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# Intake of selected nutraceuticals and the clinical condition of patients with mental disorders

Agnieszka Wendołowicz, Ewa Stefańska, Dorota Jankowska, Napoleon Waszkiewicz, Lucyna Ostrowska

#### Summary

Aim: The aim of this research was to assess the impact of nutraceutical intake on the mental condition of patients affected by depression and schizophrenia.

**Material and methods:** The research covered a group of 156 patients with depression and 116 patients with schizophrenia ranging in age from 18 to 65 years. The clinical condition of the patients was assessed on the basis of: the age of onset, average number of episodes per year of the disease and the average duration of the disease. A quantitative assessment of diet by means of a 24-hour dietary recall was carried out.

**Results:** It was stated that choline was a nutritional factor that has a significant impact on the clinical condition of depression. The study also revealed that the nutritional factors having a significant impact on the reduction of the number of schizophrenia episodes are: tyrosine, vitamin  $B_1$ ,  $B_9$ , magnesium and copper, whereas the increase in the number of episodes was related to phenylalanine intake.

**Conclusions:** Patients with mental disorders require individual nutritional education and control over the nutrient intake in their diet and their concentration in the blood serum. If the patient is unable to balance their diet, supplementation with proper preparations should be considered.

nutrition, bioactive compounds, mental health

#### INTRODUCTION

Epidemiological studies indicate that the prevalence of mental disorders is rising systematically and that this phenomenon is global. According to the WHO data, depression occurs among

Agnieszka Wendołowicz<sup>1</sup>, Ewa Stefańska<sup>1</sup>, Dorota Jankowska<sup>2</sup>, Napoleon Waszkiewicz<sup>3</sup>, Lucyna Ostrowska<sup>1</sup>

<sup>1</sup>Department of Dietetics and Clinical Nutrition, Medical University of Bialystok, Head of Department prof. Lucyna.Ostrowska <sup>2</sup>Department of Statistics and Medical Informatics, Medical University of Bialystok, Head of Department prof. Tomasz Burzykowski <sup>3</sup>Department of Psychiatry, Medical University of Bialystok, Head of Department prof. Napoleon Waszkiewicz **Correspondence address:** estef@umb.edu.pl about 350 million people in the world [1]. It was stated in the EZOP study that severe depression occurred among 3% of the Poles subjected to the study. It is estimated that 0.9-17.1 persons out of 100 may experience an episode of severe depression throughout their lifetime [2]. The global prevalence of schizophrenia amounts to 50 million patients, 33 million of whom live in developing countries. The annual incidence of schizophrenia is estimated to 7-40/100,000 persons and the incidence risk in the general population throughout their lifetime in all countries is similar and amounts to about 1% [1]. In Poland, it is estimated that about 400,000 patients are affected by schizophrenia [2].

Depression is of a multi-factor nature and includes genetic predispositions, physical condition of the body and stress factors [2]. In the etiopathogenesis of schizophrenia, the role of genetic, biochemical, viral, neurophysiological and neuropathological factors is taken into consideration. Persons with mental disorders constitute a group susceptible to somatic afflictions [3-4]. These persons' poor health conditions result from low physical activity, smoking, overuse of psychoactive substances and an improper diet. Proper function of the central and peripheral nervous system depends on the diet. The cells of the nervous system need nutrients to build and maintain their structure as well as to sustain their function [5-6]. All that people feel – emotions, desires, the awareness of existence - depends on the brain and the neurotransmitters that operate therein. Any deviation from their proper operation has an impact on all the systems and organs in the human body; however, the nervous system is the most sensitive of them all [7]. Bioactive nutrition components that, thanks to their properties, show effects improving the body functions and determining the proper functioning of the nervous system are, among others, amino acids (tryptophan, tyrosine, phenylalanine), dietary fibre, polyunsaturated fatty acids such as eicosapentaenoic and docosahexaenoic acids, vitamins such as vitamin C, vitamin D, vitamin E, folic acid, choline, vitamin  $B_{1}$ , vitamin  $B_{6}$ , vitamin  $B_{12}$  and minerals: calcium, magnesium, sodium, potassium, iron, zinc, copper, selenium and iodine [8-9]. Deficiency of B vitamins in the body can result in psychiatric diseases such as depression, hysteria, hypochondria and can cause myelin degradation. Low levels of folic acid, vitamin  $B_{1}$ ,  $B_{6}$ ,  $B_{12}$ can affect levels of neurotransmitters such as serotonin and dopamine, which are important for mood [6, 9-11]. A large number of observational studies show lower choline in patients with psychosis [10]. Vitamins C, E, are nonenzymatic dietary antoxidants which may be beneficial in dealing with oxidative stress in depression and schizophrenia as they break free radical-chain reactions [6]. Mental disorders may also be associated with a deficiency of unsaturated fatty acids from the n-3 family and an elevated level of n-6 acids in phospholipids. Docosahexaenoic acid (DHA), which is necessary for the brain to work properly, and eicosapentaenoic acid (EPA), which has anti-inflammatory properties, as structural components, they play a significant role in the human nervous system [9].

Among the patients affected by mental disorders, the risk of occurrence of diet-related diseases is higher than in the case of the general population and, therefore, the monitoring of nutraceuticals intake in the all-day food rations of these persons deserves particular attention.

That is why the aim of this research was to assess the impact of the intake of selected nutraceuticals on the mental condition of patients with depression and schizophrenia.

#### MATERIALS AND METHODS

#### Study participants

The research covered a group of 272 persons ranging in age from 18 to 65 years: 156 patients with depression (109 women and 47 men) and 116 patients with schizophrenia (53 women and 63 men) (ambulatory patients under the supervision of the Mental Health Outpatient Clinic). The patients participating in the research were informed about the objective and the methods of the conducted research. Each patient signed a written consent for this research. The research obtained an approval from the local Bioethics Committee No.R-I-002/325/2011 and No.R-I-002/370/2014. The research was conducted in accordance with the Declaration of Helsinki. Body measurements such as height, body mass, were taken by personnel trained in standard procedures. Body mass index (BMI) was calculated as weight in kilograms divided by the square of height in metres.

