



Antipsychotic prescribing and drug-related readmissions in multimorbid older inpatients: a post-hoc analysis of the OPERAM population

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Received: 16 August 2023 / Accepted: 1 January 2024 / Published online: 17 February 2024
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Abstract

Background Limited data are available on characteristics associated with antipsychotic use in multimorbid older adults.

Aim Primary: to identify patient characteristics associated with antipsychotic prescribing in a multimorbid population of older inpatients with polypharmacy. Secondary: (1) to observe if antipsychotics use during an index hospitalisation was associated with a drug related admission (DRA) within one year, and (2) to describe these cases of antipsychotic-related readmissions.

Method This was a secondary analysis of the OPERAM randomized controlled trial. Multivariate analysis assessed the association between characteristics and comorbidities with antipsychotic use. An expert team assessed DRA occurring during the one-year follow-up.

Results Antipsychotics were prescribed to 5.5% (n = 110) patients upon admission while 7.7% (n = 154) inpatients received antipsychotics at any time (i.e. upon admission, during hospitalisation, and/or at discharge). The most frequently prescribed antipsychotics were quetiapine (n = 152), haloperidol (n = 48) and risperidone (n = 22). Antipsychotic prescribing was associated with dementia (OR = 3.7 95%CI[2.2;6.2]), psychosis (OR = 26.2 [7.4;92.8]), delirium (OR = 6.4 [3.8;10.8]), mood disorders (OR = 2.6 [1.6;4.1]), ≥ 15 drugs a day (OR = 1.7 [1.1;2.6]), functional dependency (Activities of Daily Living score < 50/100) (OR = 3.9 [2.5;6.1]) and < 2 units of alcohol per week (OR = 2.2 [1.4;3.6]). DRA occurred in 458 patients (22.8%) within one year. Antipsychotic prescribing at any time was not associated with DRA (OR = 1.0 [0.3;3.9]) however contributed to 8 DRAs, including 3 falls.

Conclusion In this European multimorbid polymedicated older inpatients, antipsychotics were infrequently prescribed, most often at low dosage. Besides neuro-psychiatric symptoms, risk factors for inhospital antipsychotic prescribing were lower functional status and polymedication.

Keywords Antipsychotic agents · Drug-related admission · Multimorbidity · Older patients

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Impact statements

- Older in-patients appear to be prescribed lower doses of antipsychotics suggesting awareness of the risks and/or use for off-label indications, where acceptable alternatives exist.
- Factors associated with antipsychotic use in older patients with multimorbidity and polypharmacy were not all related to psychotic features (e.g., polypharmacy and functional dependency) in our study.
- Indication for antipsychotics should be reassessed on a regular basis to avoid inappropriate use.
- Although drug-related readmissions were not associated with antipsychotic use in our population, this drug class should be used with caution in older adults in order to avoid adverse drug events.

Introduction

Antipsychotics have been first approved for the treatment of schizophrenia and other psychosis. Their off-label use has nowadays been extended to the treatment of other psychiatric diseases such as behavioural and psychological symptoms associated with dementia, bipolar disorder, major depressive disorder, anxiety, or agitation [1].

Because of physiological changes, an increased number of pathologies, and polypharmacy (i.e. more than five chronic drugs [2]), older patients are more at risk of deleterious adverse drug events, sometimes leading to loss of autonomy or mortality [3]. About 10–30% of hospital admissions in older patients are related to medicines [4–7]. Therefore, it is essential to regularly assess the benefit-risk balance of each prescribed medicine, using existing tools, such as the Beers Criteria [8] or the STOPP/START list [9], that highlight many conditions where antipsychotic use is inappropriate. Indeed, older patients using antipsychotics are exposed to a higher risk of sedation, postural hypotension and falls, confusion, pneumonia, stroke, hip fractures, metabolic syndrome, increased QT interval, and extrapyramidal symptoms (EPS) than younger adults [1], leading to emergency department visits and increased mortality rate [10, 11]. In addition, antipsychotic use is prone to the prescribing cascade [12], leading to an additional risk of adverse drug events.

