Review

By Prof. Snezha Zlateva Zlateva, MD, PhD

Of a PhD thesis for awarding the educational and scientific degree "Doctor of Philosophy" with candidate Dr. Svetla Milcheva Borisova

By the order of the Rector of the Medical University "Prof. Dr. Paraskev Stoyanov - Varna № P-109-217/25.05.2022 and by decision of the Faculty Council at the Faculty of Medicine of Medical University "Prof. Dr. Paraskev Stoyanov - Varna with Protocol № 1 I was elected chairman of the scientific jury and appointed to prepare a review regarding the degree "Doctor of Philosophy" awarding procedure of Dr. Svetla Milcheva Borisova.

Dissertation topic: "Screening questionnaire application in the assessment of alcoholusing patients in a clinical sample"

Field of higher education: 7. Healthcare and Sports

Professional division: 7.1. Medicine Scientific speciality: psychiatry

Scientific supervisor. Prof. Hristo Vassilev Kozhuharov, MD, PhD

PhD Program: Full time

Department of Psychiatry and Medical Psychology, Faculty of Medicine, Medical

University "Prof. Dr. Paraskev Stoyanov", Varna

Candidate: Dr. Svetla Milcheva Borisova

Reviewer. Prof. Snezha Zlateva Zlateva, MD, PhD

Dr. Svetla Milcheva Borisova has submitted all the necessary documents 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.

1. Biographical data:

Dr. Svetla Milcheva Borisova graduated with excellent grades from Medical University "Prof. Dr. Paraskev Stoyanov" – Varna in 2002. After graduation, she worked as a general practitioner, and later began specialization in psychiatry at the Department of Psychiatry and Medical Psychology at Medical University "Prof. Dr. Paraskev Stoyanov" - Varna. She worked first as a resident in 2008 and after 2013 till

2021 - as a psychiatrist at the Second Clinic of the Department of Psychiatry and Medical Psychology at "Sveta Marina" – Varna hospital. From 2019 she is a teaching assistant at the Department of Psychiatry and Medical Psychology at Medical University "Prof. Dr. Paraskev Stoyanov" - Varna.

Qualifications: specialty in psychiatry. Fluent in English and French. Very good computer skills.

Additional courses: trainings at the Department of Psychiatry and Medical Psychology – Medical University - Varna topics: "To develop brain science, to actively stimulate better treatment and to improve mental health" (2012), "Cognitive Disorders in Mental Disorders" (2013); Training at the College of Private Psychiatry Conference (2013); Postgraduate school in CNS, Istanbul, Turkey (2014); Humphrey Fellowship Program, USA (2017-2018) USA, RHAB 691 GR Counseling techniques class - Virginia Commonwealth University, USA (2017-2018), PSYC 671 GR Independent Readings and Research course - Virginia Commonwealth University, USA (2017-2018).), SPSS Training course, Virginia Commonwealth University, USA, (2018), Chief Resident Immersion Training, Boston Medical Center, USA (2018).

Teaching activities: Dr. Svetla Milcheva started teaching psychiatry (Programs in English) in 2019 to students (Medicine and Dental Medicine) at the Department of Psychiatry and Medical Psychology of Medical University "Prof. Dr. Paraskev Stoyanov" – Varna.

2. Relevance of the topic

The dissertation topic is based on the important and relevant issue of a validation of a screening questionnaire for alcohol use disorders. It focuses on the objective assessment of alcohol-related disorders and the need to use a validated methodology with established value in Bulgaria. The problem is topical and socially significant due to the alcohol consumption levels which are increasing in the country, the negative demographic trends, and the huge etiological and clinical diversity of alcoholrelated conditions. Patients with risky, harmful alcohol use and dependence seek medical care at all levels of the health care system from primary to hospital care and in every specialty. Such patients are hospitalized not only in psychiatric clinics, but also often undergo treatment in internal medicine, toxicology, gastroenterology, surgery, and neurology clinics. Doctors, as well as medical specialists of all specialties take care of patients with such problems. Therefore, objective assessment of alcohol intake is essential not only in treating patients with alcohol use disorders, but also in treatment of patient with underdiagnosed risky and harmful alcohol

Moreover, many patients with an alcohol problem deny its existence and thus make the diagnostic and treatment process more difficult.

The study subject is the use of alcohol, and the topic is focused on risky and harmful alcohol use and has a specific applied relevance - the validation of a screening test methodology for the identification of alcohol use disorders (AUDIT). The test has been used in Bulgaria for decades without any confirmation of its screening value. The presented work of the PhD student is an attempt to answer the question whether the above-described instrument is a valid screening questionnaire for alcohol use disorders in Bulgaria while the focus is maintained on both the use of alcohol (as current and significant problem) and the need for objective assessment and screening for risky and harmful alcohol use in Bulgaria.

