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## PROGINS PROGESTERONE RECEPTOR POLYMORPHISM IN HEALTHY WOMEN AND PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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## PROGINS ПОЛИМОРФИЗЪМ НА ПРОГЕСТЕРОНОВИЯ РЕЦЕПТОР ПРИ ЗДРАВИ ЖЕНИ И ПАЦИЕНТИ СЪС СИСТЕМЕН ЛУПУС ЕРИТЕМАТОДЕС

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### РЕЗЮМЕ

### ABSTRACT

#### ВЪВЕДЕНИЕ

Системният лупус еритематодес (СЛЕ) е хронично аутоимунно заболяване, което засяга преди всичко жени в репродуктивна възраст. Половите хормони с имunosупресивно действие и съответно техните рецептори могат да играят важна роля за развитието и прогресията на аутоимунните заболявания. Затова настоящото проуч-

#### INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that affects mostly women in reproductive age. Consequently, the sex hormones with immunosuppressive effects and their receptors could play an important role for the autoimmune disease onset and progress. Therefore, the present study aimed to investigate the PROGINS Alu

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ване имаше за цел да сравни разпределението на PROGINS полиморфизма на прогестероновия рецептор при здрави жени и пациентки със СЛЕ.

## МАТЕРИАЛИ И МЕТОДИ

Бяха изследвани 220 жени на средна възраст  $41.13 \pm 11.87$  години (20–68), Разпределението на PROGINS алела беше проучено при 115 пациентки с лупус и 105 здрави контроли чрез RFLP анализ.

## РЕЗУЛТАТИ

Мутантният PROGINS Alu insertion алел беше установен при 15.45% от изследваните жени, докато обичайните алели бяха наблюдавани при 84.55% от участниците в проучването. Не се установиха съществени различия в разпределението на генотипните честоти на PROGINS полиморфизма при пациентите със СЛЕ в сравнение с контролната група ( $p = 0.208$ ), въпреки че честотата на хомозиготния PROGINS генотип беше по-висока при здравите отколкото при болните жени (4.76% срещу 0.87%). Полиморфизмът на прогестероновия рецептор не показва значима връзка с възрастта на поява, тежестта или клиничните симптоми на заболяването ( $p > 0.05$ ).

## ЗАКЛЮЧЕНИЕ

PROGINS полиморфизмът не е свързан със специфични клинични характеристики при жените с лупус. Необходими са допълнителни изследвания в други етнически групи, за да се установи специфичното влияние на полиморфизма на прогестероновия рецептор върху склонността към развитие на СЛЕ, както и за изясняване на съществуващите зависимости между стероидните хормони, рецепторните полиморфизми и автоимунните заболявания.

## INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic inflammatory autoimmune disease more prevalent in women with gender ratio of female to male of 9:1 (Weckerle CE, Niewold, 2011). This female predominance remains unexplained, although several different hypotheses have been proposed (Weckerle CE, Niewold, 2011, Hughes

insertion polymorphism in progesterone receptor gene in female lupus patients and healthy women.

## MATERIALS AND METHODS

Two hundred and twenty Caucasian women (mean age  $41.13 \pm 11.87$  years (20–68)) were included in the study. The PROGINS allele distribution was investigated in 115 lupus patients and 105 healthy women by RFLP analysis.

## RESULTS

PROGINS variant allele (Alu insertion) was found in 15.45% of the investigated women, while the wild type progesterone receptor allele (N) was carried by 84.55% of the group. No significant differences in the genotype frequencies of progesterone receptor PROGINS polymorphism in patients and controls were observed ( $p = 0.208$ ), although the prevalence of homozygous Alu insertion genotype was more common in controls than in patients (4.76% vs. 0.87%). The progesterone receptor polymorphism did not influence the clinical manifestation, severity of the disease or the age of SLE onset ( $p > 0.05$ ).

## CONCLUSIONS

PROGINS Alu insertion polymorphism is not associated with a specific clinical phenotype in Bulgarian SLE female patients. Further studies in other ethnic groups are needed to establish the precise influence of the PROGINS polymorphism on the SLE susceptibility as well as to clarify the genetic susceptibility to autoimmune disorders and the precise influence of the steroid hormones and their receptor polymorphisms.

GC, 2012). Steroid hormones could play an important role as modulators of the autoimmune disease onset and progress. Generally, they are implicated in the immune response, with estrogens being enhancers of at least the humoral immune response, and androgens, glucocorticoids and progesterone as natural immunosuppressors (Cutolo et al., 2004).

Recent studies indicate that progesterone and synthetic progestins could influence the risk of autoimmune processes differently depending on their levels and the presence of various progesterone receptors expressed in immune organs, immune cells or tissues targeted by the immune attack (Hughes GC, 2012). Progesterone could modulate the proliferation of stimulated T-cell, cytokine secretion, antibody production and macrophageal function (Zen et al., 2010). Decreased progesterone levels have been described in juvenile SLE patients, but the clinical significance of luteal dysfunction for the disease manifestation is unclear (Medeiros et al., 2009).

The progesterone receptor (PR) is a ligand-activated transcription factor existing in two isoforms: A (PRA) and B (PRB), resulting from the presence of 164bp additional amino acids at the N-terminus and alternative promoter usage (Romano et al., 2007; Stenzig et al., 2012). More than 670 single nucleotide polymorphisms have been identified in the human PR gene, many of them associated with increased risk for developing ovarian, endometrial, and breast cancer, pre-term labor and delivery, recurrent abortions, and migraine-associated vertigo in females (Tait et al., 2008). The most extensively studied polymorphic variant of the progesterone receptor is termed PROGINS haplotype. This complex consists of (1) an intronic 306-bp Alu insertion in intron 7, (2) a G/T substitution in exon 4 that results in amino acid substitution V660L (rs1042838) and (3) a silent base pair change C/T in exon 5 resulting in H770H (rs1042839). The Alu insertion and two single nucleotide polymorphisms (SNPs) are in complete linkage disequilibrium (Rockwell, 2012; Stenzig et al., 2012). Potential role of PR polymorphisms has not been previously investigated in patients with SLE. Therefore, the present study aimed to investigate the PROGINS Alu insertion in progesterone receptor gene in female lupus patients in comparison to healthy women.

## MATERIALS AND METHODS

### SUBJECTS

Two hundred and twenty Caucasian women (mean age  $41.13 \pm 11.87$  years [20–68]) were included in the study. One hundred and fifteen patients fulfilled the modified 1997 American College Rheumatology (ACR) classification criteria for systemic lupus erythematosus (Hochberg, 1997). The Systemic Lupus International Collaborating Clinics/ACR (SLICC) index (Stoll et al. 1996), the presence of Raynaud's phenomenon and Sicca syndrome were documented. All women underwent complete general assessment and the previous and current medication with corticosteroids and immunosuppressors was registered. One hundred and five controls were collected from the medical staff and students, all healthy volunteers – women without known connective tissue diseases. The experimental protocol was explained to all participants and written informed consent was obtained prior to the inclusion in the current study. The study was approved by the institutional ethic commission.

### GENETIC ASSAY

All participating women provided peripheral blood samples for DNA collected in EDTA tube. The genomic DNA was extracted through a standard salt extraction procedure. Genotyping for the PR Alu insertion polymorphism was performed by PCR-RFLP analysis. The control group of women was used only for a comparison of genetic polymorphism frequency. The Alu insertion was used as the indicator of the PROGINS allele. Primers used for amplification were: (F) 5'-GGCAGAAAGCAAAATAAAAAGA-3', (R) 5'-AAAGTATTTTCTTGCTAAATGTC-3' (Gimenes et al, 2010). PCR reaction was carried out in a total volume of 15  $\mu$ l, with 0.7 pM final concentration for each primer. Thermocycling conditions were 94° C for 5 min for an initial denaturation step, followed by 30 cycles of 94° C for 30 sec, 55° C for 60 sec, 72° C for 90 sec, followed by a final extension of 72° C for 5 min. The amplification

products were separated on 2% agarose gel and visualized with ethidium bromide under UV light. The PCR product presenting a single band of 149 bp referred homozygous individual without Alu insertion (marked as N/N genotype). The presence of one 149 bp band and one 455 bp band was an indication of heterozygous individual with one 306 bp Alu insertion allele and one allele without it (marked as N/Alu ins). The presence of single 455 bp band indicated individual with Alu insertion on both alleles. These samples were designated as Alu ins / Alu ins.

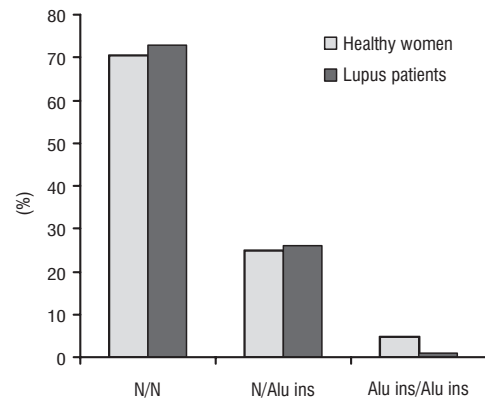
### STATISTICS

The distribution of all investigated genotypes in healthy females was in agreement with the Hardy-Weinberg equilibrium. The results were presented as mean  $\pm$ SD (median) for continuous variables or as a frequency (%) for dichotomous variables. Categorical data were analyzed through  $\chi^2$  test or Fisher's exact test. After a Kolmogorov-Smirnov test for normality of the distribution differences between two groups were established with an independent t-test or Mann-Whitney test. All results were considered significant at the 0.05 level. Statistical analysis was conducted through SPSS v. 11 for Windows (SPSS, Chicago, IL, USA).

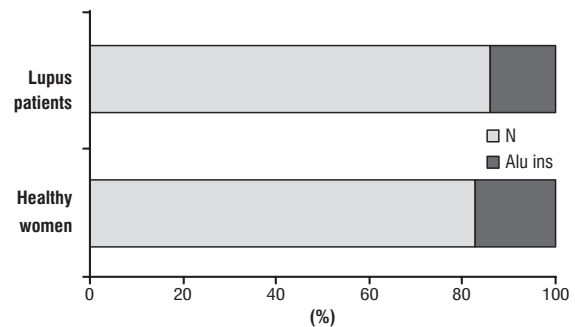
### RESULTS

PROGINS variant allele (Alu insertion) was found in 15.45% of the investigated women, while the wild type progesterone receptor allele (N) was carried by 84.55% of the group. No significant differences in the genotype frequencies of progesterone receptor PROGINS polymorphism in patients and controls were observed ( $p=0.208$ ), although the prevalence of Alu ins / Alu ins genotype was more common in controls than in patients (4.76% vs. 0.87%) (Figure 1). Considering clinical characteristics of the SLE patients, the presence of PROGINS Alu insertion polymorphism was not significantly

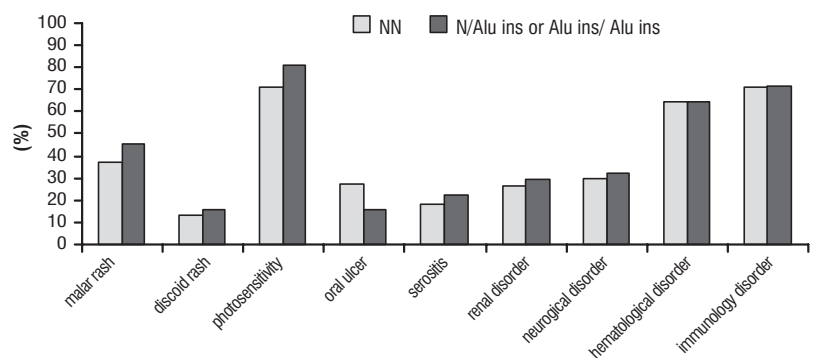
related to any ACR criterion (Figure 2). The progesterone receptor polymorphism did not influence the development of Raynaud's phenomenon or Sjögren syndrome, the severity of the lupus, or the age of disease onset ( $p>0.05$ ).



**Figure 1A.** Genotype frequencies of the progesterone receptor polymorphism in patients with systemic lupus erythematosus and healthy controls.



**Figure 1B.** Allele frequencies of the progesterone receptor polymorphism in patients with systemic lupus erythematosus and healthy controls ( $p>0.05$ ).



**Figure 2.** Allele frequencies of the progesterone receptor polymorphism in lupus patients with several ACR criteria ( $p>0.05$  for all).

Additionally, it was not related to any treatment plan ( $p > 0.05$ , data not shown).

## DISCUSSION

PROGINS polymorphism is a variant allele of the human PR gene, containing a 306-bp Alu direct repeat insertion of the PV/HS-1 Alu sub-family in intron G in the hormone-binding domain encoding region of the gene (Rowe et al., 1995). According to Stenzig et al. the PROGINS PR variants did not functionally differ from the wild type progesterone receptors (Stenzig et al., 2012). In opposite, in other experimental studies PROGINS polymorphic variant has been associated with reduced progestin actions (Romano et al., 2007). Reduced stability of the PROGINS transcripts, reduced transactivation activity of the PROGINS variant and less efficient inhibition of cell proliferation in ovarian cells expressing the PROGINS variant have been described (Romano et al., 2007). Progesterone has a protective effect on the ovarian and endometrial carcinogenesis, but it stimulates cell proliferation in the breast. Therefore, an increased risk for ovarian/endometrial malignancies and reduced risk for breast cancer could be expected in PROGINS female carriers (Giacomazzi et al., 2012).

Accordingly, the impairment of the progesterone immunosuppressive effects might lead to increased susceptibility for autoimmune diseases and exacerbations during pregnancy. Considering the important ethnic differences in polymorphism distribution we investigated the PROGINS Alu insertion in a group of healthy Bulgarian women. In the present study the PROGINS allele distribution was similar to those described in Caucasian populations from the United States, Australia and Brazil (Near et al., 2011; Giacomazzi et al., 2012).

Emerging evidence indicates that progesterone could play an important role in the immune system regulation outside of the context of pregnancy. The impaired hormone action could enhance susceptibility to development of infectious or inflammatory diseases (Tait et

al., 2008). Nevertheless, progesterone receptor polymorphisms were extensively studied only in patients with pregnancy complications or female reproductive disorders, but not in women with autoimmune diseases. Experimental studies described an impaired estrogen priming of progesterone receptors in uterus and perhaps thymus of lupus prone mice (Dhaher et al., 2000). However, the prevalence of PROGINS Alu insertion alleles did not differ between the patients with lupus and healthy women, although the homozygous Alu insertion genotype was very rare in SLE patients. The polymorphic allele was not significantly related to any ACR criterion. Probably, the PROGINS polymorphism is not associated with a specific clinical phenotype or specific manifestations of the disease in SLE patients. To the best of our knowledge this is the first study focused on the role of the progesterone receptor polymorphism in patients with lupus. However, no definitive conclusions could be drawn considering the low prevalence of homozygous polymorphic genotypes in the investigated groups. Further studies in other ethnic groups are needed to establish the precise influence of the PROGINS polymorphism on the SLE susceptibility as well as to clarify the genetic susceptibility to autoimmune disorders and the precise influence of the steroid hormones and their receptor polymorphisms.

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## RELATION BETWEEN BURNOUT SYNDROME, PERSONALITY TRAITS, AND MALADAPTIVE COPING AMONG PRISON STAFF

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## ВРЪЗКА МЕЖДУ БЪРНАУТ СИНДРОМ, ЛИЧНОСТОВИ ЧЕРТИ И МАЛАДАПТИВНИ КОПИНГ СТРАТЕГИИ СРЕД СЛУЖИТЕЛИ В ЗАТВОРИ

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### РЕЗЮМЕ

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#### РЕЗЮМЕ

Местата за лишаване от свобода са предизвикателни и опасни за работа. Извършеният литературен преглед посочва високо ниво на бърнаут синдром сред затворническия персонал, водещ до редица отрицателни последици.

#### ЦЕЛ

Целта на това изследване е да се проучи дали личностовите характеристики и маладаптивни

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### ABSTRACT

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#### ABSTRACT

Correctional environments are challenging and dangerous places of employment. The made literature review identifies high level of burnout among prison staff, leading to negative outcomes.