Despite the risk of severe adverse effects and the availability of tools to assess the treatment, 77% of antipsychotics prescribed to older patients still have an inappropriate indication, such as agitation, aggressiveness, and anxiety [2, 3].

Given the risks of antipsychotic medicines, it seems important to investigate the profile of patients who are receiving these therapies. The majority of previous studies focus on long-term nursing home residents, or patients with psychosis or dementia [13] because of the high prevalence of long-term antipsychotic use in these populations [14–18]. However, it could be useful to increase knowledge about the factors associated with antipsychotic prescribing and drug-related readmissions (DRA) in a multimorbid population of older adults with polypharmacy, regardless of their place of living.

Aim

The main objective of our study was to identify patient characteristics associated with antipsychotic prescribing in a multimorbid population of older inpatients with polypharmacy from 4 countries. Secondary objectives were, (1) to observe if exposure to antipsychotics during index hospitalisation was associated with a DRA within one year, and (2) to describe these cases of antipsychotic-related readmissions.

Ethics approval

The OPERAM trial received approval from the ethics committees of each site: ID 2016–01200 (Cantonal Ethics Committee Bern, Switzerland), ID 15–522/D (Medical Research Ethics Committee Utrecht, Netherlands), 2016/20JUL/347–Belgian registration No: B403201629175 (Comité d’Ethique Hospitalo-Facultaire Saint-Luc-UCL) and ID ECM 4 (o) 07/02/17 (Cork University Teaching Hospitals Clinical Ethics Committee, Cork, Republic of Ireland). This post-hoc analysis was exempted from further ethical committee approval.

Method

Design and participants

This was a secondary analysis of the “Optimizing thERapy to prevent Avoidable hospital admissions in the Multimorbid elderly” (OPERAM) trial [19]. The OPERAM trial was a randomized multicentre controlled study that evaluated the impact of a structured medication review during the index hospitalisation (i.e. when each patient was included in the trial), on DRA in a multimorbid population (≥ 3 chronic medical conditions) of older adults (over 70 years) with polypharmacy (≥ 5 chronic medications).

This study recruited 2008 patients, between 2016 and 2020, in four centers (i.e., Inselspital, Bern, Switzerland; University Medical Centre and St. Antonius hospital,

Utrecht; the Netherlands, Cork University Hospital, Cork, Ireland; and St. Luc University Hospital, Brussels, Belgium) [19, 20].

Exclusion criteria were planned transfer to palliative care within 24 h after admission and report of any structured drug review by a clinician within two months before enrolment.

The 2008 patients of the OPERAM population were included in the present analysis.

Variables

All variables used in this post-hoc analysis were collected during the OPERAM trial.

Patient characteristics associated with antipsychotic prescribing during the hospital stay

Patient characteristics included age, sex, body mass index, education level, nursing-home living in the past 6 months, smoking status, alcohol consumption, functional status assessed using activities of daily living (ADL) score [21], with a lower score indicating a higher level of dependency, history of falls and patient allocation (i.e. intervention or control) in the OPERAM study.

Main indications and adverse effects of antipsychotics in older patients were used, as available at index hospitalisation: dementia, psychosis, confusion, anxiety, mood disorder, hip fracture, type 2 diabetes, stroke, increased QT interval, postural hypotension, pneumonia, dyskinesia, Parkinsonism and other extrapyramidal symptoms.

To identify factors associated with antipsychotic prescribing, the length of stay during the index hospitalisation and information on the antipsychotic medications were also included: anatomical therapeutic chemical (ATC) codes (ATC/DDD Index 2021), type (i.e. first generation or atypical antipsychotic), start and stop dates, dosage (expressed as prescribed daily dose/defined daily dose ratio) and frequency. All ATC drugs with the code N05A were included except for lithium (N05AN01) and prochlorperazine (N05AB04). The ratio prescribed daily dose (PDD) or defined daily dose (DDD) upon admission was included as a variable. The PDD at any time of the OPERAM study was calculated individually for each patient by adding the antipsychotic doses over the day. According to the WHO, DDD is the average maintenance dose per day for a drug used in his main indication (i.e. psychosis for the antipsychotic class) [22]. A ratio of less than 1 will indicate that the patient's dose is lower than the assumed average maintenance dose per day for the treatment of psychosis with this medication.

