PPN

Personalized Psychiatry and Neurology

Review

Changes in Platelet Level and Activation as Hematological Biomarkers of Antipsychotic-Induced Systemic Inflammatory Response: Narrative Review

Regina F. Nasyrova*, Natalia A. Shnayder*, Anastasiia A. Abramenko, Zarema T. Taygibova, Elmar O. Guseynov

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

* Correspondence: regina_nmrcpn@mail.ru (R.F.N.), naschnaider@yandex.ru (N.A.S.)

Citation: Nasyrova R.F., Shnayder N.A., Abramenko A.A., Taygibova Z.T., Guseynov E.O. Changes in platelet level and activation as hematological biomarkers of antipsychotic-induced systemic inflammatory response: narrative review. *Personalized Psychiatry and Neurology* 2026; 6 *(2)*: 10 - 28. https://doi.org/10.52667/2712-9179-2026-6-2-10-28

Chief Editor:
Nikolay G. Neznanov, D Med Sci, Professor

Received: 10 February 2026
Accepted: 10 June 2026
Published: 15 June 2026

Publisher's Note: V.M. Bekhterev NMRC PN stays neutral with regard to jurisdictional claims in published maps and institutional affiliations.

Abstract: Research over the last decade has shown that schizophrenia spectrum disorders (SSDs) cannot be viewed exclusively as a neurotransmitter pathology. A significant proportion of patients, especially those in the acute phase and with treatment resistance, exhibit signs of low-grade inflammation (LGI), which is associated with cardiovascular comorbidity, including the risk of venous thromboembolism (VTE). The role of antipsychotics (APs), which are the mainstay of SSDs therapy, in the development of VTE remains controversial. On one hand, preclinical *in vitro* and *in vivo* studies demonstrate an antiplatelet effect of APs. This effect is mediated through blockade of adenosine diphosphate (P2Y1 and P2Y2) and serotonin (5-HT2A) receptors, and inhibition of thromboxane A2. On the other hand, clinical in vivo studies indicate the persistence or even increase of procoagulant platelet activity and LGI, which significantly elevates the risk of VTE in patients with SSDs during long-term AP treatment. **Materials and Methods:** In this narrative review, we analyzed and summarized the results of preclinical and clinical studies on biomarkers of AP-induced platelet activation, as well as their prognostic role in assessing VTE risk in patients with SSDs. **Results:** As a result, the knowledge of psychiatrists regarding the potential negative impact on platelet hemostasis has been updated for first- and new-generation APs. It has been shown that asenapine and amisulpride carry the highest risk of developing AP-induced VTE. Haloperidol and droperidol have a dose-dependent risk of VTE. An increased risk of AP-induced pathological bleeding is observed with the use of quetiapine, thioridazine, thiothixene, and flupentixol. **Conclusion:** The diverse effects of APs on platelet hemostasis have been demonstrated. This underscores the need for a differentiated approach to selecting APs and the complexity of predicting the additive effect during AP polytherapy. Dynamic monitoring of hematological biomarkers (platelet and inflammatory) is important for reducing the risk of developing VTE in patients with SSDs.

Keywords: *platelets, schizophrenia spectrum disorders, antipsychotic, hematological biomarker, platelet hemostasis, low-grade inflammation, venous thromboembolism, pulmonary embolism, pathological bleeding, hematological adverse reaction.*

1. INTRODUCTION

Schizophrenia spectrum disorders (SSDs, ICD-X: F20 - F29) are characterized by a diverse clinical picture [1] and are associated with the risk of developing somatic pathologies, particularly cardiovascular diseases, venous thromboembolism (VTE), including deep vein thrombosis of the extremities and pulmonary embolism (PE) [2]. Antipsychotic drugs (APs) are the main class of medications used for SSDs, and numerous studies have associated their use with the risk of platelet hemostasis impairment [3,4]. However, in routine clinical practice, psychiatrists rarely or often fail to consider even standard platelet biomarkers [5] (**Table 1**).

In recent years, low-grade inflammation (LGI), induced by APs intake in patients with SSDs, has been considered a mechanism increasing the risk of AP-induced VTE [10]. For a long time, SSDs were viewed primarily as a neurotransmitter pathology. However, accumulated data from preclinical (*in vivo* and *in vitro*) and clinical (*in vivo*) studies convincingly demonstrate that a significant proportion of patients with SSD, especially in the acute phase of the illness, exhibit signs of LGI: increased C-reactive protein (CRP) and pro-inflammatory cytokines (interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF-α), etc.), as well as shifts in peripheral blood cell ratios [11,12].

Table 1. Standard platelet biomarkers in adult patients with schizophrenia spectrum disorders taking antipsychotics.

Platelet biomarker	Reference values	Brief description	Clinical role	References
PLT, $10^9/л$	M: 180-320*10^9/L F: 157-371*10^9/L	Absolute platelet count per unit volume of blood	Increased PLT* Decreased PLT**	[6]
MPV, fL ($10^{-15}л$)	9.1 – 11.9 fL	Mean cytometric platelet size	Increased MPV * Decreased PLT * *	[7] [8]
PCT, %	0.15-0.4 %	The proportion of blood volume occupied by platelets	Increased PCT * Decreased PCT * *	[9]
PDW, %	10-20 %	Degree of platelet size heterogeneity	Increased PDW * Decreased PDW ***	[8]

Note: ** - increased risk of venous thromboembolism, including deep vein thrombosis, pulmonary embolism and its branches; ** - increased risk of pathological bleeding, including spontaneous and low-traumatic hematomas, nosebleeds, uterine and rectal bleeding, hemorrhages in internal organs; *** - rarely has independent clinical significance. Abbreviations: PLT - Platelets, MPV - mean platelet volume, PDW - platelet distribution width, PCT - plateletcrit, P-LCR - platelet - large cell ratio; fL - femtoliter, VTE - venous thromboembolism, M- male, F- female.*

A logical question arose: "Is this inflammation merely a concomitant background, or does it have pathogenetic significance and, moreover, can it be modified under the influence of AP therapy?" Concurrently, experimental studies in animal models, humans, and cell lines established that APs are not inert concerning platelets. APs can block adenosindiphosphate (ADP)-receptors P2Y1/P2Y12, modulate the platelet-activating factor (PAF) pathway, and suppress thromboxane A2 synthesis [13, 14]. *In vitro*, many APs exhibited an antiplatelet effect. Consequently, they should protect patients from VTE and possibly even reduce LGI by inhibiting platelet activity. However, during long-term AP intake, despite the direct inhibitory effect of APs on platelets, signs of their activation and subsequent hypercoagulation persisted or even increased [15].

Studies using the thrombodynamics method have demonstrated that in patients with SSD undergoing AP monotherapy, procoagulant activity does not normalize, and the risk of VTE persists or even increases [10]. Moreover, in patients with treatment-resistant schizophrenia (TRS) receiving clozapine, the highest values of hematological pro-inflammatory biomarkers for VTE were recorded [11, 12]. It became evident that standard quantitative parameters of platelet hemostasis (Table 1), including platelet count (PLT), mean platelet volume (MPV), platelet distribution width (PDW), plateletcrit (PCT), and the platelet-to-lymphocyte ratio (PLR), do not reflect the functional state of platelets under conditions of LGI. The need arose for a differentiated assessment of platelet levels and their functional activation. Also important is the verification of changes in the levels of additional platelet biomarkers (receptor, secretory, or procoagulant), which are altered during long-term AP intake and are associated with interindividual variability in response to psychopharmacotherapy [10,13,14]. We have hypothesized that platelets and hematological biomarkers of their activation may serve as an integral link connecting three key components (APs, LGI, and platelet hemostasis impairment) in patients with SSDs in the short and long term.

The aim of this narrative review is to update psychiatrists' knowledge on the role of hematological biomarkers of platelet activation and associated LGI for effective stratification of patients with SSD based on the degree of risk of AP-induced VTE.

2. MATERIALS AND METHODS

An analysis was conducted of available clinical studies on the adverse drug reactions (ADRs) of first- and new-generation APs on LGI, platelet hemostasis, and the risk of VTE in patients with SSDs, as well as on the relationship between AP-induced metabolic syndrome and secondary platelet dysfunction. The search for sources was carried out in the eLIBRARY, PubMed, Google Scholar, Cochrane, and Lens databases for the period 2020–2025. The review included original studies, systematic reviews, meta-analyses, clinical observations, and preclinical (experimental) studies (*in vitro* and *in vivo*). Additionally, the authors analyzed the official prescribing information for APs available in the State Register of Medicines in Russia [16] and the Food and Drug Administration (FDA) in the USA [17].

3. RESULTS

The meta-analysis by Zheng Y. et al. [12] demonstrated that the PLR is the most accessible quantitative index reflecting the risk of developing AP-induced VTE. However, PLR is not a sensitive hematological biomarker for distinguishing between patients with SSDs undergoing AP therapy and healthy controls. This explains the insufficiency of routine hematological tests for assessing AP-induced LGI and VTE, and also justifies the need to search for additional biomarkers of platelet activation.

Most studies acknowledge that PLT, MPV, PDW, and PCT (**Table 1**) are only suitable for primary screening of AP-induced hematological ADRs. This explains the importance of understanding the role of additional biomarkers of AP-induced platelet activation and their role in the risk of AP-induced VTE (**Table 2**). Such biomarkers may reflect key stages of activation, degranulation, and interaction of platelets with the inflammatory cascade and LGI [8,12,15].

Screening and additional hematological biomarkers of AP-induced VTE can help differentially assess:

(1) the expression of adhesion molecules (e.g., P-selectin, GPIb) that facilitate contact with the endothelium and leukocytes;

(2) the intensity of intracellular signaling pathways (via serotonin levels, activity of platelet 5-HT2A receptors, thromboxane A2 production);

(3) the degree of platelet degranulation and release of pro-inflammatory biomarkers (β-thromboglobulin, PF4);

(4) the final coagulation activity (via the GPIIb/IIIa complex) [18, 23, 26].

It is known that in a resting platelet, P-selectin is located inside the platelet within α-granules. Upon platelet activation, the granules fuse with the platelet membrane, and P-selectin is expressed on the surface. Here, P-selectin performs two key functions: it mediates platelet adhesion to the damaged vascular wall and facilitates binding to leukocytes, forming monocyte-platelet aggregates (MPAs). A portion of P-selectin is cleaved from the platelet membrane and enters the bloodstream. The level of its soluble form in the systemic circulation correlates with the severity of SSDs [40].

The activated αIIbβ3 complex (GPIIb/IIIa) is a receptor responsible for platelet aggregation. At rest, it is inactive. However, upon receiving an activating signal, GPIIb/IIIa changes its spatial conformation and acquires the ability to bind fibrinogen and von Willebrand factor (vWF) [41].

