

## REVIEW

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In accordance with Order No. R-109-517/16.12.2025 of the Rector of the Medical University – Varna, and decision under Protocol No. 1/23.12.2025, I have been appointed to prepare a review in a procedure for awarding the educational and scientific degree "Doctor (PhD)".

Dissertation thesis titled:

"Diagnostic Dynamics in Patients with a First Psychotic Episode Following the Use of Psychoactive Substances", submitted for public defense before a scientific jury for awarding the educational and scientific degree "Doctor (PhD)" in professional field 7.1 Medicine, scientific specialty "Psychiatry" (03.01.20).

The author of the dissertation is Dr. Danko Tonev Avramov, PhD candidate at the Department of Psychiatry and Medical Psychology, Faculty of Medicine, Medical University – Varna.

Scientific supervisor: Assoc. Prof. Deyan Hrusafov, MD, PhD, Department of Psychiatry and Medical Psychology, Medical University – Varna.

## RELEVANCE AND SIGNIFICANCE OF THE TOPIC

The topic of the presented dissertation is highly relevant and of substantial scientific and practical importance for contemporary psychiatry. The first psychotic episode represents a critical moment in the development of psychotic disorders, and the presence of psychoactive substance use significantly complicates the diagnostic process, therapeutic decisions, and long-term prognosis. In clinical practice, serious difficulties often arise in distinguishing between primary psychosis and substance-induced psychotic disorder, especially in the early stages of illness.

Against the background of increasing psychoactive substance use, including cannabis and stimulants, the issue of diagnostic dynamics in the first psychotic episode acquires not only clinical but also major public health significance. In this sense, the choice of topic is fully justified and corresponds to priority directions in modern psychiatric science.

#### BRIEF BIOGRAPHICAL DATA

Dr. Danko Tonev Avramov graduated in Medicine from the Medical University “Prof. Dr. Paraskev Stoyanov” – Varna (2019). Since 2019 he has worked as a physician at University Hospital “St. Marina” – Varna. He was an assistant at the Department of Psychiatry and Medical Psychology at the Medical University – Varna in the period 2020–2025. He obtained a specialty in Psychiatry in 2024. His scientific interests are in psychopharmacology, biological psychiatry, and psychotic disorders. He is the author of scientific publications and reports related to psychosis and psychoactive substance use.

#### GENERAL CHARACTERISTICS OF THE DISSERTATION

The dissertation comprises 149 pages and contains 60 figures and 43 tables and is prepared in accordance with the requirements of the Medical University – Varna for awarding the educational and scientific degree “Doctor (PhD)”. It is logically structured and includes an introduction, an extensive literature review, clearly formulated aims, objectives and hypotheses, appropriately described materials and methods, detailed results, in-depth discussion, conclusions, and stated scientific and applied contributions.

#### LITERATURE REVIEW

The literature review is detailed, well systematized, and critically analyzed. The main historical and contemporary concepts of psychosis are presented, as well as the current classification systems (ICD-10, ICD-11, DSM-5). Special attention is paid to psychotic disorders associated with psychoactive substance use, as well as to diagnostic and prognostic difficulties in the first psychotic episode.

A positive impression is made by the inclusion of the Bulgarian contribution to the doctrine of psychoses, which demonstrates respect for the national psychiatric school and in-depth knowledge of the subject. The literature review provides a solid theoretical basis for formulating the aims and hypotheses of the study.

#### AIM, OBJECTIVES, AND HYPOTHESES

The aim of the dissertation is clearly and specifically formulated — to track diagnostic dynamics in patients with a first psychotic episode depending on the presence of psychoactive substance use. The set objectives and working hypotheses are logically grounded, consistent, and fully correspond to the main aim of the study.

#### MATERIALS AND METHODS

The methodological approach used is appropriate and consistent with modern requirements for clinical psychiatric research. Two comparable groups of patients with a first psychotic episode were studied — with and without psychoactive substance use. Validated clinical instruments and standardized methods for assessment of symptomatology and functional status were applied. The statistical data processing is correct and allows reliable interpretation of the results.

#### RESULTS AND DISCUSSION

The results are presented in detail and consistently, clearly reflecting the set aims and testing the formulated hypotheses. Patients with psychoactive substance use show earlier onset, are more often male, and have lower social and occupational functioning. Their clinical picture is dominated by acute, high-intensity positive symptoms and behavioral disorganization, which complicates early diagnosis.

Patients without substance use show a more homogeneous and gradual clinical presentation with greater early diagnostic stability.

The two-year follow-up demonstrates significantly higher diagnostic change in the substance-use group. Some initially diagnosed with substance-induced psychosis later meet criteria for schizophrenia-spectrum or affective disorders, supporting the role of substances as triggering rather than sole causal factors.

PANSS scores show significant reduction of positive symptoms in both groups, more pronounced in the substance-use group, while negative symptoms are more persistent. GAF assessment shows persistently lower functioning in the substance-use group, associated with more hospitalizations and worse outcomes.

Overall, psychoactive substance use is associated with greater diagnostic instability, more complex course, and poorer functional outcome.

## CONCLUSIONS

The study leads to clear and clinically significant conclusions confirming the initial aims and hypotheses. Psychoactive substance use significantly influences onset, symptom profile, diagnostic stability, and functional outcome. Diagnostic instability and later diagnostic transformation are more common in the substance-use group, while diagnoses are more stable and predictable without substance use.

Integrated treatment approaches addressing both psychosis and substance use are necessary.

## SCIENTIFIC AND APPLIED CONTRIBUTIONS

The dissertation provides a systematic national analysis of diagnostic dynamics in first psychotic episode with and without psychoactive substance use. It identifies clinical and prognostic factors related to diagnostic change and offers practical clinical guidance — especially the need for caution in early diagnosis and for long-term follow-up with reassessment.

It also emphasizes functional and social outcomes as key long-term indicators.

## RECOMMENDATIONS FOR FUTURE RESEARCH

Future studies may extend follow-up duration and differentiate more precisely between substance classes. Greater focus on integrated therapeutic and rehabilitation strategies is recommended.

## FINAL STATEMENT

The presented dissertation is a completed, independent, and scientifically significant study that fully meets the requirements of the Medical University – Varna for awarding the educational and scientific degree “Doctor (PhD)”.

I strongly recommend that Dr. Danko Tonev Avramov be awarded the educational and scientific degree “Doctor (PhD)” in Psychiatry.

Reviewer:

Заличено на основание чл. 5,  
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