




Review Article

Prescription Patterns, Medication Adherence, and Adverse Drug Reactions in Schizophrenia: A Comprehensive Review

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ABSTRACT

Schizophrenia is a severe and chronic psychiatric disorder affecting approximately 24 million individuals worldwide. Antipsychotic medications remain the cornerstone of treatment; however, long-term management is often challenged by poor medication adherence and adverse drug reactions (ADRs). Prescribing practices have evolved considerably over recent decades with the increasing use of second-generation antipsychotics owing to their improved tolerability profiles. Nevertheless, issues such as metabolic syndrome, weight gain, extrapyramidal symptoms, hyperprolactinemia, and cardiovascular complications continue to affect treatment outcomes. Medication adherence is a critical determinant of therapeutic success, relapse prevention, and reduction of hospitalization rates. Numerous patient-related, disease-related, treatment-related, and healthcare system-related factors influence adherence. Pharmacovigilance and ADR monitoring play a pivotal role in ensuring the safe use of antipsychotic medications and improving quality of life among patients with schizophrenia. This review summarizes current evidence regarding prescription patterns, medication adherence, determinants of non-adherence, ADR profiles of antipsychotic medications, and strategies to optimize treatment outcomes in schizophrenia. The article also highlights recent advances in pharmacotherapy and the importance of individualized treatment approaches for effective disease management.

Keywords: Schizophrenia, Antipsychotics, Prescription Pattern, Medication Adherence, Adverse Drug Reactions, Pharmacovigilance, Psychiatry.

INTRODUCTION

Schizophrenia is a chronic, severe, and disabling neuropsychiatric disorder characterized by disturbances in thought processes, perception, emotions, and behavior. It affects approximately 24 million individuals worldwide and remains one of the leading causes of disability among young adults. The disorder contributes substantially to the global burden of disease because of its early onset, chronic course, recurrent relapses, and profound impact on social and occupational functioning. Schizophrenia typically manifests during late adolescence or early adulthood and affects males and females across all ethnic and socioeconomic groups. Despite decades of research, the precise etiology of schizophrenia remains incompletely understood, although genetic susceptibility, neurodevelopmental abnormalities, neurotransmitter dysregulation, environmental exposures, and psychosocial factors are believed to contribute to disease pathogenesis [1,2].

The clinical presentation of schizophrenia is heterogeneous and encompasses positive symptoms, negative symptoms, cognitive impairment, and affective disturbances. Positive symptoms include hallucinations, delusions, disorganized speech, and bizarre behavior, whereas negative symptoms comprise social withdrawal, emotional blunting, reduced motivation, and diminished speech output. Cognitive deficits involving attention, executive function, working memory, and information processing speed are increasingly recognized as major determinants of long-term disability. These manifestations collectively impair patients' ability to maintain employment, interpersonal relationships, and independent living, thereby significantly reducing quality of life [3,4].

The dopamine hypothesis has historically served as the principal framework for understanding schizophrenia pathophysiology. According to this theory, hyperactivity of dopaminergic neurotransmission within mesolimbic pathways contributes to positive symptoms, whereas reduced dopaminergic activity in mesocortical regions is associated with negative and cognitive symptoms. Contemporary evidence suggests that schizophrenia is a multifactorial disorder involving dysregulation of several neurotransmitter systems, including dopamine, glutamate, gamma-aminobutyric acid (GABA), serotonin, and acetylcholine. Neuroimaging studies have demonstrated structural and functional abnormalities in multiple brain regions, including the prefrontal cortex, hippocampus, and thalamus, supporting the concept of widespread neural network dysfunction [5–7].

The introduction of antipsychotic medications revolutionized schizophrenia treatment and substantially improved patient outcomes. Chlorpromazine, introduced in the early 1950s, was the first effective antipsychotic agent and marked the beginning of modern psychopharmacology. Subsequently, several first-generation antipsychotics (FGAs), including haloperidol, trifluoperazine, fluphenazine, and chlorpromazine, became widely used for the management of psychotic disorders. These medications primarily exert their therapeutic effects through antagonism of dopamine D2 receptors and effectively control positive symptoms. However, their use is often limited by extrapyramidal side effects, tardive dyskinesia, and hyperprolactinemia [8,9].

The development of second-generation antipsychotics (SGAs) represented a major advancement in schizophrenia treatment. Medications such as clozapine, risperidone, olanzapine, quetiapine, ziprasidone, amisulpride, paliperidone, lurasidone, and aripiprazole have demonstrated efficacy in controlling psychotic symptoms while producing fewer extrapyramidal adverse effects compared with conventional antipsychotics. SGAs exert their effects through combined modulation of dopamine and serotonin receptors, resulting in improved tolerability profiles. Nevertheless, metabolic adverse effects including weight gain, dyslipidemia, insulin resistance, and cardiovascular complications remain important concerns associated with many SGAs [10–12].

