

# MEDICAL COMORBIDITIES IN PATIENTS WITH UNIPOLAR DEPRESSION

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## REZUMAT

**Objective:** Tulburarea depresivă recurentă reprezintă una din cele mai prevalente tulburări psihice de pe întreg globul și, în consecință, constituie o problemă majoră de sănătate publică. Scopul principal al lucrării a fost acela de a releva nivelele de comorbiditate la pacienții depresivi și de a stabili factorii care o influențează. **Material și metode:** Am realizat un studiu retrospectiv pe 248 pacienți internați în Clinica noastră în perioada 2001-2005 cu diagnosticul de tulburare depresivă recurentă conform ICD-10. Rezultatele au fost supuse prelucrării statistice. **Rezultate:** Datele socio-demografice au fost în consens cu literatura internațională. Cifrele de prevalență privind comorbiditatea cu bolile cardiovasculare și cerebrovasculare au fost semnificativ mai mari la pacienții depresivi comparativ cu datele de prevalență în populația județului Timiș. Prezența bolilor somatice au crescut riscul de depresie, iar depresia, în sine, a fost un factor de risc pentru apariția anumitor boli somatice. Bolile cardiovasculare s-au asociat cu trăsăturile de personalitate de cluster C, conform DSM-IV. Analiza în interiorul lotului de depresivi a indicat că bolile osteo-articulare cresc independent riscul de suicid, iar comorbiditățile totale cresc frecvența spitalizărilor. De asemenea, vârsta crescută și nivelul educativ scăzut au favorizat apariția comorbidității somatice. **Concluzii:** Comorbiditatea somatică constituie o importantă problemă la pacienții cu depresie. Factori precum trăsăturile de personalitate, nivelul educațional și vârsta contribuie la apariția comorbidității somatice. **Cuvinte cheie:** Tulburare depresivă, prevalență, comorbidități somatice, factori de risc, spitalizare

## ABSTRACT

**Objective:** Recurrent depressive disorders are the most prevalent psychiatric disorders worldwide, raising several major problems related to public health. The main objective of our study was to reveal the levels of comorbidity in depressive patients and to establish which factors influence it. **Material and methods:** We have conducted a retrospective study on 248 patients admitted in our Clinic between 2001 and 2005 with the diagnosis of recurrent depressive disorders, according to ICD-10 criteria. Two control samples were selected: one with bipolar affective disorder and other with persistent delusional disorder. The results were statistically analyzed. **Results:** The socio-demographic data were in consensus with international literature. The prevalence figures for cardiovascular diseases and cerebrovascular diseases were constantly higher in the studied sample of depressive patients, as compared with the prevalence reported in Timiș county population. Somatic diseases increase the risk for depression and depression itself increases the risk for some somatic disease. The cardiovascular diseases were associated with cluster C personality traits. The analysis within the depressive sample reveals that musculoskeletal diseases increase the risk of suicide and the total comorbidities increase the frequency of hospitalization. Also, aging and educational level were correlated with somatic comorbidity. **Conclusion:** Somatic comorbidity represents an important issue in depressive patients. Factors as personality traits, educational level and age influence the somatic comorbidity in depressive patients.

**Key Words:** Depressive disorders, prevalence, somatic comorbidities, risk factors, hospitalization

## INTRODUCTION

Both clinical and epidemiological studies reveal that depression is the most prevalent psychiatric disorders existing around the world with highest level of comorbid conditions.<sup>1-3</sup> According to The Global Burden of Disease concept, conceived and estimated by Murray and Lopez, depression, though frequent,

is currently under diagnosed.<sup>4,5</sup> The estimates for 1990 performed by aforementioned authors reveal that depression ranked fourth regarding the global costs related to all diseases and, moreover, in 2020 depression will be on second place. Among the factors that increase the economical and clinical importance of depression, somatic co-morbidity is a significant one. Medical co-morbidity increase both direct and indirect costs of depression. The indirect costs represents the majority of costs related to clinical depression due to the lost of productivity and professional disability. Along with patient's professional problems, there are frequently repercussions on patient's family members related to professional neglecting.<sup>6,7</sup> The most frequent somatic co-morbidities of depression include cardiovascular disease, neurological disease, diabetes mellitus, neoplastic diseases, etc.<sup>8-12</sup> There are several biological mechanisms incriminated in pathogenesis of depression and some of somatic diseases like:

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autonomic dysfunctions, serotonergic and anti-platelet dysfunctions, endothelial dysfunction, etc. Moreover, it is possible that medical co-morbidities are responsible for therapeutic resistance and thereafter for increasing the costs of depression.<sup>12</sup>

From a categorical approach, we can say that the syndromes of depression can be found in a large variety of psychic disturbances, as: mourning, adaptation disorders (more precisely, the depressive reaction), depression associated with the use of psychoactive drugs (during both consume and withdrawal periods), drug-induced depression (e.g. by interferon, cortical steroids, oral contraceptives, etc), depression induced by a somatic illness (a systemic illness with consequences upon the functioning of the CNS, like the Cushing disease, or a primary neurological illness associated with depressive symptoms), and so on. In the next pages we will address the problem of major depression in the frame of affective mood disorders, according to diagnostic criteria of DSM-IV and ICD-10.

Despite the fact that major depression is one of the addressable psychic disorders, we should mention some problems related to the diagnostic and the natural course of depression. Unfortunately, depression is often under diagnosed because of the presence of other psychic disorders, due to its complex clinical picture. Specifics related to age should always be taken into consideration, as some subjects from extreme age groups can be sometimes misdiagnosed. For example, depression in children is often manifest thorough an irritable disposition, while depression in adolescents can take the form of behavioral modifications, or educational failure (due to the extremely important impact of the depression upon the cognitive functioning), and in elderly people it is often discussed the problem of masked depression (confusion with somatic complains and the neglect of depressive mood). Even it is less "trendy", this concept is now discussed again by the international experts, possibly due to the significant economical consequences it has, induced by the large (and often inefficient) use of the health services by this category of patients. The second problem discussed concerns the natural course of major depression, an illness with high recurrence. Studies have indicated that 30% of the patients remain depressive one year after the disorder has been first diagnosed, 18% after two years and 12% after five years. On the other side, despite a high response rate to antidepressant medication (according to some studies up to 75-80%), 50% of the patients will still experience at least one depressive episode in the future. We should also consider the problem of the resistant (to

medication) depression, for which the most common causes are: associated comorbidity (either with another psychiatric disorder, especially alcohol consumption and personality disorders, or with some somatic illnesses, like hypertension, diabetes mellitus, digestive diseases, etc), the lack of an adequate therapeutic treatment (related to the administered medication's dose and period of administration) but also the lack of social support (especially for elderly people, who, apart from the loss of professional and social status through retirement must also face loneliness).

## OBJECTIVE

Our purposes were to reveal the level of somatic co-morbidity in depression and to find the factors that may influence the occurrence of somatic diseases in this type of patients. Often, the relationship between somatic diseases and depression is quite complex, and is bidirectional one. The sequencing of the occurrences gives us the precious data regarding causality between two distinct conditions. For these reasons we have chosen to perform a retrospective study.

The hypotheses for all samples were as follows:

a. According with our clinical observations and literature data we supposed that the frequencies of high blood pressure, coronary artery disease, diabetes mellitus, malignant tumors and cerebro-vascular diseases are higher in depressive patients that in our county population.

b. Several socio-demographical characteristics may exert their influences on somatic diseases occurrences in depressive patients.

c. We supposed that the preexistent somatic disease could increase the risk of depression and that depression once occurred increases the risk for some somatic diseases.

d. Antipsychotic drugs, the personality factors, stressful life events and familial history may exert their influences on co-morbidity.

e. Depression could have more important consequences on professional ability than other psychiatric conditions.

## MATERIALS AND METHODS

The present study is a part of the doctoral studies performed by Dr. Virgil Enatescu. The retrospective research took place by viewing the medical records of the patients hospitalized in the Psychiatric Clinic from Timișoara between 2001 and 2005. The study patients were selected on the basis of the following inclusion

criteria: presence of recurrent depressive disorder, bipolar affective disorder and persistent delusional disorder, and age between 18-65 years. Exclusion criteria were represented by psychiatric comorbidities, with the exception of dysthymia and personality disorders. The patients selected were divided in three groups, depending on the principal diagnostic. The study sample was represented by depressive patients and control samples by bipolar and persistent delusional disorders.