#### AIM

The purpose of this study is to examine whether personal characteristics and maladaptive coping is related to burnout among prison staff.

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стратегии за справяне са свързани с бърнаут синдрома сред затворническия персонал.

## МАТЕРИАЛ И МЕТОДИ

Данните са събрани от 114 мъже и 87 жени, работещи в два български затвора, използвайки въпросник, попълнен анонимно. Четири основни конструкции – демографски и личностови характеристики, оценка на бърнаут по метода на Бойко, и някои отрицателни стратегии за справяне – бяха включени в използвания въпросник. Всички анализи бяха проведени с помощта на SPSS за Windows, v.17.0.

## РЕЗУЛТАТИ

Честотата на бърнаут синдрома е 73.13% (n=147) сред участниците в проучването. Съгласно резултатите от t-теста на Стюdent съществува статистически значима връзка между употребата на алкохол и медикаменти и синдром на изпепеляване ( $p < 0.05$ ). Интровертните служители в затворите показват по-високи напрежение, резистенция, изтощение и бърнаут, отколкото екстривертните членове на персонала. Намерихме сигнификантна корелация между трите компонента на бърнаут и дименсията интроверсия ( $p < 0.01$ ).

## ЗАКЛЮЧЕНИЕ

Личностната черта интроверсия е от значение при прогнозиране нивото на бърнаут сред надзирателите. Бърнаут синдромът и неговите три измерения сигнификантно корелират с консумацията на алкохол и употребата на медикаменти.

**Ключови думи:** бърнаут синдром, служители в затвори, екстраверсия-интроверсия, копинг стратегии

## МАТЕРИАЛS AND METHODS

Data was collected from 114 men and 87 women working in two Bulgarian prisons using questionnaire completed anonymously. Four major constructs – demographic and personality characteristics, burnout assessment using Boiko's method, and some negative coping skills – were included in a used questionnaire. All analyses were conducted using SPSS for Windows, v. 17.0.

## RESULTS

The prevalence of burnout syndrome is found to be 73.13% (n=147) among the study participants. According to the outcomes of the Student's t-test, there is statistically significant association between the alcohol and substance use and burnout syndrome ( $p < 0.05$ ). The introverted prison officers indicate higher strain, resistance, exhaustion, and burnout than the extroverted members of staff. We found a significant correlation between all three components of burnout and introversion ( $p < 0.01$ ).

## CONCLUSION

The personality trait introversion is important in predicting level of burnout among warders. Burnout syndrome and its three dimensions are significantly related to alcohol consumption and substance use.

**Key words:** burnout syndrome, prison staff, extraversion-introversion, coping

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## INTRODUCTION

Burnout is a prolonged response to chronic emotional and interpersonal stressors on the job [14]. This syndrome has mostly been studied in human service professions. More recent studies had suggested that burnout could be found in other occupations, e.g. physicians [17],

teachers [4], police [14] and prison officers [8]. There has been little research on correctional staff burnout [13]. Armstrong and Griffin [2] regard prisons as unique working environments as very few other institutions are charged with the primary duty of supervising and securing a population that can be unwilling and potentially

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violent. Research has found that the perceived dangerousness of the job, as a result of threats and inmate violence is a significant cause of burnout for many correctional officers. Burnout may have many negative consequences for prison staff such as health problems, excessive alcohol intake, increased cigarette smoking, substance use and abuse [12]. Personality traits are also related to burnout. The role of temperament as antecedence for burnout process is supported in many studies [5, 10, 15].

### AIM

The purpose of this study is to examine whether personal characteristics and maladaptive coping is related to burnout among prison staff.

### MATERIALS AND METHODS

A cross-sectional study was carried out with 201 correctional officers working in the Regional Prison of Pazardzhik and the Regional Prison of Sliven during June-December 2012. The only qualification in the sample selection was that the employee has direct contact with inmates. The respondents comprised 56.72% males and 43.28% females, and ranged in age from 23 to 62 years, the mean age was 41.32, with a standard error of 0.54. Tenure ranged from 1 to 33 years, the mean tenure was 11.71 years, with a standard error of 0.50. About 38.31% of the participants indicated the highest education level, and most of them (72.64%) were married. Police officers were 70.15%, inspectors – 29.85%. The all available staff at prisons was asked to complete the survey anonymously and on a voluntary basis. Four major constructs – demographic and personality characteristics, burnout assessment, and some negative coping skills – were included in a used questionnaire. Six demographic characteristics were selected – gender, age, education, marital status, job position, and tenure. A Bulgarian version of Boiko's method (84 items), translated and adapted, was used to measure burnout in the sample. The presence and level of burnout

syndrome among correctional officers was assessing using this method [18] for diagnostics of the severity of symptoms and the phases of formation and completion of the occupational burnout process. Eysenck Personality Questionnaire (EPQ) is a questionnaire to assess the personality traits of a person [7]. The questionnaire contains 86 items and answers are given on a Yes-No scale. Eysenck initially conceptualizes personality as two, biologically-based independent dimensions of temperament measured on a continuum: Extraversion-Introversion and Neuroticism-Stability. Further research demonstrates the need for a third category of temperament: Psychoticism-Socialization. The destructive coping – smoking, alcohol consumption, and substance use and abuse were assessed with the questionnaire with only two possible answers (yes/no) without asking participants the name of the medication taken.

**Statistical analyses:** All analyses were conducted using SPSS for Windows, v. 17.0. Descriptive statistics, Student's t-test and Pearson correlation of all study variables were processed. Statistical significance was defined as p-value < 0.05 (two-tailed).

### RESULTS

The prevalence of burnout syndrome is found to be 73.13% (n=147) among the study participants. Next, we measured the association between a high level of job burnout and negative coping skills among correctional officers. According to the outcomes of the Student's t-test, there is statistically significant association between the alcohol and substance use and burnout syndrome (Table 1).

Results show that the levels of burnout and its subscales are higher among prison staff used alcohol excessively. All three dimensions of burnout are statistically significant associated with psychotropic substance use among respondents.

Table 2 presents the results of burnout components means concerning the personality trait extraversion-introversion. As can be seen

the introverted correctional officers indicate higher strain, resistance, exhaustion, and burn-out than the extroverted members of staff.

Based on the results reported in Table 2 we used a Pearson correlation between burn-out and its subscales and personality trait introversion. We found a significant correlation between all three components of burnout and introversion (Table 3).

## DISCUSSION

Prison work places officers in situations where reaction, speed, coordination and the capacity to make rapid decisions and accurate judgments under pressure is critical, and inefficient mental and emotional responses to stress can significantly impair these abilities [14]. One possible outcome of these prolonged and chronic stress-

**Table 1.** Relation between maladaptive coping and burnout and its three dimensions

Burnout and its subscales Maladaptive coping	Strain Mean ± SE	Resistance Mean ± SE	Exhaustion Mean ± SE	Burnout Mean ± SE
<b>Smoking</b>	30.98±2.16	42.79±1.70	32.79±1.89	106.56±5.19
<input type="checkbox"/> No	32.38±2.43	46.69±2.08	33.28±2.08	112.35±5.92
<input type="checkbox"/> Yes				
<b>Alcohol use</b>	29.99±1.62**	43.31±1.37*	31.86±1.39**	105.16±3.93**
<input type="checkbox"/> No	44.73±5.85**	54.27±4.21*	42.36±5.61**	141.36±14.33**
<input type="checkbox"/> Yes				
<b>Substance use</b>	29.89±1.51***	43.31±1.29**	31.10±1.26***	104.30±3.61***
No	73.00±9.94***	73.63±5.27**	79.00±6.21***	225.63±17.02***
Yes				

\* p-value is < 0.05.

\*\* p-value is < 0.01.

\*\*\* p-value is < 0.001.

**Table 2.** Relation between personality characteristics and burnout and its components

Burnout & subscales Personality trait	Strain Mean ± SE	Resistance Mean ± SE	Exhaustion Mean ± SE	Burnout Mean ± SE
Extraversion	25.36±2.28***	39.19±1.88***	27.72±2.02***	92.27±5.49***
Introversion	58.29±5.83***	64.82±5.14***	56.53±6.31***	179.65±15.22***

\*\*\* p-value is < 0.001.

**Table 3.** Correlations between burnout and its subscales and introversion

Pearson's rho	Introversion	Strain	Resistance	Exhaustion	Burnout
<b>Introversion</b>	1	0.215**	0.268***	0.225**	0.260***
Correlation Coefficient		0.002	0.000	0.001	0.000
Sig. (2-tailed)					
<b>Strain</b>		1	0.670***	0.781***	0.920***
Correlation Coefficient			0.000	0.000	0.000
Sig. (2-tailed)					
<b>Resistance</b>			1	0.686***	0.862***
Correlation Coefficient				0.000	0.000
Sig. (2-tailed)					
<b>Exhaustion</b>				1	0.914***
Correlation Coefficient					0.000
Sig. (2-tailed)					
<b>Burnout</b>					1
Correlation Coefficient					
Sig. (2-tailed)					

\*\* p-value is < 0.01.

\*\*\* p-value is < 0.001.

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ors at the work place is burnout. We have found a very high level of burnout in our sample. A problem that often results from burnout is substance and alcohol abuse or other behaviors that can become self-destructive. These behaviors can be described as coping mechanisms to relieve the emotional pain of burnout that ultimately can pose major problems for anyone involved. Prison officers that are emotionally exhausted are often left feeling incompetent, lack energy, and have fewer alternatives to choose from when problem solving. One negative way of solving problems is psychotropic medication abuse with alcohol. Many studies have reported that a high level of exposure to job strain increases the risk of consuming psychotropic substances [3, 16]. Over the past 20 years, the prevalence of psychotropic drug use among workers has been reported to be between 3.9% and 19.5% [11]. In the current study the substance use among correctional officers is 3.98%. Until this day, little is known about the prevalence of psychotropic drug use among correctional officers [11]. A correctional facility is a work environment where a high level of exposure to psychosocial risk factors is often present and the warders face difficult conditions in their daily work. Some researchers [6] assert that police officers often self-medicate with alcohol to forget the things they have seen. For people whose primary reason for drinking is to reduce or escape from distress, drinking is more likely to occur when they experience stress.

A discussion of the coping process is incomplete without examining the personal factors that influence the choice of coping strategy, and the relationship between personality variables and burnout. Most frequently reported predictors of burnout among prison staff are personality characteristics [1]. In our study the application of the Eysenck Personality Inventory has shown that introversion is a significant correlation with burnout and all three subscales. Our results agree with the findings of similar studies in the field [9]. Personality determines the way the person interprets events and conceives

the interaction between self and the environment. Introverts are chronically over-aroused and jittery and are therefore in need of peace and quiet to bring them up to an optimal level of performance. Introverts have a preference for internalising own energy and do not speak their minds as extraverts. Not ventilating own experiences of stressors, increases the risk of exhaustion. It can thus be argued that introverted correctional officers in our sample are more likely to suffer from exhaustion. Correctional officers high in introversion become more vulnerable to burnout. We have indicated the possibility that personality plays an important role in the development of burnout.

## CONCLUSION

It was found high level of burnout among correctional staff. The personality trait introversion is important in predicting level of burnout among warders. Generally, correctional officers do not have effective coping skills. Burnout syndrome and its three dimensions are significantly related to alcohol consumption and substance use. Future studies need to assess and explore the effectiveness of burnout reduction strategies.

## ACKNOWLEDGEMENTS

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## JOB SATISFACTION AMONG EMPLOYEES IN MEDICAL UNIVERSITY

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## УДОВЛЕТВОРЕНОСТ ОТ ТРУДА СРЕД ПРЕПОДАВАТЕЛИ В МЕДИЦИНСКИ УНИВЕРСИТЕТ

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### РЕЗЮМЕ

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Удовлетвореността от труда изразява субективната преценка за трудовата дейност. Тя се влияе най-вече от икономически фактори – размер на заплащане, стимули, перспективи за разтеж и др. Тези условия са общовалидни и действат в системата на здравеопазването и медицинското образование. С оглед на субект-субектната същност на медицинската професия, удовлетвореността от практикуването ѝ се влияе от едно специфично условие – културата на пациента. За удовлетвореността от труда при групата от високо квалифицирани специалисти, работещи в университетските болници и преподаващи в медицинските университети, към проблема култура на пациента, се наслагва и този за интеркултурността на средата в медицински университет. В предлаганата статия се публикуват данни, показващи зависимостта между изграждането на общата преценка за удовлетвореност от труда сред работещи в УМБАЛ и в МУ, в контекста интеркултурност.

Ключови думи: удовлетвореност, медицинско образование, здравеопазване

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### ABSTRACT

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Job satisfaction expresses the subjective evaluation for work activity. It is influenced mainly by economic factors- amount of payment, stimuli, perspectives for development etc. These conditions are universal and are at work in the healthcare system and medical education. With a view to the subject-subject essence of the medical profession, satisfaction from practicing it is influenced by a specific condition- the culture of the patient. On job satisfaction in the group of highly-qualified specialists working in the university hospitals and teaching in the medical universities, in addition to the problem of patient culture, the problem of interculturality in the environment of the medical university is added. In the present article are published data revealing the dependence between developing a general evaluation of job satisfaction among employees in UMHAT (University Multiprofile Hospital for Active Treatment) and MU in the intercultural context.

**Key words:** satisfaction, medical education, healthcare



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## INTRODUCTION

The concept 'satisfaction' creates a notion of the fact to what extent an employee is content with the satisfaction of his own needs and achieves his desires, due to higher motivation for work, efficiency and positive morality'(8). It is connected with positive experiences of a personality, group or society. The interest in studying the psychological aspect of satisfaction appears in the middle of the XX<sup>th</sup> century when special attention is paid to satisfaction from the work done. The opinion is expressed that it is a collective attitude to separate aspects of the practical activity- content, conditions, and situation. It is presented as 'cognitive-affective process' (3:5; 4).

Job satisfaction is the most studied attitude. It is accepted that it determines people's behavior in their practical activities. Only the person satisfied by his work is able to put more efforts, as well as to reveal strife for affirmation at the workplace. The presence of job satisfaction correlates with the presence of motivation for long-term commitment with the organization's (institution's) activities, with partaking in its organizational values etc.

The legislation defining the framework for safety and hygiene standards at work, work process management, work standardization, technology of production etc. define the criteria according to which an objective evaluation of working conditions is established. But job satisfaction evaluation is not objective, it is a value determined by each person. It expresses the subjective opinion on the nature of relationships generated in the process of the practical activities, from the conditions in which it is implemented, from its organization etc. In this sense satisfaction is an indicator for the quality of life. It may be suggestive of the individual adaptation to work as well as to the efficiency and contribution of the individual to the joint work activity.

Job satisfaction is a complex value. Its positive or negative indication is formed under the influence of a peculiar 'mix' of conditions exerting psychological impact. The intertwining of

multiple aspects in the study of the phenomenon 'job satisfaction' suggests the presentation of the problems in different contexts – personal, social, economic, etc.

In the psychological literature the statement that satisfaction is influenced by three basic components: the abilities possessed and work skills, nature of relationships generated in the work process and the received payment and stimuli, is quite common.

The complex of mechanisms regulating the individual work activity which is important for defining job satisfaction, may be expressed by the position of the individually oriented attitude and by the term 'fully functioning person' introduced by Carl Rogers (2: 178–181). This personality accepts as a challenge the change in the social environment and its conditions.

Job satisfaction is a function of the personal outlooks on life. On the one hand it combines the subjective evaluation of the nature of the changes in the work environment, on the other- perceives emotionally the relationships involved in the work process. Therefore the personality refracts the overall practical activity through his/her individual peculiarities- mentality, temperament, value model.

Quite often in scientific literature the economic dependence of job satisfaction is emphasized, of its dependence on the quantitative expression of the remuneration as an instrument for achieving satisfaction. This conception finds expression in Frederick Taylor's principle of the so-called 'economic man' (9). According to him the minimal level of work payment is bound with the implementation of basic tasks. Stimulation is done by a system of additional remuneration. This system operates through the implementation of tasks which level is above the minimal. If in the material production the dependence efficiency- salary is a condition for higher intensity of work, then the problem acquires a different aspect and is considered in another context when satisfaction from non-material production is evaluated- healthcare education, social activities etc. With it the sub-

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jective evaluation for adequacy between payment and efforts exerted, skills, competences etc., the 'material' with which work is done is of crucial importance.

