New use of psychotropic medication after hospitalization among people with dementia

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Abstract

Objectives: Psychotropic medication is commonly used among people with dementia (PWD), but it shows modest efficacy and it has been associated with severe adverse events. Hospitalizations are an opportunity for medication management as well as treatment recommendations for outpatient physicians. The aim of this study was to assess factors associated with new use of psychotropic medication after hospitalization among PWD.

Methods: We conducted a retrospective dynamic cohort study from 2004 to 2015 using claims data from a German health insurance company. PWD were identified by an algorithm that included ICD-10 diagnosis and diagnostic measures. The medication classes included were antidepressants, antipsychotics, anxiolytics or hypnotics/sedatives, and Alzheimer’s medication. The assessment period was up to 30 days after discharge from the hospital across four hospitalizations.

Results: The main predictors for new use of psychotropic medication were similar across medication classes. Neuropsychiatric symptoms (NPS) and the need of care were associated with higher odds of new use of antidepressants, antipsychotics, and anxiolytics or hypnotics/sedatives. A hospital stay due to dementia was an independent predictor for new use across medication classes as well. Delirium increased the odds for new use of antipsychotics and anxiolytics or hypnotics/sedatives.

Conclusions: Factors associated with new use of psychotropic medication included delirium, NPS, and the need of care in PWD. The findings highlight the need for preventive interventions and non-medical treatment options in regards to delirium and NPS as well as for a more intensive use of screening tools for inappropriate medication use among PWD.

KEYWORDS
claims data, dementia, hospitalization, psychotropic medication

1 | INTRODUCTION

Psychotropic medications are often used to treat behavioral and neuropsychiatric problems among people with dementia (PWD). However, the use of psychotropic medication has a limited efficacy and can be accompanied by severe adverse events. Evidence suggests that using psychotropic medication is associated with a higher risk of mortality, falls and fractures, hospitalizations.
accumulation of hospital days,\textsuperscript{12} and deterioration.\textsuperscript{13,14} Consequently, lists of potentially inappropriate medication for older adults, such as the Beers criteria and the Screening Tool of Older Persons’ potentially inappropriate prescriptions/screening tool to alert to right treatment (STOPP/START) generally advice against prescription of these drugs for PWD, unless stringently indicated.\textsuperscript{15,16} Nevertheless, psychotropic medications are commonly prescribed among PWD in the community, nursing home, and during hospitalization.\textsuperscript{17-21}

Hospitalizations are common among PWD and can lead to an increase in prescribed medication,\textsuperscript{22-24} but hospital stays could also be regarded as an opportunity for an improved medication management. Since hospitalizations can also have an immediate impact on outpatient care and prescribing of medication, it is of utmost importance to understand which factors influence the prescription of psychotropic medications and to identify high-risk groups. This would contribute to developing appropriate measures to reduce the initiation of inappropriate prescribing of psychotropic medications.

In general, studies have shown that psychotropic medication use increases with care dependency,\textsuperscript{3} history of psychiatric diseases,\textsuperscript{25,26} and behavioral and psychological symptoms.\textsuperscript{2,3} Nevertheless, there is a lack of studies assessing risk factors for new use of psychotropic medication among PWD specifically after hospitalization. A recent study among hospitalized PWD focused on anticholinergic agents which include some of the psychotropic medications, and discovered that the presence of comorbid psychiatric conditions played a major role in prescribing.\textsuperscript{27} However, this study only focused on a single hospital stay and prevalent use of medication.

Hence the aim of this study was to comprehensively assess factors associated with new use of psychotropic medication after hospitalization across multiple hospital stays among PWD.

2 | METHODS

2.1 | Study Design

A retrospective dynamic cohort study was conducted based on claims data of a German health insurance plan from 2004 to 2015. The database itself consists of a statutory health insurance sample beginning in 1998 (18.75% random sample of all subjects insured by "Allgemeine Ortskrankenkasse [AOK] Hessen").\textsuperscript{28} Patient informed consent was not required by law as the study was based on pseudonymous data and the utilization of the database for research purposes was approved by the Ministry of Social Affairs of Hesse. Starting in 2006, cohort entry and cohort exit was possible in every year of the study period. Eligible for cohort entry were all members of the statutory health insurance aged \(\geq\)55 years during the study period with information on age and sex, and a continuous insurance period of at least 2 years prior to cohort entry. The baseline period started 2 years prior to cohort entry to assess pre-existing comorbidities and medication use. Reasons for cohort exit were limited to death, end of insurance period, or end of study period. End of insurance period which was very rare (1.9% of patients during the period of investigation) relates to participants switching to a different health insurance plan.