The instruments used were: the retrospective data sheet for collecting data in longitudinal research and additional data sheet for depressive sample. Along with medical records we examined all medical and surgical documents, psychological examinations results, biological examinations results, and social investigations, all of these being attached to medical records. The stressful life events were noted as follow: triggering events if occurred within one year before onset of depression, vulnerabling events if occurred more than one year before onset of depression and maintaining events if occurred after the onset of depression. The data on smoking was inconstantly mentioned in medical records so it wasn't possible to analyze this item. The data were stored by Microsoft Excel file and processed using Epi Info and SPSS for Windows version 8.0.0. Statistical analysis comprised parametric and non parametric methods. The odds ratios (OR) were calculated. The minimal limit for confidence interval was > 1. For comparison, we used the data for the general adult population from Timis County.

## RESULTS

### A. Groups description

The patients included were divided into three groups:

1. Study group encompasses 248 patients with recurrent depressive disorder, 24.6% males, average age = 49.43 yrs, SD = 8.54.

2. Control group 1 encompasses 44 patients with bipolar affective disorder, 31.8% males, average age = 41.88 yrs, SD = 10.88.

3. Control group 2 encompasses 59 patients with persistent delusional disorder, 28.8% males, average age = 48.22 yrs, SD=8.15.

Comparative analysis regarding homogeneity of demographical variables indicates:

#### a. Age at the current admission

In all three samples the differences between average ages were tested with Levene test that indicates

no significant differences between depressives and delusionals ( $F = 0.036, p = 0.85$ , that means high homogeneity). (Fig. 1) But there were significant differences between bipolar group, on one side, and persistent delusional and depressive groups, on the other side, regarding age of onset ( $F = 5.77, p = 0.017$ ) and total duration of disorders. We took into account these existing differences in order to interpret and analyze the data.

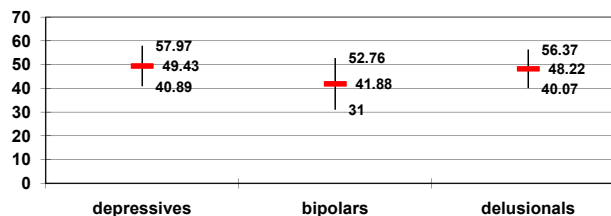


Figure 1. Current average age in the three samples (+/- 1 SD).

### b. Gender distributions

There were no significant differences in gender distribution in all three groups when  $\chi^2$  Test was performed ( $\chi^2=1.26; p=0.53$ ), showing a good homogeneity of the samples. (Fig. 2)

Gender distribution in depressive patients was in concordance with international literature.<sup>13</sup>

The higher prevalence of depression in females could be related to socio-cultural considerations, the role of a female in a couple being less rewarding than that of a male.<sup>14</sup>

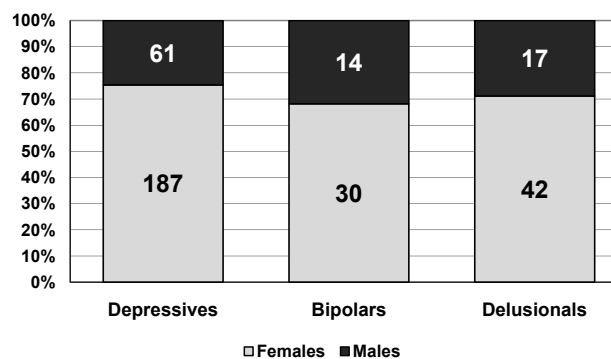


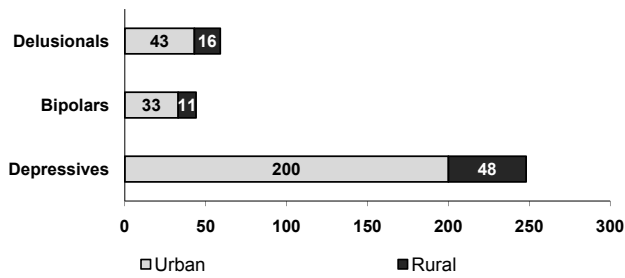
Figure 2. Gender distribution in all three samples.