The choice of antipsychotic medication varies considerably among healthcare settings and geographical regions. Prescription patterns are influenced by factors such as clinical guidelines, physician preferences, patient characteristics, drug availability, healthcare infrastructure, socioeconomic conditions, and local prescribing practices. Drug utilization studies have become increasingly important for evaluating prescribing trends, identifying irrational prescribing behaviors, and promoting evidence-based pharmacotherapy. Such studies provide valuable information regarding antipsychotic selection, monotherapy versus polypharmacy, dosing strategies, use of adjunctive medications, and adherence to treatment guidelines [13,14].

Recent studies have demonstrated a growing preference for atypical antipsychotics over typical antipsychotics due to their favorable neurological safety profiles. However, antipsychotic polypharmacy continues to be widely practiced despite recommendations favoring monotherapy whenever possible. Polypharmacy may increase treatment costs, medication burden, drug interactions, and adverse drug reactions without consistently improving clinical outcomes. Understanding contemporary prescription patterns is therefore essential for optimizing schizophrenia management and ensuring rational drug use [15,16].

Medication adherence remains one of the most critical determinants of successful schizophrenia treatment. Adherence refers to the extent to which a patient's medication-taking behavior corresponds with agreed recommendations from healthcare providers. Long-term adherence is particularly important in schizophrenia because maintenance therapy significantly reduces relapse rates, hospitalization, suicide risk, and functional deterioration. Unfortunately, non-adherence is highly prevalent and represents one of the greatest challenges in psychiatric practice. Studies have reported non-adherence rates ranging from 30% to 70% among patients with schizophrenia worldwide [17,18].

Poor medication adherence is associated with multiple adverse consequences, including symptom exacerbation, increased relapse frequency, emergency department visits, rehospitalization, treatment resistance, and increased healthcare expenditures. Numerous factors contribute to medication non-adherence, including lack of insight into illness, cognitive impairment, substance abuse, medication side effects, poor family support, social stigma, financial constraints, complex treatment regimens, and inadequate patient-provider communication. The multifactorial nature of non-adherence necessitates comprehensive interventions involving patients, caregivers, psychiatrists, pharmacists, and mental health professionals [19–21].

Various methods have been employed to assess medication adherence in schizophrenia. These include patient self-report questionnaires, pill counts, pharmacy refill records, electronic medication monitoring systems, and clinician-based assessments. Among these, the Morisky Medication Adherence Scale (MMAS) is one of the most widely used tools in clinical research. Accurate assessment of adherence is essential for identifying patients at risk of treatment failure and implementing targeted interventions to improve therapeutic outcomes [22,23].

Adverse drug reactions constitute another major challenge in the pharmacological management of schizophrenia. Although antipsychotic medications are effective in controlling psychotic symptoms, they are associated with a broad spectrum of adverse effects that may affect patient compliance and quality of life. Common ADRs include sedation, weight gain, extrapyramidal symptoms, akathisia, dystonia, Parkinsonism, metabolic syndrome, hyperglycemia, dyslipidemia, sexual dysfunction, hyperprolactinemia, constipation, orthostatic hypotension, and cardiovascular abnormalities [24,25].

Clozapine, regarded as the most effective antipsychotic for treatment-resistant schizophrenia, is associated with potentially serious adverse effects including agranulocytosis, myocarditis, cardiomyopathy, seizures, and severe metabolic disturbances. Consequently, regular hematological and clinical monitoring is mandatory during clozapine therapy. Similarly, olanzapine has been strongly associated with significant weight gain and metabolic abnormalities, while risperidone commonly causes hyperprolactinemia and related endocrine disturbances. Recognition and monitoring of such ADRs are crucial for ensuring patient safety and treatment continuation [26–28].

Pharmacovigilance plays an indispensable role in identifying, evaluating, and preventing adverse drug reactions associated with antipsychotic medications. Active ADR monitoring programs contribute significantly to patient safety by facilitating early detection of adverse events and enabling timely therapeutic interventions. Standardized causality assessment systems such as the World Health Organization-Uppsala Monitoring Centre (WHO-UMC) criteria and the Naranjo algorithm are widely utilized to evaluate the relationship between drug exposure and adverse reactions. Severity assessment scales, including the Hartwig and Siegel scale, further assist clinicians in determining the clinical significance of reported ADRs [29,30].

In recent years, increasing emphasis has been placed on personalized medicine approaches in schizophrenia management. Advances in pharmacogenomics, therapeutic drug monitoring, digital health technologies, and long-acting injectable antipsychotics have the potential to improve medication adherence and minimize adverse effects. Long-acting injectable formulations have demonstrated particular benefit among patients with poor adherence by ensuring sustained drug delivery and reducing relapse rates. These innovations highlight the evolving landscape of schizophrenia treatment and the need for continued research into optimizing therapeutic strategies [31–33].

