

ORIGINAL RESEARCH

# Clinical Profile of Schizophrenia in Children and Adolescents: Diagnosis, Symptoms and Prognosis

Hurşit FERAH KAYA<sup>1</sup>, Ayşegül Tuğba HIRA SELEN<sup>2</sup>

<sup>1</sup> Necmettin Erbakan University Faculty of Medicine, Department of Child and Adolescent Psychiatry, Konya, Türkiye.

<sup>2</sup> Konya City Hospital, Konya, Türkiye.

## ABSTRACT

Schizophrenia is a psychiatric disorder with a wide clinical spectrum that significantly impairs the functionality of the individual. It is less common under 18 years of age and clinical symptoms, diagnosis, treatment and follow-up processes differ from adult schizophrenia in certain aspects. This study aims to evaluate the sociodemographic and clinical characteristics of patients diagnosed with early-onset schizophrenia (EOS) and childhood-onset schizophrenia (COS). In this retrospective study, 83 children and adolescents diagnosed with schizophrenia according to DSM-5 criteria were analyzed. Sociodemographic characteristics, age at first symptom, duration of diagnosis, comorbidities and treatment processes of the patients were analyzed. The mean age at diagnosis of schizophrenia was  $14.42 \pm 2.46$  years. The mean time between the first psychiatric symptom and the diagnosis of schizophrenia was  $11.1 \pm 1.56$  months. The mean age of starting the first psychiatric treatment was  $13.26 \pm 3.10$  years and the mean age of starting the most commonly used drug group, antipsychotic drugs, was  $13.93 \pm 2.82$  years. Comorbid psychiatric disorders were common, with ADHD and intellectual disability being the most frequently observed. In addition, 19% of the patients had a history of psychiatric disorders in their mothers and 20% in their fathers. Our study highlights the delays in the diagnostic process and the prevalence of comorbid disorders by determining the sociodemographic and clinical characteristics of patients diagnosed with EOS and COS. It is emphasized that early diagnosis and intervention processes should be strengthened, individualized treatment approaches should be adopted, and long-term functionality of patients should be increased with multidisciplinary approaches.

**Keywords:** Childhood-onset schizophrenia. Early-onset schizophrenia. Sociodemographic characteristics. Comorbid psychiatric disorders.

## Çocuk ve Ergenlerde Şizofreninin Klinik Profili: Tanı, Belirtiler ve Prognoz

## ÖZET

Şizofreni geniş bir klinik yelpazesi olan bireyin işlevselliğini belirgin olarak bozan psikiyatrik bir bozukluktur. 18 yaşın altında daha nadir görülmekte ve klinik belirtiler, tanı, tedavi ve takip süreçleri erişkin dönem şizofrenisinden bazı yönleri ile ayrılmaktadır. Bu çalışma, erken başlangıçlı şizofreni (EOS) ve çocukluk başlangıçlı şizofreni (COS) tanısı almış hastaların sosyodemografik ve klinik özelliklerini değerlendirmeyi amaçlamaktadır. Retrospektif olarak tasarlanan bu çalışmada DSM-5 kriterlerine göre şizofreni tanısı almış 83 çocuk ve ergen hasta incelenmiştir. Hastaların sosyodemografik özellikleri, ilk semptom yaşı, tanı alma süresi, komorbiditeleri ve tedavi süreçleri analiz edilmiştir. Hastaların ortalama şizofreni tanısı alma yaşı  $14,42 \pm 2,46$  yıl olarak belirlenmiştir. İlk psikiyatrik semptomun ortaya çıkışı ile şizofreni tanısı alma arasında geçen süre ortalama  $11,1 \pm 1,56$  ay olarak saptanmıştır. İlk psikiyatrik tedaviye başlama yaşı ortalama  $13,26 \pm 3,10$  yıl ve en sık kullanılan ilaç grubu olan antipsikotik ilaçlara başlama yaşı ortalama  $13,93 \pm 2,82$  yıl olarak saptanmıştır. Komorbid psikiyatrik bozukluklar yaygındı ve en sık DEHB ve entelektüel yeti yitimi gözlemlendi. Ayrıca, hastaların %19'unun annesinde ve %20'sinin babasında psikiyatrik bozukluk öyküsü saptanmıştır. Çalışmamız, EOS ve COS tanısı alan hastaların sosyodemografik ve klinik özelliklerini belirleyerek, tanı sürecinde yaşanan gecikmelere ve komorbid bozuklukların yaygınlığına dikkat çekmektedir. Erken tanı ve müdahale süreçlerinin güçlendirilmesi, bireyselleştirilmiş tedavi yaklaşımlarının benimsenmesi ve multidisipliner yaklaşımlar ile hastaların uzun vadeli işlevselliğinin artırılması gerektiği vurgulanmaktadır.

