Original article

Comorbidity of Somatic Illnesses on People With Treated Mental Disorders – A New Challenge in Medicine

Romana Marušić [1,2], Adriana Levaković [2], Dunja Degmečić [2,3], Tatjana Bačun [2,4*]

1 Department of Internal Medicine, National Memorial Hospital Vukovar, Croatia
2 Faculty of Medicine, J.J. Strossmayer University, Osijek, Croatia
3 Department of Psychiatry, University Hospital Centre, Osijek, Croatia
4 Division of Endocrinology, Department of Internal Medicine, University Hospital Centre, Osijek; Croatia

*Corresponding author: Tatjana Bačun, tbacun@gmail.com

Abstract

Aim. Comorbidities pose a major challenge for 21st century medicine. The mutual pathophysiological effect of one disease on another can significantly affect their course and prognosis. The aims of this study were to examine the frequency of comorbidities and the most common psychiatric and somatic comorbidities and to determine the difference in the incidence of certain diseases by gender and age.

Methods. Data were recorded in several groups: demographic characteristics, psychiatric and somatic diagnoses classified according to gender, age, and the legally determined ability to work, and correlations of somatic and psychiatric diagnoses.

Results. The most common psychiatric diagnoses in men were post-traumatic stress disorder (PTSD) (25%) and alcoholism (23%), while in women these were recurrent depressive disorder (19%) and psychosis (10%). A statistically significant difference was found in the incidence of alcoholism and PTSD, which are more common in men than in women. The most common somatic diseases in both sexes were arterial hypertension (M = 33%, F = 46%) and diabetes mellitus (M = 18%, F = 32%). Statistically significant differences were found in the frequency of hypertension ($p = 0.03$) and epilepsy ($p = 0.002$), which are more common in men. The ratio alcoholism-hypertension ($p = 0.03$), alcoholism-diabetes ($p < 0.0001$), alcoholism-COPD ($p < 0.001$) was statistically significant.

Conclusion. It is extremely important to improve the multidisciplinary approach and cooperation in treatment in order to reduce the number of hospitalizations, emergency interventions and suicides and to improve the patients' quality of life and life expectancy.

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Introduction

Comorbidity indicates the presence of two or more different diseases or disorders simultaneously and poses a major challenge for 21st century medicine (1). People with a chronic physical illness are 1.5 to 2 times more likely to develop a mental disorder (2).

It is estimated that 25% of the general population has some form of mental disorder. Of these, as many as 68% have one or more physical comorbidities (3). Due to the extended average lifespan, the prevalence of multimorbidity is increasing; in Australia, it is 75% for people aged 65 to 74 and over 80% for people aged 75 and above. A study conducted in Ontario showed a multimorbidity of 7 to 35 % in people between the ages of 18 and 65 (4). In Croatia, the prevalence of multimorbidity is 79.8 % for people over 65 (5).

Mental disorders are a major public health problem that has a significant impact on the health of people with chronic diseases and can change the course of their illness and their prognosis. Depression is present in 40% of people with hypertension; the prevalence is 36.6% in men and as much as 63.4% in women. In somatically healthy individuals with depressive disorder, the risk of coronary heart disease is increased 1.5- to 2-fold, while in individuals with coronary heart disease, the risk of myocardial infarction is increased 1.5- to 4.5-fold (2). Some studies show that the prevalence of depressive disorders in people with diabetes ranges from 8 to 15% (6). Only 25% to 50% of people with diabetes who suffer from depression get diagnosed and treated (7). The risk of complications of the disease is increased as much as 4 times due to the reduced ability to regulate glucose metabolism (1, 8). Other studies show that as many as 47.6% of young people with insulin-dependent diabetes develop a mental disorder after ten years, most often one year after diagnosis (2).

The cost of hospital treatment of patients with comorbid depression was increased 1.5-fold compared with other patients. The positive correlation of psychological comorbidities with the length of hospital stays, doctor visits, and longer sick leave has also been proven, which leads to a reduced quality of life and higher treatment costs (2). One study showed that every fifth person in physical rehabilitation suffers from a comorbid mental disorder. This has an adverse effect on the outcome of rehabilitation due to the patient's reduced motivation, cooperation, and active participation in the rehabilitation process (9).

