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Original Study

# Use of Medications of Questionable Benefit During the Last Year of Life of Older Adults With Dementia

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## ABSTRACT

*Objectives:* To investigate the prevalence and factors associated with the use of medications of questionable benefit throughout the final year of life of older adults who died with dementia.
*Design:* Register-based, longitudinal cohort study.
*Setting:* Entire Sweden.
*Participants:* All older adults (≥75 years) who died with dementia between 2007 and 2013 (n = 120,067).
*Measurements:* Exposure to medications of questionable benefit was calculated for each of the last 12 months before death, based on longitudinal data from the Swedish Prescribed Drug Register.
*Results:* The proportion of older adults with dementia who received at least 1 medication of questionable benefit decreased from 38.6% 12 months before death to 34.7% during the final month before death ($P < .001$ for trend). Among older adults with dementia who used at least 1 medication of questionable benefit 12 months before death, 74.8% remained exposed until their last month of life. Living in an institution was independently associated with a 15% reduction of the likelihood to receive ≥1 medication of questionable benefit during the last month before death (odds ratio 0.85, 95% confidence interval 0.88–0.83). Antidementia drugs accounted for one-fifth of the total number of medications of questionable benefit. Lipid-lowering agents were used by 8.3% of individuals during their final month of life (10.2% of community-dwellers and 6.6% of institutionalized people, $P < .001$).
*Conclusion:* Clinicians caring for older adults with advanced dementia should be provided with reliable tools to help them reduce the burden of medications of questionable benefit near the end of life.

Medications are part of the daily care provided to people with dementia, from diagnosis to the end of life. In a context of limited life expectancy, as dementia progresses and leads to ever-greater impairments, it is recommended to reconsider the goals of care and to shift from disease-targeted therapies to a more palliative approach.[1] Good prescribing requires progressively reducing treatments aimed at prolonging survival and to focus on comfort care to manage burdensome symptoms, relieve psychological distress, and support caregivers.[2–4]

Several authors have pointed out the need to reconsider the appropriateness of medication use near the end of life.[1,5–7] Yet, previous studies suggest that many individuals with life-limiting illnesses are exposed to medications whose benefit in terms of comfort and quality of life is questionable.[8] In 2008, a consensus panel composed of experts in geriatrics and palliative medicine defined a list of medications deemed "never appropriate" for older adults with advanced dementia.[1] However, no study has investigated the use of these drugs across care settings. Thus, there is limited generalizability of findings to the overall population.

Using register-based, longitudinal data with national coverage in Sweden, we aimed to measure the prevalence of medications of questionable benefit over the course of the last 12 months of life of

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LM and DLV contributed equally.

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older adults with dementia, and to investigate the factors associated with the use of these medications.

## Methods

### Study Design and Data Sources

This was a nationwide cohort study of older adults with dementia who died in Sweden between January 1, 2007, and December 31, 2013. Death certificate data were obtained from the Swedish National Board of Health and Welfare and were linked at the individual level with several other registries with national coverage: the Swedish Prescribed Drugs Register, the Social Services Register, the National Patient Register, and the Education Register. The Regional Ethical Review Board in Stockholm, Sweden, approved the study (no. 2013/1941–31/3).

### Study Population

We included all deceased individuals aged ≥75 years at time of death who were either diagnosed with dementia (International Classification of Diseases, 10th revision codes F00, F01, F02, F03, F051, G30, and G311 reported in the National Patient Register during the final 2 years of life or mentioned as contributing cause of death) or prescribed antidementia drugs in the final 2 years of life (Anatomical Therapeutic Chemical [ATC] codes N06DA and N06DX01). A total of 131,337 individuals fulfilled these criteria. Among those, older adults with missing cause of death and decedents with no prescription data available over the course of the last 3 months before death were excluded from the study population ($n = 11,270$; 8.6%).