**Anahtar Kelimeler:** Çocukluk çağı başlangıçlı şizofreni. Erken başlangıçlı şizofreni. Sosyodemografik özellikler. Komorbid psikiyatrik bozukluklar.

**Date Received:** February 5, 2025

**Date Accepted:** March 24, 2025

## Authors' ORCID Information:

Hurşit FERAH KAYA: 0000-0001-8611-0435

Ayşegül Tuğba HIRA SELEN: 0000-0003-1065-5548

Dr. Hurşit FERAH KAYA

Necmettin Erbakan Üniversitesi Tıp Fakültesi, Yunus Emre,

Meram Tıp Fakültesi Hst. No:281, 42090, Meram/Konya,

Türkiye

Phone: +90 555 524 54 59

E-mail: [drhurshitferahkaya@gmail.com](mailto:drhurshitferahkaya@gmail.com)

Schizophrenia is a complex psychiatric disorder characterized by a broad clinical spectrum of positive and negative symptoms that significantly impair an individual's functionality. While the age of onset varies across studies, the disorder is generally reported to emerge during late adolescence and early adulthood<sup>1</sup>. Research indicates that the peak onset period of schizophrenia is approximately 20.5 years<sup>2</sup>. Schizophrenia is usually diagnosed in the twenties, but the neurodevelopmental processes that cause the disorder are thought to occur during childhood and adolescence<sup>3</sup>. The American Academy of Child and Adolescent Psychiatry classifies cases with onset before the age of 13 as childhood-onset schizophrenia (COS) and cases with onset before the age of 18 as early-onset schizophrenia (EOS)<sup>4</sup>. The prevalence of EOS in the general population is estimated at approximately 0.25%, whereas COS is rarer, with an estimated prevalence of around 0.05%. While COS and EOS fundamentally represent similar disorders and share diagnostic criteria with adult-onset schizophrenia (AOS), they differ in terms of neurobiology, clinical presentation, prognosis, and treatment processes<sup>2,5</sup>.

Although EOS and COS are less common than AOS, studies indicate that initial symptoms of schizophrenia appear before the age of 18 in approximately 18% of individuals later diagnosed with schizophrenia in adulthood<sup>2</sup>. Assessments of premorbid symptoms reveal significant deficits in social, motor, and language skills among individuals with EOS and COS. Additionally, these patients frequently present with comorbid neurodevelopmental disorders, such as attention-deficit/hyperactivity disorder (ADHD), autism spectrum disorder (ASD), and obsessive-compulsive disorder (OCD)<sup>6,7</sup>. EOS and COS exhibit a broad range of initial symptoms and are associated with an insidious onset of psychotic symptoms<sup>8</sup>.

In the long term, they are reported to differ from adult cases by demonstrating more severe negative symptoms, pronounced cognitive impairments, and a more treatment-resistant course<sup>6</sup>. The subtle progression of psychotic symptoms in younger patients, along with the predominance of negative symptoms, can contribute to delays in diagnosis and subsequent treatment. A follow-up study found that only 32% of patients initially presenting with symptoms received a schizophrenia diagnosis at the first evaluation, but this figure increased to 40% upon further assessments<sup>9</sup>. Additionally, the duration of untreated psychosis in COS and EOS is reported to be longer than in AOS<sup>9</sup>. Studies suggest that delays in schizophrenia diagnosis and untreated psychosis are associated with increased symptom severity and poorer long-term cognitive and functional outcomes<sup>10,11</sup>.