Due to the high incidence of comorbidities of physical and mental illnesses, it is important to conduct preventive examinations, personalized pharmacotherapy and psychotherapy, and educational programs for medical professionals. An integrative approach and timely recognition and treatment can reduce mortality, morbidity, and overall treatment costs (10).

The aims of our research were to examine the frequency of comorbidities and the most common psychiatric and somatic comorbidities and to determine the difference in the incidence of certain diseases by gender and age.

Patients and methods

Patients and study design

The research was organized as a cross-sectional study with historical data. It was approved by

the Ethics Committee of the Faculty of Medicine Osijek, Josip Juraj Strossmayer University

in Osijek. The study was conducted on 137 subjects who were hospitalized at the Clinic for Psychiatry of the Clinical Hospital Center Osijek. Data were collected from the hospital information system of the Clinical Hospital Center Osijek over a period of one year. Inclusion criterion was diagnosis of any somatic illness in psychiatric patients.

Methods

Data were categorized in several groups: demographic characteristics of respondents, psychiatric and somatic diagnoses classified

according to gender, age, and the legally determined ability to work (up to 65 years), and correlations of somatic and psychiatric diagnoses. To examine the correlation between somatic and psychiatric diagnoses, only diagnoses for which frequency was higher than 3% (N ≥ 7 for psychiatric, N ≥ 5 for somatic diagnoses) in total population and somatic diagnoses that are applicable in both genders came into consideration.

Statistical analysis

R software was used to perform statistical analysis of the collected data. Descriptive data are expressed in frequency and share for nominal variables and arithmetic and standard deviation for numerical variables that have a normal distribution. The normality of distribution was examined using the Kolmogorov-Smirnov test. Differences of category variables were tested by binomial, $\chi 2$, and Fisher's exact test, and the degree of correlation was examined by the ϕ test. Differences of numerical variables with normal distribution were tested by Student's t-test. The level of statistical significance was set at $p < 0.05$.

Results

The study included 137 respondents, of whom 95 (70%) were men and 42 (30%) were women. The mean age of men was 55.9 ± 12.1 (22 to 87) and women 56.9 ± 13.5 (16 to 80). Of the 137 respondents, 2% were aged between 18 and 30, 76% were between 30 and 65, and 23% were over 65. A statistically significant difference was found in the number of respondents by sex, in the group aged 35 to 65 years ($p < 0.0001$). Respondents were divided according to employment into employed, unemployed, and retired ones: A statistically significant difference was found between retired men and women ($p < 0.0001$) (Table 1).

Table 1. Demographic characteristics of respondents

	Male	Female	Total	p
Age	55.9±12.2	56.9±13.5		0.68
Age category				
16-30	2(20%)	1(2%)	3(2%)	0.56
30-65	73(77%)	30(71%)	103(76%)	**< 0.0001**
65 +	20(20%)	11(26%)	31(23%)	0.15
Employment status				
Employed	15(16%)	3(7%)	18(13%)	< 0.05
Unemployed	22(23%)	16(39%)	38(28%)	0.41
Retired	57(60%)	22(54%)	79(59%)	**< 0.0001**

The most common psychiatric diagnoses in men were post-traumatic stress disorder (PTSD) (25%), alcoholism (23%), recurrent depressive disorder (13%), while in women the most common ones were recurrent depressive disorder (19%), psychosis (10%), alcoholism, PTSD, and anxiety-depressive disorder (7%). A statistically significant difference was found in the incidence of alcoholism and PTSD, which were more common in men than in women (Table 2).

Table 2. Psychiatric diagnoses of respondents

	Male	Female	Total	p
Alcoholism	33(23%)	4(7%)	37(18%)	**< 0.0001**
Recurrent depressive disorder	18(13%	11(19%)	29(14%)	0.26
PTSD*	35(25%)	4(7%)	39(19%)	**< 0.0001**
Psychoorganic syndrome	7(5%)	2(3%)	9(4%)	0.18
Anxiety-depressive disorder	3(2%)	4(7%)	7(3%)	1
Psychosis	8(6%)	6(10%)	14(7%)	0.79
Another inorganic psychotic disorder	1(1%)	0(0%)	1(0%)	
Pervasive developmental disorder	0(0%)	1(2%)	1(0%)	
Mild mental retardation	4(3%)	1(2%)	5(2%)	0,27
Delirium tremens	3(2%)	0(0%)	3(1%)	
Organic insane disorder	1(1%)	3(5%)	4(2%)	0,62
Schizophrenia	6(4%)	3(5%)	9(4%)	0.5
Borderline depressive decompensation	4(3%)	3(5%)	7(3%)	1
Depressive disorder	10(7%)	3(5%)	13(6%)	0.09
Bipolar affective disorder	2(1%)	4(7%)	6(3%)	0.68
Crisis	1(1%)	4(7%)	5(2%)	0.37
OCD*	3(2%)	0(0%)	3(1%)	
Schizoaffective disorder	2(1%)	3(5%)	5(2%)	1
Organic emotionally labile disorder	0(0%)	3(5%)	3(1%)	
Anorexia nervosa	1(1%)	0(0%)	1(0%)	