Regarding bipolar and persistent delusional patients, the explanation for higher female prevalence was related to alcohol induced co-morbidity, which represented exclusion criteria, that was higher than in depressive patients, especially in males, in congruence with other studies.<sup>15</sup>

### c. Residence

The patients from all three groups were more frequently from urban areas. (Fig. 3) Thus, we found no significant differences ( $\chi^2=2.10; p=0.35$ ), with good homogeneity regarding this item. As in other

important studies, the psychiatric patients, generally, and depressive patients, especially, come from urban areas.<sup>16</sup>



**Figure 3.** Distribution by residence.

### B. Analysis of cumulated group (all three samples)

#### 1. The prevalence of somatic co-morbidities in depressive patients compared with official data from Timiș County regarding the prevalence of some chronic diseases.

We compared the prevalence of the five most frequent medical diseases in depressive patients (high blood pressure- HBP, coronary artery disease- CAD, diabetes mellitus-DM, malignant tumors and neurological diseases) to their prevalence in the general population of Timiș County in the same time slot (2001-2005). The data for general population were

obtained from the County Office for Public Health.

We observe a higher prevalence for most chronic diseases in the depressive group compared with the general population. For a more accurate estimate regarding the difference between observed prevalence figures, especially because the sizes of the two comparison group are quite different, we applied  $\chi^2$  Test, and looked for significance of the difference and odds ratio. The results are presented in Table 3.

As we can observe, despite the fact all prevalence figures are constantly higher in depressive patients than in the general population of our county, this has no real significance in all cases. Constantly significant are the differences regarding high blood pressure, coronary artery disease and cerebro-vascular diseases. Regarding diabetes mellitus and malignant tumors, there are annual variations in respect with level of differences significance.

The high co-morbidity of cardiovascular diseases and neurological disease in depressive patients was documented by several clinical and epidemiological studies.<sup>17,18</sup>

#### 2. The specific socio-demographical characteristics in depressive group that determines the occurrence of somatic diseases.

The socio-demographical characteristics that

**Table 1.** Prevalence of HBP, CAD, diabetes mellitus, malignant tumors and cerebro-vascular diseases in Timis county population between 2001 and 2005.

Year	Total Population	BPH		CAD		DM		Malignant tumors		Cerebro-vascular diseases	
		No.	Prev. (%)	No.	Prev. (%)	No.	Prev. (%)	No.	Prev. (%)	No.	Prev. (%)
2001	673942	24688	3.66	13263	1.97	12831	1.90	8991	1.33	3576	0.53
2002	674985	38214	5.66	22404	3.32	16006	2.37	9542	1.41	5421	0.80
2003	656418	42228	6.43	25016	3.81	17460	2.66	10346	1.58	6306	0.96
2004	655632	43373	6.62	25165	3.84	18940	2.89	11043	1.68	6064	0.92
2005	655718	45560	6.95	25853	3.94	20994	3.20	11855	1.81	6175	0.94

**Table 2.** Prevalence of HBP, CAD, DM, malignant tumors and cerebro-vascular diseases in depressive group between 2001 and 2005

Year	Total Population	BPH		CAD		DM		Malignant tumors		Cerebro-vascular diseases	
		No.	Prev. (%)	No.	Prev. (%)	No.	Prev. (%)	No.	Prev. (%)	No.	Prev. (%)
2001	40	15	37.50	6	15.00	5	12.50	0	0.00	5	12.50
2002	44	16	36.36	3	6.82	3	6.82	0	0.00	2	4.55
2003	53	21	39.62	16	30.19	2	3.77	3	5.66	2	3.77
2004	63	12	19.05	6	9.52	5	7.94	2	3.17	6	9.52
2005	48	13	27.08	9	18.75	3	6.25	1	2.08	1	2.08

**Table 3.** The difference significance between prevalence of HBP, CAD, DM, malignant tumors and cerebro-vascular diseases recorded in general population and in depressive study group, between 2001 and 2005.

Year	Population	BPH	CAD	Diabetes mellitus	Malignant tumors	Cerebro-vascular D.
2001	X <sup>2</sup> ; p	120; <0.001*	35.20; <0.001*	24.04; <0.001*	0 cases in depressive	108.43; <0.001*
	OR	15.78*	8.79*	7.36*		26.78*
2002	X <sup>2</sup> ; p	77.62; <0.001*	1.68; 0.195	2.08; 0.149	0 cases in depressive	7.73; 0.005*
	OR	9.52*	2.13	3.01		5.88*
2003	X <sup>2</sup> ; p	96.95; <0.001*	100.54; <0.001*	0.25; 0.61	5.70; 0.016*	4.41; 0.035*
	OR	9.54*	10.91*	1.44	3.75*	4.04*
2004	X <sup>2</sup> ; p	15.76; <0.001*	5.52; 0.018*	5.72; 0.016*	0.84; 0.358	50.79; <0.001*
	OR	3.32*	2.64*	2.90*	1.91	11.28*
2005	X <sup>2</sup> ; p	30.09; <0.001*	27.78; <0.001*	1.44; 0.23	0.02; 0.88	0.67; 0.412
	OR	4.97*	5.62*	2.02	1.16	2.24