The essence of work in healthcare and education is subject-subject. It includes empathic listening, assistance, working overtime including during rest days etc., i.e. the prerequisites for more active interpersonal relationships are present and thence greater emotional load. In practice, the complex evaluation of satisfaction in the non-material production contains elements influencing the individual on a psychological level, which concerns his/her quality of life.

The constant 'press' on work time in healthcare- observing schedules, working on duty, performing planned activities etc., combined with the emotional aspect of the interpersonal relationships with diseased, their relatives, colleagues are at the root of psychic stress connected with labor in the work place. The emotional load leads to psychological tension, arouses mental fatigue and physical exhaustion. The influence of emotions in the work process in the healthcare system is confirmed by a sociological study conducted by Confederation of Independent Trade Unions (CITU) in Bulgaria (2009). According to it 20% of participants experience negative emotions during work activities and for 30% work bears positive experiences i.e. half of the participants, in one way or another, are subject to emotional impact which has reflection on them. A total of  $\frac{3}{4}$  of the participants in the study fall in the category 'reporting on satisfaction from work' (5: 10).

The organization of the work process is one of the conditions having negative influence on job satisfaction in healthcare. The presence of negativism concerning work organization in the hospital environment combined with lack of satisfaction from work organization in the specialized higher education medical school are prerequisites for emotional load in greater degree in the group of doctors who apart from the therapeutic activities, have teaching duties. Their work remuneration, the distribution of their time among medical, teaching and scientific work, doing consultancy, administrative duties etc. are characteristic for the work done

by that group of highly qualified specialists. They not only form the image of the academic society in medical universities but also guarantee the quality of student training and the level of research of the university.

A peculiarity of the work of the doctor teaching at MU is a combination of requirements expected from his work as a doctor and educator. On the one hand, his work as a physician is influenced by the legislative and moral requirements expected from the employees in healthcare. It is defined by the doctor-patient relationship. On the other hand, it is influenced by the post 'lecturer' and is charged with engagements in the execution of his teaching and academic work load. It is affected by the lecturer-student relationships. Physician's satisfaction from the work he/she does is influenced by the expectations of his patients for „higher quality control“ (48.2%), „better doctor-patient relationship“ (42.8%), „quicker medical service“ (39.9%) etc., as well as by his own expectations as part of the healthcare system „better payment“ (60.2%), „better qualification of healthcare managers“ (53.5%), „more precise organization of physician's labor“ (53.1%) etc. (1: 19-26). Satisfaction of the physician as a teacher is influenced by the expectations for a more efficient education as well as by the student's motivation to acquire quality training which will make them competitive specialists on the international labor market etc.

The presence of the higher education medical schools on the international market of higher education, the strife for higher rating, the educational standards in the field of the medical education etc. are external factors which exert influence on medical universities and therefore on the teacher. The doctor-teacher has to be mentally prepared for the work in two working environments and the fulfillment of two professional roles. Thus job satisfaction of the doctor teaching at MU is a sum of the satisfaction of the different activities done in two different working environments – hospital and educational.

The participation in a work process in which clinical and teaching practice are combined

within the framework of UMHAT and MU, suggests a necessity of keeping up-to-date and developing, of building up skills and competences in the free time. According to the satisfaction indicator 'daily duration of the workday', despite the readings for the level of satisfaction, 'a long duration of the working time, of the working time on weekends and holidays, ... low average amount of the actual use of the paid annual leave' is present (6: 11) – i.e. the achieving job satisfaction especially of one having complex nature in one degree or another reflects on the health of the teacher.

For the physician combining medical with teaching practice, work with students may be perceived as a professional challenge. The grounds for this statement lay in the conclusions of the Annual Report of the Society of specialists on human resource management in Canada (2011) (7: 9–10). In it are presented results from studies referring to the satisfaction of employees from different fields including the field of services, social and healthcare activities. The results show that the professional challenges, insurance of a job offering the use of the skills and interests of the worker, the creation of positive relationships in the work team are some of the conditions creating a positive evaluation of satisfaction. The work on improving working conditions with a view to increase in satisfaction is connected with career development, training and qualifications, with trust in the management and effective communication with it.

The generalized conclusion on job satisfaction of the doctor – teacher is defined not only by the listed conditions but is also influenced by the peculiarities of each separate work environment. For example, in the last years in the medical universities in Bulgaria the peculiarity interculturality is present- as a consequence of the education of a considerable number of foreign students in Bulgarian medical universities.

The change in the culture of the environment changes the language communication in it and forces conformity with the cultural dif-

ference. In this way nonspecific for the medical profession culture factors influence satisfaction of the doctor- teacher.

The dependence of job satisfaction of doctors teaching at MU on the results from the work in the hospital and academic environment assumes that the change in the working conditions of one of them would reflect on the overall evaluation of satisfaction.

Interculturality is a contemporary problem in the medical education and to what extent it reflects on the estimation of job satisfaction of the doctor- teacher is among the questions studied in 2012 at MU Plovdiv. It encompasses 115 lecturers from all medical universities in Bulgaria. The participants are divided in four groups. Two of them are comprised only of employees working in an academic environment- at MU Plovdiv and MU in the country. The third group includes practicing doctors who are also teachers, who among work with students in the auditorium, practice therapeutic work at the University hospitals. The fourth is comprised of doctors who work in clinics of a University hospital and do not teach.

The results from the analysis reveal the presence of satisfaction among 51.3% of the studied, which confirms the findings of the cited study of the Institute for social and trade-union studies at CITU (5: 8–13) (fig. 1).



**Fig. 1.** Job satisfaction in the educational environment in medicine.

The highest satisfaction from the working conditions is registered among those who work in only one working environment. The relative share of the teachers satisfied by the conditions in which the educational process takes place is 53.12%. Close to it is satisfaction in the group of doctors who practice only the medical profession (52.39%). In contrast to the two groups practicing one profession on one working place, the highest relative share in the category 'lack of satisfaction (30.00%)' is recorded the doctors who are also teachers at MU. (table 1).

Apart from the recording of satisfaction, of significance is the degree at which it is displayed. According to satisfaction under the criterion "effectiveness in working with a group of mixed ethnicity" the greatest number of participants have marked "average degree". Among the teachers working only at MU, the average degree of satisfaction is 46.90%, and among these who combine the clinical with teaching work it is 40.00%.

The comparison of the results from all groups reveals a statistically significant difference ( $\chi^2 = 24.566$ ,  $df = 6$ ,  $P = 0.000$ ). It may be stated that the estimate for satisfaction from teaching at MU is influenced by the factor interculturality in the educational environment in medicine. In a greater degree it reflects on the teachers performing specialized training in the University hospital clinics, than on those teaching theoretical disciplines at MU.

Labour activity in a complex work environment (UMHAT and MU) in the context of interculturality is the cause for lack of satisfaction among 53.30% of doctors. The Data analysis for the variable 'not satisfied' reveals a statistically significant difference ( $\chi^2 = 16.34$ ,  $df = 2$ ,  $p < 0.000$ ). It may be stated that satisfaction from teaching is influenced by the factor 'efficiency of teaching in the respective subject' in the context of interculturality. It depends on conditions like 'level of foreign language communicative competence (teacher's and student's), peculiarities of the working environment, work in one or more working environments.

The summary of the results reveals that satisfaction of the doctor teacher depends on the interculturality as an educational peculiarity in a specialized medical university which is not typical for these kinds of higher education schools. Satisfaction from teaching depends on the fact to what extent the work performed is resultant as well as whether it is done only in the university auditorium or in the combined clinical environment of University Hospital.

The conclusions from the study in MU- Plovdiv may serve as a basis of comparison with the level of satisfaction of the teacher from each specialized university- economic, technical, agrarian etc. Where the specialized training of the students is done in a combined educational environment and where the effectiveness from education is influenced by interculturality as a peculiarity of the environment.

**Table 1.** Satisfaction from the working place according to the subject of activity  
Удовлетвореност от работната среда според предмета на дейност

	Doctors with teaching load (n = 30)		Teachers at MU (n = 64)		Doctors (UMHAT and GP) (n = 21)		Total (n = 115).	
	бр.	%	бр.	%	бр.	%	бр.	%
satisfaction	14	46.67	34	<b>53.12</b>	11	<b>52.39</b>	59	<b>51.30</b>
lack of satisfaction	9	<b>30.00</b>	11	17.19	4	19.04	24	20.87
no answer	7	23.33	19	29.69	6	28.57	32	27.83
total	30	100.0	64	100.0	21	100.0	115	100.0

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## COGNITIVE IMPAIRMENTS AND QUALITY OF LIFE IN PATIENTS WITH SUPRATENTORIAL BRAIN TUMORS: A COMPARATIVE PROSPECTIVE STUDY OF THEIR DYNAMICS AND CORRELATIONS

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## КОГНИТИВНИ НАРУШЕНИЯ И КАЧЕСТВО НА ЖИВОТ ПРИ ПАЦИЕНТИ СЪС СУПРАТЕНТОРИАЛНИ МОЗЪЧНИ ТУМОРИ: СРАВНИТЕЛНО, ПРОСПЕКТИВНО ПРОУЧВАНЕ НА ТЯХНАТА ДИНАМИКА И ВЗАИМНА ЗАВИСИМОСТ

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### РЕЗЮМЕ

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**ЦЕЛ:** Да се проследи динамиката на когнитивните нарушения и качеството на живот при пациенти, страдащи от супратенториални мозъчни тумори и да се установи взаимовръзката между тези показатели.

**МАТЕРИАЛ И МЕТОДИ:** Извършено е сравнително, проспективно проучване за период от

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### ABSTRACT

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**AIM:** The objective of the present study is to follow up the dynamics of cognitive impairments and quality of life (QOL) in patients suffering from supratentorial brain tumors and establish the relationships between these variables.

**MATERIAL AND METHODS:** A comparative prospective three point neuropsychological assessment

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7 месеца чрез трикратно прилагане на набор невропсихологични тестове върху група от 38 пациента, оперирани по повод на супратенториални мозъчни тумори и върху контролна група от 41 пациента, оперирани по повод на дегенеративни заболявания на лумбалния дял на гръбначния стълб. В рамките само на тестовата група сме приложили и две скали, за да оценим функционалния статус и качеството на живот на пациентите, страдащи от мозъчни тумори.

**РЕЗУЛТАТИ:** Пациентите, страдащи от мозъчни тумори са показали по-лоши резултати при всички невропсихологични тестове в сравнение с пациентите от контролната група. Пациентите с мозъчни тумори са показали значимо и трайно подобрене по отношение на някои от изследваните когнитивни показатели и качеството им на живот в следоперативния период. Корелациите между когнитивните показатели и тези за оценка на качеството на живот се засилват в рамките на периода на проследяване.

**ЗАКЛЮЧЕНИЕ:** Неврокогнитивните функции и показателите за оценка на качеството на живот са взаимно свързани. Следователно, влошаването на когнитивните функции при пациентите със супратенториални мозъчни тумори трябва да се избягва, за да се запази по-добро качество на живот при тези пациенти. Комбинацията от прилагането на невропсихологични тестове и скали за оценка на качеството на живот може да се изпозва като адекватно средство за оценка на изхода от проведеното лечение.

**Ключови думи:** мозъчен тумор, лечение, когнитивен дефицит, качество на живот

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## INTRODUCTION

The impairment of neurocognitive functioning resulting in behavioral, emotional, and intellectual difficulties, occurs in nearly all patients with brain tumors and eventually compromises their independence [22]. This impairment is related to a combination of various factors, including the tumor itself and the associated treatment with surgery, radiotherapy, chemotherapy, the presence of psychological distress

for a period of 7 months was performed on 38 patients who were operated for supratentorial brain tumors and 41 control patients who underwent surgery for lumbar degenerative diseases. In addition, we applied two commonly used scales to evaluate functional status and QOL of the patients from the brain tumor group only.

**RESULTS:** The brain tumor patients scored significantly worse on all neuropsychological tests compared to the patients from the control group. The brain tumor group experienced significant and permanent overall improvement in some cognitive domains and quality of life in the postoperative period. The correlations between cognitive impairments and quality of life have become stronger during the longitudinal follow-up.

**CONCLUSION:** Neurocognitive functions and QOL are correlated. Therefore, neurocognitive decline in brain tumor patients should be avoided in order to preserve better QOL. The combination of neuropsychological and QOL assessment may be used as a valuable outcome measure in brain tumor clinical trials.

**Key words:** Brain tumor, Treatment, Cognitive deficit, Quality of life

and comorbidity [3,15,24,28]. Not surprisingly, neurocognitive function assessments have been incorporated as major components of patient assessments, along with common and widely used questionnaires to assess health-related QOL [14]. Two of the most commonly used tools to evaluate functional status and QOL in neuro-oncology are the Karnofsky Performance Status Scale (KPS) and the European Organization for Research and Treatment of Cancer (EORTC)

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Core Quality of Life Questionnaire version 3.0 (QLQ-C30) [5,6]. Indeed, neurocognitive function has been demonstrated to be a valid predictor of long-term QOL [10,11].

The aim of the present study is to prospectively investigate the type of cognitive impairments and the dynamics of quality of life (QOL) in patients suffering from supratentorial brain tumors and establish the relationships between both outcome measures.

## **MATERIAL AND METHODS**

### **SUBJECTS**

The study was conducted at the Department of Neurosurgery of the Medical University of Plovdiv between 2010 and 2012. The supratentorial brain tumors were diagnosed by means of neuroimaging examinations – CT and/or MRI with contrast enhancement. All cases were discussed by a neurosurgeon, neurologist and psychiatrist to rule out comorbidity. Patients from the brain tumor and control groups were selected according to inclusion and exclusion criteria. Inclusion criteria were as follows: Bulgarian language speakers and nationality, age between 16 and 72 years, education of 7 and more years, signing an informed consent, absence of any history of neurological, mental and traumatic brain disease, previous neurosurgical brain interventions, decompensated chronic somatic diseases, alcohol abuse and drug addictions, clinically evident aphasia of any type and motor impairment of the dominant hand. Exclusion criteria were refusal to sign the informed consent, KPS<60, failure to meet the above-mentioned inclusion criteria. Thus, the present study included a total of 38 patients (16 males and 22 females) undergoing surgery for supratentorial brain tumors and 41 control patients (19 males and 22 females) admitted for surgery of lumbar degenerative diseases. Both groups did not differ significantly by age, sex and education and met the reliability criteria for group comparison. The brain tumor group had a mean age of  $55.08 \pm 1.67$  (SD 10.27, range:

17 to 72 years) and mean years of education of  $10.82 \pm 0.41$  (SD 2.51). The control group had a mean age of  $55.73 \pm 1.60$  (SD 10.27, range: 22 to 72 years) and mean years of education was  $10.80 \pm 0.38$  (SD 2.40). According to the WHO Classification of Tumors of the Central Nervous System [21], the study included 12 cases of Meningioma Gr. I and 3 cases of Meningioma Gr. II&III; 4 cases of low-grade gliomas (Gr. II); 13 cases of high-grade gliomas (Gr. III&IV); and 5 cases of metastatic brain tumors. One case of epidermoid tumor (cholesteatoma) was also included. 21 of the brain tumors were located in the right cerebral hemisphere, 14 – in the left cerebral hemisphere and 3 had bilateral localization. Eighteen patients with malignant tumors received additional postoperative radiotherapy and 8 patients – additional postoperative chemotherapy.

### **NEUROPSYCHOLOGICAL AND QOL ASSESSMENT**

Patients were tested by one trained specialist in a convenient environment without distractive factors. A battery of widely used and standardized tests were applied to evaluate different cognitive functions with special focus on memory, attention and executive functions (Table 1).

