

Review

From Assoc. Prof. Vessela Stoyanova Stoyanova, MD, PhD

Department of Psychiatry and Medical psychology, Medical University – Sofia

External member of the academic jury by order № P-109-217/25.05.22 of the Rector of Medical University- Varna

Regarding dissertation thesis “**Screening questionnaire application in the assessment of alcohol-using patients in a clinical sample**” for awarding the academic degree” Doctor of Philosophy” in the higher education field 7.1 Medicine to Svetla Milcheva Borisova, enrolled in a full-time PhD program “Psychiatry”, professional field 7.1 Medicine with order № P-109-56/01.02.2019 and completed the program with an approved proposal for thesis defense № P-109-217/25.05.2022.

This statement is prepared in accordance with the requirements of the Academic Staff Development Act of the Republic of Bulgaria and the Academic Staff Development Regulations of Medical University "Prof. Dr. Paraskev Stoyanov" – Varna for awarding the academic degree "Doctor of Philosophy".

Biographical data: Dr.Svetla Milcheva Borisova graduated with a master's degree in medicine and professional qualification as a medical doctor in 2002. During 2002-2006 she worked as a general practitioner. After that, from 2008 to 2012 she worked as a resident in the second psychiatric clinic of UMHAT "Sveta Marina" – Varna. Since 2013, after defending her specialty in Psychiatry, she held the position of a psychiatrist at the same institution. In 2019 she was appointed teaching assistant at the Department of Psychiatry and Medical Psychology, Medical University – Varna, and continued working as a psychiatrist at the abovementioned clinic of UMHAT "Sveta Marina" – Varna. Dr. Borisova actively participates in the diagnostic process, treatment, and expert consultations at the medical institution where she works. Since 2019, she was actively involved in the research and teaching activities of the Department of Psychiatry and Medical Psychology in Varna as a teaching assistant. In 2019 she was also enrolled in a Ph.D.

program at the same department. She had participated in several projects and trainings as part of different qualifications programs. Some of her specializations are related to methodology, analysis, and statistics in scientific research. She has 4 publications for 2013-2018, including in journals with an impact factor in co-authorship with reputable names in the field of addictions. She is also involved as a co-author in the creation of textbooks and manuals for nurses, students, and specializing physicians.

The structure of the dissertation is designed according to the requirements and contains 166 pages with 29 figures, 45 tables, and 4 annexes. It contains a literature review; aim, objectives, materials, and methods; results; discussion; conclusions, and contributions. The bibliographic reference comprises 156 sources, of which 16 are in Bulgarian and 140 are in English.

The synopsis is presented in 46 pages and reflects the dissertation accordingly. There is a technical error on the title page that is about to be corrected as the thesis is for the award of the academic degree "Doctor of Philosophy".

Relevance of the topic: alcohol is a psychoactive substance with significant health effects, and there is still no uniform internationally accepted control mechanism. The use of alcohol and its effects are considered to lie along a spectrum rather than categorically, with multiple psychosocial factors as well as cultural factors determining attitudes of the society toward alcohol use. In our country, according to the NCPHA, in a 2014 study, alcohol use was reported by 65.7% of the respondents, with $\frac{1}{4}$ of them using alcohol on a regular basis. At the same time, the effects of alcohol use are individually determined and should be examined from a biopsychosocial aspect. Often there is a denial of the problem, and the consequences are not only psychosocial but also somatic, involving considerable costs for diagnosis and treatment of complications. In this context, early identification (diagnosis) through reliable and convenient tools is essential to prevent the problem from worsening and preventing complications.

