Received: 22 September 2025 | Revised: 18 March 2026 | Accepted: 19 March 2026

DOI: 10.1002/bcp.70553

ORIGINAL ARTICLE

Psychotropic medication use among community dwellers with and without Parkinson's disease – A nationwide cohort study

Noora Nieminen[1] | Anna-Maija Tolppanen[1,2] | Valtteri Kaasinen[3,4] | Marjaana Koponen[1,2] | Sirpa Hartikainen[1,2]

[1]School of Pharmacy, University of Eastern Finland, Kuopio, Finland

[2]Kuopio Research Centre of Geriatric Care, University of Eastern Finland, Kuopio, Finland

[3]Clinical Neurosciences, University of Turku, Turku, Finland

[4]Neurocenter, Turku University Hospital, Finland

Correspondence
Anna-Maija Tolppanen, School of Pharmacy, University of Eastern Finland, P.O. Box 1627, 70211 Kuopio, Finland.
Email: anna-maija.tolppanen@uef.fi

Abstract

Aims: We studied the prevalence of psychotropic use and psychotropic polypharmacy in persons with Parkinson's disease (PD) during a 10-year follow-up, because longitudinal studies on this topic are scarce although non-motor symptoms of PD are often treated with psychotropics.

Methods: The prevalence of any psychotropic, benzodiazepines and related drugs (BZDRs), antidepressants, antipsychotics in six-month time windows from five years before to five years after PD diagnosis was studied in a Finnish nationwide register-based study of 17 379 people with clinically verified PD diagnosis during 2000–2014 and compared to a matched comparison cohort without PD (n = 115 386).

Results: During the follow-up, psychotropic use increased from 18% to 35% in persons with PD and from 14% to 20% in the comparison cohort. Psychotropic polypharmacy and use of all psychotropic subgroups were more frequent in the PD than in the non-PD cohort throughout the follow-up. In comparison, cohort BZDRs were the most frequently used psychotropics during the whole follow-up. In the PD cohort, BZDRs were the most frequently used psychotropic group until three years after PD diagnosis, with the highest prevalence just before the index date (19.4%). After that, antidepressants were the most commonly used psychotropics. In the PD cohort, the psychotropic polypharmacy increased from 5% to 10% during the follow-up. The differences were not explained by dementia.

Conclusions: The results likely reflect the onset of non-motor symptoms already before diagnosis and increasing symptomatology with disease progression. Alternatively, they may reflect increased healthcare contact. Still, the findings are concerning as all psychotropics increase the risk of adverse effects including falls and fall-related fractures.

KEYWORDS

antidepressant, antipsychotic, cohort, Parkinson's disease, psychotropic use

1 | INTRODUCTION

Persons with Parkinson's disease (PD) commonly experience non-motor manifestations of the disease, such as neuropsychiatric symptoms, sleep disturbances and pain, already before the onset of the motor symptoms, and these symptoms become more prevalent during the disease progression.[1–5] Anxiety and sleep disturbances have been observed in around one-third of persons diagnosed with PD.[6,7] A similar proportion is estimated to have clinically significant depression.[8] Psychotic symptoms are estimated to affect 40% of people with PD, especially persons living with dementia.[9] In addition, pain is common, with prevalence estimates among persons with PD ranging from 30% to 85%, depending on type, classification and assessment methods of pain and duration of PD.

Psychotropic medications are used for various indications, and in PD, they are also used to treat non-motor symptoms. Antidepressants are used to treat depression and neuropathic pain[10] but also anxiety disorders,[11,12] and insomnia.[5] Benzodiazepines and related drugs may be utilized for short-term treatment of insomnia[5] and severe[11] and generalized anxiety.[12] Atypical antipsychotics, mainly clozapine and quetiapine, can be utilized for the treatment of psychotic symptoms[13] and in the later stage for neuropsychiatric symptoms of dementia.[11] However, the evidence on the efficacy and safety of psychotropics in people with PD is limited.[14,15] Psychotropic use is associated with increased risk of adverse events in older adults,[16] and the risks may be more pronounced in persons with PD, especially when psychotropics are used concomitantly. A majority of the people with PD are older adults[17] with multimorbidity[18] and multiple medications.[19] In addition, PD increases the fall risk[20] as also use of any kind of psychotropic medications.[21]

Studies on the prevalence of psychotropic use in people with PD are sparse. A cross-sectional study among PD medication users reported a prevalence of antidepressant use 22% among home-dwelling persons, and 50% in institutional settings.[22] The prevalence of antipsychotic use was approximately 10% in a small population-based study of persons with PD.[23] Further, 4.8% to 12.2% initiated antipsychotic use within a year of PD medication initiation.[24–26] In our previous studies, we have shown that the rates of antidepressant and antipsychotic initiation start to increase several years before the PD diagnosis.[27,28] So far, there are no studies assessing whether the prevalence of any psychotropic medication use, psychotropic polypharmacy or psychotropic subgroups changes over time.

The aim of this study was to investigate the prevalence of any psychotropic medication use, psychotropic polypharmacy and all psychotropic subgroups in a nationwide cohort of persons with PD and a matched comparison cohort without PD during a ten-year follow-up beginning five years before the PD diagnosis date.

What is already known about this subject

- Non-motor manifestations of Parkinson's disease (PD), such as neuropsychiatric symptoms, sleep disturbances and pain, are common already before the onset of the motor symptoms and become more prevalent as the disease progresses
- In previous, mainly cross-sectional studies, the prevalence of antidepressant use in PD varied between 22–50%, and 4.8%–12.2% initiated antipsychotics within a year of PD diagnosis. There are no longitudinal studies on psychotropic polypharmacy.
- Psychotropic medication use is associated with increased risk of adverse events in older adults, and the risks may be more pronounced in persons with PD, especially when psychotropics are used concomitantly.

What this study adds

- In this nationwide cohort study following people with PD diagnosis from 5 years before PD diagnosis until 5 years after the diagnosis, psychotropic use increased from 18.1% to 34.8% in persons with PD and from 14.2% to 20.3% in a matched comparison cohort without PD.
- Psychotropic polypharmacy and use of all psychotropic subgroups were more frequent in the PD than in the non-PD cohort throughout the follow-up. Psychotropic medication use was most prevalent in the oldest persons, and the prevalence of psychotropic polypharmacy doubled during the follow-up. The results were not explained by dementia.
- The observed common use of psychotropics, and especially psychotropic polypharmacy, is concerning due to the increased risk of adverse effects, including falls and fall-related fractures, in an older adult population with PD, who are at particularly increased risk for these events.

2 | METHODS

This study is part of the Finnish Parkinson's disease (FINPARK), a nationwide register linkage study. FINPARK contains 22 189 people with clinically confirmed PD diagnosis (ICD-10 code G20) between 1996 and 2015 who were community-dwelling at the time of diagnosis and their 148 009 matched comparison persons. This study was restricted to 17 384 persons with PD diagnosed with PD between 2000 and 2014 and their 115 424 comparison persons without PD.