Three time periods were considered: 1) having an antipsychotic at any time during the index hospital stay (i.e. upon admission, during hospitalisation, and/or at discharge),

2) on admission and 3) at the discharge of the index hospitalisation.

Association between antipsychotic prescribing and drug-related readmission

In the OPERAM trial, patients had follow-up contact with the research team at months 2, 6 and 12 post-discharge of the index hospitalisation. Readmission letters and other relevant information regarding any readmission were collected, anonymised and blinded to the intervention group so they could be adjudicated as DRA [19, 20]. The adjudication process to determine whether these readmissions were DRAs, was performed by a pair of physicians and pharmacists who applied a structured chart review including the use of triggers to detect potential adverse drug reactions and the WHO-UMC system classification to check for causality [23, 24].

The occurrence of hospitalisation, the date of readmission and the presence of a DRA with an antipsychotic listed as causing or contributing medication were used to analyse the factors associated with DRA. Since data on the medication of patients were collected during the index hospitalisation, patients who started an antipsychotic medication during the follow-up were not included in the “antipsychotic” group.

Statistical analysis

To detect (1) factors associated with antipsychotic prescribing, and (2) factors associated with DRA, univariate logistic regressions was first performed. The alcohol consumption variable was dichotomised into “< 2 units per week” and “≥ 2 units per week”, ADL score at baseline into “< 10” and “≥ 10” and number of drugs into “< 15” and “≥ 15” for easier interpretation. All variables with p-values < 0.2 in each univariate regression model were integrated into multivariable logistic regressions. There was no multicollinearity of any variables according to the Variance Inflation Factor (VIF) test. P-values < 0.05 were considered statistically significant. Missing data were not imputed in the analysis. Statistical analysis was performed with IBM® SPSS Statistics version 26.

Results

Participants

The OPERAM trial included 2008 patients with a median age of 79 years, 55.3% male, 55.8% having more than 15 drugs and 9.6% living in nursing homes. Among all patients, 154 (7.7%) had at least one antipsychotic at any time during the index hospitalisation (Fig. 1), of which 110 had an

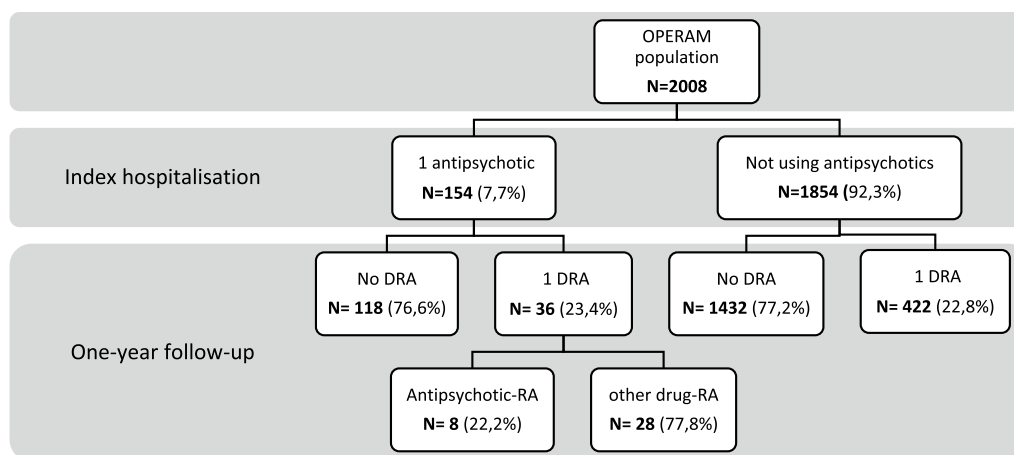


Fig. 1 Flowchart of patients. *DRA* Drug-related readmissions; *RA* Related readmission

antipsychotic on admission, 132 at discharge and one patient during the hospital stay only.

