

REVIEW

by

Prof. Radost Spiridonova Asenova, MD, DMSc

Department of Urology and General Practice, Faculty of Medicine,
Medical University - Plovdiv

Dissertation submitted for the award of the educational and scientific degree "Doctor"
professional field 7.1. Medicine,
scientific specialty "General Medicine"

Author: **Dr. Daniela Krasimirova Kostadinova**

Department: **"General Practice"**, Faculty of Medicine, Medical University "Prof. Dr. Paraskev Stoyanov" - Varna

Topic: **Management of patients with alcohol dependence in general practice**

Form of doctoral studies: **part-time**

Scientific supervisor : **Assoc. Prof. Zhenya Ruseva, MD, PhD**

The review was prepared in accordance with Order No. P-109-287/11.07.20 25 of the Vice-Rector of MU-Varna.

General presentation of the procedure and the PhD student

According to Order No. 109-287/11.07.2025 of the Vice-Rector of the Medical University - Varna and Protocol No. 1/15.07.2025 of the meeting of the Scientific Jury, I was elected as its external member with a commitment to prepare a review of the dissertation work of Dr. Daniela Krasimirova Kostadinova. The presented set of materials, provided in electronic and paper format, is in full compliance with the Regulations for Academic Development at the Medical University "Prof. Dr. Paraskev Stoyanov" - Varna and includes all required documents necessary for the procedure.

Dr. Daniela Krasimirova Kostadinova was born in 1990 in the town of Razgrad. She completed her secondary education at the "Acad. Nikola Obreshkov" High School of Natural Sciences and Mathematics in her hometown, and in 2015 she graduated as a doctor at the "Prof. Dr. Paraskev Stoyanov" Medical University - Varna. In May 2019 she obtained a specialty in

"General Medicine". In the period from February 1, 2023 to March 31, 2025 she is a part-time PhD student at the Department of General Medicine of the Medical University - Varna.

She began her professional career as a resident physician in the Emergency Department of the St. Ivan Rilski Hospital in Razgrad, and later worked as a consultant at the Dr. Velkovi Medical Center and a resident physician at the Emergency Medical Care Center in Razgrad and at the branch in Ispereh. From 2017 to the present, she has been a manager and general practitioner at Daniela Medica - APHC - IP Ltd in Razgrad.

Dr. Kostadinova has numerous additional professional qualifications in the fields of emergency medicine, ultrasound diagnostics, homeopathy, nutritional and integrative medicine. She has participated in a number of national and international scientific forums and trainings, as well as in specialized seminars and conferences in general medicine, emergency medicine, cardiology and oncology. Her scientific career began as a student with participation in scientific sessions and conferences, and subsequently continued actively with publications and reports.

She has been honored many times for her academic and professional achievements - she is the recipient of the "Outstanding Student of the Class of 2015" plaque from MU - Varna, the "Young Doctor" award (2017) from the Bulgarian Medical Union, as well as the "Worthy Doctors" award (2019).

Dr. Daniela Krasimirova Kostadinova is a member of EURACT – European Academy of Teachers in General Practice and Family Medicine, and is actively involved in the development of primary care in both clinical, research and teaching aspects.

Relevance of the topic

The topic of the dissertation is undoubtedly relevant for primary health care, as it concerns a significant medical and social problem with a direct practical focus. Bulgaria is among the countries with an unfavorable trend in terms of alcohol consumption, with an increase in recent decades and high indicators of alcohol-related morbidity and mortality. This justifies the need for scientific studies aimed at developing specific measures for early detection and effective monitoring of patients within the framework of general practice. Alcohol dependence remains one of the leading health and social problems of the 21st century, with a distinct global burden and regional characteristics. According to data from 2019, nearly 2.6 million deaths in the world are associated with harmful alcohol use, with about 25% of them affecting the age group 20–39 years. In Europe, the number of addicts is estimated at about 23 million, and the socio-economic damage amounts to tens of billions of euros annually. Against this background, the role of the general practitioner is key - screening, early recognition, and the implementation of

brief interventions have been proven to be applicable in general practice and can significantly improve the prognosis when applied consistently.