The identification of cohorts with and without PD has been described in detail previously by Hentilä et al.[27] Briefly, people with PD were identified by eligibility for reimbursement for PD medications from the Special Reimbursement Register maintained by the National Social Insurance Institution KELA, with ICD-10 code G20

recorded as the reason for reimbursement. To receive the reimbursement, patient's physician, who is required to be working in specialized unit or to be a neurologist, sends an application to KELA, where the PD diagnosis is verified, and the reimbursement is granted for the patient if the diagnostic criteria of PD are fulfilled. In this study, due to convenience, the term 'PD diagnosis date' is used instead of 'PD medication reimbursement grant date' as the time between these two dates is expected to be rather short. Over the study period 1996–2015, PD was diagnosed according to the Finnish Current Care Guideline on PD[29] which was in line with the United Kingdom Parkinson's Disease Society Brain Bank criteria. We also applied the following criteria to exclude persons with an uncertain PD diagnosis: age <35 years on the date of diagnosis, or a recorded diagnosis of a condition which may confuse the PD diagnosis $+/-2$ years of the PD diagnosis date (e.g. other neurodegenerative disorders, detailed list given in reference).[27]

Up to 7 comparison persons were identified for each person with PD from the KELA database, including all residents of Finland, and matched with PD persons with age (± 1 year), sex and place of residence on the date of PD diagnosis. The comparison persons were not allowed to have PD reimbursement code, diagnosis of dementia due to PD (ICD-10 code F02.3) or PD medication (ATC N04B) purchases ever before the index date to 12 months after. Otherwise, identical exclusion criteria were applied to the cohorts. In both cohorts, the persons had to be community-dwelling on the index date (date of PD diagnosis [grant of PD medication reimbursement]; matching date). Data on comorbidities were collected from the Care Register for Health Care, Special reimbursement register, Cancer register and Prescription register (Table S1).

Prevalence of psychotropic medication use was assessed in six-month time windows from five years before until five years after the index date. Psychotropic medication purchases were identified by Anatomical Therapeutic Chemical (ATC) classification codes from the Prescription Register, which includes all medications dispensed to community-dwelling persons in Finland with a reimbursement since 1995. The Prescription Register data does not contain the indication or the dose. Psychotropic medication groups were based on the ATC classification as follows: antidepressants (N06A), antipsychotics (N05A, excluding N05AB04 and N05AN01) and benzodiazepines and related drugs (N05BA, N05CD, N05CF). Psychotropic polypharmacy was defined as purchases from at least two different psychotropic medication groups in the same six-month time window.

Follow-up began five years before the index date and ended on five years after the index date, death or diagnosis of PD (comparison persons only), whichever occurred first. Persons who were hospitalized for >120 days in all time windows were excluded from the study population ($n = 5$ in the cohort with PD and $n = 38$ in the cohort without PD), and persons who were hospitalized >120 days in a specific time window were excluded from that time window. The final study population included 17 379 persons with PD and 115 386 comparison persons without PD. The prevalence of psychotropic medication use was calculated using the number of persons alive in that time window as the denominator. Information on comorbidities, psychotropic medications and analgesics before the follow-up, and information on dementia during the follow-up were extracted from national registers Table S1).

Characteristics of cohorts were compared using standardized mean differences (SMD). Prevalence of psychotropic use between the PD and comparison cohort during the study period was compared using a population-averaged panel data model with generalized estimating equations logistic regression model. The models were adjusted for age, sex, time window and calendar year. To evaluate whether the higher risk of dementia in PD explains the difference in psychotropic use rates, dementia was included as a time-varying covariate in these models. In addition, PD*dementia interaction term was included to assess the impact of dementia in the PD and comparison cohort. The analyses were conducted by using Stata MP14.2.

Register maintainers have approved the FINPARK study plan, and this permit has been updated with the National Health and Social Data Permit Authority Findata (permit decision number THL/6660/14.02.00/2020). Data were pseudonymized before submission to the research team, and study participants were not contacted. Therefore, according to Finnish legislation (Act on the Secondary Use of Health and Social Data 552/2019), the study has been granted an exemption from requiring ethics approval or informed consent.

3 | RESULTS

The final cohorts included 17 379 people with PD and 115 386 people without PD (Table 1). The mean age in the cohort with PD at the index date was 70.9 and 70.5 in the cohort without PD. In both cohorts, over half were men. The prevalence of comorbidities was similar between the cohorts, with all|SMD|below 0.1. Antidepressant and antipsychotic use was more common in the PR cohort before the follow-up (|SMD|0.11 for both).

The prevalence of any psychotropic medication use was higher in the cohort with than without PD during the whole study period (Figure 1 A, Table 2). Five years before PD diagnosis, 18.1% of persons with and 14.2% without PD used psychotropic medications. The difference between the cohorts started to increase two years before the index date. On the index date, 30.3% of the cohort with PD and 18.8% of the cohort without PD used at least one psychotropic medication, and after that, the difference slightly increased, being 34.8% in the PD and 20.3% in the non-PD cohort at the end of follow-up. Altogether 35.3% of the PD cohort and 11.1% of the comparison cohort developed dementia during the follow-up (Table 1).

Persons with PD than without PD used more frequently all psychotropic subgroups during the whole follow-up time (Figure 1B-D). In the PD cohort, benzodiazepines and related drugs (BZDR) were the most commonly used psychotropic medication group before the index date, highest just before the index date (19.4%), and after that, slightly decreased to the end of follow-up (17.0%) (Figure 1D). In comparison, cohort BZDRs were the most frequently used psychotropic group during the whole follow-up (10.7% in the beginning and 13.8% at the end of follow-up). Antidepressant use increased during the whole follow-

TABLE 1 The characteristics of cohorts with and without Parkinson's disease (PD) before the follow-up and mortality and incidence of dementia during the follow-up. Data are given as N (%) unless otherwise indicated and differences are calculated as standardized mean difference (SMD).