The median age of antipsychotic users at any time of index hospitalisation was 80, and 50.6% were male. The most common comorbidities in this group were type 2 diabetes (27.3%), mood disorders (27.3%), dementia (26.6%), delirium (24.0%) and stroke (14.9%). In non-users of antipsychotics, the most frequent comorbidities were type 2 diabetes (29.8%), stroke (15.5%) and pneumonia (8.6%) (Table 1).

Regarding their antipsychotic medication, the median PDD/DDD ratio at any time was 0.125 (IQR = 0.187) and the most frequently prescribed antipsychotics were quetiapine ($n = 152$; mean PDD/DDD ratio = 0.37; SD = 0.99), haloperidol ($n = 48$; mean PDD/DDD ratio = 0.37; SD = 0.99) and risperidone ($n = 22$; mean PDD/DDD ratio = 0.39; SD = 1.06). (Fig. 2).

Patient characteristics associated with antipsychotic prescribing during the hospital stay

Results of the univariate regression are shown in eTable 2.

In the multivariable regression (Table 2), antipsychotic prescribing at any time of the index hospitalisation was associated with dementia (OR = 3.73; 95%CI [2.24; 6.19]), psychosis (OR = 26.19 95%CI [7.39; 92.80]), delirium (OR = 6.41 95%CI [3.79; 10.81]), mood disorders (OR = 2.60 95%CI [1.65; 4.11]), alcohol consumption lower than 2 units per week (OR = 2.20 95%CI [1.36; 3.57]), ADL score below 50/100 (OR = 3.96 95%CI [2.55; 6.15]) and the prescription of 15 drugs or more (OR = 1.67 95%CI [1.07; 2.58]).

Antipsychotic prescribing on admission and at the discharge of the index hospitalisation was associated with the same variables as at any time during the hospitalisation except for the number of drugs (OR = 1.58 95%CI [0.95;

2.61]) that were not significantly associated with antipsychotic prescribing on admission (Table 2).

Association between antipsychotic prescribing and drug-related readmission

Among the 133 patients with an antipsychotic at the discharge of the index hospitalisation, 29 had an all-causes DRA during the one-year follow-up.

All-causes DRA within one year after index hospitalisation was not associated with having an antipsychotic prescribed at the discharge of the index hospitalisation (OR = 0.71 95%CI [0.46; 1.10]). The use of more than 15 drugs (OR = 2.78 95%CI [2.19; 3.53]) at any time of the index hospitalisation was the only significant variable positively associated with DRA (eTable 3).

Case reports of antipsychotic-related readmissions

The expert panel detected eight antipsychotic-related readmissions among the 36 patients (22.2%) with a DRA and using an antipsychotic at any time of the index hospitalisation. An antipsychotic was the main reason for admission for five patients and was a contributory reason for admission for three patients.

Of the eight antipsychotic-related readmissions, six were caused by atypical antipsychotics. Antipsychotic-related readmissions were due to an adverse drug reaction in seven cases, the other causes being overuse ($n = 1$) and underuse ($n = 1$).

Antipsychotic-related readmissions included falls ($n = 3$), confusion/delirium ($n = 3$) and acute renal impairment ($n = 2$).

Although the number of patients was low, it was noted that a low PDD/DDD ratio was detected in patients being treated with quetiapine (i.e. range: 0.03 to 0.06). Patients

Table 1 Baseline characteristics according to antipsychotic prescribing patterns during the index hospitalisation