The neuropsychological assessment was carried out at three time points: baseline (prior to surgery), at the end of the 1st and the 7th postoperative month. The tests were administered in the following order: 1) The Mini-Mental State Examination (MMSE) is a scale for global cognitive evaluation with maximum score 30 [9]. Patients with MMSE<24 indicating the presence of dementia were not included. 2) The Stroop Test (ST) consists of three sets of stimuli administered for 45 seconds each: (a) color words printed in black ink; (b) color patches or colored X's; and (c) color words printed in incongruous colored ink (e.g., the word „RED“ printed in blue ink). The participant must read the color words on the first sheet, the colors on the second sheet, and the color of the ink (i.e., not the words) on the third



**Table 1.** Neuropsychological Test Battery for Cognitive Assessment

Neuropsychological Tests	Cognitive Domains
MMSE	Global cognitive functioning
Stroop Test	Selective attention, executive control
Trail-Making Test Parts A&B	Part A – Visual scanning, information processing speed and motor planning Part B – divided attention and shifting, executive functions
Go/No-go Test	Decision making, executive motor control
Verbal Fluency (semantic and phonemic)	Semantic Fluency – semantic memory Phonemic Fluency – executive functions
Digit Span Forward & Backward	Forward – short-term memory Backward – working memory
Digit-Symbol Test	Visual scanning, mental flexibility, sustained attention, psychomotor and information processing speed
Clock Drawing Test	Planning within executive functions and constructive abilities

sheet. In the latter task, the normal tendency to read the words, rather than the color of the ink in which the words are printed, elicits a significant slowing in reaction time called the „Stroop effect“ or the „interference effect“ [2,25]. We compared the results from the raw scores of the third part only. 3) Trail-Making Test parts A and B (TMT A and B). The subject must first draw lines to consecutively connect randomly scattered numbered circles on one work sheet (Part A) and then connect the same number of consecutively numbered and lettered circles on another work sheet by alternating between two sequences (Part B). The subject is urged to connect the circles „as fast as you can“ without lifting the pencil from the paper. The result is registered by the time needed to complete any of the parts in seconds and lesser time indicates better result. The maximum time allowed for each part is 300 seconds [19]. 4) Go/No-go Test (GNG) – in the first part, the subject is instructed to follow strictly the examiner’s taps with the index finger on a table (once for once; twice for twice). In the second part, the instructions are changed and every time the examiner taps twice, the subject should tap once on the table and if he taps once, the subject must not answer. 25 stimuli are administered for each part and the number of correctly performed actions is registered [19]. We compared

the results from the raw scores of the second part only. 5) Verbal fluency tasks are phonemic and semantic and are administered for 1 minute each. Semantic fluency task (SFT) requires participants to say as many words as possible within a certain category (e.g., animals). Phonemic fluency task (PFT) requires participants to say as many words as possible beginning with a specific letter, in our case the letter ‘M’. The maximum count of words with ‘M’ and animals is registered [2]. 6) Digit Span Test Forward and Backward (DSF and DSB). Both parts consist of seven pairs of random number sequences that the examiner reads aloud at the rate of one per second. In the DSF, the participant should remember and reproduce as many numbers as he can in exactly the same order. In the DSB, the participant is asked to reproduce the previously remembered series of digits in the reverse order. The highest number of correctly reproduced series of digits is registered [19]. 7) Digit-Symbol Test (DST) requires participants to fill in the corresponding symbol in an empty box below randomly sequencing digits from 1 to 9 in accordance with the sample „digit-symbol“ pairs given at the top of the page. The number of correctly coded digit-symbol pairs within 90 seconds is registered [19]. 8) Clock Drawing Test (CDT) – the participant is given a pencil and asked to draw the screen of a clock,

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to put the hours within the screen and to place the hands of the clock showing 10 past 11. The result is registered on a standard 10-point scale [26]. The total time for test battery administration was also recorded.

Besides the neuropsychological testing, functional status and QOL of the patients with brain tumors were also evaluated by means of the KPS and the EORTC QLQ-C30 version 3.0 [1,16]. The best-known instrument, KPS, has been widely used for many years to measure the physical functioning of patients. The EORTC QLQ-C30 (version 3.0) is a 30-item questionnaire composed of multi-item scales and single items that reflect the multidimensionality of the QOL construct. It combines five functional scales {physical (PF), role (RF), emotional (EF), cognitive (CF) and social functioning (SF)}, three symptom scales {fatigue (FA), pain (PA), and nausea/vomiting (NV)}, a global health and QOL scale, six single items assessing additional symptoms commonly reported by cancer patients {dyspnea (DY), appetite loss (AP), sleep disturbance (SL), constipation (CO) and diarrhea (DI)}, as well as the perceived financial impact (FI) of the disease and treatment.

### STATISTICAL ANALYSES

It is hypothesized that the neurocognitive functioning of brain tumor patients is significantly worse as compared to the control group and may impact the patient's QOL. The raw scores from the neuropsychological tests were used for comparisons. The raw scores from the QLQ-C30 (version 3.0) for each domain and single item were transformed to give a value between 0–100. For the five functional scales and the global health status/QOL scale, item responses were recorded so that a higher score represented a better level of functioning. For the symptom-oriented scales and items, a higher score corresponded to a severer level of symptoms [8]. The KPS scores range from 0 to 100 and high scores indicate a patient's better ability to perform normal activities of daily

living or his/her lesser degree of dependency on others for assistance. In order to establish the dynamics and relationship between these parameters we used descriptive, parametric, nonparametric, correlation and linear model analyses. All analyses were performed by the SPSS software. Scores were presented as mean ( $\pm$ SE). Kolmogorov-Smirnov Test was used to test for normality of distribution. Most of the scores were non-normally distributed and were, therefore, compared by nonparametric methods. The numerical comparisons between consecutive measurements (dependent groups) were assessed by Friedman within the whole group comparisons and by Wilcoxon test in pairwise comparisons. The pairwise comparisons between two independent groups were made by Mann-Whitney U test. A p-value  $< 0.05$  was considered to be statistically significant in all analyses. Spearman correlations were determined between neurocognitive test scores and KPS and QLQ-C30 measurements at baseline, 1st and 7th postoperative month. To test the hypothesis of factor influence of cognitive impairments on QOL, we used linear modeling. As dependent variables we used differences in mean scores of QOL scales between baseline and 7th month (KPS; global health/QOL and functional scales in QLQ-C30) and applied forward stepwise introduction of mean score of overall dynamics of cognitive tests as predictors. In order to increase predictive power and accuracy automatic actions were taken to trim outliers, replace missing values, change measurement level from continuous to ordinal and some categories were merged to maximize association with target variable. If a variable was transformed the original was excluded from the analysis and the transformed variable was included instead. Records were excluded in case of missing predictor or target, frequency weight missing or less than one after rounding or a regression weight missing, negative or zero. Models were considered acceptable if their accuracy was 50% or higher at p-value  $< 0.05$ .

**Table 2.** Comparative Assessment of Mean Test Scores between Brain Tumor and Control Groups

Cognitive Tests	Baseline			1 <sup>st</sup> month			7 <sup>th</sup> month						
	Brain tumor group (n=38)		P-value	Brain tumor group (n=38)		P-value	Brain tumor group (n=38)		P-value				
	Mean ±SE	SD	Mean ±SE	SD	Mean ±SE	SD	Mean ±SE	SD					
Time (min)	43,76±1,71	10,51	28,37±0,70	4,48	33,03±1,16	7,12	26,55±0,55	3,37	33,41±1,66	9,69	25,22±0,54	3,27	<0.001
MMSE	25,39±0,47	2,93	29,76±0,08	0,49	27,03±0,55	3,39	29,66±0,08	0,53	26,03±0,60	3,48	29,85±0,07	0,42	<0.001
ST	24,13±1,89	11,66	46,98±1,38	8,85	32,24±2,24	13,82	49,46±1,44	9,23	30,00±2,39	13,96	49,24±1,31	8,37	<0.001
TMT A	104,47±10,52	64,87	55,85±2,68	17,18	79,53±7,45	45,95	53,41±2,40	15,34	86,44±8,95	52,20	53,44±2,26	14,49	<0.001
TMT B	236,84±12,36	76,18	95,51±5,25	33,63	185,34±12,27	75,61	83,78±3,68	23,55	202,29±15,06	87,83	83,24±3,68	23,56	<0.001
GNG	22,21±5,38	33,18	24,68±0,10	0,61	24,66±0,13	0,81	24,80±0,07	0,46	24,12±0,32	1,87	24,90±0,05	0,30	=0.01
SFT	13,84±0,95	5,87	20,00±0,47	3,03	14,45±0,66	4,05	19,63±0,43	2,77	14,47±0,92	5,34	20,00±0,44	2,81	<0.001
PFT	5,21±0,53	3,29	12,10±0,36	2,32	6,32±0,48	2,94	12,20±0,27	1,75	6,53±0,57	3,33	12,54±0,28	1,82	<0.001
DSF	4,68±0,15	0,93	6,61±0,14	0,89	4,58±0,14	0,86	6,78±0,13	0,85	4,59±0,16	0,96	6,63±0,12	0,80	<0.001
DSB	3,32±0,11	0,66	5,56±0,18	1,16	3,45±0,14	0,86	5,80±0,12	0,78	3,26±0,13	0,75	6,02±0,11	0,72	<0.001
DST	21,61±1,82	11,22	51,20±1,46	9,35	27,37±2,41	14,85	51,68±1,38	8,87	27,41±2,55	14,88	52,46±1,39	8,89	<0.001
CDT	6,53±0,39	2,42	9,90±0,05	0,30	7,84±0,43	2,66	10,00±0,00	0,00	8,15±0,42	2,46	10,00±0,00	0,00	<0.001

**Legend:** Time (min) – total time for test battery administration; MMSE – Mini-Mental State Examination; ST – Stroop Test; TMT – Trail-Making Test; GNG – Go/No-go Test; SFT – Semantic Fluency Task; PFT – Phonemic Fluency Task; DSF – Digit Span Forward; DST – Digit Span Backward; DSB – Digit Span Backward; DST – Digit Span Backward; CDT – Clock Drawing Test

**Table 3.** Dynamics of the Results from the Cognitive Tests in the Brain Tumor and Control Groups

Cognitive tests	Brain tumor group (n=38)						Control group (n=41)					
	D (T2-T1)			D (T3-T1)			D (T2-T1)			D (T3-T1)		
	Mean±SD	%	P-value	Mean±SD	%	P-value	Mean±SD	%	P-value	Mean±SD	%	P-value
Time (min)	-10,74±7,19	-23,25	<0.001	-8,88±8,19	-20,23	<0.001	-2,03±3,09	-6,18	<0.001	-3,33±4,34	-10,19	<0.001
MMSE	1,63±3,06	7,0	<0.001	0,38±2,28	1,65	NS	-0,10±0,74	-0,30	NS	0,10±0,49	-0,35	NS
ST	8,11±10,00	54,75	<0.001	5,26±12,44	46,36	<0.05	2,49±4,39	5,78	<0.01	2,27±4,84	5,70	<0.01
TMT A	-24,95±50,07	16,19	<0.001	-12,15±52,48	4,54	<0.001	-2,44±6,63	-3,01	<0.05	-2,41±6,91	-2,54	NS
TMT B	-51,50±65,27	-18,18	<0.001	-27,12±64,30	-10,38	<0.05	-11,73±18,44	-9,59	<0.001	-12,27±22,83	-9,24	<0.001
GNG	-2,82±33,26	-13,11	<0.01	-3,85±35,24	-10,31	<0.05	0,12±1,75	0,55	NS	0,22±0,57	0,94	<0.05
SFT	0,61±4,74	22,07	NS	0,09±4,71	6,55	NS	-0,37±2,15	-1,08	NS	0,00±1,90	0,64	NS
PFT	1,11±2,86	29,74	<0.05	1,09±3,87	43,43	NS	0,10±1,69	2,70	NS	0,44±1,66	5,55	NS
DSF	-0,11±0,89	-0,18	NS	-0,12±0,84	-0,32	NS	0,17±0,77	3,50	NS	0,02±0,82	7,84	NS
DSB	0,13±0,93	6,49	NS	-0,03±0,83	-1,52	NS	0,24±,92	7,77	NS	0,46±0,90	12,08	<0.01
DST	5,76±8,34	33,20	<0.001	4,65±8,02	29,17	<0.01	0,49±4,83	1,57	NS	1,27±4,61	3,14	NS
CDT	1,32±2,01	29,41	<0.001	1,32±2,80	33,75	<0.05	0,10±0,30	1,08	<0.05	0,10±,30	1,08	<0.05

**Legend:** T1 – baseline assessment; T2 – assessment at 1<sup>st</sup> postoperative month; T3 – assessment at 7<sup>th</sup> postoperative month; Time (min) – total time for test battery administration; MMSE – Mini-Mental State Examination; ST – Stroop Test; TMT – Trail-Making Test; GNG – Go/No-go Test; SFT – Semantic Fluency Task; PFT – Phonemic Fluency Task; DSF – Digit Span Forward; DST – Digit Span Backward; DSB – Digit Span Backward; CDT – Clock Drawing Test;

## RESULTS

The average time needed for test battery administration within the brain tumor group was about 43 minutes preoperatively and about 33 minutes postoperatively, whereas the control subject needed on average 28 and 26 minutes, respectively. Descriptive statistics of neuropsychological tests' mean scores for both brain tumor and control groups are presented in Table 2.

The data suggests that the brain tumor patients scored significantly worse than the control patients on all tests at each assessment. Only the difference between the mean scores from the second assessment (1<sup>st</sup> month) with the GNG test was not statistically significant but it was significant at baseline and 7<sup>th</sup> postoperative month.

The longitudinal follow-up of the dynamics of the mean scores from the cognitive tests in the brain tumor group indicates that significant and permanent postoperative improvement for the entire period was observed in the ST, TMT A and B, GNG, DST and CDT (Table 3).

Despite these improvements, the mean scores of the brain tumor patients remained significantly worse than that of the control patients, as seen in Table 2. The MMSE and Phonemic fluency scores improved significantly at the 1<sup>st</sup> month after surgery but this effect was only transient and there was no significant difference at the end of the period compared to baseline results. Despite being insignificant, the overall improvement of the mean PFT score was 43%. The SFT, DSF and DSB did not demonstrate any significant dynamics during the 7-month period, i.e., the semantic, short-term and working memory evaluated by these tests remained permanently impaired in the brain tumor group. Significant improvements on some neuropsychological tests were also observed in the control group for the entire follow-up period. Nevertheless, the percentage of improvement was considerably lower compared to those registered in the brain tumor group as seen in Table 3. We considered that this phenomenon was due to the „practice effect“ as a result of the

threefold neuropsychological assessment of the healthy control subjects.

In terms of QOL and functional status, the brain tumor patients experienced significant and permanent overall improvement as measured by the following scales: KPS, global health and QOL, EF and in some symptoms such as fatigue, nausea/vomiting, appetite loss and constipation. According to the patients' self-assessment, the improvement in RF and CF was only temporary and did not differ significantly at the end of the period compared to baseline (Table 4).

In the current study, we have established highly significant statistical correlations between the mean scores of the neuropsychological tests and the mean scores of the KPS and QLQ-C30 scales. These correlations have become stronger and increased in number with each consecutive assessment and were most prominent at the end of the study (Table 5).

The automatic linear modeling demonstrated with 52% accuracy that  $\Delta_{(T3-T1)}\text{MMSE}$  and  $\Delta_{(T3-T1)}\text{CDT}$  were statistically significant predictors of subsequent change in the  $\Delta_{(T3-T1)}\text{KPS}$ . The  $\Delta_{(T3-T1)}\text{MMSE}$  was stronger predictor ( $\beta=2.82;p=0.000$ ) than the  $\Delta_{(T3-T1)}\text{CDT}$  ( $\beta=0.92;p=0.05$ ).