Early diagnosis and intervention are crucial for mitigating symptom severity and improving long-term prognosis<sup>12</sup>. Identifying and monitoring clinical high-risk groups among children and adolescents, as well as recognizing early warning signs of psychotic disorders, provide significant opportunities for timely diagnosis and intervention.

Since schizophrenia is a rare disorder, studies examining the diagnostic process and the progress of schizophrenia in children and adolescents are very limited in Türkiye. This study aims to evaluate the sociodemographic and clinical characteristics of individuals diagnosed with EOS and COS who were admitted to our clinic. By analyzing the management and treatment processes of this patient group, we seek to contribute to a more comprehensive understanding of schizophrenia in children and adolescents and to emphasize the importance of early intervention programs in clinical practice.

## Material and Method

This retrospective study was designed using data from the Child and Adolescent Psychiatry outpatient clinic database at Necmettin Erbakan University, Faculty of Medicine. The study sample comprised patients diagnosed with schizophrenia over the past 10 years. Psychiatric diagnoses were made by child psychiatrists based on the DSM-5 diagnostic criteria. In addition to psychiatric diagnoses, sociodemographic characteristics (age, gender, parental age and education level, socioeconomic status), the onset of symptoms, the timing of schizophrenia diagnosis, family history, treatment, and follow-up processes were recorded. The study was approved by the Non-Interventional Clinical Research Ethics Committee of Necmettin Erbakan University (06.09.2024-2024/5165) and conducted in accordance with the principles of the Helsinki Declaration.

## Statistical Analysis

The data were analyzed using SPSS (Statistical Package for the Social Sciences) version 25.0. Descriptive statistics (mean, standard deviation, frequency, and percentage) were used to summarize the data. Relationships between categorical variables were assessed using the chi-square test. A significance level of  $p < 0.05$  was considered statistically significant.

## Results

97 patients diagnosed with schizophrenia were identified in our database. However, 14 individuals were excluded due to missing data, resulting in a final

## Schizophrenia in Children and Adolescents

study group consisting of 83 participants (46 males, 37 females). The participants' ages ranged from 6 to 18 years, with a mean age of  $13.86 \pm 3.13$  years. Among the participants, 37 were continuing their high school education, while 10 had discontinued formal schooling. Approximately 20% of participants belonged to single-parent households, 33% had three siblings, and 45% were the firstborn child in their family. The sociodemographic data of the participants are summarized in Table I.

**Table I.** Sociodemographic and clinical characteristics of the participants

	Mean	SD
<b>Age</b>	13.86	3.13
<b>Mother's age</b>	41.42	4.29
<b>Father's age</b>	43.72	3.61
	n	%
<b>Gender, Male/Female</b>	46/37	55.4/44.6
<b>Education level</b>		
Illiterate	10	12.0
Primary school	36	43.4
Secondary school	37	44.6
<b>Comorbidity</b>		
Organic comorbidity, Yes/No	18 / 65	21.7 / 78.3
Psychiatric comorbidity	54 / 29	65.1 / 34.9
ADHD	16	19.3
ID	15	18.1
OCD	8	9.6
MDD	3	3.6
AD	3	3.6
ASD	2	2.4
CD	2	2.4
BPD	2	2.4
Diğer	3	3.6
<b>Mother's education level</b>		
	n	%
Illiterate	20	24.1
Primary school	54	65.1
Secondary school	7	8.4
University	2	2.4
<b>Father's education level</b>		
	n	%
Illiterate	17	20.5
Primary school	50	60.2
Secondary school	14	16.9
University	2	2.4
<b>Economic Level</b>		
	n	%
Low	49	59.0
Middle	24	29.0
High	10	12.0
<b>Family Structure</b>		
	n	%
Nuclear	57	68.7
Extended	10	12.0
Fragmented	16	19.3

SD = standard deviation, n= number of cases  
 ADHD: attention deficit/hyperactivity disorder, ID: intellectual disability, OCD: obsessive compulsive disorder, MDD: major depressive disorder, AD: anxiety disorder, ASD: autism spectrum disorder, CD: conduct disorder, BPD: bipolar disorder