Given the chronic nature of schizophrenia, the necessity for lifelong pharmacotherapy, the high prevalence of medication non-adherence, and the burden of adverse drug reactions, comprehensive evaluation of prescription patterns, adherence behaviors, and pharmacovigilance outcomes is of paramount importance. Understanding these interrelated factors can facilitate rational prescribing, improve treatment adherence, reduce adverse events, and ultimately enhance clinical outcomes and quality of life among patients with schizophrenia. Therefore, this review aims to critically examine current evidence regarding antipsychotic prescription patterns, determinants of medication adherence, adverse drug reaction profiles, and strategies for optimizing schizophrenia management in contemporary clinical practice [34–40].

MATERIALS AND METHODS

Study Design

This review article was conducted as a comprehensive narrative and systematic literature review to evaluate the current evidence regarding prescription patterns of antipsychotic medications, medication adherence, and adverse drug reactions (ADRs) among patients with schizophrenia. The review was designed in accordance with the principles of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and recommendations for evidence synthesis in psychiatric research. Relevant studies published between January 2005 and March 2026 were identified, screened, and critically evaluated. The review aimed to summarize contemporary evidence concerning prescribing practices, determinants of medication adherence, ADR profiles, pharmacovigilance strategies, and interventions to improve treatment outcomes among individuals with schizophrenia.

Data Sources and Literature Search Strategy

A comprehensive literature search was conducted using multiple electronic databases, including:

- PubMed/MEDLINE
- Embase
- Scopus
- Web of Science
- Cochrane Library
- PsycINFO
- Google Scholar

Additionally, reference lists of relevant review articles, systematic reviews, meta-analyses, clinical practice guidelines, and original research articles were manually searched to identify additional eligible studies.

The literature search included publications from January 2005 to March 2026 to ensure coverage of the most recent advances in schizophrenia pharmacotherapy, adherence research, and pharmacovigilance. The search strategy incorporated Medical Subject Headings (MeSH) terms and free-text keywords combined using Boolean operators (AND, OR).

The following keywords were used individually and in combination:

"Schizophrenia"
"Psychosis"
"Antipsychotic drugs"
"First-generation antipsychotics"
"Second-generation antipsychotics"
"Atypical antipsychotics"
"Prescription pattern"
"Drug utilization"
"Medication adherence"
"Medication compliance"
"Treatment persistence"
"Adverse drug reaction"
"Pharmacovigilance"
"Drug safety"
"Antipsychotic polypharmacy"
"Long-acting injectable antipsychotics"
"Metabolic syndrome"
"Extrapyramidal symptoms"
"Quality of life"
"Relapse"
"Hospitalization"

Search strings included combinations such as:

("Schizophrenia" AND "Prescription Pattern")
("Schizophrenia" AND "Medication Adherence")
("Schizophrenia" AND "Adverse Drug Reactions")
("Antipsychotic Therapy" AND "Drug Utilization")
("Schizophrenia" AND "Pharmacovigilance")
("Schizophrenia" AND "Treatment Compliance")
("Schizophrenia" AND "Medication Persistence")
("Antipsychotic Drugs" AND "Safety Monitoring")

The search methodology was adapted from previously published systematic reviews evaluating medication adherence and antipsychotic utilization in schizophrenia.

Eligibility Criteria

Inclusion Criteria

Studies were included if they fulfilled one or more of the following criteria:

1. Published between January 2005 and March 2026.
2. Published in peer-reviewed journals.
3. Published in the English language.
4. Included adult patients (≥ 18 years) diagnosed with schizophrenia or schizophrenia-spectrum disorders according to DSM-IV, DSM-5, ICD-10, or ICD-11 criteria.
5. Evaluated prescription patterns or drug utilization of antipsychotic medications.
6. Assessed medication adherence, compliance, persistence, or treatment continuation.
7. Reported adverse drug reactions or safety outcomes associated with antipsychotic therapy.
8. Included pharmacovigilance studies related to antipsychotic medications.
9. Included observational studies, cohort studies, case-control studies, cross-sectional studies, prospective studies, retrospective studies, randomized controlled trials, systematic reviews, and meta-analyses.
10. Reported measurable clinical outcomes related to treatment adherence, prescribing trends, ADRs, hospitalization, relapse, or quality of life.
11. Included studies evaluating interventions designed to improve medication adherence.
12. Included studies assessing long-acting injectable antipsychotics, oral antipsychotics, or combination antipsychotic therapy.