Key points

- The percentage of new users was 1.8%, 7.1%, 2.1%, and 2.5% across hospitalizations for antidepressants, antipsychotics, anxiolytics or hypnotics/sedatives, and Alzheimer’s medication, respectively.
- 83.0%, 61.9%, 56.9%, and 88.1% of new users received antidepressants, antipsychotics, anxiolytics or hypnotics/sedatives, and Alzheimer’s medication for more than 6 weeks.
- Delirium and neuropsychiatric symptoms were associated with significantly increased odds of new psychotropic medication use.
- Hospital stays due to dementia and the need of care were predictors for new use of psychotropic medication.

2.2 | Ascertainment of dementia, delirium and neuropsychiatric symptoms

A detailed description of the algorithm used to identify PWD has been previously provided elsewhere.\textsuperscript{29} In brief, dementia was defined as two confirmed outpatient diagnoses in the same or consecutive 3-month periods or one inpatient diagnosis. The application of at least one appropriate diagnostic measurement was required as well and included testing of cerebrospinal fluid, computed tomography scan and magnetic resonance imaging of the head, or positron-emission tomography of the brain. To determine the type of dementia all dementia diagnoses in the first year after cohort entry were considered. Since no specific ICD-10 code for mixed dementia exists, it was defined as the presence of Alzheimer’s disease (AD) and vascular dementia types according to ICD-10 coding. Repeat switching of specific dementia types or switching from a specific to an unspecified dementia type lead to an assignment to other/unknown dementia.

The following coded diagnoses of delirium and neuropsychiatric symptoms (NPS) (ICD-10 code) were assessed during hospitalization: delirium (F05), depression (F32, F33, F06.3) sleeping disorder (G47, F51), aberrant motor behavior (R25), agitation (R45.1, R46.3), hallucination (R44), acute psychotic state (F06.0-F06.2, F23), delusional disorder (F22), apathy (R45.3), anger (R45.4), violence (R45.6, F91), hostility (R45.5), anxiety (F41), and somnolence (R40.0). Since aberrant motor behavior has no specific ICD-10 code we used the mentioned ICD-10 code as a proxy.
2.3 | Dispensation of psychotropic medications

Outpatient dispensation of psychotropic medication was assessed using the anatomical therapeutic chemical classification system. Psychotropic medication was differentiated according to the following medication classes: antidepressants (N06A), antipsychotics (N05A), anxiolytics or hypnotics/sedatives (N05B, N05C), and Alzheimer’s medication (N06DA02-04, N06DX01). The exact date of the dispensation from the pharmacy was used to determine new use for each class of medication within 30 days after discharge from the hospital. New use for each psychotropic medication class was defined as the first dispensation of the medication. Hence, participants were eligible for new use when there was no dispensation during the baseline period or prior to the respective hospitalization. There was no information available on medications given to PWD by hospital physicians during the hospital stay. The duration of psychotropic medication prescribing was assessed by adding the package sizes in form of the DDD (eg, 100 DDDs last theoretically for 100 days) to the date of the initial dispensation from the pharmacy. New users were then grouped into short-term (< 6 weeks) and long-term (≥6 weeks) users.

2.4 | Statistical analysis

The associations between potential determinants with new use of each of the medication classes after hospitalization were analyzed using logistic regression models to compute odds ratios (OR) with corresponding 95% confidence interval (CI). The observation time began at the day of discharge from the hospital and ended 30 days after discharge, or on the day of the first dispensation of the analyzed medication, a new hospitalization or cohort exit (death or end of insurance period), whichever came first. First, the estimates were derived separately for up to four rounds of hospitalizations per participant after dementia diagnosis to explore possible trends, and second the association of possible predictors with new use of psychotropic medication after any of the four hospitalizations was estimated jointly to increase the power of the analyses. To account for clustering effects in the joint analyses, logistic regression models with a sandwich estimate using the covariance matrix were computed.\(^\text{20}\) In case the first dementia diagnosis was an inpatient diagnosis, this was considered the first hospitalization.

Potential determinants considered included age, sex, comorbidities present at baseline, delirium and NPS during hospitalization, main discharge diagnosis (reflects the main reason for the hospital stay as determined by the hospital physicians), year of hospitalization, type of dementia, time since cohort entry, and need of care. The need of care is based on care services reimbursed by the statutory care insurance, is established by a qualified nurse or physician by assessing the ability to perform activities of daily living, and reflects the dependency on care. At the time of the study the need of care was classified into three levels in the German health care system. All statistical analyses were done using SAS 9.4 (SAS Institute Inc., Cary, N.C., USA).