Glycoprotein Ib (GpIb) is a receptor for vWF. It is known that GpIb is responsible for the initial adhesion of platelets to the vascular wall in areas of high shear blood flow. Upon platelet activation, a portion of GpIb receptors can cluster together or be cleaved from the platelet surface (a phenomenon known as "shedding"). Both processes reflect the degree of platelet activation and damage [42, 43].

Thanks to the studies by Wu C.C. et al. [14] and Kosidou S. et al. [13], it is known that assessing the platelet receptor status allows not only to confirm the very fact of their activation but also to understand which specific receptor pathways of platelet activation are associated with the adverse effects of APs and the risk of VTE (**Table 3**).

One of the key pathways of AP-induced alteration of platelet hemostasis is realized through the blockade of P2Y1 and P2Y12 receptors, which leads to the suppression of ADP-induced platelet aggregation. This mechanism is the basis for the antiplatelet effect observed *in vitro* [14].

Concurrently, APs interfere with the platelet-activating factor (PAF) signaling cascade. As shown by Kosidou S. et al. [13], some APs (e.g., fluphenazine, trifluoperazine, and chlorpromazine) are capable not only of inhibiting PAF-induced platelet aggregation but also (at increased concentrations) of causing platelet lysis with the release of intracellular contents into the extracellular space. Furthermore, APs affect arachidonic acid metabolism by suppressing the synthesis of thromboxane A2 and its stable metabolite, thromboxane B2 (TXB2). The reduction in platelet aggregation due to AP-induced blockade of the cyclooxygenase pathway has been confirmed experimentally [14].

Consequently, APs simultaneously affect three key points of platelet activation:

(1) ADP receptors;

(2) the PAF-dependent cascade;

(3) the cyclooxygenase pathway.

However, the clinical outcome of this effect depends on the concentration of the AP in the patient's blood, the duration of AP intake, and the baseline LGI in the specific patient with SSDs.

Table 2. Additional biomarkers of hemostasis, systemic inflammation, and platelet activation in patients with schizophrenia spectrum disorders taking antipsychotics.

Platelet biomarker	Reference values	Brief description	Clinical role	References
		A. Platelet activation biomarkers		
P-selectin (CD62P), ng/mL	20 – 60 ng/mL	Transmembrane glycoprotein that acts as a cell adhesion molecule and as one of the mediators of the systemic inflammatory response	Increased P-selectin level is a biomarker of increased risk of AP-induced VTE	[18]
Activated complex IIb/IIIa (integrin αIIbβ3), %	50 – 90 %	Reflecting the percentage of platelet aggregation after the addition of activators (ADP, collagen, thrombin)	Increased level of integrin αIIbβ3 is a biomarker of increased risk of AP-induced VTE (due to suppression of GPIIb/IIIa activation and alteration of fibrinogen structure)	[13, 19, 20]
TXB2, ng/mL	< 100 ng/mL	Biomarker reflecting the degree of platelet activation via the cyclooxygenase pathway	Increased TXB2 level is a biomarker of increased risk of AP-induced VTE	[21]
PF4, ng/mL	< 10 ng/mL	Chemokine protein that is produced by platelet alpha-granules and released into the blood upon their activation	Increased PF4 level is a biomarker of increased risk of AP-induced VTE	[22]
β-TG, ng/mL	20 – 35 × 10^{-12} g/L	Chemokine protein released by platelets upon their degranulation; it reflects the degree of platelet activation in the blood	Increased β-TG level is a biomarker of increased risk of AP-induced VTE	[23]
CD40L, pg/mL	2000 – 5000 pg/mL	Reflects platelet activation and their pro-inflammatory activity	Increased CD40L level is a biomarker of increased risk of AP-induced VTE, hypercholesterolemia, and cardiovascular risk	[24, 25]
GpIb	ND	Membrane protein, the main component of the platelet glycoprotein Ib-IX-V complex, which binds von Willebrand factor, leading to platelet adhesion and aggregation	Increased GpIb level is a biomarker of increased risk of AP-induced VTE	[26]
5-*HT2A*	50 – 220 ng/mL (blood serotonin)	Serotonin 2A receptors on platelets reflect the state of the serotonergic system. By competitively binding to 5-HT2AR, APs trigger intracellular signaling pathways, increasing calcium levels, which leads to changes in platelet shape, enhanced aggregation, and clot stabilization, contributing to hemostasis and inflammation	Increasing the level of serotonin in the blood is a biomarker for an increased risk of AP-induced VTE (typical for AP with high affinity for 5-HT2A)	[27]
PAF	ND	Powerful phospholipid mediator, capable of inducing platelet aggregation and dilating blood vessels, participates in pro-inflammatory reactions	Increasing the level of PAF is a biomarker for an increased risk of AP-induced VTE (due to platelet activation)	[28]

Table 2. *Continuation*

Platelet biomarker	Reference values	Brief description	Clinical role	References
		B. Inducers of thrombogenesis		
ADP	ND	Low-molecular-weight platelet activator released from their dense granules, activating their aggregation	Increasing the level of ADP is a biomarker for an increased risk of AP-induced VTE	[13]
vWF, U/ml	0.5–1.5 U/ml	Large multimeric plasma glycoprotein that plays a central role in hemostasis, activating platelet aggregation	Increasing the level of vWF is a biomarker for an increased risk of AP-induced VTE	[15]
Collagen, ng/mL	ND	Biomarker that activates platelet aggregation, triggering a pathological process through direct binding to $\alpha 2\beta 1$ (integrin) and GPVI receptors, leading to the replacement of damaged tissue with connective tissue	Increasing the level of collagen is a biomarker for an increased risk of AP-induced VTE	[29]
		C. Biomarkers of endothelial damage		
TF (tissue factor, coagulation factor III, CD142), pg/ml	ND	When the vascular endothelium is damaged, TF comes into contact with blood and binds factor VIIa, triggering a cascade of blood coagulation and platelet aggregation	Elevated TF level is a biomarker of increased risk for AP-induced VTE	[30]
Thrombomodulin, ng/ml	20 – 50 ng/ml	Thrombomodulin is an indicator of vascular endothelial damage (e.g., in AP-induced endothelial dysfunction)	Increasing the level of thrombomodulin is a biomarker for an increased risk of AP-induced VTE	[31]
		D. Biomarkers of fibrinolysis		
D-dimer, ng/ml	< 500 ng/ml	Reflects fibrinolytic activity	Elevated D-dimer level is a biomarker of increased risk for AP-induced VTE	[32]
TAT-complex, ng/ml	ND	Reflects the level of thrombin in the vascular system	Increasing the level of TAT is a biomarker for an increased risk of AP-induced VTE	[33]
		D. Coagulation tests		
APTT, sec	25.1 – 36.6 sec	Clot formation time upon addition of specific reagents	Decreased APTT level is a biomarker for an increased risk of AP-induced VTE	[34, 35]
Antithrombin III, %	75 – 125 %	Glycoprotein that suppresses thrombin formation and inhibits factors IXa and Xa	Decreased level of antithrombin III is a biomarker for an increased risk of AP-induced VTE	[36]
INR	0.8 – 1.2	Standardized indicator of the prothrombin test that allows comparison of results obtained from different laboratories	Decreased INR level is a biomarker for an increased risk of AP-induced VTE	[35]

Table 2. *Continuation*

Platelet biomarker	Reference values	Brief description	Clinical role	References
PTT, sec	9 – 13 sec	Biomarker reflecting the time required for blood clotting	Decreased PT rate is a biomarker for an increased risk of AP-induced VTE	[37]
PTI	Up to 26 years: 69.0 – 121.0 26 – 46 years: 69.0 – 143.0 Over 46 years: 67.0 – 149.0	The percentage ratio of the clotting time of control plasma (standard indicator of a healthy person) to the clotting time of a specific patient	Increasing the level of PI is a biomarker for an increased risk of AP-induced VTE	[38]
		E. Inflammatory biomarkers		
CRP, mg/L	< 5 mg/L	Highly sensitive acute-phase protein produced by the liver in response to inflammation or tissue damage	CRP is a biomarker of AP-induced LGI and increased risk of AP-induced VTE	[39]
PLR	61 – 239	Ratio of the absolute platelet count to the absolute lymphocyte count	Increased PRL level is a biomarker for an increased risk of AP-induced LGI	[2]
P-LCR, %	13 – 43 %	Large platelet count** or **Count of large platelets	Increased P-LCR is a biomarker for an increased risk of AP-induced LGI	[2]

Note: *5-HT2A – hydroxytryptamine 2A; ADP - adenosine diphosphate; AP – antipsychotic; APTT - activated partial thromboplastin time; β-TG - beta-Thromboglobulin; CD40L - CD40 ligand; CRP - C-reactive protein; GpIb - Glycoprotein I beta; GPIIb/IIIa -Glycoprotein II beta/III alpha; GPVI - Glycoprotein VI; INR - International Normalized Ratio; MPV - Mean Platelet Volume; PAF - Platelet-Activating Factor; PCT – Plateletcrit; PDW - Platelet Distribution Width; PF4 - Platelet factor 4; P-LCR - Platelet - Large Cell Ratio; PLR - Platelet-to-Lymphocyte Ratio; PLT – Platelets; PT - prothrombin time; PTI - prothrombin index; TAT - Thrombin-antithrombin complex; TF- Tissue Factor; TXB2- Thromboxane B2; VTE - venous thromboembolism; vWF- von Willebrand Factor.*

Table 3. Effect of different generations of antipsychotics on platelet activation.