*PTSD – Post-traumatic stress disorder, OCD – Obsessive-compulsive disorder

Of the somatic diagnoses, the most common diagnoses in both sexes were arterial hypertension (M = 33%, F = 46%), diabetes mellitus (M = 18%, F = 32%) and epilepsy (M = 15%, F = 8%). Statistically significant differences were found in the frequency of arterial hypertension (p = 0.03) and epilepsy (p = 0.002), which were more common in men (Table 3).

Table 3. Somatic diagnoses of respondents

	Male	Female	Total	p
Arterial hypertension	41(33%)	23(46%)	64(36%)	**0.03**
Diabetes mellitus	23(18%)	16(32%)	39(22%)	0.34
Epilepsy	19(15%)	4(8%)	23(13%)	**0.002**
COPD*	5(4%)	2(4%)	7(4%)	0.45
Liver cirrhosis	1(1%)	0(0%)	1(1%)	
Gastric ulcer	2(2%)	0(0%)	2(1%)	
Pneumonia	2(2%)	0(0%)	2(1%)	
Hashimoto's thyroiditis	0(0%)	1(2%)	1(1%)	
Multiple sclerosis	1(1%)	0(0%)	1(1%)	
Lumbosacral pain	2(2%)	0(0%)	2(1%)	
Esophagitis	0(0%)	0(0%)	0(0%)	
Chronic gastritis	5(4%)	0(0%)	5(3%)	
Venous ulcer	1(1%)	0(0%)	1(1%)	
Pulmonary embolism	0(0%)	1(2%)	1(1%)	
NHL*	1(1%)	0(0%)	1(1%)	
Angina pectoris	3(2%)	0(0%)	3(2%)	
Esophageal cancer	1(1%)	0(0%)	1(1%)	
Psoriasis	4(3%)	0(0%)	4(2%)	1
Prostate hyperplasia	5(4%)	0(0%)	5(3%)	
Parkinson's disease	3(2%)	0(0%)	3(2%)	
Acute renal failure	1(1%)	0(0%)	1(1%)	
Cystitis	1(1%)	0(0%)	1(1%)	
Hepatitis	1(1%)	0(0%)	1(1%)	
Cervicobrachial syndrome	0(0%)	1(2%)	1(1%)	
GERD*	1(1%)	0(0%)	1(1%)	
SLE*	0(0%)	2(4%)	2(1%)	
Urine retention	1(1%)	0(0%)	1(1%)	
Hodgkin's disease	1(1%)	0(0%)	1(1%)	

*COPD – Chronic obstructive pulmonary disease, NHL – Non-Hodgkin's lymphoma, GERD – Gastroesophageal reflux disease, SLE – Systemic lupus erythematosus

Since we were interested in the frequency of psychiatric diagnoses among respondents, we divided them into groups based on their employment status and age. The most common illness-related psychiatric diagnoses among retired respondents were recurrent depressive disorder (31%), PTSD (26%), and alcoholism (12%). Unemployed respondents were most often diagnosed with alcoholism (25%), recurrent depressive disorder (16%), and PTSD (14%). Similar diagnoses were most common among employed respondents: alcoholism (33%) and

PTSD (11%). $\chi 2$ showed a significant statistical difference in the number of patients with PTSD and recurrent depressive disorder among retired, unemployed, and employed respondents under the age of 65 (Table 4).

