UDC/УДК: 615.065:615.214.21:616.008.9
https://doi.org/10.30895/2312-7821-2025-478

Review | Обзор

Circulating MicroRNAs Are Promising Biomarkers for Assessing the Risk of Antipsychotic-Induced Metabolic Syndrome (Review): Part 1

Natalia A. Shnayder[1,2,✉], Regina F. Nasyrova[1,3], Nikolai A. Pekarets[1], Violetta V. Grechkina[1], Marina M. Petrova[2]

[1] Institute of Personalized Psychiatry and Neurology,
V.M. Bekhterev National Medical Research Center for Psychiatry and Neurology,
3 Bekhterev St., St Petersburg 192019, Russian Federation

[2] Shared Core Facilities "Molecular and Cell Technologies",
Prof. V.F. Voino-Yasenetsky Krasnoyarsk State Medical University,
1 Partisan Zheleznyak St., Krasnoyarsk 660022, Russian Federation

[3] Tula State University,
92 Lenin Ave, Tula 300012, Russian Federation

✉ **Natalia A. Shnayder** naschnaider@yandex.ru

ABSTRACT

INTRODUCTION. Antipsychotic-induced metabolic syndrome (AIMetS) is a common adverse reaction to the pharmacotherapy of psychiatric and addiction disorders. However, interindividual variability in the metabolism of antipsychotics may limit the sensitivity and specificity of known blood-based biochemical biomarkers of AIMetS for assessing the safety of psychopharmacotherapy and the risk of AIMetS in patients with schizophrenia spectrum disorders. In recent years, circulating microRNAs have been considered as new and promising epigenetic biomarkers of AIMetS.

AIM. This study aimed to evaluate the potential of circulating microRNAs as epigenetic biomarkers for the prediction and early diagnosis of AIMetS.

DISCUSSION. The authors analysed the results of academic and clinical research published from 2012 to 2024 with a focus on the role of circulating microRNAs involved in the key AIMetS pathogenesis and progression pathways. This review presents novel international approaches to using primary and additional clinical and biochemical biomarkers of AIMetS and demonstrates the advantages of microRNAs as epigenetic biomarkers of AIMetS. The article summarises data on the roles of microRNAs in the mechanisms of AIMetS development (oxidative stress, systemic inflammation, adipocyte differentiation, lipid and glucose metabolism, appetite regulation, and changes in neuropeptide Y and orexin expression, leptin sensitivity, and testosterone, thyroid and parathyroid hormone levels).

CONCLUSIONS. Detecting changes in the expression of circulating microRNAs in easily accessible samples (blood, saliva, urine, etc.) is a promising alternative method for predicting and diagnosing AIMetS. The second part of this review will explore the role of circulating microRNAs as epigenetic biomarkers for developing the main manifestations of MetS and AIMetS and will classify microRNA signatures according to the risk of developing AIMetS.

Keywords: antipsychotics; antipsychotic-induced metabolic syndrome; metabolic syndrome; early diagnosis; circulating microRNAs; adverse drug reaction; epigenetic biomarker; personalized risk assessment; mental disorders

For citation: Shnayder N.A., Nasyrova R.F., Pekarets N.A., Grechkina V.V., Petrova M.M. Circulating microRNAs are promising biomarkers for assessing the risk of antipsychotic-induced metabolic syndrome (review): Part 1. *Safety and Risk of Pharmacotherapy*. 2025;13(3):344–356. https://doi.org/10.30895/2312-7821-2025-478

Funding. The study was performed without external funding.
Disclosure. The authors declare no conflict of interest.

Циркулирующие микроРНК — перспективные биомаркеры для оценки риска развития антипсихотик-индуцированного метаболического синдрома (обзор): часть 1

Н.А. Шнайдер[1,2,✉], Р.Ф. Насырова[1,3], Н.А. Пекарец[1], В.В. Гречкина[1], М.М. Петрова[2]

[1] Институт персонализированной психиатрии и неврологии,
Национальный медицинский исследовательский центр психиатрии и неврологии имени В.М. Бехтерева,
ул. Бехтерева, д. 3, Санкт-Петербург, 192019, Российская Федерация

[2] Центр коллективного пользования «Молекулярные и клеточные технологии»,
Красноярский государственный медицинский университет имени профессора В.Ф. Войно-Ясенецкого,
ул. Партизана Железняка, д. 1, г. Красноярск, 660022, Российская Федерация

[3] Федеральное государственное бюджетное образовательное учреждение высшего образования
«Тульский государственный университет»,
пр. Ленина, д. 92, г. Тула, 300012, Российская Федерация

✉ **Шнайдер Наталья Алексеевна** naschnaider@yandex.ru

РЕЗЮМЕ

ВВЕДЕНИЕ. Антипсихотик-индуцированный метаболический синдром (АИМетС) является распространенной нежелательной реакцией при фармакотерапии психических расстройств и болезней зависимости. Однако чувствительность и специфичность известных биохимических биомаркеров в крови могут быть недостаточными для оценки безопасности психофармакотерапии и риска развития АИМетС в связи с индивидуальными различиями метаболизма антипсихотиков у пациентов с расстройствами шизофренического спектра. Циркулирующие микроРНК в крови рассматриваются как новые перспективные эпигенетические биомаркеры АИМетС.
ЦЕЛЬ. Оценить возможность использования циркулирующих микроРНК как эпигенетических биомаркеров для прогнозирования и ранней диагностики АИМетС.
ОБСУЖДЕНИЕ. Проведен анализ результатов фундаментальных и клинических исследований роли циркулирующих микроРНК, влияющих на основные звенья патогенеза и прогрессирования АИМетС, опубликованных в период 2012–2024 гг. Представлены новые международные подходы к использованию основных и дополнительных клинических и биохимических биомаркеров АИМетС, показаны преимущества использования микроРНК в качестве эпигенетических биомаркеров АИМетС. Приведены обобщенные данные о роли микроРНК в механизмах развития АИМетС, включая окислительный стресс, системное воспаление, дифференцировку адипоцитов, метаболизм липидов и глюкозы, регуляцию аппетита, изменение экспрессии нейропептида Y, чувствительности к лептину, экспрессии орексина, уровней тестостерона, тиреоидных гормонов и паратиреоидного гормона.
ВЫВОДЫ. Выявление изменений уровня экспрессии циркулирующих микроРНК в доступных образцах (кровь, слюна, моча) перспективно как одна из альтернативных методологий прогнозирования и диагностики АИМетС. Во второй части обзора будет рассмотрена роль циркулирующих микроРНК как эпигенетических биомаркеров развития основных проявлений МетС, АИМетС, а также распределение сигнатур микроРНК в зависимости от риска развития АИМетС.