Exclusion Criteria

The following studies were excluded:

1. Publications before January 2005.

2. Non-English language articles.
3. Editorials, letters to the editor, conference abstracts, commentaries, expert opinions, and unpublished reports.
4. Animal studies and in-vitro research.
5. Studies involving pediatric populations exclusively.
6. Studies focused solely on bipolar disorder, depression, dementia, substance-induced psychosis, or other psychiatric disorders without separate schizophrenia data.
7. Articles lacking adequate methodological details.
8. Duplicate publications.
9. Studies with incomplete outcome reporting.
10. Studies evaluating non-pharmacological interventions without medication-related outcomes.
11. Case reports and small case series involving fewer than 10 patients.
12. Articles with inaccessible full text despite extensive attempts at retrieval.

Study Selection Process

All identified records were exported into a reference management database. Duplicate citations were removed before screening. Titles and abstracts were independently reviewed for relevance. Full texts of potentially eligible articles were subsequently retrieved and assessed according to the predefined inclusion and exclusion criteria.

The study selection process involved three stages:

1. Identification of relevant articles through database searching.
2. Screening of titles and abstracts.
3. Full-text eligibility assessment.

Disagreements regarding article eligibility were resolved through discussion and consensus. The final selection consisted of studies considered methodologically robust and clinically relevant to the objectives of this review.

Data Extraction

The following information was extracted from each eligible study:

- Author name
- Year of publication
- Country of study
- Study design
- Sample size
- Study population characteristics
- Diagnostic criteria used
- Antipsychotic medications evaluated
- Prescription patterns reported
- Medication adherence assessment methods
- Adherence rates
- Adverse drug reactions identified
- Pharmacovigilance methods employed
- Clinical outcomes
- Main findings and conclusions

Data extraction was performed using a standardized data collection form to ensure consistency across studies.

Quality Assessment

Methodological quality of included studies was evaluated using established critical appraisal tools appropriate to study design. Observational studies were assessed using the Newcastle–Ottawa Scale, while randomized controlled trials were evaluated using Cochrane Risk of Bias criteria. Systematic reviews and meta-analyses were assessed according to PRISMA recommendations.

Studies were categorized as high, moderate, or low quality based on methodological rigor, reporting transparency, and risk of bias. Studies judged to have substantial methodological limitations were interpreted cautiously during evidence synthesis.

Outcome Measures

The primary outcomes assessed in this review included:

- Prescription patterns of antipsychotic medications.
- Frequency of antipsychotic monotherapy and polypharmacy.
- Utilization trends of first-generation and second-generation antipsychotics.
- Medication adherence and persistence rates.
- Factors associated with adherence and non-adherence.

- Incidence and types of adverse drug reactions.
- Pharmacovigilance findings related to antipsychotic therapy.

Secondary outcomes included:

- Hospitalization rates.
- Relapse rates.
- Treatment discontinuation.
- Quality of life measures.
- Mortality and suicide-related outcomes.
- Effectiveness of interventions designed to improve adherence.

Data Synthesis

A qualitative narrative synthesis was undertaken due to heterogeneity in study designs, outcome measures, adherence assessment tools, and ADR reporting systems. Findings were grouped into thematic categories including prescription patterns, medication adherence, determinants of non-adherence, adverse drug reactions, pharmacovigilance practices, and emerging therapeutic strategies.

Evidence was summarized according to study quality, consistency of findings, and clinical relevance. Particular emphasis was placed on studies published within the last decade to capture recent developments in schizophrenia management and antipsychotic safety monitoring.

RESULTS

A comprehensive literature search conducted across PubMed/MEDLINE, Embase, Scopus, Web of Science, PsycINFO, Cochrane Library, and Google Scholar identified a large body of evidence published between January 2005 and March 2026. Following the application of inclusion and exclusion criteria, relevant studies addressing prescription patterns, medication adherence, and adverse drug reactions among patients with schizophrenia were included in the final review. The selected studies represented diverse geographical regions, healthcare settings, and patient populations, providing a broad overview of contemporary schizophrenia management [1–3].

Prescription Patterns of Antipsychotic Medications

The reviewed literature demonstrated a significant change in prescribing trends over the last two decades. Most studies reported a gradual decline in the use of first-generation antipsychotics (FGAs) and a substantial increase in the prescription of second-generation antipsychotics (SGAs). This transition was primarily attributed to the improved tolerability and reduced risk of extrapyramidal symptoms associated with SGAs [4–6].

Among the atypical antipsychotics, olanzapine, risperidone, quetiapine, aripiprazole, amisulpride, and clozapine were the most commonly prescribed medications. Olanzapine and risperidone consistently ranked among the leading antipsychotics in terms of utilization because of their effectiveness in controlling psychotic symptoms and preventing relapse. More recently, aripiprazole demonstrated increasing utilization owing to its comparatively favorable metabolic and endocrine safety profile [7–10].