	Total (N = 2008) n (%)	Antipsychotic prescribing			
		No antipsychotic (n = 1854) n (%)	At any time during the IH (n = 154) n (%)	On admission of the IH (n = 110) n (%)	At discharge of the IH (n = 132) n (%)
Age, median [IQR], years	79.0 [74–84]	78.5 [74–84]	80.0 [75–85]	79.0 [75–85]	80.0 [75–85]
Sex, male	1110 (55.3%)	1032 (55.7%)	78 (50.6%)	56 (50.9%)	65 (49.2%)
Nursing-home residents ^a	192 (9.6%)	154 (8.3%) ^c	38 (24.7%)	28 (25.5%)	33 (25.0%)
BMI, median [IQR]	26.2 [23.4–29.7]	26.2 [23.5–29.8]	25.7 [23.1–29.0]	25.8 [23.1–29.2]	25.6 [23.1–28.7]
<i>Trial site</i>					
Bern (Switzerland)	822 (40.9%)	721 (38.9%)	101 (65.6%)	68 (61.8%)	87 (65.9%)
Louvain (Belgium)	388 (19.3%)	374 (20.2%)	14 (9.1%)	13 (11.8%)	12 (9.1%)
Utrecht (the Netherlands)	452 (22.5%)	436 (23.5%)	16 (10.4%)	6 (5.4%)	16 (12.1%)
Cork (Ireland)	346 (17.2%)	323 (17.4%)	23 (14.9%)	23 (10.9%)	19 (14.4%)
Education level ^b		^e	^d		
Less than high school	595 (30.1%)	546 (29.9%)	49 (32.0%)	34 (30.9%)	43 (32.6%)
High school	909 (45.5%)	835 (45.7%)	74 (48.4%)	51 (46.4%)	62 (46.9%)
University	475 (24.0%)	445 (24.4%)	30 (19.6%)	24 (21.8%)	26 (19.7%)
<i>Alcohol consumption</i>					
< 2 units per week	1343 (66.9%)	1214 (65.5%)	129 (83.8%)	93 (84.5%)	113 (85.6%)
≥ 2 units per week	665 (33.1%)	640 (34.5%)	25 (16.2%)	17 (15.5%)	19 (14.4%)
Smokers ^a	158 (7.9%)	142 (7.7%) ^c	16 (10.4%)	14 (12.7%)	12 (9.1%)
<i>Functional dependency</i>					
ADL < 50/100	204 (10.2%)	151 (8.1%)	53 (34.4%)	37 (33.6%)	44 (33.3%)
ADL ≥ 50/100	1804 (89.8%)	1703 (91.9%)	101 (65.6%)	73 (66.4%)	88 (66.7%)
Number of falls, medical history, median [IQR]	0 [0–1]	0 [0–1]	1 [0–2]	1 [0–2]	1 [0–2]
Length of stay of the IH, median [IQR], days	7 [3–10]	7 [3–10]	8 [4–12]	7 [3–11]	8 [4–12]
<i>Intervention group</i>					
Intervention	963 (48.0%)	887 (47.8%)	76 (49.4%)	57 (51.8%)	65 (49.2%)
Control	1045 (52.0%)	967 (52.2%)	78 (50.6%)	53 (48.2%)	67 (50.8%)
<i>Daily drugs, number</i>					
< 15	888 (44.2%)	854 (46.1%)	34 (22.1%)	25 (22.7%)	27 (20.5%)
≥ 15	1120 (55.8%)	1000 (53.9%)	120 (77.9%)	85 (52.7%)	105 (79.5%)
Dementia	118 (5.9%)	77 (4.1%)	41 (26.6%)	34 (30.9%)	36 (27.3%)
Psychosis	14 (0.7%)	4 (0.2%)	10 (6.5%)	10 (9.1%)	9 (6.8%)
Delirium	97 (4.83%)	60 (3.23%)	37 (24.0%)	18 (16.4%)	33 (25.0%)
Anxiety	38 (1.9%)	31 (1.7%)	7 (4.5%)	6 (5.5%)	7 (5.3%)
Mood disorders	199 (9.9%)	157 (8.5%)	42 (27.3%)	34 (30.9%)	39 (29.5%)
Hip fractures	55 (2.7%)	51 (2.7%)	4 (2.6%)	2 (1.8%)	4 (3.0%)
Type 2 diabetes	594 (29.6%)	552 (29.8%)	42 (27.3%)	31 (28.2%)	35 (26.5%)
Stroke	311 (15.5%)	288 (15.5%)	23 (14.9%)	13 (11.8%)	22 (16.7%)
Increased QT-interval	20 (1.0%)	18 (0.9%)	2 (1.3%)	2 (1.8%)	2 (1.5%)
Postural hypotension	64 (3.2%)	57 (3.1%)	7 (4.5%)	4 (3.6%)	6 (4.5%)
Pneumonia	172 (8.6%)	160 (8.6%)	12 (7.8%)	7 (6.4%)	11 (8.3%)
Dyskinesia	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Parkinsonism	5 (0.2%)	4 (0.2%)	1 (0.6%)	1 (0.9%)	1 (0.7%)
Other extrapyramidal symptoms	68 (3.4%)	65 (3.5%)	3 (1.9%)	2 (1.8%)	2 (1.5%)

