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## ORIGINAL ARTICLE



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# Potentially inappropriate medications in nursing homes and the community older adults using the French health insurance databases

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#### Abstract

**Purpose:** Potentially inappropriate medications (PIMs) have become a major issue in improving prescribing practices and reducing the risk of adverse drug events in older people. However, very few studies have compared exposition to PIMs controlling for differences in demographic and health between nursing home residents (NHRs) and community-dwelling older adults (CDOAs). This study aimed to assess the prescribing pattern of PIMs between NHRs and CDOAs.

**Methods:** We conducted a cross-sectional study over three months in 2019 using the French Health Insurance databases. The study population included 274 971 NHRs and 4 893 721 CDOAs aged 75 years or over. The prevalence ratio (PR) between NHRs and CDOAs of 17 PIM indicators, based on the Beers and STOPP criteria lists, was assessed using multivariable robust Poisson regression adjusted for age, sex, diseases, and polypharmacy.

**Results:** During the study period, 54% of NHRs and 29% of CDOAs received at least one PIM. After adjustment, the prevalence of PIMs was 33% higher among NHRs compared to CDOAs (aPR = 1.33; 95% CI [1.33-1.34]). NHRs received PIMs related to benzodiazepines (aPR = 1.43; 95% CI [1.42-1.43]), anticholinergic drugs (aPR = 1.29; 95% CI [1.27-1.31]), and at least three central nervous system-active drugs (aPR = 1.94; 95% CI [1.92-1.96]) more frequently. Prevalence of PIMs related to non-steroidal anti-inflammatory drugs (aPR = 0.50; 95% CI [0.48-0.52]) and longacting benzodiazepines (aPR = 0.84; 95% CI [0.82-0.85]) was lower among NHRs.

**Conclusion:** The NHRs were at greater risk for PIM than CDOAs, although differences exist according to the category of PIMs. As the population is aging, it is essential to promote and evaluate interventions in NHs and the community to enhance medication optimization.

#### KEYWORDS

nursing homes, older adults, pharmacoepidemiology, potentially inappropriate medications

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#### **Key Points**

- Potentially inappropriate medications (PIMs) are drugs that should be avoided whenever possible because of the higher risk of adverse drug events in older adults compared to younger adults.
- Using the French Health Insurance databases, we compared the prevalence of PIMs in nursing home residents and community-dwelling older individuals over three months in 2019.
- After adjustment for age, gender, and 17 chronic diseases, the prevalence of PIMs was 33% higher among nursing home residents compared to community-dwelling older adults.
- However, nursing home residents were less likely to receive long-acting benzodiazepines and inappropriate use of non-steroidal anti-inflammatory drugs than community-dwelling older individuals.
- Both nursing home residents and community-dwelling older adults were more likely to receive PIMs if they had polypharmacy or psychiatric disorders.

#### **Plain Language Summary**

Potentially inappropriate medications (PIMs) are drugs that should be avoided whenever possible in older adults due to poor efficacy or a higher risk of adverse effects. Few studies have compared exposition to PIMs between nursing home residents (NHRs) and community-dwelling older adults (CDOAs). Using the French Health Insurance databases, this study compared 17 PIMs indicators among 274 971 NHRs and 4 893 721 CDOAs aged 75 years or over in 2019. Over a three-month period, 54% of NHRs and 29% of CDOAs received at least one PIM. The prevalence of PIMs was 33% higher among NHRs compared to CDOAs after controlling for differences in demographic and health characteristics between groups. Of note, PIMs related to anticholinergic drugs and co-prescription of central nervous system-active drugs were more frequent among NHRs. On the contrary, PIMs related to non-steroidal anti-inflammatory drugs and long-acting benzodiazepines were less frequent among NHRs. In conclusion, NHRs were globally at greater risk for PIMs than CDOAs in this study, although some PIMs were less frequent among NHRs. As the population is aging, it is essential to promote and evaluate interventions in NHs and the community to enhance medication optimization.

## 1 | INTRODUCTION

As multimorbidity (co-occurrence of two or more medical conditions) increases with age, medication use is common among older adults.<sup>1,2</sup> Polypharmacy, as well as age-related changes in pharmacokinetic and pharmacodynamic properties of medications, make medication safety a critical challenge in older adults.<sup>3,4</sup> Indeed adverse drug reactions (ADRs) are estimated to account for approximately 9% of hospitalizations in older adults.<sup>5</sup>

In this context, particular attention should be paid to the appropriateness of medication for older adults.<sup>6</sup> Potentially inappropriate medications (PIMs) are drugs that should be avoided whenever possible in older adults due to a poor benefit-risk ratio in old age. The use of PIMs in older adults has been associated with an increased risk of ADRs, falls, functional decline, hospitalization, and cost of care.<sup>7</sup> Multiple PIM lists have been drawn up based on expert consensus to assess and improve the quality of prescription practices for older adults.<sup>8</sup>

Nursing home residents (NHRs) are particularly vulnerable to ADRs as they tend to be frailer and have a higher disease burden than community-dwelling older adults (CDOAs).<sup>9</sup> Projections in Europe

predict that the population aged 75 to 84 years will expand by 56% over the 2019–2050 period.<sup>10</sup> As the population is aging, the number of NHRs is increasing. In France, 8.8% of people over the age of 75 years live in institutions, and the number of dependent older adults is expected to increase from 15% to 33% between 2015 and 2030.<sup>11,12</sup>

