

Cochrane for Clinicians

Putting Evidence into Practice

Schizophrenia: Use of Antipsychotic Drugs for Maintenance Therapy

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Clinical Question

Does maintenance therapy with antipsychotic drugs prevent symptom relapse in patients with schizophrenia?

Evidence-Based Answer

Compared with placebo, using antipsychotic drugs for maintenance therapy in patients with schizophrenia is associated with relapse prevention at seven to 12 months (number needed to treat [NNT] = 3; 95% CI, 2 to 3). (Strength of Recommendation [SOR]: A, based on consistent, good-quality patient-oriented evidence.) Hospitalizations are less likely among individuals receiving maintenance therapy with antipsychotics (NNT = 8; 95% CI, 6 to 14). (SOR: A, based on consistent, good-quality patient-oriented evidence.) People taking antipsychotic drugs are more likely to experience adverse effects, including movement disorders (number needed to harm [NNH] = 20; 95% CI, 14 to 50) and weight gain (NNH = 25; 95% CI, 20 to 50).¹ (SOR: A, based on consistent, good-quality patient-oriented evidence.)

Practice Pointers

Schizophrenia is the most common psychotic disease, with an estimated prevalence of 0.25% to 0.64% in the U.S. population.² Given the limited access to psychiatrists in many parts of the country, family physicians are often called on to screen,

diagnose, and treat a variety of psychiatric conditions, including schizophrenia.^{3,4} In particular, family physicians may be in a position to counsel patients and families on the benefits and risks of continuing antipsychotic medications for the treatment of schizophrenia. This Cochrane review aimed to answer questions about whether maintaining antipsychotic therapy prevented relapse of schizophrenia symptoms, reduced hospitalizations, improved quality of life and social functioning, or was associated with adverse effects.

The Cochrane review included 75 randomized controlled trials involving 9,145 patients with schizophrenia or schizophrenia-like illness and compared those taking antipsychotic medications with those taking placebo.¹ The included trials were published between 1959 and 2017.

The primary outcome was whether antipsychotic drugs were effective at preventing relapse of psychotic symptoms among individuals with schizophrenia or schizophrenia-like illness. The meta-analysis found that these medications were effective at preventing symptom relapse at seven to 12 months (NNT = 3; 95% CI, 2 to 3). Individuals receiving antipsychotic drugs were also less likely to be hospitalized compared with those taking placebo (NNT = 8; 95% CI, 6 to 14).

Quality of life and social functioning may be better for patients receiving antipsychotics, based on low- and moderate-certainty evidence, respectively. No statistically significant differences were identified between groups for likelihood of employment or death from suicide.

Individuals receiving antipsychotic drugs were more likely to experience movement disorders (NNH = 20; 95% CI, 14 to 50) and weight gain (NNH = 25; 95% CI, 20 to 50). In both cases, the rate of adverse effects associated with the antipsychotic medication increased over time, with no statistically significant differences identified during the first three months of treatment. There was a trend toward increased sedation among those treated with antipsychotics vs. placebo, but the difference was not statistically significant.

A practice guideline from the American Psychiatric Association recommends that patients with schizophrenia whose symptoms have

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CME This clinical content conforms to AAFP criteria for CME. See CME Quiz on page 338.

improved with antipsychotic use continue treatment. It also states that when antipsychotic drugs are administered on a long-term basis, adverse effects such as movement disorders and weight gain are common. For this reason, the American Psychiatric Association recommends preventive interventions such as early intervention for weight gain and regular screening for lipid and glucose abnormalities. Similarly, patients should be monitoring for movement disorders, with a continual discussion around benefits and adverse effects associated with the medications in the context of shared medical decision-making.⁴

The practice recommendations in this activity are available at <http://www.cochrane.org/CD008016>.

