

Understanding Antipsychotic Polypharmacy in Real-World Practice

Medication adherence, adverse events, cognition, and resource utilization under antipsychotic polypharmacy in schizophrenia

ANTIPSYCHOTIC POLYPHARMACY IN REAL-WORLD PRACTICE^{1,2}

Antipsychotic polypharmacy:
the concurrent use of ≥ 2 antipsychotics¹⁻³

10%-40%

of patients with schizophrenia receive antipsychotic polypharmacy in contemporary real-world and registry studies, despite guidelines noting that evidence supporting combined antipsychotic treatment remains inconsistent.¹⁻⁵

Antipsychotic polypharmacy may occur more frequently in patients with complex clinical presentations, including but not limited to:

- › greater illness severity
- › repeated relapse
- › aggression

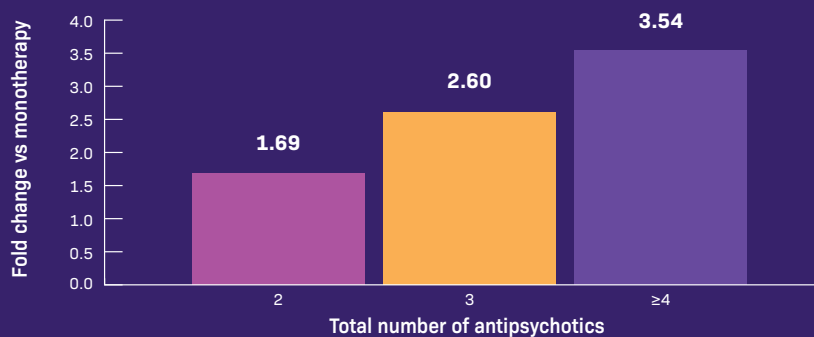
High-quality evidence from randomized controlled trials showing clear benefits of antipsychotic polypharmacy compared with single-agent treatment is lacking.^{1,4}

ANTIPSYCHOTIC POLYPHARMACY AND MEDICATION ADHERENCE^{1,6}

Medication nonadherence occurs in up to 60% of people with schizophrenia.^{7,8}

In the study at right, complete nonadherence was more than double among patients on antipsychotic polypharmacy (13.4%) compared with those on monotherapy (5.6%).⁹

In a therapeutic drug monitoring study of blood samples from 24,239 patients, each additional antipsychotic added to a regimen was associated with an increased risk of nonadherence compared with monotherapy:^{9*}



*Therapeutic drug monitoring analysis of blood samples from patients treated with oral antipsychotics between 2005 and 2017 in Norway. Nonadherence was defined as at least one undetectable serum concentration of the prescribed antipsychotic.⁹

ANTIPSYCHOTIC POLYPHARMACY AND ADVERSE EVENTS^{1,6}

Observational studies show that antipsychotic polypharmacy is associated with higher total daily antipsychotic doses compared with monotherapy.^{1,4}

Exposure to multiple medications may be linked to:^{1,6}



Metabolic abnormalities



Drug-drug interactions



Anticholinergic burden



Sedation/somnolence



Extrapyramidal symptoms



Cognitive impairment

Recent receptor occupancy modeling data suggest that when two antipsychotics with similar receptor targets are combined at usual doses, their effects are additive, and may result in total receptor occupancy above the therapeutic window.^{1,10}

THE IMPACT OF ANTIPSYCHOTIC POLYPHARMACY ON COGNITIVE FUNCTION^{1,11}

Higher relative antipsychotic exposure and anticholinergic burden may be associated with reduced cognitive function in people with schizophrenia, as shown by reductions in several cognitive domains, including:^{11*}

- › Brief Assessment of Cognition in Schizophrenia total score
- › Verbal memory
- › Working memory
- › Motor speed
- › Attention and speed of information processing

*Based on retrospective study results. These results must be interpreted carefully, and causality between medication and cognitive performance cannot be established.¹¹

ANTIPSYCHOTIC POLYPHARMACY AND RESOURCE UTILIZATION^{1,12}

A systematic review of 81 US observational studies published between January 1, 2008, and June 1, 2018, showed that patients receiving antipsychotic polypharmacy incurred higher annual medical costs.¹²

\$24,045–\$29,344

Mean total annual cost associated with adding an additional antipsychotic medication, driven largely by medication expenditure:¹²

Inpatient costs*	Outpatient costs	Medication costs
\$1,932–\$2,172	\$2,173–\$2,610	\$8,615–\$12,523

*Inpatient costs reflect the sum of acute hospital and psychiatric hospital costs for antipsychotic augmentation.¹²

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