Table 4. Psychiatric diagnoses according to the employment status

	Retired		Unemployed	Employed	
	> 65	< 65	> 65	< 65	p
Alcoholism	5(12%)	10(12%)	13(25%)	9(33%)	0.8
Psychosis	5(12%)	0(0%)	4(8%)	2(7%)	
PTSD*	2(5%)	21(26%)	7(14%)	3(11%)	**0.0004**
Schizophrenia	2(5%)	5(16%)	2(4%)	0(0%)	
Borderline depressive decompensation	0(0%)	3(4%)	2(4%)	2(7%)	0.98
Depressive disorder	5(12%)	2(2%)	5(10%)	2(7%)	0.63
Bipolar affective disorder	0(0%)	4(5%)	1(2%)	1(4%)	0.5
Mixed anxiety-depressive disorder	0(0%)	3(4%)	3(6%)	1(4%)	0.85
Recurrent depressive disorder	5(12%)	25(31%)	8(16%)	2(7%)	**< 0.0001**
Organic emotionally labile disorder	3(7%)	0(0%)	0(0%)	0(0%)	
Mild mental retardation	0(0%)	2(2%)	0(0%)	1(4%)	
Crisis	1(2%)	1(1%)	1(2%)	287%)	0.96
Psychoorganic syndrome	10(24%)	5(6%)	0(0%)	0(0%)	
Organic delusional disorder	2(5%)	0(0%)	1(1%)	1(4%)	
Anorexia nervosa	0(0%)	0(0%)	1(2%)	0(0%)	
Schizoaffective disorder	0(0%)	0(0%)	4(8%)	0(0%)	
Pervasive developmental disorder	0(0%)	0(0%)	0(0%)	0(0%)	
Delirium tremens	1(2%)	0(0%)	0(0%)	1(4%)	
OCD*	0(0%)	0(0%)	0(0%)	0(0%)	

