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#### ONLINE JOURNAL OF HEMATOLOGY AND MEDICINE

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ONLINE JOURNAL OF HEMATOLOGY AND MEDICINE (OJHM) is an interdisciplinary open access online journal focusing primarily on blood diseases. The journal publishes original contributions in non-malignant and malignant hematological diseases. It also covers all the areas related to the hematological field that takes care of diagnosis and treatment of blood disease. Particular editorial interest is addressed to: Inherited and Acquired Clotting Disorders, Antiphospholipid Syndrome, Clinical Management of Bleeding Diseases, Coagulopathies, Hemophilia, Platelets Disorders, Thrombotic Disorders. Manuscripts should be presented in the form of original articles, editorials, reviews, short communications, or cases report, all submissions are rigorously peer reviewed.

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# HEMATOLOGY & MEDICINE

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## Letter to the Editor

# Clinical Dental Protocol for the Management of Patients with Hemophilia

#### Introduction.

Hemophilia, a congenital bleeding disorder characterized by a deficiency of factor VIII (hemophilia A) or factor IX (hemophilia B), presents significant challenges in dental care. Oral manifestations and the risk of bleeding during clinical procedures require careful planning and close coordination between dental professionals and hematologists. This protocol is a practical guidance tool based on my clinical experience and the most recent recommendations from the World Federation of Hemophilia (WFH).

# **Objective**

To provide a safe and updated clinical guide for the dental care of patients with hemophilia, emphasizing the prevention of bleeding events, appropriate planning of procedures, and interdisciplinary collaboration.

## Preoperative evaluation

- Comprehensive medical history focusing on type and severity of hemophilia, bleeding history, presence of inhibitors, and current treatment.
- Consultation with the treating hematologist to determine need for prophylactic measures.
- Evaluation of the type of dental procedure and its hemorrhagic risk.
- Preoperative testing when invasive procedures are planned.

# Procedures by risk level

- Non-invasive procedures: cleaning, fluoride application, sealants, oral health education.
- Low-risk procedures: simple restorations, orthodontics without extractions.
- **High-risk procedures**: extractions, periodontal surgery, endodontics.

# Local Hemostatic Management

- Tranexamic Acid (TXA): Antifibrinolytic agent that prevents fibrin clot degradation. Can be used as mouthwash (10 ml of 5% solution, held for 2 minutes, 3–4 times/day for 5–7 days), gauze application, or oral form under medical supervision.
- Absorbable Gelatin Sponges: Applied directly into the socket, reabsorbed in 4–6 weeks.
- Oxidized Regenerated Cellulose\*\*: Promotes clot formation and stabilization.
- Microfibrillar Collagen\*\*: Enhances platelet adhesion, used in persistent bleeding.
- Trichloroacetic Acid (TCA)\*\*: Contraindicated due to its caustic effect and risk of necrosis.

# Postoperative care

- Relative rest.
- Clear instructions regarding diet, hygiene, and alarm signs.
- Continued use of TXA as needed.
- Clinical follow-up within 24–48 hours.

#### Prevention and Education

Preventive care is fundamental. Proper brushing with soft-bristled brushes, daily flossing, alcohol-free rinses, fluoride treatments, and regular dental visits (every 3–6 months) help avoid invasive procedures. Educating patients and families on oral hygiene and involving medical teams are essential to prevent complications. Like in healthy individuals, prevention is the key—but for patients with bleeding disorders, it is even more crucial.

### **Special Considerations**

Older adults and patients with hematological conditions due to medication (e.g., chemotherapy, anticoagulants) face similar bleeding risks. I have seen how what appears to be a simple extraction can turn into a complex situation without proper assessment. Compassionate, adapted care is essential for all these individuals.

## Advances in Hemophilia Treatment

- Extended half-life clotting factors prolong protection.
- Non-replacement therapies promote endogenous coagulation.
- Personalized prophylaxis plans allow better planning of dental procedures.

#### **Final Reflection**

This protocol is not just a technical guide: it is a reflection of my commitment to caring for patients. Each case is unique, each person deserving of attention, preparation, emotional compromise and respect.