Antipsychotic	Mechanism of influence on platelet hemostasis	Clinical role (risk level)	Reference
	A. First-generation antipsychotics		
Haloperidol	Therapeutic concentration in blood: inhibits platelet biomarkers and P-selectin expression, integrates into the platelet plasma membrane and alters the relative spatial arrangement of phospholipid-consuming enzymes, thereby changing the rate of enzyme-catalyzed reactions High concentration in blood: causes thrombocytopenia and suppression of P-selectin expression, inhibits platelet MAO and 5-HT2A	Increased risk of bleeding (ND)	[14,46]
	High concentration in blood: increases plasma protein coagulation and suppresses platelet disaggregation via P2Y1 and P2Y12 receptors	Increased risk of VTE (ND)	
Droperidol	Therapeutic concentration in blood: does not typically inhibit platelet indicators (GpIb, GpIIb-IIIa) or P-selectin expression High concentration in blood: causes thrombocytopenia and suppression of P-selectin expression	Increased risk of bleeding (ND)	[14,45,47]
	High concentration in blood: increases plasma protein coagulation and suppresses platelet disaggregation via P2Y1 and P2Y12 receptors	Increased risk of VTE (ND)	
Zuclopenthixol	Therapeutic concentration in blood: causes thrombocytopenia (exact mechanism unknown, likely through immune-mediated platelet destruction)	Increased risk of bleeding (rarely)	[48]
	Mechanism of increased VTE risk is unknown	Increased risk of VTE (very rarely)	
Levomepromazine	High concentration in blood: inhibits ATP- and 5-HT2A-induced platelet aggregation, reduces ATP production, reduces platelet size, inhibits membrane vesiculation, causes thrombocytopenia	Increased risk of bleeding (ND)	[49,50]
Loxapine*	Therapeutic concentration in blood: inhibits 5-HT2A-induced platelet aggregation, causes thrombocytopenia, significantly reduces blood coagulation	Increased risk of bleeding (ND)	[51]
Periciazine	High concentration in blood: increases 5-HT2A-induced platelet aggregation	Increased risk of VTE (ND)	[52]
Perphenazine	Therapeutic concentration in blood: competitively inhibits platelet MAO activity, causes thrombocytopenia High concentration in blood: induces platelet lysis via PAF, a potent thromboinflammatory mediator	Increased risk of bleeding (ND)	[13,53,54]
Pimozide*	Therapeutic concentration in blood: does not typically inhibit platelet indicators High concentration in blood: causes thrombocytopenia, inhibits the phosphoinositide (PI) signaling pathway, integrates into the platelet plasma membrane and alters the relative spatial arrangement of phospholipid-consuming enzymes, thereby changing the rate of enzyme-catalyzed reactions, significantly reduces blood coagulation	Increased risk of bleeding (ND)	[44]
Prochlorperazine*	Therapeutic concentration in blood: inhibits platelet aggregation, causes significant thrombocytopenia (possible agranulocytosis), integrates into the platelet plasma membrane and alters the relative spatial arrangement of phospholipid-consuming enzymes, thereby changing the rate of enzyme-catalyzed reactions; inhibits the metabolism of PIP and PIP2 in platelets	Increased risk of bleeding (ND)	[44,55]

Table 3. *Continuation*

Antipsychotic	Mechanism of influence on platelet hemostasis	Clinical role (risk level)	Reference
Sulpiride	High concentration in blood: suppresses bone marrow hematopoiesis	Increased risk of bleeding (ND)	[56]
Thioproperazine	ND	ND	[57]
Thioridazine	Therapeutic concentration in blood: causes thrombocytopenia, inhibits ATP- and 5-HT2A-induced platelet aggregation, reduces ATP production, reduces platelet size, inhibits membrane vesiculation	Increased risk of bleeding (rarely)	[58]
Thiothixene*	Therapeutic concentration in blood: causes thrombocytopenia (exact mechanism unknown, likely through immune-mediated platelet destruction)	Increased risk of bleeding (rarely)	[59]
Trifluoperazine	Therapeutic concentration in blood: causes thrombocytopenia High concentration in blood: >50 μM – induces platelet lysis, reaching 30 – 40% at 100 μM. In the non-lytic range (0 – 50 μM): causes pronounced inhibition of arachidonic acid release and phosphatidylcholine breakdown, which was complete at 25 μM. Phosphatidylinositol breakdown was partially inhibited (by approximately 50%) at 25 μM TFP, with further inhibition at higher concentrations being minimal	Increased risk of bleeding (ND)	[60,61]
Flupentixol	High concentration in blood: causes thrombocytopenia, likely through immune-mediated platelet destruction	Increased risk of bleeding (rarely)	[62]
Fluphenazine	Therapeutic concentration in blood: typically inhibits platelet indicators, causes thrombocytopenia, reduces platelet size, decreases platelet membrane microviscosity. High concentration in blood: causes pronounced thrombocytopenia and reduced coagulation	Increased risk of VTE (ND)	[63,64,65,66]
	High concentration in blood: enhances 5-HT2A-induced platelet aggregation and increases platelet 5-HT2A receptor binding sites	Increased risk of bleeding (ND)	
Chlorpromazine	Therapeutic concentration in blood: inhibits ATP- and 5-HT-induced platelet aggregation, reduces ATP production, reduces platelet size, inhibits membrane vesiculation. High concentration in blood: reduces blood coagulation	Increased risk of bleeding (commonly)	[67,68,69]
	High concentration in blood: increases 5-HT2A-induced platelet aggregation	Increased risk of VTE (ND)	
Chlorprothixene	Therapeutic concentration in blood: causes thrombocytopenia, likely through immune-mediated platelet destruction	Increased risk of bleeding (rarely)	[70]
	High concentration in blood: mechanism of VTE is unknown	Increased risk of VTE (very rarely)	
	B. Second-generation antipsychotics		
Asenapine	ND	Increased risk of VTE (rarely)	[71]
Amisulpride	Therapeutic concentration in blood: may cause VTE due to antagonism of platelet 5-HT2A receptors, stimulation of ADP-induced platelet aggregation, or indirectly (due to the development of hyperprolactinemia)	Increased risk of VTE (rarely)	[72,73]
Ziprasidone	ND	ND	[74]
Quetiapine	Therapeutic concentration in blood: integrates into the platelet membrane and alters the relative spatial arrangement of phospholipid-consuming enzymes, thereby potentially destroying platelets and altering the rate of enzyme-catalyzed reactions	Increased risk of bleeding (uncommonly)	[44,75]

Clozapine	Therapeutic concentration in blood: integrates into the platelet plasma membrane and alters the relative spatial arrangement of phospholipid-consuming enzymes, can destroy platelets and alter the rate of enzyme-catalyzed reactions. Causes thrombocytopenia or thrombocytosis.	Increased risk of bleeding (very rarely)	[44,76,77]
	High concentration in blood and long-term use: may cause thrombocytosis and increase platelet aggregation	Increased risk of VTE (very rarely)	
Lurasidone	High concentration in blood: inhibits 5-HT2A-induced platelet aggregation	Increased risk of bleeding (ND)	[78,79]
Olanzapine	Therapeutic concentration in blood: causes thrombocytopenia of unclear origin, likely due to immune-mediated platelet destruction and direct bone marrow suppression	Increased risk of bleeding (very rarely)	[80,81,82,83]
	High concentration in blood: increases platelet aggregation due to structural similarity between olanzapine and platelet receptors in patients with olanzapine-induced MS	Increased risk of VTE (ND)	
Paliperidone	Therapeutic concentration in blood: may cause a decrease in the levels of coagulation factors VIII and IX	Increased risk of bleeding (rarely)	[72,84,85,86,87]
	High concentration in blood and long-term use: may cause VTE, CTEPH, due to a decrease in the level of endogenous NO in blood plasma and reduced expression of *NOS* gene mRNA	Increased risk of VTE (very rarely)	
Risperidone	Therapeutic concentration in blood: may cause thrombocytopenia, presumably due to effects on the bone marrow	Increased risk of bleeding (uncommonly)	[85,88,89]
	High concentration in blood and long-term use: may induce VTE and CTEPH by reducing the level of endogenous NO in blood plasma and decreasing expression of the mRNA of the gene encoding eNOS	Increased risk of VTE (rarely)	
Sertindole*	High concentration in blood and/or long-term use: may increase platelet aggregation due to affinity for 5-HT2A receptors and activation of 5-HT2A-induced platelet aggregation	Increased risk of VTE (ND)	[72, 90]
	C. Third-generation antipsychotics		
Aripiprazole	Mechanisms of thrombocytopenia and VTE development have not been studied	Increased risk of bleeding (ND). Increased risk of VTE (ND)	[91]
Brexpiprazole	ND	Increased risk of VTE (ND)	[92]
Cariprazine	ND	Increased risk of VTE (ND)	[93]

Note: *ND – no data; * - the drug is not registered in the Russian Federation; according to the World Health Organization (WHO) classification, adverse reactions are presented according to their frequency of occurrence (where applicable) as follows: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1000 to <1/100), rare (≥1/10,000 to <1/1000), very rare (<1/10,000), frequency unknown (cannot be estimated from the available data). Abbreviations: ADP - adenosine diphosphate, AP – antipsychotic; VTE – venous thromboembolism; PE – pulmonary embolism; eNOS – endothelial nitric oxide synthase; CTEPH - chronic thromboembolic pulmonary hypertension, MAO - monoamine oxidase, TFP - trifluoperazine, 5-HT - hydroxytryptamine, PAF - Platelet-Activating Factor, PI - Phosphoinositide, GpIb - Glycoprotein Ib, GPIIb/IIIa - Glycoprotein IIb/IIIa, P-selectin, D-dimer, PIP - Phosphatidylinositol Phosphate, MS – metabolic syndrome.*

4. DISCUSSION

This narrative review demonstrates that the negative effect of first- and new-generation APs on platelet hemostasis is multidirectional, which can be either dose-dependent [94] or dose-independent [95], and depends on the duration of AP intake. In this regard, assessing the risk of AP-induced VTE or bleeding at the start of AP therapy is a challenging task.

To assess the safety profile of antipsychotics, the data presented in **Table 3** are insufficient. Therefore, we ranked the adverse effects of APs on the hemostatic system: VTE and hemorrhage.

The **Figures 1-2** presented clearly demonstrate the incidence of VTE and hemorrhage during APs using (red - high incidence, yellow - moderate, green - rare). The information shown in the figures includes only those drugs with reliable data; others were excluded from the analysis due to insufficient study of the effect.