^aMissing values = 10; ^bmissing values = 29; ^cmissing values = 10; ^dmissing values = 1; ^emissing values = 28

ADL score Activity of daily living score, the maximum score is 20, lower score indicates higher functional dependency; *BMI* Body mass index; *IH* Index hospitalisation, *IQR* Interquartile range

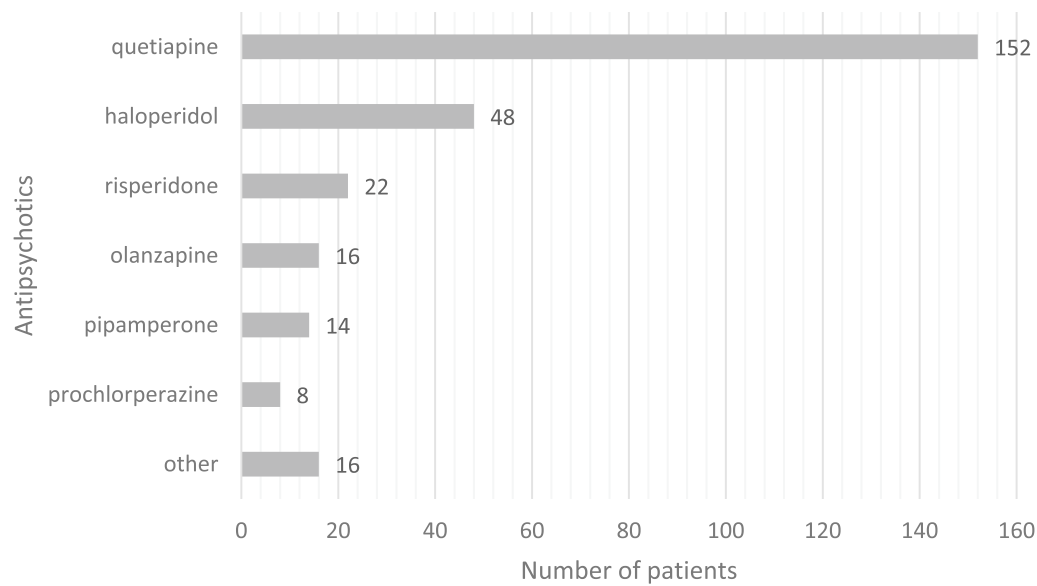


Fig. 2 Prescribed antipsychotics at any time during index hospitalisation (i.e. upon admission, during hospitalisation, and/or at discharge among the 2008 OPERAM patients)

Table 2 Patient characteristics associated with antipsychotic prescribing for inpatients, compared to no antipsychotic use, included in the multi-variable logistic regression