3 | RESULTS

3.1 | Sample characteristics

Characteristics of PWD identified through the algorithm are shown in Table 1. The study population consisted of 8110 PWD, of whom 61% were female. PWD were on average about 79.5 years old at the time of cohort entry. Nearly half of PWD (49.5%) had a coded diagnosis of other/unknown types of dementia, 30.1% of vascular dementia, 16.6% of AD, 2.0% of Lewy body dementia, and 1.8% of frontotemporal dementia. Furthermore, antidepressants, antipsychotics and anxiolytics or hypnotics/sedatives were dispensed to 34.4%, 37.3%, and 22.9% of PWD prior to cohort entry, respectively. The most common comorbidities at baseline included bone/joint diseases (58.7%), cardiovascular diseases (57.7%), diabetes (35.8%) and depression (34.9%). Delirium was prevalent in 14.3% of PWD at baseline.

| TABLE 1 | Characteristics of the study population
|---|---|
| | N = 8110 |
| Demographic and dementia characteristics | |
| Sex (female N, %) | 4947 (61.0) |
| Age in years at baseline (mean, SD) | 79.5 (7.7) |
| Years of follow-up (median, IQR) | 2.2 (3.4) |
| Reasons for leaving study (N, %) | |
| Deceased | 4871 (60.1) |
| End of study period | 3082 (38.0) |
| End of insurance period | 157 (1.9) |
| Type of dementia (N, %) | |
| Alzheimer’s dementia | 1346 (16.6) |
| Vascular dementia | 2443 (30.1) |
| Lewy-Body-Dementia | 165 (2.0) |
| Frontotemporal dementia | 144 (1.8) |
| Other, unknown | 4012 (49.5) |
| Use of Alzheimer’s disease medication (N, %) | |
| Antidepressants | 1730 (21.4) |
| Antipsychotics | 1307 (16.1) |
| Anxiolytics, hypnotics/sedatives | 1462 (18.1) |
| Other comorbidities at cohort entry (N, %) | |
| Cardiovascular diseases | 4679 (57.7) |
| Neurologic diseases | 1435 (17.7) |
| Depression | 2830 (34.9) |
| Delirium | 1160 (14.3) |
| Pulmonary diseases | 1590 (19.6) |
| Diabetes | 2903 (35.8) |
| Bone/Joint diseases | 4761 (58.7) |
| Cancer | 1663 (20.5) |
| Other comorbidities | 2214 (27.3) |

*Rivastigmine, galantamine, donepezil or memantine.
*Chronic kidney disease, alcohol abuse, dehydration.
3.2 | New use of psychotropic medication

The number of new users, short- and long-term users for each medication class according to the different hospitalizations are presented in Table 2. The lowest percentage of new use was seen for antidepressants, with 1.3% to 2.3% new users and a total of 218 new users across hospitalizations. In contrast, the highest percentage of new use was observed for antipsychotics, with 5.0% to 8.9% new users and a total of 829 new users across hospitalizations. Anxiolytics or hypnotics/sedatives and Alzheimer's medication had a varying percentage of new use from 1.2% to 3.2% with a total of 304 new users and 1.6% to 3.5% with a total of 394 new users, respectively. Among medication classes, new users of Alzheimer's medication had the highest percentage of long-term users (88.1%) followed by new users of antidepressants (83.0%), antipsychotics (61.9%) and anxiolytics or hypnotics/sedatives (56.9%).

3.3 | Predictors of new use of psychotropic medication

Predictors of new use of the various classes of psychotropic medication are shown in Tables 3–5 and S1. No associations were seen between age and sex and the outcomes in any of the models, and therefore results for these sociodemographic variables are not displayed.

The factors associated with new use of antidepressants are displayed in Table 3. PWD with anxiety during any hospitalization had a significantly higher odds for new use of antidepressants (OR: 4.52, 95% CI 1.16-17.61). PWD with depression during any hospitalization had a significantly higher odds for new use of antidepressants as well (OR: 2.95, 95% CI 2.25-3.87). Compared to all remaining main discharge diagnoses, a diagnosis of dementia was associated with significantly increased new use of antidepressants (OR: 2.17, 95% CI 1.28-3.67). The need of care was a predictor for new use of antidepressants. In particular, PWD who were in need of level one, level two or level three care had a significantly increased odds of new antidepressants use (Level 1 care: OR 1.50, 95% CI 1.06-2.13; Level 2 care: OR 1.88, 95% CI 1.32-2.68; Level 3 care: OR 1.59, 95% CI 1.05-2.42).

