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Grade Methods in Evaluation of Clinical Scales Data to Measure Therapy Effectiveness

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The present paper describes how the grade approach has been applied to investigate a dataset from diagnostic questionnaires and scales obtained after completion of clinical therapy. It is shown that more regular copula data structures are observed after therapy. Grade methodology gives a valuable insight into effects of therapy. Moreover, grade exploration reveals new hidden variables and splits the questionnaire data into four more regularly monotone dependent segments, closely connected with level of improvement and external or internal controllability. Finally, two sets of homogeneous and ordered clusters of patients obtained before therapy as well as four segments obtained after therapy receive characterizations from the therapy effectiveness point of view, which may be useful in future medical therapeutic decisions. All analyses were performed using the GradeStat program.

K e y w o r d s: clinical data exploration, grade decomposition, neurotic disorders, Rotter scale

1. Introduction and Essential Results

Grade approach has recently been applied [1] to analyze and visualize a dataset from diagnostic clinical questionnaires and psychological scales collected from patients just before a ten-week therapeutic treatment of complex psychotherapy in the Department of Neuroses at the Psychiatry Clinic of the Medical University in Lublin (Poland). At present we supplement our investigation with exploration of the data obtained (for these patients and the same observable variables) after the completion of the clinical therapy.

Similarly as in the paper mentioned above the patients' records after the therapeutic treatment contain the measurements of the following first line variables: the Rotter Internal-External Control Scale [2], the Neurotic Disorders Scale of Bizoń

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and the "O" Symptom Check List of Aleksandrowicz [3], consisting of 13 subscales that concern intensity of various neurotic symptoms. Two set of clusters were formed in [1] on the basis of these first line variables. The remaining variables, called second line variables (because they were not involved in cluster making) are in particular: demographic variables (marriage status, gender, age and education) and medical classifications (in terms of ICD-10). Moreover, they include the global results of the "O" Symptom Check List of Aleksandrowicz (the sums of the results of all subscales) collected before and after therapy. These two variables denoted *SUM1* and *SUM2* are used to define a therapy improvement level as follows

$$level\ of\ improvement = ((SUM1 - SUM2)/SUM1) \cdot 100\%$$

After the grade decomposition of the post therapy data described in Section 2 we obtained four subsets of patients' records differing mostly in *level of improvement*, Rotter scale values and ICD-10 classifications. These four subsets form a kind of a 2×2 polythetic classification of the whole post-therapy dataset, i.e. the whole dataset is polythetically cross-classified by two variables: Locus of Control denoted LOC (internal or external) and *level of improvement* (higher or lower). By the polythetic cross-classification we mean that the division concerning these two variables is not exact: each subset consists of a group of patients with a significant majority of patients with LOC and a level of improvement belonging to four categories defined by these two variables (cf. Table 1) and each segment is also possibly homogenous with respect to the first line variables.

Table 1. Four segments of patients due to a grade polythetic cross-classification of the post therapy data with respect to LOC and a level of improvement

Patients with LOC	Level of improvement	
	lower	higher
external	segment1 $n_1 = 30$	segment2 $n_2 = 19$
internal	segment3 $n_3 = 15$	segment4 $n_4 = 16$

The segment 1 is dominated by the patients with anxious and depressive disorders diagnosed; neurotic disorders are diagnosed in the majority of cases in the segments 2 and 4; the adjustment disorders and anxious, depressive disorders are the most frequent diagnoses of patients in the segment 3.

The results of grade decomposition could lead to important conclusions concerning medical treatment, in particular about qualifying patients to a specific type of therapy. Grade polythetic cross-classification, which is described in Sections 2 and 3, seems to be a valuable tool to decompose mixtures formed by several segments with possibly regular monotone dependent data sets.

Note that two-segment grade decomposition of the pre-therapy data for the same set of patients was also performed and seven resulting homogenous and ordered clusters are described in [1]. It is therefore interesting to compare the post therapy and the pre-therapy data from two points of view: firstly basing on post-therapy segmentation onto 4 segments, secondly on pre-therapy clustering onto 7 clusters. This is done in Section 3 and 4.