	Antipsychotic at any time (N = 1989)		Antipsychotic on admission (N = 1988)		Antipsychotic at discharge (N = 1989)	
	OR [CI 95%]	p-value	OR [CI 95%]	p-value	OR [CI 95%]	p-value
Age	0.99 [0.97; 1.03]	0.902			1.00 [0.97; 1.03]	0.967
Sex: Male					0.92 [0.60; 1.40]	0.697
Nursing-home residents ^a	1.60 [0.97; 2.65]	0.067	1.55 [0.89; 2.69]	0.120	1.56 [0.92; 2.65]	0.102
Alcohol < 2 units/week	2.20 [1.36; 3.57]	0.001*	2.17 [1.23; 3.82]	0.007*	2.51 [1.45; 4.33]	0.001*
Smokers ^a			1.89 [0.97; 3.66]	0.061		
ADL score < 50/100	3.96 [2.55; 6.15]	< 0.001*	3.49 [2.12; 5.76]	< 0.001*	3.36 [2.10; 5.39]	< 0.001*
Numbers of drugs ≥ 15	1.67 [1.07; 2.58]	0.022*	1.58 [0.95; 2.61]	0.076	1.83 [1.13; 2.95]	0.014*
Dementia	3.73 [2.24; 6.19]	< 0.001*	4.90 [2.89; 8.32]	< 0.001*	3.42 [2.03; 5.82]	< 0.001*
Psychosis	26.19 [7.39; 92.80]	< 0.001*	33.63 [9.22; 122.65]	< 0.001*	21.19 [6.31; 71.17]	< 0.001*
Delirium	6.41 [3.79; 10.81]	< 0.001*	2.28 [1.19; 4.63]	0.013*	6.37 [3.71; 10.94]	< 0.001*
Anxiety	2.06 [0.79; 5.33]	0.138	2.38 [0.85; 6.67]	0.098	2.47 [0.95; 6.37]	0.063
Mood disorders	2.60 [1.65; 4.11]	< 0.001*	2.75 [1.66; 4.53]	< 0.001*	2.89 [1.79; 4.65]	< 0.001*
Parkinsonism			1.41 [0.02; 102.28]	0.876		

CI Confidence interval; OR Odds ratio

with risperidone had a PDD/DDD of 0.70 and 1.60, the second patient being previously diagnosed with a psychotic disorder.

Discussion

The prevalence of antipsychotic use in our population of 2008 older patients with multimorbidity and polypharmacy was 7.7% at any time of hospitalisation. The doses were mostly low compared to standard doses for the psychosis treatment. Antipsychotic prescriptions increased during the hospital admission, rising from 110 to 132 patients.

OPERAM intervention had no impact on antipsychotic prescribing. Patients with dementia, psychosis, delirium and mood disorders had unsurprisingly a higher rate of antipsychotic prescriptions. Antipsychotics users also had significantly lower alcohol consumption, a higher number of medicines prescribed and a higher functional dependency. There was no difference between groups of patients who had an antipsychotic at any time, at admission or at the discharge of index hospitalisation. These results are similar to previous findings of a trial focusing on home-living patients, where patients with dementia, over 85 and with a lower ADL score had an increased frequency of antipsychotic prescribing. [25] However, the OPERAM patients, despite having many comorbidities and receiving polypharmacy, were slightly younger (median age = 79.0 IQR[74–84]) and had a more robust profile (i.e. 89.8% of patients with ADL score $\geq 50/100$ and 9.6% of patients were living in nursing-home) compared to patients of this previous trial.

In this study, the presence of antipsychotic use on admission, at discharge or at any time during the index hospitalisation was not significantly associated with all-cause DRA within a year. However, antipsychotics are frequently described in the literature as medications with a high risk of adverse drug events (i.e. 11 antipsychotic-related adverse drug events on 100 patients over 65 [26]). Of the 2008 included patients, only 0.4% ($n=8$) were readmitted because of an antipsychotic, while figures of 4% are described in the literature [27]. Antipsychotics are frequently reported as a cause of emergency visits (aOR 1.86; 95% CI[1.41–2.46]) [10] or DRA. [26, 28] This proportion varies by population and adverse reactions reported. The divergence may be due to the small number of patients under antipsychotic in the OPERAM population and to the inclusion of robust older patients, regardless of their living situation, pathologies and hospitalisation wards (except no recruitment in psychiatric units) while most other studies have focused on patients with a diagnosis of psychosis [10, 29] or living in nursing homes [3]. Moreover, our patients used mainly low-dose antipsychotics and for an unknown duration.

