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## Comment on : Decrease of anticholinergic drug use in nursing home residents in the United States

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2021-07

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Aalto , U L , Kautiainen , H & Pitkälä , K H 2021 , ' Comment on : Decrease of anticholinergic drug use in nursing home residents in the United States ' , Journal of the American Geriatrics Society , vol. 69 , no. 7 , pp. 2033-2035 . <https://doi.org/10.1111/jgs.17182>

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<http://hdl.handle.net/10138/353340>

<https://doi.org/10.1111/jgs.17182>

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1 **Comment on:** Decrease of Anticholinergic Drug Use in Nursing Home Residents in the United  
2 States, 2009 to 2017

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4 **Changes in the use of anticholinergic drugs depend on the criteria**

5 *To the Editor:* We read the article by Malagaris and colleagues<sup>1</sup> with great interest. They showed a  
6 significant decrease in prescriptions of drugs with high anticholinergic potential defined by the  
7 Anticholinergic Cognitive Burden (ACB) scale<sup>2</sup> in nursing home (NH) residents over time. In our  
8 previous study, we observed a stable or even an increasing trend in anticholinergic drug use defined  
9 by the Anticholinergic Risk Scale (ARS)<sup>3</sup> in a Finnish long-term care population from 2003 to  
10 2017.<sup>4</sup> Due to the well-known differences between the various anticholinergic criteria, we wanted to  
11 further explore whether using the ACB scale<sup>2</sup> would affect our results in this population and what  
12 might be the reasons behind the different temporal pattern.

#### 13 **Methods**

14 Data from our previous study were used.<sup>4</sup> Altogether 4297 residents in NHs (years 2003, 2011, and  
15 2017) and 4565 residents in assisted living facilities (ALFs) (years 2007, 2011, and 2017) in  
16 Helsinki participated. Residents' medication was a point prevalence on the data collection date. The  
17 use of drugs with high anticholinergic potential was identified by the ACB scale<sup>2</sup> and further  
18 categorized according to their therapeutic class as suggested.<sup>1</sup>

19 The unadjusted hypothesis of linearity was tested using the Cochran–Armitage test or analysis of  
20 variance with an appropriate contrast. The adjusted hypothesis of linearity (orthogonal polynomial)  
21 was evaluated using generalized link models (e.g., analysis of covariance and logistic models) with  
22 appropriate distribution and link function. Models included age, sex, Charlson Comorbidity Index<sup>5</sup>,  
23 and mobility as covariates.

## 24 **Results**

25 In all cohorts, most of the residents were female and the mean age was around 84 years. A dementia  
26 diagnosis and dependency in mobility became more prevalent over time. There was no significant  
27 trend in the proportion of users of anticholinergic drugs in NHs from 2003 to 2017, but in ALFs an  
28 increasing trend was observed from 2007 to 2017. Antipsychotics and antidepressants were the  
29 most prevalent drug classes with high anticholinergic burden. The proportion of users of ACB  
30 antipsychotics increased in both facilities over the years. In contrast, the use of ACB antidepressants  
31 practically disappeared in both NHs and ALFs, and the same pattern was observed in the use of  
32 urinary antispasmodics and hydroxyzine. (Table 1)

## 33 **Discussion**

34 The use of drugs with high anticholinergic potential according to the ACB remained stable or even  
35 increased over the years. This happened even though many ACB drugs are no longer available in  
36 Finland. Furthermore, there was a significant increase in the antipsychotic use, which is worrisome  
37 considering that the residents commonly had cognitive impairment. Our results markedly differed  
38 from those of Malagaris and colleagues, as they found an overall decreasing trend in anticholinergic  
39 prescriptions irrespective of therapeutic class. The recently published UK study among older people  
40 showed a significant increase in the prevalence of anticholinergic drugs over 20 years.<sup>6</sup>

41 Our study investigating the prevalence of anticholinergic drug use is not directly comparable with  
42 the study of Malagaris and colleagues focusing on the prescription rates. However, some points of  
43 discussion may be raised. The various anticholinergic criteria define anticholinergic drugs and their  
44 anticholinergic potential differently, resulting in varying prevalence rates and predicted outcomes.<sup>7-9</sup>

45 Even one single commonly used drug may have a significant effect on the anticholinergic use  
46 observed, as we showed in our previous study in which the increased use of mirtazapine was mainly  
47 responsible for the overall increasing trend in antidepressant use over the years.<sup>4</sup> The ACB scale

48 does not include mirtazapine in drugs with high anticholinergic potential, which likely explains the  
49 low and even decreasing prevalence of antidepressant use in our present study. The increase in  
50 dementia diagnoses and possible related neuropsychiatric symptoms in the latter cohorts is likely to,  
51 at least partly, be the explanation behind the increasing prevalence of antipsychotics, despite  
52 guidelines advising non-pharmacological treatment. Furthermore, unlike several other criteria<sup>9</sup>,  
53 quetiapine is defined as high anticholinergic according to the ACB scale. Quetiapine explains most  
54 of the increase in the use of antipsychotics. Old neuroleptics have practically disappeared from the  
55 drug lists of our latest cohorts.

