REVIEW

Medical faculty (MF) - Sofia University "St. Kliment Ohridski" and MF – Medical University (MU) of Plovdiv, member of the scientific jury according to Order No. R-109-301/ 07.06.23 of the Medical University "Prof. Dr. Paraskev Stoyanov" - Varna and on the basis of Protocol No. 1/16.06.2023 of the first meeting of the scientific jury

REGARDING: Defense of the dissertation work of ***Dr. Alexandra Krasimirova Yankova-Aleksieva***, for the award of the educational and scientific degree **"Doctor"** in the field of higher education 7. "Health and sports", professional direction 7.1. "Medicine", scientific specialty " Occupational Diseases" at the Prof. Dr. Paraskev Stoyanov Medical University - Varna, on the ***topic " Shift Work Sleep Disorders"*** with scientific supervisor *Prof. Dr. Veselinka Dimitrova Nestorova, MD.*

I. Defense procedure

According to the order of the Rector of the MU "Prof. Dr. Paraskev Stoyanov" - Varna No. R-109-301/ 07.06.23, considering report with entry No. 102-1078/ 02.05.2023 by Prof. Dr. Zornitsa Zlatarova-Angelova, MD - Head of the Department "Optometry and Occupational Diseases", with decision under Protocol No. 206/ 23.05.2023 of the Faculty Council and Report with entry No. 104-576/ 01.06.2023 by Prof. Antonia Dimova-Yordanova, MD - Dean of the Faculty of Public Health at the MU "Prof. Dr. Paraskev Stoyanov" - Varna, I have been appointed as a member of the Scientific Jury for the preparation of a review of the dissertation work of Dr. Alexandra Krasimirova Yankova-Aleksieva - PhD student in full-time study.

This review is in accordance with the requirements of the Law on the Development of the Academic Staff of the Republic of Bulgaria, the regulations for its application and the Regulations for the Development of the Aacademic Staff at the MU - Varna.

According to the procedure for the defense of the dissertation, Dr. Alexandra Krasimirova Yankova-Aleksieva has submitted all the necessary materials.

Dr. Alexandra Yankova has successfully passed the exam to cover the doctoral minimum in the specialty "Occupational Diseases" and in a foreign language.

She has the required ORCID registered profiles with ORCID ID: https://orcid.org/0000-0002-6293-9625, with Google Scholar at the Internet address:https://scholar.google.com/citations?view_op=list_works&hl=en&user=flFw6goAAAAJ and with Researchgate at the Internet address: https://www.researchgate.net/profile/Aleksandra-Yankova.

Information maps of the National Center for Information and Documentation (NACID) have been created in Bulgarian and English (on electronic media - flash memory) in Word.

The scientific study was approved by the Research Ethics Committee at the MU-Varna.

The dissertation work has been approved and referred for defense by the faculty council of the Department of Optometry and Occupational Diseases at the Medical University "Prof. Dr. Paraskev Stoyanov" on April 20, 2023.

II. Brief biographical data and professional qualifications

Dr. Alexandra Krasimirova Yankova-Aleksieva was born on 25/08/1991 in the city of Ruse, where she completed her secondary education at the "St. Konstantin-Kyril

the Philosopher" in 2010. In 2016, she graduated with honors from the MU - Varna as a "Master" in the specialty "Medicine" (Diploma for higher education OKS "Master", MUV series No. 002964, Reg. No. 004344/ 11.11.2016), and in 2023 acquired a specialty in "Nervous Diseases" (Specialty Certificate No. 4839, Reg. No. 025995/10.02.2023).
Dr. Yankova began her professional career as a resident physician in the Second Neurology Clinic of Sveta Marina UMBAL EAD - Varna in October 2016. Since May 2018, she has been a physician specializing in "Nervous Diseases" and a regular assistant at the Department of Occupational Diseases, Department of Optometry and Occupational Diseases, MU - Varna, and since 2019 she is also a full-time doctoral student at the Department of Occupational Diseases.
Her main professional and scientific interests are in the field of sleep disorders, cerebrovascular diseases, electromyography and neurological complications of occupational diseases.
She is fluent in written and spoken English and Russian.
Her good theoretical and practical knowledge in the field of neurology and occupational diseases she applies daily in her practice as a doctor and teacher.
She has good teamwork, communication and organizational skills.
She is a member of the Bulgarian Medical Union, the Bulgarian Society of Neurology and the European Stroke Organization.