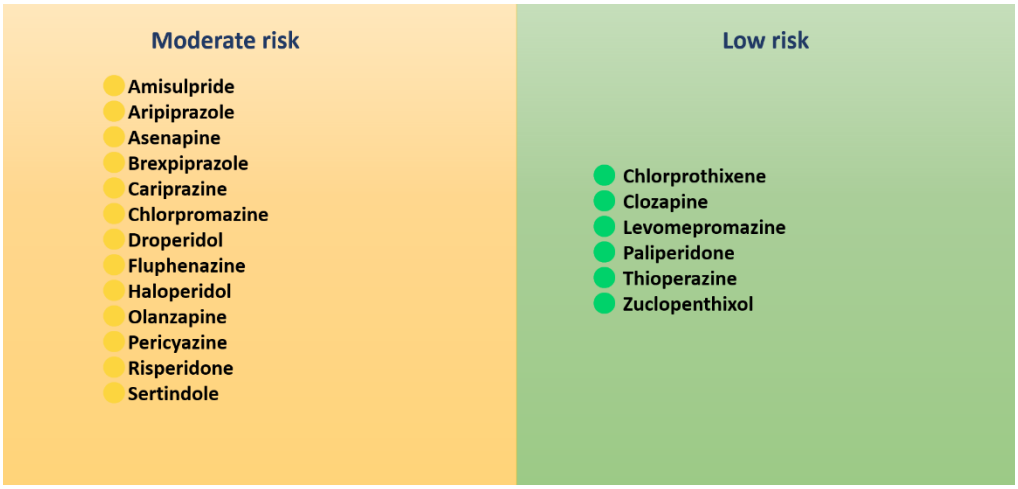

Figure 1. Antipsychotic-induced risk of developing venous thromboembolism

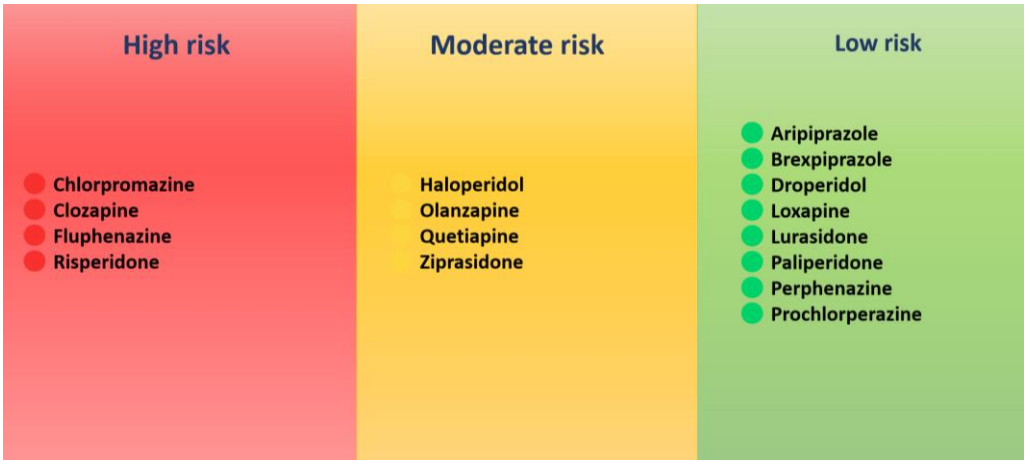

Figure 2. Antipsychotic-induced pathological bleeding.
Note: *the incidence of hemorrhage during antipsychotics using (red - high incidence, yellow - moderate, green - rare).*

Probably, a significant contribution to the risk of developing AP-induced VTE is made by still insufficiently studied genetic biomarkers that determine the interindividual variability in the risk and nature of AP-induced ADRs from platelet hemostasis (for example, polymorphism of genes encoding platelet receptors and key biomarkers that activate platelet adhesion and aggregation) [96]. Polymorphism of genes encoding platelet receptors (*HTR2A, P2Y12*), cytochrome P450 system enzymes (*CYP2D6, CYP3A4*), as well as transporter proteins (*ABCB1*), may explain the

interindividual variability in response to APs [97, 98]. A promising direction for managing the risk of platelet hemostasis disorders is the development of personalized monitoring approaches that take into account both platelet biomarkers and the results of pharmacogenetic testing (PGx) before prescribing APs with a high risk of hematological ADRs.

Furthermore, the risk of developing AP-induced VTE may be influenced by increased platelet aggregation associated with LGI in patients with AP-induced metabolic syndrome and AP-induced central/visceral obesity [99]. The information we have compiled on the effect of APs on platelet hemostasis is presented in **Table 3** and demonstrates that the highest risk of developing AP-induced VTE, including deep vein thrombosis of the extremities, PE and its branches, is probably associated with asenapine (≥1/10,000 to <1/1,000 cases) and amisulpride (≥1/10,000 to <1/1,000 cases). A dose-dependent risk, where the frequency of VTE increases in patients only when taking the maximum daily dose (MDD), is associated with haloperidol and droperidol. A low or very low risk of developing VTE is noted with the use of aripiprazole (frequency unknown), zuclopenthixol (<1/10,000 cases), clozapine (<1/10,000 cases), olanzapine (frequency unknown), paliperidone (<1/10,000 cases), risperidone (≥1/10,000 to <1/1,000 cases), fluphenazine (frequency unknown), chlorprothixene (<1/10,000 cases), and chlorpromazine (frequency unknown). However, their use increases the risk of AP-induced pathological bleeding, including nosebleeds, low-traumatic and spontaneous bleeding, subcutaneous hematomas, and (very rarely) gastrointestinal bleeding. Such hematological ADRs are observed with the use of quetiapine (≥1/1,000 to <1/100 cases), thioridazine (≥1/10,000 to <1/1,000 cases), thiothixene (≥1/10,000 to <1/1,000 cases), and flupentixol (≥1/10,000 to <1/1,000 cases).

Furthermore, the risk of developing hematological ADRs may be influenced by the platelet lifespan. According to various sources, platelets circulate in the systemic bloodstream for 7 to 10 days [100]. However, there are many modifiable and non-modifiable factors associated with a reduction in the platelet lifecycle (**Figure 3**) [15, 101, 102, 103, 104], which increases the risk of developing pathological bleeding in patients with SSDs taking maximum daily doses of APs. However, it is important to remember that the body strives to replenish the pool of missing cells, therefore it releases young and large platelets into the systemic circulation. These possess increased activity, leading to a paradoxical increase in the risk of VTE during long-term AP intake [105].

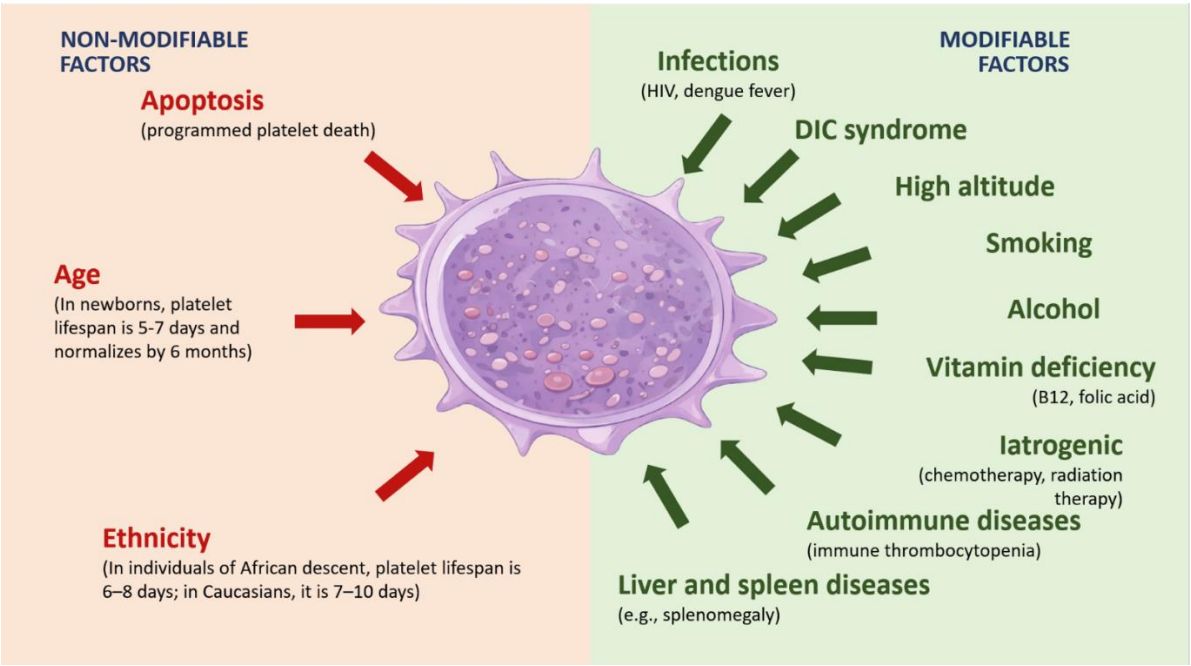

Figure 3. Factors influencing platelet lifespan.

Note: *HVI- human immunodeficiency virus, DIC - disseminated intravascular coagulation, B12- cyanocobalamin.*

Table 4. Results of clinical studies on antipsychotic-induced changes in platelet hemostasis in patients with schizophrenia spectrum disorders.

Platelet parameter	Study design	Antipsychotics studied	General sample characteristics	Clinical significance	Reference
PLT, PTT, PTI	Open-label, randomized, cross-over, two-period, two-sequence, single-center comparative clinical study, *in vivo*	Aripiprazole Olanzapine	Main group: 24 healthy volunteers (12 men and 12 female), aged 18 to 65 years	Aripiprazole and olanzapine may decrease PLT and PTI. Aripiprazole may increase PTT	[121]
ND	Open-label observational study, *in vivo*	AP1 and AP2	Main group: 42 patients taking APs with idiopathic VTE	AP1 significantly increase the risk of VTE in men and women under 60 years of age. Chlorpromazine and thioridazine have a very high risk of VTE	[118]
MPV	Retrospective observational comparative study, *in vivo*	AP1 and AP2	Main group: 60 patients with paranoid schizophrenia taking only APs Control group: 30 healthy volunteers	APs significantly increase MPV levels	[119]
Fibrinogen	Open-label study, *in vitro*	Clozapine	Blood from healthy adult volunteers	Clozapine increases the thrombogenic properties of fibrinogen	[76]
Fibrinogen, PAI-1, antithrombin III, CRP, leptin	Open-label comparative study, *in vivo*	Clozapine, Olanzapine	Main group: 29 patients with paranoid schizophrenia taking clozapine, 29 patients with paranoid schizophrenia taking olanzapine, 29 patients with paranoid schizophrenia taking APs. Control group: first-degree relatives of patients taking clozapine (23), olanzapine (11)	APs increase CRP and antithrombin III levels; olanzapine increases PAI-1 and leptin levels	[120]
PAF, ADP	Open-label comparative study, *in vitro*	Quetiapine, Perphenazine	Blood from healthy adult volunteers	Perphenazine inhibits PAF and ADP-induced platelet aggregation pathways	[13]

Note: *PLT – platelets; PT - prothrombin time; PTI -prothrombin index; ND – no data; AP1 - first-generation antipsychotics; AP2 - new-generation antipsychotics; VTE - venous thromboembolism; MPV - mean platelet volume; PAI-1 - plasminogen activator inhibitor-1; CRP - C-reactive protein; PAF - platelet-activating factor; ADP - adenosine diphosphate.*

Table 5. Results of preclinical studies on antipsychotic-induced changes in platelet hemostasis in patients with schizophrenia spectrum disorders.