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References

1. Ceraso A, Lin JJ, Schneider-Thoma J, et al. Maintenance treatment with antipsychotic drugs for schizophrenia. *Cochrane Database Syst Rev*. 2020;(8):CD008016.
2. National Institute of Mental Health. Schizophrenia. Accessed December 14, 2020. <https://www.nimh.nih.gov/health/statistics/schizophrenia.shtml>
3. National Council Medical Director Institute. The psychiatric shortage: causes and solutions. March 28, 2017. Accessed December 14, 2020. https://www.thenationalcouncil.org/wp-content/uploads/2017/03/Psychiatric-Shortage_National-Council-.pdf?dof=375ateTbd56
4. Keepers GA, Fochtmann LJ, Anzia JM, et al. *The American Psychiatric Association Practice Guideline for the Treatment of Patients with Schizophrenia*. 3rd ed. Published online September 2020. Accessed February 20, 2021. <https://psychiatryonline.org/doi/pdf/10.1176/appi.books.9780890424841>

Interventions to Improve Use of CPAP Machines in Adults with Obstructive Sleep Apnea

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Clinical Question

Are educational, supportive, behavioral, or mixed intervention strategies effective at increasing compliance with continuous positive airway

pressure (CPAP) in patients with obstructive sleep apnea (OSA)?

Evidence-Based Answer

Behavioral interventions increase CPAP use (mean difference [MD] = 1.31 hours per night; 95% CI, 0.95 to 1.66) compared with usual care. These interventions also increase CPAP adherence, measured by participants using their machine four or more hours per night, from 371 to 501 per 1,000 patients (number needed to treat [NNT] = 8; 95% CI, 5 to 23). Supportive interventions may slightly increase CPAP use (MD = 0.70 hours per night; 95% CI, 0.36 to 1.05) vs. usual care, and they increase CPAP adherence from 601 to 717 per 1,000 patients (NNT = 9; 95% CI, 5 to 56). The benefits of educational and mixed interventions are unclear because of low-quality evidence.¹ (Strength of Recommendation: A, based on consistent, good-quality patient-oriented evidence.)

Practice Pointers

OSA causes sleep fragmentation and can lead to excessive daytime sleepiness, mood changes, and impairments in cognition, memory, and driving competence. OSA increases the risk of cardiovascular, cerebrovascular, and metabolic morbidity.² CPAP is first-line treatment for OSA, and consistent use can improve sleep quality and associated symptoms.³ A large systematic review and meta-analysis showed that CPAP had no effect on cardiovascular outcomes in patients with OSA; however, in most randomized controlled trials, patients used CPAP less than four hours per night.⁴ The effectiveness of CPAP on OSA symptoms directly correlates to duration of compliance, with more than four hours of adherence to therapy demonstrating improvements in sleep quality, daytime sleepiness, fatigue, and depressive symptoms.⁵

This Cochrane review included 41 studies with 9,005 participants.¹ It evaluated the effectiveness of educational, supportive, behavioral, and mixed interventions on CPAP compliance compared with usual care, which was defined as providing background information and general instructions for CPAP use.¹ Most participants were CPAP naive. Educational interventions aimed to improve patient knowledge and understanding of OSA in general or CPAP treatment specifically and were delivered in various formats (written, group, video, in-person). Supportive

interventions used automated feedback from the CPAP machine that triggered a clinician intervention or scheduled a follow-up visit to encourage CPAP use. Behavioral interventions included motivational enhancement therapy, social cognitive theory, transtheoretical/stages of change model, and cognitive behavior therapy to improve compliance. Mixed interventions were any combination of the previous interventions. The authors used total CPAP hours per night and total number of participants who used the machine four or more hours per night to measure CPAP compliance. Patient-oriented outcomes of daytime sleepiness and quality of life could not

be evaluated because of inconsistency in measurement among studies.

Based on high-certainty evidence, behavioral interventions demonstrated a significant benefit (MD = 1.31 more hours per night of CPAP use compared with usual care; 95% CI, 0.95 to 1.66). They also increased the number of participants adhering to therapy, assessed by using their machine for four or more hours per night, from 371 to 501 per 1,000 (NNT = 8; 95% CI, 5 to 23). Patients using behavioral interventions were less likely to withdraw from therapy based on a decrease in study withdrawals from 146 to 101 per 1,000 (NNT = 22; 95% CI, 13 to 33).