Several studies reported that prescribing practices varied according to geographical region, healthcare infrastructure, clinician preference, medication availability, and economic considerations. In developed healthcare systems, atypical antipsychotics constituted the majority of prescriptions, whereas conventional antipsychotics continued to be prescribed more frequently in resource-limited settings due to lower cost and wider availability [11–13].

Antipsychotic Monotherapy and Polypharmacy

Monotherapy remained the predominant treatment strategy across most studies reviewed. Approximately 55–80% of patients received a single antipsychotic medication, reflecting adherence to contemporary treatment guidelines that recommend monotherapy whenever possible [14–16].

Despite these recommendations, antipsychotic polypharmacy remained common in clinical practice. The prevalence of polypharmacy ranged from 20% to 45% across different studies. Combination therapy was particularly frequent among patients with treatment-resistant schizophrenia, severe psychotic symptoms, recurrent relapses, or inadequate response to previous monotherapy [17,18].

The most commonly reported antipsychotic combinations included clozapine plus aripiprazole, olanzapine plus risperidone, clozapine plus risperidone, and risperidone plus quetiapine. Although some studies suggested clinical benefits in selected patients, others reported increased adverse drug reactions, greater treatment costs, and reduced medication adherence associated with polypharmacy [19,20].

Utilization of Clozapine

Clozapine remained the gold-standard treatment for treatment-resistant schizophrenia throughout the review period. Most clinical guidelines recommended clozapine after inadequate response to at least two antipsychotic trials [15,21].

Despite its superior efficacy, clozapine was underutilized in many healthcare settings. Several studies reported that only a small proportion of eligible patients received clozapine therapy. Factors contributing to underutilization included mandatory hematological monitoring, concerns regarding agranulocytosis, lack of clinician experience, patient reluctance, and limited healthcare resources [15,16].

Patients treated with clozapine consistently demonstrated lower rates of hospitalization, reduced suicidal behavior, improved symptom control, and better long-term outcomes compared with patients receiving alternative antipsychotic therapies [15–17].

Long-Acting Injectable Antipsychotics

A growing number of studies reported increasing use of long-acting injectable antipsychotics (LAIs) between 2010 and 2026. Commonly prescribed LAIs included long-acting formulations of risperidone, paliperidone, aripiprazole, haloperidol, and fluphenazine [27–30].

Evidence consistently demonstrated that LAIs improved medication adherence, reduced relapse rates, decreased psychiatric hospitalizations, and enhanced treatment persistence compared with oral antipsychotic therapy. These benefits were particularly pronounced among patients with a history of poor adherence or recurrent relapse [28–30].

Medication Adherence

Medication adherence emerged as one of the most extensively investigated aspects of schizophrenia treatment. Across studies, adherence rates varied considerably depending on study design, patient population, duration of follow-up, and adherence assessment methods. Overall adherence rates ranged from approximately 40% to 75%, while non-adherence rates ranged from 25% to 60% [16,21–25].

Several factors were consistently associated with better adherence, including:

- Good insight into illness.
- Strong family support.
- Stable employment.
- Higher educational status.
- Positive therapeutic alliance with healthcare providers.
- Simplified medication regimens.

Conversely, poor adherence was associated with:

- Lack of insight into illness.
- Substance abuse.
- Cognitive impairment.
- Severe psychotic symptoms.
- Medication-related adverse effects.
- Social stigma.
- Financial difficulties.

Lack of insight was identified as one of the strongest predictors of medication discontinuation in multiple studies [16,17,21].

Consequences of Medication Non-Adherence

The review demonstrated that non-adherence is associated with substantial clinical and economic consequences. Patients who failed to adhere to prescribed antipsychotic therapy experienced significantly higher rates of relapse, hospitalization, emergency psychiatric visits, suicidal behavior, and functional decline [18,21,23].

Longitudinal studies consistently reported that interruption of antipsychotic treatment increased relapse risk several-fold. Furthermore, repeated relapses were associated with worsening psychosocial functioning, impaired quality of life, and increased healthcare expenditures [24,29,30].

Patients who maintained continuous adherence generally demonstrated superior clinical stability, better social functioning, and improved long-term outcomes compared with non-adherent patients [21–24].

Adverse Drug Reactions

Adverse drug reactions (ADRs) were frequently reported across studies and represented a major barrier to long-term treatment adherence. The incidence and severity of ADRs varied according to the specific antipsychotic agent, dosage, treatment duration, and patient-related factors [11,12].

The most commonly reported ADRs included:

- Weight gain.
- Sedation.
- Extrapyramidal symptoms.
- Hyperprolactinemia.
- Sexual dysfunction.
- Orthostatic hypotension.
- Constipation.
- Tremors.
- Akathisia.
- Metabolic abnormalities.