2. Grade Decomposition of Post Therapy Data into Four Segments

The post-therapy data form a patients/variables table with the records of 80 patients (rows) and 15 first-line variables (columns). All variables in the post-therapy data have the index 2 attached to their names to distinguish them from the pre-therapy observations. The names of the post-therapy first line variables are:

- *I-E Rotter2* (scale with values from 0 to 23, with low values indicating internal LOC and high values indicating external LOC);
- *Bizoń2* (higher values of the scale are believed to reflect stronger neurotic disorders);
- 13 subscales in the Aleksandrowicz questionnaire: *fear2, depression2, anxiety2, hypochondria2, somatic symptoms2, hysteria2, neurasthenia2, psychasthenia2, derealization2, compulsions2, sexual disorders2, sleep disorders2, social difficulties2.*

Similarly as in [1] the patients and the variables are ordered by the GCA (Grade Correspondence Analysis) procedure, so that the strength of monotone dependence of the data table measured by grade correlation ρ^* is maximal. The result is presented in Fig. 1 by means of the so called overrepresentation map (explained in [1]). Under this GCA ordering the patients at the top of vertical axis tend to have possibly large values of the most left variables (hypochondria2, somatic symptoms2, compulsions2) and small values of right variables (Rotter2), while the patients at the bottom of vertical axis tend to have small values of the most left variables and very large values of Rotter2.

The records of external-controllability patients, i.e. patients with external LOC (dark arrow-shaped markers), tend to concentrate at the bottom of the map, while the records of internal-controllability patients, i.e. those with internal LOC (light rectangular markers), tend to concentrate in the upper part of the map.

The patients most strongly outlying from the GCA ordering are specified as outliers from regularity and marked on the left side of the map. Thus the whole total set of 80 patients after therapy (named TOTAL2) is divided into two subsets: a subset called FIT2 which consists of the patients better fitted to the GCA trend and a subset OUT2 consisting of the outliers from regularity. The overrepresentation maps of the subsets FIT2 and OUT2 are given in Fig. 2 and Fig. 3 respectively after their subsequent transformation by GCA.

