

# Prescription and Nonprescription Anticholinergic Medication Linked to Increased Risk of Dementia

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## Abstract

A brief overview of a study published in JAMA Internal Medicine entitled: Cumulative Use of Strong Anticholinergic Medications and Incident Dementia.

**Keywords:** Dementia; Alzheimer's dementia; OTC; Anticholinergic medication; Cough medication; Cold medication

## Study

Recently, JAMA Internal Medicine, a peer-reviewed journal by the American Medical Association, published a study on the topic of common anticholinergic medications and the risk they attribute to the development of incident dementia and Alzheimer's dementia. The study design was a prospective population-based cohort study with the objective to examine whether the cumulative use of anticholinergic medication posed a higher risk for the development of dementia. Participants in the study were 3,434 adults who were 65 years of age or older without dementia when they entered the study pool. The recruitment of participants occurred over a number of years with replacement of those participants who died during the investigational period. In the study all participants were followed up every two years and data for the study was collected through September 20, 2012 [1]. Participants were followed and cumulative exposure to anticholinergic medications was tracked using pharmacy dispensing data. For purposes of the study, prescription and nonprescription anticholinergic medication use was examined for the previous ten years with the most recent twelve months being excluded to avoid use due to prodromal symptoms [1]. Drug dispensing data that was followed included drug name, strength, route, dose, and date dispensed [1]. To judge exposure to medications a standard daily dose (SDD) was calculated based on the minimum effective dose recommended for use in elderly adults and the amount dispensed for each prescription that was filled by a participant [1]. The SDD was then used to calculate a cumulative standard daily dose (TSDD) that compensated for varying effects and strengths of different anticholinergic medications, over time, so that the overall burden of these medications could be followed [1]. Exposure was broken into periods: no use, 1-90 days, 91-356 days, 366-1095 days, and greater than 1095 days (3 years) [1]. The most common drugs taken by participants in the study were tricyclic antidepressants, first-generation antihistamines, and antimuscarinics. As an example: a person would reach the highest level of exposure if they took a first-generation antihistamine such as Benadryl, daily, for more than three years. Results of the study were adjusted for individual demographics, health status and behaviors, as well as comorbidities.

## Results and Discussion

The results of the study showed a direct correlation between cumulative use of anticholinergic medications and development of dementia [1]. The most common drugs, of the three most offending classes, taken by participants in the study were doxepin, chlorpheniramine, and oxybutynin [1]. Of the participants in the study,

797, which represent 23% of the total, developed dementia. Further, 637 of those who developed dementia developed Alzheimer's type dementia [1]. This is the first study of its kind to show a dose related correlation, as the study indicated a 10-year positive dose-response relationship between cumulative anticholinergic use and dementia<sup>1</sup>. Participants in the highest class of exposure (> 3 years), with the highest TSDD, had a significantly increased risk for developing dementia (1.54, 1.21-1.96) or Alzheimer's dementia (1.63, 1.21-1.96) and participants in the second highest risk category had only slightly lower risk of developing dementia.

Concerning the results of the study Science Daily, an online resource reporting on new research topics, quoted the lead author of the study Dr. Shelly Grey: "Older adults should be aware that many medications - including some available without a prescription, such as over-the-counter sleep aids - have strong anticholinergic effects and should tell their health care providers about all their over-the-counter use" [2]. Dr. Grey is a professor, vice chair of curriculum and instruction, and director of the Geriatric Pharmacy Program for the University of Washington. On how physicians can help to alter the future of this scenario of anticholinergic induced dementia, Grey responded: "Providers should regularly review their patients drug regimen", and "If providers need to prescribe a medication with anticholinergic effects because it is the best therapy, they should use the lowest effective dose and stop therapy if it is ineffective" [2].

The results of this study are not altogether surprising as other studies have previously implicated anticholinergic medications in the development of dementia. In one 2014 study, Kalisch et al. [3] concluded, that use of anticholinergic medication is associated with greater risk of hospitalization for confusion and dementia.

Due to the nature of these findings, is important for physicians to complete a few tasks related to geriatric anticholinergic prescribing, or prescribing in general for that matter:

1. Ask patients about non-prescription medication use in addition

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to normal prescription medications and any other dietary or nutritional supplements.

2. Educate patients on benefits and side effects of all medications and supplements.
3. Prescribe the lowest possible dose effective for a given condition.
4. Discontinue any medications causing undesired side effects in favor of suitable medications.
5. Monitor geriatric patients requiring anticholinergic medication regimens at each visit for signs and symptoms of developing dementia.

The bottom line is that the study has shown that anticholinergic

medications across the board, whether prescription or nonprescription, are implicated in the development of dementia with a trend toward Alzheimer's dementia if used chronically. Finally, the medical community, in general, should be aware of these findings and implement steps to reduce the number of patients who will develop dementia solely from increased anticholinergic medication load.

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