	Cohort with PD	Cohort without PD	SMD
	N = 17 379	N = 115 386	
Age at index date, years (mean, 95%CI)	70.9 (70.8–71.1)	70.5 (70.4–70.6)	−0.05
Sex			0.01
Women	7752 (44.6%)	51 033 (44.2%)	
Men	9627 (55.4%)	64 353 (55.8%)	
Comorbidities			
Schizophrenia	221 (1.3%)	1080 (0.9%)	−0.03
Other mood disorders	590 (3.4%)	2666 (2.3%)	−0.07
Bipolar disorder	130 (0.8%)	450 (0.4%)	−0.05
Epilepsy	226 (1.3%)	1156 (1.0%)	−0.03
Asthma/chronic obstructive pulmonary disease	1052 (6.1%)	7006 (6.1%)	<0.01
Cardiovascular disease	6030 (34.7%)	38 529 (33.4%)	−0.03
Stroke	516 (3.0%)	3737 (3.2%)	0.02
Diabetes	1411 (8.1%)	8724 (7.6%)	−0.02
Cancer	266 (1.5%)	1629 (1.4%)	−0.01
Head injury	483 (2.8%)	3557 (3.1%)	0.02
Substance abuse	287 (1.7%)	2560 (2.2%)	0.04
Medication use			
Antiepileptics	487 (2.8%)	2127 (1.8%)	−0.06
Antidepressants	1489 (8.6%)	6737 (5.8%)	−0.11
Antipsychotics	653 (3.8%)	2304 (2.0%)	−0.11
Benzodiazepines/related drugs	2591 (14.9%)	14 529 (12.6%)	−0.07
Opioids	498 (2.9%)	2821 (2.4%)	−0.03
Paracetamol	357 (2.1%)	2203 (1.9%)	−0.01
Non-steroid anti-inflammatory drugs	4525 (26.0%)	28 318 (24.5%)	−0.03
Deaths during the follow-up	3897 (22.4%)	16 605 (14.4%)	−0.20
Median survival since PD diagnosis (interquartile range), years	3.0 (1.7–4.0)	2.7 (1.4–3.9)	−0.16
Dementia during the follow-up	3861 (22.2%)	7072 (6.1%)	−0.47
Median time since PD diagnosis (interquartile range), years	2.6 (1.0–3.7)	3.0 (1.7–4.0)	−0.12

up in both cohorts (7.6% at the beginning and 19.2% at the end of follow-up in PD, and in comparison, cohort 5.0% and 8.4%, respectively) (Figure 1B). In the PD cohort, the prevalence of antipsychotic use increased during the whole follow-up from 3.9% to 10.7% (Figure 1 C). In the comparison cohort, the prevalence was quite stable but slightly increased to the end of follow-up (from 2.0% to 3.3%).

PD was consistently associated with a higher prevalence of any psychotropic use, as well as use of different psychotropic groups (Table 2), with the strongest associations observed for antipsychotics and antidepressants. All associations remained after adjusting for dementia as a time-varying covariate, although this adjustment had the strongest effect on antipsychotic use. Association of dementia with psychotropic use was similar in people with and without PD (Figure S1). The use of any psychotropic, especially antidepressant and BZDR use, was more common in women than in men in both cohorts, and the shape of prevalence curves was similar between sexes (Figure 2). There was no difference in antipsychotic use between women and men in the PD cohort after the index date (Figure 2C).

Use of any psychotropic medication was most common in the oldest age group (age ≥80 years at the index date) in both cohorts (Figure 3). In the PD cohort, the prevalence of any psychotropic medication use at the oldest age group increased from 24.8% to 40.1% during the study period, but remained nearly constant after the diagnosis (Figure 3 A). During the same time, the prevalence of any psychotropic medication use in 60–79-year-old persons with PD increased from 17.4% to 36.2% and in the youngest age group (<60 years) from 12.7% to 25.6%. Prevalence of use increased more steadily and moderately in the cohort without PD (Figure 3 B).

The proportion of persons who had purchased at least two different groups of psychotropics increased from 5.2% to 10.4% in the cohort

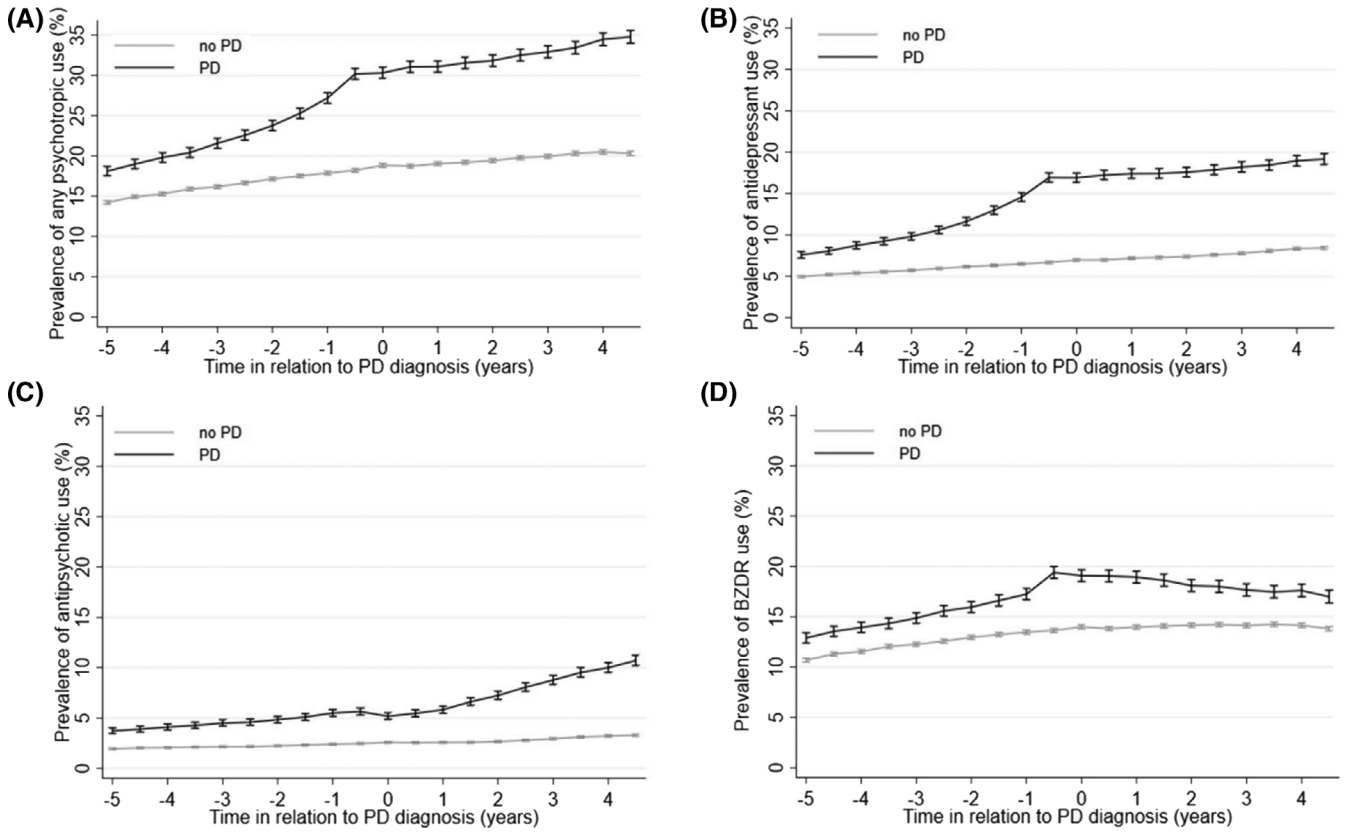

FIGURE 1 Prevalence of a: psychotropic drug use, B: antidepressant drug use, C: antipsychotic drugs use and D: benzodiazepine and related drugs (BZDR) use in cohort with Parkinson's disease (PD) and in cohort without PD from five years before to five years after index date. Index date is 0 in the x-axis.