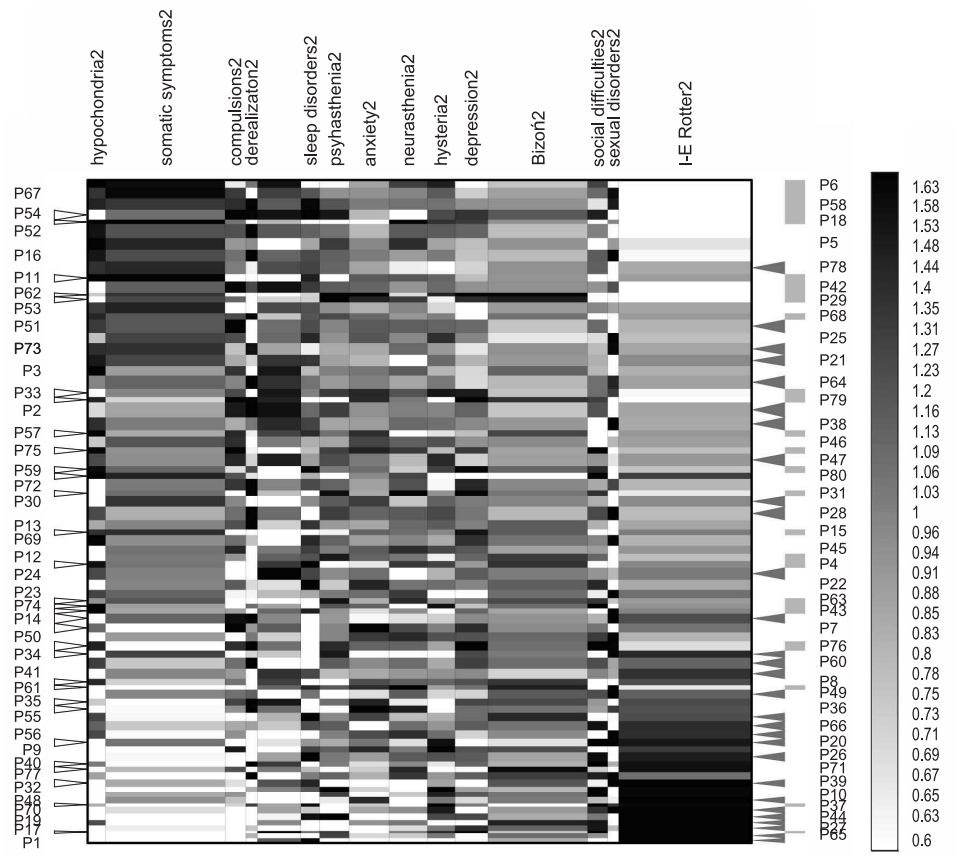

Fig. 1. The post-GCA overrepresentation map presenting patients/variables table after therapy for 15 first line variables and 80 the same patients (coded P1, P2, … P80). At the right side of the map dark arrow-shaped markers are attached to the patients with high external-controllability and light rectangular markers are attached to the patients with high internal-controllability. White arrow-shaped markers at the left side of the map are attached to the patients most outlying from the positive dependence pattern. The values of grade density are determined according to the scale of grey given at the right side of the map. The values of ρ^* and τ are 0.202 and 0.136, the regularity index τ_{max}/τ_{abs} is 0.47

The GCA ordering of the variables in FIT2 differs only slightly from that in TOTAL2, while the GCA ordering of OUT2 is more different. In both these subsets a special role in the ordering is played by the position of *social difficulties* which aspires to be one of main variables in FIT2, similarly as *sexual disorders* in OUT2.
It is worth special attention that in TOTAL2, FIT2 and OUT2 the GCA ordering of variables is mainly determined by I-E Rotter scale situated always on right. Subset FIT2 is strongly dominated by highly external-controllable patients (25 external, 6 internal) on the contrary to subset OUT2 with internal-controllable people in majority (only 4 external to 20 internal). This apparent controversy is due to strongly different marginal distributions of Rotter in FIT2 and in OUT2, as it is seen on

the histograms presented in Fig. 4. Generally, it is strongly advocated to supplement overrepresentation maps with histograms of variables.

Now we decompose the subsets FIT2 and OUT2 onto upper and lower segments in such a way that the lower part in FIT2 is the largest possible which does not contain internal-controllable patients, while the upper part in OUT2 contains no external-controllable patients. The division of FIT2 and OUT2 onto the lower and upper part ensures possibly high homogeneity of each of four parts . The lines differing the upper and lower parts are shown in Fig. 2 and Fig. 3. In the segment 1 (the upper part of FIT2) there are 11 external-controllable and 6 internal-controllable patients. In the segment 2 (the lower part of FIT2) there are no internal-controllable patients. In the segment 3 (the upper part of OUT2) there are no external-controllable patients. In the segment 4 (the lower part of OUT2) there are only 4 external-controllable and 8 internal-controllable patients.

It will be shown in the next section that a significant improvement has been achieved in the segment 2 with external-controllable patients and the segment 4 with internal-controllable patients in the majority. There was no improvement in the segment 1 (with more external than internal-controllability) and a rather low level of improvement is noted in the segment 3 of internal-controllable patients.

