the following instruments were used :

1. Present State Examination—PSE (Wing *et al.*, 1974)
2. Brief Psychiatric Rating Scale—BPRS (Overall & Gorham, 1962).

The PSE interview schedules were used to derive "syndrome" profile of each patient. For this "Syndrome Check List" of the PSE was also used. The severity of manifest psychopathology was judged on the basis of ratings on BPRS. The work status of the patient and course of the disorder as well as clinical outcome were assessed on the basis of structured clinical interview.

Data Analysis : The data analyses were carried out by using appropriate parametric and non-parametric statistical tests. Chi square test, Z test and Product Moment Co-efficient of Correlation were used. Stepwise multiple regression analyses were performed to assess the direction and strength of predictor variables.

For "stepwise multiple regression", outcome measures viz. clinical outcome, course of the disorder, severity of disorder and work status at follow-up were classed as dependent variables and socio-demo-

graphic, PSE and BPRS variables were classed as independent variables.

Results

At the time of intake, the cohort of the patients studied included 112 subjects. These patients were followed-up for a period ranging from 18 months to 30 months (mean 22.9 months, S.D 4.23 months). Of the 112 patients included in the study, 91 patients were traced and reassessed. The details of how the patients were assessed at follow-up have been provided by us in one of our earlier works (Kulhara & Chandiramani, 1988).

A comparison of the follow-up and dropout groups was carried out and is shown in table 1. It is obvious from this comparison that the follow-up and drop

out groups do not show statistically significant difference on any of the demographic and clinical variables.

The relationship between various socio-demographic and clinical variable (independent variables) and outcome measures (dependent variables) was studied by subjecting the data to correlational and multiple regression analyses. The list of independent variables, 47 in number, is appended (see appendix).

In the first step of the analysis, a correlation matrix consisting of the dependent variable i. e. clinical outcome, work outcome, course of the disorder and severity of illness at follow-up and the 47 independent variables was generated.

"r" values obtained were subjected to computation for deriving "z" transformation values. It was observed that

TABLE 1. Comparison between follow-up and Dropout groups*

Variable		Follow-up group (n=91)	Drop-out group (n=21)
Age in years :	Mean	28.64	28.04
	S.D.	8.42	9.66
Sex :	Male	52	7
	Female	39	14
Formal Education :	Upto 10 years	42	14
	More than 10 yrs	49	7
Residence :	Urban	63	15
	Rural	28	6
Duration of illness :	Upto 6 months	36	8
	More than 6 Months	55	13
Treatment status :	Treated as out-patient	48	8
	Hospitalised	43	13
Family history of Schizophrenia :	Present	25	2
	Absent	66	19
Marital status :	Single	38	7
	Married	53	14
Severity of illness at intake :	Mean	5.16	4.90
	S.D.	0.71	0.70

*X² test or Z test did not reveal any significant difference.

"r" values—0.21 only were statistically significant. Of the 47 independent variables which entered correlational analysis, only 18 items approached statistically significant level of correlation with outcome variables. These results are shown in Table 2. This table also shows variables which had correlation of 0.19 or 0.20 with the measures of outcome.

From table 2 it is apparent that only 4 independent variable e. g. duration of illness, diagnosis of schizophrenia according to the criteria of Feighner *et al.* (1972), diagnosis according to DSM-III (American Psychiatric Association, 1980)

and impersistence at work during follow-up had significant correlation with all outcome variables (see table 2).

Global clinical outcome also correlated well with gender of the patient, place of residence, incoherent speech on PSE (Wing *et al.*, 1974) at intake, PSE syndrome of non-specific psychosis and diagnosis according to ICD-9 (Table 2). Course of the disorder over the period of follow-up was also found to correlate well with PSE syndrome of non specific psychosis and poor premorbid work record (Table 2).