56 Even a moderate anticholinergic burden has been shown to have an association with poor outcomes  
57 in older, cognitively frail people.<sup>10</sup> By excluding drugs with lower anticholinergic potential and  
58 measuring exclusively the use of high potential drugs, the results might appear to be an  
59 underestimation of the true anticholinergic burden.

60 Despite extensive research on anticholinergic drugs, so far there is a lack of clear evidence  
61 regarding which anticholinergic scale would be optimal and how to best recognize the most  
62 deleterious anticholinergic drug use or burden as regards the clinical outcomes.

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73 **Conflicts of interest:** The authors (UA, HK, KP) report no conflicts of interest.

74 **Author contributions:** Study concept and design, analysis and interpretation of data (UA, HK,  
75 KP), preparation and revising of manuscript (UA, KP), final approval (UA, HK, KP).

76 **Sponsor's role:** None.

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116 Table 1. Characteristics of residents in nursing homes (in 2003, 2011, and 2017) and assisted living  
 117 facilities (in 2007, 2011, and 2017).

| Characteristics of residents  | Nursing home  |               |              | P for trend         | Assisted living facility |               |               | P for trend         |
|---|---------------|---------------|--------------|---------------------|--------------------------|---------------|---------------|---------------------|
|   | 2003 (n=1979) | 2011 (n=1568) | 2017 (n=750) |                     | 2007 (n=1336)            | 2011 (n=1556) | 2017 (n=1673) |                     |
| Females, n (%)  | 1597(81)      | 1209(77)      | 580(77)      | 0.013               | 1041(78)                 | 1217(78)      | 1210(72)      | <0.001              |
| Mean age, years (SD)  | 84(8)         | 85(8)         | 84(8)        | 0.34                | 83(7)                    | 84(7)         | 84(8)         | 0.006               |
| Dementia, n (%)   | 1374(69)      | 1188(77)      | 581(78)      | <0.001              | 798(60)                  | 1090(70)      | 1302(78)      | <0.001              |
| Bed- or wheelchair-bound, n (%)                                       | 598(30)       | 947(60)       | 427(57)      | <0.001              | 195(15)                  | 446(29)       | 508(30)       | <0.001              |
| Mean CCI (SD)   | 2.1 (1.2)     | 2.4(1.5)      | 2.1(1.3)     | 0.39                | 2.1(1.4)                 | 2.4(1.5)      | 2.0(1.3)      | 0.001               |
| Mean number of regularly used drugs (SD)                              | 7.9(3.5)      | 7.3(3.3)      | 8.3(3.3)     | 0.94                | 8.3(3.5)                 | 8.8(3.8)      | 9.0(3.7)      | <0.001              |
| Users of anticholinergic drugs <sup>b</sup> , n (%)                   | 501(25)       | 277(18)       | 156(21)      | 0.17 <sup>a</sup>   | 247(18)                  | 330(21)       | 344(21)       | 0.010 <sup>a</sup>  |
| Users of antipsychotics <sup>b</sup> , n (%)                          | 240(12)       | 245(16)       | 151(20)      | <0.001 <sup>a</sup> | 161(12)                  | 288(19)       | 331(20)       | <0.001 <sup>a</sup> |
| Users of antidepressants <sup>b</sup> , n (%)                         | 96(5)         | 13(1)         | 2(0)         | <0.001 <sup>a</sup> | 36(3)                    | 15(1)         | 11(1)         | 0.004 <sup>a</sup>  |
| Users of gastrointestinal drugs or antiemetics <sup>b,c</sup> , n (%) | 17(1)         | 0(0)          | 0(0)         | *                   | 0(0)                     | 1(0)          | 0(0)          | *                   |
| Users of anti-Parkinson drugs <sup>b</sup> , n (%)                    | 7(0)          | 0(0)          | 0(0)         | *                   | 0 (0)                    | 0 (0)         | 0 (0)         | *                   |
| Users of urinary antispasmodics <sup>b</sup> , n (%)                  | 60(3)         | 2(0)          | 0(0)         | *                   | 31(2)                    | 10(1)         | 0(0)          | *                   |
| Users of hydroxyzine, n (%)   | 142(7)        | 26(2)         | 4(1)         | <0.001 <sup>a</sup> | 30(2)                    | 26(2)         | 6(0)          | <0.001 <sup>a</sup> |

118 Data are expressed as n (%) unless otherwise specified.

119 CCI = Charlson Comorbidity Index<sup>5</sup>; SD = standard deviation



120 \* Not applicable; <sup>a</sup> adjusted for age, sex, dementia diagnosis, and mobility; <sup>b</sup> high (score 3) anticholinergic  
121 drugs defined by the Anticholinergic Cognitive Burden (ACB) scale<sup>2</sup>; <sup>c</sup> including scopolamine, hyoscyamine,  
122 or promazine  
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