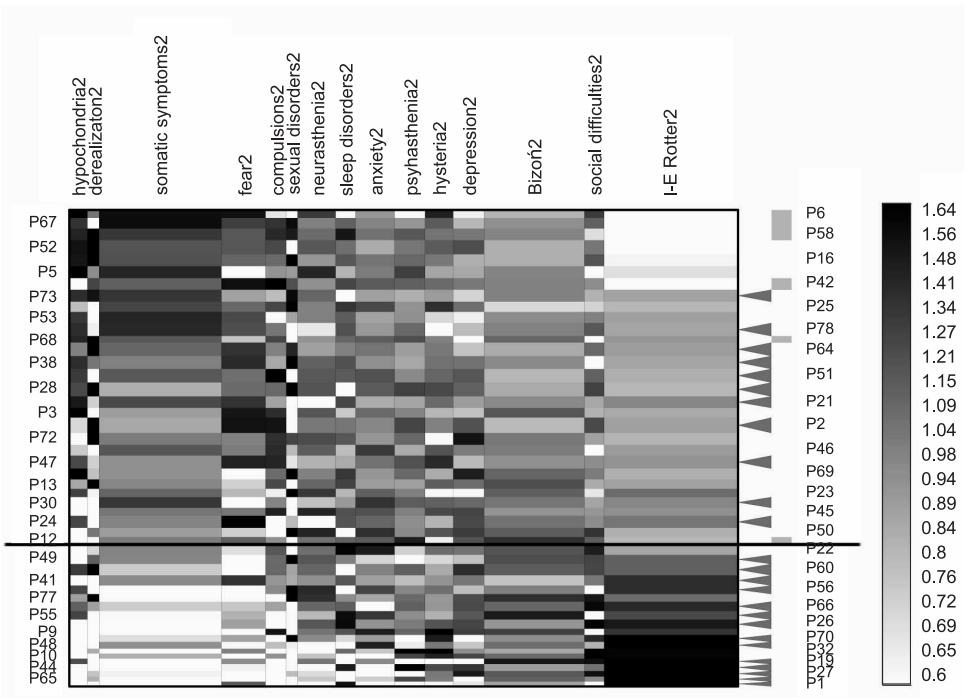

Fig. 2. The post-GCA overrepresentation map for the FIT2 subset after therapy (markers at right and patients' labels have the same meaning as in Fig. 1). The patients' records are divided into the upper and lower segment. The values of ρ^* and τ are 0.211 and 0.142, the regularity index τ_{max}/τ_{abs} is 0.57

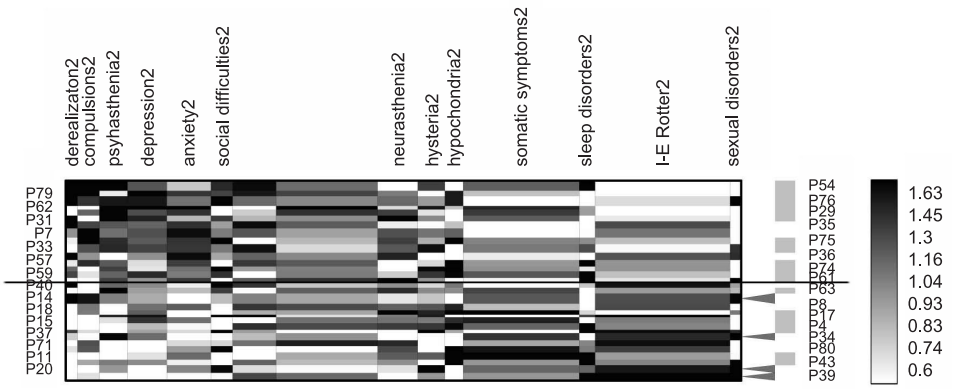

Fig. 3. The post-GCA overrepresentation map for the OUT2 subset after therapy (markers at right and patients' labels have the same meaning as in Fig. 1). The patients' records are divided into the upper and lower equal segment. The values of ρ* and τ are 0.221 and 0.148, the regularity index τ_{max}/τ_{abs} is 0.41