*PTSD – Post-traumatic stress disorder, OCD – Obsessive-compulsive disorder

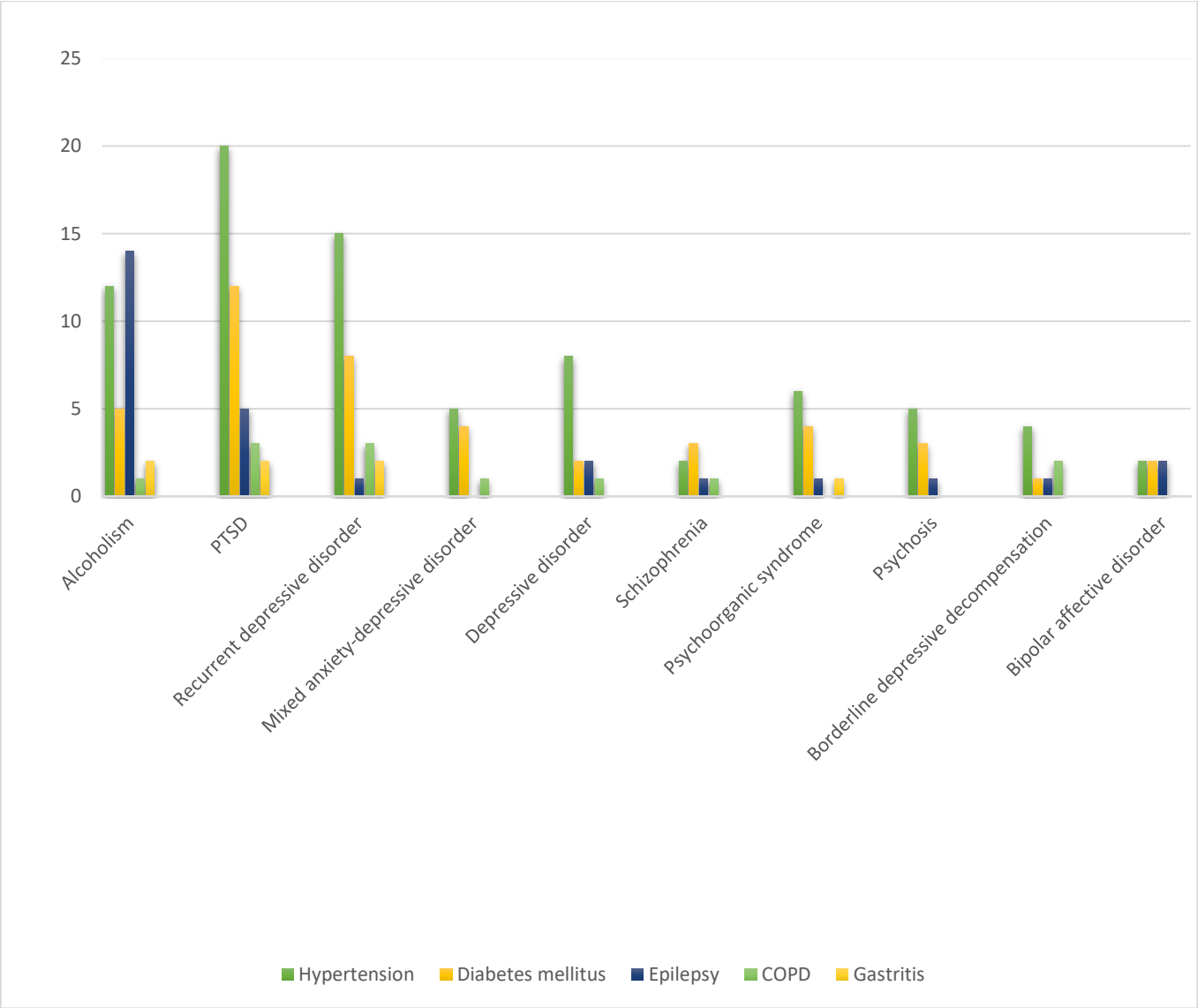

Figure 1. Correlation of somatic and psychiatric diagnoses

*** PTSD – Post-traumatic stress disorder, COPD – Chronic obstructive pulmonary disease**

With the aim of roughly determining the correlation of somatic and psychiatric diagnoses, a graph was made to reflect that correlation (Figure 1).

We took the most significant diagnoses from the graph and made a matrix in which we tested the statistical significance and correlation of the most common diagnoses:

1. Psychiatric diagnoses: alcoholism, recurrent depressive disorder, PTSD, mixed anxiety-depressive disorder, schizophrenia, depressive disorder

2. Somatic diagnoses: hypertension, diabetes mellitus, epilepsy, COPD, gastritis.

The ratios alcoholism-hypertension ($p = 0.03$), alcoholism-diabetes mellitus ($p < 0.0001$), alcoholism-COPD ($p < 0.001$) were statistically significant, which means that respondents treated for alcoholism had a lower risk for hypertension, diabetes, and COPD, although the correlation was almost equal to zero ($\Phi 1 = 0.03$, $\Phi 2 = 0$, $\Phi 3 = 0.004$) (Table 5).

Table 5. Correlation of somatic and psychiatric disorders

		HYPERTENSION				DIABETES MELLITUS				EPILEPSY				COPD				GASTRITIS		
		Yes	No	p	ϕ	Yes	No	p	ϕ	Yes	No	p	ϕ	Yes	No	p	Φ	Yes	No	p
Alcoholism	Yes	12	25	0.03	0.03	5	32	**<0.0001**	0.18	14	23	0.18		1	36	<0.001	0.004	2	35	0.62
	No	52	45			59	38			50	47			6	92			1	94	
Recurrent depressive disorder	Yes	15	14	0.678		8	21	1		1	28	**0.03**	0.03	3	26	0.17		2	27	0.3
	No	49	56			31	74			22	83			4	101			3	102	
PTSD	Yes	20	19	0.7		12	27	0.84		5	34	0.46		3	36	0.41		2	37	0.63
	No	44	51			27	68			18	77			4	91			3	92	
Psychoorganic syndrome	Yes	6	3	0.31		4	5	0.45		1	8	1		0	9			1	8	0.29
	No	58	67			35	90			22	103			7	118			4	121	
Mixed anxiety-depressive disorder	Yes	5	2	0.26		4	3	0.19		0	7			1	6	0.32		0	7	
	No	59	68			35	92			23	104			6	121			5	122	
Psychosis	Yes	5	4	0.74		3	6	0.72		1	8	1		0	9			0	9	
	No	59	66			36	89			22	103			7	118			5	120	
Schizophrenia	Yes	2	6	0.28		3	5	0.69		1	7	1		1	7	0.36		0	8	
	No	62	64			36	90			22	104			6	120			5	121	
Borderline depressive decompensation	Yes	4	3	0.7		1	6	0.67		1	6	1		2	6	0.056		0	7	
	No	60	67			38	89			22	105			5	121			5	122	
Depressive disorder	Yes	8	4	0.23		2	10	0.5		2	10	1		1	11	0.49		0	12	
	No	56	66			37	85			21	101			6	116			5	117	
Bipolar affective disorder	Yes	2	4	0.69		2	4	1		2	4	0.27		0	6			0	6	
	No	62	66			37	91			21	107			7	121			5	123	

* PTSD – Post-traumatic stress disorder, COPD – Chronic obstructive pulmonary disease

Discussion

Comorbidities of physical and mental disorders occur with high frequency, and they are most often present in people over 65 years of age. In this study, a statistically significant difference was found in the incidence of PTSD and alcoholism in men and women; they were significantly more common in men, while recurrent depressive disorder was more common in women.