Platelet parameter	Study design	Antipsychotics studied	General sample characteristics	Clinical significance	Reference
Coagulation factors VIII and IX	Healthy rats	Paliperidone	Female Wistar rats	Paliperidone reduces coagulation factor VIII levels at a dose of 3 mg/kg/day and increases coagulation factor IX levels at a dose of 1 mg/kg, causing bleeding or VTE, respectively	[85]
Ca2+, collagen, ADP, arachidonic acid	Animal model of coronary thrombosis	Droperidol	Dogs and pigs	Droperidol inhibits collagen-induced and ADP-induced platelet aggregation and dose-dependently alters Ca2+ concentration in platelets	[45]
Platelet count, TNF-α, IL-6, IL-10, glutathione, SOD	Healthy rats	Chlorpromazine	Male rats	Chlorpromazine reduces platelet count and increases the level of proinflammatory biomarkers	[122]

Note: *VTE - venous thromboembolism; ADP - adenosine diphosphate; TNF-α - tumor necrosis factor-alpha; IL-6 - interleukin-6; IL-10 - interleukin-10; SOD - superoxide dismutase.*

This review demonstrates the importance of dynamic laboratory monitoring in patients with SSDs taking APs (especially over a long period), with assessment of the screening and additional platelet biomarkers presented in **Tables 1 and 2.** The high and very high-risk group for AP-induced VTE includes patients who have a high cardiovascular risk according to the SCORE (Systematic Coronary Risk Evaluation) scale [106] and/or a high risk of VTE according to the Wells scale at the start of AP therapy [107]. Furthermore, psychiatrists in their clinical practice should remember the validated Padua [108] and International Medical Prevention Registry on Venous ThromboEmbolism (IMPROVE VTE) [109] scores, which are used to assess the likelihood of developing VTE in hospitalized non-surgical patients [110].

Given that some APs may increase the risk of pathological bleeding even when taking medium doses (therapeutic blood concentration), useful diagnostic tools include the WHO/CTCAE (Common Terminology Criteria for Adverse Events) scales [111], the GUSTO (Global Utilization of Streptokinase and Tissue Plasminogen Activator for Occluded Coronary Arteries) classification [112], the TIMI (Thrombolysis in Myocardial Infarction) classification [113] - for assessing the severity of an already occurred bleeding, as well as the HAS-BLED (Hypertension, Abnormal renal/liver function, Stroke, Bleeding history or predisposition) scale [114], the ATRIA (Anticoagulation and Risk Factors in Atrial Fibrillation) scale [115], the ABC-HBR (Academic Research Consortium for High Bleeding Risk) [116], and the IMPROVE Bleeding Score [117] - for predicting the risk of bleeding.

We conducted a search for data from clinical and preclinical studies on the effect of APs on platelet biomarkers (**Tables 4, 5**). Despite the limited number of contemporary studies, 6 studies from the period 2000-2025 were included in **Table 4**. All studies confirm the effect of APs on platelet biomarkers and indicate an increased risk of VTE with their long-term use.

However, the analysis of available publications revealed some methodological limitations. For example, the study by Zornberg G.L. and Jick H. [118] does not specify which particular APs were taken by patients with SSDs. This makes it impossible to assess which specific drugs carry the greatest thrombogenic risk and to implement the study results into clinical practice. In a study dedicated to examining the role of MPV [119], the authors associate its increase with the risk of VTE but do not indicate the criteria (confirmed deep vein thromboses, PE, or laboratory biomarkers) by which this risk was assessed.

Other studies were more specific. For example, Ma X. et al. [76] showed that aripiprazole and olanzapine decrease platelet count and PTI, and aripiprazole also prolongs PT in healthy volunteers. This points to a potential undesirable effect of these APs on blood coagulation. An *in vitro* study demonstrated that clozapine alters the structure of fibrinogen, making clots denser and more resistant to breakdown. Carrizo E. et al. [120] showed that first-generation APs increase

levels of CRP and antithrombin III, while olanzapine increases the concentration of PAI-1 and leptin, which are biomarkers of high VTE risk in the context of AP-induced metabolic syndrome.

The effect of APs on the phenomenon of mutual aggravation between "LGI and VTE" is ambiguous. On one hand, risperidone and clozapine can reduce the level of pro-inflammatory biomarkers, presumably by suppressing CD40L expression on T-lymphocytes. On the other hand, clozapine, olanzapine, and first-generation APs (to a lesser extent) may exert procoagulant and pro-inflammatory effects, as evidenced by increased levels of CRP (a known additional biomarker of VTE risk). Kosidou S. et al. [13], using an *in vitro* model, showed that perphenazine suppresses platelet aggregation by blocking PAF- and ADP-dependent activation pathways.

Preclinical studies **(Table 5)** clarify the mechanisms of action of individual APs. A study in rats revealed that paliperidone dose-dependently affects coagulation factors VIII and IX [85], which may explain both thrombotic and hemorrhagic ADRs. A study in dogs and pigs showed that droperidol suppresses platelet aggregation induced by collagen and ADP, and alters intracellular calcium levels [45]. An experiment with chlorpromazine in rats confirmed that the AP reduces platelet count while simultaneously increasing the level of pro-inflammatory cytokines (TNF-α, IL-6), linking LGI and thrombocytopenia [122].

5. CONCLUSIONS

This review demonstrates that platelets act not merely as participants in the hemostasis system, but as active modulators of LGI, linking AP intake with LGI and hematological ADRs (both thrombotic and hemorrhagic). For risk stratification of AP-induced platelet hemostasis disorders, psychiatrists in clinical practice are recommended to monitor standard platelet biomarkers (PLT, MPV, PDW, PCT), which are the most accessible, albeit less specific. More informative are additional biomarkers of platelet activation (P-selectin, GPIIb/IIIa, CD40L, PF4, β-TG, 5-HT2A receptors, PAF), which allow for the assessment of key stages of platelet activation. The most sensitive are 5-HT2A receptors and PAF, as they are direct pharmacological targets of APs. However, the influence of these biomarkers on the development and maintenance of LGI and VTE is a subject for further large-scale studies.

Author Contributions: Conceptualization, R.F.N. and N.A.S.; formal analysis, A.A.A., Z.T.T and E.O.G.; writing — original draft preparation, A.A.A. and Z.T.T.; writing — review and editing, N.A.S., visualization, A.A.A.; supervision, N.A.S.; project administration, R.F.N. All authors have read and agreed to the published version of the manuscript.

Funding: The study was performed within the framework of the state assignment of the "Bekhterev's National Medical Research Center for Psychiatry and Neurology of the Ministry of Health of Russia" (XSOZ 2024 0012).

Institutional Review Board Statement: Not applicable.

Informed Consent Statement: Not applicable.

Data Availability Statement: Not applicable.

Conflicts of Interest: The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data, in the writing of the manuscript.

REFERENCES

1. Ji G.J., Zalesky A., Wang, Y., et al. Linking personalized brain atrophy to schizophrenia network and treatment response. *Schizophrenia Bulletin*. **2023**; *49*(1):43–52. https://doi.org/10.1093/schbul/sbac162
2. Yu Q., Weng W., Zhou H., et al. Elevated platelet parameter in first-episode schizophrenia patients: a cross-sectional study. *Journal of Interferon & Cytokine Research*. **2020**; *40*(11): 524–529. https://doi.org/10.1089/jir.2020.0117
3. Manoubi S.A., Boussaid M., Brahim O., et al. Fatal pulmonary embolism in patients on antipsychotics: case series, systematic review and meta-analysis. *Asian Journal of Psychiatry*. **2022**; 73,103105. https://doi.org/10.1016/j.ajp.2022.103105
4. Chari D., Sawhney I., Mukaetova-Ladinska E., et al. Risk factors for deep vein thrombosis and pulmonary embolism: a comparative study between acute hospital care and mental health inpatient settings for older people. *Working with Older People*. **2025**; 29(3):254–265. https://doi.org/10.1108/WWOP-06-2024-0031
5. Osimo E.F., Perry B.I., Cardinal R.N., et al. Inflammatory and cardiometabolic markers at presentation with first episode psychosis and long-term clinical outcomes: a longitudinal study using electronic health records. *Brain, Behavior, and Immunity*. **2021**; 91:117-127. https://doi.org/10.1016/j.bbi.2020.09.011
6. Li H., Li W., Zhang X., et al. Association of antipsychotic drugs with venous thromboembolism in patients with schizophrenia: a systematic review and meta-analysis. *General Psychiatry*. **2023**; 36(5):e101347. https://doi.org/10.1136/gpsych-2023-101347