Outcome in the sphere of work and

TABLE 2. *Socio-demographic Variables and Clinical Variables having High Correlation with Outcome Measures**

Variable	Global Outcome	Course	Work outcome	Severity of illness at Follow-up
1. Duration	0.41	0.41	0.38	0.38
2. Feighner's Criteria	0.22	0.33	0.22	0.21
3. DSM-III Criteria	0.37	0.43	0.43	0.41
4. Impersistence at work	0.21	0.31	0.33	0.26
5. Incoherent speech	0.27	-0.17	-0.19	-0.18
6. Non-specific psychosis	-0.26	-0.21	-0.20	-0.22
7. Poor premorbid work	0.19	0.21	0.24	0.17
8. Gender	-0.20	-0.094	-0.06	-0.13
9. Residence	0.25	0.08	0.15	0.25
10. Severity of illness at intake	0.11	0.08	0.25	0.21
11. Follow-up in the clinic	-0.06	0.09	-0.20	-0.02
12. Drug compliance during follow-up	-0.16	-0.02	-0.27	-0.10
13. ICD-9 criteria	0.22	0.20	0.16	0.27
14. Poor premorbid adjustment	0.09	0.17	0.19	0.11
15. Flattened affect	0.13	0.20	0.15	0.08
16. Loss of interest	0.19	0.13	0.14	0.06
17. Hospitalization	0.14	0.16	0.22	0.30
18. Worry	0.11	-0.20	-0.20	0.13

* "r" value—0.21 significant at $p=0.05$

employment was also found to have significant correlation with poor premorbid work record, severity of illness at intake, drug compliance during follow-up and the variable of hospitalization (Table 2).

Likewise, the severity of illness at follow-up was highly correlated with the PSE syndrome of non-specific psychosis, residence of the patient, severity of illness at the time of intake, diagnosis according to ICD-9 and hospitalization of patient as well (Table 2).

Certain socio-demographic variables like age of the patient and marital status had poor correlation with outcome measures. Family history of schizophrenia was also found to have poor correlation with outcome variables. First Rank Symptoms of Schneider (1959) did not correlate well with outcome. There was

poor correlation between diagnosis of CATEGO S+ schizophrenia and outcome. Diagnosis of schizophrenia according to RDC of Spitzer et al. (1978) also showed poor correlation with global clinical outcome, course, work outcome and severity of the disorder at follow up. PSE (Wing et al., 1974) syndromes like Nuclear Syndrome (NS), Catatonic Syndromes (CS), Depressive Delusions (DD), Residual Syndrome (RS), Auditory Hallucination (AH), Persecutory Delusions (PE) Overactivity (OV), Social Unease (SU), Irritability (IR) and Neglect (NG) also had poor correlation with the various outcome measures. These results are shown in table 3.

The measures of outcome had high correlation among themselves suggesting their interdependence. Global clinical

TABLE 3. Variable Displaying poor correlation with Outcome Measures

Variable	Global Outcome	Course	Work Outcome	Severity of illness at follow-up
1. Age	0.11	0.002	0.04	0.05
2. Family history	-0.004	0.06	0.03	0.03
3. Marital status	-0.006	-0.02	0.01	0.03
4. Diagnosis of CATEGO+	-0.05	-0.07	-0.02	0.02
5. FRS	0.03	0.01	-0.06	0.03
6. RDC diagnosis of Schizophrenia	0.05	0.09	-0.04	-0.01
7. Nuclear syndrome	0.06	0.10	0.007	0.08
8. Catatonic syndrome	0.004	0.01	0.03	-0.007
9. Depressive delusions	0.01	-0.07	-0.03	0.00
10. Residual syndrome	-0.14	-0.11	0.12	-0.08
11. Auditory hallucinations	0.011	0.10	-0.08	-0.04
12. Persecutory delusions	0.007	0.00	-0.04	0.04
13. Over activity	-0.14	-0.08	-0.03	-0.04
14. Social unease	0.15	0.08	0.007	0.09
15. Irritability	0.12	0.006	0.15	-0.10
16. Neglect	0.03	0.03	0.10	0.03

outcome had a correlation of 0.80 with course, 0.76 with work outcome and 0.89 with severity of illness at follow-up. Course of the disorder had a correlation of 0.73 with work outcome and 0.86 with severity of illness at follow-up. Work outcome had a correlation of 0.78 with severity of illness at follow-up. All these "r" values are significant at $p < 0.01$.

Stepwise multiple regression analyses were carried out to assess the strength and direction of relationships among the dependent variables i.e. outcome measures and the independent variables i.e. socio-demographic and clinical variables. Independent variables which had significant correlation ($r \geq 0.21$) were selected to enter regression equations. In addition, certain other variables which had "r" values of 0.19 and 0.20 were also fed into the regression equations.