The literature review is presented in 45 pages and covers the different bio-psycho-socio-ethical aspects of alcohol consumption. Different patterns of use are discussed, as well as different definitions of 'acceptable alcohol consumption with the highest probability of reduced risk' of

adverse consequences. The literature review shows that there are substantial international differences in the recommendations developed for alcohol (daily/weekly consumption) associated with low health risk. Alcohol consumption is viewed from different perspectives, as a socially acceptable pattern of behavior, as a comorbid anxiety condition, as a risk factor for somatic problems, and as a brain disorder per se. The need for early identification and intervention when problem drinking is identified is discussed. The epidemiological aspects of alcohol use are also analyzed, respectively the social significance of the problem and the need for quantitative and qualitative assessment strategies. The impact of COVID-19 on levels of psychosocial distress and reinforcement of manifestations of maladaptive behaviors, including increased alcohol consumption, is also examined. In the literature review, attention is also paid to the various screening instruments for the problem, and to the AUDIT test, which has been translated into Bulgarian and used in this country but has not been validated to date. This fact as well as the importance of screening motivates the Ph.D. student's academic work.

The methodology of this study covers 8 pages

The aim is specific and is limited to the validation of the AUDIT screening questionnaire, which is used for the early identification of harmful alcohol use and alcohol dependence. The objective thus set is related to the accomplishment of two sets of tasks:

- Establishing the factor structure of the AUDIT screening instrument for the Bulgarian population
- Examination of the psychometric properties of the AUDIT questionnaire - external and internal validity.

Additional analyses are planned to demonstrate the screening value of the questionnaire relative to other alcohol use/dependence questionnaires. The main hypothesis is clearly formulated to confirm the three-factor structure of the AUDIT screening instrument, its high internal consistency, and its significant correlation with other screening questionnaires and also with Spielberger's Anxiety Inventory. I consider the analysis of only demographic factors (gender and age) and not socio-demographic factors such as education, family status, occupation, as well as the lack of consideration of the comorbidity factor with both mental and somatic illnesses, to be a weakness of the study.

Material and methods. The study is cross-sectional, and empirical with two groups - patients with harmful alcohol use and healthy controls. The patients were examined from 08-12.2020 at the Second Psychiatric Clinic of UMHAT "Sveta Marina", Varna. There is a second phase when patients were examined after 12 months. Demographic data was assessed and the following self-assessment questionnaires were administered - AUDIT; AUDIT-C (short version) and CAGE to assess alcohol consumption and Spielberg's anxiety inventory (STAI-T and STAI-S). Inclusion and exclusion criteria are clearly defined.

The statistical methods used to analyze the data are descriptive statistics; correlation analysis; internal consistency testing using Cronbach's alpha; exploratory factor analysis; identification of the factor structure of the AUDIT; sensitivity and specificity analysis of the methodology (ROC curve) and analyses to confirm the screening value of the scale in relation with other screening instruments.

The results are presented on 55 pages. A patient group of 33 individuals was formed, leaving 22 at the second follow-up stage. The main diagnoses were F10.1 (3 patients, 9.09%) and F 10.3 (30 patients, 90.91%). The mean age of this group is 43.52 (± 8.772) with two distribution peaks for age - around 40 years and after 55 years, with a male predominance (75.76%).

The control group consisted of 128 individuals with comparable mean age but is more homogeneous and with equal gender distribution. The patient group, in addition to the controls, is compared in relation to demographic parameters to a patient group of 242 individuals who underwent treatment in the same clinic in 2019 for sex and age comparison, and the study methodology does not describe that such a comparison will be conducted. The demographic parameters in the patient group are comparable to those of 2019. Comparative data and descriptive statistics are presented in both forms - tables and figures, which presents an unnecessary duplication of information. The screening instruments scores received are analyzed, there is a comparison by sex and age, there is a numeric assessment and assessment by proportion, and are presented in tables. Anxiety is assessed as both state and trait parameters in both study groups, with higher values found in the patient group without making it clear whether the differences are statistically significant. It is noteworthy that in both groups anxiety as a trait parameter has higher levels than state anxiety, despite the current pandemic situation in which

the study is conducted and it would be interesting to analyze this result. High reliability of the instruments used is assessed, with Cronbach's α within a range, for the control and patient groups respectively, from: 0.770 to 0.848 for AUDIT; 0.692 to 0.801 for AUDIT-C; 0.831 to 0.935 for STAI-S and 0.812 to 0.892 for STAI-T. A significant part of the results section is devoted to the correlation analysis, which demonstrated significant correlation coefficients, which in the patient group were most pronounced between state anxiety and trait anxiety, between the regular and short versions of the AUDIT, and between the two screening questionnaires AUDIT and CAGE. The correlation between the screening questionnaires in the control group was also pronounced and statistically significant. High test-retest reliability of the instruments used was also found after 12 months in 22 patients. It is not clear in the results discussed for what reasons 1/3 of the patients (11 individuals) dropped out.

