

Review of a PhD Dissertation

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Member of the Scientific Jury based on Order No. P-109-436/17.10.2025 of the Rector of
Medical University "Prof. Dr. Paraskev Stoyanov", Varna, Bulgaria

Regarding: *Iliana Dimitrova Mechkarova, MD, DMD obtaining the educational and scientific
degree "Doctor of Philosophy" in the scientific specialty "Surgery", field of higher education "7.
Healthcare and Sport", professional field "7.1. Medicine".*

Topic of the dissertation: "Microbiological profile of purulent-septic diseases in
maxillofacial surgery"

Scientific supervisor: Assoc. Prof. Yanko Georgiev Yankov, MD, PhD

I. Brief autobiographical information about the doctoral student

Iliana Mechkarova, MD, DMD holds two master's degrees – in Dental Medicine and
Medicine, as well as a bachelor's degree in Health Management, which provides her with in-
depth and comprehensive knowledge in the field of healthcare. This broad medical background is
complemented by experience as a research associate at the university clinic in Rostock, Germany,
where she gained valuable experience in in vitro laboratory research.

After specializing in oral surgery at University Hospital "Sveta Marina", Varna, Bulgaria,
Iliana Mechkarova focused her efforts on defending her dissertation, which she began as a regular
doctoral student in the "Surgery" doctoral program at the Department of General and Operative
Surgery of the Faculty of Medicine at Medical University "Prof. Dr. Paraskev Stoyanov", Varna,
Bulgaria. Within her doctoral program, she applied her interdisciplinary knowledge to study the
microbiological profile of purulent-septic diseases in maxillofacial surgery and she participated in
writing articles published in accredited scientific journals.

II. General presentation of the dissertation

This review has been prepared in my capacity as a member of the Scientific Jury, appointed
by Order No. P-109-436 of the Rector of Medical University "Prof. Dr. Paraskev Stoyanov",
Varna, Bulgaria, dated 17.10.2025.

I have thoroughly familiarized myself with the dissertation, its abstract, and the attached scientific publications on the topic. The dissertation by Iliana Mechkarova is a serious and in-depth scientific study dedicated to the microbiological profile of purulent-septic diseases in maxillofacial surgery. The problem is of extreme importance for clinical practice in maxillofacial surgery, as timely and adequate therapy for these infections is a key to preventing severe complications and ensuring a favorable outcome for patients.

The submitted set of documents and materials is in full compliance with the requirements of the Law for the Development of Academic Staff in the Republic of Bulgaria and its Implementing Regulations at Medical University "Prof. Dr. Paraskev Stoyanov", Varna, Bulgaria.

The doctoral student has submitted two scientific publications, which not only cover the minimum national requirements for quantitative and qualitative indicators for obtaining the educational and scientific degree "Doctor of Philosophy", but also demonstrate active research activity and the ability to validate results.

The topic is extremely relevant, given the growing antibiotic resistance, the frequency of deep infectious processes in the orofacial region, the significant risk of spread to the mediastinum and CNS, and the need for local microbiological analysis to optimize empirical therapy.

The dissertation reflects the current understanding that regional microbiological characteristics determine clinical strategy.

III. Analysis of the Literature Recenzia

One of the strong elements of the dissertation is its literature review, which spans over 55 pages and is exceptionally systematic and comprehensive. The doctoral student approached the task with research precision, structuring the review into logically sequential sections:

- **Anatomical features.** This section begins with a precise analysis of the anatomical features of the maxillofacial region and the neck, emphasizing the fascias and interfascial spaces. The detailed description of the superficial and deep cervical fascia, as well as potential spaces such as the submandibular, parapharyngeal, and retropharyngeal spaces, demonstrates a deep understanding of the mechanisms of infection spread. The importance of the "dangerous space" and the "dangerous triangle of the face" as pathways for life-threatening complications is correctly highlighted.