The first set of stepwise multiple regression was between global clinical

outcome as a dependent variable and 11 independent variable which had "r" values ≥ 0.19 . The results of this analysis are shown in table 4. Duration of illness had maximum influence on outcome followed by PSE Syndrome of incoherent speech, DSM-III diagnosis of schizophrenia, residence of the patient and so on. F values for all the variables was significant at $p < 0.005$. Total variance explained by all independent variables taken together was 34.22%. Poor premorbid work record and ICD-9 diagnosis did not contribute appreciably to the multiple co-efficient of correlation and Feighner's criteria, loss of interest and impersistence at work did not reach statistical significance.

As regards the course of the disorder over the period of follow up, results of stepwise multiple regression indicate that 6 independent variables namely, diagnosis of schizophrenia as per DSM-III cri-

TABLE 4. *Stepwise multiple regression : Global clinical outcome and certain socio-demographic and clinical variables.*

Independent variable	Step	R	R ²	F*
Duration †	1	0.413	0.170	18.323**
Incoherent speech	2	0.460	0.211	11.185**
DSM-III Criteria	3	0.497	0.247	9.513**
Residence	4	0.535	0.286	8.633**
Gender	5	0.552	0.304	7.439**
Non specific psychosis	6	0.565	0.319	6.570**
Poor premorbid work record	7	0.573	0.328	5.810**
ICD-9 criteria	8	0.578	0.334	5.146**
Feighner's criteria	9	0.582	0.338	4.604
Loss of interest	10	0.585	0.342	4.159
Impersistence at work at intake	11	0.585	0.342	3.734

*d.f. = 11, 90

**Significant at $p < 0.005$

Total variation explained by all independent variables = 34.228%

teria, duration of the illness, PSE Syndromes of loss of interest, affective flattening and non-specific psychosis, and imperistence at work at the time of admittance to the study contribute significantly to the prediction of the course. ICD-9 diagnosis, Feighner's criteria and poor premorbid work record do not add significantly to the variance explained by the independent variables as a composite set. The total variance explained by all these variables as a set is 31.13%.

When the relationship between work outcome and predictor variables is considered, DSM-III diagnosis of schizophrenia emerges as the most significant variable. Other variables which have prognostic implication are regular drug intake during follow-up, imperistence at work at the time of entry into the study, severity of illness at intake, syndrome of non specific psychosis, loss of interest and poor premorbid work record. Variables like Feighner's criteria for diagnosis of schizophrenia, duration of illness, hospitalization of the patient at the time of entry into the study, regularity of follow-up visits to the clinic and poor premorbid

adjustment do not increase the multiple correlation (R) appreciably. These results are shown in table 6.

An attempt was made to assess the predictive value of various variables in ascertaining severity of illness at follow-up. For this 10 variables entered multiple regression equations. DSM-III criteria of diagnosis of schizophrenia was found to be the most powerful predictor. Place of origin of the patient, hospitalization of the patient at intake, duration of illness and clinical features like PSE syndromes of incoherent speech and non-specific psychosis were important in prediction. Severity of illness at intake was found to be a poor predictor of severity of illness at follow-up. Diagnosis of schizophrenia according to ICD-9 concept of the disorder as well as according to Feighner's criteria and imperistence at work at intake were also found to be poor predictors and did not add appreciable to the value of R. These results are shown in table 7.

Thus, from stepwise multiple regression on this data set it is apparent that DSM-III diagnosis of schizophrenia,

TABLE 5. *Stepwise Regression : Course of the Disorder and certain Socio-demographic and Clinical Variables*

Independent variable	Step	R	R ²	F*
DSM-III Criteria	1	0.433	0.187	20.525**
Duration	2	0.478	0.228	13.040**
Loss of interest	3	0.509	0.259	10.134**
Affective Flattening	4	0.533	0.284	8.523**
Non-specific psychosis	5	0.542	0.293	7.059**
Imperistence at work	6	0.552	0.304	6.139**
ICD-9 criteria	7	0.558	0.311	5.348
Feighner's criteria	8	0.558	0.311	4.626
Poor premorbid work record	9	0.558	0.311	4.062