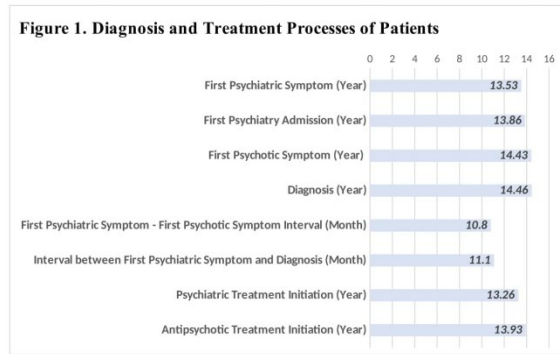
43 patients initially presented with internalizing problems (depression, anxiety disorders etc.), while 40 patients sought consultation due to externalizing issues (ADHD, conduct disorder, etc.). No statistically significant gender differences were found regarding internalizing and externalizing problems ( $\chi^2=0.91$ ,  $p=0.338$ ). Negative symptoms were the first psychotic symptoms in 43% of patients, while delusions were the most frequently observed positive psychotic symptom, present in 25% of cases. Additionally, 65% of participants had comorbid psychiatric disorders, including attention-deficit/hyperactivity disorder (ADHD) and intellectual disability. Eighteen participants had a history of organic medical conditions, primarily epilepsy.

The mean age at the onset of initial psychiatric symptoms was  $13.53 \pm 2.89$  years, whereas the onset age of the first psychotic symptom was  $14.43 \pm 2.78$  years. The mean duration between the first psychiatric symptom and the first psychotic symptom was  $10.8 \pm 1.43$  months, while the mean interval between the first psychiatric symptom and the diagnosis of schizophrenia was  $11.1 \pm 1.56$  months. The mean age at schizophrenia diagnosis was  $14.42 \pm 2.46$  years, with initial psychiatric treatment being initiated at  $13.26 \pm 3.10$  years and antipsychotic treatment commencing at  $13.93 \pm 2.82$  years. Antipsychotic medications were the most commonly prescribed first-line treatment (65%), followed by selective serotonin reuptake inhibitors (SSRIs) (14%). 22 patients required hospitalization for treatment and follow-up. Furthermore, five participants had a history of suicide attempts, while nine had a history of substance use. The clinical characteristics of the patients are presented in Table II and Figure 1.

**Table II.** Clinical characteristics of patients and diagnosis/treatment processes

<b>First Psychiatric Symptom</b>	<b>n</b>	<b>%</b>
Symptoms of Externalisation	43	51.8
Symptoms of Internalisation	40	48.2
<b>First Psychotic Symptom</b>	<b>n</b>	<b>%</b>
Negative Symptoms	36	43.4
Hallucination	21	25.3
Delusion	14	16.9
Dysorganised Behaviour	7	8.4
Dysorganised Speech	5	6.0
<b>Variables</b>	<b>Mean</b>	<b>SD</b>
First Psychiatric Symptom (Year)	13.53	2.80
First Psychiatry Admission (Year)	13.86	3.13
First Psychotic Symptom (Year)	14.43	2.75
Diagnosis (Year)	14.46	2.34
First Psychiatric Symptom - First Psychotic Symptom Interval (Month)	10.8	1.43
First Psychiatric Symptom - Diagnosis Interval (Month)	11.1	1.56
Psychiatric Treatment Initiation (Year)	13.26	3.20
Antipsychotic Treatment Initiation (Year)	13.93	2.82

SD = standard deviation, n= number of cases

**Figure 1:***Diagnosis and Treatment Processes of Patients*

Examination of family history revealed that the participants' mothers (mean age:  $41.42 \pm 4.29$  years) and fathers (mean age:  $43.72 \pm 3.61$  years) had an educational level of primary school in approximately 50% of cases, and 59% of families had a low socioeconomic status. Additionally, psychiatric disorders were identified in 19% of mothers and 20% of fathers.

## Discussion and Conclusion

In this study, we conducted a detailed evaluation of the sociodemographic and clinical characteristics of children and adolescents diagnosed with schizophrenia. The mean age of the participants was  $13.86 \pm 3.13$  years. The majority of the patients had negative first psychotic symptoms. The mean age of the first psychotic symptoms was  $13.53 \pm 2.89$  years, and the mean age of the first psychotic symptoms was  $14.43 \pm 2.78$  years. The mean time between the first psychiatric symptom and the diagnosis of schizophrenia was  $11.1 \pm 1.56$  months, and the mean age of the diagnosis was  $14.42 \pm 2.46$  years.