## DISCUSSION

The present study demonstrates that the cognitive domains which are significantly impaired in brain tumor patients in comparison with the control group are as follows: divided, sustained and selective attention; semantic, short-term and working memory; psychomotor and information processing speed; executive functions including planning, decision making, mental flexibility and executive control. These findings are in accordance with other publications [7,18,28,32,35]. The follow-up of the dynamics of cognitive impairments within the 7-month period points out that the cognitive domains which may be considerably ameliorated over time as a result of the treatment are: divided, sustained and selective attention, psychomotor and information processing speed and

**Table 4.**

Mean Scores and Dynamics of the Results from the KPS and QLQ-C30 in the Brain Tumor Group

Scales	Baseline		1 <sup>st</sup> month		D (T <sub>2</sub> -T <sub>1</sub> )		7 <sup>th</sup> month		D (T <sub>3</sub> -T <sub>1</sub> )	
	Mean ±SE	SD	Mean±SD	SD	Mean ±SE	P-value	Mean ±SE	SD	Mean±SD	P-value
KPS	70,79±1,27	7,84	84,47±1,72	10,58	13,68±8,83	<0.001	80,59±2,23	13,01	8,82±10,08	<0.001
<b>QLQ-C30 version 3.0</b>										
Global Health/QOL	37,50±3,34	20,57	64,47±2,98	18,35	26,97±19,12	<0.001	55,39±3,53	20,61	17,65±21,49	<0.001
<b>Functional Scales</b>										
PF	73,16±3,95	24,33	79,30±3,10	19,10	6,14±23,11	NS	71,76±3,80	22,14	-1,76±20,91	NS
RF	64,91±4,52	27,89	77,19±4,05	24,94	12,28±26,76	<0.01	75,49±4,18	24,36	8,82±27,29	NS
EF	57,89±4,68	28,86	76,75±3,75	23,10	18,86±27,03	<0.001	69,12±4,04	23,53	11,27±25,45	<0.05
CF	60,53±4,97	30,61	71,49±4,26	26,25	10,96±30,08	<0.05	58,82±4,73	27,60	-2,94±32,43	NS
SF	77,19±4,85	29,87	79,39±3,95	24,33	2,19±31,99	NS	80,39±4,01	23,38	3,43±23,85	NS
<b>Symptom scales</b>										
FA	40,94±4,04	24,93	28,95±3,85	23,75	-11,99±26,14	<0.01	29,41±3,89	22,70	-9,48±25,82	<0.05
NV	19,30±5,05	31,13	3,51±2,00	12,35	-15,79±30,00	<0.01	5,88±2,71	15,83	-13,73±33,20	<0.05
PA	34,21±4,74	29,24	13,60±3,82	23,52	-20,61±31,34	<0.01	19,12±4,11	23,97	-15,69±26,25	<0.01
DY	15,79±4,99	30,74	10,53±4,37	26,96	-5,26±27,43	NS	11,76±3,69	21,53	-4,90±27,38	NS
SL	28,95±4,90	30,19	23,68±4,85	29,92	-5,26±29,54	NS	21,57±5,24	30,58	-9,80±36,26	NS
AP	18,42±5,14	31,67	7,02±3,12	19,23	-11,40±32,21	<0.05	6,86±2,74	15,95	-13,73±32,94	<0.05
CO	13,16±3,67	22,65	6,14±2,47	15,22	-7,02±22,14	NS	0,00±0,00	0,00	-10,78±19,63	<0.01
DI	5,26±2,00	12,32	3,51±1,68	10,37	-1,75±13,30	NS	3,92±2,34	13,64	-1,96±18,24	NS
FI	34,21±6,22	38,35	29,82±4,83	29,80	-4,39±35,66	NS	36,27±5,52	32,17	1,96±40,98	NS

**Legend:** T<sub>1</sub> – baseline assessment; T<sub>2</sub> – assessment at 1<sup>st</sup> postoperative month; T<sub>3</sub> – assessment at 7<sup>th</sup> postoperative month; KPS – Karnofsky Performance Scale; PF – Physical Functioning; RF – Role Functioning; EF – Emotional Functioning; CF – Cognitive Functioning; SF – Social Functioning; FA – Fatigue; NV – Nausea/Vomiting; PA – Pain; DY – dyspnea; SL – Sleeplessness; AP – Appetite Loss; CO – Constipation; DI – Diarrhea; FI – Financial Impact

**Table 5.**Significant Correlations between the Mean Scores of Cognitive Tests and KPS/QLQ-C30 Scales at 7<sup>th</sup> Month

Assessment at 7 <sup>th</sup> month	KPS	QL	PF	RF	CF	SF
MMSE	0.68**	0.41*	0.56**	0.47**	-	0.58**
ST	0.76**	0.55**	0.61**	0.43*	0.39*	0.54**
TMT A	-0.64**	-0.44**	-0.59**	-0.39*	-0.50**	-0.36*
TMT B	-0.83**	-0.56**	-0.63**	-0.48**	-0.40*	-0.49**
SFT	0.61**	0.50**	0.61**	0.45**	0.41*	0.45**
PFT	0.69**	0.41*	0.54**	0.35*	-	0.43*
DSF	0.49**	0.40*	0.41*	-	-	-
DSB	0.64**	0.54**	0.45**	0.34*	-	0.54**
DST	0.72**	0.50**	0.64**	0.43*	0.42*	0.43*
CDT	0.53**	0.41*	0.47**	0.45**	0.42*	0.41*

\*\* Correlation is significant at the 0.01 level (2-tailed)

\* Correlation is significant at the 0.05 level (2-tailed)

**Legend:** MMSE – Mini-Mental State Examination; ST – Stroop Test; TMT – Trail-Making Test; SFT – Semantic Fluency Task; PFT – Phonemic Fluency Task; DSF – Digit Span Forward; DSB – Digit Span Backward; DST – Digit-Symbol Test; CDT – Clock Drawing Test; KPS – Karnofsky Performance Scale; QL – Global Health/QOL; PF – Physical Functioning; RF – Role Functioning; CF – Cognitive Functioning; SF – Social Functioning;

some components of the executive functions such as planning, mental flexibility, decision making and executive control. The capability of executive control assessed by the Stroop Test was the domain which demonstrated the highest improvement rate with over 46% for the entire follow-up period. Despite the positive dynamics, these domains remain considerably impaired and the patients with brain tumors do not reach the level of functioning of the patients from the control group at any time point. Solely, the capability of decision-making evaluated by the GNG test nears that of normal subjects at the 1<sup>st</sup> postoperative month. Improvement of cognitive functioning during the period of clinical follow-up was mentioned in several studies after removal of brain lesions [4,12,27,31,33,34].

As a result of the treatment, the brain tumor patients also significantly and permanently improved their functional status, global QOL and RF measured by the KPS and the QLQ-C30, respectively. Indeed, the QOL usually improves after surgical treatment [23]. As we also observed, the baseline KPS and QOL assessment are generally lower compared to the postoperative evaluations which implicates the idea that the tumor itself and the deficits it causes are the major factors contributing to poor preoperative QOL [5,29].

The mean scores of the global health and QOL were most strongly correlated with the mean scores of TMT B and ST whereas the KPS correlates well with TMT B, ST, DST and MMSE. Therefore, it indicates that the impairment of executive functions may have substantial impact on patients' QOL. Additionally, by means of linear modeling, it was demonstrated that the change of the global cognitive status evaluated by the MMSE is a strong predictor influencing the dynamics of the functional status (KPS). Thus, the poorer MMSE score entails impaired ability to perform normal activities of daily living and higher degree of dependency on others for assistance, an observation also shared by others [30].

This study established multiple correlations between cognitive functions and QOL which increase in strength and number during the follow-up period. In fact, cognitive deterioration may predict subsequent decline in QOL [20]. Hence, neurocognitive functions are important determinants of the QOL of patients suffering from brain tumors [13,15,17].

## CONCLUSION

This study confirms the hypothesis that cognitive functions and QOL in patients with supratentorial brain tumor are closely connected. Therefore, prevention of neurocognitive deterioration should be an important clinical target in order to provide proper level of well-being. The combined assessment of cognitive functioning and QOL has been outlined as a valuable outcome measure in brain tumor clinical trials which may ultimately affect future decisions making regarding the choice of the optimal treatment regimens.

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## CHANGES IN MACRONUTRIENT INTAKE OF INTERNET FITNESS COMMUNITY MEMBERS DURING A FIVE-YEAR PERIOD

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## ПРОМЕНИ В КОНСУМАЦИЯТА НА МАКРОНУТРИЕНТИ ПРИ УЧАСТНИЦИ В ИНТЕРНЕТ ФИТНЕС ОБЩНОСТ ЗА ПЕРИОД ОТ ПЕТ ГОДИНИ

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### РЕЗЮМЕ

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До този момент фактическото влияние на тренировъчния опит върху приема на нутриенти не е изследвано. Целта на това проучване беше да провери хипотезата, че през годините на активни тренировки натрупващият се опит от фитнеса повлиява диетичния прием на макронутриенти при непрофесионално практикуващи бодибилдинг и че този ефект зависи от специфичните цели, които човек си е поставил. Сред потребителите на популярен български фитнес форум е проведено лонгитудинално ретроспективно проучване на развитието с многократно измерване, използвайки документален метод и метод на анализ на съдържанието. При хора с различни тренировъчни цели през годините

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### ABSTRACT

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To this moment the actual quantitative impact of training experience on nutrient intake has not been investigated. The aim of this study was to test the hypothesis that over the years of active training the accumulated fitness experience affects the dietary macronutrient intake of individuals practicing bodybuilding unprofessionally and that effect depends on the specific training goals set before the individuals. A longitudinal retrospective developmental study with adopted repeated measures design was conducted among the users of a popular Bulgarian fitness forum using documentary research method and content analysis. There was a significant difference in the changes during the years for people with different training goals in daily protein intake

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имаше значителни различия в промените на белтъчния дневен прием –  $F(7.27, 274) = 22.2, p < 0.001, \eta^2 = 0.37$ , – въглехидратния дневен прием –  $F(7.79, 293.25) = 5.24, p < 0.001, \eta^2 = 0.12$ , – и дневния прием на мазнини –  $F(12, 452) = 4.75, p < 0.001, \eta^2 = 0.11$ . Тренировъчният опит, водещ до развитие на спортна култура през годините, е свързан със значителни изменения в дневния прием на макронутриенти. Тези различия варират значително между хората с различни тренировъчни цели. Резултатите показват нуждата от промоция на здравословния начин на живот сред младите хора чрез подкрепа на Интернет фитнес общността и осигуряване на достоверна и съвременна информация за храненето.

**Ключови думи:** спортна култура, макронутриенти, Интернет, фитнес

–  $F(7.27, 274) = 22.2, p < 0.001, \eta^2 = 0.37$ , – daily carbohydrate intake –  $F(7.79, 293.25) = 5.24, p < 0.001, \eta^2 = 0.12$ , – and daily fat intake –  $F(12, 452) = 4.75, p < 0.001, \eta^2 = 0.11$ . Training experience leading to development of sports culture over the years was associated with significant alterations in the daily macronutrient intake. Those differences varied significantly across people with different training goals. The findings demonstrate the necessity for promotion of healthy lifestyle among younger people through supporting the Internet fitness community and providing scientifically sound and up-to-date nutritional information.

**Keywords:** sports culture, macronutrients, Internet, fitness

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## INTRODUCTION

Compelling evidence suggests that young people in modern societies often have poor dietary habits. (6, 5, 7) On the other hand, spreading sports culture is associated with balanced and regular meal consumption. (13, 19) Sport, as a highly diversified social phenomenon comprising different types of physical activity, (2) possesses the unique potential to educate, attract, motivate and inspire people to take care for their health. (3) For example, having a less-frequent intake of unhealthy foods and not skipping meals were associated with decreased odds of learning difficulties and behavioural problems in Norwegian adolescents, (26, 27) and favourable effects of night-time consumption of protein or carbohydrates on the next-morning metabolism were observed in sporting males. (24) Sport is an ideal setting for health promotion and prioritising it might contribute to achieving positive health in youngsters. (8, 11, 20) Moreover, the obesity in men is rising and the potential of sports clubs to engage men in health promotion activities is increasingly recognised. (17) However, intensive training has been associated with some negative nutri-

tional practices which might be due to misinformation. (9, 15, 29, 30)

A report at the International conference of young scientists – Plovdiv, 2013, based on a survey among Bulgarian young people involved with fitness activities presented findings that the majority of them had raised their medical culture, were interested in medical research and were generally more involved in health promotion after they started training. (10) The term „sports culture“, on which the concept of this paper is based, comprises all psycho-social practices arising from the care for one's own body which in time transcend the plane of initial aesthetic or self-esteem needs and become manifestations of certain epistemological necessities.

To this moment the actual quantitative impact of training experience and the general knowledge of healthy nutritional principles, which it cultivates, on nutrient intake has not been investigated.

The **aim** of this study was to test the hypothesis that over the years of active training the accumulating fitness experience affects the dietary macronutrient intake of individu-

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als practicing bodybuilding unprofessionally and that effect depends on the specific training goals set before the individuals.

## MATERIAL AND METHODS

### STUDY DESIGN

In the period February 3 – August 1, 2013 a longitudinal retrospective developmental study with adopted repeated measures design was carried out using documentary research method and content analysis (16, 31) among the users of the most popular internet fitness forum in Bulgaria ([www.bb-team.org](http://www.bb-team.org)) with 54 000 registered users and 900 000 posts per month at the beginning of the study. The concept of participating in the forum is for each participant to keep daily records describing workout and dietary practices as well as the alterations in anthropometrics, attitudes and everyday experiences. This detailed information permitted the author to select 117 users about whom the necessary data was available in the archives of the forum for the period of 5 years (2008–2012). For each of the years September was analysed because it presented everyday data for each of the users. The data was extracted and organized by the author. *Sample size estimation* – The determined maximum number of participants calculating for 95% degree confidence and an error of 5% from the mean value of the daily macronutrient intake was 117. *Variables* – Anthropometric characteristics (body weight and height), demographic data (age, residence, gender, educational attainment), eating habits (protein, carbohydrates and fat daily intake) and training habits (number of workouts per week and training goals). The continuous data were registered for a representative day of the month after the author made sure that there were not considerable variations in food consumption for that month. The macronutrients were registered as mean grams per kilogram body weight per day. The assessment of the macronutrient content of different food products

was performed using the nutritional value of foods tables published in the 2007 edition of „Choose Your Foods: Exchange Lists for Meal Planning“.(2) *Selection criteria* – Inclusion criteria – non-steroid or supplement users; clearly described training and everyday routines. Additional content analysis of posts during the whole period permitted the author to ensure that the users did not report any major health, financial or other issues that might have affected their nutritional practices. *Statistical analyses* – Wilcoxon's signed ranks test was used to compare differences in residence in 2008 and 2012. The main analyses used were within subjects and split-plot ANOVAs with Bonferroni's post-hoc correction. To check the normality of the distribution Shapiro-Wilk test and graphical analysis were used. The variables included in the ANOVAs met or approximated normal distribution. (14, 22) Pearson's and Spearman's correlation analyses and the criterion of significance level of  $P < 0.05$  (two-tailed) were used. Missing values were replaced with automated multiple imputation. Statistical data processing was performed using the software SPSS v.21.

### RESULTS

Mean age of participants in September 2008 was 23.5 ( $\pm 5.5$ ) ranging 18 – 41 years. The majority were male (79.5%,  $n = 93$ ). In 2008 13.7% were resident in a village, 22.2% in a small town and 64.7% in a big city, while in 2012 those relative shares were 5.1%, 20.5% and 74.4% respectively – ( $Z = -3.84$ ,  $p < 0.001$ ). Nearly one third of the participants (29.9%) were training in order to lose weight, 37.6% wanted to gain muscle mass, 22.2% aimed to develop functionality and 10.3% worked out in order to achieve positive health or just for tonus. A reduction in the number of workouts per week was observed. No meaningful and significant correlations could be found between the macronutrient consumption and any of the other demographic or workout related variables for the different training goals.

## EFFECT OF FITNESS TRAINING EXPERIENCE ON MACRONUTRIENT INTAKE

The macronutrient intake during the five-year period is presented at table 1.