*d.f. for F values : 9,90 **Significant at $p < 0.005$. Total variance explained = 31.13%

TABLE 6. *Stepwise Regression: Work outcome and certain Socio-demographic and Clinical variables.*

Independent variable	Step	R	R ²	F*
DSM-III Criteria	1	0.437	0.190	20.965
Drug intake during follow-up	2	0.503	0.253	14.934
Impersistence at work (at intake)	3	0.537	0.288	11.775
Non-specific psychosis	4	0.571	0.326	10.385
Severity of illness at intake	5	0.588	0.345	8.993
Loss of interest	6	0.599	0.358	7.334
Poor premorbid work record	7	0.607	0.368	6.920
Feighner's criteria	8	0.612	0.374	6.144
Duration of illness	9	0.628	0.394	5.871
Follow-up in the clinic	10	0.629	0.395	5.232
Hospital status	11	0.629	0.395	4.703
Poor premorbid adjustment	12	0.629	0.395	4.257

*d.f. for F values: 12, 90 (All F values significant at $p < 0.005$). Total variance explained = 39.56%

TABLE 7. *Stepwise Regression: Severity of illness at follow-up and certain socio-demographic and clinical variables*

Independent variable	Step	R	R ²	F*
DSM-III criteria	1	0.418	0.174	18.882
Residence	2	0.482	0.232	13.293
Hospital status	3	0.528	0.278	11.206
Duration	4	0.562	0.315	9.929
Incoherent speech	5	0.583	0.339	8.764
Non-specific psychosis	6	0.596	0.355	7.705
ICD-9 diagnosis	7	0.606	0.367	6.897
Feighner's criteria	8	0.609	0.370	6.042
Impersistence at work	9	0.611	0.373	5.363
Severity of illness	10	0.612	0.374	4.791

*d.f. for F value: 10, 190 (All F value significant at $p < 0.005$). Total variance explained = 37.45%

(duration of illness, and PSE syndrome of non-specific psychosis are important predictors of outcome measures.

Discussion

Since the follow-up and drop-out groups do not differ significantly on any of the socio-demographic and clinical variables and as the rate of follow-up is reasonably high (82%) the results of the study can be generalized to the entire cohort.

The salient feature of the present study is that various diagnostic definitions of schizophrenia differ in prediction of outcome. DSM-III (American Psychiatric Association, 1980), Feighner et al. (1972) and ICD-9 (World Health Organization, 1978) diagnosis of schizophrenia were found to be significantly correlated with all of the four outcome measures. GATEGO (Wing et al., 1974), RDC (Spitzer et al., 1978) and FRS of Schneider (1959) had poor correlation with outcome. In this respect our findings are in agreement with the findings of Brockington et al. (1978), Kendell et al. (1979), Helzer et al., (1981, 1983) and Endicott et al. (1986).

DSM-III (American Psychiatric Association, 1980), criteria for the diagnosis of schizophrenia was found to be superior to other diagnostic definitions in prediction of outcome. In this respect, our findings are in agreement with the findings of McGlashan (1986) and Endicott et al. (1986). Furthermore, combining DSM-III criteria of diagnosis with duration of illness significantly increased multiple correlation (R) as well as the variance explained by the set of predictor variables. In this respect also, our findings reflect the trend reported by Helzer et al. (1981, 1983).

In the present study, PSE (Wing et al. 1974) syndromes of incoherent speech, and non-specific psychosis, gender and

the place of origin of the patients, and poor premorbid work record also contributed significantly to multiple correlation (R). Many earlier studies have also remarked on prognostic importance of these variables; incoherent speech and non-specific psychotic symptoms (World Health Organization, 1979), gender of the patient (World Health Organization, 1979, McGlashan, 1986) lack of urbanization (Sethi et al., 1987; World Health Organization, 1979) and poor premorbid work record (Brown et al., 1966; Vaillant, 1962). These earlier studies have considered these variables individually, the present study by virtue of multivariate analysis, has the advantage of considering them together.