In our research, PTSD is almost four times more common in men. It is estimated that 3 to 6% of the population suffers from PTSD. Seeing as some studies show that about 49.8% of people who were in the war develop PTSD, these findings can be related to the Croatian War of Independence in the early 1990s. PTSD was most often diagnosed in retired respondents under the age of 65 (26% of respondents), which

we can also attribute to the recent Croatian war history. Although several studies show increased incidence of somatic diseases in patients who suffer from PTSD, our study did not show a statistically significant correlation between PTSD and certain somatic diseases (11, 12, 13). One of the possible reasons could be a small number of participants in our study. PTSD is often associated with physical comorbidities ranging from nonspecific dizziness, tinnitus, and blurred vision to chronic pain, diabetes, cardiovascular, respiratory, and gastrointestinal diseases. There is also increased risk of cancer, arthritis, autoimmune and inflammatory diseases. In our study, the most common somatic disease in patients with PTSD was hypertension. A high ratio of patients with PTSD have unhealthy lifestyles and habits such as heavy smoking, low physical activity, and obesity, which lead to development of vascular, degenerative, and other types of somatic disorders (14). As many as 80% of people have at least one mental disorder with PTSD, the most common being depressive disorder, generalized anxiety disorder, and addictive disorder. Due to non-cooperation, the frequency of hospitalizations and relapses is high (15). Therefore, it is important to identify individuals suffering from this disease, encourage them to cope with the problem, and take care of their mental and physical health to avoid further consequences and comorbidities (16).

In our study, the most common mental disorder in women was recurrent depressive disorder (19%). The most common comorbidity with a recurrent depressive disorder was hypertension (4). Studies have shown that individuals with depression are more likely to develop hypertension, strokes, and ischemic heart disease. There is a pathophysiological connection between depression and hypertension because both disorders are characterized by increased sympathetic tone and increased secretion of adrenocorticotropic hormone and cortisol. Moreover, depressed patients may have difficulty adhering to their therapy regimen, resulting in poor blood pressure control (17). The prevalence of depression is 10 to 15%, with over 350 million people currently affected. Risk factors for developing depression disorder include stressful events, genetic predisposition, disability, illness, previous treatment for depression disorder and sleep problems. Somatic chronic diseases increase the risk of developing depression due to reduced quality of life, difficulty coping with diagnosis, pain, and rejection of the environment (4). Also, the prevalence of depression in people who suffer from at least one chronic illness is 9.3 to 23% and differs greatly from people who do not suffer from any chronic disorder (3.2 %). Increased prevalence of depressive disorders has been noticed in people suffering from cardiovascular diseases (17-27%), diabetes (11-31%), and arthritis (10-24%) (4, 17).

In this research, 25% of men and 7% of women were treated for alcoholism. It is estimated that 43% of the world's population consumes alcohol (18). In Croatia, about 6% of the population suffers from alcohol dependence, which amounts to about 250,000 people (19). Spirits (44.8 %) and beer (34.3 %) are most often consumed. Alcoholism is twice as common in men than in women, with the highest frequency between the ages of 20 and 24 (18). Alcoholics have twice the risk of developing other mental illnesses; these are most often anxiety disorders, affective disorders, personality disorders. Psychiatric disorders are thought to precede the development of alcoholism, except for obsessive-compulsive disorder and depression, which occur after alcohol use disorder (20). In addition, there is also a great link with various physical comorbidities.