Series of one-way within subjects ANOVAs were conducted to compare the effect of fitness training experience on macronutrient intake over the five years according to the different workout goals. When Mauchly's Test indicated that the assumption of sphericity had been violated, the degrees of freedom were corrected using Greenhouse-Geisser estimates of sphericity. The ANOVAs revealed the following **profiles related to goals**:

- **people whose goal was to lose weight:** there was significant effect of fitness training experience on the daily protein intake,  $F(1.977, 67.204) = 28.869$ ,  $p < 0.001$ ,  $\eta^2 = 0.46$ ; a significant difference between daily protein intake in the years 2008 and 2009, 2010, 2011, 2012; 2009 and 2010, 2011, 2012; 2010 and 2012; 2011 and 2012. Fitness training experience significantly affected the daily carbohydrate intake,  $F(2.15, 73.13) = 11.42$ ,  $p < 0.001$ ,  $\eta^2$

$= 0.25$ . There was a significant difference between daily carbohydrate intake in the years 2008 and 2011, 2012; 2009 and 2011, 2012. There was also significant effect of fitness training experience on the daily fat intake,  $F(2.73, 92.79) = 27.41$ ,  $p < 0.001$ ,  $\eta^2 = 0.45$ . There was a significant difference between daily fat intake in the years 2008 and 2011, 2012; 2009 and 2012; 2010 and 2012; 2011 and 2012.

- **people whose goal was to gain muscle mass:** there was significant effect of fitness training experience on the daily protein intake,  $F(1.99, 85.85) = 7.29$ ,  $p < 0.001$ ,  $\eta^2 = 0.15$ . There was a significant difference between daily protein intake in the years 2008 and 2010, 2012; 2009 and 2012; 2011 and 2012. There was significant effect of fitness training experience on the daily carbohydrate intake,  $F(1.93, 83.03) = 37.33$ ,  $p < 0.001$ ,  $\eta^2 = 0.47$ . There was a significant difference between daily carbohydrate intake in the years 2008 and 2009, 2010, 2011, 2012; 2009 and 2010, 2011, 2012; 2010 and 2011, 2012; 2011 and 2012. There was also significant effect of fitness training experience on the daily fat intake,  $F(4, 172) = 25.32$ ,  $p < 0.001$ ,  $\eta^2 = 0.37$ . There was

**Table 1.**

Distribution of the macronutrients in g/kg/day depending on the fitness goals over the five years (2008–2012)

Year	Macronutrient (g/kg/day)	Fitness goal			
		Weight loss	Muscle gain	Functionality	Tonus
2008	Protein	2.98 (± 0.28)	2.34 (± 0.44)	2.30 (± 0.53)	1.92 (± 0.39)
	Carbohydrates	1.02 (± 0.20)	3.39 (± 0.41)	3.38 (± 0.49)	1.76 (± 1.19)
	Fat	0.89 (± 0.30)	1.92 (± 0.42)	2.22 (± 0.51)	1.34 (± 0.58)
2009	Protein	2.82 (± 0.27)	2.41 (± 0.42)	2.37 (± 0.53)	2.03 (± 0.43)
	Carbohydrates	1.07 (± 0.25)	3.35 (± 0.42)	3.41 (± 0.48)	1.76 (± 1.19)
	Fat	0.97 (± 0.27)	1.51 (± 0.69)	2.35 (± 0.53)	1.78 (± 0.40)
2010	Protein	2.66 (± 0.32)	2.56 (± 0.44)	2.23 (± 0.46)	2.00 (± 0.36)
	Carbohydrates	1.14 (± 0.28)	3.23 (± 0.49)	3.33 (± 0.44)	1.42 (± 0.41)
	Fat	1.03 (± 0.22)	2.15 (± 0.47)	2.63 (± 0.61)	2.2 (± 0.65)
2011	Protein	2.56 (± 0.34)	2.67 (± 0.49)	2.10 (± 0.37)	2.07 (± 0.31)
	Carbohydrates	1.20 (± 0.21)	3.24 (± 0.46)	3.25 (± 0.37)	1.78 (± 1.05)
	Fat	1.14 (± 0.23)	2.41 (± 0.56)	2.99 (± 0.64)	1.98 (± 0.36)
2012	Protein	2.41 (± 0.38)	2.78 (± 0.47)	2.10 (± 0.33)	2.05 (± 0.33)
	Carbohydrates	1.26 (± 0.28)	3.07 (± 0.49)	3.11 (± 0.43)	1.25 (± 0.87)
	Fat	1.53 (± 0.46)	2.51 (± 0.52)	2.85 (± 0.74)	2.03 (± 0.30)

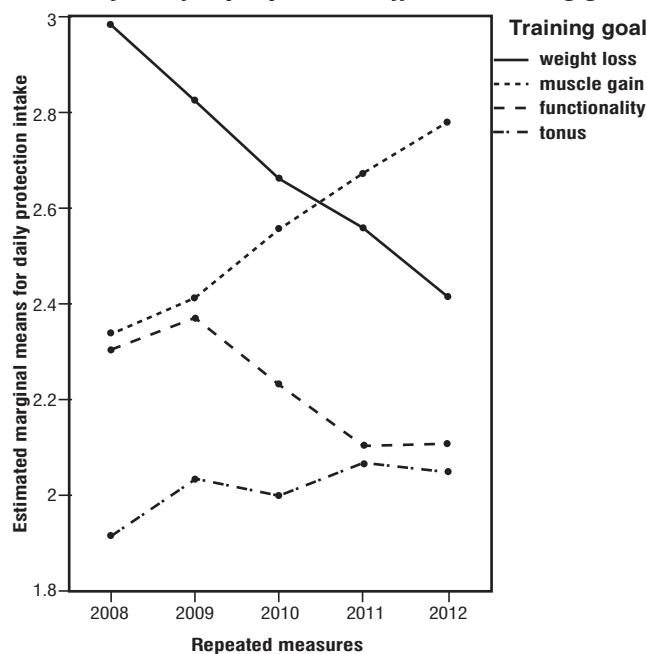
a significant difference between daily fat intake in the years 2008 and 2009, 2011, 2012; 2009 and 2010, 2011, 2012; 2010 and 2012.

- people whose goal was to develop functionality:** there was significant effect of fitness training experience on the daily protein intake,  $F(2.08, 52.11) = 10.96$ ,  $p < 0.001$ ,  $\eta^2 = 0.31$ . There was a significant difference between daily protein intake in the years 2008, 2009, 2011; 2009 and 2010, 2011, 2012. There was significant effect of fitness training experience on the daily carbohydrate intake,  $F(1.87, 46.76) = 3.28$ ,  $p = 0.049$ ,  $\eta^2 = 0.12$ . There was a significant difference only between daily carbohydrate intake in the years 2009 and 2012. There was significant effect of fitness training experience on the daily fat intake,  $F(4, 100) = 10.86$ ,  $p < 0.001$ ,  $\eta^2 = 0.3$ . There was a significant difference between daily fat intake in the years 2008 and 2011, 2012; 2009 and 2011, 2012; 2010 and 2011.
- people who worked out only for good health and tonus:** there was not a significant effect of fitness training experience on the daily protein intake -  $F(2.31, 25.36) = 0.32$ ,  $p = 0.761$ ,  $\eta^2 = 0.03$  - and on the daily carbohydrate intake -  $F(4, 44) = 2.032$ ,  $p = 0.105$ ,  $\eta^2 = 0.16$ . There was significant effect of fitness training experience on the daily fat intake,  $F(2.43, 26.72) = 6.93$ ,  $p = 0.002$ ,  $\eta^2 = 0.39$ . There was a significant difference between daily fat intake in the years 2008 and 2010.

Difference between the changes in macronutrient consumption over the years for people with different workout goals

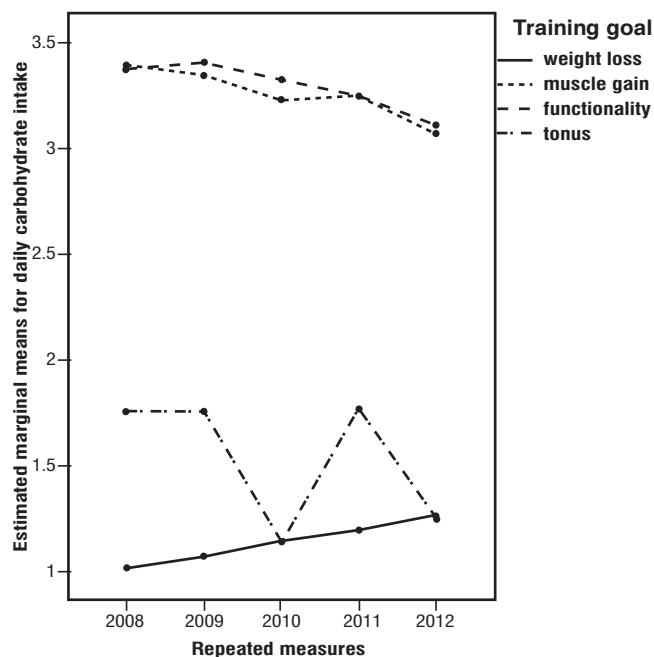
The results from the split-plot ANOVAs indicated that there was a significant difference in the changes over the years for the people with different training goals in daily protein intake -  $F(7.27, 274) = 22.20$ ,  $p < 0.001$ ,  $\eta^2 = 0.37$ , - daily carbohydrate intake -  $F(7.79, 293.25) = 5.24$ ,  $p < 0.001$ ,  $\eta^2 = 0.12$ , - and daily fat intake -  $F(12, 452) = 4.75$ ,  $p < 0.001$ ,  $\eta^2 = 0.11$ . For daily protein intake there was no significant difference ( $p > 0.05$ ) except between people with muscle gain and functionality goals for 2008 and 2009; between weight loss and muscle gain goals for 2010 and 2011; and between functionality and tonus goals for 2011 and 2012. (Figure 1)

**Figure 1.**  
Differences in the changes in protein consumption over the years for people with different training goals



For daily carbohydrate intake there was no significant difference ( $p > 0.05$ ) except between people with functionality and muscle gain goals for the whole period; and between weight loss and tonus for 2010 and 2012. (Figure 2)

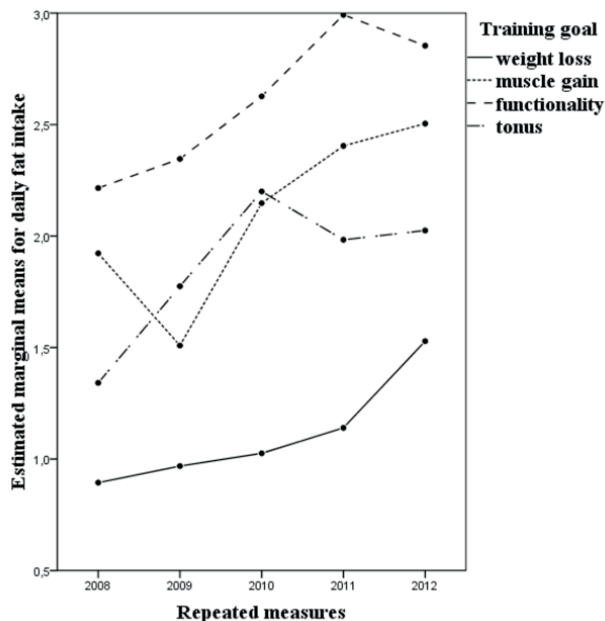
**Figure 2.**  
Differences in the changes in carbohydrate consumption over the years for people with different training goals



For daily fat intake there was no significant difference ( $p > 0.05$ ) only in the changes between people with muscle gain and tonus goals for 2009 and 2010. (Figure 3)

**Figure 3.**

*Differences in the changes in fat consumption over the years for people with different training goals*



## DISCUSSION

Overall, our findings suggest that when people aiming to lose weight became more experienced in fitness training, they consumed significantly less protein and more carbohydrate and fat per day, changing their eating habits from the popular very high-protein, low-fat and low-carbohydrate diet which, although effective, has been associated with some health concerns to more balanced meals. (4, 25)

For muscle gainers the nutritional habits changes resulted in the reduction of high-carbohydrate intake (1, 21) and in graduate increase in protein and fat-intake characteristic of the popular high-fat diets, where the major energy source is from fat-rich foods. (12, 18, 23)

People, whose goal was to develop functional capacity, demonstrated similar trend over the years to those observed in muscle-gainers, but

only in reference to carbohydrate consumption. Otherwise, their protein intake was significantly lower than muscle-gainers and the fat intake was significantly higher. The results suggest that, when people were training for achieving positive health and for tonus, the training experience accumulated during the years did not significantly alter their daily macronutrient intake except for fat intake which increased significantly only during the first two years.

According to the American Dietetic Association, Dieticians of Canada, and the American College of Sports Medicine carbohydrate recommendations for athletes range from 6 to 10 g/kg body weight per day, protein recommendations for endurance and strength-trained athletes range from 1.2 to 1.7 g/kg body weight per day and the fat should not be supplying the majority of caloric intake. (28) Overall, the studied bodybuilders had higher mean daily protein intake than the recommended with only people training for tonus approximating the upper limit. On the contrary, no one reached the 6 g/kg carbohydrate intake.

## SPORTS CULTURE AS A SOCIAL PHENOMENON – A COMPREHENSIVE DISCUSSION OF THE QUANTITATIVE FINDINGS IN THE LIGHT OF A QUALITATIVE RESEARCH

The initial motivation of the users to begin working out in a gym (mainly good looks and boosting self-esteem) gradually transcended into a specific social position and worldview. The concern with everyday routine and maintaining optimal caloric and nutrient intake cultivated discipline in the users and altered their social priorities towards a healthier lifestyle and restriction of unhealthy nutritional practices. Over the time, the users became more and more involved in dietetic research and novel guidelines for optimal sports nutrition. Their major information source was Internet where they read articles and exchanged experience and information. When the users advised others about some nutritional regimen, they frequently supported their preference with references for internet publications. They showed extensive knowledge about human

metabolism, nutritional value of foods, quality of food sources and optimal food preparation. Some of the problematic nutritional practices (like ketogenic diets) might be attributed to the inability of common bodybuilders, despite their best efforts, to select the most appropriate and scientifically sound information sources about dietetics. These findings are based on observations among many of the users of the forum and are not restricted to the included 117 people. Hence, it is quite plausible that the changes in macronutrient intake might be due to a great extent to the sports culture of the internet fitness community.

### LIMITATIONS

The major limitations of the present study are typical for self-report and retrospective studies, namely some socio-cultural factors, impacting on the nutritional practices, might have been omitted and others generalized. There is a possibility for reporting bias as well. It is controversial whether sports culture is the sole determinant of the dietary changes. Future research should replicate these results in other countries and in bodybuilders who do not belong to internet fitness community in order to verify the conclusions of this paper. Also different types of protein, carbohydrates and fat should be assessed.

### CONCLUSION

Training experience leading to development of sports culture over the years might be associated with significant alterations in the daily macronutrient intake. Those differences varied significantly across people with different training goals – muscle-gainers and people developing functionality orientated towards high-fat, normal-protein and carbohydrate diets, while those aiming to lose weight or working out just for tonus – towards more balanced diets. These findings might be used to promote healthy lifestyle among younger people through supporting the internet fitness community and providing scientifically sound and contemporaneous nutritional information.

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**LEGAL EFFECTS OF EARLY DISCHARGE  
FROM HOSPITAL IN CASES OF ACUTE EXOGENOUS POISONING  
(MODEL REPRESENTATION)**

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**ПРАВНИ ПОСЛЕДИЦИ ПРИ ПРЕЖДЕВРЕМЕННА  
ДЕХОСПИТАЛИЗАЦИЯ ПРИ ОСТРО ЕКЗОГЕННО ОТРАВЯНЕ**

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**РЕЗЮМЕ**

Съвременното състояние на медицинската помощ у нас, особено в областта на спешната медицина, осъществявана в лечебните заведения със стратегическа здравна значимост и медико-икономическите ѝ измерения, поставят за решаване тежки правни, медицински и икономически проблеми.

Проучването цели да установи специфичните последици (правни и финансови) за изпълнителя на болнична помощ, при случаи с невъзможността за завършване на клиничната пътека, съгласно условията на финансиране на болничната помощ от НЗОК, както и да подпомогне ръководители на клиници/отделения за предотвратяване на случаите на преждевременна дехоспитализация и преодоляване на пречките за завършване на лечението.