Ключевые слова: антипсихотики; антипсихотик-индуцированный метаболический синдром; метаболический синдром; ранняя диагностика; циркулирующие микроРНК; нежелательная реакция; эпигенетический биомаркер; персонализированная оценка риска; психические расстройства

Для цитирования: Шнайдер Н.А., Насырова Р.Ф., Пекарец Н.А., Гречкина В.В., Петрова М.М. Циркулирующие микроРНК — перспективные биомаркеры для оценки риска развития антипсихотик-индуцированного метаболического синдрома (обзор): часть 1. *Безопасность и риск фармакотерапии*. 2025;13(3):344–356. https://doi.org/10.30895/2312-7821-2025-478

Финансирование. Работа выполнена без спонсорской поддержки.
Потенциальный конфликт интересов. Авторы заявляют об отсутствии конфликта интересов.

INTRODUCTION

Antipsychotics (APs) are treatment of choice for schizophrenia spectrum disorders (SSD); however, they are associated with a higher risk of antipsychotic-induced metabolic syndrome (AIMetS) [1]. Metabolic syndrome (MetS) is a cluster of pathological conditions, including central (abdominal) obesity, high blood pressure (BP), fasting hyperglycaemia, triglyceridaemia, and decreased serum high-density lipoprotein cholesterol (HDL-C) [2]. Increased MetS prevalence in many countries [3] leads to higher mortality rates [4] and the economic burden [5]. According to the International Diabetes Federation (IDF), 20–25% of the world adult population has MetS, and the probability of premature mortality in MetS patients is three times higher than without the syndrome[1].

AIMetS prevalence is high and ranges from 37 to 63%, including its main components: weight gain / waist circumference, dyslipidemia, insulin resistance / type 2 diabetes mellitus, and arterial hypertension [6]. AIMetS plays a crucial role in increased risk of premature mortality in SSD patients, mainly of cardiovascular diseases [7]. Negative metabolic AP effects affect more than half of psychiatric patients, children and adolescents being the highest-risk groups, which is a serious obstacle to long-term treatment of socially significant diseases, including SSDs [8, 9].

Since prolonged use of APs (more than 3 months) can contribute to AIMetS, international clinical guidelines underline the need for initial physical and laboratory examination of naive patients (prior to AP prescription), as well as subsequent monitoring of clinical and laboratory (biochemical, hormonal) markers for the early detection and treatment of this adverse drug reaction (ADR) [10]. Expanding knowledge about the individual tolerance of well-established typical / atypical APs and the search for new AIMetS biomarkers can help improve the safety of SSD pharmacotherapy and minimise the risk of a drug-induced metabolic disorder [11, 12].

The AIMetS mechanisms are not yet clear enough, therefore psychiatrists have access to only a few mitigating (reduced AP dosage or discontinued active SSD therapy with the AP that caused this condition) or alternative actions (optimised lifestyle and diet of an SSD patient) for correcting this AP-induced ADR [13]. This highlights the importance of finding new ways to predict and timely diagnose AIMetS, using, among others, epigenetic biomarkers that predict the risk of adverse reactions following psychopharmacotherapy with a higher sensitivity than classical approaches do [14]. Such promising epigenetic biomarkers include circulating small non-coding ribonucleic acids (microRNAs) [15–17] that play an important role in the regulation of various physiological and pathological processes.

The aim is to evaluate the potential of circulating microRNAs as epigenetic biomarkers for the prediction and early diagnosis of AIMetS.

The analysed fundamental and clinical studies concentrated on circulating microRNAs as epigenetic biomarkers of the main MetS and AIMetS mechanisms, which was included in the Google Scholar, PubMed, Scopus, eLibrary.ru databases for 2014–2024. Search keywords: “метаболический синдром”, “антипсихотик”, “антипсихотик-индуцированный метаболический синдром”, “эпигенетический биомаркер”, “микроРНК”, “metabolic syndrome”, “antipsychotic”, “antipsychotic-induced metabolic syndrome”, “epigenetic biomarker”, “microRNAs”. Inclusion criteria: access type – open access to the full-text publication in the Russian or English language; publication type – original article, systematic review, meta-analysis, and Cochrane review. Exclusion criteria: duplicate publications, dissertations, and thesis abstracts published under the copyright.

[1] The IDF consensus worldwide definition of the metabolic syndrome. IDF; 2006. https://idf.org/media/uploads/2023/05/attachments-30.pdf

The analysed publications assessed changes in the expression levels of circulating microRNAs (plasma, serum, exosomes, mononuclears).

MAIN PART

Diagnostic criteria for antipsychotic-induced metabolic syndrome

According to the new IDF[2] definition (2023), to diagnose MetS, a patient must have central obesity (increased waist circumference (*Table 1*, published on the journal website[3]) compared with ethnic norms) plus any two of the following markers: serum triglycerides (TG) >150 mg/dL (1.7 mmol/L) or specific treatment of triglyceridemia; serum HDL-C <40 mg/dL (1.03 mmol/L) in men and <50 mg/dL (1.29 mmol/L) in women or specific treatment of this lipid metabolism disorder; increased systolic blood pressure ⩾130 mmHg, increased diastolic blood pressure ⩾85 mmHg or treatment of previously diagnosed hypertension; fasting plasma glucose >100 mg/dL (5.6 mmol/L) or previously diagnosed type 2 diabetes mellitus (if >100 mg/dL (5.6 mmol/L), a glucose tolerance test is strongly recommended). In 2023, the IDF experts also developed additional clinical and laboratory (biochemical, hormonal) MetS markers (*Table 2*, published on the journal website[4]; the Table also adapted materials from [14, 18, 19].

Biomarkers can be used not only to classify and assess the individual risk of developing and progressing mental disorders and comorbid diseases in a patient, but to assess the safety and risk of standard and novel therapeutic strategies [20], including the risk of both primary and secondary MetS in SSD patients (drug-induced), as is the case with AIMetS [8]. In recent years, the pattern of AIMetS laboratory biomarkers has expanded significantly as a result of Russian and foreign fundamental and clinical studies *(Table 3)*.

Considering the study results of these laboratory biomarkers, it is proposed to diagnose three degrees of AIMetS in SSD patients receiving AP for 3 months or more: specific, possible, and probable [14].