In line with previous studies, one of the key findings of our research is that schizophrenia was found to be more prevalent among males<sup>4</sup>. Additionally, more than 10% of participants had discontinued their education. Individuals diagnosed with EOS and COS are reported to experience significant impairments in academic functioning, with frequent disruptions in their educational trajectories<sup>7</sup>. Schizophrenia adversely affects cognitive capacity and social skills, while also leading to motivational deficits, which can contribute to increased dropout rates from school<sup>8</sup>. Therefore, in addition to symptom management through pharmacological treatment, providing educational support and implementing individualized educational programs for individuals with schizophrenia may help mitigate academic functional impairments.

In our study, about 20 per cent of the participants came from broken families. This finding suggests a bidirectional relationship. Family structure has been identified as a significant factor in the development of psychiatric disorders in children and adolescents, and studies indicate that children from single-parent families have a higher risk of developing EOS<sup>13</sup>. Family conflicts, limited social support, and economic difficulties observed in fragmented families may increase the risk of psychopathology<sup>14</sup>. Furthermore, children raised in unstable family environments are more likely to be exposed to stressors, which could exacerbate neurodevelopmental vulnerabilities<sup>15</sup>. Additionally, the burden of having a family member with a chronic psychiatric disorder, along with the challenges of diagnosis, treatment, and follow-up, may further contribute to family stress and disrupt family integrity. This finding suggests a bidirectional relationship. Therefore, strengthening family support systems and providing mental health support to caregivers could play a crucial role in improving the prognosis of children and adolescents diagnosed with schizophrenia.

Participants in our study presented with externalizing symptoms (e.g., hostility, aggression, impulsivity) and internalizing symptoms (e.g., depression, anxiety, social withdrawal) at similar rates. Our findings support the notion that schizophrenia in children and adolescents presents with a heterogeneous clinical profile<sup>18</sup>. Some studies suggest that internalizing symptoms are more common in the prodromal phase, particularly anxiety and depressive symptoms in EOS cases<sup>9</sup>. However, externalizing symptoms are also noteworthy clinical indicators, particularly in the presence of comorbid ADHD and conduct disorder, where they tend to be more pronounced<sup>16</sup>. Thus, a comprehensive clinical assessment that evaluates both internalizing and externalizing symptoms simultaneously is essential for developing effective early intervention strategies. Another key finding of our study was that there were no significant gender differences in the prevalence of internalizing or externalizing symptoms. This suggests that schizophrenia in childhood and adolescence manifests across a broad spectrum of psychopathology, independent of gender. Although previous research has reported that males exhibit more externalizing symptoms while females present with more internalizing symptoms, our study did not observe this distinction<sup>17</sup>. The fact that externalization and internalization problems did not differ between genders in our study can be explained by several factors. Firstly, although it is traditionally accepted that men are more externalized (aggression, anger outbursts) and women are more internalized (depression, anxiety), modern social dynamics may have reduced these differences. In addition, the fact that women participate more in business life and

## Schizophrenia in Children and Adolescents

social life and men receive more psychosocial support may eliminate the difference between the sexes in terms of the expression of symptoms.

Regarding psychotic symptoms, 43% of participants initially exhibited negative symptoms, while delusions were the most commonly reported positive symptom (25%). Our findings align with previous literature indicating that negative symptoms predominate in EOS<sup>18</sup>. The early predominance of negative symptoms may prevent families and social circles from recognizing the disorder, contributing to diagnostic delays<sup>19</sup>. Therefore, early identification and appropriate management of negative symptoms in children and adolescents is of paramount importance. The presence of comorbid psychiatric disorders, including ADHD and intellectual disability in 65% of participants, underscores the strong association between EOS/COS and neurodevelopmental disorders. Neurodevelopmental impairments are considered significant risk factors for schizophrenia and further complicate patients' academic and social functioning [20]. Moreover, the presence of organic medical conditions, particularly epilepsy, in 18 participants highlights the neurobiological and neurological underpinnings of schizophrenia. The relationship between epilepsy and schizophrenia has been extensively studied, with research suggesting shared neurobiological mechanisms underlying both conditions<sup>21</sup>.