Проучени са (case series) случаи на ОЕО, лекувани в Клиника по клинична токсикология на УМБАЛ „Свети Георги“ ЕАД – Пловдив през 2012 – 2103 г., при които пациентите, след като получат медицинска помощ, напускат лечебното

**ABSTRACT**

The current state of the medical services in Bulgaria, especially urgent medicine services, provided by hospitals with strategic position among the providers of medical care, sets forth serious medical, legal and economic problems.

The specific effects (legal and financial) of early discharge are analyzed, as the provider of medical help could not finish the protocol of the Clinical Path, according to the conditions of the payment for delivering of healthcare by the National Insurance Fund, as well as to sets forth some ideas in order to help the managers of words to prevent cases of early discharge and overcome the obstacles against completing the treatment.

The analysis provides ten case studies of patients with acute exogenous poisoning, refusing to continue their hospitalization after being treated in the Toxicology word of University hospital „Saint George“ in Plovdiv, Bulgaria and therefore the pro-

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заведение преди завършване на пълния алгоритъм на клиничната пътека.

Изяснени са предвидения в закона ред за дехоспитализация (отказ от лечение), дефиницията за клинична пътека и случаите, при които тя се смята за незавършена. Анализирани са съдебна практика в тази насока. Обосновано се критикува действащата към момента правна уредба.

Изводите на статията насочват към предложения за изменение на нормативната уредба и преразглеждане на дефиницията за завършена клинична пътека, така че едновременно да бъде зачетено правото на пациента по всяко време да откаже лечение и правото на изпълнителя на болнична помощ да получи заплащане на разходите, направени за лечението на пациентите.

**Ключови думи:** Преждевременна дехоспитализация, здравни и правни последици, информирано съгласие, остри екзогенни отравяния.

tol, required by the Clinical Path, could not be considered as completed.

The specific regulation, concerning the early discharge, the definition of „clinical path“ and the cases, when it is considered as „not completed“ and the current legislation are reasonably criticized in the article. Practice on different court case is included as well.

The conclusions are aimed to provide specific recommendations for changes of the legislation and revising the definition of the completed protocol of the clinical path in order to respect both the right of the patient to refuse medical help at any moment during the treatment and the right of the provider of medical services to receive payment for the costs made during the treatment.

**Key words:** early discharge; medical and legal effect; informative consent; acute exogenous poisoning;

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## INTRODUCTION

Art. 90 from The Health act, stipulates that the patient has the right to refuse medical help at every moment of his hospitalization. It is very important to mention that the patient could not receive medical help without informed consent or in case of refusal, except in special cases, provided expressly by the law. If the patient is treated against his/her will, his/her rights would be infringed.

Patients with Acute Exogenous Poisoning (AEP), especially cases, caused by alcohol, narcotics, suicide attempts, very often declare their will against any medical help, even before the protocol of the Clinical Path being concluded. Part of the patient would leave the hospital while other part would refuse specific medical procedures, required by the protocol. There are patient who refuse to sign informed consent and this act is equal to refusal. Therefore we have to discuss the question why the right of the patient to refuse medical help at any time of the treatment is considered as a problem.

## REPRESENTATION AND ANALYSIS

The payment coming from the National Health Insurance Fund (NHIF) to the hospitals, according to the Individual contracts between the providers of hospital care and the Regional Health Insurance Fund (RHIF) is the main financial source of the hospitals. The conditions of payment are provided in the National Frame Contract.

At the same time the method of payment and evaluation of the medical help, provided to the insured persons, are detailed by Ordinances, issued by the Council of Ministers (for example Ordinance № 366/2011 and Ordinance № 353/2012).

All of those above mentioned Acts define specific requirements that should be followed by the provider of medical care in order to receive payment for the services provided to the insured persons. Part of those requirements are included in the protocols of the Clinical Paths, which structure and content are defined in the NFC. The Clinical Paths (CP) and Clinical Proce-

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dures cover the range of the health care, paid (fully or partly) by the NHIF.

The following analysis shall study only the concept of the „completed Clinical Path“ in the context of the right of every patient to refuse health care and leave the hospital before completing the full protocol of the CP and problems following this decision.

The conditions, called AEP are treated in Toxicology Clinics and Words, providing medical help, defined from CP № 291 to № 296, NFC 2012, appendix 16. Ordinance № 366/27.12.2011 of the Council of Ministers provides that NHIF shall pay the medical help, delivered to the patient in case the protocol of the CP is fully completed. How the „completed CP“ is defined in the legislation? The legal definition, according to the § 1, p. 1 NFC 2012, stipulates that all the basic diagnostic and therapeutic procedures part of the protocol must be provided. Even more, the patient should stay at the hospital as much time as it is calculated in the protocol.

Therefore, only completed CPs are paid by the NHIF to the provider of medical help. Argumentum per a contrario, in case of not completed CP, the NHIF shall not pay for the health care provided. The above mentioned is expressively specified in the Ordinance № 366: *„In case that a patient if treated and the CP is not completed, the medical care shall not be paid. Exceptions could be made in case of exitus letalis when the minimum hospital stay was not completed but all the diagnostic, therapeutic or surgery procedures were followed.“* In other words, if the patient refuses medical help before completing his minimum hospital stay, the provider of medical help shall not be paid. However, those articles should be discussed together with art. 30, NFC 2012, where it is stipulated that the providers of medical care are obliged not to require any payment from the insured persons for the medical care, paid by the NHIF. Argumentum per a contrario, the provider of medical care could require payment for all the services, provided to the patients, which are not paid by the NHIF.

Therefore, in cases of early discharge due to the patient right to refuse any medical help, the patient is required to pay the expenses, made by the hospital in order to provide health care. Actually, the early discharge is an obstacle against the hospital to receive payment for the treatment of the patient. This obstacle, according to us, is an objective one, as the hospital could not detain the patient against his will. At the same time, expenses have been done by the healthcare institution that should be covered.

### THE ANALYSIS

Ten cases in the Toxicology word in University Hospital „Saint George“ were analyzed in order to describe the consequences of this problem. The data have been compared with the information, reported by the Agency „Medical audit“. The legal practice and court cases were examined as well in order to provide accurate model of the relations between patient-provider of hospital care-NHIF.

We discovered that the characteristic of the patient with AEP is associated directly with the problem. The causes of the AEP are directly related with the social status of the patients. Usually these are patients with history of addictions, both alcoholic and/or drugs; chronic health problems; low incomes or social status. This could be added to their attitude as they are usually aggressive, the communication is difficult and they could not be easily convinced or informed about their rights and the effects of early discharge.

The analysis describe also that the patients themselves have an acceptable argument against the right of the hospital to request payment for them, as they are insured persons and the early discharge is a right, provided by the Health act and could not be followed by negative financial effects. This contradiction leads to a controversy between the patient and the provider of hospital care, as the first one has paid his health insurance and has the legal right to leave the hospital earlier that it is provided in

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the protocols, while the second one has provided medical care.

There were also disputes between hospitals and NHIF before 2012, which have been resolved in favor of the hospitals. The motives of the court match our conclusions, suggested in the report. The Court has decided that it is not acceptable to punish the hospitals by not paying for the health care provided, because the patient has the right to refuse medical help at any time of his hospitalization. Those cases, according to the Court, are equal to the cases when the patient dies before the protocol is completed, as both events are not under the control of the provider. Those decisions have been made before the changes of the Ordinances of the Council of Ministers when the death cases were the only exception of the rule that providers shall not receive payment in cases of incomplete protocols. In addition, another amendment has been done in Ordinance №49/2010 r. As this legal act provides, the early discharge should be certified by the patient by signing a declaration. Part of the text, included in it, says: *„I am aware that I shall pay for all the medical care provided, in case my early discharge prevents the hospital to receive payment by the NHIF or Ministry of Health.“*

As a result of the described provisions of the legal acts, the hospitals bear significant financial loss and the patients are forced to pay for the treatment or stay in the hospital against their will, while the NHIF saves money for medical care that should be paid. The same situation could be described in the Toxicology Clinic at Hospital „Saint George“. 186 patient treated in 2012 have declared their will to be discharged earlier than it is provided in the CPs. The number of those patients from January to August 2013 is 87.

During the study of the representative model, when 10 randomized cases were studied, we discovered that in 70% of those patients AEP has been caused by alcohol or/and drugs and the cost of treatment of half of them was

between 700 BGL–1500 BGL. Only 5% of the studied cases cost the hospital just 150 BGL. The Agency „Medical Audit“ reported recently the same data, relevant to all the hospitals. 509 cases of early discharge were reported by 21 hospitals for 6 months period. 63% of them left the hospital without signing the declaration, required by Ordinance 49/2010 and only 7.28% paid for their treatment. *„Those cases generate significant loss for all the hospitals“*-reported *„Medical audit“*.

In conclusion, we must state that this problem leads to negative effects to both hospitals and patients, and positive financial effect to the public body-NHIF.

## **CONCLUSIONS AND RECOMMENDATIONS:**

1. Changes of the legislation is needed and the cases of early discharge should be considered as equal to death cases, when the clinical path could not be completed due to objective obstacles.
2. Another way to resolve the problem is to remove the requirement of minimum hospital stay in the protocols of the CPs, so they could be considered as completed by following the main procedures, provided by them.
3. The CP's as a method for payment of the providers of hospital care should be replaced by the diagnostic related groups
4. Specific measures should be recommended by the hospitals in order to limit the negative effects of the early discharge:
  - Cooperation between toxicologists and psychiatrics when difficult patients (suspicious for psychiatric problems, aggressive patient, etc.)
  - Preparation of clear hospital protocols, regarding the informed consent, refusal of medical help, providing health care against the patients' will in order to protect both patients and medical staff's rights and preventing conflicts.
  - Cooperation with the administration of the hospital and building specific models of relations between Court, Police, Prosecution and other bodies when it is needed.

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2. National Frame Contract (2006, 2009, 2012, 2013)
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## ALLERGIC REACTIONS TO SUBSTANCES WITH UNKNOWN PHYSICOCHEMICAL CHARACTERISTICS

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## АЛЕРГИЧНИ РЕАКЦИИ ОТ СУБСТАНЦИИ С НЕИЗВЕСТЕН ФИЗИКО-ХИМИЧЕН СЪСТАВ

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### РЕЗЮМЕ

Алергичните реакции засягат лица упражняващи различни професии. Когато е налице пряка причинно-следствена връзка или се обективизира сенсибилизация към конкретно вещество (материал) с който пациентът е в професионален контакт, диагностиката не представлява проблем. Нерядко, обаче, особено в производства със засекретен характер, установяването на субстанциите отключващи алергичните реакции е силно затруднено или невъзможно поради неизвестния физико-химичен състав на материалите и/или липсата на специализирана апаратура за тяхната детекция.

Друг проблем, който поражда интереса на специалистите от различни области – алерголози, дерматолози, токсиколози, е доколко алергичните заболявания при работещите в секретни производства лица са проява на сенсibili-

### ABSTRACT

Allergic reactions affect people practicing different professions. Establishing the diagnosis is not a problem if there is a direct causal relation present or sensibilization to a specific substance (material) is objectified. However it is not a rare case for the substance to be unknown when it includes manufacture of secretive character or when revealing of the substances is hindered or impossible due to unknown physicochemical content of the materials and/or lack of special equipment for their detection. Another problem that attracts the interest of different specialists (allergologists, dermatologists, toxicologists) is whether allergic diseases in people working at private manufactures are resulting from the potential of certain materials to sensitize the organism or they are caused by other mechanisms-toxic, irritative etc. That is why the presented clinical case would provoke the interest of military med-

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зиращия потенциал на определен материал или са породени от други механизми – токсични, иритативни или други.

Ето защо представеният от нас клиничен случай би предизвикал интереса както на специалистите във военната медицина, така и на работещите в медицински заведения от общ профил специалисти.

**Ключови думи :** алергични реакции, професионална експозиция, субстанции с неизвестен физико-химичен състав.

icine specialists as well as the occupied with general medicine physicians.

Key words: allergic reaction, professional exposure, substances with unknown physicochemical content

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## INTRODUCTION

In different manufactures substances with known as well as unknown physico-chemical content are used (1,2,4). This also applies to military industry especially in manufactures of private and secretive character.

Similar conclusion could be drawn about the pathogenetic mechanisms and types of influence in people exposed to such materials. Some of the materials that the presented by us patient had been exposed to are with familiar pathogenic mechanisms and the diseases they can cause. The health harming effects of nitrobenzene compounds like trinitrotoluene (TNT) that our patient has been in daily contact with at the work place are well known (3,6).

Another kind of materials that the patient had been in professional contact with belong to the group of organic solvents and synthetic polymers –acetone, benzine, paraphenylenediamine, polyethylene polyamide. It is known about them that their toxicity depends on their physicochemical properties like volatility, water and fat solubility quotient etc. A considerable part of the materials the patient had been exposed to has other harmful for the health effects (3,4,6,7,8,9,10,14,15).

Due to the private character and content of those substances and materials the etiological and pathogenetic reasons for the caused allergic reactions are complex to discover (11,12, 13).

## CASE PRESENTATION

The patient is a 53 year old male who was hospitalised in the Departement of Occupational Diseases and Allergology – University Hospital „St. George“ Plovdiv in 2012. A source of information is the official medical documentation of the patient – medical history with paraclinical examinations and tests, epicrisis, data from the outpatient documentation, medical counselling with other specialists.

Professional background and risk factors of the working environment are summarized below.

The patient reported 35 years of work at a military factory. The materials she had been in contact with could be divided into two groups:

- 1) Substances with familiar physicochemical content and properties: TNT, acetone, paraphenyldiamine, polyethylene polyamide, benzene.
- 2) Materials reported by the patient as ones with unknown chemical content and properties: oil resembling liquid without a specific odor and black colored powdery substance.
  - Resin – like substance that was dark in color and with specific odor that according to the patient was used for the production of plastic, laminate and PVC products, polishing laquer .
  - Powder – like substance that according to the patient was used for the production of rubber and latex products.
  - Silver coloured granules that also have metallic glimmer, according to the patient they were used for the production of metal products.

## GENERAL AND ORIENTED HISTORY OF ALLERGIES

The onset of the allergic symptoms was in 2001 when the patient got an itchy rash localized on the parts of the body, mainly hands, that had been in contact with the previously mentioned substances. The exanthema was accompanied by burning and itching sensations and redness. Sometimes the rash appeared along with edema of the soft tissue, especially on the lips. After the end of the working shift and during the days off work the intensity of symptoms decreased with increasement during work hours.

In the last 2 – 3 years the exanthema had been almost permanent and despite the therapeutic courses it often exacerbated expanding to wider areas, including such that had not been in contact with the substances. The patient was on long – term local corticosteroid and antihistamine therapy. Exacerbations of the allergic symptoms were present.

## PHYSICAL EXAMINATION DATA

Good general appearance. Clear consciousness. Adequate. Afebrile. Pale skin. Pale pink visible mucosa. Angioneurotic edema mainly on the lower lip. Itchy urticarial rash on the axillar area, chest and feet. (picture 2 and 3)

No pathologies of the respiratory and cardiovascular condition are detected.

The results of hematologic, biochemical and immunologic tests do not show any diverstions from the normal levels (table 1).

Epicutaneous skin testing was conducted with materials that the patient had been in professional contact with. The test was positive (++) for acetone, polyethylene polyamine, benzine, paraphenyldiamine, TNT. (table 2) Epicutaneous skin testing with the substances of unknown origin was also positive (++) (table 3).

The used therapeutic scheme included application of systemic corticosteroids in combination with antihistamines.

The patient was discharged in good general state and asymptomatic.

The definitive diagnosis in the epicrisis was urticaria and contact allergic dermatitis with professional etiology, chronic recidive course, often exacerbations.