Specific AIMetS is marked by: ⩾3 MetS clinical criteria (according to the current IDF international criteria or the National Cholesterol Education Program Adult Treatment Panel III (ATP III) / National Cholesterol Education Program Adult Treatment Panel III-advanced (ATP III-A)[5] while taking APs for ⩾3 months as a mono- or polytherapy; ⩾3 additional AIMetS blood biomarkers (plasma and serum) and ⩾3 AIMetS markers of in urine.

Possible AIMetS shows 1 to 3 MetS clinical criteria in accordance with current international criteria (ATP III, ATP III-A or IDF) while taking APs for ⩾3 months as a mono- or polytherapy; 1 to 3 blood biomarkers (plasma and serum) or 1 to 3 biomarkers in urine.

Probable AIMetS is marked by the lack of MetS clinical criteria (in accordance with ATP III, ATP III-A or IDF criteria) after ⩾3 months of taking APs as a mono- or polytherapy; the presence of individual (single) biomarkers of MetS in blood (plasma and serum) and/or single biomarkers in urine.

However, absence of the above clinical and laboratory MetS biomarkers in patients with mental disorders within 3 months of AP therapy does not exclude the risk of AIMetS in the future if AP is continued. Dynamic monitoring of these biomarkers is important in patients with possible AIMetS (once every three months) and with probable AIMetS (once every six months) [14].

Sensitivity and specificity of laboratory (biochemical and hormonal) AIMetS biomarkers can vary in a wide range depending on the environmental factors (geography and climate, nutrition, and sociocultural factors), age and gender of patients with mental disorders,

[2] The IDF consensus worldwide definition of the metabolic syndrome. IDF; 2006. https://idf.org/media/uploads/2023/05/attachments-30.pdf
[3] https://doi.org/10.30895/2312-7821-2025-478-tabl1-2
[4] https://doi.org/10.30895/2312-7821-2025-478-tabl1-2
[5] National Cholesterol Education Program High Blood Cholesterol ATP III Guidelines At-A-Glance: Quick Desk Reference. https://www.nhlbi.nih.gov/files/docs/guidelines/atglance.pdf

Table 3. Primary and additional blood-based laboratory biomarkers of antipsychotic-induced metabolic syndrome[6] [14, 21–26]

Biomarker	Reference value	Levels in MetS	MetS symptom
Primary laboratory biomarkers			
Glucose, mg/dL	<100	High	Insulin resistance
Insulin, μU/mL	2.6–24.9	High	Insulin resistance
Apolipoprotein B, g/L	0.6–1.33	High	Insulin resistance Dyslipidaemia Central obesity
High-density lipoproteins, mmol/L	0.7–1.7	Low	Insulin resistance
Low-density lipoprotein cholesterol, mmol/L	<2.6	High	Dyslipidaemia Central obesity
Uric acid, μmol/L	M: 202.3–416.5 F: 142.8–339.2	High	Obesity
Aldosterone, pg/mL	25–315	High	High blood pressure
C-peptide, ng/mL	1.1–4.4	High	Insulin resistance
Additional laboratory biomarkers			
Sialic acid, mmol/L	2.00–2.33	High	Coronary heart disease Systemic inflammation
Adiponectin, g/L	0.6–1.33	Low	Insulin resistance
Chimerin, ng/mL	116.00–157.50	High	Central obesity Coronary heart disease
Ghrelin, ng/L	0–100	Low	Central obesity
Leptin, ng/mL	M: 2–5.6 F: 3.7–11.1	High	Insulin resistance Leptin resistance
Omentin, ng/mL	M (18–29 years): 200–960 M (30–39 years): 252–712 M (40–49 years): 272–784 F (15–29 years): 242–764 F (30–37 years): 236–560 F (38–49 years): 220–600	Low	Central obesity Endothelial dysfunction Coronary heart disease
Parathyroid hormone, pg/mL	15.0–65.0	High	Cardiovascular diseases
Testosterone, nmol/L	M (18–55 years): 8.64–29.0 F (18–55 years): 0.29–1.67	Low	Central obesity
Thyroid-stimulating hormone, μIU/mL	0.27–4.2	High	Cardiovascular diseases
Total bilirubin, μmol/L	<21	Low	Oxidative stress
Adipocyte fatty acid-binding protein, ng/mL	<6.2	High	Central obesity Cardiometabolic diseases
Serum soluble ligand CD40, ng/mL	<3.5	High	Systemic inflammation Coronary heart disease
Cystatin C, mg/L	0.5–1.2	High	High blood pressure
Ferritin, μg/L	M: 20–250 F: 10–120	Contradictory	Oxidative stress
Fibrinogen, g/L	1.8–3.5	High	High blood pressure Coronary heart disease
Fibroblast growth factor 21, pg/mL	M: 3.6–1021.4 F: 65.3–1209.8	High	Central obesity Atherosclerosis

[6] https://www.biovendor.com/file/5881/PDS_67_HOME_ENG.004.A_EV.pdf?version=202303080807
https://www.abcam.com/products/elisa-kits/human-mcp-1-elisa-kit-ab179886.html
https://practical-haemostasis.com/Fibrinolysis/pai_1.html
https://www.athensresearch.com/products/human-proteins/retinol-binding-protein-human-plasma-rbp-4
https://www.randox.com/superoxide-dismutase-ransod/

Table 3 (continued)

Biomarker	Reference value	Levels in MetS	MetS symptom
Monocytic chemotactic protein-1, pg/mL	4.7–300.0	High	Coronary heart disease
Plasminogen activator inhibitor-1, ng/mL	5.0–40.0	High	Insulin resistance Coronary heart disease
Retinol-binding protein 4, μg/mL	11.0–40.0	High	Central obesity Insulin resistance Cardiovascular diseases
Tumour necrosis factor alpha, pg/mL	<8.1	High	Coronary heart disease
Oxidised low-density lipoprotein, IU/L	26.0–117.0	High	Oxidative stress Systemic inflammation
Apolipoprotein A1, g/L	M: >1.2 F: >1.4	Low	Insulin resistance Dyslipidaemia Central obesity
Free fatty acids, ng/mL	M: 8.3–10.9 F: 11.4–13.6	High	Insulin resistance
Superoxide dismutase type 1 (in red blood cells), U/g	1200.0–2000.0	Low	Oxidative stress Systemic inflammation
Gamma-glutamyl transferase, U/g	M: 10.0–71.0 F: 6.0–42.0	High	Oxidative stress Systemic inflammation
Lipoprotein-associated phospholipase A, ng/mL	<200.0	High	Cardiovascular diseases
Vitamin D (25-hydroxycholecalciferol), ng/mL	30.0–100.0	Low	Cardiovascular diseases
Vitamin E (tocopherol), μg/mL	5.0–18.0	Low	Oxidative stress

The table is prepared by the authors

Note. MetS, metabolic syndrome; M, male; F, female.

as well as sampling and storage of samples. This encourages researchers to look for new AIMetS biomarkers that would have a better stability profile in blood samples, as well as a good reproducibility of research results in various laboratories. Circulating microRNAs are promising epigenetic biomarkers [15–17] that may contain data on the environment and lifestyle impact on the health of an SSD patient, and also allow monitoring the effectiveness of treatments applied for this mental disorder [27–30].