\*Statistically significant

influence the occurrence of some chronic medical diseases were higher current age and age of onset, and the decreased level of education. (Table 4)

**Table 4.** Socio-demographical characteristics influencing physical health.

Inducing factors	Statistical Test	Significance
Age of onset	Pearson	0.419; p<0.001*
Current age	Pearson	0.351; p<0.001*
Total duration of disorder	Pearson	0.087; p=0.10
Educational level	Kendall	-0.151; p=0.001*
	Spearman	-0.179; p=0.001*
Primary versus middle studies	Test T	1.91; p=0.58
Primary versus university studies	Test T	4.162; p<0.001*
Middle versus university studies	Test T	3.175; p=0.002*

\*Statistically significant

Other studies found that educational level exerts an influence on physical health status.<sup>19</sup> We consider that along with residency (differences between urban versus rural areas), in our country, the educational level is a true factor that influences the recognition of most important health issues and the prompt referral to specialists. These deficiencies have repercussions on all medical and surgical diseases.

### 3. The interrelation between somatic diseases and depression.

To demonstrate the relationship between depression and somatic diseases, we performed tables of convergence for the onset and current episode of depression. (Tables 5, 6)

**Table 5.**

	+	DEPRESSION	-
S O M A T I C D I S E A S E	+	156	47
	-	92	56

X<sup>2</sup> = 8.21; p=0.004; OR = 2.02 (1.24<OR<3.31)

**Table 6.**

	+	SOMATIC DISEASE	-
D E P R E S S I O N	+	210	38
	-	60	43

X<sup>2</sup> = 28.63; p<0.001; OR = 3.96 (2.27<OR<6.91)

For the somatic diseases existing at the onset of disorders, as risk factor for the occurrence of bipolar and persistent delusional disorders, we obtained X<sup>2</sup> = 8.21; p = 0.004; OR = 0.49 (0.30 < OR < 0.81). Therefore, we can say that somatic diseases do not represent risk factor for mentioned psychiatric disorders. Regarding unipolar depression, somatic diseases proved to have some influence on the occurrence of depression: X<sup>2</sup> = 8.21; p = 0.004; OR = 2.02 (1.24 < OR < 3.31). This result was supported by

other studies, the most representative being the study conducted by Cuijpers et al.<sup>20</sup> We found that digestive diseases was most frequent associated with depression occurrence,  $X^2 = 6.69$ ;  $p = 0.009$ ;  $OR = 2.65$  ( $1.24 < OR < 5.81$ ). In part, we consider this result as an artifact allowed by ICD-10 diagnostic criteria. More exactly, a representative part of digestive diseases was the pathology called as „functional” that could be one facet of depressive expressions that precedes clinical diagnostic. On the other hand, there could be some common underlying mechanisms that promote both depression and some of somatic conditions, such as serotonergic dysfunctions.<sup>21</sup>

Conversely, depression once occurred represent a risk factor ( $X^2 = 28.63$ ;  $p < 0.001$ ;  $OR = 3.96$  ( $2.27 < OR < 6.91$ )) for some of the somatic diseases. (Table 6)

Persistent delusional and bipolar disorders were not found to be risk factors for any somatic diseases were found ( $X^2 = 28.63$ ;  $p < 0.001$ ;  $OR = 0.25$  ( $0.14 < OR < 0.44$ )).

Statistical analysis showed that the risk to develop somatic diseases is twice in depressive subjects during onset and current episode period. We underline that this result is not due to aging process, the same process is present in the control samples but the risk isn't significant.

Moreover, several studies indicated that depression has increased the risk for some somatic diseases, as in coronary artery disease, this risk being higher than in general population, in younger subjects.