The depression degree assessment was made by means of the Hamilton Depression Rating Scale (17-point scale version) on the basis of the age of onset, the number of episodes per year of the disease and the average duration of the disease in years [12]. The group included patients diagnosed with recurrent depressive disorders lasting up to 5 years. Current antidepressant treatment consisted of one antidepressant (selective serotonin reuptake inhibitors-SSRI) and one sedative used on an as-needed basis. In the group of studied patients, 44% received sertraline, 27% escitalopram, 21% paroxetine, 8% citalopram.

The course of schizophrenia was assessed on the basis of the age of onset, the number of episodes per year of the disease and the average duration of the disease in years. Patients from the schizophrenia group had received atypical or typical antipsychotic drugs for at least a year before their inclusion in the study and they were psychiatrically stable. 40% of patients have been receiving 1 neuroleptic, 60% patients-2 or 3 neuroleptics, concomitantly. The most commonly used were: olanzapine, risperidone, haloperidol and clozapine. Persons abusing psychoactive substances, diagnosed with other mental disorders, cognitive disorders, or nutritional disorders were excluded from the study.

#### Nutritional Assessment

Among all the patients, a 24-hour dietary recall from 3 weekdays was used for quantitative assessment of the diet and next the results were averaged. A 24-hour dietary recall was collected by a qualified dietician. Data obtained by this method inform about usual food consumption. The size of food portions was determined on the basis of photo album of food provided by the National Food and Nutrition Institute in Warsaw [13]. The assessed patients did not use any additional vitamin-mineral supplementation.

While assessing the nutraceuticals intake, such as amino acids (tryptophan, tyrosine, phenylalanine), polyunsaturated fatty acids (such as eicosapentaenoic and docosahexaenoic acid), vitamins, (such as vitamin C, vitamin D, vitamin E, folic acid, vitamin  $B_{1,}$  vitamin  $B_{6,}$  vitamin  $B_{12}$ ) and minerals (calcium, magnesium, sodium, potassium, iron, zinc, copper, iodine), was used the computer program Diet 5.0 recommended and developed by the National Food and Nutrition Institute in Warsaw, taking into account the loss of nutrients during food processing (Diet 5.0 package for planning and ongoing assessment of the individual diet (license agreement No. HBBxtpINI). Dieta 5 was constructed based on a previously developed and validated Nutritive Value Tables of Food Products containing database of nutritional values of Polish food products and dishes.

Due to the fact that there are no publications concerning the choline and selenium content in foodstuffs, the American database (United States Department of Agriculture – Agricultural Research Service – USDA Food Composition Databases) was used for the assessment [14].

#### **Statistical Analysis**

Statistical analysis of the obtained results was performed using the Statistica 12.0 software by StatSoft. Parameters of descriptive statistics were used to describe continuous variables, and for categorized variables, percentages of individual values were used. The  $\chi^2$  test was used in order to assess relations between nominal values. To compare the clinical characteristics between patients Mann-Whitney U test was performed.

In the statistical analysis of correlations between pairs of quantitative variables, the Spearman rank correlation was used. The multiple linear regression for a multivariate analysis with stepwise variables elimination (full model was taking into consideration the intake of all abovementioned nutraceuticals). A p-value less than 0.05 was considered statistically significant.

#### RESULTS

The characteristics of the participants in the present study are shown in Table 1. (Tab.1).

Analysed		Women		Men			
characteristics	Group with depression n=109	Group with schizophrenia n=53	р	Group with depression n=47	Group with schizophrenia n=63	р	
	Mean ±SD	Mean ±SD		Mean ±SD	Mean ±SD		

Table 1. Characteristics of study participants.

Age (years)	46.6	40.3	<0.001	43.9	39.7	0.153
	±11.97	±11.01		±12.44	±12.43	
BMI [kg/m²] (%)						
<18.5	5	2	0.008	0	0	<0.001
18.5-24.9	34	62		13	71.5	
25.0-29.9	33	21		59	17.5	
≥30	28	15		28	11	
		Ма	rital status (%)			
Single	22.9	54.9	<0.001	28.3	74.5	<0.001
Married	56.9	19.6		65.2	10.0	
Divorced	11.0	13.7		6.5	14.5	
Widow/	9.2	11.8		0	0	
Widower						
		Place	of residence (%	)		
City	57.8	80.4	0.008	69.6	69.1	0.013
Town	11.0	3.9		6.5	14.5	
Village	31.2	15.7		23.9	16.4	
		Educa	tional backgrour	nd		
Elementary education	12.4	5.9	<0.001	17.4	29.1	<0.001
Vocational education	22.5	15.6		28.3	25.5	
Secondary education	49.5	45.1		37.0	32.7	
Higher education	15.6	33.4		17.3	12.7	
	·	Ту	pe of work (%)		·	
Pensioner	25.7	42.0	<0.001	22.2	63.5	<0.001
Physical work	40.4	18.0		42.2	23.1	
Intellectual work	33.9	40.0		35.6	13.4	

A mean age of women with depression was 46.6±11.97 years and it was significantly higher compared to women with schizophrenia 40.3±11.01 years, (p=0.001). On the other hand, the mean age of men was higher in the group with depression 43.9±12.44 years compared to the group with schizophrenia 39.7±12.43 years, but the difference was not statistically significant (p=0.153). The mean BMI of women with depression was 27.0 (range 17.2 to 45.7) and 25.6 (range 17.3-42.2) kg/m<sup>2</sup> in women with schizophrenia. The mean BMI of men with depression was 27.7 (range 19.1-38.7) and 24.9 (range 18.7-41.3) kg/ m<sup>2</sup> in men with schizophrenia. A significantly larger group of people with BMI $\geq$ 25 kg/m<sup>2</sup> was in women and men with depression compared to groups with schizophrenia. It was found that both in the compared groups of women and men, significantly more patients with depression were married, had secondary education and intellectual work as compared with the patients with schizophrenia.