Epigenetic biomarkers of antipsychotic-induced metabolic syndrome

Advance in epigenomics opened up new possibilities, allowing SSD diagnosis and control and predicting an adverse response to psychopharmacotherapy more accurately, efficiently, and quickly [30, 31] than using standard approaches based on the previously proposed clinical and biochemical MetS and AIMetS markers [15, 16]. Candidate epigenetic biomarkers are selected from a huge number of molecules produced by cells and tissues in case of MetS and AIMetS during preclinical and clinical studies, including microRNAs and histone posttranslational modifications that can be analysed in a wide range of biological samples (blood plasma, serum, saliva, urine, breast milk, fresh and frozen tissues, formalin-fixed paraffin-embedded tissues, etc.). MicroRNAs are stable and reproducible during sample processing and can be used for MetS and AIMetS prediction and their early diagnosis (identification) in SSD patients, as well as for clarifying natural course and outcome [30].

MicroRNAs are small non–coding single-stranded RNAs (19–25 nucleotides) involved in transcriptional and post-transcriptional regulation of gene expression through specific interactions with target genes [32]. MicroRNAs play an important role in the regulation of various physiological and pathological processes involved in MetS and AIMetS mechanisms, including oxidative stress [33, 34], systemic inflammation [35, 36], adipocyte

Table 4. Roles of circulating microRNAs in the mechanisms of antipsychotic-induced metabolic syndrome pathogenesis

Pathogenetic mechanism	Role of circulating microRNAs	References
Oxidative stress	Inhibition of oxidative stress: miR-19b, miR-20a, miR-24, miR-99a, miR-125b, miR-141, miR-152, miR-200a, miR-200c, miR-210, miR-221, miR-455, miR-601, miR-626	[33, 34]
	Induction of oxidative stress: miR-1, miR-21, miR-23b, miR-27a, miR-28, miR-29, miR-34a, miR-92a, miR-93, miR-101, miR-106b, miR-128, miR-129, miR-140, miR-142, miR-144, miR-146, miR-148, miR-153, miR-155, miR-181c, miR-193b, miR-320, miR-365, miR-375, miR-383, miR-495, miR-503, miR-802	
Systemic inflammation	Anti-inflammatory effect: miR-7, miR-9, miR-10a, miR-15a, miR-16, miR-24, miR-31, miR-124, miR-125, miR-126, miR-142, miR-143, miR-146, miR-149, miR-150, miR-210, miR-223, miR-363	[35, 36]
	Pro-inflammatory effect: miR-21, miR-23a, miR-27a, miR-29a, miR-34a, miR-34c, miR-92a, miR-132, miR-138, miR-155, miR-200, miR-let7a	
Regulation of adipogenesis, development of central obesity	Inhibition of adipogenesis and prevention of central obesity: miR-27, miR-27a, miR-30c, miR-33a, miR-33b, miR-130, miR-145, miR-146a, miR-155, miR-181, miR-182, miR-200b, miR-236, miR-363, miR-344, miR-448, miR-4429	[35, 37–39]
	Induction of adipogenesis and central obesity: miR-17, miR-20a, miR-21, miR-103, miR-128-1, miR-143, miR-144, miR-146b, miR-148a, miR-194, miR-210, miR-322, miR-375, intronic miR-378	
Changes in lipid metabolism	Inhibition of lipid metabolism: miR-30c, miR-33a, miR-33b, miR-34a, miR-128-1, miR-144, miR-148a, miR-223, miR-246b	[38, 60]
	Induction of lipid metabolism: miR-7, miR-27a, miR-27b, miR-122	
Changes in high-density lipoprotein cholesterol homeostasis	Upregulation of high-density lipoprotein levels: no data	[38, 40, 41]
	Downregulation of high-density lipoprotein levels: miR-33a, miR-33b, miR-128-1, miR-144, miR-148b	
Changes in low-density lipoprotein cholesterol homeostasis	Upregulation of low-density lipoprotein levels: miR-128-1, miR-148a	[40, 42]
	Downregulation of low-density lipoprotein levels: miR-30c	
Changes in atherogenesis	Inhibition of atherogenesis: miR-30c	[38, 41, 42]
	Induction of atherogenesis: miR-33,miR-144	
Development of fatty hepatosis (fatty liver disease)	Contribution to fatty hepatosis development: miR-34a	[38]
	Prevention of fatty hepatosis development: miR-27a, miR-122, miR-223	
Changes in insulin sensitivity	Reduction of insulin sensitivity: miR-let7 (muscle tissue), miR-15b, miR-19, miR-29, miR-33a/b (liver), miR-103 (adipose tissue), miR-107 (adipose tissue), miR-143, miR-155, miR-223, miR-378 (liver), miR-451-1, miR-802 (liver)	[35, 38, 43–45]
	Improvement of insulin sensitivity: no data	
Changes in insulin expression and secretion by B-cells in the islets of Langerhans	Inhibition of insulin expression and secretion: miR-7a, miR-26a, miR-29, miR-124a, miR-130a, miR-130b, miR-152, miR-187, miR-200, miR-204, miR-375, miR-802	[38, 46–50]
	Activation of insulin expression and secretion: miR-24, miR-26, miR-30d, miR-148, miR-182	

Table 4 (continued)