Simultaneously, with aging process the differences in mentioned risk disappear and became equal for both category of people.<sup>22</sup> The increased risk for myocardial infarct, coronary artery disease and cerebro-vascular diseases was found in depression by Van der Kooy et al.<sup>23</sup> Depression conferred a risk for the somatic diseases mentioned similar to that conferred by diabetes and smoking. On the other hand, depression once occurred increases significantly the risk for a unfavorable outcome of pre-existing somatic diseases by unhealthy behaviors, lack of adherence to treatment, auto-destructive thoughts etc.

Table 7 presents the analysis of whether depressive disorders represent a risk factor for the occurrence of different somatic diseases.

The results show that depression increases the risk for high blood pressure almost twice, for digestive and musculoskeletal diseases approximately three-fold, for nutrition and metabolic diseases four-fold (especially for type 2 diabetes) and for gynecologic disease almost five-fold. All these results were in concordance with international studies. The predisposition of depressive subjects to develop high blood pressure was explained by a autonomic dysfunction including catecholaminergic hyperactivity and decreased heart rate variability.<sup>24,25</sup> Depression increases the risk for gastrointestinal diseases both in functional (e.g. irritable bowel syndrome) and in organic (e.g. Crohn's disease) disorders.<sup>26</sup> Musculoskeletal diseases were also associated with significant levels of depression.<sup>27,28</sup>

**Table 7.** Unipolar depression as risk factor for the occurrence of somatic diseases.

Somatic disease	$X^2$	p	OR	OR limits
High blood pressure	4.92	0.03*	1.87	1.04<OR<3.39
Coronary artery disease	1.74	0.24	1.61	0.76<OR<3.49
Other cardiological diseases	8.32	0.012*	0.13	0.02<OR<0.73
Cardiological disease total	3.95	0.06	1.66	0.98<OR<2.84
Digestive diseases	12.62	<0.001*	2.70*	1.49<OR<4.92*
Musculoskeletal diseases	13.49	<0.001*	3.29*	1.63<OR<6.74*
Nutrition and metabolic diseases	6.34	0.011*	4.24*	1.19<OR<17.95*
Endocrinological diseases	0.21	0.65	1.21	0.49<OR<3.07
Gynecologic diseases	11.94	<0.001*	4.70*	1.73<OR<13.89*
Nephrological diseases	0.08	0.77	1.14	0.43<OR<3.09
Urological diseases	1.91	0.16	1.89	0.71<OR<5.31
Neurological diseases	0.11	0.74	1.16	0.476<OR<2.94
Hematological diseases	0.23	0.63	1.47	0.27<OR<10.40
Respiratory diseases	2.04	0.15	2.77	0.75<OR<12.03
Other diseases	20.69*	<0.001*	8.07*	2.72<OR<26.93*

\*statistically significant

Among the significant risk factors for diabetes, depression was an important one.<sup>29</sup> On the one hand, depression has well-known endocrine substrates represented especially by HPA (hypothalamic-pituitary-adrenal) axis dysfunctions. This may result in hormonal changes and in consequence to the development of gynecologic diseases. On the other hand, this result could be an artifact because the most frequent gynecologic disease was represented by uterine fibroids that increases in prevalence in a naturally manner, as degenerative changes occur simultaneously with advancing in age.<sup>30</sup>

#### 4. Unipolar depression and work ability.

The changes in work status depending on diagnosis, was tested by  $\chi^2$ , the resulting data is presented in Table 8.

**Table 8.** Table of convergence for study group, depending on diagnosis and the changes in the professional status.

		+ WORSENING OF PROFESSIONAL STATUS -	
D E P R E S S I O N	+	105	143
	-	41	62

$\chi^2=0.19$ ;  $p=0.66$ ;  $OR=1.11$  ( $0.68 < OR < 1.82$ )

Despite the magnitude of impact, we can observe that depression itself doesn't represent a significant risk factor for loss professional ability in comparison with other psychiatric diagnosis (in our case with persistent delusional and bipolar disorder). While in bipolar patients the loss of academic skills is due to cognitive impairments, in depressive there are subjective reasons, as worthlessness or low self-esteem, rather than objective dysfunctions. We must outline that the loss of professional status and retirement in depressive subjects are not particular for our country as a merely social phenomenon. For example, in Finland there are studies that revealed similar results despite the evident advantage to be employed.<sup>31</sup>