Table 2 shows the clinical condition of the patients (tab.2). Among the patients with depression, the mean number of points scored in the Hamilton Depression Rating Scale was significantly higher in the group of women (15.27±6.80) compared to the group of men (12.58±6.68) (p=0.031). The average number of episodes per year of the disease was 0.60±0.46 in the group of women with depression and it was lower than in the group of men with depression where it amounted to 0.80±0.71 (the difference was not statistically significant). The duration of the disease in the

group of women with depression was  $2.30\pm0.94$  years on average, whereas in the group of men –  $1.88\pm0.92$  years on average (p=0.356). It was stated that among women with depression, the highest percentage concerned the patients affected by the disorder for over 5 years (58.2%), 19.4% of wom-

en have been affected for one up to five years and 27.8% of them for less than one year. In the group of men, the highest percentage of 47.7% has been affected for less than one year, then 36% has been affected for longer than five years and 15.9% of men have been affected for one up to five years.

Analysed		Women			Men		р				
characteristics	Mean±SD	Me	Scope	Mean±SD	Me	Scope					
Group with depression											
Age of onset	37.74±12.12	38.00	16-63	35.73±11.59	35.00	18-65	0.316				
Hamilton Depression Rating Scale	15.27±6.80	15.50	2-33	12.58±6.68	12.00	4-31	0.031				
Average number of episodes per year of the disease	0.60±0.46	0.57	0.08-2.14	0.80±0.71	0.67	0.04-3.00	0.207				
Duration of the disease (in years)	2.30±0.94	3	1-5	1.88±0.92	2	1-3	0.356				
Group with schizophren	nia										
Age of onset	28.12±9.22	26.00	15-53	25.90±9.44	22.00	12-56	0.183				
Average number of episodes per year of the disease	0.94±0.77	0.73	0.08-3.00	0.83±0.63	0.62	0.25-3.00	0.778				
Duration of the disease (in years)	2.55±0.71	3	1-3	2.58±0.69	3	1-3	0.765				

Table 2. Clinical condition of the patients.

#### SD:standard deviation, Me-median

The mean age of onset among women with schizophrenia was 28±9.22 years and it was higher than in the group of men where it was 25.90±9.44 years, (p=0.183). The mean number of episodes per year of disease was (0.94±0.77) in the group of women with schizophrenia compared to the group of men  $(0.83\pm0.63)$ (p=0.778). The mean duration of the disease in the group of women with schizophrenia was 2.55±0.71 years, whereas in the group of men it was 2.58±0.69 years (p=0.765). Furthermore, it was stated that the highest percentage of patients with schizophrenia have been affected for more than 5 years (68.1% of woman and 70.6% of men). It was observed among patients with schizophrenia that 19.1% of women and 17.6% of men have been affected for one up to five years, whereas 12.8% of women and 11.8% of men have been affected for less than one year.

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Table 3 and 4 present the average energy value of daily food rations and the average consumption of selected nutrients by the studied participants. In the study groups of women no statistically significant differences were observed in the consumption of evaluated nutrients, but the food rations of women with depression were characterized by a lower energy value and the content of most of the assessed nutrients as compared to the food rations of women with schizophrenia. The food rations of men with recognized depression were characterized by higher content of the majority of assessed nutrients as compared to the food rations of men with schizophrenia. Men demonstrated statistically significant differences in the supply of vitamin C (p=0.030), whose intake was significantly higher in the men with depression compared to the men with schizophrenia.

Variables	Women	with dep	ression	Women v	vith schize	ophrenia	р
	Mean±SD	Me	Scope	Mean±SD	Me	Scope	
Energy (kcal/d)	1689.6±565.2	1645.0	721.7 – 3593.7	1848.6±558.3	1777.9	830.2-3252.3	0.233
Tryptophan (mg/d)	809.3±314.5	752.8	221.6 - 2043.4	787.4±221.8	777.1	361.9-1301.8	0.972
Tyrosine (mg/d)	2213.39±884.72	2107.9	838.9-5909.7	2231.0±728.2	2165.9	1008.5-4094.7	0.859
Phenylalanine	2821.9±1086.9	2659.7	1073.5 – 7377.3	2816.4 ±778.0	2846.4	1325.7-4668.3	0.759
Eicosapentaenoic acid (g/d)	0.02±0.09	0.00	0.00 – 0.52	0.05±0.31	0.00	0.00 – 2.20	0.952
Docosahexaenoic acid (g/d)	0.06±0.20	0.00	0.00-1.59	0.15±0.95	0.00	0.00-6.68	0.952
Fibre (g/d)	17.3±7.2	6.8	2.8 - 54.4	19.3±8.0	18.6	4.2 – 51.8	0.203
Vitamin A (µg/d)	718.0±451.7	619.6	89.8-2799.2	802.9±506.1	629.9	119.0-2562.6	0.558
Vitamin D (µg/d)	2.0±1.5	1.6	0.2-9.7	2.1±1.6	1.5	0.1-8.1	0.982
Vitamin E (mg/d)	5.9±4.1	4.7	1.2-25.8	7.1±5.0	5.2	2.0-25.0	0.408
Vitamin C (mg/d)	60.1±44.4	45.9	2.5-257.5	62.2±55.2	40.6	0.2-268.3	0.918
Vitamin B <sub>1</sub> (mg/d)	1.3±0.4	1.3	0.2-2.5	1.2±0.4	1.1	0.5-2.5	0.541
Vitamin B <sub>6</sub> (mg/d)	1.3±0.4	1.2	0.5-3.1	1.3±0.4	1.3	0.6-2.3	0.662
Folic acid (µg/d)	186.5±66.7	180.45	39.7 – 376.6	211.1±87.9	204.9	67.5-455.3	0.274
Vitamin B <sub>12</sub> (µg/d)	2.3±1.1	2.1	0.6-5.8	2.2±0.8	2.2	0.9-4.1	0.861
Choline(mg/d)	207.4±109.4	198.7	23.7-518.0	196.4±98.4	190.7	78.3-528.2	0.739
Calcium (mg/d)	473.7±271.9	446.0	61.3-1366.9	542.4±318.7	494.4	76.1-1390.5	0.533
Magnesium (mg/d)	261.2±95.2	249.8	73.8-613.5	285.9±116.5	271.5	90.0-617.5	0.398
Sodium (mg/d)	3309.0±1084.9	3336.1	704.5-5972.1	3098.3±1097.7	2902.4	416.4-5391.1	0.465
Potassium (mg/d)	2888.8±1102.4	2793.1	661.9-8638.2	3044.8±1704.0	2713.0	758.4-9200.5	0.938
lron (mg/d)	9.7±3.8	8.4	3.1-19.7	8.8±3.1	9.1	3.9-26.2	0.349
Zinc (mg/d)	8.8±2.7	8.6	2.8-19.1	8.8±2.4	8.8	4.3-14.8	0.994
Copper (mg/d)	1.0±0.8	0.8	0.4 - 8.8	0.9±0.3	0.9	0.3-8.6	0.861
lodine (µg/d)	122.7±63.0	118.7	0.0-256.5	118.1±63.7	107.7	16.1 – 341.4	0.651
Selenium (µg/d)	69.2±24.7	69.4	17.2-135.0	75.8±29.8	68.9	32.1-193.7	0.829