Pathogenetic mechanism	Role of circulating microRNAs	References
Changes in glucose metabolism	Inhibition of gluconeogenesis and glucose metabolism: miR-7a, miR-26a, miR-27, miR-29, miR-33b, miR-103, miR-107, miR-124, miR-130a, miR-130b, miR-143, miR-152, miR-155, miR-187, miR-200, miR-204, miR-336, miR-375, miR-378, miR-451-1, miR-466b, miR-802	[38, 43–50]
	Induction of glycogenesis and glucose metabolism: miR-19, miR-24, miR-26, miR-27a, miR-30d, miR-33, miR-148, miR-182	
Changes in appetite regulation	Suppression of appetite: miR-33, miR-103	[51–54, 56]
	Stimulation of appetite: miR-let7a, miR-7a, miR-9, miR-30e, miR-100, miR-132, miR-141, miR-145, miR-200a, miR-218, miR-342, miR-383, miR-384-3p, miR-429, miR-488	
Changes in neuropeptide Y expression	Increased of the neuropeptide Y expression: miR-708, miR-2137	[51, 55]
	Downregulation of NPY expression: miR-let7b, miR-29b, miR-33, miR-140- miR-143, miR-503	
Changes in leptin sensitivity	Improvement of leptin sensitivity: miR-let7a, miR-9, miR-30e, miR-132, miR-145, miR-218, miR-342	[35, 56]
	Reduction of leptin sensitivity: miR-15a, miR-16, miR-33, miR-200a, miR-200b, miR-223, miR-363, miR-429, miR-532	
Changes in orexin expression	Upregulation of orexin expression: нет данных / no data	[58, 59]
	Downregulation of orexin expression: miR-137, miR-637, miR-654, miR-665	
Changes in testosterone expression	Upregulation of testosterone expression: miR-15a, miR-320	[60]
	Downregulation of testosterone expression: miR-150	
Changes in thyroid hormones expression	Upregulation of thyroid hormone expression: miR-21, miR-146, miR-214	[61]
	Downregulation of thyroid hormone expression: miR-27, miR-155, miR-181, miR-200a, miR-221, miR-224, miR-246, miR-383, miR-425	
Changes in parathyroid hormone expression	Upregulation of parathyroid hormone expression: miR-27b, miR-136b, miR-146b, miR-503	[62]
	Downregulation of parathyroid hormone expression: miR-24	

The table is prepared by the authors

Note. miR, microRNA.

differentiation and central obesity [35–37], lipid and glucose metabolism [35, 38–50], regulation of appetite changes [51–54, 56], changes in: neuropeptide Y (NPY) expression [51, 56, 57], leptin sensitivity [36, 56, 57], orexin expression [58, 59], testosterone levels [60], thyroid hormones [61] and parathyroid hormone [62] *(Table 4)*. The signature of circulating microRNAs in AIMetS patients receiving AP differs from that in naive patients (before AP prescription) and in healthy people [33–56, 58–62].

Over the recent years, an extensively discussed hypothesis is that circulating microRNAs can participate in initiation and modification of the development and severity [36, 63, 64] for both AIMetS and MetS associated with SSD itself [65-67]. In addition, polymorphic variants in microRNA-coding genes and/or in the binding sites of target genes and microRNAs can alter the expression levels of circulating microRNAs in the blood, which is also associated with MetS and AIMetS risk and severity in patients with mental disorders [68, 69].

Circulating microRNAs are promising biomarkers of AIMetS occurrence and severity in SSD patients due to the simple and accessible obtaining of biological samples. Over the past 10 years, Russian and foreign studies have demonstrated that circulating micro-

RNAs and their mediated regulation of the metabolic response to APs can be considered as a basic level of epigenetic control for various pathogenetic AIMetS mechanisms and individual variability in AP safety in general, including the risk of therapeutic resistance to APs [70].

CONCLUSIONS

Despite its frequent occurrence in psychopharmacotherapy, the problem of early AIMetS detection is far from being resolved. The first part of this review describes approaches to the spectrum and assessment of the main and additional clinical / laboratory MetS markers in SSD patients in general and AIMetS in particular. Previously used classical biomarkers (biochemical, hormonal) are individually variable and influenced by both environmental factors and sample preparation / storage of biological samples, which affects their *ex vivo* stability.

Circulating microRNAs are involved in the initiation and modification of the development of all AIMetS manifestations, including oxidative stress, systemic inflammation, adipocyte differentiation, lipid and glucose metabolism, appetite regulation, changes in neuropeptide Y expression, leptin sensitivity, orexin expression, testosterone levels, thyroid hormones, and parathyroid hormone. MicroRNAs are promising as AIMetS prognostic and diagnostic biomarkers, as they are detected in easily accessible samples (blood, saliva, urine), are highly stable in the stored biological samples (including during multiple cycles of freezing and thawing), better reproducibility, and higher sensitivity in individual patients compared with classical biomarkers.

The second part of the review will consider the role of specific circulating microRNAs as epigenetic biomarkers of the main AIMetS domains. The authors will also describe their ideas on the gradation of microRNA signatures in SSD patients depending on AIMetS risk (low, medium, high) and discuss the prospects for their clinical use in the psychiatric practice.

References / Литература

1. Pillinger T, McCutcheon RA, Vano L, et al. Comparative effects of 18 antipsychotics on metabolic function in patients with schizophrenia, predictors of metabolic dysregulation, and association with psychopathology: A systematic review and network meta-analysis. *Lancet Psychiatry*. 2020;7(1):64–77. https://doi.org/10.1016/S2215-0366(19)30416-X
2. Shpilevskaya YR, Shtonda MV. Metabolic syndrome: The modern aspects of diagnostic and treatment. *Medical News*. 2021;(5):4–8 (In Russ.). EDN: HCJBZE
3. Ferrari CKB. Chapter 6. Epidemiology of metabolic syndrome: Global scenario. In: Mukhopadhyay S, Mondal S, eds. *Metabolic syndrome: From mechanisms to interventions*. Academic Press; 2024. P. 59–71. https://www.doi.org/10.1016/B978-0-323-85732-1.00038-4
4. Li W, Qiu X, Ma H, Geng Q. Incidence and long-term specific mortality trends of metabolic syndrome in the United States. *Front Endocrinol (Lausanne)*. 2023;13:1029736. https://www.doi.org/10.3389/fendo.2022.1029736
5. Chong KS, Chang YH, Yang CT, et al. Longitudinal economic burden of incident complications among metabolic syndrome populations. *Cardiovasc Diabetol*. 2024;23(1):246.
6. Akinola PS, Tardif I, Leclerc J. Antipsychotic-induced metabolic syndrome: A review. *Metab Syndr Relat Disord*. 2023;21(6):294–305. https://doi.org/10.1089/met.2023.0003
7. Penninx BWJH, Lange SMM. Metabolic syndrome in psychiatric patients: Overview, mechanisms, and implications. *Dialog Clin Neurosci*. 2018;20(1):63–73. https://doi.org/10.31887/DCNS.2018.20.1/bpenninx
8. Libowitz MR, Nurmi EL. The burden of antipsychotic-induced weight gain and metabolic syndrome in children. *Front Psychiatry*. 2021;12:623681. https://doi.org/10.3389/fpsyt.2021.623681
9. Correll CU, Manu P, Olshanskiy V, et al. Cardiometabolic risk of second-generation antipsychotic medications during first-time use in children and adolescents. *JAMA*. 2009;302(16):1765–73. https://doi.org/10.1001/jama.2009.1549
10. Keepers GA, Fochtmann LJ, Anzia JM, et al. The American Psychiatric Association Practice Guide-