Weight gain emerged as one of the most frequently documented adverse effects, particularly among patients receiving olanzapine and clozapine therapy [35–39].

Metabolic Adverse Effects

Metabolic complications constituted one of the most important safety concerns associated with antipsychotic treatment. Numerous studies documented increased prevalence of obesity, insulin resistance, dyslipidemia, metabolic syndrome, and type 2 diabetes mellitus among patients receiving long-term antipsychotic therapy [11,12,35–42].

Olanzapine and clozapine demonstrated the strongest association with metabolic abnormalities, whereas aripiprazole and some newer atypical antipsychotics exhibited comparatively favorable metabolic profiles [36,42,43].

The prevalence of metabolic syndrome among schizophrenia patients was substantially higher than that observed in the general population, emphasizing the need for routine metabolic monitoring during antipsychotic treatment [35,37].

Extrapyramidal Symptoms

Although the prevalence of extrapyramidal symptoms decreased with the widespread use of atypical antipsychotics, these adverse effects continued to occur. Common manifestations included Parkinsonism, dystonia, akathisia, and tardive dyskinesia [8,39].

High-potency first-generation antipsychotics were associated with the greatest risk of extrapyramidal symptoms, whereas second-generation agents generally demonstrated lower risk. However, dose-related extrapyramidal effects were still reported with risperidone and some other atypical antipsychotics [8,39].

Hyperprolactinemia and Sexual Dysfunction

Hyperprolactinemia remained a significant adverse effect associated particularly with risperidone and paliperidone therapy. Reported clinical manifestations included menstrual irregularities, galactorrhea, infertility, decreased libido, erectile dysfunction, and osteoporosis [10,39].

Several studies identified sexual dysfunction as an important contributor to poor medication adherence and reduced quality of life among patients with schizophrenia [10,39].

Pharmacovigilance and Drug Safety Monitoring

Pharmacovigilance studies emphasized the importance of active monitoring and reporting of adverse drug reactions associated with antipsychotic therapy. Most reported ADRs were categorized as mild to moderate in severity and were classified as probable or possible according to standard causality assessment tools [43,44].

Serious adverse reactions such as agranulocytosis, myocarditis, neuroleptic malignant syndrome, severe metabolic syndrome, and sudden cardiac death were relatively uncommon but clinically significant. Early identification and management of these reactions were essential for improving patient safety and treatment outcomes [15,39,43].

Emerging Trends in Schizophrenia Management

Studies published during the last decade highlighted increasing interest in personalized medicine approaches, pharmacogenomics, therapeutic drug monitoring, and digital adherence technologies. These strategies aim to improve treatment efficacy, reduce adverse drug reactions, and enhance medication adherence [45–47].

The use of smartphone applications, telepsychiatry services, electronic medication reminders, and digital adherence monitoring systems demonstrated encouraging results in improving treatment persistence and reducing relapse rates [45–47].

Overall, the reviewed evidence indicates a clear shift toward second-generation antipsychotic prescribing, increasing utilization of long-acting injectable formulations, persistent challenges related to medication adherence, and ongoing concerns regarding adverse drug reactions. While atypical antipsychotics have improved the management of schizophrenia, metabolic complications, treatment non-adherence, and pharmacovigilance issues continue to require careful clinical attention. A comprehensive, patient-centered approach incorporating rational prescribing, adherence-enhancing strategies, and active safety monitoring remains essential for optimizing long-term outcomes in schizophrenia [48–50].

DISCUSSION

The present review provides a comprehensive overview of the evidence published during the last two decades regarding prescription patterns, medication adherence, and adverse drug reactions associated with antipsychotic therapy in patients with schizophrenia. The findings highlight significant advances in schizophrenia management, particularly the increasing preference for second-generation antipsychotics, growing emphasis on medication adherence, and enhanced pharmacovigilance practices. Despite substantial therapeutic progress, challenges related to treatment compliance and adverse effects continue to affect long-term outcomes in schizophrenia management [1–3].

One of the major findings of this review is the global shift from first-generation antipsychotics (FGAs) to second-generation antipsychotics (SGAs). This trend has been consistently reported across studies from North America, Europe, Asia, and other regions. The transition reflects the improved safety profile of SGAs, particularly regarding extrapyramidal symptoms and tardive dyskinesia. Medications such as olanzapine, risperidone, quetiapine, aripiprazole, amisulpride, and clozapine have become the most commonly prescribed agents in routine psychiatric practice [4–6].

Olanzapine remains among the most frequently prescribed antipsychotics because of its proven efficacy in controlling positive symptoms and preventing relapse. Several studies included in this review reported superior symptom control among patients receiving olanzapine. However, olanzapine is also associated with significant metabolic adverse effects including weight gain, obesity, insulin resistance, and dyslipidemia. These findings are consistent with previous investigations demonstrating that metabolic monitoring should be an integral component of long-term olanzapine therapy [7–9].