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#### Conflicts of Interest

The authors declare no conflict of interest.

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# Case Report

# Prophylaxis with Extended Half-Life Factor VIII in a Patient with Moderate Hemophilia A and Ischemic Heart Disease: A Case Report

#### Abstract.

This case report describes the management of a 53-year-old male with moderate hemophilia A and a complex cardiovascular history, including HIV and HCV infections, who experienced a non-Q myocardial infarction requiring dual antiplatelet therapy and percutaneous coronary intervention. The patient was successfully managed with prophylaxis using extended half-life (EHL) recombinant factor VIII (turoctocog alfa pegol) during and after cardiac procedures. This report highlights the challenges and strategies in balancing bleeding and thrombotic risks in hemophilia patients with cardiovascular comorbidities and discusses the rationale for factor level targets during antithrombotic therapy.

**Keywords**: hemophilia A, extended half-life factor VIII, ischemic heart disease, dual antiplatelet therapy

#### Introduction

Hemophilia A is an X-linked bleeding disorder caused by deficiency of coagulation factor VIII (FVIII), with moderate forms defined by FVIII activity between 0,01 and 0,05 IU/mL [1]. Advances in therapy have increased life expectancy, resulting in a growing prevalence of age-related comorbidities, including cardiovascular disease (CVD) [2]. Managing acute coronary syndromes in hemophilia is challenging due to the need for antithrombotic therapy, which increases bleeding risk[3]. Extended half-life (EHL) FVIII products allow for more stable factor levels and less frequent infusions, potentially improving safety in this setting [4]. We report a case of a middle-aged man with moderate hemophilia A, HIV, HCV. and heterozygous Factor V Leiden mutation, who developed an acute myocardial infarction and underwent successful percutaneous coronary intervention (PCI) with EHL FVIII prophylaxis.

# Report of the case

A 53-year-old male with moderate hemophilia A (baseline FVIII 0,045 IU/mL), HIV infection (on antiretroviral therapy with bictegravir, emtricitabine, and tenofovir since 1985), HCV positivity (since 1990), and heterozygosity for Factor V Leiden presented to the emergency department with acute retrosternal chest pain. About his medical history, hemophilia A was diagnosed in childhood. Previous antihemorrhagic treatments included cryoprecipitate, plasma-derived and recombinant FVIII, and, since 2018, turoctocog alfa and subsequently turoctocog alfa pegol. He has several comorbidities: HIV (managed with bictegravir/emtricitabine/tenofovir), HCV, history of multiple traumatic fractures (radius/ulna, clavicle, ribs), meniscal injury, lumbar disc disease (L4-L5 discopathy, L5-S1 herniation), frequent migraines treated with triptans, and previous use of non-steroid anti-inflammatory drugs (NSAIDs). On December 28, 2023, the patient was diagnosed with a non-Q myocardial infarction. He underwent coronary angiography and primary PCI with drug-eluting stent placement on the left circumflex artery, followed by further PCI on additional branches two days later. No procedural complications occurred.

For peri-procedural hemostasis, 3000 IU (43 IU/kg) of turoctocog alfa pegol was administered prior to angiography and primary PCI, followed by a daily dose of 3,000 IU for several days post-intervention. Maintenance therapy consisted of 3,000 IU every other day during dual antiplatelet therapy (aspirin and ticagrelor) to ensure sustained hemostatic coverage. Factor VIII activity levels were closely monitored, demonstrating 0,435 IU/mL at 15 hours post-infusion, declining to 0,296 IU/mL by 39 hours. After six months of therapy, a 24-hour post-infusion FVIII level of 0,364 IU/mL was observed, suggesting stable pharmacokinetics. Based on these data, trough levels were estimated to remain >10% with a dosing interval of every 3.5 days, supporting the feasibility of an extended-interval prophylactic regimen in this setting. Laboratory data are resumed in Figure 1.

