

To the Chairman of the Scientific Jury,  
By Order No. R-1436/20.03.2025  
To the Rector of the Medical University, Plovdiv

Attached: Review  
By Prof. Dr. Stoyanka Vladeva, MD

On the competition for awarding the educational and scientific degree "Doctor" in the field of Higher Education 7. Health and Sports, professional field 7.1. Medicine, under the doctoral program "Rheumatology"

Contact address:

Prof. Dr. Stoyanka Vladeva, MD

Thracian University, Stara Zagora, Faculty of Medicine

Stara Zagora, ul. "Armeyska" № 11

E-mail: stoyanka.vladeva@trakia-uni.bg

The review was prepared in connection with the procedure for awarding the ONS "Doctor" to Dr. Aleksandar Marinkov, PhD student in independent training at the Department of "Propaedeutics of Internal Medicine "Prof. Dr. Anton Mitov", Faculty of Medicine, Medical University - Plovdiv with a dissertation on the topic: "SPREAD AND CLINICAL SIGNIFICANCE OF COVID-19 INFECTION IN PATIENTS WITH RHEUMATOLOGICAL DISEASES IN BULGARIA" with scientific supervisor: Prof. Dr. Rositsa Karalilova, MD and Scientific Consultant Prof. Dr. Rositsa Dimova, MD, MU-Plovdiv, Faculty of Public Health, Department of "Health Management and Health Economics"

The review was prepared in accordance with the requirements of the Law on the Administration of Health and Welfare of the Republic of Bulgaria, the Regulations for its implementation and the Regulations for Academic Development of MU-Plovdiv.

## I Education and Qualifications

Dr. Aleksandar Marinkov was born on September 19, 1988 in the city of Dimitrovgrad, Serbia. In 2007 he graduated with honors from the MU "Dr. Milenko Hadžić", and in 2013 he graduated from the Medical University of Plovdiv. Since 2018, he has won a competition for an assistant professor at the Department of Propaedeutics of Internal Medicine, Faculty of Medicine, Medical University - Plovdiv. Since 06.04.2022, he has been enrolled in doctoral studies of independent preparation with the supervisor Prof. Dr. Rositsa Karalilova, MD in the same scientific unit.

Dr. Marinkov has acquired a clinical specialist in "Rheumatology" since 2018. He currently works as a rheumatologist at the Clinic of Rheumatology, University Hospital "Kaspela" in Plovdiv with the Head Prof. Dr. Anastas Batalov, MD.

## II. Relevance of the topic

The global COVID-19 pandemic has raised many questions about the algorithms of behavior in some of the most vulnerable patients - those with chronic diseases. Since the beginning of the COVID-19 pandemic, there has been a lot of unclear and contradictory data on the frequency of COVID-19 infection, the severity of the course of the disease in patients with chronic diseases, as well as the influence of concomitant therapy on these processes. Establishing the exact number of COVID-19 patients among patients with chronic rheumatic diseases, the severity of the course and possible post-infectious complications is extremely relevant and has an enormous practical benefit for daily clinical activity. The pathogenesis of this infectious disease includes the synthesis of proinflammatory cytokines, which also play a central role in inflammatory and systemic rheumatic diseases. It is important to comprehensively analyze the causes, patterns and factors - both external and internal, which are important for the course of Corona Virus infection in patients with acute and chronic joint diseases.

I believe that Dr. Aleksandar Marinkov's topic is relevant and significant both for rheumatology and for other areas of healthcare such as social medicine, health economics, general medicine, health management, as well as for the pharmaceutical industry.

## III. Structure of the dissertation

The dissertation is written on 138 standard typewritten pages and is structured in the accepted manner in the relevant sections. It contains 26 figures, 14 tables and 6 appendices. The presented dissertation is in accordance with the requirements of MU-Plovdiv for structuring and volume content – it includes the following sections: Introduction - 2 pages; Literature review - 31 pages;

Aim and objectives - 2 pages; Materials and methods - 15 pages; Results - 32 pages; Discussion - 25 pages, Conclusions - 1 page; Bibliography - 152 sources.; Appendices - 30 pages. The abbreviations used are correctly reflected.

The introduction outlines the significance of the research problem.

#### Literature review

The doctoral student demonstrates in-depth knowledge in the field of the researched issue, which is illustrated by a comprehensive and well-structured literature review, which broadly addresses the issues related to the problem. It examines some of the most important rheumatological diseases such as rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, systemic lupus erythematosus, progressive systemic sclerosis, vasculitis, Sjögren's syndrome, polymyositis/dermatomyositis, gout and osteoarthritis. The influence of the known impact of COVID-19 treatment on rheumatic diseases, as well as the vaccination against COVID-19 in patients with rheumatic diseases, has been studied.

In the dissertation, Dr. Alexander Marinkov sets a clearly defined goal - to assess the impact of the COVID-19 pandemic on patients with rheumatic diseases in Bulgaria.

To achieve the set goal, Dr. Marinkov formulates six research tasks. The tasks are specific, feasible and meet the defined goal in the dissertation work. They have both clinical and socio-economic scope with the possibility of a wide scale of analysis.