III. Publications and scientific activity

Dr. Alexandra Krasimirova Yankova-Aleksieva is the author of 3 full-text scientific publications, 2 of which in Bulgarian periodicals on the problem of her dissertation work and 1 in the Electronic Journal of General Medicine - an English multidisciplinary peer-reviewed medical journal. She is the lead author of all three publications and therefore has a major role in carrying out the research, preparing and producing the publications and presenting the scientific results in the scientific articles. Two of the publications are in 2022 and the third in 2023, which shows the topicality of the subject.
Also attached are 4 dissertation-related active participations in scientific forums, 3 of which were presented at national congresses with international participation, in which she was the third author, and 1 - at an anniversary scientific conference as a leading author.

IV. Structure of the dissertation

The dissertation presented for review is structured according to the accepted standards of a dissertation for obtaining the scientific degree "Doctor" and according to the requirements specified in the Regulations for the Development of the Academic Staff of the MU - Varna. It was developed in a volume of 114 standard pages in eleven sections with an adequate ratio: introduction (1 page), literature review (34 pages), aim and tasks (1 page), material and methods (3 pages), results (45 pages), discussion (5 pages), conclusions (1 page), contributions (1 page), literature (9 pages), publications and scientific events related to the dissertation work (1 page), appendices (9 p.). It is illustrated with 46 figures and 13 tables and contains 4 appendices.
The bibliographic reference consists of 198 sources, of which 4 are in Cyrillic and 194 are in Latin. About 50% of the citations are from the last ten years, and 30% - from the last five years.

V. Relevance of the dissertation work

An increasing number of workers are employed and work unusual hours with non-standard work time, which include shift and night work, extended work shifts, weekend work, variable working hours, etc. These trends cover 76% of the workforce in the European Union, according

to data from the European Foundation for the Improvement of Living and Working Conditions. Shift work is associated with a number of specific physiological, health and social problems for the individual. Changes in circadian biological rhythms are one of the most important physiological problems in shift work, they deepen with the number of consecutive night shifts, they have an adverse effect on the duration and quality of sleep. According to data from the International Classification of Sleep Disorders, 2-5% of shift workers suffer from shift work sleep disorder with manifestations of insomnia and/or excessive sleepiness on non-working days as well. These workers have an increased risk of a number of socially significant diseases - cardiovascular, diabetes mellitus, metabolic, gastrointestinal, depression, reproductive, etc.
That is why studies of sleep quality and disorders and the effect of sleep disorders on the health status of shift workers are relevant, important and necessary for successful prevention, early diagnosis, timely therapy and their adequate control, they are a significant modern problem.
The relevance of the dissertation also lies in the insufficiently clarified role of the risk factors of the work environment in the etiology and pathogenesis of sleep disorders during shift work.

VI. Literature review

Dr. Yankova-Aleksieva has made a multifaceted and in-depth literature review, logically structured, presented in 34 standard pages. She presented in depth and sufficient concreteness the experience of others on the problem, which testifies to a very good awareness of sleep disorders and shift work sleep disorders. The various sleep disorders, their characteristics, etiology and conditioning by the shift work regime are indicated. Chronic illnesses have been described during shift work, which further increase the risk of developing sleep disorders. The various possibilities for diagnosis and follow-up of sleep disorders are comprehensively presented. The vast amount of information has been skilfully synthesized and analyzed, highlighting controversial and poorly clarified issues.
The literature review shows knowledge of the essence of the problem by the doctoral student, who creatively and critically evaluated the literature data.

VII. Aim and tasks

The analysis of the literature data allows to logically formulate, in accordance with the world scientific research in this direction, a clear scientifically based goal of her work and the resulting five specific well-defined tasks necessary to achieve the added goal.
Five substantiated scientific hypotheses are also formulated upon which to build her research.

VIII. Materials and methods

One hundred workers without sleep disorders were studied, of which 50 had a shift work schedule for $\geq$ 2years and 50 had a regular schedule from 9:00 a.m. to 5:00 p.m., a control group. The Pittsburg Sleep Quality Index (PSQI), Insomnia Severity Index (ISI) and Epworth Sleepiness Scale (ESS) were used to assess sleep quality and the presence of insomnia and excessive sleepiness with high reliability, respectively.
In order to objectify sleep disorders, a polysomnographic study was performed, through which the duration, latency and efficiency of sleep, number of awakenings, Apnea-Hypopnea Index and number of periodic movements of the lower limbs were determined.
Variation, alternative, correlation and graphic analyses were applied for statistical processing of the obtained results by means of the software programs SPSS and GraphPad Prism, allowing a full analysis and reliable evaluation of the data.
The methods used are modern, adequate, informative and reliable for the assessment of sleep disorders during shift work.

IX. Main results and contributions

The results obtained from Dr. Yankova's research corresponded to the tasks set. They were presented clearly, illustrated very well with figures and tables.