line for the treatment of patients with schizophrenia. *Am J Psychiatry*. 2020;177(9):868–72. https://doi.org/10.1176/appi.ajp.2020.177901
11. Bernardo M, Rico-Villademoros F, García-Rizo C, et al. Real-world data on the adverse metabolic effects of second-generation antipsychotics and their potential determinants in adult patients: A systematic review of population-based studies. *Adv Ther*. 2021;38(5):2491–512. https://doi.org/10.1007/s12325-021-01689-8
12. Limankin OV. Personalized psychiatry: Achievements and prospects. *Personalized Psychiatry and Neurology*. 2021;1(2):126–7. https://doi.org/10.52667/2712-9179-2021-1-2-126-127
13. Castellani LN, Costa-Dookhan KA, McIntyre WB, et al. Preclinical and clinical sex differences in antipsychotic-induced metabolic disturbances: A narrative review of adiposity and glucose metabolism. *J Psychiatr Brain Sci*. 2019;4:e190013. https://doi.org/10.20900/jpbs.20190013
14. Khasanova AK, Dobrodeeva VS, Shnayder NA, et al. Blood and urinary biomarkers of antipsychotic-induced metabolic syndrome. *Metabolites*. 2022;12(8):726. https://doi.org/10.3390/metabo12080726
15. Mironova OI, Berdysheva MV, Elfimova EM. MicroRNA: A clinician's view of the state of the problem. Part 2. MicroRNA as a biomarker. *Eurasian Heart Journal*. 2023;(2):64–71 (In Russ.). https://doi.org/10.38109/2225-1685-2023-2-64-71
16. Dexheimer PJ, Cochella L. MicroRNAs: From mechanism to organism. *Front Cell Dev Biol*. 2020;8:409. https://www.doi.org/10.3389/fcell.2020.00409
17. Pozniak T, Shcharbin D, Bryszewska M. Circulating microRNAs in medicine. *Int J Mol Sci*. 2022;23(7):3996. https://www.doi.org/10.3390/ijms23073996
18. Gayoso-Diz P, Otero-González A, Rodriguez-Alvarez MX, et al. Insulin resistance (HOMA-IR) cut-off values and the metabolic syndrome in a general adult population: Effect of gender and age: EPIRCE cross-sectional study. *BMC Endocr Disord*. 2013;13:47. https://doi.org/10.1186/1472-6823-13-47
19. Karpel'ev VA, Filippov YI, Tarasov YV, et al. Mathematical modeling of the blood glucose regulation system in diabetes mellitus patients. *Annals of the Russian Academy of Medical Sciences*. 2015;70(5):549–60 (In Russ.). https://doi.org/10.15690/vramn.v70.i5.1441
20. Bethesda M. Biomarkers Definitions Working Group. Biomarkers and surrogate endpoints: preferred definitions and conceptual framework. *Clin Pharmacol Ther*. 2001;69(3):89–95. https://doi.org/10.1067/mcp.2001.113989
21. Vulf MA, Shunkina (Skuratovskaia) DA, Hung V, et al. Chemerin as a potential regulator of mitochondrial quality control in obese patients. *Medical Immunology (Russia)*. 2021;23(4):881–6 (In Russ.). https://doi.org/10.15789/1563-0625-CAA-2227
22. Behnoush AH, Shobeiri P, Bahiraie P, et al. Chemerin levels in chronic kidney disease: A systematic review and meta-analysis. *Front Endocrinol (Lausanne)*. 2023;14:1120774. https://www.doi.org/10.3389/fendo.2023.1120774
23. Alieva AM, Teplova NV, Reznik EV, et al. Diagnostic and prognostic aspects of omentin in cardiovascular diseases. *Russian Cardiology Bulletin*. 2024;19(1):16–22 (In Russ.). https://doi.org/10.17116/Cardiobulletin20241901116
24. Pobozheva IA, Panteleeva AA, Polyakova EA, et al. Subcutaneous adipose tissue omentin-1 in coronary artery disease patients. *Medical Genetics*. 2020;19(11):21–30 (In Russ.). https://doi.org/10.25557/2073-7998.2020.11.21-30
25. Lorente L, Martín MM, Varo N, et al. Association between serum soluble CD40 ligand levels and mortality in patients with severe sepsis. *Crit Care*. 2011;15(2):R97. https://www.doi.org/10.1186/cc10104
26. Wang MN, Han YB, Li Q, et al. Higher serum retinol binding protein 4 may be a predictor of weak metabolic control in Chinese patients with type 2 diabetes mellitus. *J Int Med Res*. 2012;40(4):1317–24. https://www.doi.org/10.1177/147323001204000410
27. Brandão-Lima PN, de Carvalho GB, Payolla TB, et al. Circulating microRNAs showed specific responses according to metabolic syndrome components and sex of adults from a population-based study. *Metabolites*. 2022;13(1):2. https://www.doi.org/10.3390/metabo13010002
28. Solís-Toro D, Mosquera Escudero M, García-Perdomo HA. Association between circulating microRNAs and the metabolic syndrome in adult populations: A systematic review. *Diabetes Metab Syndr*. 2022;16(1):102376. https://www.doi.org/10.1016/j.dsx.2021.102376
29. Xavier G, Mauer J, Ota VK, et al. Influence of antipsychotic drugs on microRNA expression in schizophrenia patients – a systematic review. *J Psychiatr Res*. 2024;176:163–72. https://doi.org/10.1016/j.jpsychires.2024.06.010
30. García-Giménez JL, Seco-Cervera M, Tollefsbol TO, et al. Epigenetic biomarkers: Current strategies and future challenges for their use in the clinical laboratory. *Crit Rev Clin Lab Sci*. 2017;54(7–8):529–50. https://doi.org/10.1080/10408363.2017.1410520
31. Neznanov NG. A paradigm shift to treat psychoneurological disorders. *Personalized Psychiatry and Neurology*. 2021;1(1):1–2.