Table 3. Mean content of selected nutrients in daily food rations of the studied women

SD-standard deviation, Me-median, ns-not statistically significant

Table 4. Mean content of selected nutrients in c	daily food rations of the studied men
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Variables	Men	with depre	ssion	Men wi	hrenia	р	
	Mean ±SD	Me	Scope	Mean±SD	Me	Scope	
Energy (kcal/d)	2066.1±634.0	1969.4	1006.1-3526.8	2052.3±639.8	2044.0	734.2-3502.2	0.987
Tryptophan (mg/d)	1001.2±403.0	933.5	327.6-2698.7	922.5±309.8	881.1	254.2-1779.2	0.772
Tyrosine (mg/d)	2683.6±936.1	2455.2	1353.5-5176.3	2569.8±913.1	2472.8	824.5-5643.3	0.899
Phenylalanine	3321.4±1136.3	3235.3	900.0 - 5650.0	3331.4±1060.1	3200.9	1026.3-6078.9	1.000
Eicosapentaenoic acid (g/d)	0.01±0.03	0.00	0.00-0.18	0.02±0.10	0.00	0.00-0.68	0.637
Docosahexaenoic acid (g/d)	0.03±0.07	0.00	0.00-0.39	0.11±0.24	0.02	0.00-1.03	0.631

Fibre (g/d)	18.2±6.1	17.8	7.5-32.0	15.9±5.3	15.8	2.2-30.7	0.259
Vitamin A (µg/d)	1068.7±1368.1	777.6	69.5-8775.0	897.6±1137.0	696.2	46.8-8601.7	0.801
Vitamin D (µg/d)	2.5±1.6	1.9	0.7-2.5	3.0±3.1	2.0	0.4-22.1	0.985
Vitamin E (mg/d)	7.5±6.1	5.3	1.5-25.7	5.6±3.5	4.9	0.9-22.9	0.664
Vitamin C (mg/d)	81.4±96.9	50.8	4.8-539.4	49.6±48.3	34.7	0.0-250.2	0.030
Vitamin B <sub>1</sub> (mg/d)	1.5±0.5	1.50	0.8-3.1	1.4±0.6	1.5	0.3-4.8	0.376
Vitamin B <sub>6</sub> (mg/d)	1.9±0,5	1.9	0.9-3.0	1.7±0.6	1.7	0.3-3.7	0.186
Folic acid (µg/d)	267.4±131.6	225.0	71.8-588.7	213.8±74.2	218.8	38.3-393.2	0.937
Vitamin B <sub>12</sub> (µg/d)	3.2±2.7	2.5	0.9-16.5	3.1±2.8	2.7	0.6-16.2	0.902
Choline (mg/d)	205.9±105.7	182.7	30.0-423.8	234.0±157.8	216.1	27.9-763.2	0.857
Calcium (mg/d)	620.3±541.6	416.7	85.4-2758.2	475.9±332.3	390.3	118.2-1881.3	0.532
Magnesium (mg/d)	296.2±108.1	282.6	145.2-656.9	252.5±80.5	251.4	50.9 – 451.7	0.084
Sodium (mg/d)	4238.9±1287.7	4329.2	1603.0-6975.9	4039.5±1392.7	3967.3	1383.7-7091.1	0.677
Potassium (mg/d)	3221.0±866.6	3299.7	1660.2 – 4522.7	2956.9±1080.3	2918.4	527.6-7147.9	0.216
Iron (mg/d)	12.5±9.5	10.5	5.3-20.2	10.3±3.4	10.0	2.4-18.0	0.679
Zinc (mg/d)	11.2±3.4	10.7	5.3-18.3	10.1±3.5	9.2	2.9-20.0	0.321
Copper (mg/d)	1.1±0.4	1.0	0.5-2.8	0.9±0.2	0.9	0.2-1.5	0.431
lodine (µg/d)	142.6±51.1	140.9	15.0-244.5	134.1±56.4	131.8	8.2-259.8	0.696
Selenium (µg/d)	68.3±20.5	69.4	23.4-113.9	77.6±38.2	76.2	11.2-186.4	0.594

SD-standard deviation, Me-median, ns-not statistically significant

Table 5. Analysis of correlation between the amount of provided nutrients and aggravation of depression in the group of men
and women subjected to the study.