SUMMARY TABLE

Comparison of Various Interventions plus CPAP vs. Usual Care plus CPAP

Outcomes	Anticipated absolute effects* (95% CI)			Participants (RCTs)	Quality of evidence
	Risk with usual care plus CPAP	Risk with intervention plus CPAP	NNT* (95% CI)		
Educational interventions					
Device use	Mean of 1.97 to 5.1 hours per night	MD = 0.85 hours per night (0.32 to 1.39)	—	1,128 (10)	Very low
N deemed adherent (≥ 4 hours per night)	558 per 1,000	765 per 1,000 (654 to 849)	5 (3 to 10)	1,019 (7)	Very low
Supportive interventions					
Device use	Mean of 1.75 to 4.9 hours per night	MD = 0.70 hours per night (0.36 to 1.05)	—	1,426 (13)	Moderate
N deemed adherent (≥ 4 hours per night)	601 per 1,000	717 per 1,000 (619 to 797)	9 (5 to 56)	376 (2)	Low
Behavioral interventions					
Device use	Mean of 1.48 to 5.1 hours per night	MD = 1.31 hours per night (0.95 to 1.66)	—	578 (8)	High
N deemed adherent (≥ 4 hours per night)	371 per 1,000	501 per 1,000 (414 to 587)	8 (5 to 23)	549 (6)	High
Withdrawal	146 per 1,000	101 per 1,000 (70 to 143)	22 (13 to 33)	939 (10)	High
Mixed interventions					
Device use	Mean of 2.6 to 5.5 hours per night	MD = 0.82 hours per night (0.20 to 1.43)	—	4,509 (11)	Very low
N deemed adherent (≥ 4 hours per night)	741 per 1,000	830 per 1,000 (755 to 886)	11 (7 to 71)	4,015 (9)	Very low
Withdrawal	129 per 1,000	83 per 1,000 (40 to 161)	—	4,956 (11)	Very low

CPAP = continuous positive airway pressure; MD = mean difference; NNT = number needed to treat; RCT = randomized controlled trial.

*—The risk in the intervention group (and its 95% CI) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95% CI).

Supportive interventions increased CPAP use (MD = 0.70 hours per night; 95% CI, 0.36 to 1.05) and increased adherence to therapy from 601 to 717 per 1,000 participants (NNT = 9; 95% CI, 5 to 56) compared with usual care, although these results were based on moderate- and low-certainty evidence, respectively. The benefits of educational and mixed interventions to improve CPAP compliance were uncertain due to low-quality evidence.

This Cochrane review supports the use of behavioral interventions to improve CPAP compliance. Although the studies used various behavioral intervention techniques, the key concept is to engage or interact with the patient in some way. The American Academy of Sleep Medicine strongly recommends educational interventions and conditionally recommends behavioral and troubleshooting (similar to supportive) interventions.³ The Department of Veterans Affairs/Department of Defense clinical practice guideline also includes recommendations for educational, behavioral, and supportive interventions to improve adherence to CPAP therapy in patients with OSA.⁶ Both guidelines recommend using these interventions during the initiation phase of CPAP therapy.^{3,6}

The practice recommendations in this activity are available at <http://www.cochrane.org/CD007736>.

Editor's Note: The NNTs and CIs reported in this Cochrane for Clinicians were calculated by the authors based on raw data provided in the original Cochrane review.

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References

1. Askland K, Wright L, Wozniak DR, et al. Educational, supportive and behavioural interventions to improve usage of continuous positive airway pressure machines in adults with obstructive sleep apnoea. *Cochrane Database Syst Rev.* 2020;(4):CD007736.
2. Kapur VK, Auckley DH, Chowdhuri S, et al. Clinical practice guideline for diagnostic testing for adult obstructive sleep apnea: an American Academy of Sleep Medicine clinical practice guideline. *J Clin Sleep Med.* 2017;13(3):479-504.
3. Patil SP, Ayappa IA, Caples SM, et al. Treatment of adult obstructive sleep apnea with positive airway pressure: an American Academy of Sleep Medicine clinical practice guideline. *J Clin Sleep Med.* 2019;15(2):335-343.
4. Yu J, Zhou Z, McEvoy RD, et al. Association of positive airway pressure with cardiovascular events and death in adults with sleep apnea: a systematic review and meta-analysis. *JAMA.* 2017;318(2):156-166.
5. Wang Y, Ai L, Luo J, et al. Effect of adherence on daytime sleepiness, fatigue, depression and sleep quality in the obstructive sleep apnea/hypopnea syndrome patients undertaking nasal continuous positive airway pressure therapy. *Patient Prefer Adherence.* 2017;11:769-779.
6. The Management of Chronic Insomnia Disorder and Obstructive Sleep Apnea Work Group; Department of Veterans Affairs; Department of Defense. VA/DoD clinical practice guideline for the management of chronic insomnia disorder and obstructive sleep apnea. 2019;1-152. Accessed July 20, 2020. <https://www.healthquality.va.gov/guidelines/CD/insomnia/VADoDSleepCPGFinal508.pdf> ■