32. O'Brien J, Hayder H, Zayed Y, Peng C. Overview of microRNA biogenesis, mechanisms of actions, and circulation. *Front Endocrinol (Lausanne)*. 2018;9:402. https://www.doi.org/10.3389/fendo.2018.00402
33. Saha S. Role of microRNA in oxidative stress. *Stresses*. 2024;4(2):269–81. https://doi.org/10.3390/stresses4020016
34. Włodarski A, Strycharz J, Wróblewski A, et al. The role of microRNAs in metabolic syndrome-related oxidative stress. *Int J Mol Sci*. 2020;21(18):6902. https://www.doi.org/10.3390/ijms21186902
35. Carvalho GB, Brandão-Lima PN, Payolla TB, et al. Circulating miRNAs are associated with low-grade systemic inflammation and leptin levels in older adults. *Inflammation*. 2023;46(6):2132–46. https://www.doi.org/10.1007/s10753-023-01867-6
36. Das K, Rao LVM. The role of microRNAs in inflammation. *Int J Mol Sci*. 2022;23(24):15479. https://www.doi.org/10.3390/ijms232415479
37. Engin AB, Engin A. Adipogenesis-related microRNAs in obesity. *ExRNA*. 2022;4:16. https://www.doi.org/10.21037/exrna-22-4
38. Agbu P, Carthew RW. MicroRNA-mediated regulation of glucose and lipid metabolism. *Nat Rev Mol Cell Biol*. 2021;22(6):425–38. https://www.doi.org/10.1038/s41580-021-00354-w
39. Dong M, Ye Y, Chen Z, et al. MicroRNA 182 is a novel negative regulator of adipogenesis by targeting CCAAT/enhancer-binding protein α. *Obesity (Silver Spring)*. 2020;28(8):1467–76. https://doi.org/10.1002/oby.22863
40. Wagschal A, Najafi-Shoushtari SH, Wang L, et al. Genome-wide identification of microRNAs regulating cholesterol and triglyceride homeostasis. *Nat Med*. 2015;21(11):1290–7. https://www.doi.org/10.1038/nm.3980
41. Cheng J, Cheng A, Clifford BL, et al. MicroRNA-144 silencing protects against atherosclerosis in male, but not female mice. *Arterioscler Thromb Vasc Biol*. 2020;40(2):412–25. https://www.doi.org/10.1161/ATVBAHA.119.313633
42. Irani S, Iqbal J, Antoni WJ, et al. MicroRNA-30c reduces plasma cholesterol in homozygous familial hypercholesterolemic and type 2 diabetic mouse models. *J Lipid Res*. 2018;59(1):144–54. https://doi.org/10.1194/jlr.M081299
43. Trajkovski M, Hausser J, Soutschek J, et al. MicroRNAs 103 and 107 regulate insulin sensitivity. *Nature*. 2011;474(7353):649–53. https://doi.org/10.1038/nature10112
44. Liu W, Cao H, Ye C, et al. Hepatic miR-378 targets p110α and controls glucose and lipid homeostasis by modulating hepatic insulin signalling. *Nat Commun*. 2014;5:5684. https://doi.org/10.1038/ncomms6684
45. Kornfeld JW, Baitzel C, Könner AC, et al. Obesity-induced overexpression of miR-802 impairs glucose metabolism through silencing of Hnf1b. *Nature*. 2013;494(7435):111–5. https://doi.org/10.1038/nature11793
46. Xu H, Du X, Xu J, et al. Pancreatic β cell microRNA-26a alleviates type 2 diabetes by improving peripheral insulin sensitivity and preserving β cell function. *PLoS Biol*. 2020;18(2):e3000603. https://doi.org/10.1371/journal.pbio.3000603
47. Ofori JK, Salunkhe VA, Bagge A, et al. Elevated miR-130a/miR130b/miR-152 expression reduces intracellular ATP levels in the pancreatic beta cell. *Sci Rep*. 2017;7:44986. https://doi.org/10.1038/srep44986
48. Belgardt BF, Ahmed K, Spranger M, et al. The microRNA-200 family regulates pancreatic beta cell survival in type 2 diabetes. *Nat Med*. 2015;21(6):619–27. https://doi.org/10.1038/nm.3862
49. Zhang F, Ma D, Zhao W, et al. Obesity-induced overexpression of miR-802 impairs insulin transcription and secretion. *Nat Commun*. 2020;11(1):1822. https://doi.org/10.1038/s41467-020-15529-w
50. Melkman-Zehavi T, Oren R, Kredo-Russo S, et al. miRNAs control insulin content in pancreatic β-cells via downregulation of transcriptional repressors. *EMBO J*. 2011;30(5):835–45. https://doi.org/10.1038/emboj.2010.361
51. Price NL, Fernández-Tussy P, Varela L, et al. microRNA-33 controls hunger signaling in hypothalamic AgRP neurons. *Nat Commun*. 2024;15(1):2131. https://www.doi.org/10.1038/s41467-024-46427-0
52. Taouis M. MicroRNAs in the hypothalamus. *Best Pract Res Clin Endocrinol Metab*. 2016;30(5):641–51. https://www.doi.org/10.1016/j.beem.2016.11.006
53. Zhang D, Yamaguchi S, Zhang X, et al. Upregulation of mir342 in diet-induced obesity mouse and the hypothalamic appetite control. *Front Endocrinol (Lausanne)*. 2021;12:727915. https://www.doi.org/10.3389/fendo.2021.727915
54. Sangiao-Alvarellos S, Pena-Bello L, Manfredi-Lozano M, et al. Perturbation of hypothalamic microRNA expression patterns in male rats after metabolic distress: impact of obesity and conditions of negative energy balance. *Endocrinology*. 2014;155(5):1838–50. https://www.doi.org/10.1210/en.2013-1770
55. Mak KWY, He W, Loganathan N, Belsham DD. Bisphenol A alters the levels of miRNAs that directly and/or indirectly target neuropeptide Y in murine hypothalamic neurons. *Genes (Basel)*. 2023;14(9):1773. https://www.doi.org/10.3390/genes14091773
56. Derghal A, Djelloul M, Azzarelli M, et al. MicroRNAs are involved in the hypothalamic leptin sensitivity. *Epigenetics*. 2018;13(10–11):1127–40.