DSM-III criteria for the diagnosis of schizophrenia and duration of the disorder were found to be the two most important prognostic predictors of the course of the disease over the period of follow-up. Three clinical variables i.e. PSE syndromes (Wing et al., 1974) of loss of interest, affective flattening and non-specific psychosis also contributed significantly to multiple correlation (R). Interestingly enough impersistence at work at the time of intake was the other variable which had significant influence on the course. Thus, the composite set of variable for predicting the course of the disorder is somewhat different from the set of variables which was earlier identified in relation to the global clinical outcome.

Prognostic variables for the prediction of work outcome are dominated by variables which reflect social interactions and work potential of an individual. It cannot be denied that impersistence at work, poor premorbid work record and loss of interest are tendencies which would adversely affect work performance of an individual. These together with poor drug intake during the period of follow-up

would make it exceedingly difficult for any patient to work efficiently. Though we have found these variables as a group to be a potent predictor of work outcome, many investigations have found these individually to be of prognostic importance (Stroffelmayer *et al.*, 1983; Strauss & Carpenter, 1978; World Health Organization, 1979; Moller *et al.*, 1982).

Variable which predicted severity of illness as a dimension of outcome were almost similar to the variables associated with the prediction of global clinical outcome though their relative contributions in terms of multiple correlation (R) were different. Hospital status *i.e.* whether or not the patient was hospitalized at the time of intake emerged as an influential variable in determining the severity of the illness at follow-up. Curiously enough, severity of illness at the time of admittance into the study did not appreciably increase the variance explainable by this set of variables.

Though most of the variables entering regression equation have significant correlation with the measures of outcome, total variance explained by these variables is also not insubstantial and ranged from 31.13% to 39.56%. The amount of outcome variance explained by the sets of predictor variables of the present work is almost similar to the ones obtained by McGlashan (1986). Our figures of total variance are also superior to those reported in the International follow-up study of Schizophrenia (World Health Organization, 1979). However, a large portion of variance still remains unexplained. Social support available to the patient, social and familial patterns of interactions, and expressed emotions are other important variables which may be contributing to prognosis and may account for some of the unexplained variance.

CONCLUSION

Our data and findings indicate that

3 variables *i.e.* DSM-III (American Psychiatric Association, 1980) diagnosis of schizophrenia, duration of the disorder and PSE syndrome non-specific psychosis are the variables which individually and collectively have significant properties of prediction of outcome in schizophrenia. It is suggested that these can be used as a set in predicting prognosis of schizophrenia in our country. However, replication of our findings by other workers from our country will greatly enhance the validity of this set of predictor variables. Perhaps, adding variables of social support, family interactions and expressed emotions may make the list of prognostic variables in schizophrenia more complete. A great deal of work though still remains to be done.

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APPENDIX

List of variables which were used in correlation analyses.

1. Gender of the patient
2. Age
3. Residence
4. Duration of illness
5. Hospital status
6. Family history of schizophrenia
7. Marital status at intake
8. Severity of illness at intake
9. Follow-up in the clinic
10. Drug intake during follow-up
11. CATEGO S + diagnosis of schizophrenia
12. Schneider's FRS
13. Spitzer *et al* (RDC) diagnosis of schizophrenia
14. Feighner's diagnosis of schizophrenia
15. DSM-III diagnosis of schizophrenia
16. ICD-9 diagnosis of schizophrenia
17. Poor pre-morbid adjustment
18. Poor pre-morbid work record
19. Impersistence at work at intake
20. Nuclear syndrome (NS)
21. Catatonic syndrome (CS)
22. Incoherent speech (IS)
23. Residual syndrome (RS)
24. Depressive delusions (DD)
25. Simple depression (SD)
26. Generalized anxiety (GL)
27. Hysteria (HT)
28. Affective flattening (AF)
29. Auditory hallucinations (AH)
30. Persecutory delusion (PE)
31. Delusions of reference (RE)
32. Sexual and fantastic delusions (SF)
33. Visual hallucinations (VH)
34. Overactivity (OV)
35. Slowness (SL)
36. Non-specific psychosis (NP)
37. Special features of depression (ED)
38. Agitation (AG)
39. Self neglect (NG)
40. Tension (TE)
41. Lack of energy (LE)
42. Worry (WO)
43. Irritability (IR)
44. Social unease (SU)
45. Loss of interest and concentration (IE)
46. Hypochondriasis (HE)
47. Other symptoms of depression (OD)