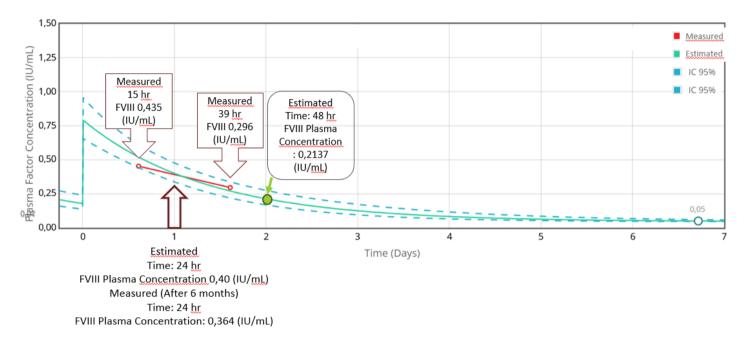


Fig. 1: Measured and estimated FVIII Plasma concentration after infusion of Turotoctog Alfa Peg 3000 UI (43,8 IU/Kg) every other day (Modified from Wapps Hemo App - 2024 McMaster University, Canada)

The patient was discharged on dual antiplatelet therapy and EHL FVIII prophylaxis. No thrombotic or major bleeding events occurred during one year of follow-up. The patient remained adherent to therapy, and FVIII levels were maintained above 0,20 IU/mL, as recommended for patients on dual antiplatelet therapy[3][4]. Regular cardiology and hematology follow-up was arranged, including lipid profile monitoring and cardiovascular risk assessment.

#### Discussion

This case highlights the complexity of managing hemophilia patients with acute coronary syndromes. Extended life expectancy in hemophilia has led to increasing encounters with CVD, and the need for antithrombotic therapy poses a significant bleeding risk[2][3]. EHL FVIII products, such as turoctocog alfa pegol, provide more stable and sustained FVIII levels, reducing the risk of bleeding during periods of increased antithrombotic exposure[4][5]. Guidelines recommend maintaining FVIII levels above 15-30% during dual antiplatelet therapy and above 1-5% during single antiplatelet therapy[3][6]. In this patient, regular EHL FVIII infusions allowed safe administration of dual antiplatelet therapy without bleeding complications. The presence of HIV and HCV, as well as genetic thrombophilia (heterozygous FV Leiden), further complicated the risk profile, underscoring the need for individualized, multidisciplinary management[2][7]. Potential contributors to the patient's coronary artery disease include chronic HIV infection and antiretroviral therapy, both associated with accelerated atherosclerosis and metabolic

disturbances[7][8]. The use of triptans and NSAIDs may also have increased vascular risk[9][10]. This case supports the growing evidence that hemophilia does not provide protection from atherosclerosis and that standard cardiovascular risk factors must be addressed[2][3][7].

#### Conclusion

EHL FVIII prophylaxis enabled safe management of acute coronary syndrome and dual antiplatelet therapy in a patient with moderate hemophilia A and multiple cardiovascular risk factors. This case underscores the importance of individualized prophylaxis regimens, regular monitoring, and multidisciplinary care in hemophilia patients with complex comorbidities.

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# Letter to the Editor

# Increased European Presence Through Liaison and Ambassadors

#### Introduction.

Save One Life, a nonprofit organization dedicated to improving the lives of people with bleeding disorders in developing and underserved countries, is expanding its footprint in Europe with a more structured approach. As an originally American organization, with headquarters near Boston, Massachusetts, and most board members also based in the USA, it is important to have representatives on the ground in Europe as well. As part of this strategic growth, the organization had already in 2016 established a liaison in Germany and has now in 2025 also appointed ambassadors in

Italy, the United Kingdom, and the Netherlands. This expansion marks a pivotal moment in Save One Life's commitment to global equity in hemophilia care. The liaison and ambassadors are appointed to promote Save One Life in Europe. This role also includes developing partnerships with national hemophilia foundations, pharmaceutical companies, academic institutions, and foundations throughout Europe, ensuring that resources are effectively channeled to countries and individuals most in need.