Understanding of the problem

Dr. Daniela Krasimirova Kostadinova demonstrates in-depth knowledge of the Bulgarian and international experience in the researched issue, presenting an analytical assessment of the available scientific information. The literature review shows knowledge of the problem in its historical, etiopathogenetic and clinical perspective. Definitions and criteria according to ICD-10 and DSM - IV /5 are presented, distinctions between risky use, abuse and dependence, as well as concepts of tolerance, withdrawal and neuroadaptation with an emphasis on the role of the mesocorticolimbic system and dopamine pathways. The biopsychosocial model and various typologies are examined, seeking a connection between individual, family, cultural and genetic factors and the development of chronic alcohol disease. Epidemiological data are presented - global and national trends, risk groups, social and economic consequences - compared with clinical manifestations: from intoxication and withdrawal to psychosis, cognitive disorders and somatic damage (liver, cardiovascular, etc.). Particularly valuable is the focus on diagnostic and screening approaches – questionnaires, biological and imaging methods – as well as the clearly outlined role of GPs in prevention, early referral and long-term follow-up, which directly justifies the research goal of the dissertation.

Characterization and evaluation of the dissertation work and contributions

Structurally, the work strictly follows the academic requirements for a dissertation: a clearly developed introduction, literature review, aim, tasks and working hypotheses, materials, design and methods, own results, discussion, conclusion, findings, contributions, applications and a list of publications and literature. The content is consistently and logically arranged, which makes it easier to follow the argumentation and verification of scientific statements. The text is scientifically and stylistically sound, with good terminological unity and correct use of abbreviations. There is a rich illustration through figures and tables, especially in the sections with results, where graphic representations help to understand trends and interrelationships. The bibliography includes a wide range of sources in Cyrillic and Latin, which testifies to a thorough knowledge of the international and national context. The total volume is over 140 pages, which

corresponds to the scale of the research task and allows for a full presentation of the data and interpretations.

The main goal is formulated clearly and practically: to establish the frequency of risky alcohol consumption, assess physical and mental impairments, and develop a model for monitoring and medical examination of risky and dependent individuals within the framework of general practice. Specific tasks logically arise from the goal – from determining the level of consumption and its relationship with age and gender, through assessing psychosomatic and social harms, to validating a combined screening approach and creating a practical algorithm for medical examination. The formulated thesis and working hypothesis are consistent with the goals and address a current gap in the practice of the general practitioner.

The design of the study is adequate and precisely aligned with the set goals and objectives. A population-based survey was conducted in primary care with a large sample of 610 individuals over 18 years of age, divided into seven age groups (18–24, 25–34, 35–44, 45–54, 55–64, 65–74 and over 75 years). The recruitment of participants was carried out during the preventive annual examinations at the primary care outpatient clinic "Daniela Medica - APHC - IP" in the city of Razgrad, which guarantees representativeness of different gender, age and social groups.

The study covers several main areas: socio-demographic characteristics (gender, age), specifics of alcohol consumption, laboratory data (ASAT, ALT, GGT) and ultrasound diagnostics of the liver. The combination of these measures – questionnaire, biochemical and instrumental – ensures triangulation of evidence and increases the reliability of the results. The specialized questionnaire used contains 14 closed questions, based on AUDIT and adapted to the Bulgarian population, which guarantees cultural relevance and high applicability in general practice.

Clinical and laboratory examinations were conducted using standard methods, and the ultrasound examination was performed with a Sonofine device EUS B, which allows high accuracy in assessing liver structure. All ethical standards were met, and the study was approved by the Ethics Committee.

IBM was applied for the analysis and interpretation of the data. SPSS Statistics v .19. In addition to descriptive statistics (frequencies, means, standard errors and deviations), cross-tabulations, association coefficients, statistical hypothesis tests, correlation analysis, as well as reliability and validity assessment (Cronbach's α , factor analysis) were performed. The results

are richly illustrated with tables and graphs, which facilitates their practical interpretation and increases their accessibility for general practitioners.

The methodology is consistent and comprehensive, allowing for both an objective assessment of the extent of alcohol consumption and validation of the proposed combined screening procedure. This makes the dissertation a significant contribution to clinical practice.

The results obtained cover the full spectrum of the tasks set and are presented in detail in the sections for descriptive and correlation analysis, reliability and validity testing, as well as in the development of an own model. A high relative share of risky and problematic use was established among the studied population (over one third of the participants showed deviations according to the questionnaire), with men in the active age group (30–49 years) standing out with significantly higher values compared to women. Statistically significant relationships were found between high alcohol consumption and laboratory indicators – increased levels of ASAT, ALT and GGT, as well as ultrasound changes in the liver, found in a significant part of patients with risky use. In addition to somatic damage, the analysis also shows the presence of psycho-emotional and social problems, more often registered in dependent patients compared to control groups.