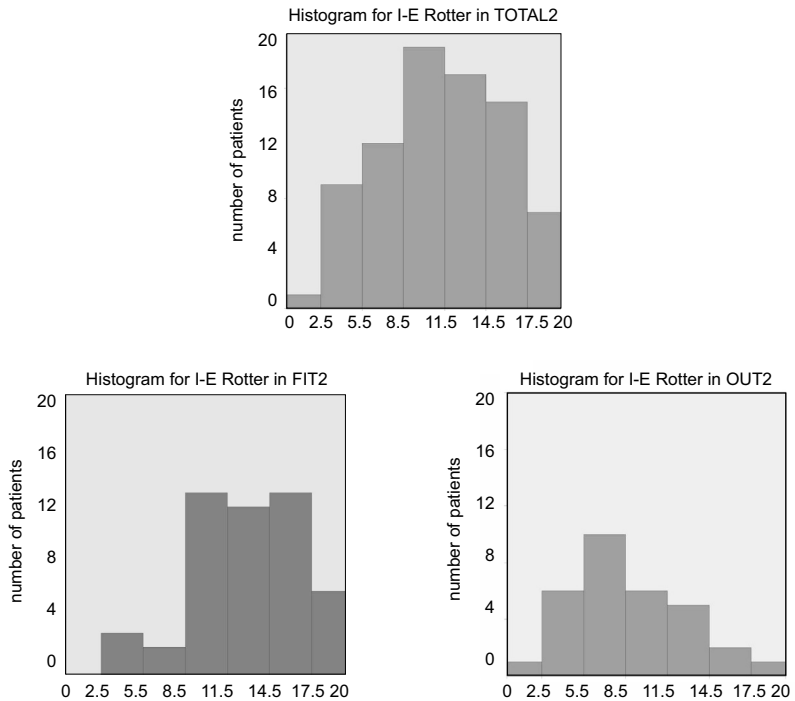

Fig. 4. The histograms for I-E Rotter scale which determines the trend in TOTAL2, FIT2 and OUT2

As a result, we obtain a 2×2 table anticipated in Section1. This table satisfies the requirement of the polythetic cross-classification with respect to the external/internal-controllability and a lower/higher level of improvement.

3. Comparison of Post-therapy and Pre-therapy Data Referred to Post-therapy Data Segmentation

This section intends to investigate the nature of post therapy effects basing on four segments which have been constructed in Section 2. These segments will be described now by Figs 5, 6 summarizing the information obtained before and after therapy concerning global results of the "O" questionnaire as well as the Bizoń and Rotter scales, a level of improvement and values of some of second line variables. It is noticeable that a significant improvement has been achieved in the segment 2 dominated by the external-controllability patients most of whom were diagnosed with neurotic disorders (F48.9 in ICD-10) as well as in the segment 4 dominated by the women diagnosed with neurotic and personal disorders (F48.9, F60.8). The smallest improvement is noted in the segment1, where the dominating diagnosis are anxious and depressive disorders (F41).

	SUM1 of "O"	SUM2 of "O"	% improvement	BIZOŃ1	BIZOŃ2	ROTTER1	ROTTER2	% women	% married	mean age	level of education	F41	F43.2	F48.9	F60.8	numbers of patients
segment1	447	433	1	78	79	12.1	11.9	60	57	34	3.7	12	5	7	8	30
segment2	353	222	36	71	61	13.6	15.1	58	53	34	3.6	3	3	8	3	19
FIT2	411	351	15	75	72	12.7	13.2	59	55	34	3.65	15	8	15	11	49

Fig. 5. The characterization of the segments 1 and 2 of FIT2 by the mean values of SUM of "O", Bizoń and Rotter average results before and after therapy, a level of improvement and selected second line variables (note that the total numbers of diagnoses attached to the patients may differ in each segment from the respective total numbers of patients as only four most frequent diagnoses are taken into account in the table and moreover a patient may be diagnosed with more than one diagnosis)

	SUM1 of "O"	SUM2 of "O"	% improvement	BIZOŃ1	BIZOŃ2	ROTTER1	ROTTER2	% women	% married	mean age	level of education	F41	F43.2	F48.9	F60.8	numbers of patients
segment3	308	253	10	65	60	7.5	6.8	40	33	28	3.8	4	5	3	4	15
segment4	337	199	36	65	48	11.3	10.3	81	44	31	3.3	3	2	7	9	16
OUT2	323	225	24	65	54	9.5	8.6	61	39	29	3.5	7	7	10	13	31

Fig. 6. The characterization of the segments 3 and 4 of OUT2 by means of SUM of "O", Bizoń and Rotter average results before and after therapy, level of improvement and selected second line variables

It is possible to explore the character of patients' post therapy improvement. Tables 2 and 3 present the mean level of particular neurotic disorders measured by subscales of the Aleksandrowicz questionnaire before and after therapy in the particular segments of patients. In the segments 2 and 4, where the mean level of improvement achieves as much as 36%, we also note a significant improvement of *somatic symptoms*, *fear, anxiety and depression*. Furthermore, a considerable reduction of *neurasthenia* in the segment 2 and reduction of *psychasthenia* in the segment 4 are observed. On the other hand, in the segment 1 there is the highest mean level of neurotic symptoms both before and after therapy, and only 1% of the mean global improvement. Moreover, during the therapeutic cycle *anxiety* increases on average in the segments 1 and 3.