	Women with depression								
Analysed characternistics	Hamilton De Rating S	epression Scale	Number of epi of the o	sodes per year disease	Duration of the disease				
	r	r p		r p		р			
Dietary fibre (g/d)	-0.02	ns	-0.17	ns	-0.10	ns			
Vitamin A (µg)	0.07	ns	-0.12	0.031	-0.07	ns			
Vitamin C (mg)	0.11 ns		0.17	ns	-0.13	ns			
Choline (mg)	-0.35	0.026	-0.02	ns	-0.02	0.045			
Calcium (mg)	0.07 ns		-0.04	ns	-0.19	0.019			
Magnesium (mg)	0.03 ns		-0.19	ns	-0.11	ns			
Potassium (mg)	0.00	ns	-0.05	ns	-0.06	ns			
Zinc (mg)	0.06	ns	-0.11	ns	-0.08	ns			
lodine (µg)	0.06	ns	-0.06	ns	0.07	ns			
		Men with de	epression						
	1	n=4	7						
Analysed characterristics	Hamilton Depression Rating Scale		Number of epi of the o	sodes per year disease	Duration of the disease				
	r	р	r	р	r	р			
Dietary fibre (g/d)	0.21	ns	-0.30	0.013	-0.21	ns			

Vitamin A (µg)	0.13	ns	-0.16	ns	-0.23	ns
Vitamin C (mg)	0.00	ns	-0.20	ns	-0.31	0.041
Choline (mg)	0.05	ns	-0.15	ns	-0.09	ns
Calcium (mg)	0.18	ns	-0.32	ns	-0.06	ns
Magnesium (mg)	0.06	ns	-0.10	0.020	-0.07	ns
Potassium (mg)	0.05	ns	-0.51	0.012	-0.24	ns
Zinc (mg)	0.37	0.041	-0.03	ns	-0.05	ns
lodine (µg)	0.34	0.048	-0.07	ns	-0.01	ns

r – Spearman's rank correlation coefficient; p – critical value of significance test for Spearman's rank correlation coefficient; ns-not statistically significant

The relationship between the energy value of diet and supply of selected nutraceuticals with the severity of depression and schizophrenia was analysed among the examined patients.

The statistically significant results are presented in tables 5 and 6 (tab.5, tab.6). Regardless of sex, statistically significant correlations between aggravation depression and schizophrenia and the energy value of the diet, the content of basic nutrients and between the intake of phenylalanine, tyrosine, tryptophan and polyunsaturated fatty acids and aggravation of these diseases were not stated.

 Table 6. Analysis of correlation between the amount of provided nutrients and aggravation of schizophrenia in the group of men and women subjected to the study.

Analysed characteristic	nalysed characteristic Women with s				Men with schizophrenia n=63			
	Number of year of t	episodes per he disease	Duration of the disease		Number of episodes per year of the disease		Duration of the disease	
	r	р	r	р	r	р	r	р
Vitamin C (mg)	-0.06	ns	-0.02	ns	-0.21	ns	-0.32	0.027
Folic acid (µg)	-0.05	ns	-0.01	ns	-0.10	0.029	-0.20	ns
Selenium (µg)	-0.06 0.004		-0.27	0.020	0.09	ns	0.05	ns

r - Spearman's rank correlation coefficient; p - critical value of significance test for Spearman's rank correlation coefficient;

ns-not statistically significant

It was stated in the group of women with depression that choline intake in the diet correlated significantly and negatively with the aggravation of depression (measured by means of the Hamilton Depression Rating Scale) (r=-0.35; p=0.02) and with the duration of disease (r=-0.017; p=0.045). Negative correlations were also stated between the amount of provided vitamin A and the number of episodes per year of disease (r=-0.12; p=0.031) as well as between the calcium intake and the duration of disease ( r=-0.19; p=0.019 ).

A negative, statistically significant correlation between the amount of consumed dietary fibre and the number of episodes per year of disease (r=-0.30; p=0.013) as well as between vitamin C intake and the duration of the disease (r=-0.31; p=0.041) as well as a negative correlation between potassium intake in the diet and the number of episodes occurring within a year (r=-0.51; p=0.012) and between magnesium intake and the number of episodes per year of disease (r=-0.10; p=0.020) were stated in the group of men with depression. Furthermore, a statistically significant correlation between zinc intake and the aggravation of depression was measured with the use of the Hamilton Depression Rating Scale (r=0.37; p=0.041) as well as between iodine intake and the aggravation of depression (r=0.34; p=0.048) were stated in the group of men with depression.

While assessing the correlation between schizophrenia and the intake of bioelements in diet,

it was stated that in the group of women only selenium intake correlated with the number of episodes per year of disease (r=-0.06; p=0.004) and duration of the disease (r=-0.27; p=0.020). A statistically significant negative correlation between the amount of folic acid provided in the diet and the number of episodes per year of disease (r=-0.10; p=0.029) was stated in the group of men with schizophrenia. There was also a negative statistically significant correlation between the supply of vitamin C and the duration of the disease in the group of men with schizophrenia (r=-0.32; p=0.027).

The results of the analysis of multiple regressions assessing the correlation between the intake of chosen nutraceuticals in an all-day food ration and the aggravation of depression was presented in table 7 (tab.7). It was proved that a diet low in choline intake has an impact on the aggravation of symptoms of depression in 81% (regardless of sex).

Table	7. Analysis	of linear re	egression	after stepv	vise variable	elimination	in the	group	with o	depression.
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Model after stepwise variables elimination						
	Variable	Standardised beta coefficient	Significance level p	R <sup>2</sup>		
Depression aggravation – Hamilton Depression Rating Scale	Choline	-0.25	0.011	0.81		

p - critical value of coefficients significance test in regression analysis;

R<sup>2</sup> – coefficient of determination

In the group with schizophrenia, it was stated that a high phenylalanine intake in the diet elevated the number of episodes of schizophrenia, whereas a high intake of tyrosine, vitamin  $B_{1,}$ folic acid, magnesium and copper could impact a decrease of the number of those episodes (the intake of these nutraceuticals could have impact on the occurrence of schizophrenia episodes in 30%) (Table 8).

Table 8. Analysis of linear regression after stepwise variable elimination in the group with schizophrenia.

