

**To the Chairperson of the Scientific Jury,
Appointed by Order
of the Rector of MU-Varna
No. P-109-282/30.07.2026**

Opinion

by Assoc. Prof. Ralitsa Nikolaeva Robeva, MD, PhD,
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Endocrinology "Acad. Ivan Penchev",
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Member of the scientific jury
by Order of the Rector of MU-Varna No. P-109-282/30.07.2026

Regarding the dissertation work for PhD degree:
Field of higher education: 7. Healthcare and Sports; Accredited Doctoral Program: Pediatrics;
Professional Field: 7.1. Medicine

by Vilhelm Ruslanov Mladenov, MD
PhD student at the Department of Pediatrics,
Medical University "Prof. Dr. Paraskev Stoyanov" – Varna

Dissertation Title: " Polycystic Ovary Syndrome in Adolescence – Contemporary Aspects and
Directions for Diagnosis"

Scientific Supervisor: Prof. Violeta Mihova Iotova, MD, PhD, DSc

I. Brief biographical reference

Vilhelm Ruslanov Mladenov, MD graduated from the First English Language High School and subsequently completed his medical studies at the Medical University of Varna in 1995. He qualified as a pediatrician in 2002 and obtained a second specialization in pediatric endocrinology in 2007. From 2003 to 2009, he worked as a pediatrician in the Pediatric Department of St. Anna Multiprofile Hospital for Active Treatment in Varna. Since 2009, he has served as a pediatric endocrinologist at the First Pediatric Clinic of St. Marina University Hospital in Varna, and since 2017, he has been an assistant professor at the Department of Pediatrics at the Medical University of Varna. In 2020, he enrolled as a full-time PhD student in the same department, and on December 4, 2024, he has completed his doctoral program being eligible to defend his thesis. Throughout his career as a physician and academic teacher, Dr. Mladenov has gained extensive theoretical and practical experience, establishing himself as a leading specialist in the fields of diabetes and gonadal pathology in children and adolescents. In 2011, he was awarded an ESPE scholarship, enabling him to undergo specialized training at a world-leading center for Disorders of Sex Development (DSD) in Ghent, Belgium. V. Mladenov has participated in numerous courses and scientific forums organized by ESPE and ISPAD/VAPES. Between 2011 and 2025 alone, he attended a total of eight postgraduate courses organized by ISPAD/VAPES. In 2023, he was invited as a guest lecturer to the National Conference on Pediatric Endocrinology (with international participation) in Timișoara, Romania. V. Mladenov holds numerous certifications, including those in ultrasonography, DXA scanning (bone and adipose tissue), and treatment with insulin pumps and CGM. He is a member of the Bulgarian Society of Endocrinology (2006), ESPE (2025), ISPAD (2006), the Varna Society of Pediatric Endocrinology (2012), the Bulgarian National Association of Pediatric Endocrinology, the Bulgarian Society of Human Genetics and Genomics, and the Bulgarian Medical Association. V. Mladenov is fluent in English and possesses advanced skills in working with information technology systems.

II. Purpose, relevance, and significance of the topic

This study aims to investigate diagnostic approaches to PCOS in adolescence, thereby improving and enriching the diagnostic options for young women with the syndrome. Key objectives include: assessing the clinical and laboratory profiles of adolescent patients with PCOS; investigating new potential diagnostic biomarkers for adolescent PCOS, such as AMH and FAI, and establishing corresponding cut-off values; identifying potential correlations between hormonal biomarkers,

clinical and ultrasound parameters, obesity, and metabolic abnormalities; determining the prevalence of metabolic disorders (dyslipidemia, impaired glycemic control, insulin resistance, hyperinsulinism, arterial hypertension) in adolescent patients with PCOS; and evaluating the sensitivity and specificity of selected miRNAs as diagnostic markers for adolescent PCOS, while exploring potential associations with hyperandrogenism, polycystic ovarian morphology, and metabolic disorders. The study addresses a highly relevant topic, considering the limited data in the literature on PCOS in this specific age group. It focuses on a very common issue of significant public health importance that might affect the nation's reproductive health. It should be noted that the accurate diagnosis of PCOS during adolescence is a fundamental prerequisite for appropriate treatment and the prevention of numerous subsequent complications in adulthood, including metabolic, cardiovascular, and oncological diseases, as well as infertility. The tasks undertaken fully align with the objectives of the dissertation and provide an opportunity to expand knowledge regarding the role of various diagnostic markers in adolescent girls with PCOS. A valuable approach is the comparison of patients not only with healthy controls but also with adolescent girls suffering from other hyperandrogenic conditions. Investigating selected miRNAs as diagnostic markers for PCOS represents a novel diagnostic approach that could contribute to the early diagnosis of the syndrome. All of this underscores the immense theoretical and practical significance of the presented work.