Table 2. Comparison of the mean level of neurotic symptoms before and after therapy in the segments of FIT2

	hypochondria1	hypochondria2	derealization1	derealizaton2	somatic symptoms1	somatic symptoms2	fear1	fear2	compulsions1	compulsions2	sexual disorders1	sexual disorders2	neurasthenia1	neurasthenia2	sleep disorders1	sleep disorders2	anxiety1	anxiety2	psychasthenia1	psychasthenia2	hysteria1	hysteria2	depression1	depression2	social difficulties1	social difficulties2
segment1	22	20	13	12	135	130	50	46	20	21	13	11	40	36	19	19	34	38	28	29	27	26	29	29	19	17
segment2	14	6	10	5	93	51	33	19	14	10	10	7	32	22	17	12	33	22	24	18	25	18	29	20	20	15
FIT2	19	15	12	9	119	99	43	36	18	17	12	9	37	31	18	16	33	32	27	25	26	23	29	25	19	16

Table 3. Comparison of the mean level of neurotic symptoms before and after therapy in the segments of OUT2

	hypochondria1	hypochondria2	derealization1	derealization2	somatic symptoms1	somatic symptoms2	fear1	fear2	compulsions1	compulsions2	sexual disorders1	sexual disorders2	neurasthenia1	neurasthenia2	sleep disorders1	sleep disorders2	anxiety1	anxiety2	psychasthenia1	psychasthenia2	hysteria1	hysteria2	depression1	depression2	social difficulties1	social difficulties2
segment3	14	10	12	9	71	54	30	25	16	15	8	4	30	22	10	8	27	30	21	20	20	14	27	26	15	13
segment4	12	9	11	3	102	64	40	19	13	7	6	7	27	19	16	8	25	15	21	9	20	13	25	14	15	9
OUT2	13	9	12	6	87	59	35	22	14	11	7	6	29	20	13	8	26	22	21	14	20	13	26	20	15	11

4. Comparison of Post-therapy and Pre-therapy Data Referred to Pre-therapy Data Clustering

The pre-therapy clustering described in [1] divided the whole set of 80 patients into two parts denoted FIT1 and OUT1, which were subsequently divided into ordered

clusters 1–4 in FIT1 and 5-7 in OUT1. This clustering does not take into account any post therapy information. Therefore, we may pose a question whether it has a really meaningful predictive value.

The post therapy segmentation described in Sections 2 and 3 of the present paper divided the considered set of 80 patients into two parts denoted FIT2 and OUT2, with FIT2 consisting of the segments 1 and 2, while OUT2 consisting of the segments 3 and 4. The segments 2 and 4 were shown to form possibly homogeneous although different groups of 19 and 16 patients, a majority of whom gained a substantive level of improvement as a result of therapy. Which of seven pre-therapy clusters most strongly contributed to the segments 2 and 4, consisting mostly of the patients who benefited from therapy? From which clusters do the patients come to such hopeless segment 1?

The flow of patients from the pre-therapy clusters to the post-therapy segments is illustrated with a map in Fig 7. The number of patients from the i-th cluster ($i = 1, 2,\ldots,7$) to the j-th segment ($j = 1, 2, 3, 4$) is inscribed into the cell at the intersection of row i and column j. The columns 4 and 2 in the middle show the segments with the majority of patients who benefited from therapy, whereas column 1 is the segment the most strongly dominated by the patients of therapeutic failure. The map is the first step to construct a discriminant rule which, after assigning a new patient from one of the seven clusters, will qualify (or not) this person for therapy. Additional valuable information can be obtained from the ICD-10 diagnoses and demographic data, as well as from current experience (cf. Tables 4–7).