Model after stepwise variables elimination						
Number of episodes per year of the disease	Variable	Standardised beta coefficient	Significance level p	R <sup>2</sup>		
	Phenylalanine	1.01	0.049	0.30		
	Tyrosine	-0.95	0.040	-		
	Vitamin B <sub>1</sub>	-0.38	0.027			
	Folic acid	-0.46	0.022			
	Magnesium	-0.58	0.001			
	Copper	-1.38	0.002			

p - critical value of coefficients significance test in regression analysis;

R<sup>2</sup> - coefficient of determination

### DISCUSSION

It was stated that both in the compared groups of women and men, significantly more patients with depression were married, had secondary education and intellectual work as compared with the patients with schizophrenia. Similar results were obtained in studies of other authors [15-16]. Literature shows a relationship between a health-promoting lifestyle and several socio-demographic factors. The most important lifestyle modifying factors are gender, age and education [15]. The socio-demographic factors can influence the lifestyle, but they are also closely connected with psychiatric disorders.

Many studies show the co-occurrence of positive correlations between the occurrence of excessive weight and obesity and severity of mental disorders [10-11]. It has been found that a long term effect of stress factors causing disturbances on the hypothalamic-pituitary-adrenal axis, primarily through an increased release of hypothalamic corticotropin and vasopressin. Hypothalamic corticotropin and vasopressin act synergistically to potentiate the release of adrenocorticotropin and cortisol. The consequence of neuroendocrine changes is an activation of lipoprotein lipase, which leads to lipid accumulation in adipocytes [17]. Our own studies showed a higher percentage of people with BMI over 25 kg/m<sup>2</sup> in the group of patients with depression than with schizophrenia.

Changes in nutritional behaviours may occur among patients affected by mental disorders consisting in the avoidance or the excessive consumption of defined groups of products and dishes, which in consequence may result in the development of severe nutritional deficiencies or excesses that, if they persist for a long time, can contribute to disturbances in the proper functioning of the nervous system [18]. Proper nutrition is one of essential health determining factors. On the basis of the analysis of the available literature, it should be noted that there is a limited number of studies assessing the diet and nutritional state of persons affected by mental diseases. Numerous studies were rather focused on metabolic troubles related to the unhealthy lifestyle of these patients [17].

Improper amounts and/or portions of consumed nutrients in relation to the physiological needs of the body may lead to their deficiency or excess. A consequence of an unbalanced diet can be disturbances in the course of physiological processes determining homoeostasis of the body, the ageing rate and occurrence of many afflictions. The results from epidemiological cohort studies indicate that nutritional deficiencies are related to the increase in the incidence of certain mental disorders [17-18]. The conducted studies reported lower consumption of most of the assessed nutrients in the food rations of women compared to men, which could be due to the dietary preferences of the respondents, but also to the lower usual consumption of food by the compared groups.

In this research, in the group of men with depression, a low dietary fibre intake correlated significantly with the aggravation of depression symptoms. The fermentation of particular fractions of dietary fibre occurs thanks to bacteria in the human gastrointestinal tract. Dietary fibre has an impact on gastrointestinal microbiota and it is a prebiotic that causes changes in its composition and multiplication of beneficial bacteria [19-20]. Microbiota in turn has an impact on CNS through the modulation of pro-inflammatory and anti-inflammatory cytokines concentration, production of numerous neuromediators and on the expression of their receptors in the brain through interactions with enteric and autonomic nervous system and through regulation of the HPA axis (hypothalamic-pituitary-adrenal axis) response. While there are some reports of an essential role of the immune system and proinflammatory cytokines in inflammatory pathogenesis of depression [20]. Dietary fibre also has impact on fat absorption and cholesterol metabolism through bonding of bile salts. Soluble fibre in the form of beta-glucan and pectins as well as non-soluble fibre and lignins increase excretion of sterols from the body. Bile acids, their salts and cholesterol contained there may be adsorbed onto fibre or dissolved and retained in water absorbed by dietary fibre. Thanks to these properties, bile acids are excreted from the body, cholesterol is directed to synthesis of bile acids which leads to a decrease of the amount of cholesterol available for lipoprotein synthesis and in consequence to reduce its concentration in the blood. Therefore, a proper dietary fibre content in the diet of patients with depression and schizophrenia seems to be very important in the prevention of lipid disorders. Other researchers stated that regular consumption of vegetables and fruits that are a source of dietary fibre may contribute to additional rare occurrences of further episodes of depression [21]. Likewise, on the basis of a GA-ZEL cohort study, it was stated that regular consumption of vegetables and fruits was linked to a decreased risk of occurrence of further episodes of depression [22].

In the group of men with depression and schizophrenia, a negative correlation between low intake of vitamin C and the aggravation of symptoms of the disease was stated. Randomized double-blind, placebo-controlled tri-

al studies showed that vitamin C elevated the mood and decreased the severity of depression [23].Research conducted in Japan suggest that a deficiency in vitamin C increases the prevalence of depressive symptoms [24].

Accumulation of antioxidants in the brain and nervous tissue is much slower than in other tissues [25]. In other studies, correlations between low vitamin C intake with simultaneous low level of this vitamin in blood serum and an increased risk of occurrence of ischaemia and decrease in mental capacity [25-26].

In the present research, a negative correlation between an insufficient amount of choline intake and the aggravation of depression was stated. Too low choline intake in the diet leads to changes in the composition of cell membranes, their structure and functions. A disturbed homoeostasis entails a loss of plasticity, impairment of synapses, apoptosis, neurodegeneration and increase in the risk of development of mild forms of cognitive disorders [27-29].

On the basis of the conducted in-house research, a negative correlation between a low magnesium intake and aggravation of symptoms of depression among men. Similarly, very low intake of this mineral was directly associated with depressive symptoms in the US National Health and Nutrition Examination Survey [30].Magnesium along with zinc, iron and copper are important glutamatergic transmission modulators related to etiopathogenesis of depression. Moreover, according to the available literature, the magnesium deficiency is related to a series of chronic diseases, including diabetes, arterial hypertension and lipid disorders. Magnesium deficiencies are one of the factors contributing to the development of insulin resistance that impairs the efficiency of energy metabolism and decreases the ability to physical work and has a negative impact on glucose level in the blood [31-34].