In our study, the mean age at onset of initial psychiatric symptoms was 13.53 years, while the mean age at onset of psychotic symptoms was 14.43 years. Literature suggests that EOS typically has an insidious onset, which can delay diagnosis<sup>9</sup>. The average interval between the first psychiatric symptom (whether internalizing or externalizing) and the onset of psychotic symptoms was 10.8 months, while the mean duration from the first psychiatric symptom to schizophrenia diagnosis was 11.1 months. In other words, non-psychotic psychiatric symptoms often precede psychotic symptoms, and schizophrenia is diagnosed approximately one year after the initial symptoms emerge. This finding highlights that diagnostic delays in EOS and COS remain a significant concern. Various factors may contribute to these delays. Firstly, psychotic symptoms in childhood and adolescence may be misattributed to neurodevelopmental disorders (e.g., ADHD or ASD) or mood disorders<sup>7</sup>. Additionally, the early predominance of negative symptoms may obscure the clinical detection of psychotic processes<sup>22</sup>. Conducting detailed family history assessments and carefully evaluating symptom progression may help reduce diagnostic delays. Our study also found that the mean age at initiation of psychiatric treatment was 13.26 years, while the mean age at initiation of antipsychotic treatment was 13.93 years. Many children and

adolescents exhibiting early psychiatric symptoms initially receive treatment for anxiety, depression, or behavioral problems, with antipsychotic treatment introduced only when psychotic symptoms become more apparent<sup>23</sup>. This could explain the gap between clinical diagnosis and the commencement of antipsychotic treatment. Our findings emphasize the need for improved early intervention strategies in EOS and COS. These findings underscore the importance of early recognition and careful monitoring of psychiatric symptoms in children and adolescents at risk for schizophrenia. Implementing structured screening protocols and increasing awareness among clinicians could help minimize diagnostic delays and ensure timely initiation of appropriate treatment strategies.

Our study also found that 22 patients required hospitalization. Hospitalization rates in EOS and COS are generally high, likely due to the severity of symptoms and greater treatment resistance in this patient group<sup>24</sup>. Additionally, five participants had a history of suicide attempts, while nine had a history of substance use. Previous research has corroborated the high prevalence of suicide risk and substance use among children and adolescents with schizophrenia<sup>20</sup>. Suicide attempts and social withdrawal are particularly common in patients with predominant negative symptoms<sup>22</sup>. Therefore, early identification of suicide risk and a multidisciplinary approach to managing EOS and COS patients are essential.

An examination of family history revealed that 50% of participants' parents had only a primary school education, and 59% were classified as having low socioeconomic status. Low socioeconomic status and lower parental education levels have been identified as major risk factors for the development of psychiatric disorders in children<sup>7</sup>. Additionally, psychiatric disorders were identified in 19% of mothers and 20% of fathers, with schizophrenia specifically diagnosed in 10% of both mothers and fathers. Genetic predisposition is a well-established risk factor for schizophrenia and other psychotic disorders, with individuals having a parent diagnosed with schizophrenia being at significantly greater risk than the general population<sup>16</sup>. These findings underscore the interplay between biological and environmental factors in schizophrenia development. Early identification and intervention strategies for high-risk groups may help improve disease outcomes.

Our study has several limitations. First, as a retrospective study, we were unable to track long-term functional outcomes or treatment responses, limiting our ability to draw definitive conclusions about disease progression and treatment efficacy. Second, our sample size was relatively small and drawn from a single center, which may restrict the generalizability of our findings. Future studies should replicate our

findings across diverse geographical and cultural settings. Lastly, our study did not use a scale to assess positive and negative symptoms in more detail, which may have limited the comprehensive assessment of negative symptoms and cognitive impairments. Future research should incorporate long-term follow-up data and evaluate the effectiveness of early intervention programs for managing EOS and COS.

This study provides valuable insights into the sociodemographic and clinical characteristics of individuals diagnosed with EOS and COS, highlighting critical findings regarding diagnosis and management. Enhancing early screening programs, adopting multidisciplinary approaches, and implementing individualized treatment strategies are essential for optimizing the care and long-term functionality of affected individuals. Future prospective and large-scale studies may further refine our understanding of EOS and COS and contribute to the development of more effective intervention strategies.