### C. Analysis on depressive sample

#### 1. Somatic diseases as influencing factors on depression outcome.

We found that musculoskeletal diseases increased independently the risk of suicide almost twice

( $\chi^2=4.99$ ;  $p = 0.03$ ;  $OR = 2.14$  ( $1.04 < OR < 4.47$ ). On the one hand, it is well-known that depression is accompanied by low level for pain perception. This results from noradrenergic and serotonergic neurotransmitters deficiency (these neuro-mediators modulates pain transmission form periphery to brain through spinal tracts). This finding is supported by Linsley and Martin study that found significant low back pain symptoms (51.70%) in those who committed suicide.<sup>32</sup>

#### 2. Somatic co-morbidity as risk factor for increasing direct cost of depression.

In order to test the linking between number of somatic comorbidities at the onset of depression and the frequency of subsequent admissions for depression disorder, we used Pearson Correlation Test. On one hand, there is a direct correlation between number of somatic diseases at the onset of depression and the number of admissions in a psychiatric hospital per year ( $r = 0.16$ ;  $p = 0.009$ ). Among somatic diseases cardiovascular disease significantly increased the number of subsequent psychiatric hospitalizations ( $r = 0.14$ ;  $p = 0.021$ ). It could be possible that somatic disease worsen the course of depression by psychogenic and/or biological ways. Other studies found that cardiovascular diseases associated with depression leads to more hospitalizations compared to those having just cardiovascular disease without depression.<sup>33</sup> In consequence we can affirm that somatic comorbidities increases the direct costs of depression along with the indirect costs related to lost of productivity.

#### 3. The role of stressful life events on depression occurrence and somatic diseases co-morbidity.

Despite the significant role of triggering stressful life events in onset of depression, there was no influence of stressful life events on somatic comorbidities occurrence. (Table 9) This result was according to kindling theory that stressful life events are significant at the onset of depression but diminish with the new recurrences of depression.<sup>34</sup>

**Table 9.** Average number of stressful life events depend on event's type and differences significance.

Type of event	Mean	S.D.	Difference
Vulnerating - Triggering	0.57	0.91	$t = - 3.04$ ; $p = 0.003$
Triggering - Triggering	0.75	0.62	$t = 6.19$ ; $p < 0.001$
Maintaining - Vulnerating	0.43	0.72	$t = 2.26$ ; $p = 0.024$
Maintaining - Maintaining	0.57	0.91	
Maintaining - Maintaining	0.43	0.72	

**4. The influence of personality structure profile on somatic co-morbidity in depression.**

We analyzed the structure of personality depend on personality cluster existing in DSM-IV diagnostic manual. Although in our national health system the medical data are collected according with ICD-10 manual, there was possible to convert ICD-10 diagnostics in DSM-IV diagnostics according to conventional agreement. Cluster C personality that include obsessive-compulsive personality, anxious personality and dependent personality, was most represented in studied sample. We found that cluster C personality traits was significant more correlated ( $p = 0.024$ ) with cardiovascular disease occurrence. A dimensional approach of personality could be better in studying medical co-morbidity in depressives. Thus, several articles indicate that high levels of neuroticism, as five-factor model perspective on personality, were found in those who developed somatic co-morbidities.<sup>35</sup> It is well-known that cluster C traits of personality are high correlated with neuroticism from dimensional approach of personality structure.

**5. Antipsychotic drugs as inductor of somatic diseases in depressive patients.**

In order to test this hypothesis we used unpaired T Test, applying for the number of co-morbidities at the onset of depression, at the current episode and for acquired co-morbidity during the evolution of depression. (Table 10)

**Table 10.** The influence of antipsychotic treatment on number of somatic co-morbidities in depressive patients.

	<b>Without antipsychotics</b>	<b>With antipsychotics</b>	<b>Significance</b>
Number of co-morbidities at the onset	1.19; SD 1.36	1.42; SD1.43	0.20
Number of co-morbidities at the current episode	2.65; SD 2.03	2.29; SD 1.86	0.14
Number of acquired co-morbidities	1.46; SD 1.77	0.87; SD 1.46	<b>0.004*</b>

The antipsychotic treatment alone is not a sufficient argumentation for somatic co-morbidity appearance. The number of total acquired somatic co-morbidity was higher in group without antipsychotic drugs indicating that this type of co-morbidity is related to a depressive phenomenon rather than caused by side effects of antipsychotic medications. We must outline that in depressive disorder the duration of psychotic symptoms is shorter than in bipolar or in persistent

delusional disorder so the antipsychotic treatment is administrated inconstantly and for well-delimited period of time. There is the possibility that studies in larger groups disagree with our findings.