Estimates for new use of antipsychotics are shown in Table 4. PWD with delirium (OR: 2.13, 95% CI 1.66-2.74), delusion, hallucination or acute psychotic state (OR: 2.47, 95% CI 1.64-3.70), agitation, anger or hostility (OR: 1.73, 95% CI 1.48-2.02) during any hospitalization were at a significantly increased odds for new use of antipsychotics. Main discharge diagnoses of dementia (OR: 3.01, 95% CI

### TABLE 2  Number of new users, short-term and long-term users per medication class and hospitalization

| Hospitalization | Antidepressants | Antipsychotics | Anxiolytics, hypnotics/sedatives | Alzheimer medication |
|-----------------|----------------|----------------|----------------------------------|----------------------|
| **First hospitalization** | | | | |
| Eligible (N) | 4842 | 4555 | 5684 | 5886 |
| New users (N, %) | 62 (1.3) | 229 (5.0) | 68 (1.2) | 92 (1.6) |
| Short-term | 3 (4.8) | 79 (34.5) | 40 (58.8) | 7 (7.6) |
| Long-term | 59 (95.2) | 150 (65.5) | 28 (41.2) | 85 (92.4) |
| **Second hospitalization** | | | | |
| Eligible (N) | 3528 | 3284 | 4151 | 4441 |
| New users (N, %) | 81 (2.3) | 284 (8.6) | 96 (2.3) | 128 (2.9) |
| Short-term | 18 (22.2) | 110 (38.7) | 50 (52.1) | 16 (12.5) |
| Long-term | 63 (77.8) | 174 (61.3) | 46 (47.9) | 112 (87.5) |
| **Third hospitalization** | | | | |
| Eligible (N, %) | 2363 | 2273 | 2787 | 3070 |
| New users (N, %) | 43 (1.8) | 202 (8.9) | 82 (2.9) | 106 (3.5) |
| Short-term | 12 (27.9) | 76 (37.6) | 49 (59.8) | 17 (16.0) |
| Long-term | 31 (72.1) | 126 (62.4) | 33 (40.2) | 89 (84.0) |
| **Fourth hospitalization** | | | | |
| Eligible (N, %) | 1565 | 1525 | 1840 | 2099 |
| New users (N, %) | 32 (2.0) | 114 (7.5) | 58 (3.2) | 68 (3.2) |
| Short-term | 4 (12.5) | 51 (44.7) | 34 (58.6) | 7 (10.3) |
| Long-term | 24 (87.5) | 63 (55.3) | 24 (41.4) | 61 (89.7) |
| **Any hospitalization** | | | | |
| Eligible (N, %) | 12 298 | 11 637 | 14 462 | 15 496 |
| New users (N, %) | 218 (1.8) | 829 (7.1) | 304 (2.1) | 394 (2.5) |
| Short-term | 37 (17.0) | 316 (38.1) | 131 (43.1) | 47 (11.9) |
| Long-term | 181 (83.0) | 513 (61.9) | 173 (56.9) | 347 (88.1) |
2.12-4.27) were associated with significantly increased new use of antipsychotics compared to all remaining main discharge diagnoses. While people with vascular dementia (OR: 0.72, 95% CI 0.57-0.91) were at a significantly lower odds for new use of antipsychotics compared to people with AD, Lewy body dementia was associated with increased odds for new antipsychotic use (OR: 1.35, 95% CI 1.01-1.80). The need of care was associated with a significantly increased odds for new use of antipsychotics across all hospitalizations (Level 1 care: OR 2.95, 95% CI 2.32-3.76; Level 2 care: OR 3.30, 95% CI 2.57-4.24; Level 3 care: OR 4.01, 95% CI 3.00-5.37).

The results for new use of anxiolytics or hypnotics/sedatives are reported in Table 5. PWD with delirium (OR: 1.45, 95% CI 1.07-1.97), agitation, anger or hostility had a significantly higher odds of new use of anxiolytics or hypnotics/sedatives (OR: 2.03, 95% CI 1.67-2.48). In addition, a main discharge diagnosis of dementia (OR: 2.16, 95% CI 1.44-3.23) was significantly associated with new use of anxiolytics or hypnotics/sedatives compared to all remaining main discharge diagnoses. Furthermore, the need of care was associated with an increased odds of new use of anxiolytics or hypnotic/sedative use as well (Level 1 care: OR 2.02, 95% CI 1.44-2.84; Level 2 care: OR 3.02, 95% CI 2.17-4.20; Level 3 care: OR 3.32, 95% CI 2.29-4.80).

