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Use of antipsychotics in adults with dementia

New study identifies a wider range of associated harm

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The linked study by Mok and colleagues (doi:10.1136/bmj-2023-076268) provides new insights into the risks associated with use of antipsychotics in dementia care.[1] This population based matched cohort design compared the incidence of serious adverse outcomes, including stroke, venous thromboembolism, myocardial infarction, heart failure, fracture, pneumonia, and acute kidney injury, in adults (≥50 years) with dementia who were prescribed antipsychotics versus those who did not use antipsychotics.

Using data from the Clinical Practice Research Datalink (CPRD) database in England, the study included 35 339 adults with dementia who had just been prescribed antipsychotics for the first time, within a broader population of 173 910 adults with dementia. The authors found significantly increased risks for nearly all evaluated adverse outcomes in antipsychotic users, with especially steep increases for pneumonia (hazard ratio 2.19, 95% confidence interval 2.10 to 2.28), acute kidney injury (1.72, 1.61 to 1.84), stroke (1.61, 1.52 to 1.71), and venous thromboembolism (1.62, 1.46 to 1.80) within the first 90 days after a prescription.

Mok and colleagues' research expands the number and type of documented risks associated with antipsychotics in the management of dementia. Their study discovered that risks extend beyond stroke and mortality to include a wider range of serious adverse health outcomes. Risks were found to be highest shortly after treatment initiation, underscoring the need for increased caution in the early stages of treatment. By distinguishing between typical and atypical antipsychotic agents and detailing drug specific risks, the findings of this study will equip healthcare professionals with more nuanced data to help guide personalized treatment decisions.

The authors acknowledge that information on indications for antipsychotic treatment was unavailable. This study limitation is important because understanding the specific indications for antipsychotic treatment (eg, for behavioral and psychological symptoms of dementia, or for other reasons) could provide deeper insights into the study's findings, particularly about the risk-benefit balance of antipsychotic use in adults with dementia.

The authors minimized the risk of confounding using propensity score methods to adjust for observable characteristics that might influence the initiation of antipsychotic treatment. However, they also confirmed that unlike randomized controlled trials, which can account for both observed and unobserved differences between treatment groups, their study could only adjust for observed differences—acknowledging a limitation inherent to all observational research: the inability to fully account for all potential confounding factors.

Widely used

Antipsychotics are widely used to manage behavioral and psychological symptoms of dementia despite well documented and substantial risks of harm (including higher mortality).[2-4] International guidelines advise restricting use to adults with severe behavioral and psychological symptoms of dementia,[5,6] but the rate of prescribing has risen in recent years, most notably during the covid-19 pandemic as a result of increased distress caused by loneliness, social isolation measures, and reduced access to alternative treatments.[7]

Mok and colleagues highlight the need for careful justification of antipsychotic use in dementia care, including a comprehensive assessment of the benefits weighed against a broader range of serious harms than previously acknowledged. Duration of treatment should be minimized, the need for treatment should be regularly reassessed, non-drug options should be explored first, and guidelines should be updated to reflect the wider spectrum of risks associated with antipsychotics.

Perhaps the biggest challenge to reducing use of these drugs is the relative scarcity of effective non-drug alternatives. One review found only a few interventions—including cognitive stimulation, selected behavior management therapies, and specific types of education for caregivers and residential care staff—to have some evidence of any lasting effectiveness.[8] Their implementation, too, often required substantial resources, such as highly trained staff with adequate time and specialized equipment, and the drugs were usually ineffective for patients with severe symptoms.

Using antipsychotics for the management of dementia related behaviors requires nuanced decision making after careful assessment, informed by a personalized approach.[9] Mok and colleagues call for a critical re-evaluation of antipsychotic use in this clinical setting. Their study clearly identified a broader spectrum of adverse effects than previously acknowledged, and it advocates for a comprehensive review of risks and benefits, prioritization of non-drug strategies, and exploration of alternative therapies. Increased priority on more patient centric care, tailored care plans, regular reassessment of management options, and a move away from the overprescription of antipsychotics is overdue.

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1 Mok PLH, Carr MJ, Guthrie B, etal. Multiple adverse outcomes associated with antipsychotic use in people with dementia: population based matched cohort study. *BMJ* 2024;385:e076268.

2 Steinberg M, Lyketsos CG. Atypical antipsychotic use in patients with dementia: managing safety concerns. *Am J Psychiatry* 2012;169:-6. doi: 10.1176/appi.ajp.2012.12030342 pmid: 22952071

3 Reus VI, Fochtmann LJ, Eyler AE, etal. The American Psychiatric Association Practice Guideline on the Use of Antipsychotics to Treat Agitation or Psychosis in Patients With Dementia. *Am J Psychiatry* 2016;173:-6. doi: 10.1176/appi.ajp.2015.173501 pmid: 27133416

4 Kheirbek RE, Fokar A, Little JT, etal. Association Between Antipsychotics and All-Cause Mortality Among Community-Dwelling Older Adults. *J Gerontol A Biol Sci Med Sci* 2019;74:-21. doi: 10.1093/gerona/glz045 pmid: 30753301

5 NICE. Dementia: Assessment, management and support for people living with dementia and their carers. NICE guideline [NG97]. 2018. https://www.nice.org.uk/guidance/ng97

6 Rabins PV, Blacker D, Rovner BW, etalAPA Work Group on Alzheimer's Disease and other DementiasSteering Committee on Practice Guidelines. American Psychiatric Association practice guideline for the treatment of patients with Alzheimer's disease and other dementias. Second edition. *Am J Psychiatry* 2007;164(Suppl):-56.pmid: 18340692

7 Luo H, Lau WCY, Chai Y, etal. Rates of Antipsychotic Drug Prescribing Among People Living With Dementia During the COVID-19 Pandemic. *JAMA Psychiatry* 2023;80:-9. doi: 10.1001/jamapsychiatry.2022.4448 pmid: 36696128

8 Kales HC, Gitlin LN, Lyketsos CG. Assessment and management of behavioral and psychological symptoms of dementia. *BMJ* 2015;350:. doi: 10.1136/bmj.h369 pmid: 25731881

9 Treloar A, Crugel M, Prasanna A, etal. Ethical dilemmas: should antipsychotics ever be prescribed for people with dementia? *Br J Psychiatry* 2010;197:-90. doi: 10.1192/bjp.bp.109.076307 pmid: 20679257