At the same time, a statistically significant (p=0.048), medium (r=0.34) positive correlation between the amount of iodine intake in the diet and aggravation of depression symptoms among men was observed in this research. Iodine is the first element that is necessary for the production of triiodothyronine  $T_3$  and thyroxine  $T_4$ , hormones in the thyroid gland that have an impact on proper cell differentiation

and maturation of brain and nervous system cells [35].

A statistically significant (p=0.029) weak (r=-0.10) negative correlation between low folic acid intake and aggravation of schizophrenia symptoms was also stated in the group of men subjected to the study. In the research conducted among patients with neuropsychiatric disorders, a low level of the serotonin metabolite – 5-hydroxyindoleacetic acid (5-HIAA) in the cerebrospinal fluid was stated and supplementation with folates restored a proper concentration of this acid [27]. It was also proved that folic acid is a donor of methyl groups used in the reactions of the methylation of homocysteine to methionine. Among others, vitamin  $B_{12}$  participates in this process [36].

A correlation between low selenium intake and the aggravation of the disease was observed in the group of women with schizophrenia. In the central nervous system characterised by a high quantity of phospholipids, selenium as a component of glutathione peroxidase indirectly prevents the oxidative stress through limitation of the number of lipid peroxides [37]. There are some reports on adverse impact of selenium deficiency on the brain function through disturbance of neurotransmitters activity [38-39]. A low selenium level was associated with a significantly more frequent occurrence of anxiety, disorientation and aggression. Furthermore, selenium participates in thyroid hormones metabolism and its deficiency may lead to thyroid dysfunction [40-41].

In the group of men with depression, a positive correlation between zinc consumption and aggravation of the disease was stated.

Zinc concentration in blood serum remains in close connection with inflammatory processes whose activation occurs in the course of mental disorders. The presence of vitamin A and E supports the absorption of zinc. Zinc is necessary for the proper development and functioning of the brain. An important role of this element results from the fact that it modulates the transmission of nervous signals in synapses in the central nervous system [37]. Neurons containing zinc cations in complex with glutamate, also known as glutamatergic, occur in brain areas such as the cerebral cortex, limbic system structures that are responsible for regulation of emotions, reception

and processing of sensual experiences, that is to say olfaction, gustation, hearing, vision or pain perception as well as learning processes of memory forming processes [38].

To sum up, it can be stated that nutritional factors may contribute to the aggravation of both assessed disorders and for that reason nutritional advice should be provided for these groups of patients.

#### CONCLUSIONS

- It was stated that, among the assessed nutraceuticals, the strongest connection with the occurrence of depression is attributable to a low intake of choline in the diet; furthermore, significant correlations between the aggravation of the disease and low intake of vitamin A and calcium in the diet was observed among women, whereas among men with depression to a low vitamin C, magnesium and potassium intake and a higher intake of zinc and iodine.
- 2. It was proved that, among the assessed nutraceuticals, the phenylalanine intake in the diet had the strongest impact on an increase of the number of schizophrenia episodes, whereas the intake of tyrosine, vitamin B<sub>1</sub>, folic acid, magnesium and copper had a positive impact on a decrease of the number of episodes of this disease. At the same time, negative correlations between the aggravation of schizophrenia and the intake of folic acid and vitamin C was stated among men, whereas in the group of women it was between a low intake of selenium in the diet and the aggravation of this disease.
- 3. Patients with mental disorders require nutritional education and control of the nutrients in their diet as well as their concentration in the blood serum. If the patient is unable to balance their diet, a supplementation with proper preparations should be considered.

## **Conflict of Interest** The authors declare that they have no conflict of interest.

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#### REFERENCES

- World Health Organization. Depression. [cited 2019 Jan 22]. Available from https://www.who.int/en/news-room/factsheets/detail/mental-disorders/.
- Kiejna A, Piotrowski P, Adamowski T, Moskalewicz J, Wciórka J, Stokwiszewski J et al. The prevalence of common mental disorders in the population of adult Poles by sex and age structure. Psychiatr Pol. 2015; 49(1): 15-27.
- Gondek TM, Królicka A, Piotrowski P, Kiejna A. The European studies on mortality in schizophrenia. Psychiatr Pol. 2015; 49(6): 1139–1148.
- Jaaro-Peled H, Ayhan Y, Pletnikov MV, Sawa A. Review of pathological hallmarks of schizophrenia: comparison of genetic models with patients and nongenetic models. Schizophr Bull. 2010; 36(2): 301–313.
- Dipasquale S, Pariante CM, Dazzan P, Aguglia E, McGuire P, Mondelli V. The dietary pattern of patients with schizophrenia: a systematic review. J Psychiatr Res. 2013; 47(2): 197-207.
- Kim EJ, Lim SY, Lee H J, Lee JY, Choi S, Kim SY et al. Low dietary intake of n-3 fatty acids, niacin, folate, and vitamin C in Korean patients with schizophrenia and the development of dietary guidelines for schizophrenia. Nutr. Res. 2017; 45: 10-18.
- Vermeulen E, Brouwer IA, Stronks K, Bandinelli S, Ferrucci L, Visser M et al. Inflammatory dietary patterns and depressive symptoms in Italian older adults. Brain Behav Immun. 2018; 67: 290-298.
- Saluk-Juszczuk J, Kołodziejczyk J, Babicz K, Królewska K. Functional food-a role of nutraceuticals in cardiovascular disease prevention. Kosmos. 2010; 3(4): 527-538.
- Glibowski P, Misztal A. Effect of diet on mental well-being. Bromat Chem Toksykol. 2016; 49(1): 1-9.
- Aucoin M, LaChance L, Cooley K, Kidd S. Diet and Psychosis: A Scoping Review. Neyropsychobiology. 2020; 79: 20-42.
- Łojko D. Czy dieta w chorobie dwubiegunowej ma znaczenie? Psychiatr. Pol. 2018; 52: 783-795.
- Hamilton MA. A rating scale for depression. J Neurol Neurosurg Psych. 1960; 23: 56–62.
- Szponar L, Wolnicka K, Rychlik E. Album of photographs of food products and dishes. Warsaw: National Food and Nutrition Institute; 2000.
- USDA (US Department of Agriculture), 2013. USDA National Nutrient Database for Standard Reference, release 26. Agricultural Research Service. [cited 2017 Jul 20]. Available from: http://:ndb.nal.usda.gov/ndb/nutrients/index/.
- Ślusarz R, Borzyszkowska A, Szrajda J, Fidecki W, Haor B. Wpływ wybranych czynników socjodemograficznych na występowanie zaburzeń depresyjnych wśród kobiet. Problemy Pielęgniarstwa. 2011; 19(1): 21-26.