3. Structure of the dissertation:

The dissertation covers 166 pages, contains 29 figures and 45 tables. The bibliography includes 156 titles, of which 16 titles are in Cyrillic and 140 - in Latin. Most of the cited sources are from recent years.

The dissertation is structured according to the classical model and includes: Table of Contents - 3 pages; Abbreviations - 1 page; Basic concepts - 3 pages; Introduction - 4 pages; Literature review - 46 pages; Methodology (aim, objectives and hypotheses, methods of data collection and analysis, description of the sample, organization and conduct, and limitations and restrictions of the empirical study) - 7 pages; Results - 56 pages; Discussion - 17 pages; Conclusions - 1 page; Contributions - 1 page; References - 16 pages; Appendices - 8 pages.

The literature review is a critical analysis of the sources used to justify both the significance of the issues and the elements included in the empirical study design. The relevance of issues is derived not only from data on increased alcohol use in Bulgaria in recent years (in pandemic context), but also from contemporary demographic trends in Bulgaria.

In the literature review, the relevance of the topic is based on data from national and international studies and is also related to the possibilities for follow-up interventions such as brief intervention based on screening for risky and harmful alcohol use. Some specific aspects are highlighted: definition of terms related to risky and low-risk consumption in Bulgaria; the estimation of alcohol intake in national surveys; fragmented data related to the prevalence of alcohol use disorders.

The making process of the AUDIT screening questionnaire, which is the focus of the dissertation, is investigated, with special attention paid to the lack of statistical analyses on the psychometric characteristics of the Bulgarian version of the questionnaire.

The literature review is relevant to the dissertation topic and provides well-presented and analyzed theoretical and research material. Major issues related to alcohol consumption and recommendations for global intake are examined.

The literature review includes the following areas: 1. Alcohol as a psychoactive substance; 2. The Standard drink concept; 3. Alcohol use spectrum and patterns; 4. The development process of the disorder - from alcohol use to dependence; 5. The anxiety impact on alcohol use in a pandemic context; 6. Epidemiological aspects related to alcohol intake; 7. Alcohol use disorders identification questionnaires; 8. Significance of the screening with the Alcohol Use Disorders Identification test and Interventions.

The Methodology section describes the aim and objectives of the study. The aim the study is clearly and precisely formulated and fully in line current psychometric trends. The aim is the AUDIT screening methodology validation for identification of cases of risky, harmful alcohol use and alcohol dependence. Thus stated, the aim directs to the solution of two main tasks related to the factor structure of the AUDIT questionnaire and the analysis of the validity of the questionnaire. The tasks are specific and precisely defined: to identify the factor structure of the AUDIT screening instrument for the Bulgarian population; to conduct external and internal validity analysis of the AUDIT questionnaire, as well as analyses to demonstrate the screening value of the questionnaire in relation to other questionnaires identifying alcohol use/dependence. Four hypotheses are defined suggesting: a factor structure of the questionnaire, relations between the questionnaire and other screening methodologies, high internal consistency of the questionnaire, and high sensitivity of the questionnaire.

The study included 161 participants aged 18-75 years, divided into two groups - a group of individuals with harmful alcohol use/dependence and a control group of healthy volunteers. The study was conducted between 2020 and 2022. Participants from the harmful use/dependence group were enrolled in the study in two phases (12 months between the first and the second phase). They were recruited from a group of patients hospitalized at the Second Psychiatric Clinic of the University Hospital "St. Marina" - Varna from August 2020 to November 2021. The patients were discharged from the hospital and exclusion criteria were related to the presence of withdrawal, delirium or psychotic symptoms. The participants of the control group were 128 individuals. Participants were included in accordance with the inclusion and exclusion criteria and were randomly selected.

Data collection methods included structured interview on demographic data, Alcohol Use Disorders Identification Test (AUDIT), CAGE questionnaire, Anxi ety Inventory.

Methods of statistical analyses included descriptive statistics, internal consistency – Cronbach's alpha, exploratory factor analysis, identification of the factor structure of the scale, sensitivity and specificity analysis of the methodology (ROC curve) and area

under the curve (AUC), reliability and validity assessment of the AUDIT questionnaire and correlation analyses.

Statistical analises were performed with statistical package SPSS - 19 and 21 - form for expert science. Factor analysis as well as sensitivity and specificity analyses of interest and illustrate a tendency towards the use of validated questionnaires in clinical practice, which are adapted to Bulgarian conditions.