#### Ethics Committee Approval Information:

Ethical Board: Necmetin Erbakan Üniversitesi İlaç ve Tıbbi Cihaz Dışı Araştırmalar Etik Kurulu

Date: 06.09.2024

Degree No: 2024/5165

#### Researcher Contribution Statement:

Idea and design: H.F.; Data collection and processing: A.T.H.S.; H.F.; Analysis and interpretation of data: H.F.; A.T.H.S.; Writing of significant parts of the article: H.F.

#### Support and Acknowledgement Statement:

This study received no financial support.

#### Conflict of Interest Statement:

The authors of the article have no conflict of interest declarations.

## References

- Alkelai A, Greenbaum L, Shohat S, Povysil G, Malakar A, Ren Z, et al. Genetic insights into childhood-onset schizophrenia: The yield of clinical exome sequencing. *Schizophr Res* 2023;252:138–45. <https://doi.org/10.1016/j.schres.2022.12.033>.
- Solmi M, Radua J, Olivola M, Croce E, Soardo L, Salazar de Pablo G, et al. Age at onset of mental disorders worldwide: large-scale meta-analysis of 192 epidemiological studies. *Mol Psychiatry* 2022;27:281–95. <https://doi.org/10.1038/s41380-021-01161-7>.
- Lieberman JA, Perkins D, Belger A, Chakos M, Jarskog F, Boteva K, et al. The early stages of schizophrenia: speculations on pathogenesis, pathophysiology, and therapeutic approaches. *Biol Psychiatry* 2001;50:884–97. [https://doi.org/10.1016/S0006-3223\(01\)01303-8](https://doi.org/10.1016/S0006-3223(01)01303-8).
- McClellan J, Stock S. Practice Parameter for the Assessment and Treatment of Children and Adolescents With Schizophrenia. *J Am Acad Child Adolesc Psychiatry* 2013;52:976–90. <https://doi.org/10.1016/j.jaac.2013.02.008>.
- Liu Y, Guo W, Zhang Y, Lv L, Hu F, Wu R, et al. Decreased Resting-State Interhemispheric Functional Connectivity Correlated with Neurocognitive Deficits in Drug-Naïve First-Episode Adolescent-Onset Schizophrenia. *Int J Neuropsychopharmacol* 2018;21:33–41. <https://doi.org/10.1093/ijnp/pyx095>.
- Tor J, Dolz M, Sintés A, Muñoz D, Pardo M, de la Serna E, et al. Clinical high risk for psychosis in children and adolescents: a systematic review. *Eur Child Adolesc Psychiatry* 2018;27:683–700. <https://doi.org/10.1007/s00787-017-1046-3>.
- Taylor JH, Huque ZM. Commentary: Schizophrenia prevention and prodromal psychosis in children and adolescents. *J Child Psychol Psychiatry* 2021;62:674–6. <https://doi.org/10.1111/jcpp.13408>.
- Baykal S, Bozkurt A, Çobanoğlu Osmanlı C, Önal BS, Şahin B, Karadoğan ZN, et al. A comparison of clinical characteristics and course predictors in early- and childhood-onset schizophrenia. *Early Interv Psychiatry* 2025;19. <https://doi.org/10.1111/eip.13594>.
- Stentebjerg-Olesen M, Pagsberg AK, Fink-Jensen A, Correll CU, Jeppesen P. Clinical Characteristics and Predictors of Outcome of Schizophrenia-Spectrum Psychosis in Children and Adolescents: A Systematic Review. *J Child Adolesc Psychopharmacol* 2016;26:410–27. <https://doi.org/10.1089/cap.2015.0097>.
- Coulon N, Godin O, Bulzacka E, Dubertret C, Mallet J, Fond G, et al. Early and very early-onset schizophrenia compared with adult-onset schizophrenia: French FACE-SZ database. *Brain Behav* 2020;10. <https://doi.org/10.1002/brb3.1495>.
- Howes OD, McCutcheon R, Agid O, de Bartolomeis A, van Beveren NJM, Birnbaum ML, et al. Treatment-Resistant Schizophrenia: Treatment Response and Resistance in Psychosis (TRRIP) Working Group Consensus Guidelines on Diagnosis and Terminology. *Am J Psychiatry* 2017;174:216–29. <https://doi.org/10.1176/appi.ajp.2016.16050503>.
- Hashimoto K. Recent Advances in the Early Intervention in Schizophrenia: Future Direction from Preclinical Findings. *Curr Psychiatry Rep* 2019;21:75. <https://doi.org/10.1007/s11920-019-1063-7>.
- Morgan C, Fearon P, Lappin J, Heslin M, Donoghue K, Lomas B, et al. Ethnicity and long-term course and outcome of psychotic disorders in a UK sample: The ÆSOP-10 study. *Br J Psychiatry* 2017;211:88–94. <https://doi.org/10.1192/bjp.bp.116.193342>.
- Uher R, Zwickler A. Etiology in psychiatry: embracing the reality of poly-gene-environmental causation of mental illness. *World Psychiatry* 2017;16:121–9. <https://doi.org/10.1002/wps.20436>.
- Rutter M. Annual Research Review: Resilience – clinical implications. *J Child Psychol Psychiatry* 2013;54:474–87. <https://doi.org/10.1111/j.1469-7610.2012.02615.x>.
- Kim-Cohen J, Caspi A, Moffitt TE, Harrington H, Milne BJ, Poulton R. Prior Juvenile Diagnoses in Adults With Mental Disorder. *Arch Gen Psychiatry* 2003;60:709. <https://doi.org/10.1001/archpsyc.60.7.709>.
- Solmi M, Seitidis G, Mavridis D, Correll CU, Dragioti E, Guimond S, et al. Incidence, prevalence, and global burden of schizophrenia - data, with critical appraisal, from the Global Burden of Disease (GBD) 2019. *Mol Psychiatry* 2023;28:5319–27. <https://doi.org/10.1038/s41380-023-02138-4>.
- Driver DI, Thomas S, Gogtay N, Rapoport JL. Childhood-Onset Schizophrenia and Early-onset Schizophrenia Spectrum Disorders. *Child Adolesc Psychiatr Clin N Am* 2020;29:71–90. <https://doi.org/10.1016/j.chc.2019.08.017>.
- Remschmidt H, Theisen F. Early-onset schizophrenia. *Neuropsychobiology* 2012;66:63–9. <https://doi.org/10.1159/000338548>.
- Hollis C. Developmental precursors of child- and adolescent-onset schizophrenia and affective psychoses: diagnostic specificity and continuity with symptom dimensions. *Br J Psychiatry* 2003;182:37–44. <https://doi.org/10.1192/bjp.182.1.37>.
- Williams JA, Burgess S, Suckling J, Lalouis PA, Batool F, Griffiths SL, et al. Inflammation and Brain Structure in