TABLE 2 The association between Parkinson's disease (PD) and psychotropic use during the follow-up, adjusted for age, sex, calendar year of index date and time), with additional adjustment for dementia.

	Odds ratio (95% confidence interval)			
	Any psychotropic drug	Antipsychotics	Antidepressants	Benzodiazepines and related drugs
No adjustment for dementia				
No PD	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
PD	2.06 (2.00–2.13)	3.76 (3.50–4.03)	2.94 (2.82–3.07)	1.35 (1.30–1.40)
Additional adjustment for dementia as a time-dependent covariate				
No PD	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
PD	1.98 (1.92–2.04)	2.12 (1.92–2.33)	2.61 (2.50–2.73)	1.37 (1.32–1.41)

with PD, with a sharp increase around the diagnosis date (Figure 4 A) and from 3.0% to 4.6% in the cohort without PD (Figure 4 B). The proportion of those with purchases from all three psychotropic categories in the same time window was below 1.8% during the study period in the cohort with PD, and below 0.7% in the cohort without PD.

4 | DISCUSSION

To our knowledge, this is the first nationwide longitudinal study on the prevalence of psychotropic medication use and psychotropic polypharmacy in people with PD. Psychotropic medication use increased during the follow-up in both cohorts, and it was higher in the PD than in the comparison cohort, already five years before the PD diagnosis, until the end of follow-up.

The use of psychotropics before PD diagnosis might reflect non-motor depressive and anxiety symptoms, sleep disturbances and pain, occurring already years before the PD diagnosis.[1,2,30–32] A steep increase within one year before the PD diagnosis might be explained by more frequent health care contacts due to the non-motor symptoms, including symptoms prompting the psychotropic prescribing, and thus emphasise the difference

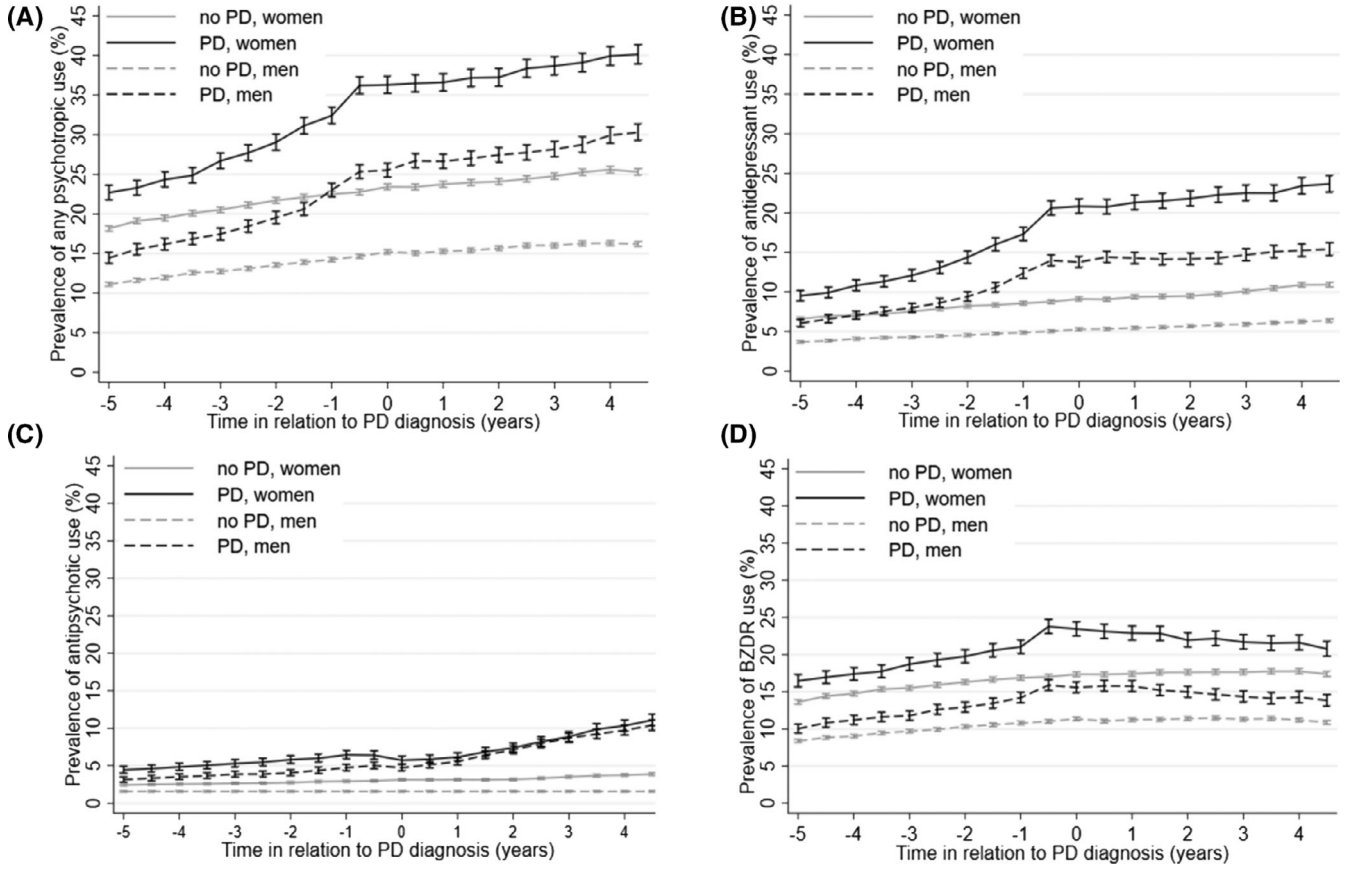

FIGURE 2 Prevalence of a: psychotropic drug use, B: antidepressant drug use, C: antipsychotic drugs use and D: benzodiazepine and related drugs (BZDR) use by men and women in cohort with Parkinson's disease (PD) and in cohort without PD five years before and five years after index date. Index date is 0 in the x-axis.