The study has several limitations in relation to its duration and sample parameters it covers a period of one year and 4 months during an unprecedented pandemic situation on a global scale. The total number of individuals studied was 161, and both samples were randomly derived and randomised. However, the findings cannot be generalized due to the small sample size. The collected data provide information for conclusions about the validity of the test methodology inferred from the results of the derived psychometric characteristics. Future aspects related to standardization of the AUDIT test methodology will need data analysis from a larger nationally representative sample.

In the Results section, the following main aspects are addressed:

- •Descriptive statistics and distribution by age, sex (and diagnosis for the harmful alcohol use/dependence group) in the two groups compared to a larger patients' sample. The results obtained with the descriptive statistics method revealed many young persons hospitalized with an alcohol use disorder
- •Descriptive statistics and distribution according to results of screening questionnaires and anxiety questionnaires. The distribution according to the AUDIT, AUDIT-C and CAGE questionnaires in each of the groups, as well as anxiety inventory results, is discussed in detail.
- •Scale reliability analyses the results of internal consistency studies of the scales used are described
- ·Correlation analyses results of comparison between scales are described
- •Exploratory factor analysis was conducted, and ROC curves were derived with sensitivity and specificity analysis of the first three questions of the AUDIT scale.

The statistical methods used for analysis are interesting and illustrate a trend towards the use of validated questionnaires in clinical practice that are adapted to Bulgarian conditions. The description of the results in the groups could be arranged differently and could follow a pattern facilitating comparability of results. The Discussion section discusses the results obtained in several areas. A comparison between the two groups has been made. Comparisons with results from other studies of the psychometric properties of the scale are more sparingly described. The results obtained are described in a fragmented way and their comparability presents a difficulty that could be overcome with a more detailed description. However, the results obtained confirm and add to the knowledge on the AUDIT questionnaire for the

identification of alcohol use disorders and have great practical value. The conclusions are related to the results of the analyses conducted in descriptive statistics and distribution according to the results of the screening questionnaires for harmful use of alcohol and anxiety, the results of the analyses conducted on Cronbach's alpha coefficient, correlation analyses and factor analysis. The presence of young people hospitalized with alcohol use disorder in active working age is a finding regarding the significance of the topic.

4. Main scientific contributions

The contributions are clearly formulated and have mainly theoretical and practical aspect. The first two contributions related to the identification of the psychometric characteristics of the AUDIT screening questionnaire and its validation are of substantial importance. Similar studies have not been conducted in the country and for this reason I believe that they enrich the existing data regarding the Bulgarian version of the questionnaire.

The contribution in relation with the identified prevalence of alcohol use only affects the study sample.

5. Description and evaluation of the submitted materials:

Dr. Svetla Milcheva presents 3 publications published in recognized scientific journals. In one of the publications (closely related to the topic of the dissertation) she is the only author, which according to the Regulations for the Development of the Academic Staff of Medical University-Varna gives her the required score, the criteria indicators in the Regulations for the Development of the Academic Staff of the Medical University-Varna for the Degree of "Doctor of Philosophy" award are met. The summary is prepared in accordance with the requirements, includes only the main results of the research and contains 12 figures and 19 tables.

6. Critical Notes:

The description of the results in the groups could be arranged differently and could follow a pattern facilitating comparability of results.

Conclusion:

The dissertation on "Screening questionnaire application in the assessment of alcoholusing patients in a clinical sample" is topical, has a contributory theoretical and practical aspect and directs attention to the objective assessment of alcohol consumption and the possibilities to apply screening questionnaires with proven screening value in the country. Basic concepts related to alcohol use as a current and significant problem, spectrum and patterns of use are discussed with special attention paid to low-risk consumption as a basis for future preventive strategies, which is underestimated in our country. The dissertation is aimed at improving the possibilities for objective assessment of alcohol consumption against the background of data from national and global surveys and in the light of contemporary demographic trends in Bulgaria.

The presented work satisfies the requirements of the Law on the Development of Academic Staff in the Republic of Bulgaria and the Regulations for its implementation, as well as the requirements of the Regulations for the Development of Academic Staff at Medical University-Varna for the PhD degree acquisition.

I express my positive evaluation of this dissertation of Dr. Svetla Milcheva. I recommend the distinguished members of the scientific jury to vote in favor of awarding the degree of "Doctor of Philosophy" to Dr. Svetla Milcheva Borisova in the field of higher education 7. Healthcare and Sports, professional division 7.1. Medicine, scientific specialty "Psychiatry".

Date: 30.06.2022

Reviewer: Juzuner

Prof. Dr. Snezha Zlateva