The data are illustrated by more than twenty tables and figures that systematically present the distributions by gender and age, laboratory values, questionnaire results and correlations between them. This visual layout increases the evidentiary value of the study and facilitates its practical use by general practitioners. The discussion is analytical and in-depth, comparing the own data with the available international literature: it confirms the global trend for an increasing frequency of abuse among young people and at the same time emphasizes national specificities – higher consumption rates in Bulgaria and a distinct association with liver damage. All this gives the work not only theoretical, but also significant practical value, as the results clearly outline the need for routine screening and early follow-up within primary care.

The conclusions are clearly formulated, consistent and directly related to the results. It is striking that the author does not limit himself to descriptive findings, but proceeds to prove the strong correlation dependence in the simultaneous use of a screening questionnaire, liver enzymes and ultrasound diagnostics for detecting abuse and dependence, and on this basis develops an algorithm for long term care with high practical and applied value. The number of conclusions is six and they cover the key axes of the study – frequency, gender and age

differences, health and social impairments, screening efficiency and organizational model of follow-up.

The contributions are clearly formulated and have an original and applied character. For the first time in our country, an original complex methodology for screening for alcohol abuse and dependence in general practice has been developed, including an original questionnaire with a rating scale adapted to the national context, and an empirically supported algorithm for follow-up and long term care. The statistically reliable effectiveness of the proposed combined procedure has been proven. These contributions are immediately transferable in the daily work of the general practitioner and can support the systematic introduction of routine screening, early referral and coordinated follow-up of at-risk patients.

In conclusion, the dissertation work is scientifically correct, methodologically consistent and practically significant. Dr. Krasimirova demonstrates a thorough analysis of the problem, skillfully combines quantitative and qualitative risk measures and offers a working model for the management of patients with alcohol dependence in general practice. I accept the scientific contributions presented.

Assessment of the publications and personal contribution

In connection with the dissertation work, Dr. Daniela Krasimirova Kostadinova has presented three publications in national peer-reviewed journals - in "General Medicine", "GP News - Gastroenterology" and "Science Endocrinology", in all of which she is the first author. They are closely related to the goals and objectives of the dissertation and cover the main areas of research: the pilot empirical study, the metabolic-biochemical and nutritional aspects of alcohol dependence. Scientific activity is complemented by participation in reports at specialized forums, where the author has presented the results to a professional audience and sought feedback for practical application.

The personal contribution of the doctoral student is clear – from the conceptualization of the study, the development of an original questionnaire and clinical charts, through the organization and conduct of the field study with a large sample and combined methods (survey, biochemistry, ultrasound), to the statistical processing and analytical interpretation of the results. On this basis, an original algorithm for screening and dispensary assessment of patients with risky alcohol use and dependence has been proposed, which is of high practical value for general practitioners. The publications and scientific presentations convincingly reflect the

independent work and significant personal contribution of Dr. Krasimirova to the researched issues.

Abstract

The abstract for the dissertation is formatted according to the requirements and objectively reflects the main results of the dissertation.

CONCLUSION

The dissertation work of Dr. Daniela Krasimirova Kostadinova represents a complete, original and scientifically based study, which contains clearly defined contributions in the field of general practice and has high practical value. The work is in full compliance with the requirements of the Law on the Development of Academic Staff in the Republic of Bulgaria, the Regulations for the Implementation of the Law and the Regulations of MU - Varna. The presented materials and results demonstrate in-depth knowledge of the problem, skillful application of modern research methods and a systematic approach to the analysis and interpretation of data. I believe that a scientific study has been conducted on a current and socially significant problem in general practice, and clear conclusions and recommendations have been formulated with direct applicability for general practitioners.

Because of the above, I give my convinced positive assessment of the dissertation work, the abstract, the achieved results and the contributions, and I propose to the esteemed scientific jury to award the educational and scientific degree "Doctor" to Dr. Daniela Krasimirova Kostadinova in the scientific specialty "General Medicine", professional field 7.1. Medicine, field of higher education 7. Health Care and Sports.

20.08.2025

City of Plovdiv

Reviewer:

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§1, б. „Б“ от Регламент (ЕС)
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Prof. Radost Spiridonova Asenova, MD, DMSc

Department of Urology and General Practice

Faculty of Medicine, Medical University of Plovdiv