### A European Liaison: Building Regional Bridges

The appointment of Marelle Hart, a former Doctors without Borders employee and mother of two sons with hemophilia, as a Europe-based liaison in Germany, was a major step toward enhancing the organization's coordination, outreach, and advocacy across the world. Situated at the heart of Europe, the liaison serves as a vital point of contact between Save One Life and patient organizations, treatment centers, and potential donors. The liaison's presence helps to create continuity, cultural awareness, and real-time responsiveness-key ingredients in long-term program success. However, Europe is a continent of different languages, in contrast to the USA, and therefore the organization was on the look out for more ambassadors who have now been installed as added value. Together the liaison and ambassadors now speak six languages and are spread across Europe in order to divide tasks.

# National Ambassadors: New Voices for More Impact

To complement its centralized efforts, Save One Life has enlisted dedicated ambassadors in Italy, the United Kingdom, and the Netherlands, each serving as an advocate, fundraiser, and community connector in their respective countries. Appointed are:

- In Italy, Gianluca Sottilotta, a hematologist and editor of an online magazine on bleeding disorders. Sottilotta speaks fluent Italian, Spanish and English.
- In the United Kingdom, Lila Mann, a health care market researcher who runs a Facebook group for bleeding disorders. Mann speaks fluent English and French.
- In the Netherlands, Ana van Schalkwyk, a mother of a son with hemophilia, and a data-driven product designer. Van Schalkwyk speaks fluent Portuguese and English.

The ambassadors work closely with hemophilia associations and treatment centers to raise awareness about global disparities and to foster engagement with the wider bleeding disorders community. Their work includes organizing fundraising events and sharing patient stories to inspire empathy and action.

They focus on outreach and education, engaging with the robust hemophilia community to highlight the ongoing needs of individuals in less-resourced regions. By leveraging connections with medical professionals, youth groups, and donors, the ambassadors play a crucial role in expanding the charity's supporter base and help to connect corporate and philanthropic partners with Save One Life's mission.

## Regional Focus, Global Mission

The new structure allows the organization to draw on Western Europe's wealth of expertise, advocacy networks, and philanthropic potential. With a liaison and ambassadors on the ground, the organization can better tailor its outreach, respond to emerging challenges, and build sustainable collaborations.

Since its establishment in 2001, Save One Life empowers individuals with bleeding disorders to lead healthier, more independent lives, one person at a time. Through its program, Project SHARE, the organization has donated over 167 million units of life-saving clotting factor to patients in 77 countries, addressing the critical shortage of treatment options in these regions.

Beyond medical aid, Save One Life offers direct financial assistance programs in 14 countries. This is done in four ways: Through sponsorships, the organization is enabling children with bleeding disorders to afford basic needs. The organization also provides scholarships for higher education and micro-enterprise grants to support small business initiatives, fostering long-term independence. Last but not least, Save One Life finances summer camps for children with bleeding disorders.

The needs in developing countries certainly outweigh the needs in Europe. But even within Europe, significant disparities exist in access to diagnosis, treatment, and quality of life, Therefore Romania is one of the 14 countries where Save One Life runs its programs. Other countries are based in Africa, Asia and South-America.

## A Vision of Equity in Hemophilia Care

Founder Laurie Kelley explains, "We believe that every person with a bleeding disorder deserves a chance to live a healthy, fulfilling life, no matter where they were born. By expanding our presence in Europe, we're creating stronger, more agile support networks that will uplift communities for generations to come."

As Save One Life continues to evolve, its European team plays a central role on a voluntary basis in reshaping what humanitarian engagement can look like: rooted in local relationships, driven by global solidarity, and focused always on the human stories behind the statistics.

#### Conflicts of Interest

The author declares no conflict of interest.

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# **Original Manuscript**

# Ozonated PRP (PRP-O<sub>3</sub>) Application for the Reduction of Pain and Inflammation in Patients with Hemophilic Arthropathy: A Pilot Study

#### Abstract.

Arthropathy represents one of the most debilitating complications in individuals with congenital bleeding disorders, significantly impairing quality of life due to chronic pain and persistent joint inflammation. This pilot study explored the use of ozonated platelet-rich plasma (PRP-O<sub>3</sub>) as a regenerative and anti-inflammatory therapeutic alternative. Five patients with various types and severities of hemophilia, and one patient with Von Willebrand disease, received intra-articular PRP-O<sub>3</sub> injections. Preliminary clinical outcomes indicated significant improvement in inflammatory symptoms and pain perception, with no complications or adverse events reported. These findings suggest that PRP-O<sub>3</sub> may represent a safe, cost-effective, outpatient therapeutic option for the complementary management of hemophilic arthropathy, encouraging a more integrative and less invasive approach. Controlled clinical trials are recommended to confirm its efficacy and to establish standardized protocols.