The factors associated with new use of Alzheimer's medication are shown in Table S1. PWD with delusion, hallucination, or an acute psychotic state during any hospitalization had a significantly increased odds for new use of Alzheimer's medication (OR: 1.97, 95% CI 1.18-3.28). Additionally, a main discharge diagnosis of dementia (OR: 3.14, 95% CI 1.94-5.08) was significantly associated with new use of Alzheimer's medication. People with vascular dementia (OR: 0.50, 95% CI 0.33-0.75) or other/unknown types of dementia (OR: 0.59, 95% CI 0.42-0.83) had a significantly lower odds for new use of Alzheimer's medication compared to people with AD.

### Table 3: Factors associated with new use of antidepressants after hospitalization displayed as odds ratios (OR)

| Time of hospitalization | Delirium and neuropsychiatric symptoms | Main discharge diagnosis | Type of dementia | Need of care |
|-------------------------|----------------------------------------|--------------------------|-----------------|-------------|
| First hospitalization   |                                       |                          |                 |             |
| OR (95% CI)             | Nevents: 62                            | Reference                | Reference       | Reference   |
| Second hospitalization  |                                       | Reference                | Reference       | Reference   |
| OR (95% CI)             | Nevents: 81                            | Reference                | Reference       | Reference   |
| Third hospitalization   |                                       | Reference                | Reference       | Reference   |
| OR (95% CI)             | Nevents: 43                            | Reference                | Reference       | Reference   |
| Fourth hospitalization  |                                       | Reference                | Reference       | Reference   |
| OR (95% CI)             | Nevents: 32                            | Reference                | Reference       | Reference   |
| Any hospitalization     |                                       | Reference                | Reference       | Reference   |

**Note:** Additional adjustment included age at baseline, sex, comorbidities at baseline, eating disorders or somnolence during hospitalization, year of hospitalization, time since cohort entry.

*aEstimation of association not possible due to very low number of cases.

**bPhysical violence, sleep disturbances, aberrant motor behavior.**
DISCUSSION

This comprehensive study assessed factors that are associated with new use of psychotropic medication among PWD after hospitalization. It adds to the literature by focusing on new use of different medication classes after multiple hospitalizations. The main predictors of new use were similar across medication classes and included delirium and NPS, main discharge diagnosis of dementia, and the need of care.

Currently, to our knowledge, there are no comparable studies assessing predictors of new use of psychotropic medications that focused on hospitalizations among PWD, hence we can only make a limited comparison with the existing literature.

Delirium (antipsychotics, and anxiolytics or hypnotics/sedatives), delusion, hallucination or acute psychotic state (antipsychotics, Alzheimer's medication), agitation, anger or hostility (antipsychotics, and anxiolytics or hypnotics/sedatives), anxiety (antidepressants) or depression (antidepressants) during hospitalizations were especially pronounced factors associated with new use of psychotropic medication. One study among community-dwelling people with AD showed that a history of psychiatric disorders is associated with an increased risk for psychotropic medication use and psychotropic polypharmacy.26 Another study among PWD living in the community or nursing homes showed that NPS are associated with prescriptions of antipsychotics, antidepressants and hypnotics/sedatives while another study of hospitalized elderly specifically identified delirium as a risk factor for antipsychotics prescriptions.31,32

Since agitation, delusions and acute psychotic symptoms are common in delirium and form an important and frequent part of the NPS and may be treated with antipsychotics it was expected that delirium and NPS during hospitalization increase the odds for new use of psychotropic medication.