7. Khoodoruth M.A.S., Tarteel H., Sami O., et al. Peripheral inflammatory and metabolic markers as potential biomarkers in treatment-resistant schizophrenia: insights from a Qatari cohort. *Psychiatry Research*. **2025**; 344:116307. https://doi.org/10.1016/j.psychres.2024.116307
8. Ekwere T.A., Effiong J.H. Assessing the risk of venous thromboembolism in psychiatric patients on antipsychotic medication using platelet indices. *International Journal of Medical and Health Sciences*. **2017**;6(3):134-138. https://doi.org/10.9790/6737-0603134138
9. Zhdanov R.I., Doinikova A.N., Zhdanova S.I., et al. Correlation between haemostatic and vegetate nervous system parameters under examination stress. *Zhurnal Vyssheinervnoi Deiatelnosti imeni I. P. Pavlova.* **2016**; 66(2):202–208. (In Russian)
10. Brusov O.S., Karpova N.S., Oleichik I.V., et al. The decrease in procoagulant activity of blood during combined therapy with antidepressants and antipsychotics in patients with endogenous mental disorders. *Zh. Nevrol. Psikhiatr. Im. S. S. Korsakova*. **2021**; 121(4):30-36. https://doi.org/10.17116/jnevro202112104130 (in Russian)
11. Morozova M.A., Burminsky D.S., Beniashvili A.G., et al. Association of the effectiveness of therapy for an acute psychotic episode in patients with schizophrenia with the activity of platelet enzymes. *Psikhiatriya.* **2023**; 21(3):6-15. https://doi.org/10.30629/2618-6667-2023-21-3-6-15 (in Russian)
12. Zheng Y., Zhou X., Chen K., et al. Neutrophil/lymphocyte ratio is increased in the acute phase of schizophrenia and regardless the use and types of antipsychotic drugs. *BMC Psychiatry*. **2024**; 24(1): 876. https://doi.org/10.1186/s12888-024-06330-w
13. Kosidou S., Zannas Z., Ofrydopoulou A., et al. Psychotropic and neurodegenerative drugs modulate platelet activity via the PAF pathway. *Neurochemistry International*. **2025**; 191:106073. https://doi.org/10.1016/j.neuint.2025.106073
14. Wu, C.C., Tsai, F.M., Chen, M.L., et al. Antipsychotic drugs inhibit platelet aggregation via p2y1 and p2y12 receptors. *Biomed Res Int.* **2016**; 2016: 2532371. https://doi.org/10.1155/2016/2532371
15. Zheng C., Liu H., Tu W., et al. Hypercoagulable state in patients with schizophrenia: different effects of acute and chronic antipsychotic medications. *Therapeutic Advances in Psychopharmacology*. **2023**; 13: 20451253231200257. https://doi.org/10.1177/20451253231200257
16. State Register of Medicines. Available at: https://grls.pharm-portal.ru/grls
17. U.S. Food and Drug Administration (FDA). Available at: https://www.fda.gov
18. Wallaschofski H., Eigenthaler M., Kiefer M., et al. Hyperprolactinemia in patients on antipsychotic drugs causes adp-stimulated platelet activation that might explain the increased risk for venous thromboembolism: pilot study. *Journal of Clinical Psychopharmacology*. **2003**; 23(5):479-483. https://doi.org/10.1097/01.jcp.0000088914.24613.51
19. National Center for Biotechnology Information (NCBI). Glycoprotein IIb/IIIa Inhibitors. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; **2023**. Available at: https://www.ncbi.nlm.nih.gov/books/NBK554376/
20. Ogłodek, E.A., Just, M.J., Grzesińska, A.D., et al. The impact of antipsychotics as a risk factor for thromboembolism. *Pharmacological Reports*. **2018**; 70(3): 533-539. https://doi.org/10.1016/j.pharep.2017.12.003
21. Patrono C., Rocca B. Measurement of thromboxane biosynthesis in health and disease. *Front. Pharmacol.* 2019; 10:1244. https://doi.org/10.3389/fphar.2019.01244
22. Takada Y.K., Wu C.Y., Takada Y. PF4 autoantibody complexes cause activation of integrins αiibβ3 and αvβ3 and possible subsequent thrombosis and autoimmune diseases. *Int. J. Mol. Sci.* **2025**; 26(21):10260. https://doi.org/10.3390/ijms262110260
23. Patti G., Nenna A., Spadoni F., et al. β-thromboglobulin as a biomarker of platelet activation and predictor of cardiovascular events: a systematic review and meta-analysis. *Stroke.* 2025; 56(3): 712-723. https://doi.org/10.1161/STROKEAHA.124.049972
24. Marengo M., Migliori M., Merlotti G., et al. Role of the cd40-cd40 ligand pathway in cardiovascular events, neurological alterations, and other clinical complications of chronic hemodialysis patients: protective role of adsorptive membranes. *Blood Purification*. **2023**; 52(1): 27-42. https://doi.org/10.1159/000530808
25. Tourjman V., Kouassi É., Koué M.È., et al. Antipsychotics' effects on blood levels of cytokines in schizophrenia: a meta-analysis. *Schizophrenia Research*. **2013**; *151*(1-3): 43–47. https://doi.org/10.1016/j.schres.2013.10.011
26. Zhang Y., Ehrlich S.M., Zhu Q., Du S. Signaling mechanisms of the platelet glycoprotein Ib-IX complex. *Platelets.* **2022**; 33(6): 823-832. https://doi.org/10.1080/09537104.2022.2071852
27. Hajjiah A., Maadarani O., Bitar Z., et al. Antipsychotic drugs may contribute to venous thromboembolism – a case report and review of literature. *JRSM Open*. **2023**; 14(1): 20542704221132142. https://doi.org/10.1177/20542704221132142
28. National Center for Biotechnology Information (NCBI). Platelet-Activating Factor. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; **2024**. Available at: https://www.ncbi.nlm.nih.gov/books/NBK557392/
29. Ollivier V., Syvannarath V., Gros A., et al. Collagen can selectively trigger a platelet secretory phenotype via glycoprotein VI. *PloS One*. **2014**; 9(8): e104712. https://doi.org/10.1371/journal.pone.0104712
30. Hering J., Amann B., Angelkort B., Rottmann M. Thrombin-antithrombin III-complex and prothrombin fragment F1+2 in arterial and venous blood of patients with peripheral arterial disease. *Vasa.* **2003**; 32(4): 193-197. https://doi.org/10.1024/0301-1526.32.4.193
31. Hemant G., Indranil B., Alireza R.R. Thrombomodulin: a multifunctional receptor modulating the endothelial quiescence. *Journal of Thrombosis and Haemostasis.* **2024**; 22(4): 905-914. https://doi.org/10.1016/j.jtha.2024.01.006
32. Zaidi S.R.H., Rout P. Interpretation of blood clotting studies and values (PT, PTT, aPTT, INR, anti-factor Xa, D-dimer) [Updated 2025]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; **2025.** Available at: https://www.ncbi.nlm.nih.gov/books/NBK604215/

33. Ishioka M., Yasui-Furukori N., Sugawara N., et al. Hyperprolactinemia during antipsychotics treatment increases the level of coagulation markers. *Neuropsychiatr. Dis. Treat.* **2015**; 11:477-484. https://doi.org/10.2147/NDT.S75176
34. Santoro R.C., Molinari A.C., Leotta M., Martini T. Isolated prolongation of activated partial thromboplastin time: not just bleeding risk. *Medicina (Kaunas, Lithuania)*. **2023**; 59(6):1169. https://doi.org/10.3390/medicina59061169
35. Chornenki N.L.J., Fralick M., Sholzberg M. International normalized ratio and activated partial thromboplastin time testing. *CMAJ:Canadian Medical Association journal*. **2022**; 194(33):E1135. https://doi.org/10.1503/cmaj.220629
36. Hsu E., Moosavi L. Biochemistry, Antithrombin III. [Updated 2023 Sep 4]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; **2025**. Available from: https://www.ncbi.nlm.nih.gov/books/NBK545295/
37. Dorgalaleh A., Favaloro E.J., Bahraini M., Rad F. Standardization of Prothrombin Time/International Normalized Ratio (PT/INR). *International Journal of Laboratory Hematology*. **2021**; 43(1):21–28. https://doi.org/10.1111/ijlh.13349
38. Croquet V., Vuillemin E., Ternisien C., et al. Prothrombin index is an indirect marker of severe liver fibrosis. *Eur. J. Gastroenterol. Hepatol*. **2002**; 14(10): 1133-1141. https://doi.org/10.1097/00042737-200210000-00015
39. Carrizo E., Fernández V., Quintero J., et al. Coagulation and inflammation markers during atypical or typical antipsychotic treatment in schizophrenia patients and drug-free first-degree relatives. *Schizophrenia Research*. **2008**; 103(1-3): 83–93. https://doi.org/10.1016/j.schres.2008.03.004
40. Pinjari O.F., Dasgupta S.K., Okusaga O.O. Plasma soluble P-selectin, Interleukin-6 and S100B protein in patients with schizophrenia: a pilot study. *Psychiatr. Q.* **2022**; 93(1): 335-345. https://doi.org/10.1007/s11126-021-09954-3
41. Ma Y.Q., Xu Z., Zhu J. Integrin αIIbβ3. In: Gresele, P., López, J.A., Angiolillo, D.J., Page, C.P. (eds) Platelet Physiology I. Platelets in Thrombotic and Non-Thrombotic Disorders. Springer, Cham. **2025**. doi: 10.1007/978-3-031-96340-7_12
42. Debaene C.B., Feys H.B.A.B., Six K.R.A. Shedding light on GPIbα shedding. *Current Opinion in Hematology*. **2024**; 31(5):224-229. https://doi.org/10.1097/MOH.0000000000000826
43. Chawla D., Saad E., Khairi T., Padmanabhan A. Severe persistent heparin-induced thrombocytopenia in a renal transplant patient. *Thrombosis Research*. **2019**; 183:106–107. https://doi.org/10.1016/j.thromres.2019.10.014
44. Oruch R., Hodneland E., Pryme I.F., Holmsen H. Psychotropic drugs interfere with the tight coupling of polyphosphoinositide cycle metabolites in human platelets: a result of receptor-independent drug intercalation in the plasma membrane?. *Biochimica et Biophysica Acta*. **2008**; 1778(10): 2165–2176. https://doi.org/10.1016/j.bbamem.2008.04.007
45. Bertha B.G., Sill J.C., Berger I., et al. High-dose droperidol protects against experimental coronary thrombosis in dogs and pigs and attenuates aggregation of porcine platelets and Ca2+ mobilization in human platelets. *Anesthesiology*. 1993; 78(4):733–743. https://doi.org/10.1097/00000542-199304000-00017
46. Instructions for medical use of the drug - Haloperidol. Available at: https://cdn.pharm-portal.ru/69jxs7cjr4n4gdc2acy5y4x8/instructions/%D0%9B%D0%A1-000645/InstrImg_2021_05_26_1469341/ae771f5a-f866-47eb-84b0-40eec18a8908.pdf
47. Instructions for medical use of the drug - Droperidol. Available at: https://cdn.pharm-portal.ru/69jxs7cjr4n4gdc2acy5y4x8/instructions/%D0%9B%D0%9F-_N_001100_-_%D0%A0%D0%93-RU_/InstrImg_2022_09_09_1486781/1fa961c9-e598-45c1-bf20-3e4593c1c915.pdf
48. Instructions for medical use of the drug - Zuclopenthixol. Available at: https://cdn.pharm-portal.ru/69jxs7cjr4n4gdc2acy5y4x8/instructions/%D0%9B%D0%9F-_N_011913_-_%D0%A0%D0%93-RU_/InstrImg_2026_02_02_1525913/f35eb14c-aac7-480e-a721-3372c5a54974.pdf
49. Instructions for medical use of the drug - Tizercin. Available at: https://cdn.pharm-portal.ru/69jxs7cjr4n4gdc2acy5y4x8/instructions/%D0%9B%D0%9F-_N_000079_-_%D0%A0%D0%93-RU_/InstrImg_2021_5_27_1469415/%D0%9B%D0%9F-%E2%84%96(000079)-(%D0%A0%D0%93-RU)[2020]_0.pdf
50. Singh A.N., Barlas C., Saeedi H., Mishra R.K. Effect of loxapine on peripheral dopamine-like and serotonin receptors in patients with schizophrenia. *Journal of Psychiatry & Neuroscience*. **2003**; 28(1), 39–47.
51. Instructions for medical use of the drug - Periciazine. Available at: https://cdn.pharm-portal.ru/69jxs7cjr4n4gdc2acy5y4x8/instructions/%D0%9B%D0%9F-_N_006400_-_%D0%A0%D0%93-RU_/InstrImg_2024_12_03_1511622/4d5ae6f6-4c61-4a1e-ac54-9b11b5f75fa7.pdf
52. Suzuki O., Seno H., Kumazawa T. In vitro inhibition of human platelet monoamine oxidase by phenothiazine derivatives. *Life Sciences*. **1988**; 42(21): 2131–2136. https://doi.org/10.1016/0024-3205(88)90127-0
53. Instructions for medical use of the drug - Perphenazine. Available at: https://cdn.pharm-portal.ru/69jxs7cjr4n4gdc2acy5y4x8/instructions/%D0%9B%D0%9F-_N_012481_-_%D0%A0%D0%93-RU_/InstrImg_2025_12_22_1524535/f9bd41a0-8a03-4601-9c1c-55e39a0fd4b0.pdf
54. Mcfarland R.B. Fatal drug reaction associated with prochlorperazine (compazine). report of a case characterized by jaundice, thrombocytopenia, and agranulocytosis. *American Journal of Clinical Pathology*. **1963**; *40*:284–290. https://doi.org/10.1093/ajcp/40.3.284
55. Instructions for medical use of the drug - Sulpiride. Available at: https://cdn.pharm-portal.ru/69jxs7cjr4n4gdc2acy5y4x8/instructions/%D0%9B%D0%9F-_N_008846_-_%D0%A0%D0%93-RU_/InstrImg_2025_03_25_1515313/f930f6cd-1fec-4bbd-90ff-58f13153ac3f.pdf
56. Instructions for medical use of the drug - Thioproperazine. Available at: https://cdn.pharm-portal.ru/69jxs7cjr4n4gdc2acy5y4x8/instructions/%D0%9F_N014904_01/InstrImg_2021_03_30_5409/ca8cddcb-52b5-4fa9-b5bf-7980b83c8eab.pdf