**Keywords:** Hemophilia, hemophilic arthropathy, platelet-rich plasma, ozone therapy, joint pain, intraarticular injection

#### Introduction

Hemophilia is an X-linked hereditary disorder caused by a deficiency in clotting factor VIII (Hemophilia A) or IX (Hemophilia B), essential to the coagulation cascade. Clinically, it presents with spontaneous bleeding, particularly in muscles and joints, leading to progressive chronic arthropathy with recurrent pain and inflammation. Autologous platelet-rich plasma (PRP) is a platelet concentrate rich in growth factors with regenerative and anti-inflammatory properties. Medical ozone therapy involves the therapeutic use of an oxygen-ozone mixture, widely applied in the management of inflammatory and degenerative conditions with a favorable safety profile. The combination of PRP enriched with ozone may enhance the individual benefits of each therapy, offering a simultaneous regenerative and anti-inflammatory approach for hemophilic patients.

# **Objective**

To preliminarily evaluate the clinical effectiveness and safety of intra-articular ozonated PRP (PRP-O<sub>3</sub>) for reducing joint pain and inflammation in patients with hemophilic arthropathy.

#### **Methods**

Five patients with confirmed congenital bleeding disorders and arthropathy due to bleeding history were selected; Patient 1: Male, 13 years old, with severe Hemophilia A complicated by bilateral ankles and left knee arthropathy. Patient 2: Male, 23 years old, moderate Hemophilia A and bilateral ankles and right knee arthropathy. Patient 3: Male, 23 years old, mild Hemophilia A: bilateral ankles and left elbow arthropathy



Patient 4: Male, 34 years old, moderate Hemophilia B complicated by right knee and left shoulder arthropathy. Patient 5: Female, 49 years old, Von Willebrand disease: left ankle arthropathy. The used procedure was: blood extraction and PRP preparation via open centrifugation followed by an immediate ozonation of the platelet concentrate, then an intra-articular injection of PRP-O<sub>3</sub> into affected joints. Exclusion criteria included acute hemarthrosis, advanced arthropathy with joint space loss, active infection, or severe comorbidities. Patients were informed about the procedure, expected benefits, and absence of complications. Range of motion was assessed before and after the injections as part of the clinical evaluation.

#### **Results**

All patients reported subjective pain reduction in the days following the injection. Clinical assessment revealed reduced joint edema. No adverse events or complications were observed. The procedure was outpatient, required no hospitalization or additional prophylactic coverage, and no post-procedure bleeding was recorded. Functional improvement in joint range of motion was noted in most cases.

#### **Conclusions**

Intra-articular injection of ozonated PRP represents a safe, accessible, and potentially beneficial therapeutic strategy for managing hemophilic arthropathy. This minimally invasive approach avoids early surgical intervention or immunosuppressive medication. Further studies with larger cohorts and longer follow-up are needed to confirm its efficacy and to develop standardized clinical protocols.

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#### Conflicts of Interest

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# HEMATOLOGY & MEDICINE

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# Letter to the Editor Early onset in psychosis

Dear Editor,

the decision to address this complex topic was motivated by the fact that it concerns an age group that is usually less affected – adolescents - compared to adults. Nonetheless, it must not be considered less important, as prompt intervention can reduce the risk of disorder progression, the difficulty of early assessment, and the ability to determine and prevent outcomes