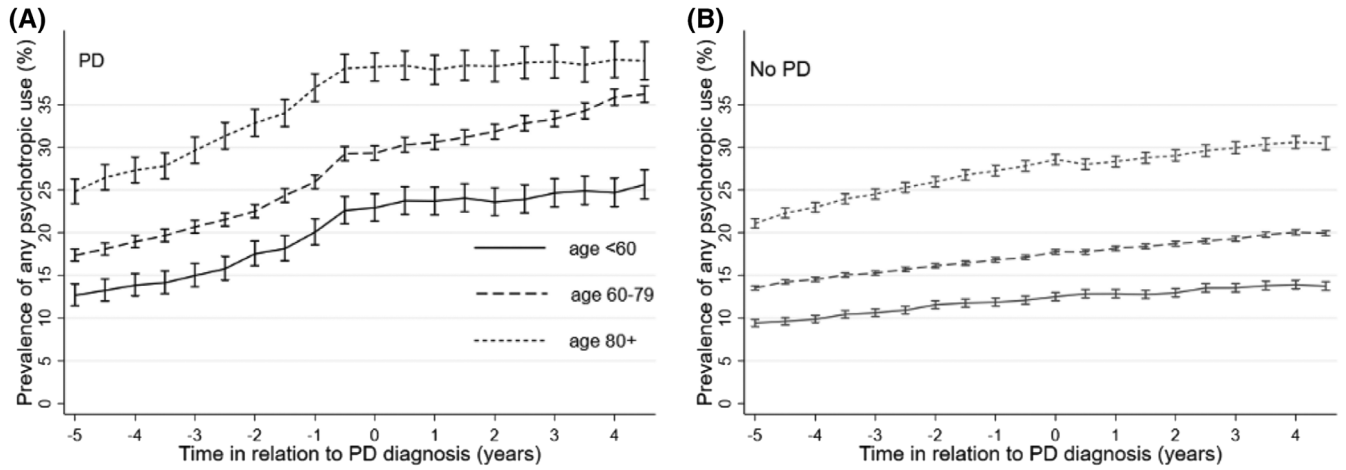

FIGURE 3 Prevalence of psychotropic drug use by age groups a: cohort with Parkinson's disease (PD) and B: cohort without PD five years before and five years after index date. Index date is 0 in the x-axis.

between PD and the comparison cohort immediately before the index date.

In both cohorts, the highest prevalence of psychotropics was due to BZDRs before the PD diagnosis. Although BZDR use remained high in the PD cohort, it began to decline slightly after the index date. This might be due to their several adverse effects and events, like negative effects on cognition,[33,34] and increased risk of falls and related fractures in older adults with PD, with a high risk of falling[21,35] as the risks can often be greater than the expected benefits.[34] BZDRs can be used for short-term insomnia maximum of two weeks according to Finnish

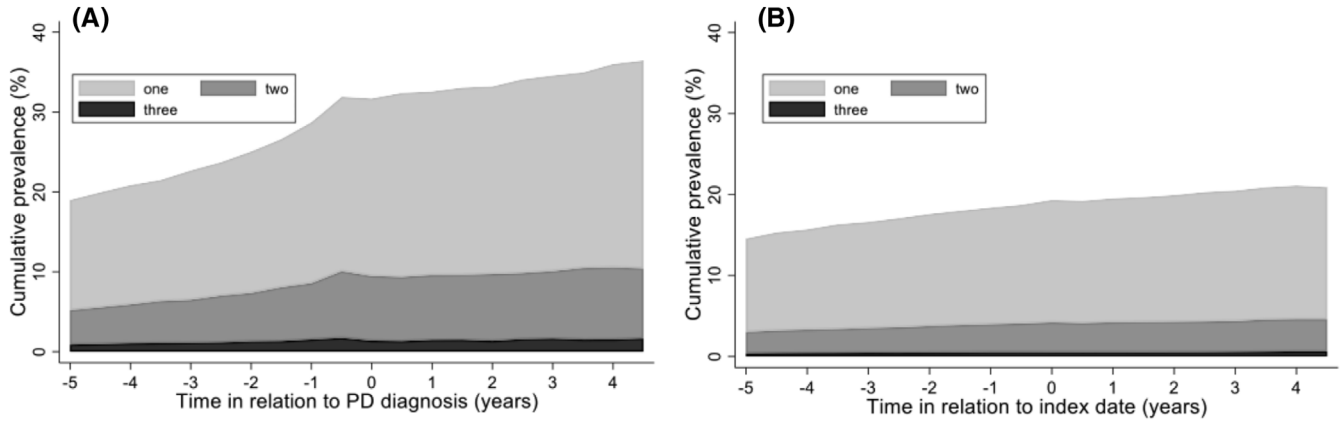

FIGURE 4 Prevalence of psychotropic monotherapy, concomitant use of psychotropics from two and three different psychotropic groups in cohort with Parkinson's disease (PD) (A) and in cohort without PD (B) five years before and five years after index date. Index date is 0 in the x-axis.

current care guidelines,[36] but benzodiazepines should not be used to treat anxiety in older adults[37] which may partially explain a decline in long-term use of these medications in Finland.[38]

An increasing prevalence of antidepressants until index date is in line with our previous finding of increased antidepressant initiation rates in the FINPARK cohort years before the PD diagnosis, with a peak incidence in the last time window prior to the PD diagnosis.[27] The increase in prevalence of antidepressant use after the PD diagnosis was rather similar in both cohorts, and prevalence close to that reported in a Swedish cross-sectional register-based study (22% in community-dwelling users of PD medications and 10% in comparison persons).[22] However, the results are not directly comparable, as the Swedish study included all users of PD medications aged 65 or older, regardless of duration or indication of PD medications.

In the PD cohort, antidepressants became the most common psychotropic medication group three years after PD diagnosis. This might reflect the several indications and increased prevalence of symptoms being treated. Based on a meta-analysis, in the PD population, the prevalence of depression varied from 2.7% to 90%, depending on the study population, methods and assessment of depression.[8] In the same meta-analysis, the prevalence of clinically significant depression was 35%, which is considerably higher than antidepressant use in our study at any time point after PD diagnosis. Comparable prevalence of anxiety disorder (34%) was found in a multicentre study with 342 persons with idiopathic PD in movement disorder clinics in the United States, Europe and Australia.[6] In that study anxiety was defined according DSM IV criteria and among participants with anxiety disorder 12% met criteria for multiple anxiety disorders. Lower prevalences of antidepressant use in our study are expected, as pharmacotherapy is just one treatment option and other treatment options exist, including non-pharmacological interventions and the adjustment of dopaminergic medication treatment of PD.[11] However, antidepressants are used to treat other non-motor symptoms of PD, like neuropathic pain and insomnia.[5,10] Neuropathic pain in PD can be classified to a radicular pain (prevalence between 14% and 35%) and to a central PD related pain (prevalence between 4% and 10%)[39] and these can be treated by serotonin-norepinephrine reuptake inhibitors and tricyclic antidepressants.[10] In addition, antidepressants with histamine effects in low doses, such as mirtazapine, can be used for the treatment of insomnia.[40]

Before the PD diagnosis, the prevalence of antipsychotic use was also higher in the cohort with PD than without PD from the first-time window and increased slightly until the diagnosis date. This is in line with findings of our recent incidence study in this same population, which showed an increase in the initiation of antipsychotics approximately four years prior to PD diagnosis.[28] The use stabilized around PD diagnosis. That might be explained by deprescribing antipsychotic medication during the diagnostic process of PD to exclude possible drug-induced Parkinsonism and consequent worsening of the motor symptoms of PD.[13] Previous studies have reported that the incidence of antipsychotic initiation ranged between 4.8% and 12.2% within a year of starting PD medication in cohorts of newly diagnosed PD persons in Wales, Canada and Taiwan.[24–26] Similarly, in our study, the prevalence of antipsychotic use was 5.8% year after PD diagnosis and increased to 10.7% five years after.