In our study, the most common somatic diseases in patients treated for alcoholism were epilepsy and hypertension. Alcohol has a significant effect on the central nervous system, leading to symptoms of mania, depression, and epileptic seizures. Chronic alcohol consumption is related to multiple central and peripheral nervous system dysfunctions due to the direct action of alcohol or its derivatives and vitamin deficiencies associated with alcoholism (21). According to data from 2012, alcohol consumption was associated with 5.5% of cancers (7.2% in men and 3.5% in women) and

with 5.8% of deaths in oncological patients (22). The most common cancers associated with alcohol use are cancers of the oral cavity, pharynx, larynx, esophagus, liver, breast, and colon. The carcinogenic potential is linearly dependent on the amount of consumed alcohol (23). Alcohol consumption has a dual effect on the cardiovascular system; it has a cardioprotective effect in small doses (one standard drink), but it is harmful in large doses (24). The consumption of two standard drinks is considered to have a protective effect in diabetes mellitus but consuming four standard drinks a day results in negative effects. Since most of the alcohol is metabolized in the liver, liver diseases are not uncommon; chronic liver diseases that lead to cirrhosis are the most often (25). Primary alcoholic dementia accounts for 10% of all dementias (26).

Arterial hypertension is the most common somatic disease in this study. It affected 33% of men and 46% of women, a total of 36% of the respondents. Hypertension and coronary heart disease cause significant morbidity in patients, reduce the quality of life, and increase treatment costs. Psychosocial factors that lead to anxiety disorders play a role in the development of hypertension. Increased autonomic excitation via the hypothalamic-pituitary axis leads to an increase in circulating catecholamines, which increases the risk of hypertension and proinflammatory conditions, which in turn leads to the development of coronary heart disease (27). Also, hypertension intensifies symptoms of anxiety and the frequency of panic attacks. In one study, a significantly higher incidence of panic attacks was noticed in patients with hypertension (17%) compared to normotensive patients (11%) (28). Other anxiety disorders are also common; monitoring cardiac activity or avoiding certain activities often results in reduced quality of life in patients with hypertension (29).

Diabetes mellitus is the second most common somatic diagnosis in our respondents (22%). We found a higher incidence in women (32%) than in men (18%). 30% of patients with diabetes suffer from a mental disorder. Patients with schizophrenia are two to four times more likely to develop diabetes compared to the general population (30). The prevalence rates of depression and anxiety are significantly higher in diabetics; some studies have reported that the risk is increased by as much as 50-100%. The correlation is two-way, depression disorder results from years of uncontrolled or poorly controlled diabetes. Depression disorder, on the other hand, activates neurohormonal and neurotransmitter changes that stimulate the hypothalamic-pituitary axis and the adrenal gland, which releases more cortisol and other hormones responsible for insulin resistance (30, 31). The prevalence of diabetes in depressed adult patients is significantly higher in women than in men. A study conducted in Saudi Arabia reported that 37% of patients with type 1 diabetes mellitus, 37.9% of patients with type 2 diabetes mellitus, and 13.6% of patients with gestational diabetes suffer from depression. Another study reported that 46.15% of patients have these comorbidities, of which 36.7% suffer from severe depression. What is more, levels of glycosylated hemoglobin (HbA1c) are significantly higher in people with depression compared with those who do not suffer from it (30).

Epilepsy affected 15% of men and 8% of women, a total of 13% of respondents. It is estimated that the most common mental illness in comorbidity with epilepsy is depression, and its incidence is about 35%. In patients in whom epilepsy is poorly controlled, the incidence is about 50%, while in patients with well-controlled seizures it is about 10 to 20% (31). One study showed that 16.7% of patients with epilepsy have some sort of anxiety disorder; most people had frequent panic attacks (81.2%). Older age of patients and later onset of epileptic seizures are associated with a higher incidence of anxiety disorders (32).

Comorbidities of physical and mental illnesses are a major challenge in medicine. The mutual pathophysiological effect of one disease on another can significantly affect the course and prognosis of the disease. Due to the diverse symptoms experienced by people with multimorbidity, diagnoses are often missed, which can lead to major consequences. It is extremely important to improve cooperation in

treatment and the multidisciplinary approach to the patient in order to reduce the number of hospitalizations, emergency interventions, suicides and improve the patients' quality of life and life expectancy.

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Administrative, technical or logistic support: RM, AL, DD, TB
Analysis and interpretation of data: RM, AL, DD, TB
Conception and design: RM, AL, DD, TB
Critical revision of the article for important intellectual content: RM, AL, DD, TB
Drafting of the article: RM, AL, DD, TB
Final approval of the article: RM, AL, DD, TB
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Obtaining funding: RM, AL, DD, TB
Provision of study materials or patients: RM, AL, DD, TB
Statistical expertise: RM, AL, DD, TB
Other: RM, AL, DD, TB