## **Psychotic Disorders**

The term "psychotic" indicates a loss of "judgment of reality," which is usually associated with symptoms such as hallucinations and delusions, and with a blurring of the boundaries of the Self. Mental disorders have traditionally been considered as distinct, episodic, and categorical conditions. This viewpoint has been challenged by evidence showing that many disorders are recurrent, chronic, and exist along a continuum. Over time, researchers have examined the structure of psychopathology,

considering dimensionality, persistence, and recurrence of mental disorders over twenty years, from adolescence to middle age. In particular, psychoses are a group of psychiatric disorders currently recognized by the presence of symptoms that, in addition to the lived experience of the affected individual, are characterized by novelty (hence the concept of "positive" symptoms), which are associated with a loss of contact with reality and generally with a lack of insight—that is, the degree of awareness and understanding that the individual has of being ill. Extensive data confirm that 50-60% of males and only 20-30% of females have their first hospital admission around age 25. Regarding course and outcome, it is evident that the prognosis is better in women, including clinical measures such as duration of hospitalization and relapses, as well as factors like social adaptation and marriage. Although a relatively high number of males utilize residential facilities, it is more common for women to live with their families or relatives. Research areas that have garnered significant attention include genetics, biochemistry, neurophysiology, psychoendocrinology, neuromorphology, and neuropsychology. Current understanding suggests a multifactorial etiology for mental disorders, with the "stress-diathesis" model serving as a framework that integrates biological, psychosocial, and environmental factors. This has spurred the development of new approaches for recognizing the onset of psychosis and intervening early, focusing particularly on prodromal phases. Many young people seek medical attention during the acute phase, often presenting symptoms and signs underestimated by their environment and healthcare providers. This early, untreated period is known as DUP (Duration of Untreated Psychosis). Its duration is a key factor influencing prognosis—particularly regarding remission of positive symptoms. Specifically, DUP refers to the time elapsed from the onset of the first psychotic symptoms to the initiation of treatment. The literature demonstrates that reducing DUP benefits outcomes in youths experiencing psychosis, motivating the expansion of specialized early intervention services across Europe and worldwide, especially in Australia, the United States, and Canada. Prodromal phases are characterized by fluctuating symptoms, with periods that may seem more critical but tend to remit quickly in early stages. There may be significant social withdrawal and cognitive deterioration before the first full-blown psychotic episode, which constitutes a rupture in the individual's development and is often more traumatic and difficult to remission. Early signs include disturbances and behavioral alterations such as social withdrawal, irritability, suspiciousness, paranoia, aggression, stereotypies, and bizarre behaviors.