- **Pathophysiology of purulent inflammation.** This section provides a comprehensive overview of the cellular and humoral mechanisms of purulent inflammation. The discussion of vasodilation, increased vascular permeability, neutrophil chemotaxis, and phagocytosis is presented clearly and correctly. The distinction between abscess and phlegmon is precise, emphasizing the diffuse nature and high risk of spread in phlegmon.

- **Classification by origin.** The doctoral student provides an adequate classification of purulent-septic diseases in the MFR according to their origin – odontogenic and non-odontogenic infections. This differentiation is crucial for the empirical selection of antibiotic therapy, which is directly related to the dissertation's aim.

- **Microbiological etiology.** This most extensive section demonstrates exceptionally in-depth knowledge. The doctoral student skillfully presents the concept of the polymicrobial nature of infections and microbial synergy, especially the interactions between facultative and strict anaerobes. The detailed description of the main groups of pathogens – Gram-positive cocci

(*Staphylococcus aureus*, CoNS, *Streptococcus* spp. – viridans, anginosus, *S. pyogenes*), Gram-negative bacteria (Enterobacteriaceae, *Pseudomonas aeruginosa*, *Acinetobacter baumannii*, *Prevotella*, *Porphyromonas*, *Fusobacterium*), and Gram-positive anaerobic cocci – is of high scientific value. The emphasis on virulence factors and molecular mechanisms of resistance (MRSA, ESBL, carbapenemases) is of significant practical importance. Special attention is paid to the challenges in diagnosing anaerobes, which is directly related to the methodology of the student's own research.

• **Principles of therapy and antimicrobial resistance.** The review concludes with a contemporary discussion of therapeutic principles, including the importance of empirical therapy, de-escalation, and surgical drainage. The discussion of the main antibiotic groups used in maxillofacial surgery (penicillins, clindamycin, metronidazole, cephalosporins) is adequate. Particularly valuable is the section dedicated to antimicrobial resistance, where the doctoral student convincingly outlines global and local challenges, including the increasing incidence of MRSA, ESBL-producing bacteria, and resistance in anaerobes.

The conclusions drawn from the literature review are logically and convincingly synthesized, summarizing the key challenges and substantiating the need for the student's own research. These conclusions demonstrate that the doctoral student has mastered the topic in depth and is capable of identifying significant problems and gaps in scientific knowledge. Overall, the literature review is of an exceptionally high standard, systematic, current, and demonstrates the doctoral student's excellent orientation in the global scientific literature on the problem.

IV. Topicality and significance of the chosen topic

The topic of the dissertation is not merely current, but strategically important in the context of contemporary challenges in medicine, especially the spread of antimicrobial resistance (AMR). The maxillofacial region is anatomically specific, with a rich microbial background, which makes purulent-septic processes here particularly insidious and often life-threatening. Empirical antibiotic therapy, often necessary in emergency situations, is only effective if it relies on current and region-specific epidemiological data.

In this sense, creating a "microbiological map" for purulent-septic diseases in Bulgaria is of great importance. The dissertation directly addresses the gap in knowledge about the local microbiological landscape, which is critical for optimizing therapeutic protocols, reducing treatment failures, reducing resistance, and improving patient prognosis. This is a work with a strong translational focus – a direct transfer of scientific data into clinical practice.

V. Aim and objectives of the study

The main **aim** of the dissertation is formulated with scientific precision and clarity: to conduct an in-depth retrospective analysis of the microbiological profile of purulent-septic diseases in the maxillofacial region treated at the Clinic of Maxillofacial Surgery at University Hospital "Sveta Marina", Varna, Bulgaria over a 10-year period, with the ultimate ambition of creating an up-to-date "microbiological map" for the region. This aim is ambitious but entirely achievable with the chosen methodology and the scale of the research.