## Schizophrenia in Children and Adolescents

- Schizophrenia and Other Neuropsychiatric Disorders. *JAMA Psychiatry* 2022;79:498. <https://doi.org/10.1001/jamapsychiatry.2022.0407>.
22. Remschmidt H, Theisen FM. Schizophrenia and related disorders in children and adolescents. *Neurodev. Disord.*, Vienna: Springer-Verlag; n.d., p. 121–41. [https://doi.org/10.1007/3-211-31222-6\\_7](https://doi.org/10.1007/3-211-31222-6_7).
23. Correll C, Arango C, Fagiolini A, Giordano G, Leucht S, Salazar de Pablo G. Finding the Right Setting for the Right Treatment During the Acute Treatment of Individuals with Schizophrenia: A Narrative Review and Clinical Practice Guideline. *Neuropsychiatr Dis Treat* 2024;Volume 20:1293–307. <https://doi.org/10.2147/NDT.S459450>.
24. Cheng X, Zhang H, Zhang J, Xu P, Jin P, Fang H, et al. Comparison of clinical characteristics and treatment efficacy in childhood-onset schizophrenia and adolescent-onset schizophrenia in mainland China: A retrospective study. *Early Interv Psychiatry* 2021;15:1721–9. <https://doi.org/10.1111/eip.13121>.