The progressive social withdrawal and isolation observed in these cases are closely linked to these symptoms, which remain stigmatized and discriminated against. Functional decline occurs both before and, to a greater extent, after the onset of psychosis and is a major predictor of negative prognosis, including transition to psychosis. Despite this broad symptomatology, patients, families, and the social network including teachers, friends, and healthcare professionals—often fail to recognize the risk state, tending to underestimate these episodes and prolonging DUP, which negatively influences the course and prognosis of the disorder. The term At Risk Mental State (ARMS) refers to a condition of increased risk for developing psychosis in young people aged 14 to 30, who experience perceptual, mood, and behavioral alterations that may be early signs of psychotic disorders. Various terminology surrounds ARMS, linked to the conceptualization of conditions at risk of psychosis onset. These include different prodromal symptom profiles that can help predict transition. A primary goal of this work is to clarify these terminologies. Early and prompt intervention in these risk states can positively influence the disorder's course, delaying or preventing the first episode of psychosis (FEP). In conceptualizing mental states at risk, the temporal aspect is crucial, necessitating careful observation and monitoring of psychological and behavioral changes over recent months and years. Early signals include declines in functioning and well-being in key areas such as relationships and education, often triggered by recent psychosocial stressors. ARMS is based on the concepts of biological, genetic, and psychosocial vulnerability, with family history of psychosis or other mental disorders being a major risk factor. Additional risk factors include past episodes of non-psychotic symptoms (e.g., depression, panic attacks, anxiety, dissociative episodes, obsessive traits), adverse life events (e.g., socioeconomic hardship, social marginalization, belonging to minority groups), and significant life changes (bereavements, relocations, relationship terminations, job loss) that may act as triggers. Substance and alcohol use are also relevant considerations. While ARMS indicates a general risk state influenced by predisposing and precipitating factors, it is possible to specify the most predictive symptoms of psychosis. This work was notably developed in Australia by McGorry and Yung, who initially defined the prodromal condition as Clinical High Risk (CHR), later establishing specific diagnostic criteria related to attenuated and transient psychotic symptoms to define Ultra High Risk (UHR). Similarly, in Europe, a set of Basic Symptoms (BS) has been identified, which can be combined with UHR criteria to delineate at-risk states for psychosis onset. This conceptualization allows differentiation between early and late at-risk states: in early prodromal stages, basic symptoms and functional decline predominate, while in later stages, closer to transition, UHR symptoms are more prominent. The diagnostic criteria for UHR were developed to evaluate this risk in youths aged 14 to 30, including the presence of attenuated psychotic symptoms (APS), brief and limited psychotic symptoms (BLIPS), genetic risk, and functional decline. Recently, APS have been incorporated into DSM-5, Section III, as part of future diagnostic considerations. These involve at least one symptom—delusions, hallucinations, or disorganized speech—in a mild and attenuated form, present for at least the past month, with onset or worsening within the last year, and causing distress or functional impairment. BLIPS refer to psychotic symptoms that appeared within the past year, are not persistent, and tend to remit spontaneously. These include ideas of reference, magical thinking, perceptual disturbances, paranoid ideation, and bizarre speech. Alongside positive symptoms like APS and BLIPS, early and subtle negative symptoms such as social withdrawal, academic or work difficulties, deteriorating interpersonal relationships, and a general decline in quality of life are also important. UHR individuals often exhibit suicidal ideation and have a history of self-injurious behavior. Regarding BS, these are subjective disturbing experiences affecting various psychological and cognitive domains, such as thought disturbances, perception issues, language problems, and attention difficulties. They have been categorized into two groups: COPER (Cognitive-Perceptive Basic Symptoms) and COGDIS (Cognitive Disturbances). It is hypothesized that COGDIS are more specific for schizophrenia and indicate a nearer-term risk of psychosis compared to COPER. The current use of UHR and BS approaches in identifying and treating at-risk youths is ongoing. Another emerging research area involves Self Disorders (SD)—anomalous subjective experiences related to perceiving oneself as a unique and stable entity. These modifications of self-experience, particularly of the

core self, are common in psychotic states and in CHR individuals, supporting their inclusion in risk assessment alongside UHR and BS criteria.

#### **EOS/VEOS: Clinical Profiles**

Studies on basic symptoms in children and adolescents have utilized the Bonn Scale for the Assessment of Basic Symptoms (BSABS), regardless of frequency of occurrence. Research indicates that, similar to adults, basic symptoms are reported across various diagnostic groups in youth. Adolescents with schizophrenia, like adults, exhibit higher levels of basic symptoms than other diagnostic categories. Case analyses suggest that basic symptoms may hold particular significance for predicting psychosis in children and adolescents, especially thought interference, perseveration, disturbances in differentiating imagination from perception, slowed thinking, and concentration difficulties. Patients diagnosed with ICD schizophrenia, schizotypic, or delusional disorders tend to have higher BSABS scores, whereas those without such diagnoses score lower. The number of basic symptoms within the BSABS categories remains fairly stable over time, indicating that these symptoms may reflect a trait-like aspect of psychopathological development. However, due to differences in assessment tools and the developmental context, these results cannot be directly compared to adult data. Currently, evidence regarding their predictive validity remains limited, although some indications suggest their potential as markers for psychosis onset in youth. Strategies to prevent severe outcomes of psychotic disorders include early diagnosis and intervention. The ultra-high risk and basic symptom criteria have primarily been developed using adult samples, but preliminary studies suggest some transferability to pediatric populations. Nevertheless, certain attenuated psychotic symptoms in youth may lack sufficient specificity, and brief psychotic episodes without observable behavioral changes are difficult to classify in children. Similarly, the validity of basic symptoms criteria in children and adolescents remains under investigation. To address these limitations, the pediatric and adolescent version of the Schizophrenia Proneness Instrument (SPI-CY) has been developed, incorporating risk criteria tailored for younger populations.

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#### Conflicts of Interest

The authors declare no conflict of interest.

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