The four **objectives** set are logically sequential and operationally defined, leading step-by-step to the achievement of the main aim:

1. determining the overall etiological structure of infections;
2. comparative analysis of the microbiological profile in odontogenic and non-odontogenic origins;
3. tracking the dynamics of the main causative agents over time, comparing two five-year periods;
4. analysis of the frequency of polymicrobial infections and samples with no proven causative agent.

I believe that the aim and objectives are adequate for the scope and requirements of a doctoral dissertation, demonstrating a clear understanding of the research problem.

VI. Methodology, structure, and volume of the dissertation

The dissertation is impeccably structured, encompassing all necessary components: introduction, extensive and critical literature review, clearly defined aim and objectives, detailed materials and methods, presentation of results, in-depth discussion, conclusions, contributions, and a comprehensive bibliography. The total volume of 133 pages is adequate, and the content is illustrated with 13 original figures and 13 tables that effectively visualize the presented data. The bibliography includes 140 sources, predominantly foreign language, which indicates excellent familiarity with international scientific thought.

The study's methodology is an exceptionally strong aspect. Basing the research on a retrospective analysis of an enormous clinical material – 1735 patient samples over a 10-year period (2015-2024) – ensures high statistical power and significance of the results. The choice of adequate statistical methods for descriptive statistics, as well as the stratification of the material according to the origin of the infection, guarantee the reliability of the obtained data. The methodical execution is at a high academic level and fully corresponds to the stated research objectives.

The "Results" and "Discussion" sections represent the core of the dissertation, demonstrating high scientific maturity, analytical acumen, and critical thinking ability on the part of the doctoral student. The presented empirical material is exceptionally rich and systematized, and its in-depth analysis in the "Discussion" section is precisely compared with current international data and leading theoretical concepts in the field. Iliana Mechkarova does not merely describe her findings but skillfully interprets them, deriving important clinical implications and explaining the observed phenomena with complex factors such as antibiotic pressure, the nosocomial environment, and even the influence of the COVID-19 pandemic. This complex vision emphasizes the translational nature of the research – a direct bridge between the laboratory and the patient's bedside.

VII. Main results, discussion, and scientific contributions

Among the main results forming the basis of the dissertation, the following stand out:

- **Creation of an up-to-date "microbiological map" for the MFR in the region.** This is a fundamental contribution that provides an empirically justified basis for the selection of initial

antibiotic therapy. This map is not merely a statistical compilation but an invaluable tool for clinicians, especially given the significant proportion of samples without an isolated pathogen or with resident flora.

- **Documentation of a "staphylococcal shift".** An original and extremely important scientific contribution is the identification of an alarming trend towards an increase in coagulase-negative staphylococci as leading pathogens, displacing traditional streptococci. Tracking this dynamic over time is an alarm signal for the need to re-evaluate current therapeutic algorithms.

- **Etiological differentiation based on the origin of the infection.** The dissertation convincingly demonstrates the differences in the microbiological profile between odontogenic and non-odontogenic infections, with this distinction being a key to guiding adequate therapy.

- **Emphasis on the role of fungi and methodological challenges with anaerobes.** The study highlights the increasing importance of *Candida* spp. as co-pathogens, as well as the need for adequate anti-anaerobic coverage, given the proven methodological difficulties in isolating them.

- **Formulation of specific clinical recommendations.** A strong point of the dissertation is that it is not limited to findings but offers scientifically substantiated guidelines for improving diagnostic and therapeutic strategies, which directly enhances the quality of medical care.

The most significant and original contributions of the dissertation are:

1. **This is the first "microbiological map" of its kind with a detailed description of the microbiological profile.**

The dissertation makes a fundamental contribution to local clinical practice by creating the first large-scale and up-to-date "microbiological map" of purulent-septic diseases in the maxillofacial region for the Varna area, covering a ten-year period. This extensive retrospective analysis of over 1700 clinical samples is unprecedented in Bulgarian conditions and provides an invaluable database. The analysis reveals a complex microbiological picture, including a high proportion of polymicrobial resident microflora and a significant percentage of sterile samples, which unequivocally confirms the challenges in etiological diagnosis. This finding precisely underscores the critical need for local epidemiological data for adequate empirical antibiotic therapy, especially when rapid results are impossible or ambiguous.