57. Instructions for medical use of the drug - Thioridazine. Available at: https://cdn.pharm-portal.ru/69jxs7cjr4n4gdc2acy5y4x8/instructions/%D0%9B%D0%9F-_N_010434_-_%D0%A0%D0%93-RU_/InstrImg_2025_06_25_1518539/8e02b14b-28e4-4671-bc6b-77f36d2b7268.pdf
58. Balon R., Berchou R., Zethelius M. Thrombocytopenia associated with chlorpromazine, haloperidol and thiothixene: a case report. *Canadian Journal of Psychiatry*. **1987**; 32(2):149–150. https://doi.org/10.1177/070674378703200213
59. Holmsen H., Daniel J.L., Dangelmaier C.A., et al. Differential effects of trifluoperazine on arachidonate liberation, secretion and myosin phosphorylation in intact platelets. *Thrombosis Research*. **1984**; 36(5), 419–428. https://doi.org/10.1016/0049-3848(84)90298-6
60. Instructions for medical use of the drug - Trifluoperazine. Available at: https://cdn.pharm-portal.ru/69jxs7cjr4n4gdc2acy5y4x8/instructions/%D0%9F_N015130_01/InstrImg_2023_06_19_1496225/ec94b864-40ea-4d0a-9936-5c6d71c60144.pdf
61. Instructions for medical use of the drug - Flupentixol. Available at: https://cdn.pharm-portal.ru/69jxs7cjr4n4gdc2acy5y4x8/instructions/%D0%9B%D0%9F-005281/InstrImg_2021_12_20_1476543/d8f8ef36-89a0-41b5-9b0a-50efa003a0df.pdf
62. Holt R.J. Neuroleptic drug-induced changes in platelet levels. *Journal of ClinicalPpsychopharmacology*. **1984**; 4(3):130–132.
63. Zubenko G.S., Cohen B.M. In vitro effects of psychotropic agents on the microviscosity of platelet membranes. *Psychopharmacology*. 1984; 84(2):289–292. https://doi.org/10.1007/BF00427463
64. Pandey S.C., Sharma R.P., Janicak P.G., Marks R.C., Davis J.M., Pandey G.N. Platelet serotonin-2 receptors in schizophrenia: effects of illness and neuroleptic treatment. *Psychiatry Research*. **1993**; 48(1):57–68. doi: 10.1016/0165-1781(93)90113-u
65. Instructions for medical use of the drug - Fluphenazine. Available at: https://cdn.pharm-portal.ru/69jxs7cjr4n4gdc2acy5y4x8/instructions/%D0%9B%D0%9F-_N_004077_-_%D0%A0%D0%93-RU_/InstrImg_2024_01_24_1501346/fbc57572-788e-457b-b8c7-bdc20110bb79.pdf
66. Holmsen H., Rygh, T. Chlorpromazine makes the platelet plasma membrane permeable for low-molecular weight substances and reduces ATP production. *Biochemical Pharmacology*. **1990**; 40(2), 373–376. doi: 10.1016/0006-2952(90)90701-l
67. Warlow C., Ogston D., Douglas A.S. Platelet function after the administration of chlorpromazine to human subjects. *Haemostasis*. **1976**; 5(1):21–26. https://doi.org/10.1159/000214115
68. Instructions for medical use of the drug - chlorpromazine. Available at: https://cdn.pharm-portal.ru/69jxs7cjr4n4gdc2acy5y4x8/instructions/%D0%9B%D0%9F-_N_001706_-_%D0%A0%D0%93-RU_/InstrImg_2024_02_06_1501740/8e2be4ba-9a8e-41a2-9133-a7ebcb6e208d.pdf
69. Instructions for medical use of the drug - chlorprothixene. Available at: https://cdn.pharm-portal.ru/69jxs7cjr4n4gdc2acy5y4x8/instructions/%D0%9B%D0%9F-_N_000203_-_%D0%A0%D0%93-RU_/InstrImg_2021_4_28_1468593/%D0%9B%D0%9F-%E2%84%96(000203)-(%D0%A0%D0%93-RU)[2021]_0.pdf
70. Instructions for medical use of the drug - asenapine. Available at: https://cdn.pharm-portal.ru/69jxs7cjr4n4gdc2acy5y4x8/instructions/%D0%9B%D0%9F-001526/InstrImg_2020_06_13_27412/f1b2224a-ca14-4da0-b4c2-b3cfbd23bdc2.pdf
71. Şengül M.C., Kaya K., Yilmaz A., et al. Pulmonary thromboembolism due to paliperidone: report of 2 cases. *The American Journal of Emergency Medicine*. **2014**; 32(7):814.e1–814.e8142. https://doi.org/10.1016/j.ajem.2013.12.038
72. Instructions for medical use of the drug - amisulpride. Available at: https://cdn.pharm-portal.ru/69jxs7cjr4n4gdc2acy5y4x8/instructions/%D0%9B%D0%9F-_N_012917_-_%D0%A0%D0%93-RU_/InstrImg_2025_12_30_1524945/42f0a04c-1f68-4390-ac3f-473ea03fe940.pdf
73. Instructions for medical use of the drug - ziprasidone. Available at: https://cdn.pharm-portal.ru/69jxs7cjr4n4gdc2acy5y4x8/instructions/%D0%9B%D0%9F-_N_003752_-_%D0%A0%D0%93-RU_/InstrImg_2025_09_12_1521409/97c8fb2e-61ce-404a-bdcc-6ed21d19b357.pdf
74. Instructions for medical use of the drug - Quetiapine. Available at: https://cdn.pharm-portal.ru/69jxs7cjr4n4gdc2acy5y4x8/instructions/%D0%9B%D0%9F-_N_004607_-_%D0%A0%D0%93-RU_/InstrImg_2024_03_11_1502662/e70afdef-a62b-4995-9347-c8d8bd3bba08.pdf
75. Gligorijević N., Vasović T., Lević S., et al. Atypical antipsychotic clozapine binds fibrinogen and affects fibrin formation. *International Journal of Biological Macromolecules*. 2020; 154:142-149. https://doi.org/10.1016/j.ijbiomac.2020.03.119
76. Instructions for medical use of the drug - clozapine. Available at: https://cdn.pharm-portal.ru/69jxs7cjr4n4gdc2acy5y4x8/instructions/%D0%9B%D0%9F-_N_011446_-_%D0%A0%D0%93-RU_/InstrImg_2025_09_16_1521486/b0d83477-5a93-4dc1-b590-027829ea9a62.pdf
77. Rafi M., Goyal C., Reddy P., Reddy S. Lurasidone induced thrombocytopenia: is it a signal of drug induced myelosuppression? *Indian Journal of Psychological Medicine*. **2018**; 40(2): 191–192. https://doi.org/10.4103/IJPSYM.IJPSYM_374_17
78. Instructions for medical use of the drug - Lurasidone. Available at: https://cdn.pharm-portal.ru/69jxs7cjr4n4gdc2acy5y4x8/instructions/%D0%9B%D0%9F-_N_011432_-_%D0%A0%D0%93-RU_/InstrImg_2025_09_04_1520983/728d4b45-574d-4ed3-99e3-6c687fbbc3b2.pdf
79. Bokhari S.A., Butaher H., Saleem R., Elhassan N. Olanzapine-induced thrombocytopenia in a patient with chronic schizophrenia: a case report. *Cureus*. **2024**; 16(11):e74677. https://doi.org/10.7759/cureus.74677
80. Rasras H., Beghi M., Samti M., et al. Rare and underestimated association of pulmonary embolism and olanzapine therapy; report of two cases. *Archives of Academic Emergency Medicine*. **2021**; 9(1):e17. https://doi.org/10.22037/aaem.v9i1.1063
81. Maazouzi M., Bouallala A., Haddadi Z., et al. Antipsychotic drugs as a contributing factor of pulmonary embolism: a report of 4 cases. *Radiology Case Reports*. **2023**; 18(5):1997-2000. https://doi.org/10.1016/j.radcr.2023.02.046