The two research groups were matched in terms of gender and age, and without significant differences in terms of education and length of service of the last occupation. The relative share of workers with mainly mental work was reliably higher among those with a shift work regime, resp. the relative share of workers with mostly physical labor was significantly higher among those with a regular work regime. Self-reported stress at work was significantly higher among shift workers. There were no significant differences regarding the presence of chemical, physical and biological risk factors in working conditions between the two groups.

Shift workers subjectively had significantly more impaired general condition and chronic diseases at an earlier age than controls, requiring frequent absence from work. Arterial hypertension was found in both groups without a significant difference, the carrier of the share of dyslipidemias and disc herniations at different levels of the spine was significantly higher among shift workers. No significant difference was found between the groups regarding the established other chronic diseases – bronchial asthma, chronic obstructive pulmonary disease, gastroesophageal reflux disease, gastritis, nephrolithiasis, gout, arthrosis, stroke, anxiety disorder, depression.

In the case of shift workers, reliable disturbances in the quality of sleep and sleep indicators were found at a significantly earlier age, increasing with the duration of work experience with a shift mode - reduced total sleep duration; shorter sleep latency, indicative of the presence of excessive sleepiness not only with a shift work regime, but also with available physical, chemical and biological occupational risk factors; lower sleep efficiency (ratio between total sleep time and time spent in bed trying to fall asleep); higher number of awakenings during the somnographic recording; more frequent periodic movements of the lower limbs. The relative share of workers with "poor quality" of sleep and with $\geq$10 years of shift work experience was the highest ($p=0.05$). Only shift work had a significantly increased relative risk for poor sleep quality compared to all other occupational risk factors.

Shift workers reported a significantly earlier bedtime on their non-working days compared to controls, as well as a significantly shorter time falling asleep, confirming the presence of excessive sleepiness even on days off. In workers with a shift work schedule, waking up significantly earlier than desired on days off, reduced number of hours of sleep with sleep deprivation from 1 to 3 hours, reduced sleep efficiency and increased number of awakenings, manifestations of insomnia with difficult maintenance of sleep were found.

In the discussion, Dr. Yankova-Aleksieva has compared her own results with those in modern specialized literary sources, emphasizing the novelties, differences and corroborating data established by the research in her dissertation work.

She has made five specific conclusions that accurately reflect the results of the conducted research and fully meet the set goals and objectives, each separately and in summary.

I accept the scientific-theoretical and scientific-practical contributions made by the doctoral student herself - for the first time in our country an in-depth study has been carried out on the quality of sleep and the presence of sleep disorders in shift workers, on the influence of the shift work schedule on health status of workers and occupational risk factors on sleep quality in shift workers.

Of a confirmatory nature are the findings among workers with a shift work regime: reduced sleep quality, increasing sleep disorders with age, deteriorated health status and existing chronic diseases.

The working scientific hypotheses, defined tasks and the summaries of the obtained results laid down in the dissertation work are original and authentic.

The dissertation is an original contribution of a scientific-theoretical and scientific-applied nature and enriches science and clinical practice.

X. The abstract is structured in accordance with the requirements, its content fully corresponds to the dissertation work, 46 figures and 13 tables are presented to illustrate the results obtained from the scientific research. It also contains 4 applications.

XI. Publication activity

The 3 articles published in connection with the dissertation work meet the quantitative criteria specified by the Law on the Development of the Academic Staff of the Republic of Bulgaria and the internal regulations of the MU - Varna for the publication activity of the doctoral student.

The published articles on the subject of the dissertation meet the recommended scientometric criteria of the MU - Varna for awarding the scientific degree "Doctor".

XII. Conclusion

The dissertation work of Dr. Alexandra Krasimirova Yankova-Aleksieva is on the current topic of shift work sleep disorders, it is developed thoroughly and comprehensively, it presents scientific and scientific-applied results and conclusions with an original contribution to science and meets all requirements of the Law on the Development of the Academic Staff of the Republic of Bulgaria, the Regulations for the Development of the Aacademic Staff at MU - Varna.

The dissertation shows that the doctoral student Dr. Alexandra Krasimirova Yankova-Aleksieva possesses in-depth theoretical knowledge and professional qualities and skills for independent conducting of scientific research.

All this gives me sufficient reason to confidently give my **positive assessment** of the peer-reviewed dissertation work and to suggest to the respected members of the honorable scientific jury to give their **positive vote** for awarding Dr. Alexandra Krasimirova Yankova-Aleksieva an educational and scientific degree „Doctor“ in the field of higher education 7. "Healthcare and sports", professional direction 7.1. "Medicine", scientific specialty "Occupational diseases" at Medical University "Prof. Dr. Paraskev Stoyanov" - Varna.

04/07/2023

Prepared the review:

Prof. Dr. Zlatka Stoineva-Paskaleva, MD,
member of the Scientific Jury