In our study, antipsychotic use doubled in the PD cohort during the study period, and the difference between cohorts increased after the PD diagnosis and was highest at the end of follow-up. It might be due to older age and longer duration of disease, which are risk factors for PD psychosis.[41,42] In addition, dopaminergic medication can provoke psychotic symptoms[43,44] and the risk for hallucinations can be five-fold (odds ratio compared to placebo 5.28 95% CI 2.4–11.4).[45] In a small population-based study on persons with PD, the prevalence of antipsychotic use was close to 10%[23] which is comparable to our observations in the last time windows. However, in that study, more than 96% of antipsychotic users had dementia, while the incidence of dementia in our study with a 5-year follow-up after PD diagnosis was 22.2%. According to a systematic review, the prevalence of dementia varies between 24% and 31% in the PD population[46] and neuropsychiatric symptoms of dementia might partly explain the higher

prevalence of antipsychotic use. In our study, the association between PD and antipsychotic use weakened after adjusting for dementia, but the prevalence during the study period was still over two times higher than in the comparison cohort.

This implies that the higher incidence of dementia does not explain the results, and they likely arise from the higher prevalence of psychotic symptoms in PD. After excluding other possible reasons for psychotic symptoms, such as delirium, infection, anticholinergic or other central nervous system-acting medication, the first-line treatment option is a reduction or change of dopaminergic PD medications.[12] If adequate symptom alleviation is not achieved, antipsychotics, preferably quetiapine and clozapine, could be considered.[29,47] Our previous study in the same population found that quetiapine was the most frequently initiated antipsychotic, accounting for 64% of all initiations.[28] Our data may include individuals using antipsychotic quetiapine off-label for insomnia, a practice observed in Finland and other Western countries, as well as in studies conducted in the Netherlands[40] and Denmark.[48]

Antipsychotics were the only psychotropic medication group in which a difference in use prevalence between sexes was not seen in the cohort with PD. This is in line with previous findings that the use of antipsychotics does not differ between the sexes among persons with newly diagnosed PD.[26] In a recent review, female sex has been concluded as a risk factor for neuropsychiatric symptoms in PD,[49] and in line with this, in our study antidepressants and BZDRs were more commonly used by women in the cohort with PD.

We found that psychotropic polypharmacy doubled in the PD cohort during the study period. There are only a few previous studies which are not directly comparable with our study due to major differences in study design. A cross-sectional study in a long-term care setting observed 21–26% prevalence of use for two or more psychotropics in PD persons aged 65 years or older.[50] Psychotropic medication use is presumably higher in institutionalized care, while our study population consisted of community-dwelling persons. Further, the definition of psychotropic polypharmacy is different, as we defined psychotropic polypharmacy based on the number of psychotropic drug groups. This would result in a lower prevalence than counting individual drugs.

4.1 | Strengths and limitations

Our study has several strengths. This was a nationwide, large-scale study with detailed information about changes in the prevalence of psychotropics in relation to the PD diagnosis. The PD diagnosis was clinically verified, and the studied antipsychotics and antidepressants are commonly reimbursed in Finland.[51] In addition, we used drug dispensing data, which better represents medication use than prescription data.[52]

Due to the exclusion of persons with other neurodegenerative disorders, persons with a diagnosis of Lewy body dementia were excluded. It is still under scientific debate whether PD and Lewy body dementia are expressions of the same underlying disease.[53] However, even with this exclusion, the difference between the cohorts was significant and may have been even greater if persons with Lewy body dementia had been included.

Our data might have a minor underestimation of benzodiazepines and benzodiazepine related drugs use, as some medications and some small packages are not reimbursed and thus not included in the Prescription Register data.[38] We defined polypharmacy as the purchase of two or more psychotropic groups within a 6-month time window, but it is possible that the psychotropics were not used concomitantly. Therefore, the definition may overestimate the prevalence of polypharmacy. Our study was conducted on community-dwelling persons at the time of diagnosis and contains no information about nursing home residents or hospitalized persons, as the Prescription Register does not contain information about medications used in those settings.

In conclusion, persons with PD use all psychotropic medications more frequently than the comparison population, starting as early as five years before their PD diagnosis. The prevalence of use increases further after diagnosis and continues to rise with disease duration. Psychotropic use is most prevalent in the oldest persons, and the prevalence of psychotropic polypharmacy doubled during the follow-up. The observed common use of psychotropics, and especially psychotropic polypharmacy, is concerning due to the increased risk of adverse effects, including falls and fall-related fractures, in an older adult population at high risk for these events.

ACKNOWLEDGEMENTS

Open access publishing facilitated by Ita-Suomen yliopisto, as part of the Wiley-FinELib agreement. Open access publishing facilitated by Ita-Suomen yliopisto, as part of the Wiley - FinELib agreement.

AUTHOR CONTRIBUTIONS

All the authors meet the criteria for authorship as described in the Uniform Requirements for Manuscripts submitted to Biomedical Journals. The authors contribution are as follows: Study concept and design: NN, AMT, VK, MK and SH. Acquisition, analysis, and interpretation of data: NN, AMT, MK, SH. Preparation of manuscript and/or critical evaluation of relevant intellectual content: NN, AMT, VK, MK and SH. Approval of final manuscript: NN, AMT, VK, MK and SH.

CONFLICT OF INTEREST STATEMENT

NN, MK and SH have nothing to disclose. AMT discloses research grants from the European Commission Horizon program, European Medicines Agency framework contracts, Michael J Fox Foundation for Parkinson's research and Sanofi, paid through the institution of employment outside of this work. VK discloses research grants from The Päivikki and Sakari Sohlberg Foundation, The Finnish Parkinson Foundation, The Finnish Cultural Foundation and.

Turku University Hospital (VTR-funds), paid through the institution of employment, speaker honoraria from Abbvie, Nordic Infucare, Bial, Lundbeck, Orion, Teva, Eisai, travel expenses from Nordic Infucare and participation in advisory board for Abbvie, Nordic Infucare, Merz outside of this work.

DATA AVAILABILITY STATEMENT

The data that support findings of this study are available from the corresponding author but restrictions apply to the availability of these data, and so they are not publicly available. Data are however available from the authors upon reasonable request and with permission sought from the National Social and Health Data Permit Authority Findata.