82. Instructions for medical use of the drug - Olanzapine. Available at: https://cdn.pharm-portal.ru/69jxs7cjr4n4gdc2acy5y4x8/instructions/%D0%9B%D0%9F-_N_002284_-_%D0%A0%D0%93-RU_/InstrImg_2023_05_15_1493505/35008e88-73eb-46b5-ac42-93f59f0ecc5d.pdf
83. Lin Y.C., Chen C.W., Chen B.L., Kao Y.T., Huang C.Y. A Case report of chronic thromboembolic pulmonary hypertension after long-term use of risperidone and paliperidone. *Acta Cardiologica Sinica*. **2020**; 36(5):514–516. https://doi.org/10.6515/ACS.202009_36(5).20200526A
84. Yılmaz E.D., Motor S., Sefil, F., et al. Effects of paliperidone palmitate on coagulation: an experimental study. *TheScientificWorldJournal*. **2014**; 964380. https://doi.org/10.1155/2014/964380
85. Zhang X.R., Zhang Z.J., Jenkins T.A., et al. The effect of chronic antipsychotic drug administration on nitric oxide synthase activity and gene expression in rat penile tissues. *European Neuropsychopharmacology*. **2010**; 20(4):211-217, https://doi.org/10.1016/j.euroneuro.2009.10.002.
86. Instructions for medical use of the drug - Paliperidone. Available at: https://cdn.pharm-portal.ru/69jxs7cjr4n4gdc2acy5y4x8/instructions/%D0%9B%D0%9F-_N_003795_-_%D0%A0%D0%93-RU_/InstrImg_2025_05_19_1517377/c29bba5d-e730-4ae9-b3c8-2569c8a4299d.pdf
87. Saxena S.K., Dwivedi A.K., Timothy A., et al. Risperidone-induced thrombocytopenia in a case of psychosis and neuroendocrine tumor: a case report. *Indian Journal of Psychiatry*. 2021; 63(3):311–312. https://doi.org/10.4103/psychiatry.IndianJPsychiatry_488_20
88. Instructions for medical use of the drug - Risperidone. Available at: https://cdn.pharm-portal.ru/69jxs7cjr4n4gdc2acy5y4x8/instructions/%D0%9B%D0%9F-_N_007087_-_%D0%A0%D0%93-RU_/InstrImg_2024_10_18_1509888/a5b2e6b5-3566-42d6-83d1-c829ad85f179.pdf
89. Instructions for medical use of the drug - Sertindole. Available at: https://cdn.pharm-portal.ru/69jxs7cjr4n4gdc2acy5y4x8/instructions/%D0%9B%D0%A1-000615/InstrImg_2024_04_17_1503727/2fcd58d6-5f65-474d-b196-e6a9d51aceeb.pdf
90. Instructions for medical use of the drug - Aripiprazole. Available at: https://cdn.pharm-portal.ru/69jxs7cjr4n4gdc2acy5y4x8/instructions/%D0%9B%D0%9F-_N_001283_-_%D0%A0%D0%93-RU_/InstrImg_2022_11_17_1488952/77228122-3caa-4a97-ac83-016331734041.pdf
91. Instructions for medical use of the drug - Brexipiprazole. Available at: https://cdn.pharm-portal.ru/69jxs7cjr4n4gdc2acy5y4x8/instructions/%D0%9B%D0%9F-006867/InstrImg_2022_12_05_1489336/525fdef5-8b68-4991-adb6-7816c5604c1a.pdf
92. Instructions for medical use of the drug - Cariprazine. Available at: https://cdn.pharm-portal.ru/69jxs7cjr4n4gdc2acy5y4x8/instructions/%D0%9B%D0%9F-_N_001510_-_%D0%A0%D0%93-RU_/InstrImg_2025_04_14_1516155/f8733f55-8c23-4502-8e68-f40b402395b7.pdf
93. Chen T.Y., Lin C.E., Chen L.F., Tzeng N.S. Enhanced bleeding risk in an elderly dementia patient treated with warfarin and quetiapine. *The Journal of neuropsychiatry and clinical neurosciences*. **2013**; 25(4): E25. https://doi.org/10.1176/appi.neuropsych.12090232
94. Saracoglu H., Karakukcu C., Kilic C., Simsek Y. Potential indicators of bone marrow suppression in patients with schizophrenia receiving clozapine: platelet-large cell ratio and immature granulocytes. *Psychiatry and Behavioral Sciences.* **2024**; 14(4): 123-130. https://doi.org/10.5455/PBS.20240301055535
95. Yan P., Gao B., Wang S., et al. Association of 5-HTR2A T102C and A-1438G polymorphisms with clinical response to atypical antipsychotic treatment in schizophrenia: a meta-analysis. *Neuroscience Letters.* **2022**; 770:136395. https://doi.org/10.1016/j.neulet.2021.136395
96. ClinicalTrials.gov. Pharmacogenetics and Therapeutic Drug Monitoring In Schizophrenia (PROMISE). Identifier: NCT05839613. Available at: https://clinicaltrials.gov/study/NCT05839613?tab=study
97. Ivashchenko D.V., Yudelevich D.A., Buromskaya N.I., et al. CYP2D6 phenotype and ABCB1 haplotypes are associated with antipsychotic safety in adolescents experiencing acute psychotic episodes. *Drug Metabolism and Personalized Therapy*. **2021**; 37(1), 47–53. https://doi.org/10.1515/dmpt-2021-0124
98. Singh R., Bansal Y., Medhi B., Kuhad A. Antipsychotics-induced metabolic alterations: Recounting the mechanistic insights, therapeutic targets and pharmacological alternatives. *European Journal of Pharmacology*. **2019**; 844: 231–240. https://doi.org/10.1016/j.ejphar.2018.12.003
99. Josefsson E., Vainchenker W., Chloe J. Regulation of platelet production and life span: role of bcl-xl and potential implications for human platelet diseases. *International Journal of Molecular Sciences*. 2020; 21: 1-12. https://doi.org/10.3390/ijms21207591
100. Badawy A.Z., Kandel S.H., Ahmedy I.A., et al. Evaluation of Bak and Bcl-Xl gene expression among pediatric patients with acute primary immune thrombocytopenia. *Clinical and Experimental Pediatrics*. **2025**; 68(11):901–908. doi: 10.3345/cep.2025.00997
101. Lindquist I., Olson S.R., Li A., et al. The efficacy and safety of thrombopoietin receptor agonists in patients with chronic liver disease undergoing elective procedures: a systematic review and meta-analysis. *Platelets*. **2022**; 33(1): 66–72. doi: 10.1080/09537104.2020.1859102
102. Wu X., Liu Y., Zou C., et al. Nicotine's impact on platelet function: insights into hemostasis mechanisms. *Frontiers in Pharmacology*. **2025**; 15: 1512142. https://doi.org/10.3389/fphar.2024.1512142
103. Hsu W.Y., Lane H.Y., Lin C.L., Kao C.H. A population-based cohort study on deep vein thrombosis and pulmonary embolism among schizophrenia patients. *Schizophrenia Research*. **2015**; 162(1–3): 248-252. https://doi.org/10.1016/j.schres.2015.01.012

104. Kaiser R., Anjum A., Nicolai L. Platelet heterogeneity in disease: the many and the diverse? *Blood*. **2025**; 146(24):2870–2881. https://doi.org/10.1182/blood.2025028957
105. SCORE (Systematic Coronary Risk Evaluation) scale. Available at: https://zdrav-nnov.ru/grazhdanam/kalkulyator-zdorovya/shkala-score/
106. Wells Scale for Pulmonary Embolism Probability [Internet]. MSD Manual Professional Edition. Available at: https://www.msdmanuals.com/ru/professional/multimedia/clinical-calculator/
107. Buryachkovskaya L.I., Lomakin N.V., Sumarokov A.B., Shirokov E.A. Efficacy and safety of antithrombotic therapy [venous thrombosis and pulmonary embolism]: scales and algorithms. *Therapy Journal.* **2018.** Available at: https://therapy-journal.ru/articles/Effektivnost-i-bezopasnost-antitromboticheskoi-terapii-venoznyi-tromboz-i-tromboemboliya-legochnoi-arterii-shkaly-i-algoritmy.html
108. Wilkinson K.S., Sparks A.D., Gergi M., et al. Validation of the International Medical Prevention Registry on Venous Thromboembolism (IMPROVE) risk scores for venous thromboembolism and bleeding in an independent population. *Research and Practice in Thrombosis and Haemostasis*. **2024**; 8(4):102441. https://doi.org/10.1016/j.rpth.2024.102441
109. Clinical guidelines "Deep vein thrombosis" (Russian Federation, 2025). Available at: https://diseases.medelement.com/disease/
110. National Cancer Institute. Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0. Published: November 27, 2017. Available at: https://dctd.cancer.gov/research/ctep-trials/for-sites/adverse-events/ctcae-v5-5x7.pdf
111. Bassand J.P. GUSTO (Global Utilization of Streptokinase and Tissue plasminogen activator in Occluded arteries): logic wins at last. *European Heart Journal*. 1994; 15(1):2–4. doi: 10.1093/oxfordjournals.eurheartj.a060374
112. Sobieraj D.M., White C.M., Kluger J., et al. Table 1, Thrombolysis in myocardial infarction (TIMI) Flow Grading System. In: Adjunctive Devices for Patients With Acute Coronary Syndrome Undergoing Percutaneous Coronary Intervention [Internet]. Rockville (MD): Agency for Healthcare Research and Quality (US); 2011. (Comparative Effectiveness Reviews, No. 42). Available at: https://www.ncbi.nlm.nih.gov/books/NBK84280/table/introduction.t1/
113. Lip G.Y., Frison L., Halperin J.L., Lane D.A. Comparative validation of a novel risk score for predicting bleeding risk in anticoagulated patients with atrial fibrillation: the HAS-BLED (Hypertension, Abnormal Renal/Liver Function, Stroke, Bleeding History or Predisposition, Labile INR, Elderly, Drugs/Alcohol Concomitantly) score. *Journal of the American College of Cardiology*. **2011**; 57(2): 173–180. https://doi.org/10.1016/j.jacc.2010.09.024
114. Zhu W., Fu L., Ding Y., et al. Meta-analysis of ATRIA versus CHA2DS2-VASc for predicting stroke and thromboembolism in patients with atrial fibrillation. *International Journal of Cardiology***. 2017**; 227: 436–442. https://doi.org/10.1016/j.ijcard.2016.11.015
115. Silverio A., Di Maio M., Buccheri S., et al. Validation of the academic research consortium high bleeding risk criteria in patients undergoing percutaneous coronary intervention: A systematic review and meta-analysis of 10 studies and 67,862 patients. *International Journal of Cardiology*. **2022**; 347: 8–15. doi: 10.1016/j.ijcard.2021.11.015
116. IMPROVE Bleeding Risk Assessment Score [Internet]. Practical-Haemostasis.com. Available at: https://practical-haemostasis.com/Clinical%20Prediction%20Scores/Formulae%20code%20and%20formulae/Formulae/Bleeding-Risk-Assessment-Score/Improve_bleeding_risk_assessment_score.html
117. Zornberg G. L., Jick H. Antipsychotic drug use and risk of first-time idiopathic venous thromboembolism: a case-control study. *Lancet (London, England)*. **2000**; 356(9237): 1219–1223. https://doi.org/10.1016/S0140-6736(00)02784-7
118. Semiz M., Yücel H., Kavakçı O., et al. Atypical antipsychotic use is an independent predictor for the increased mean platelet volume in patients with schizophrenia: a preliminary study. *Journal of Research in Medical Sciences*. **2013**; 18(7): 561–566.
119. Carrizo E., Fernández V., Quintero J., et al. Coagulation and inflammation markers during atypical or typical antipsychotic treatment in schizophrenia patients and drug-free first-degree relatives. *Schizophrenia Research*. **2008**; 1031(3): 83-93. https://doi.org/10.1016/j.schres.2008.03.004
120. Koller D., Almenara S., Mejía G., et al. Metabolic effects of aripiprazole and olanzapine multiple-dose treatment in a randomised crossover clinical trial in healthy volunteers: association with pharmacogenetics. *Advances in Therapy*. **2021**; 38(2): 1035–1054. https://doi.org/10.1007/s12325-020-01566-w
121. Obukohwo O.M., Ben-Azu B., Nwangwa E.K., et al. Adverse hematological profiles associated with chlorpromazine antipsychotic treatment in male rats: preventive and reversal mechanisms of taurine and coenzyme-Q10. *Toxicology Reports.* **2024**; 12:448-462. https://doi.org/10.1016/j.toxrep.2024.04.004