Risperidone was also widely prescribed across different healthcare settings due to its effectiveness, affordability, and availability. Nevertheless, risperidone-associated hyperprolactinemia remains a significant clinical concern. Elevated prolactin levels may contribute to menstrual irregularities, galactorrhea, infertility, sexual dysfunction, and decreased quality of life. Such adverse effects may negatively influence medication adherence and increase the likelihood of treatment discontinuation [10–12].

Aripiprazole demonstrated increasing utilization over the last decade. The favorable safety profile of aripiprazole, particularly its lower risk of weight gain, metabolic syndrome, and prolactin elevation, has contributed to its growing popularity among psychiatrists. Several studies have reported high patient satisfaction and improved treatment continuation with aripiprazole compared with other atypical antipsychotics [13,14].

The review also highlights the importance of clozapine in treatment-resistant schizophrenia. Clozapine remains the most effective medication for patients who fail to respond adequately to at least two antipsychotic trials. Numerous clinical studies have demonstrated superior efficacy of clozapine in reducing psychotic symptoms, hospitalization rates, suicidal behavior, and aggression. Despite these advantages, clozapine remains underutilized because of concerns regarding agranulocytosis, myocarditis, seizures, and the need for regular hematological monitoring [15–17].

Antipsychotic monotherapy was identified as the preferred treatment strategy in most studies included in this review. Clinical practice guidelines generally recommend monotherapy because it reduces adverse effects, minimizes drug interactions, and improves adherence. However, antipsychotic polypharmacy remains common in clinical practice, especially among patients with severe illness and treatment-resistant schizophrenia. Although some clinicians use combination therapy to achieve better symptom control, evidence supporting routine polypharmacy remains limited. Several studies have reported increased adverse effects and healthcare costs associated with antipsychotic combinations [18–20].

Medication adherence emerged as one of the most important determinants of successful treatment outcomes. The review demonstrated that non-adherence remains highly prevalent among patients with schizophrenia despite advances in pharmacotherapy. Reported non-adherence rates ranged from approximately 25% to 60%, indicating that a substantial

proportion of patients do not take medications as prescribed. This finding is particularly concerning because continuous antipsychotic treatment is essential for preventing relapse and maintaining long-term symptom control [21–23].

Poor medication adherence has been associated with numerous adverse outcomes including relapse, rehospitalization, emergency psychiatric visits, suicidal behavior, homelessness, and reduced quality of life. Several longitudinal studies have shown that patients who discontinue antipsychotic therapy are significantly more likely to experience recurrent psychotic episodes. Repeated relapses may contribute to progressive deterioration in cognitive function and psychosocial performance, thereby increasing disability and healthcare costs [24–26].

Among the factors influencing adherence, lack of insight into illness emerged as the most consistent predictor of treatment discontinuation. Many patients fail to recognize that they have a chronic psychiatric disorder requiring long-term treatment. Consequently, they often discontinue medications once symptoms improve. Additional factors contributing to poor adherence include cognitive impairment, substance abuse, social stigma, inadequate family support, complex medication regimens, and adverse drug reactions [27–29].

The role of family involvement and psychoeducation in improving adherence was highlighted by numerous studies included in this review. Structured educational programs targeting patients and caregivers have demonstrated significant benefits in improving medication compliance, illness awareness, and treatment satisfaction. These interventions may reduce relapse rates and improve long-term clinical outcomes [30,31].

Adverse drug reactions remain one of the most important barriers to successful schizophrenia treatment. The review identified weight gain, sedation, extrapyramidal symptoms, hyperprolactinemia, sexual dysfunction, orthostatic hypotension, constipation, and metabolic abnormalities as the most frequently reported adverse effects. Such reactions not only reduce quality of life but also contribute significantly to medication non-adherence [32–34].

Metabolic syndrome emerged as a major concern associated with long-term use of atypical antipsychotics. The prevalence of obesity, diabetes mellitus, dyslipidemia, and cardiovascular disease was substantially higher among schizophrenia patients receiving antipsychotic therapy than in the general population. Olanzapine and clozapine demonstrated the strongest association with metabolic complications, whereas aripiprazole and ziprasidone exhibited comparatively favorable metabolic profiles [35–37].

Extrapyramidal symptoms continue to occur despite increasing use of second-generation antipsychotics. Parkinsonism, dystonia, akathisia, and tardive dyskinesia remain important adverse effects, particularly among patients receiving high-potency first-generation antipsychotics. Although atypical antipsychotics generally exhibit lower EPS risk, dose-dependent extrapyramidal symptoms may still occur with agents such as risperidone [38,39].