2. **The concept of "staphylococcal shift" has been established and analyzed.**

One of the most significant and original scientific contributions is the categorical documentation of coagulase-negative staphylococci (CoNS) as the leading group of pathogenic agents (23.0%), even surpassing classical oral streptococci. Tracking the dynamics over time convincingly confirms this alarming trend, which Dr. Mechkarova adequately defines as a "staphylococcal shift." This result is an alarm signal for the changing microbiological landscape and has direct implications for rethinking empirical antibiotic regimens. The doctoral student skillfully explains this phenomenon with complex factors, among which the selective pressure from widespread antibiotic use, the potential nosocomial origin of some infections, and the specific characteristics of CoNS, such as their ability to form biofilms and high methicillin resistance (MRSE), play a leading role. This depth of analysis gives particular weight to the conclusion.

3. **Precise etiological differentiation with the identification of prognostic markers has been carried out.**

The dissertation convincingly confirms and details the differences in the microbiological profile between odontogenic (dominated by streptococci, especially from the viridans group) and non-odontogenic (dominated by staphylococci, including *S. aureus* and CoNS) infections. This

differentiation is of immense practical importance for clinicians in choosing initial antibiotic therapy. Additionally, the analysis of Gram-negative bacteria (Enterobacteriaceae) is presented as an "alarming signal" and a marker for more severe, complicated, or secondarily infected processes associated with a high risk of multidrug-resistant strains (ESBL-producers). This gives significant prognostic value to the study and aids in making more informed clinical decisions.

4. The importance of fungal co-pathogens is emphasized.

The study also highlights the high proportion of *Candida* spp. (7.9%) among the isolates, confirming them as an important co-pathogen, especially in odontogenic infections. This important finding necessitates increased attention to the risk of fungal superinfections, particularly in patients with compromised immune status or after prolonged antibiotic therapy, and points to the need for adequate fungicidal therapy.

5. Scientifically substantiated clinical recommendations have been formulated.

A strong point of the dissertation is that it goes beyond the purely descriptive nature of an epidemiological study. Iliana Mechkarova offers specific, scientifically substantiated recommendations for optimizing both therapeutic approaches (rethinking the empirical choice of antibiotic based on the local microbiological profile) and the diagnostic process (improving methods for sampling, transporting, and isolating anaerobic bacteria, whose role is likely underestimated). These recommendations are a direct and valuable contribution to clinical practice, indicating the path to improving patient care.

6. Anatomical and demographic correlations have been made.

The dissertation also confirms that over 70% of odontogenic infections originate from the mandible, which is consistent with anatomical predispositions. Additionally, the demographic analysis outlines the age group between 31 and 50 years as the most affected, with a clear predominance of males. These details enrich the epidemiological picture and support the targeting of preventive and therapeutic measures.

The discussion in the dissertation is of an exceptionally high scientific level, with Iliana Mechkarova skillfully comparing her results with leading international studies, substantiating the observed phenomena. Her ability not merely to describe, but to deeply interpret the data, deriving important clinical implications from them, is an indicator of her exceptional scientific maturity and research potential.

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VIII. Evaluation of the attached scientific publications and the doctoral student's personal contribution

The two attached scientific publications are published in reputable journals and form a substantial part of the dissertation's evidence base:

1. Yankov YG, **Mechkarova ID**. Etiological spectrum of odontogenic and non-odontogenic abscesses in oral and maxillofacial surgery. *Scr Sci Med Dent*. 2023, 9: 68-74. 10.14748/ssmd.v9i1.9130;

2. Yankov YG, **Mechkarova ID**. Microbiological spectrum, clinic and treatment of patients with phlegmons of the mouth floor. *Int J Med Sci Clin Invent*. 2023, 10(5): 6704-10.10.18535/ijmsci/v10i5.02.