ORCID

Anna-Maija Tolppanen https://orcid.org/0000-0001-9270-9268

REFERENCES

1. Schrag A, Horsfall L, Walters K, Noyce A, Petersen I. Prediagnostic presentations of Parkinson's disease in primary care: a case-control study. *Lancet Neurol*. 2015;14(1):57-64. doi:10.1016/S1474-4422(14)70287-X
2. O'Sullivan SS, Williams DR, Gallagher DA, Massey LA, Silveira-Moriyama L, Lees AJ. Nonmotor symptoms as presenting complaints in Parkinson's disease: a clinicopathological study. *Mov Disord*. 2008;23(1):101-106. doi:10.1002/mds.21813
3. Stern MB, Siderowf A. Parkinson's at risk syndrome: can Parkinson's disease be predicted? *Mov Disord*. 2010;25(Suppl 1):89-93.
4. Fereshtehnejad SM, Romenets SR, Anang JB, Latreille V, Gagnon JF, Postuma RB. New clinical subtypes of Parkinson disease and their longitudinal progression: a prospective cohort comparison with other phenotypes. *JAMA Neurol*. 2015;72(8):863-873. doi:10.1001/jamaneurol.2015.0703
5. Dhawan V, Healy DG, Pal S, Chaudhuri KR. Sleep-related problems of Parkinson's disease. *Age Ageing*. 2006;35(3):220-228. doi:10.1093/ageing/afj087
6. Leetjens AF, Dujardin K, Marsh L, Martinez-Martin P, Richard IH, Starkstein SE. Symptomatology and markers of anxiety disorders in Parkinson's disease: a cross-sectional study. *Mov Disord*. 2011;26:484-492.
7. Ylikoski A, Martikainen K, Sieminski M, Partinen M. Parkinson's disease and insomnia. *Neurol Sci*. 2015;36(11):2003-2010. doi:10.1007/s10072-015-2288-9
8. Reijnders JS, Ehrt U, Weber WE, Aarsland D, Leentjens AF. A systematic review of prevalence studies of depression in Parkinson's disease. *Mov Disord*. 2008;23(2):183-189. doi:10.1002/mds.21803
9. Schapira AHV, Chaudhuri KR, Jenner P. Non-motor features of Parkinson disease. *Nat Rev Neurosci*. 2017;18(7):435-450. doi:10.1038/nrn.2017.62
10. Attal N, Cruccu G, Baron R, et al. EFNS guidelines on the pharmacological treatment of neuropathic pain: 2010 revision. *Eur J Neurol*. 2010;17:1112-1113.
11. Mueller C, Rajkumar AP, Wan YM, et al. Assessment and Management of Neuropsychiatric Symptoms in Parkinson's disease. *CNS Drugs*. 2018;32(7):621-635. doi:10.1007/s40263-018-0540-6
12. Weintraub D, Aarsland D, Biundo R, Dobkin R, Goldman J, Lewis S. Management of psychiatric and cognitive complications in Parkinson's disease. *BMJ*. 2022;24;379:e068718.
13. Samudra N, Patel N, Womack KB, Khemani P, Chitnis S. Psychosis in Parkinson disease: a review of etiology, phenomenology, and management. *Drugs Aging*. 2016;33(12):855-863. doi:10.1007/s40266-016-0416-8
14. Seppi K, Ray Chaudhuri K, Coelho M, et al. Update on treatments for nonmotor symptoms of Parkinson's disease - an evidence-based medicine review. *Mov Disord*. 2019;34(2):180-198. doi:10.1002/mds.27602
15. Seppi K, Weintraub D, Coelho M, et al. The movement disorder society evidence-based medicine review update: treatments for the non-motor symptoms of Parkinson's disease. *Mov Disord*. 2011;26(Supply 3):42-80.
16. Johnell K, Jonasdottir Bergman G, Fastbom J, Danielsson B, Borg N, Salmi P. Psychotropic drugs and the risk of fall injuries, hospitalisations and mortality among older adults. *Int J Geriatr Psychiatry*. 2017;32(4):414-420. doi:10.1002/gps.4483
17. Tysnes OB, Storstein A. Epidemiology of Parkinson's disease. *J Neural Transm (Vienna)*. 2017;124(8):901-905. doi:10.1007/s00702-017-1686-y
18. McLean G, Hindle JV, Guthrie B, Mercer SW. Co-morbidity and polypharmacy in Parkinson's disease: insights from a large Scottish primary care database. *BMC Neurol*. 2017;17(1):126. doi:10.1186/s12883-017-0904-4
19. Csoti I, Herbst H, Urban P, Woitalla D, Wüllner U. Polypharmacy in Parkinson's disease: risks and benefits with little evidence. *J Neural Transm*. 2019;126(7):871-878. doi:10.1007/s00702-019-02026-8
20. Montero-Odasso M, van der Velde N, Martin FC, et al. World guidelines for falls prevention and management for older adults: a global initiative. *Age Ageing*. 2022;2(51):afac205. Erratum in: Age Ageing. 2023;1;52: Erratum in: Age Ageing. 2023;2:52
21. Seppala LJ, Wermelink AMAT, de Vries M, et al. Fall-risk-increasing drugs: a systematic review and meta-analysis: II. Psychotropics. *J am Med Dir Assoc*. 2018;19(4):371.e11-371.e17. doi:10.1016/j.jamda.2017.12.098
22. Haasum Y, Fastbom J, Johnell K. Use of antidepressants in Parkinson's disease: a Swedish register- based study of over 1.5 million older people. *Parkinsonism Relat Disord*. 2016;27:85-88. doi:10.1016/j.parkreldis.2016.04.015
23. Bower JH, Grossardt BR, Rocca WA, Savica R. Prevalence of and indications for antipsychotic use in Parkinson's disease. *Mov Disord*. 2018;33(2):325-328. doi:10.1002/mds.27256
24. Marras C, Kopp A, Qiu F, et al. Antipsychotic use in older adults with Parkinson's disease. *Mov Disord*. 2007;22(3):319-323. doi:10.1002/mds.21192
25. Wang MT, Lian PW, Yeh CB, Yen CH, Ma KH, Chan AL. Incidence, prescription patterns, and determinants of antipsychotic use in patients with Parkinson's disease. *Mov Disord*. 2011;26(9):1663-1669. doi:10.1002/mds.23719
26. Orayj K. Trends and contributing factors for prescribing antipsychotics in newly diagnosed Parkinson's disease patients: a population-based study. *Risk Manag Healthc Policy*. 2021;14:2443-2452. doi:10.2147/RMHP.S313212
27. Hentilä E, Tiihonen M, Taipale H, Hartikainen S, Tolppanen AM. Incidence of antidepressant use among community dwellers with and without Parkinson's disease - a nationwide cohort study. *BMC Geriatr*. 2021;21(1):202. doi:10.1186/s12877-021-02145-6
28. Lilja S, Tolppanen AM, Koponen M, Hartikainen S, Tiihonen M. Incidence of antipsychotic use among community dwellers with and without Parkinson's disease. *Parkinsonism Relat Disord*. 2022;103:69-72. doi:10.1016/j.parkreldis.2022.08.024
29. Working Group Appointed by the Finnish Medical Society Duodecim, the Finnish Neurological Society. *Parkinson's disease: current care guidelines*. The Finnish Medical Society Duodecim; 2022. (referred 17.06.2023). Available online at: www.kaypahoito.fi
30. Ishihara L, Brayne C. A systematic review of depression and mental illness preceding Parkinson's disease. *Acta Neurol Scand*. 2006;113(4):211-220. doi:10.1111/j.1600-0404.2006.00579.x
31. Bohlken J, Schrag A, Riedel-Heller S, Kostev K. Identification of prodromal presentations of Parkinson's disease among primary care outpatients in Germany. *Neuroepidemiology*. 2022;56(1):41-49. doi:10.1159/000520574
32. Schrag A, Bohlken J, Dammertz L, et al. Widening the Spectrum of risk factors, comorbidities, and prodromal features of Parkinson disease. *JAMA Neurol*. 2023;80(2):161-171. doi:10.1001/jamaneurol.2022.3902