The Materials and Methods section is described in 15 pages. The dissertation study includes 1248 patients with rheumatological diseases for a period of 2 years (2022-2024). Of the patients studied, those who had COVID-19 accounted for 28.80%, of whom 85.60% were treated at home, 11.20% underwent hospital treatment and 1.20% were treated in an intensive care unit.

The demographic and clinical characteristics of the patients and healthy controls are described in detail and comprehensively. The inclusion and exclusion criteria are well selected and clearly defined.

Dr. Alexander Marinkov gives an extremely detailed description of all methods used in the study, which shows a good knowledge. The methods include: Epidemiological method for obtaining data on the demographic characteristics of patients. A survey was conducted using a digital platform, allowing for the collection of a sufficient number of data.

Sociological method - standard individual interview, direct individual survey to obtain information from all monitored groups of patients.

The statistical program IBM SPSS, version 27 (2020) was used to analyze the data from the survey.

Results section - The results are presented logically, consistently and meet the set goals and objectives. The results are illustrated with a sufficient number of tables, figures and are well interpreted using modern statistical methods.

Results are presented in parallel for the three groups - inflammatory, degenerative and systemic diseases. The results of the survey show a 28.80% incidence of COVID-19 infection among respondents with a rheumatological diagnosis.

The main active signs in the course of the infection are given in detail by disease group. The distribution of patients according to the severity of COVID-19 illness and access to rheumatological drugs and rheumatologist during the pandemic is also presented. Overall, mild, severe and very severe forms of COVID disease do not show a significant association with drug rheumatological therapy ( $p > 0.05$  for all comparisons).

There is data on antibiotics - used by all patients (100%) with a very severe form of infection, by 91.50% with a severe form, by 83.10% with a moderate form and by 52.40% of those who had a mild illness. Vitamins, including vitamin D, were used most by patients with a severe form (81%), followed by those with a moderate form (78.70%), by 74.50% of patients with a mild form and the lowest percentage (66.70%) of patients with a very severe form. 66.70% of patients with very severe forms, 59.60% with severe forms, 52.20% with moderate forms and 21.40% with mild forms of infection were treated with corticosteroids.

The discussion is critical

In all rheumatological diagnoses, a prevalence of mild or moderate COVID-19 infection was found, with the course of patients with severe COVID-19 infection being comparable to the general population.

In almost all patients (91.60%) who had a very severe form, an exacerbation of the rheumatological disease was observed, with the percentage decreasing in milder forms and being lowest in patients with a mild form of infection (45.80%),  $p = 0.003$ . The doctoral student well summarizes and compares the results obtained with those worldwide and seeks the reasons for these differences.

There are seven conclusions and they are properly argued, corresponding to the set goal and the tasks accomplished. They synthesize the analysis of the data from the review and the own study.

The conclusion is interesting that chronic intake of corticosteroid preparations and Imuran aggravate the course of the infection and lead to a more unfavorable outcome, which determines the importance of the assessment of the basic therapy. Overall, these conclusions can contribute to a correct model of care in the case of comorbidity of the patients under consideration.

The contributions are respectively – 6 of an original nature, 2 of a scientifically applied nature and 1 of a confirmatory nature, which objectively reflect the significance of the obtained results in scientific terms and their applicability in real clinical practice. I accept their formulation and nature.

The bibliography contains 152 publications in English from the last five years. This once again emphasizes the relevance of the problem under consideration at a global level and the need for its development in our country.

The work also includes appendices that complement and enrich the dissertation work.

IV. Publications – In connection with the dissertation work, 3 publications have been made, in Bulgarian and international journals. The doctoral student also participated in a scientific project of the CPVB on the topic.

#### V. Abstract

The abstract presents the goals, objectives, results and discussion, conclusions and contributions of the dissertation work in a concise, summarized form. The results are illustrated graphically for greater demonstrativeness. The abstract gives an overall picture of the results obtained and contributions of the dissertation work.

#### VI. Comprehensive, qualitative assessment of the work

The analysis and discussion of the results show good professional preparation and demonstrate the personal participation of the doctoral candidate in writing the dissertation work.

#### VII. Conclusion

The dissertation work contains scientific, scientifically applied and applied results that represent an original contribution to science. The dissertation shows that the doctoral student Dr. Aleksandar Marinkov possesses in-depth theoretical knowledge and professional skills in the

scientific specialty "Rheumatology", demonstrating qualities and skills for independent conduct of scientific research.

Based on the cited data and taking into account the requirements of the Act on the Development of the Academic Staff in the Republic of Bulgaria (ADSRB) and the regulations for its application in the Medical University - Plovdiv, I give my positive vote and recommend to the esteemed Scientific Jury to vote positively for the award of the educational and scientific degree "Doctor" to Dr. Aleksandar Marinkov in the doctoral program in Rheumatology.

11.04. 2025

Заличено на основание  
Чл.5 §1, 6."В" Регламент (ЕС)2016/679

Prof. Dr. Stoyanka Vladeva, MD,

Stara Zagora