These demonstrate Iliana Mechkarova's ability to plan, conduct, and publish scientific research, validating her results at various stages. The second publication is particularly impressive, linking microbiological findings with clinical phenotype and treatment outcomes, demonstrating a clinical-research mindset.

The PhD student's task has been completed – setting a clinical-scientific problem, planning a study, conducting a study to prove/reject a thesis, processing the results, discussing and analyzing the importance of the data. This is an important foundation for building a successful scientist. On this basis, under the right conditions, it is possible to conduct very large and important studies of a local, regional, national, and international nature. The understanding and identification of the limitations of the study makes an extremely good impression, demonstrating critical thinking and a deep awareness of the basic idea of science.

IX. Critical Remarks and Recommendations

Dr. Mechkarova's dissertation is of an exceptionally high scientific and applied level, demonstrating a profound understanding of the problem and impeccable execution of the research plan. For this very reason, substantial critical remarks within the scope of this review are difficult to formulate. The work is comprehensive and exhaustive for the chosen methodology.

In the spirit of constructive academic dialogue and as a guide for future research, I would allow myself to suggest expanding the methodology to include modern molecular-genetic methods. More specifically, the use of techniques such as next-generation sequencing (NGS) or polymerase chain reaction (PCR) with various modifications could significantly enrich the analysis. These methods offer the possibility of extremely precise and rapid identification of microorganisms, especially fastidious bacteria such as strict anaerobes, whose isolation and identification in routine microbiological practice are associated with significant challenges and methodological limitations, as the dissertation itself notes. The implementation of such approaches would provide an even more detailed and comprehensive insight into the complex polymicrobial etiology of purulent-septic infections in the maxillofacial region. This would allow not only to confirm but also to further develop the findings on microbial synergy and the potential role of undiscovered pathogens. Such an analysis would complement the already comprehensive "microbiological map" by adding information on the full spectrum of microorganisms, including those that cannot be cultured by standard methods. This would reveal new aspects of the microbiological landscape and potential therapeutic targets. This recommendation, however, is more a vision for the future development of the scientific problem and in no way diminishes the great value, originality, and applied significance of the present dissertation, which unequivocally deserves a high evaluation. The dissertation fully achieves and exceeds its stated goals using the best available conventional methods.

In larger studies, more statistical methods could be used to prove the thesis.

The results for a lower frequency of mixed aerobic-anaerobic infections than those available in the literature suggest that further analysis of the causes should be carried out in subsequent studies.

X. Conclusion

Based on the thorough analysis performed and the high evaluation of the presented dissertation, I am firmly convinced that the work of Iliana Dimitrova Mechkarova, MD, DMD on the topic "Microbiological profile of purulent-septic diseases in maxillofacial surgery" fully meets the requirements of the Law for the Development of Academic Staff in the Republic of Bulgaria and the Regulations of Medical University "Prof. Dr. Paraskev Stoyanov", Varna, Bulgaria for obtaining the educational and scientific degree "Doctor of Philosophy".

The PhD student's task has been completed – setting a clinical-scientific problem, planning a study, conducting a study to prove/reject a thesis, processing the results, discussing and analyzing the importance of the data.

The author has demonstrated profound theoretical knowledge, excellent practical skills, and high research potential. The obtained results have undoubted scientific value and direct applicability in clinical practice, contributing to the optimization of diagnostic and therapeutic strategies.

Given the above, I give my entirely **positive vote** of the dissertation and confidently propose to the esteemed Scientific Jury to award Iliana Dimitrova Mechkarova, MD, DMD the educational and scientific degree "Doctor of Philosophy" in the scientific specialty "Surgery" in the field of higher education "7. Healthcare and Sport" and professional field "7.1. Medicine".

11.11.2025
Pleven, Bulgaria

Assoc. Professor Martin Petrov Karamanliev, MD, PhD

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