33. Billioti de Gage S, Bégaud B, Bazin F, et al. Benzodiazepine use and risk of dementia: prospective population based study. *BMJ*. 2012; 345(sep27 4):e6231. doi:10.1136/bmj.e6231
34. Ruottinen H. Parkinsonin tautiin liittyvät muut kognitiiviset ja psykiatriset oireet. Additional information (article reference nix02216 [050.042]). In: Working Group Appointed by the Finnish Medical Society Duodecim, the Finnish Neurological Society, ed. *Current care guideline: Parkinson's disease: current care guidelines*. The Finnish Medical Society Duodecim; 2022. (referred 01.03.2024). www.kaypahoito.
35. Woolcott JC, Richardson KJ, Wiens MO, et al. Meta-analysis of the impact of 9 medication classes on falls in elderly persons. *Arch Intern Med*. 2009;169(21):1952-1960. doi:10.1001/archinternmed.2009.357
36. *Insomnia: current care guidelines. Working group set up by the Finnish medical society Duodecim and the Finnish sleep research ry*. The Finnish Medical Society Duodecim; 2023. (Referred 01.03.2024). Available online at: www.kaypahoito.fi
37. Working Group Appointed by the Finnish Medical Society Duodecim, the Finnish Psychiatric Association and Finnish adolescent psychiatry Association. *Anxiety disorders: current care guidelines*. The Finnish Medical Society Duodecim; 2019. (referred 01.03.2024). Available online at: www.kaypahoito.fi
38. Kurko T, Saastamoinen LK, Tuulio-Henriksson A, et al. Trends in the long-term use of benzodiazepine anxiolytics and hypnotics: a national register study for 2006 to 2014. *Pharmacoepidemiol Drug Saf*. 2018; 27(6):674-682. doi:10.1002/pds.4551
39. Wasner G, Deuschl G. Pains in Parkinson disease--many syndromes under one umbrella. *Nat Rev Neurol*. 2012;8(5):284-294. doi:10.1038/nrneurol.2012.54
40. Kamphuis J, Taxis K, Schuiling-Veninga C, Schuiling-Veninga CC, Bruggeman R, Lancel M. Off-label prescriptions of low-dose quetiapine and mirtazapine for insomnia in the Netherlands. *J Clin Psychopharmacol*. 2015;35(4):468-470. doi:10.1097/JCP.0000000000000338
41. Zahodne LB, Fernandez HH. Pathophysiology and treatment of psychosis in Parkinson's disease: a review. *Drugs Aging*. 2008;25(8):665-682. doi:10.2165/00002512-200825080-00004
42. Zhang S, Ma Y. Emerging role of psychosis in Parkinson's disease: from clinical relevance to molecular mechanisms. *World J Psychiatry*. 2022;12(9):1127-1140. doi:10.5498/wjp.v12.i9.1127
43. Forsaa EB, Larsen JP, Wentzel-Larsen T, et al. A 12-year population-based study of psychosis in Parkinson disease. *Arch Neurol*. 2010; 67(8):996-1001. doi:10.1001/archneurol.2010.166
44. Baker WL, Silver D, White CM, et al. Dopamine agonists in the treatment of early Parkinson's disease: a meta-analysis. *Parkinsonism Relat Disord*. 2009;15(4):287-294. doi:10.1016/j.parkreldis.2008.07.004
45. Williams-Gray CH, Evans JR, Goris A, et al. The distinct cognitive syndromes of Parkinson's disease: 5 year follow-up of the CamPaIGN cohort. *Brain*. 2009;132(Pt 11):2958-2969. doi:10.1093/brain/awp245
46. Aarsland D, Zaccai J, Brayne C. A systematic review of prevalence studies of dementia in Parkinson's disease. *Mov Disord*. 2005;20(10): 1255-1263. doi:10.1002/mds.20527
47. Miyasaki JM, Shannon K, Voon V, et al. Practice parameter: evaluation and treatment of depression, psychosis, and dementia in Parkinson disease (an evidence-based review): report of the quality standards Subcommittee of the American Academy of neurology. *Neurology*. 2006;66(7):996-1002. doi:10.1212/01.wnl.0000215428.46057.3d
48. Rosenqvist TW, Osler M, Wium-Andersen MK, Wium-Andersen IK. Sedative drug-use in Denmark, 2000 to 2019: a nationwide drug utilization study. *Soc Psychiatry Psychiatr Epidemiol*. 2023;58(10):1493-1502. doi:10.1007/s00127-022-02409-5
49. Couture V, Carmel JF, Rousseau K, et al. Sex Differences in Neuropsychiatric Symptoms in Alpha-Synucleinopathies: A Systematic Review and Meta-Analysis. *Mov Disord Clin Pract*. 2024;11(11):1335-1344. doi:10.1002/mdc3.14227
50. Bhattacharjee S, Goldstone L, Warholak T. Prevalence, patterns and predictors of psychotropic polypharmacy among elderly individuals with Parkinson's disease in long term care settings in the United States. *J Parkinsons Dis*. 2016;6(1):247-255. doi:10.3233/JPD-150646
51. KELA's Research and Statistics, Statistical Database Kelasto. *Dispensations reimbursable under the NHI scheme 2008-2019*. Search performed using ATC-codes on 02.05.2024. www.kela.fi/kelas-research-and-statistics
52. Rikala M, Hartikainen S, Sulkava R, Korhonen MJ. Validity of the Finnish prescription register for measuring psychotropic drug exposures among elderly finns: a population-based intervention study. *Drugs Aging*. 2010;27(4):337-349. doi:10.2165/11315960-000000000-00000
53. Borghammer P, Okkels N, Weintraub D. Parkinson's disease and dementia with Lewy bodies: one and the same. *J Parkinsons Dis*. 2024;14(3):383-397. doi:10.3233/JPD-240002

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Nieminen N, Tolppanen A-M, Kaasinen V, Koponen M, Hartikainen S. Psychotropic medication use among community dwellers with and without Parkinson's disease – A nationwide cohort study. *Br J Clin Pharmacol*. 2026;1-10. doi:10.1002/bcp.70553