III. Structure of the dissertation

The dissertation encompasses 173 standard typewritten pages and is illustrated with 25 tables and 16 figures. The literature review covers 52 pages and provides a detailed examination of current concepts regarding the etiology and pathogenesis of PCOS, diagnostic criteria across different age groups, the syndrome's clinical features, potential new biomarkers, and age-specific therapeutic approaches recommended in current guidelines. The aim and objectives of the dissertation are clearly formulated. The research methods are described with great precision. The results are presented in a detailed and systematic manner. The discussion and conclusions span 37 pages and are interpreted within the context of international studies. The abstract is meticulously prepared, presenting the key data and conclusions of the research in detail. The bibliography is comprehensive, comprising 180 references—4 in Cyrillic and 176 in Latin script, with over 70% of the cited publications dating from the last 10 years.

IV. Scientific contributions of the thesis

Vilhelm Mladenov's dissertation is distinguished by significant scientific theoretical and practical contributions. This study is the first in the country and the second globally to examine the expression of selected miRNAs in adolescent girls with PCOS compared to control groups. For the first time (in Bulgaria and internationally), the expression of miR-320a-5p, miR-103a-5p, miR-15a-5p, and miR-194-5p was investigated in adolescent girls with PCOS, and their sensitivity and specificity as diagnostic markers for the condition were determined. This study is the first in the country and one of the few worldwide to establish the most sensitive and specific diagnostic threshold value for AMH in adolescent girls with PCOS. It is also the first in the country and one of the few globally to determine the most sensitive and specific diagnostic threshold values for androstenedione and FAI in the same age group. This is the first study in the country to comprehensively examine PCOS in adolescence through a detailed clinical and laboratory assessment that includes miRNAs analysis. A particularly important practical contribution of the work is its potential to enrich the diagnostic algorithm for PCOS in girls by introducing new, highly specific and sensitive biomarkers suitable for inclusion in current national clinical guidelines. The dissertation demonstrates the doctoral candidate's profound knowledge and extensive clinical experience regarding the subject matter.

V. Publications related to the thesis and scientific indicators

Vilhelm Ruslanov Mladenov, MD presents a total of four publications, one of which appeared in a high-impact-factor journal ranked in the top Q1 quartile. The doctoral candidate is the first author on all the publications. The results of the dissertation have been presented at four scientific forums. Additionally, a research project based on the dissertation topic was successfully conducted.

In conclusion, based on the foregoing, I consider the proposed dissertation by Vilhelm Ruslanov Mladenov, MD, titled "Polycystic Ovary Syndrome in Adolescence – Contemporary Aspects and Directions for Diagnosis" to be timely, complete, and compliant with all procedural requirements. The conclusions drawn regarding the role of certain miRNAs as diagnostic markers for PCOS hold significant scientific and theoretical value. It should be emphasized that this study is the first of its kind regarding not only the adolescent age group but also PCOS in Bulgarian female patients in general. Of particular practical importance is the comprehensive analysis of clinical and metabolic characteristics in young women with various hyperandrogenic conditions, as well as the establishment of diagnostic thresholds for key markers such as AMH and FAI in adolescence—cut-

offs that can be implemented in actual clinical practice. This could lead to more effective early diagnosis and prevention of metabolic and reproductive complications in adulthood. The presented work demonstrates that the doctoral candidate possesses exceptionally profound knowledge in the field of reproductive endocrinology. The competent analysis of the results from a clinical perspective is noteworthy, as is the stylistic and linguistic precision of the dissertation. In view of this, I provide a positive assessment and strongly recommend that the esteemed jury award Vilhelm Ruslanov Mladenov, MD the educational and scientific degree of "Doctor" in the doctoral program: Pediatrics. Professional Field 7.1: Medicine.

14.09.2026.

Sofia

Заличено на основание чл. 5,
§1, б. „В“ от Регламент (ЕС)
2016/679

Signature:

/Assoc. Prof. Ralitsa Robeva, MD, PhD/