### TABLE 4 Factors associated with new use of antipsychotics after hospitalization displayed as odds ratios (OR)

|                        | First hospitalization OR (95% CI) | Second hospitalization OR (95% CI) | Third hospitalization OR (95% CI) | Fourth hospitalization OR (95% CI) | Any hospitalization OR (95% CI) |
|------------------------|-----------------------------------|-----------------------------------|-----------------------------------|-----------------------------------|----------------------------------|
| **Delirium and neuropsychiatric symptoms** | | | | | |
| Not present            | Reference                         | Reference                         | Reference                         | Reference                         | Reference                        |
| Delirium               | 3.32 (2.18-5.04)                  | 2.61 (1.64-4.15)                  | 1.95 (1.02-3.71)                  | 1.48 (0.60-3.66)                  | 2.13 (1.66-2.74)                |
| Delusion, hallucination, acute psychotic state | 3.28 (1.64-6.56) | 1.71 (0.81-3.62) | 1.74 (0.63-4.84) | 1.93 (0.49-7.57) | 2.47 (1.64-3.70) |
| Agitation, anger, hostilitya | 1.69 (1.24-2.30) | 1.78 (1.36-2.33) | 1.83 (1.27-2.63) | 2.12 (1.29-3.48) | 1.73 (1.48-2.02) |
| Anxiety                | 5.03 (0.89-28.51)                 | 2.81 (0.52-15.17)                 | b                                 | b                                 | 1.84 (0.56-5.98)                |
| Depression             | 0.73 (0.48-1.11)                  | 0.86 (0.61-1.21)                  | 0.97 (0.63-1.49)                  | 0.95 (0.54-1.66)                  | 0.94 (0.78-1.13)                |
| **Main discharge diagnosis** | | | | | |
| All remaining          | Reference                         | Reference                         | Reference                         | Reference                         | Reference                        |
| Dementia               | 2.90 (1.61-5.24)                  | 3.61 (1.79-7.29)                  | 4.02 (1.47-10.95)                 | 2.48 (0.24-25.94)                 | 3.01 (2.12-4.27)                |
| **Type of dementia**   | | | | | |
| Alzheimer's disease    | Reference                         | Reference                         | Reference                         | Reference                         | Reference                        |
| Vascular dementia      | 0.22 (0.10-0.48)                  | 0.74 (0.39-1.43)                  | 0.98 (0.44-2.18)                  | 0.62 (0.21-1.84)                  | 0.72 (0.57-0.91)                |
| Lewy body dementia     | 1.44 (1.01-2.25)                  | 1.46 (0.73-2.31)                  | 1.26 (0.61-2.45)                  | 1.12 (0.41-2.79)                  | 1.35 (1.01-1.80)                |
| Frontotemporal dementia| 0.59 (0.20-2.39)                  | 0.23 (0.03-1.87)                  | 0.45 (0.05-3.73)                  | 0.68 (0.10-3.93)                  | 0.42 (0.19-0.92)                |
| Other/Unknown          | 0.75 (0.46-1.24)                  | 1.49 (0.85-2.61)                  | 0.88 (0.42-1.84)                  | 1.17 (0.46-3.00)                  | 0.81 (0.66-0.99)                |
| **Need of care**       | | | | | |
| No level               | Reference                         | Reference                         | Reference                         | Reference                         | Reference                        |
| Level one              | 2.90 (1.89-4.44)                  | 2.72 (1.78-4.16)                  | 2.83 (1.47-5.44)                  | 1.81 (0.70-4.71)                  | 2.95 (2.32-3.76)                |
| Level two              | 3.17 (2.00-5.03)                  | 2.72 (1.74-4.23)                  | 2.51 (1.28-4.93)                  | 4.25 (1.70-10.63)                 | 3.30 (2.57-4.24)                |
| Level three            | 3.16 (1.71-5.84)                  | 3.47 (2.08-5.79)                  | 3.66 (1.77-7.58)                  | 2.11 (0.72-6.23)                  | 4.01 (3.00-5.37)                |

Note: Additional adjustment included age at baseline, sex, comorbidities at baseline, eating disorders or somnolence during hospitalization, year of hospitalization, time since cohort entry.
aPhysical violence, sleep disturbances, aberrant motor behavior.
bEstimation of association not possible due to very low number of cases.
antipsychotics. The current evidence regarding the efficacy of antipsy-
chotics to treat or prevent delirium among hospitalized older adults
does not support the use of antipsychotics. Antipsychotics should
only be used in PWD with agitation or psychotic symptoms with the
potential of causing harm to the person and/or others and if they did
not respond to non-pharmacological treatments. According to a
recent consensus recommendation, citalopram and analgesia should
be prioritized ahead of antipsychotics for agitation, if pharmacologic
strategies were needed. In contrast, for psychosis, pharmacologic
options should be prioritized following the assessment of underlying
causes. Interestingly, people with delusion, hallucination or an acute
psychotic state had a significantly higher odds of new Alzheimer’s
medication use. The most likely explanation is that Alzheimer’s medici-
ation might reduce NPS, including delusions, which is why treatment
might have been initiated. The higher odds of receiving psychotro-
pic medication among PWD with delirium and NPS in general
highlights the need to establish early detection and (non-pharma-
ological) treatment of those symptoms, especially during
hospitalization.