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- Ito H, Kumagai T, Kimura M, Koike S, Shimizu T. Dietary intake in body mass index differences in community-based Japanese patients with schizophrenia. Iran J Public Health. 2015; 44: 639-645.
- Yu ZM, Parker L, Dummer TJB. Depressive symptoms, diet quality, physical activity, and body composition among populations in Nova Scotia, Canada: Report from the Atlantic Partnership for Tomorrow's Health. Prev Med. 2014; 61: 106-113.
- Park JY, You JS, Chang KJ. Dietary taurine intake, nutrients intake, dietary habits and life stress by depression in Korean female college students: a case-control study. J Biomed Sci. 2010; 17(Suppl.1): S40-S44.
- Dahl WJ, Stewart ML. Position of the Academy of Nutrition and Dietetics: Health Implications of Dietary Fiber. J Acad Nutr Diet. 2015; 115(11): 1861-1870.
- Rudzki L, Szulc A. Influence of intestinal microbiota on the central nervous system and its potential in the treatment of psychiatric disorders. Pharmacotherapy in Psychiatry and Neurology. 2013; 2: 69-77.
- Evrensel A, Ceylan ME. The Gut-Brain Axis: The Missing Link in Depression. Clin Psychopharmacol Neurosci. 2015; 13(3): 239-44.
- Le Port A, Gueguen A, Kesse-Guyot E, Melchior M, Lemogne C, Nabi H et al. Association between dietary patterns and depressive symptoms over time: 10-year follow-up study of the GAZEL cohort. PLoS One. 2012; 7: e.0051593.
- Khajehnasiri F, Mortazavi SB, Allameh A, Akhondzadeh S. Effect of omega-3 and ascorbic acid on inflammation markers in depressed shift workers in Shahid Tondgoyan Oil Refinery, Iran: A randomized double-blind placebo-controlled study. J Clin Biochem Nutr. 2013; 53: 36–40.
- Nguyen TTT, Tsujiguchi H, Kambayashi Y, Hara A, Miyagi S, Yamada Y et al. Relationship Between Vitamin Intake and Depressive Symptoms in Elderly Japanese Individuals: Differences With Gender and Body Mass Index. Nutrients. 2017; 9(12): 1319.
- Grosso G, Bei R, Mistretta A, Marventanto S, Calabrese G, Masuelli L et al. Effects of vitamin C on health: a review of evidence. Front Biosci. 2013; 18: 1017-1029.
- May JM. Vitamin C transport and its role in the central nervous system. Subcell Biochem. 2012; 56: 85-103.
- Kennedy DO. B Vitamins and the Brain: Mechanisms, Dose and Efficacy-A Review. Nutrients. 2016; 8(2): 68-98.

- Skripuletz T, Manzel A, Gropengießer K, Schäfer N, Gudi V, Singh V et al. Role of choline metabolites in remyelination. Brain. 2015; 138(2): 398-413.
- Michel V, Bakovic M. Editorial: choline and brain function. Cent Nerv Syst Agents Med Chem. 2012; 12(2): 69.
- Tarleton EK, Littenberg B. Magnesium intake and depression in adults. J Am Board Fam Med. 2015; 28: 249–256.
- Lingam I, Robertson NJ. Magnesium as a Neuroprotective Agent: A Review of Its Use in the Fetus, Term Infant with Neonatal Encephalopathy, and the Adult Stroke Patient. Dev Neurosci. 2018; 40(1): 1-12.
- Koning G, Leverin AL, Nair S, Schwendimann L, Ek J, Carlsson Y et al. Magnesium induces preconditioning of the neonatal brain via profound mitochondrial protection. J Cereb Blood Flow Metab. 2019; 39(6): 1038-1055.
- Vink R. Magnesium in the CNS: recent advances and developments. Magnes Res. 2016; 29(3): 95-101.
- Nichols TA, Spraker TR, Gidlewski T, Cummings B, Hill D, Kong Q et al. Dietary magnesium and copper affect survival time and neuroinflammation in chronic wasting disease. Prion.2016; 10(3): 228-250.
- Redman K, Ruffman T, Fitzgerald P, Skeaff S. Iodine Deficiency and the Brain: Effects and Mechanisms. Crit Rev Food Sci Nutr. 2016; 56(16): 2695-2713.
- McCaddon A. Vitamin B<sub>12</sub> in neurology and ageing: clinical and genetic aspects. Biochimie. 2013; 95: 1066-1076.
- Li Z, Wang W, Xin X, Song X, Zhang D. Association of total zinc, iron, copper and selenium intakes with depression in the US adults. J Affect Disord. 2018; 1: 68-74.
- Adebayo OL, Adenuga GA, Sandhir R. Selenium and zinc protect brain mitochondrial antioxidants and electron transport chain enzymes following postnatal protein malnutrition. Life Sci. 2016; 152: 145-155.
- Solovyev ND. Importance of selenium and selenoprotein for brain function: From antioxidant protection to neuronal signalling. J Inorg Biochem. 2015; 153: 1-12.
- Cardoso BR, Roberts BR, Bush AI, Hare DJ. Selenium, selenoproteins and neurodegenerative diseases. Metallomics. 2015; 7(8): 1213-1228.
- Khalili H, Ahl R, Cao Y, Paydar S, Sjölin G, Niakan A et al. Early selenium treatment for traumatic brain injury: Does it improve survival and functional outcome? Injury. 2017; 48(9): 1922-1926.