**DISCUSSIONS AND CONCLUSIONS**

Depressive experience is highly prevalent among general population and is the most frequent psychiatric disorders. The average age of onset is relatively similar in unipolar depression and persistent delusional disorder, being placed in the fifth decade of life.

In contrast with unipolar depression, bipolar individuals have the onset of their disorder at earlier age, according to some of authors in young adult periods or even in adolescence. This fact could contribute, in part, to the increased co-morbidity with somatic illnesses in unipolar depressives.

Females are more affected from depression than males, the prevalence being twice in the former. This could be determined by the complex role of women in our society (e.g. a woman must be good wife, mother and if there is possible excellent professional) and the low sense of rewarding perceived by females engaged in a couple. In bipolar and persistent delusional subjects, the higher prevalence in females could be a result of exclusion criteria related to alcohol usage more frequent in males than in females. Undoubtedly alcohol use will increase the somatic problems of psychiatric patients.

Regarding residency, there were no differences related to psychiatric diagnostic that express a poor addressability to psychiatrist of those living in rural areas.

During the comparative analysis between study group data and available data of morbidity in our county, we found that cardiovascular and cerebrovascular diseases were constantly significantly increased during entire study period (2001 - 2005). Inconstantly, in some years, we found among depressive patients a significantly increased prevalence for diabetes mellitus and malignant tumors. We consider that our findings could serve as a solid argument for future projects of researches.

The socio-demographical characteristics found to exert their influences on somatic co-morbidity were: age at the onset of disorder and current age, as well as educational level. Advancing in age is associated with increased somatic morbidity caused by natural reasons. Also, educational level is inversely correlated with number of somatic diseases in depressives and



that could be an extension of the situation existing in general population. Unfortunately, people living in rural areas have a low addressability to psychiatrist and also a low education level and this must be counteracted by informative programs in this category with increased risk for development of somatic diseases.

The comparative analysis of study group and the control groups has showed that physical health status has a significant influence on the risk of developing depression. The existence of somatic disturbances predisposes to the development of depression, partially through underlying biological mechanisms. However, this result could represent an artifact, in the sense that somatic clinical expressions could be just a facet of depressive experience misdiagnosed as a distinct somatic disease. Conversely, depression once occurred significantly increases the risk to develop some somatic diseases.

There are several explanations, from biological and psychological perspectives: depressive patients share common predisposing factors with a part of somatic illnesses, there could be a genetic link between depression and some of the somatic disorders, such as genes that codifying serotonin transporter activity, the depressive individuals present more frequent unhealthy behaviors as alcohol or other psychoactive substances use, smoking etc. Although, depression exerts a significant impact on professional ability, this is not a characteristic of depressive disorder as the percentage of retirement was similar to that found in control groups.

We consider that subjective reasons could be a reason for retirement in depressive individuals more frequently than in bipolar and persistent delusional individuals where cognitive dysfunctions persist during inter-episodic periods and professional disability is rather a rule than an exception.

Internal analysis of depressive group reveals several interesting findings. First, musculoskeletal diseases, especially those with chronic pain, such as cervical and lumbar spondylosis, increase the risk of suicide. Consequently, this category of depressives must be carefully questioned about suicidal ideation. Second, somatic diseases generally, and cardiovascular diseases especially increase the number of subsequent hospitalizations in psychiatric units. It must be analyzed to what extent physical symptoms could alert, in a false manner, about development of depressive recurrence. Or it could be possible that depressive subjects with cardiovascular co-morbidity have special and increased needs in comparison with those without somatic co-morbidity. Third, stressful life events didn't

exert direct a influence on somatic co-morbidity level in depressive subjects. Fourth, those with cluster C traits of personality have increase risk to develop cardiovascular co-morbidity, through mal-adaptive behaviors and attitudes. Finally, the antipsychotic medications is not responsible, or at least not entirely, for the occurrence of somatic illnesses. This finding could be determined by the discontinuation period of antipsychotic treatment in depression which is overlapped on psychotic manifestations period.

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