People with Lewy body dementia had a significantly higher odds
of new use of antipsychotics compared to people with AD. Studies
have shown a significantly greater total score and sub-scores for hal-
lucinations on the neuropsychiatric inventory among people with
Lewy body dementia as well as a higher risk of delirium compared to
people with AD. Although we adjusted the analysis for delirium and
NPS there might be cases with delirium or NPS that were not
coded which led to new use of antipsychotics. Another explanation
might be that delirium and Lewy body dementia share a number of
clinical features that make a differentiation between those two chal-
lenging. Hence, people with Lewy-Body-Dementia might appear to
have delirium and thus get prescribed antipsychotics. Nevertheless,
the use of antipsychotics in Levy body dementia is not advised.

### TABLE 5 Factors associated with new use of anxiolytics or hypnotics/sedatives after hospitalization displayed as odds ratios (OR)

| First hospitalization | Second hospitalization | Third hospitalization | Fourth hospitalization | Any hospitalization |
|-----------------------|------------------------|-----------------------|------------------------|--------------------|
| OR (95% CI)           | N<sub>events</sub>: 68  | OR (95% CI)           | N<sub>events</sub>: 82  | OR (95% CI)        | N<sub>events</sub>: 58  |
| Delirium and neuropsychiatric symptoms |                       |                       |                       |
| Not present           | Reference              | Reference             | Reference              | Reference          |
| Delirium              | 0.97 (0.38-2.45)       | 1.49 (0.81-2.73)      | 2.18 (1.14-4.18)       | 2.72 (1.19-6.25)   | 1.45 (1.07-1.97)       |
| Delusion, hallucination, acute psychotic state | 2.72 (0.97-7.64)       | 0.78 (0.30-2.05)      | 0.33 (0.08-1.44)       | 1.24 (0.36-4.30)   | 0.91 (0.55-1.51)       |
| Agitation, anger, hostility<sup>a</sup> | 2.39 (1.37-4.17)       | 1.92 (1.35-2.73)      | 1.84 (1.24-2.72)       | 2.13 (1.23-3.69)   | 2.03 (1.67-2.48)       |
| Anxiety               | b                      | b                     | b                      | b                  | 2.57 (0.70-9.48)       |
| Depression            | 0.78 (0.35-1.73)       | 1.13 (0.75-1.72)      | 1.30 (0.83-2.06)       | 0.85 (0.46-1.61)   | 1.11 (0.88-1.39)       |

| Main discharge diagnosis | Circulatory system | Dementia |
|--------------------------|-------------------|----------|
| OR (95% CI)              | Reference         | Reference|
| N<sub>events</sub>: 96  | 4.52 (2.05-9.97)  | 2.62 (1.22-5.65)  |
| N<sub>events</sub>: 82  | 3.41 (1.21-9.61)  | 1.13 (0.14-9.26)  |
| N<sub>events</sub>: 58  | 2.16 (1.44-3.23)  |          |

| Type of dementia          |
|--------------------------|
| Alzheimer’s disease       |
| Vascular dementia         |
| Lewy body dementia        |
| Frontotemporal dementia   |
| Other/unknown             |
| OR (95% CI)               | Reference         |
| N<sub>events</sub>:       | 1.10 (0.65-1.83)  |
| N<sub>events</sub>:       | 0.73 (0.22-2.42)  |
| N<sub>events</sub>:       | 1.42 (0.29-7.06)  |
| N<sub>events</sub>:       | 1.13 (0.57-2.25)  |

| Need of care               |
|---------------------------|
| No level                  |
| Level one                 |
| Level two                 |
| Level three               |
| OR (95% CI)               | Reference         |
| N<sub>events</sub>:       | 2.14 (0.97-4.70)  |
| N<sub>events</sub>:       | 2.75 (1.23-6.14)  |
| N<sub>events</sub>:       | 3.39 (1.27-9.10)  |

Note: Additional adjustment included age at baseline, sex, comorbidities at baseline, eating disorders or somnolence during hospitalization, year of hospitalization, time since cohort entry.

<sup>a</sup>Physical violence, sleep disturbances, aberrant motor behavior.