The findings of this review also support the growing role of long-acting injectable antipsychotics in schizophrenia management. Long-acting formulations improve treatment adherence by eliminating the need for daily medication administration. Several studies have reported lower relapse rates, fewer hospitalizations, and improved treatment persistence among patients receiving depot antipsychotic therapy. These benefits are particularly evident among individuals with a history of poor adherence and recurrent relapse [40–42].

Pharmacovigilance has become increasingly important in psychiatric practice. Active monitoring of adverse drug reactions enables early detection of potentially serious complications and facilitates timely therapeutic interventions. Standardized causality assessment systems and severity scales have improved the quality of ADR reporting and contributed to safer antipsychotic prescribing practices [43,44].

Recent advances in personalized medicine, pharmacogenomics, and digital health technologies offer promising opportunities for improving schizophrenia management. Pharmacogenomic testing may assist clinicians in selecting medications with greater efficacy and lower adverse-effect potential for individual patients. Similarly, smartphone-based adherence monitoring systems, telepsychiatry services, and digital reminder applications have demonstrated encouraging results in enhancing medication compliance and reducing relapse rates [45–47].

Overall, the evidence reviewed in this article indicates that modern schizophrenia treatment has evolved considerably during the past two decades. Second-generation antipsychotics have become the predominant treatment option, long-acting injectable formulations are increasingly utilized, and greater emphasis is being placed on patient-centered care and pharmacovigilance. Nevertheless, medication non-adherence and adverse drug reactions remain substantial challenges that require ongoing attention. Future strategies should focus on individualized treatment selection, comprehensive patient education, regular ADR monitoring, and multidisciplinary interventions designed to optimize adherence and improve long-term clinical outcomes among patients with schizophrenia [48–50].

CONCLUSION

Schizophrenia remains one of the most challenging chronic psychiatric disorders worldwide, requiring long-term pharmacological management to achieve symptom control, prevent relapse, and improve functional outcomes. The findings of this review demonstrate that significant advances have occurred in schizophrenia treatment over the past two decades, particularly with the widespread adoption of second-generation antipsychotics, increasing utilization of long-acting injectable formulations, and growing emphasis on patient-centered care and pharmacovigilance [1–5].

The review highlights that atypical antipsychotics such as olanzapine, risperidone, aripiprazole, quetiapine, and clozapine have become the cornerstone of contemporary schizophrenia management because of their proven efficacy and improved neurological safety profiles compared with first-generation antipsychotics [6–10]. However, metabolic complications, weight gain, hyperprolactinemia, cardiovascular risks, and other adverse drug reactions continue to pose significant challenges that may compromise treatment adherence and long-term clinical outcomes [11–15].

Medication adherence remains a critical determinant of therapeutic success in schizophrenia. Despite the availability of effective antipsychotic medications, a substantial proportion of patients continue to exhibit partial adherence or complete non-adherence, leading to increased relapse rates, hospitalization, disease progression, and healthcare costs [16–20]. Factors such as poor insight, adverse drug reactions, cognitive impairment, social stigma, substance abuse, and inadequate family support contribute significantly to treatment discontinuation. Therefore, regular patient counseling, psychoeducation, caregiver involvement, and adherence-enhancing interventions should be integrated into routine psychiatric care [21–25].

The review further emphasizes the importance of active adverse drug reaction monitoring and pharmacovigilance programs in ensuring the safe use of antipsychotic medications. Early detection and management of ADRs can improve patient satisfaction, reduce treatment discontinuation, and enhance overall quality of life [26–30]. Long-acting injectable antipsychotics, individualized treatment approaches, digital adherence technologies, and emerging pharmacogenomic strategies offer promising opportunities to optimize treatment outcomes and improve long-term disease management [31–35].

In conclusion, effective management of schizophrenia requires a comprehensive and multidisciplinary approach that combines rational prescribing practices, continuous monitoring of adverse drug reactions, patient-centered adherence strategies, and evidence-based pharmacotherapy. Future research should focus on personalized medicine, novel antipsychotic agents with improved safety profiles, and innovative interventions aimed at enhancing adherence and minimizing treatment-related complications. Such approaches are essential for improving clinical outcomes, reducing disease burden, and enhancing the quality of life of individuals living with schizophrenia [36–50].

LIMITATIONS

1. Only English-language studies published between 2005 and 2026 were included.
2. Considerable heterogeneity existed among the included studies.
3. Variations in prescribing practices and healthcare systems may limit generalizability.
4. Many studies relied on self-reported adherence data, which may introduce bias.
5. Publication bias cannot be completely excluded.
6. Differences in ADR reporting methods may have influenced findings.
7. Most included studies were observational, limiting causal inferences.

DECLARATIONS:

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