In 8 cases, common reasons for readmission for antipsychotics users were falls and confusion. As these patients were using low doses of antipsychotics, falls were probably induced by the antihistamine and antiadrenergic properties of the antipsychotics, causing sedation and postural hypotension [30, 31]. Of the cases of readmitted antipsychotics users, a large number were prescribed atypical antipsychotics that have anticholinergic properties (e.g., clozapine, olanzapine, quetiapine). This may explain the cases of patients being readmitted because of confusion [32].

At any time during the OPERAM study, the most frequently prescribed antipsychotics were quetiapine, haloperidol and risperidone, which confirms previous findings [33]. Interestingly, all identified cases of antipsychotic-related

adverse drug reactions in our population were related to these three drugs. In geriatric units, adverse drug reactions represent 10 to 20% of admissions [34, 35] and are the main cause of DRA [36]. As for DRA, antipsychotics are frequently named in the major classes causing adverse drug events, and their use is thus not recommended in older adults, except in psychosis or short-term use for severe agitation in neuropsychiatric conditions [26, 36–38]. Despite this, in most situations in the OPERAM population, antipsychotics were most likely used for indications other than psychosis (e.g. treatment of insomnia, anxiety or agitation). Low-dose quetiapine is increasingly being used in the treatment of insomnia despite the risks of orthostatic hypotension, weight gain and metabolic syndrome [39, 40]. Risperidone and haloperidol are frequently used for agitation and behavioural disorders in patients with dementia [41].

Our study had some limitations. First, the number of patients using antipsychotics in the OPERAM population was low and power to assess DRA might have been limited, as reflected in the rather large confidence intervals. Second, as this study was a posthoc analysis, we had to rely on the data which had previously been collected. For example, we used baseline characteristics to assess factors potentially associated with DRA occurring during the follow-up; however, it is likely that these characteristics were stable over time. Third, the indications of the antipsychotics prescribed were unknown.

The strength of our study rely on it being a secondary analysis of a multicentre international study with a large number of multimorbid and polymedicated patients included, regardless of living situation, pathology, and hospitalisation ward.

In clinical practice, antipsychotics should be reassessed on a regular basis to avoid inappropriate use. Particular attention should be paid to patients with polypharmacy, functional dependency, or using antipsychotics at low-dose. Although drug-related readmissions were not associated with antipsychotic use in our population, this drug class should be used with caution in older adults. Pharmacists have an important role in preventing side effects, optimising treatment and promoting shared decision-making relating to antipsychotic medication [42].

Conclusion

In conclusion, the findings of this analysis highlight that the use of antipsychotics in a multimorbid population of older inpatients with polypharmacy is mainly at a low dose in 8% of patients which tends to increase during hospital stay. Antipsychotic use was unsurprisingly associated with psychiatric comorbidities, but also with a higher

number of drugs, lower alcohol consumption, and greater dependence in daily living. While there was no association between antipsychotic use and drug-related readmission at one-year follow-up, the most frequent causes of antipsychotic-related readmissions were falls and delirium. Antipsychotics should continue to be used with caution in older adults.

Supplementary Information The online version contains supplementary material available at <https://doi.org/10.1007/s11096-024-01700-6>.

Funding This work is part of the project “OPERAM: Optimising theERapy to prevent Avoidable hospital admissions in the Multimorbid elderly” supported by the European Union's Horizon 2020 research and innovation program under the grant agreement No 634238, and by the Swiss State Secretariat for Education, Research and Innovation (SERI) under contract number 15.0137. OPERAM was also partially funded by the Swiss National Scientific Foundation (SNSF 320030_188549 and 325130_204361/1). Juliette Lagreula is a research fellow of the Fonds de la Recherche Scientifique-FNRS (Brussels, Belgium).

Conflicts of interest The authors have no conflicts of interest to declare.

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