All the conditions for conducting a factor analysis have been verified and confirmed. KMO (Kaiser-Meyer-Olkin) test for adequacy and Bartlett's test for specificity were used, making the results reliable and significant. The exploratory factor analysis, correlation and rotation matrices were applied to represent a modern statistical approach to confirm the three-factor structure of the AUDIT questionnaire and reject the two-factor structure.

The application of the ROC-analysis allows determining the sensitivity and specificity of the instrument used and of the first 3 questions of the AUDIT test in particular. High sensitivity and validity are demonstrated, with the highest sensitivity and validity for question 2, followed by questions 3 and 1.

The discussion is presented in 16 pages (disproportionate to the size of the results section covering 55 pages). The demographic results of the patient group are compared with the literature data. The results of the predominance of working-age individuals are highlighted, as is the wider involvement, of the male gender, but independent analyses and interpretations could be more comprehensive. Of interest is the lowering of the screening threshold for women. The usual threshold scores assessed by AUDIT are ≥ 8 . An important result that is analyzed and highlighted is that the two tools AUDIT and CAGE are comparable, but for women, the lower threshold value (≥ 5) yields a higher proportion of at-risk individuals. The three-factor model of AUDIT is confirmed and analyzed, forming the following factors: consumption; dependence; risky/harmful use. It is stressed that the short version of the questionnaire can replace the whole

questionnaire. Participants with harmful alcohol use and dependence showed higher scores on the anxiety assessment, raising the question of causal relationships in these conditions. The high sensitivity of the first three questions of the methodology is discussed, confirming its screening value in the Bulgarian sample examined. These results provide a basis for further studies of the sensitivity and specificity of the scale at different thresholds.

The conclusions and contributions reflect a realistic study design, the results obtained, and the author's analysis and discussion. There are 10 conclusions and 3 contributions that have more practical and theoretical applicability.

Dr. Borisova properly discusses several **limiting factors** that affect the study: the presence of a COVID-19 pandemic, which on the one hand is a limitation, but can be used in subsequent comparative studies by assessing the impact of the pandemic as a modifying factor; a small patient group within a relatively short period of patient inclusion; the overall sample is from the Varna region and is not nationally representative.

Research activity: In connection with the dissertation work Dr. Borisova presented three publications, in one, she is the only author and in the other- she is co-authored in a journal with impact factor.

In conclusion, the dissertation submitted in my opinion focuses primarily on screening for harmful alcohol use using the Alcohol Use Disorders Identification Test - AUDIT. There is a Bulgarian translation of the questionnaire available as the questionnaire has long been used in general practice, but without validation and without confirmation of its screening value. The validation of the AUDIT questionnaire for a sample in a Bulgarian population will allow for more accurate screening and comparability of results in relation to global standards. Its screening value, its comparability with other similar instruments, including the short 3-item version, as well as its high sensitivity and validity are indisputable results of this dissertation. These results have been objectified through the application of advanced statistical analyses, which make the obtained results reliable and of the great practical and theoretical value.

The comments and observations I have made do not substantially change the significance and credibility of the results presented.

Based on the above I believe that the dissertation submitted for my opinion on the topic “Screening questionnaire application in the assessment of alcohol-using patients in a clinical sample” meets the requirements of the Academic Staff Development Act of the Republic of Bulgaria and the regulations for its implementation as well as the Academic Staff Development Regulations of Medical University – Varna. I give a positive review and I propose to the members of the academic jury to vote in favor of awarding the academic degree "Doctor of philosophy" to Dr. Svetla Milcheva Borisova.

28.06.2022

Reviewer:

A handwritten signature in blue ink, consisting of a large, stylized initial 'V' followed by several loops and a final flourish.

Assoc. Prof. Vessela Stoyanova, MD, PhD