https://doi.org/10.1080/15592294.2018.1543507
57. Dobrodeeva VS, Abdyrahmanova AK, Nasyrova RF. Personalized approach to antipsychotic-induced weight gain prognosis. P*ersonalized Psychiatry and Neurology*. 2021;1(1):3–10. https://doi.org/10.52667/2712-9179-2021-1-1-3-10
58. Holm A, Possovre ML, Bandarabadi M, et al. The evolutionarily conserved miRNA-137 targets the neuropeptide hypocretin/orexin and modulates the wake to sleep ratio. *Proc Natl Acad Sci USA*. 2022;119(17):e2112225119. https://www.doi.org/10.1073/pnas.2112225119
59. Siegert S, Seo J, Kwon EJ, et al. The schizophrenia risk gene product miR-137 alters presynaptic plasticity. *Nat Neurosci*. 2015;18(7):1008–16. https://www.doi.org/10.1038/nn.4023
60. Azhar S, Dong D, Shen WJ, et al. The role of miRNAs in regulating adrenal and gonadal steroidogenesis. *J Mol Endocrinol*. 2020;64(1):R21–R43. https://www.doi.org/10.1530/JME-19-0105
61. Aranda A. MicroRNAs and thyroid hormone action. *Mol Cell Endocrinol*. 2021;525:111175. https://www.doi.org/10.1016/j.mce.2021.111175
62. Vaira V, Verdelli C, Forno I, Corbetta S. MicroRNAs in parathyroid physiopathology. *Mol Cell Endocrinol*. 2017;456:9–15. https://www.doi.org/10.1016/j.mce.2016.10.035
63. Martinez B, Peplow PV. MicroRNAs as potential biomarkers for diagnosis of schizophrenia and influence of antipsychotic treatment. *Neural Regen Res*. 2024;19(7):1523–31. https://doi.org/10.4103/1673-5374.387966
64. Zhang HC, Du Y, Chen L, et al. MicroRNA schizophrenia: Etiology, biomarkers and therapeutic targets. *Neurosci Biobehav Rev*. 2023;146:105064. https://doi.org/10.1016/j.neubiorev.2023.105064
65. Zaki MB, Abulsoud AI, Ashraf A, et al. The potential role of miRNAs in the pathogenesis of schizophrenia – a focus on signaling pathways interplay. *Pathol Res Pract*. 2024;254:155102. https://doi.org/10.1016/j.prp.2024.155102
66. Chan YL, Ho CSH, Tay GWN, et al. MicroRNA classification and discovery for major depressive disorder diagnosis: Towards a robust and interpretable machine learning approach. *J Affect Disord*. 2024;360:326–35. https://doi.org/10.1016/j.jad.2024.05.066
67. Ding R, Su D, Zhao Q, et al. The role of microRNAs in depression. *Front Pharmacol*. 2023;14:1129186. https://doi.org/10.3389/fphar.2023.1129186
68. Elfaki I, Mir R, Mir MM, et al. Potential impact of microRNA gene polymorphisms in the pathogenesis of diabetes and atherosclerotic cardiovascular disease. *J Pers Me*d. 2019;9(4):51. https://doi.org/10.3390/jpm9040051
69. Gottmann P, Ouni M, Zellner L, et al. Polymorphisms in miRNA binding sites involved in metabolic diseases in mice and humans. *Sci Rep*. 2020;10:7202. https://doi.org/10.1038/s41598-020-64326-4
70. Villanova F, Di Meglio P, Nestle FO. Biomarkers in psoriasis and psoriatic arthritis. *Ann Rheum Dis*. 2013;72(S2):ii104–10. https://doi.org/10.1136/annrheumdis-2012-203037

Additional information. Tables 1–2 are posted on the website of *Safety and Risk of Pharmacotherapy*. https://doi.org/10.30895/2312-7821-2025-478-tabl1-2

Дополнительная информация. Таблицы 1 и 2 размещены на сайте журнала «Безопасность и риск фармакотерапии». https://doi.org/10.30895/2312-7821-2025-478-tabl1-2

Authors' contributions. All the authors confirm that they meet the ICMJE criteria for authorship. The most significant contributions were as follows. *Natalia A. Shnayder* drafted the manuscript and revised it based on the peer-review results. *Regina F. Nasyrova* developed the general concept of the study, managed the project, and approved the final version of the manuscript for publication. *Nikolai A. Pekarets* worked with databases and drafted the manuscript. *Violetta V. Grechkina* worked with databases and prepared illustrations. *Marina M. Petrova* designed the study and edited the manuscript.

Вклад авторов. Все авторы подтверждают соответствие своего авторства критериям ICMJE. Наибольший вклад распределен следующим образом: *Н.А. Шнайдер* – написание текста рукописи и его доработка по результатам рецензирования; *Р.Ф. Насырова* – общая концепция, руководство проектом, утверждение финальной версии рукописи для публикации; *Н.А. Пекарец* – работа с базами данных, написание текста рукописи; *В.В. Гречкина* – работа с базами данных, подготовка графических материалов; *М.М. Петрова* – дизайн исследования, редактирование текста рукописи.

AUTHORS / ОБ АВТОРАХ

Natalia A. Shnayder, Dr. Sci. (Med.), Professor
ORCID: https://orcid.org/0000-0002-2840-837X
Regina F. Nasyrova, Dr. Sci. (Med.)
ORCID: https://orcid.org/0000-0003-1874-9434
Nikolai A. Pekarets
ORCID: https://orcid.org/0009-0005-5895-1778
Violetta V. Grechkina
ORCID: https://orcid.org/0000-0001-8279-4198
Marina M. Petrova, Dr. Sci. (Med.), Professor
ORCID: https://orcid.org/0000-0002-8493-0058

Шнайдер Наталья Алексеевна, д-р мед. наук, профессор
ORCID: https://orcid.org/0000-0002-2840-837X
Насырова Регина Фаритовна, д-р мед. наук
ORCID: https://orcid.org/0000-0003-1874-9434
Пекарец Николай Александрович
ORCID: https://orcid.org/0009-0005-5895-1778
Гречкина Виолетта Владимировна
ORCID: https://orcid.org/0000-0001-8279-4198
Петрова Марина Михайловна, д-р мед. наук, профессор
ORCID: https://orcid.org/0000-0002-8493-0058

Received 6 December 2024
Revised 5 March 2025
Accepted 21 March 2025
Online first 4 June 2025

Поступила 06.12.2024
После доработки 05.03.2025
Принята к публикации 21.03.2025
Online first 04.06.2025