The overwhelming majority of the patients from the clusters 1, 2 and 3 assigned to the segment 1 implies the necessity to choose another kind of therapy for the patients with a similar profile (with respect to the values of the first and second line variables), whereas the vast majority of the patients from the clusters 4, 6 and 7 in

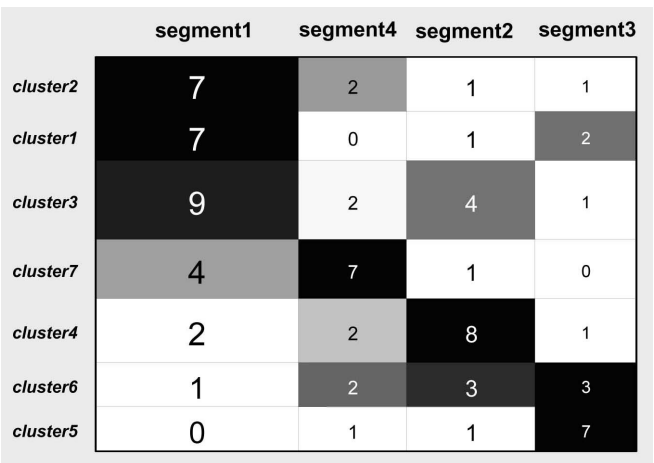

Fig. 7. The flow of patients from the pre-therapy clusters to the post-therapy segments

the segments 2 and 4 gives a positive prognosis about therapy results for the patients with a similar profile. The fact that the patients with a profile similar to the cluster 5 were assigned to the segment 3 (with the average level of improvement only 10%) does not allow too optimistic prognosis for a successful outcome of their therapy. Note that the average level of improvement overlooks the extent of improvement attained for the individual patients. From this point of view we can observe that the best results after therapy were achieved by the unmarried neurotic patients from the cluster 6, namely 40% level of global improvement, great reduction of all neurotic symptoms and neuroticism of Bizoń, and even slight decrease in values on the Rotter scale. We observe the minimal improvement (only 6%) of the youngest, educated patients from the clusters 3, and also in the cluster 5 of the single, strong internal-controllability men with anxious, depressive or adjustment disorders diagnosed. Just among those patients who do not respond to the treatment for neurosis which

Table 4. The characterization of clusters of FIT1 by means of averages of global first line variables before and after therapy as well as second line variables

	BIZON1	BIZOŃ2	SUM1 of "O"	SUM2 of "O"	% improvement	ROTTER1	ROTTER2	% married	% women	mean age	education	F41	F43.2	F48.0	F48.9	F60.8	numbers of patients
cluster1	79	75	550	422	24	9.6	9.6	50	40	38	3.2	1	4	3	0	3	10
cluster2	79	75	462	393	15	12.1	11.8	56	55	36	4.5	6	2	1	1	4	11
cluster3	74	76	382	356	6	12.4	12.9	63	63	29	3.4	3	2	2	8	6	16
cluster4	71	57	261	197	23	15	14.1	70	77	35	3.5	3	1	3	5	2	13
FIT1	75	70	402	336	16	12.4	12.3	60	60	33	3.6	13	9	9	14	15	50

Table 5. The characterization of clusters of OUT1 by means of global first line variables before and after therapy as well as second line variables

	BIZON1	BIZOŃ2	SUM1 of "O"	SUM2 of "O"	% improvement	ROTTER1	ROTTER2	% married	% women	mean age	level of education	F41	F43.2	F48.0	F48.9	F60.8	numbers of patients
cluster5	62	58	304	250	11	6.3	7.6	22	33	27	3.4	4	2	0	2	2	9
cluster6	69	57	358	206	40	10.6	10.1	22	56	32	4	2	1	0	5	2	9
cluster7	63	52	341	276	17	11.9	11.6	42	83	32	3.3	3	3	1	4	5	12
OUT1	64	55	335	247	22	9.8	9.9	30	60	30	3.5	9	6	1	11	9	30

employing the method of psychotherapy we note a slight average increase in the values of the Rotter scale after therapy – in contrast to the patients with the most substantial symptomatic improvement and concomitant decrease in the values of this scale, as it is noticeable in the clusters 6 and also in the cluster 4, formed by strongly external-controllability, rather married women.

Using the Tables 6–7, it is possible to name the kind of symptoms for which the expected changes have occurred. For example we may observe that in the cluster 3, the one with the least satisfactory effect of therapy, there are invariably depressive symptoms at the highest average level. The spectacularly greatest reduction in depression disorders (apart from other good results) is noted in the cluster 6, formed by the patients most effectively responding to therapy. On the other hand, the most considerable reduction in fears, phobias and hypochondria is achieved in the cluster 1, formed by the oldest patients with the highest neurotic symptoms.