<sup>b</sup>Estimation of association not possible due to very low number of cases.
A further common predictor across psychotropic medication classes were a main discharge diagnosis of dementia compared to all remaining main discharge diagnoses. PWD are rarely hospitalized for dementia itself which might indicate that main discharge diagnoses of dementia represent more severe cases.24,29 Although this observation is adjusted for delirium during hospitalization there also might be related reasons for prescribing psychotropic medications, such as psychosis and agitation or less severe and not coded cases of delirium, which are typically underreported when using the ICD-10 classification.45 Regardless, dementia itself without delirium or NPS is not a reason to prescribe psychotropic medication, especially when taking into account the list of possible severe adverse events. Still, as outlined above, the evidence for long-term efficacy of psychotropic medication in treating NPS is scarce, and there is a need for regular reevaluation of the risk-benefit ratio of psychotropic medication, in line with most current treatment guidelines.46 Non-pharmacological alternatives for treating NPS are urgently needed as one study has concluded that only 10% of psychotropic medication use for NPS is appropriate among PWD in nursing homes.37 On a positive note, a main discharge diagnosis of dementia was also associated with new use of Alzheimer’s medication. Alzheimer’s medication has been shown to be associated with benefits regarding cognitive, functional, and neuropsychiatric outcomes as well as mortality, nursing home placement and outcomes of hospitalization.37,39,48-52

The need of care, which reflects the ability to perform activities of daily living, dependency and utilization of care, was a strong and common predictor for new use of psychotropic medication, with the exception of Alzheimer’s medication. This is confirmed by existing evidence showing that a poor functional status, increasing dependency, and disease severity are associated with psychotropic medication use.3,32,53,54 Furthermore, associations were present across all levels of need of care compared to no need, which means that new use is common in different stages of dementia, not only more severe stages. It seems debatable to initiate treatment with psychotropic medication among PWD in need for care and at various stages of the disease considering the associations were present despite comprehensive adjustment including the main indications for medications. Another reason for new use of psychotropic medication across different levels of need of care might be higher emotional distress among nurses due to NPS, which has been shown to be associated with psychotropic medication use among nursing home residents.21 There is a need for more in depth research as to why PWD with need for care receive psychotropic medication and whether or not this is truly medically necessary.

Among new users, more than half were classified long-term users in each medication class. Longer use for antidepressants (83.0%) and Alzheimer’s medication (88.1%) seems reasonable as the main indications (depression, dementia) were the main predictors and treatment attempts with these medication classes is in line with the national guideline on dementia.55 Contrary to the guidelines that antipsychotics and anxiolytics or hypnotics/sedatives should only be cautiously used and limited in time, 61.9% and 56.9% of new users of antipsychotics and anxiolytics or hypnotics/sedatives received these medications for more than 6 weeks when assuming one daily dose per day.46,55 All things considered, early detection and treatment of delirium and NPS and tools like the Beers criteria15 or STOPP/START16 criteria should be established during transitions of care between hospital stays and care in the outpatient setting to reduce inappropriate prescription of psychotropic medications.

4.1 Strengths and weaknesses

Our study has several limitations. We analyzed data from a single German region, which limits the generalizability of our results. The analysis relied on ICD-10-GM codes for billing purposes in the health insurance system, which should ensure a high degree of validity but was not externally validated. In order to ensure a valid diagnosis of dementia, as well as the underlying etiology, diagnostic measurements as a part of our case definition and all diagnoses made in the first year after cohort entry were used. Nevertheless, the distribution of dementia subtypes seems unusual, which might impede validity of the associations between different subtypes of dementia and new use of psychotropic medication. Also, delirium and NPS are underreported when using the ICD-10 system.55 This might have led to underestimating effects in regards to delirium and NPS and new use of psychotropic medication. Although the aim of this study was to assess new use after hospitalization, it is to be noted that we did not have access to the use of medication during the hospital stay. Hence, new use might actually be a continuation of treatment beginning during the hospitalization. Furthermore, information on possible confounders including clinical parameters and family support were not available.

Among the strengths of our study is the large sample size, the novel assessment of new use of psychotropic medication classes, the differentiation between multiple hospitalizations, and the inclusion of people independently of their living situation, health status or nationality. Finally, based on the nature of the data, recall or interviewer bias was avoided.

In conclusion, we identified delirium and NPS during hospitalization, main discharge diagnoses of dementia, and the need of care as main predictors for new use of psychotropic medication after hospitalization among PWD. This highlights the need for future research to develop and implement appropriate interventions to detect delirium and NPS in early stages as well as to establish medication management across the different levels of need of care among PWD.

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CONFLICT OF INTEREST

The authors declare no potential conflict of interest.
DATA AVAILABILITY STATEMENT

The data used in this study cannot be shared as it was based on claims data of a German health insurance company, maintained by the PMV research group, and can only be used in the offices of the PMV research group.

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