### Medications of Questionable Benefit

We examined the use of medications of questionable benefit, deemed as "never appropriate" for use in patients with advanced dementia and limited life expectancy.[1] This list of medications includes acetylcholinesterase inhibitors (N06DA), memantine (N06DX01), lipid-lowering agents (C10A), cytotoxic chemotherapy (L01D), hormone antagonists (L02B), antiplatelet agents excluding aspirin (B01AC), leukotriene inhibitors (R03DC), immunomodulators (L03-L04), and sex hormones (G03). Monthly drug exposure was estimated for each of the last 12 months of life based on data from the Swedish Prescribed Drug Register, using the dispensing date, the total amount dispensed to the patient and the daily doses indicated by the prescribers (Supplementary Figure 1).[9,10]

### Characteristics of the Deceased Individuals

Individual demographic characteristics were derived from the National Cause of Death Register: sex, age at time of death, and contributing causes of death. Living arrangement at time of death (community-dwelling or institutionalized) was defined based on data from the Social Services Register. Level of education was obtained from the Education Register and categorized into "primary," "secondary," and "tertiary" education according to the International Standard Classification of Education. Place of death was defined as "usual place of living" or "hospital," based on the comparison between the discharge date of the last hospitalization and the date of death. Chronic comorbidities were identified in the National Patient Register, the National Cause of Death Register, and the Swedish Prescribed Drugs Register, following the protocol suggested by Calderón-Larrañaga and colleages.[11]

### Statistical Analysis

We first calculated the number and proportion of individuals who received at least 1 medication of questionable benefit during each of the last 12 months before death. Results were stratified by living arrangement, age, and number of chronic comorbidities. In sensitivity analyses, individuals who died from conditions indicative of "sudden" death were excluded. Second, a logistic regression model was computed to examine the factors independently associated with the use of at least 1 medication of questionable benefit during the last month before death. Variables associated with the outcome in univariate analyses ($P < .01$) were included in the multivariable analysis, with statistical significance set at $P < .001$. To explore variations in the association between living arrangement and use of medications of questionable benefit, we stratified the regression model by sex, age, level of education, and number of chronic comorbidities while adjusting for the remaining covariates. Odds ratios (ORs) and their 95% confidence intervals (95% CIs) for institution versus community are reported in a forest plot. Analyses were performed with JMP 13.0.1 (SAS Institute, Cary, NC) and Stata 14.1 (Stata Corp, College Station, TX).

## Results

### Characteristics of the Study Population

A total of 120,067 older adults with dementia who died in Sweden between January 1, 2007, and December 31, 2013, were included in the study population. Among them, 50,804 (42.3%) were living in the community and 69,263 (57.7%) were institutionalized at time of death. As shown in Table 1, community-dwelling individuals died at a younger age than individuals living in institutions (mean difference = −1.12, 95% CI −1.19 to −1.06). They also died more often in hospitals (26.6% vs 14.4%, $P < .001$), and had a higher number of diagnosed comorbidities ($P < .001$).

### Use of Medications of Questionable Benefit Over Time

The overall proportion of older adults with dementia who received at least 1 medication of questionable benefit decreased from 38.6% 12 months before death to 34.7% during the final month before death ($P < .001$ for trend). We found significant variation in this trend according to the decedents' living arrangement, age, and number of chronic comorbidities (Figure 1). After excluding antidementia drugs from the analysis, the prevalence of medications of questionable benefit during the final month of life was 19.1% (Supplementary Figure 2). We found only marginal differences in the results when excluding individuals who died from conditions indicative of a sudden death (Supplementary Figure 3).

### Type of Medications of Questionable Benefit

Table 2 presents the frequency of the different medications of questionable benefit during the 12th, 6th, and final month before death. Use of antidementia drugs decreased from 21.8% 1 year before death to 20.0% during the final month of life ($P < .001$ for trend). However, although the prescription of acetylcholinesterase inhibitors decreased by 17.4% during that period (from 16.7% to 13.8% of all decedents), use of memantine increased by 15.2% (from 6.6% to 7.6%). During the final month of life, lipid-lowering agents were used by 8.3% of individuals (10.2% of community-dwelling individuals and 6.6% of institutionalized people, $P < .001$). The proportion of women receiving sex hormones (eg, estrogens) decreased only slightly, from 10.8% to 10.2% during the last 12 months before death. The other medications of questionable benefit remained stable throughout the last year of life (Supplementary Table 1).