Finally, it can be concluded that the complex psychotherapy is not an effective method for patients with a high level of neurotic disorders and anxious and depressive disorders (F41) diagnosed, which is confirmed by clinical practice.

Table 6. Comparison of mean level of neurotic symptoms before and after therapy in clusters of FIT1

	derealization1	derealization2	hypochondria1	hypochondria2	compulsions1	compulsions2	somatic symptoms1	somatic symptoms2	sexual disorders1	sexual disorders2	fear1	fear2	sleep disorders1	sleep disorders2	anxiety1	anxiety2	hysteria1	hysteria2	neurasthenia1	neurasthenia2	social difficulties1	social difficulties2	depression1	depression2	psychasthenia1	psychasthenia2
cluster1	18	15	32	21	24	20	183	135	14	8	65	44	23	18	41	35	31	24	38	34	24	18	31	25	29	26
cluster2	18	12	25	22	21	20	128	107	17	18	49	37	20	16	36	34	27	23	44	35	19	14	31	28	28	28
cluster3	12	8	13	12	19	20	105	95	7	6	37	35	18	16	36	35	23	25	37	34	18	15	31	31	27	25
cluster4	3	3	10	5	8	8	66	53	6	4	29	22	12	8	23	19	20	14	25	15	15	11	23	18	22	17
FIT1	12	9	19	14	18	17	116	94	10	8	43	34	18	14	34	31	25	21	35	29	19	14	29	26	26	24

Table 7. Comparison of mean level of neurotic symptoms before and after therapy in clusters of OUT1

	derealization1	derealization2	hypochondria1	hypochondria2	compulsions1	compulsions2	somatic symptoms1	somatic symptoms2	sexual disorders1	sexual disorders2	fear1	fear2	sleep disorders1	sleep disorders2	anxiety1	anxiety2	hysteria1	hysteria2	neurasthenia1	neurasthenia2	social difficulties1	social difficulties2	depression1	depression2	psychasthenia1	psychasthenia2
cluster5	17	11	11	10	17	16	57	45	8	7	26	24	11	8	27	28	23	16	32	21	19	18	32	26	24	20
cluster6	15	5	12	6	19	7	81	50	13	6	36	21	16	8	32	22	24	11	37	25	19	12	31	17	24	16
cluster7	6	4	15	13	11	10	125	95	7	7	43	29	15	16	22	23	22	20	27	23	13	12	19	15	18	12
OUT1	12	6	13	10	15	11	91	67	9	7	36	25	14	11	26	24	23	16	31	23	17	14	26	19	22	16

5. Final Remarks

Grade methods described in [4] are used successfully to analyze medical data (see [5] and [6]). In exploration of multivariate medical datasets consisting of the data obtained before and after therapeutic treatment a predictive power is of particular interest. It seems that segmentation of medical data which refers to strength and regularity of dependence of multivariate datasets, possesses a predictive power and can deliver valuable prognoses for clinical practice.

It is remarkable that after therapy strength of dependence slightly improves (cf. Table 6), the more so that the number of post therapy segments is smaller than the number of pre-therapy clusters. It suggests that after therapy the levels of neurotic symptoms and internal/external controllability are somewhat "better adjusted" to the patients, or "better recognized", and that the doubtful patients were more effectively excluded from the post-therapy FIT subset, following better the main trend than it happened in the case of the pre-therapy FIT subset. This is a positive sign of therapy meaningfulness.

Table 8. Comparison of strength and regularity for the post-GCA TOTAL, FIT and OUT subsets of the patients before and after therapy

Post-GCA$_S$	Grade parameters of strength and regularity	Before therapy	After therapy
TOTAL	ρ* (Spearman rho)	0.165	0.202
	regularity index	0.44	0.47
FIT	ρ*	0.185	0.211
	regularity index	0.55	0.57
OUT	ρ*	0.202	0.221
	regularity index	0.45	0.41

Generally the paper contributes those other in statistical literature which look for new effective methods of a meaningful separation of mixtures.

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