**Table 1.**

Hematology, biochemistry and immunologic tests:

Hematology	Differential blood count	Biochemistry	Immunology
HGB – 141 g/L	Neut. – 58.9%	gluc – 5.0 mmol/l	Tot.IgE – 84.26 IU mL.
RBC – 5.02 T/L	Lymph. – 30.9%	t.prot – 72 g/l	
HCT – 0.444	Eos. – 1.1 %	alb – 44 g/l	
MCH – 27.7	Mono – 4.5%	t.bill – 12.1 mkmol/l	
MCV – 88.8	Baso – 0.6%	AST – 20 U/l	
WBC – 9.47 G/L		ALT – 14 U/l	
MCHC – 320		urea – 4.5 mmol/l	
PLT – 288 G/L		crea – 68 mkmol/l	
ESR – 10 mm		chol – 5.2 mmol/l	

Photographic material objectifying the skin and mucous syndroms of the patient:

**Table 2.** Epicutaneous skin testing of the materials of familiar origin

	Materials of the working environment	24th hour	48th hour
1	Acetone	/+ /	/+ + / noA.
2	Polyethylene polyamine	/+ /	/+ + / noA.
3	benzine	/+ /	/+ + / noA.
4	Paraphenyldiamine	/+ /	/+ + / noA.
5	TNT	/+ /	/+ + / noA.

**Table 3.** Epicutaneous testing of the presented by the patient substances with unknown origin and physico-chemical content

	Materials from the working environment	24th hour	48th hour
1	Resin – like substance	/+ /	/+ + + / noA.
2	Powder – like substance	/+ /	/+ + / noA.
3	Silver coloured granules and metallic glimmer	/+ /	/+ + + / noA.

**Table 4.** epicutaneous skin testing with substances of the standart package of occupational allergens used for detection of contact allergic dermatitis

	Materials of the working environment	24th hour	48th hour
1	Para-phenyldiaminum	/+ /	/+ + / noA.
2	N-isopropyl-N-phenyl-4-phenyldiamine	/+ /	/+ / слабо noA.
3	Nickelum (II) sulfas	/+ /	/+ + + / noA.
4	Epoxy resin	/+ /	/+ + + / noA.



Picture 1.  
*Angioneurotic edema of the lower lip*



Picture 2.  
*Urticarial rash on the left axillar area*



Picture 3.  
*right foot*



## DISCUSSION:

The used in private manufacture materials are among the broad spectrum of substances causing allergic disorders. Their chemical content and mechanisms through which they cause allergic reactions are known in some cases (3) but unfamiliar in other (2,4). Contact allergic dermatitis is one of the most common skin allergic diseases (1,5) and is often found to be with professional etiology (2,3,4). The materials and chemicals used in military industry are quoted by many authors as some of the reasons for the different in their course allergic reactions (3,4,6,7). In some patients, such as the presented here case, there was sensitization to several various by their chemical content substances present. It is very likely that those agents were the cause of the manifested in the patient allergic reactions – contact dermatitis, angioneurotic edema, urticaria. They probably played the role of unlocking agents or cofactors of the manifestation of certain types of allergic reactions. It is interesting that the patient was with diagnosed skin sensitization to substances of the standart package of occupational allergens (table 4). This package is officially certified in the EU and is used for the diagnosis of allergic dermatitis (Para-phenylendiaminum, N-isopropyl-N-phenyl-4-phenylendiamine, Nickelum II sulfas и Epoxy resin). The diagnostic differentiation of allergic skin problems such as contact dermatitis and urticaria is more of a terminological matter due to their similar and often overlapping clinical and morphological characteristics. The epicutaneous testing (patch test) is the most important lab test contributing to the confirmation of the professional etiology of the dermatitis (1). The pathogenic mechanisms could be too various, they could be IgE mediated as well as not related to IgE (1,5,7,8). The normal levels of IgE (they are tested to diagnose atopy) are also confirming the occupational etiology of the diagnosed allergic problems (1,5).

The professional etiology of contact dermatitis in the patient is based upon criterion of hygiene of labour, the positive patch test, the

positive elimination and exposure tests as well as the data in the medical documentation and medical history.(2,3,4,6).

### CONCLUSIONS:

1. The presented by us case shows that the allergic reactions in workers at manufactures with private character are not unlikely although they are rare.
2. The unknown physicochemical content of several used in the private manufactures materials causes difficulties when the diagnosis of some allergic reactions is concerned.
3. Regardless of the above mentioned circumstances the thorough knowledge of the pathogenic mechanisms of allergic reactions is a necessary condition for diagnosis and adequate treatment of such cases.

\*The photographic material is published with the written consent of the patient. Her personal data is protected by Bulgarian law and normative legislation of the University hospital.

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**ИЗКАЗАНАТА ПРИЗНАТЕЛНОСТ И ДЕКЛАРАЦИЯ ЗА КОНФЛИКТ НА  
ИНТЕРЕСИ НА СТАТИЯТА:**

**ASSISTANT PHARMACISTS' ROLE IN HEALTH PROMOTION: BULGARIAN  
NATIONAL SURVEY**

*ANGEL M. DZHAMBOV, DONKA D. DIMITROVA*  
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This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors. The authors did not participate in health promotion or practice related educational process of assistant pharmacists, do not have any relations with National Association of Bachelor Pharmacists and do not receive any benefits from conducting this study. Our interest in the topic is strictly scientific.

Грешката е допусната в ръкописа на авторите.

От редакционната колегия

The Bulgarian Medicine Journal, official edition of the Bulgarian Academy of Science and Arts, Science Division, Research Center for Medicine and Health Care is published in 4 issues per year. It accepts for publication reviews, original research articles, case reports, short communications, opinions on new medical books, letters to the editor and announcements for scientific events (congresses, symposia, etc) in all fields of fundamental and clinical medicine. The journal is published in English with exceptional reviews on significant topics in Bulgarian. The detailed abstracts and the titles of the articles, the names of the authors and institutions as well as the legends of the illustrations (figures and tables) are printed in Bulgarian and English. Bulgarian medicine is available online at the website of the Academy, publications section.

The manuscripts should be submitted in two printed copies, on standard A4 sheets (21/30 cm), double spaced, 60 characters per line, and 30 lines per standard page.

The size of each paper should not exceed 10 pages (up to 5 000 words) for original research articles, 12 pages for reviews (7 500 words), 3 pages for case reports, 2 pages for short communications, 4 pages for discussions or correspondence on scientific events on medical books or chronicles. The references or illustrations are included in this size (two 9x13 cm figures, photographs, tables or diagrams are considered as one standard page).

**The abstracts** are not included in the size of the paper and should be submitted on a separate page with 3 to 5 key words at the end of the abstract. They should reflect the most essential topics of the article, including the objectives and hypothesis of the research work, the procedures, the main findings and the principal conclusions. The abstracts should not exceed one standard typewritten page of 200 words.

Списание „Българска медицина“, издание на Българската Академия на Науките и Изкуствата, Отделение за наука, Научен център по медицина и здравеопазване, излиза в четири книжки годишно. „Българска медицина“ е достъпна онлайн на сайта на БАНИ, раздел издания.

В него се отпечатват оригинални научни статии, казуистични съобщения, обзори, рецензии и съобщения за проведени или предстоящи научни конгреси, симпозиуми и други материали в областа на клиничната и фундаменталната медицина. Списанието излиза на английски език с подробни резюмета на български и английски. Изключения се правят за обзорни статии по особено значими теми. Заглавията, авторските колективи, а също надписите и означенията на илюстрациите и в таблиците се отпечатват и на двата езика.

Материалите трябва да се предоставят в два еднакви екземпляра, напечатани на пишеща машина или на компютър, на хартия формат А4 (21 x 30 см), 60 знака на 30 реда при двоен интервал между редовете (стандартна машинописна страница). Освен това могат да бъдат изпратени като прикачени файлове по електронната поща на адресите, посочени по-долу.

Обемът на представените работи не трябва да превишава 10 стандартни страници за оригиналните статии (или 5000 думи според стандарта на англосаксонските издания) 12 страници (7 500 думи) за обзорните статии, 3–4 страници за казуистичните съобщения, 4 страници за информации относно научни прояви в България и в чужбина, както и за научни дискусии, 2 страници за рецензии на книги (монографии и учебници). В посочения обем се включват книгописът и всички илюстрации и таблици. В същия не се включват резюметата на български и английски, чий-то обем трябва да бъде около 200 думи за всяко

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**The basic structure** of the manuscripts should meet the following requirements:

### TITLE PAGE

The title of the article, forename, middle initials (if any) and family name of each author; institutional affiliation; name of department(s) and institutions to which the work should be attributed, address and fax number of the corresponding author.

### TEXT OF THE ARTICLE

#### **Titles and subtitles should be standardized.**

The original research reports should have the following structure: introduction (states the aim, summarizes the rationale for the study), subjects and materials, methods (procedure and apparatus in sufficient detail, statistical methods), results, discussion, conclusions (should be linked with the aims of the study, but unqualified statements not completely supported by research data should be avoided). These requirements are not valid for the other types of manuscripts. Only officially recognized abbreviations should be used, all others should be explained in the text. Units should be used according to the International System of Units (S. I. units). Numbers to bibliographical references should be used according to their enumeration in the reference list.

### ILLUSTRATIONS

Photographs should be presented both in the text body to indicate their location and in separate files as saved in jpeg, tif or bitmap formats.

The figures, diagrams, schemes, photos should be submitted in a separate file with: consecutive number (in Arabic figures); titles of the article and name of the first author. The explanatory text accompanying the figures should be presented along with the respective number of the figure in the main text body with space left for insertion of the figure.

(25–30 машинописни реда). Резюметата се представят на отделни страници. Те трябва да отразяват конкретно работната хипотеза и целта на разработката, използваните методи, най-важните резултати и заключения. Ключовите думи (до 5), съобразени с „Medline“, трябва да се посочат в края на всяко резюме.

**Структурата на статиите** трябва да отговаря на следните изисквания:

### ТИТУЛНА СТРАНИЦА

- а) заглавие, имена на авторите (собствено име и фамилия), название на научната организация или лечебното заведение, в което те работят. При повече от едно за ведение имената на същите и на съответните автори се маркират с цифри или звездички;
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**Забележка:** при статии от чужди автори българският текст следва английския. Точният превод от английски на български се осигурява от редакцията. Това се отнася и за останалите текстове, включително резюметата на български.

Основен текст на статията. Заглавията и подзаглавията следва да бъдат уеднаквени и различни.

Оригиналните статии задължително трябва да имат следната структура: увод, материал и методи, собствени резултати, обсъждане, заключение или извод.

Методиките следва да бъдат подробно описани (включително видът и фирмата производител на използваните реактиви и апаратура). Същото се отнася и за статистическите методи.

Тези изисквания не важат за обзорите и другите видове публикации. В текста се допускат само официално приетите международни съкращения; при използване на други съкращения те трябва да бъдат изрично посочени в текста. За мерните единици е задължителна международната система SI. Цитатите вътре в текста е препоръчително да бъдат отбелязвани само с номерата им в книгописа.

## REFERENCES

The references should be presented on a separate page at the end of the manuscript. It is recommended that the number of references should not

Exceed 20 titles for the original articles and 40 titles for the reviews; 70 % of them should be published in the last 5 years. References should be listed in alphabetical order, English first, followed by the Bulgarian ones in the respective alphabetic order. The number of the reference should be followed by the family name of the first author and then his/her initials, names of the second and other authors should start with the initials followed by the family names. The full title of the cited article should be written, followed by the name of the journal where it has been published (or its generally accepted abbreviation), volume, year, issue, first and last page. Chapters of books should be cited in the same way, the full name of the chapter first, followed by "In:" full title of the book, editors, publisher, town, year, first and final page number of the cited chapter.

### EXAMPLES:

Reference to a journal article:

1. McLachan, S. , M. F. Prumel, B. Rapoport. Cell Mediated or Humoral Immunity in Graves' Ophthalmopathy? J. Clin. Endocrinol. Metab., 78, 1994, 5, 1070-1074.

Reference to a book chapter:

2. Delange, F. Endemic Cretenism. In: The Thyroid (Eds. L. Braveman and R. Utiger). Lippincott Co, Philadelphia, 1991, 942-955.

## SUBMISSION OF MANUSCRIPTS

The original and one copy of the complete manuscript are submitted together with a covering letter granting the consent of all authors for the publication of the article as well as a statement that it has not been published previously elsewhere and signed by the first author. The procedure should be complemented via electronic submission. Manuscripts of articles accepted

## ИЛЮСТРАЦИИ И ТАБЛИЦИ

Снимките – освен в Word, за да се знае местоположението им, следва да бъдат предоставени и като отделни файлове във формат jpg, tif или bitmap.

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Книгописът се представя на отделен лист. Броят на цитираните източници е препоръчително да не надхвърля 20 (за обзорите до 40), като 70 % от тях да бъдат от последните 5 години. Подреждането става по азбучен ред (първо на латиница, после на кирилица), като след поредния номер се отбелязва фамилното име на първия автор, след това инициалите му; всички останали автори се посочват с инициалите, последвани от фамилното име (в обратен ред) до третия автор, последвани от съкращението А1. Следва цялото заглавие на цитираната статия, след него названието на списанието (или общоприетото му съкращение), том, година, брой на книжката, началната и крайната страница. Глави (раздели) от книги се изписват по аналогичен начин, като след автора и заглавието на главата (раздела) се отбелязват пълното заглавие на книгата, имената на редакторите (в скоби), издателството, градът и годината на издаване, началната и крайната страница.

for publication will not be returned to the authors.

Peer-review process: following the international standards in the field, the Editorial board has adopted double-blind peer-review policy assigned to independent referees. The authors are encouraged to submit the names of three potential referees for editorial consideration

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The editor is responsible for deciding which of the articles submitted to the journal should be published.

The editor may be guided by the policies of the journal's editorial board and constrained by such legal requirements as shall then be in force regarding libel, copyright infringement and plagiarism. The editor may confer with other editors or reviewers in making this decision.

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The editor and any editorial staff must not disclose any information about a submitted manuscript to anyone other than the corresponding author, reviewers, potential reviewers, other editorial advisers, and the publisher, as appropriate.

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The authors should ensure that they have written entirely original works, and if the authors have used the work and/or words of others that this has been appropriately cited or quoted.

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## **ПРИМЕРИ:**

Статия от списание:

1. McLachlan, S., M. F. Prumel, B. Rapoport. Cell Mediated or Humoral Immunity in Graves' Ophthalmopathy? J. Clin. Endocrinol. Metab., 78, 1994, 5, 1070-1074.

Глава (раздел) от книга:

2. Delange, F. Endemic Cretenism. In: The Thyroid (Eds. L. Braveman and R. Utiger). Lippincott Co, Philadelphia, 1991, 942-955.

## **АДРЕС ЗА КОРЕСПОНДЕНЦИЯ С АВТОРИТЕ**

Той се дава в края на всяка статия и съдържа всички необходими данни (вкл. електронна поща) на български език за един от авторите, който отговаря за кореспонденцията.

Всички ръкописи трябва да се изпращат с придружително писмо, подписани от авторите, с което потвърждават съгласието си за отпечатване в сп. „Българска медицина“. В писмото трябва да бъде отбелязано, че материалът не е бил отпечатван в други научни списания у нас и в чужбина. Ръкописи не се връщат.

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Proper acknowledgment of the work of others must always be given. Authors should cite publications that have been influential in determining the nature of the reported work.

Authorship should be limited to those who have made a significant contribution to the conception, design, execution, or interpretation of the reported study. All those who have made significant contributions should be listed as co-authors. Where there are others who have participated in certain substantive aspects of the research project, they should be acknowledged or listed as contributors.

The corresponding author should ensure that all appropriate co-authors and no inappropriate co-authors are included on the paper, and that all co-authors have seen and approved the final version of the paper and have agreed to its submission for publication.

#### **OBLIGATIONS OF THE REVIEWERS**

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**Ethical regulations:** reports with experiments on human subjects should specify whether the procedures were conducted in accordance with the ethical norms if the responsible committee on Human experimentation (local or regional) and/or with the Helsinki Declaration, as revised in 2000. Respective guidelines for animal experimentation should be considered.

#### **PROCESSING CHARGES**

Following acceptance for publication the authors are charged 5 euros per page for language editing and corrections.

#### **ADDRESS FOR SENDING OF MANUSCRIPTS AND OTHER EDITORIAL CORRESPONDENCE**

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phkumanov@lycos.com

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stojanovpisevski@gmail.com

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След положителна рецензия и одобрение на редколегията, авторите на статията дължат заплащане в размер на 10 лв. за всяка стандартна машинописна страница, с оглед на покриване разносните по английска езикова редкация на текста и коректури

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