According to literature reviews, PIM prevalence would appear to be almost 50% higher in NHRs compared to CDOAs (49% vs. 33%, respectively).<sup>7,13</sup> However, this comparison is based on juxtaposing of data from two literature reviews. The higher prevalence of PIMs in NHRs is likely partly explained by older age and a higher level of comorbidity and polypharmacy among NHRs.<sup>9</sup> A proper comparison of PIM prevalence between nursing homes (NHs) and the community would require a standardization of the criteria and the method used for data collection, as well as adjustment for differences in age and health status between groups. On this basis, it could even be hypothesized that expertise in geriatrics and health monitoring in NHs could contribute to better medication use and lower levels of PIMs in NHs. Comparison of the use of PIMs between NHs and the community would help target PIMs requiring specific attention in each setting. The main aim of this study was to describe and compare PIM prevalence between NHRs and CDOAs in France over three months in 2019, using data from the French health insurance databases. Secondly, we explored the patient-related factors associated with PIMs in each setting, to gain a further understanding of the differences between NHs and the community.

## 2 | METHODS

## 2.1 | Study design and data sources

We conducted a cross-sectional study during the second quarter of 2019 (from April 1 to June 30, 2019) on adults aged 75 years or over in France. The second quarter was chosen to avoid seasonal effects, notably winter outbreaks.

This study is based on the French Health Insurance databases (Système National des Données de Santé [SNDS]), which has previously been described as a powerful tool for epidemiological studies.<sup>14,15</sup> The French health insurance system is universal, and registration is compulsory for all French citizens. A unique anonymous individual identifier links information from three national databases, covering ambulatory care (DCIR [Données de Consommation Inter-Régime]), hospital care (PMSI [Programme de Médicalisation des Systèmes d'information]), and medico-social facilities (RESMS [Référentiel des établissements ou services médicosociaux]). The DCIR database includes reimbursed outpatient medical care, including drugs coded according to the anatomic therapeutic chemical (ATC) classification, as well as demographic information (age, sex, date of death). The PMSI database includes information on all hospital admissions and diagnoses, recorded using the International Classification of Diseases, Tenth Revision codes (ICD-10). The RESMS database contains the updated monthly list of residents of medico-social facilities, as well as administrative information on the facilities, such as the presence or absence of a pharmacy department.<sup>16</sup>

## 2.2 | Study population

This study is based on data from the French general health insurance scheme. Various schemes exist according to the beneficiary's occupational sector, of which the general scheme is the most common (covering 75% of the French population). Beneficiaries of the French general health insurance scheme aged between 75 and 110 years on the first day of the second quarter of 2019 and with at least one reimbursement for primary care in 2019 were included. We restricted the study population to those aged 75 years and over because of the increasing risk of adverse events with age and in line with previous work in France.<sup>17</sup> We compared PIM dispensing between NHRs and CDOAs (at home or receiving home care). In order to have two

independent groups, individuals who either left a NH or became a NHR during the quarter were excluded.

The type of assistance provided in NHs can vary according to the country.<sup>18</sup> In France, NHs are long-term care and assisted living facilities with on-site paramedical professionals who support individuals with varying degrees of dependency.<sup>18</sup> NHRs are usually followed by their own general practitioner. Moreover, a coordinating physician, often working part-time in the NH, is in charge of medically assessing the residents, developing and monitoring care, and managing the medical team in the NH. Community pharmacies supply the prescribed drugs for NHRs unless the NH has its own pharmacy department. In the latter case, the DCIR database does not contain any drug dispensing information, and the residents of these NHs were excluded.

## 2.3 | Indicators of PIMs

We assessed PIM indicators adapted from the 2019 Beers' criteria and 2015 STOPP criteria lists that were marketed and reimbursed in France.<sup>19,20</sup> We excluded criteria that could not be fully assessed in the DCIR database, namely those based on drug-disease or drug-syndrome interactions, as well as other criteria requiring information about drug indication or dosage (e.g., proton-pump inhibitors beyond eight weeks without justification). Our final set of criteria included 16 indicators in four therapeutic areas (Benzodiazepines [BZDs], oral Non-Steroidal Anti-Inflammatory Drugs [NSAIDs], drugs with AntiCHolinergic effects [ACH], and AntiHyperTensive drugs [AHT]), as well as an indicator of concomitant use of any combination of three or more central nervous system (CNS)-active drugs (antipsychotics, BZDs, hypnotic Z-drugs, tricyclic anti-depressants, selective serotonin reuptake inhibitors, opioids, and antiepi-leptic drugs). The molecules, ATC codes, and rationale for our set of indicators are available in Table S1.

The PIMs were defined by at least one dispensed item under the corresponding ATC code during the quarter, except for NSAIDs, for which potentially inappropriate use was defined from three dispensed items during the quarter. Criteria related to drug-drug interactions were assessed by considering that drugs delivered on the same day were used concomitantly.

## 2.4 | Other variables

Other variables included age, sex, polypharmacy, and diseases. Polypharmacy was measured as the number of drugs with different ATC codes dispensed during the quarter.<sup>21</sup> Polypharmacy was categorized into three classes: no polypharmacy (0–4 drugs), polypharmacy (5–9 drugs), and hyper-polypharmacy (≥10 drugs).

In order to adjust analyses for health status, the disease and expenditure mapping of the year 2018 was used. Disease and expenditure mapping is an algorithm tool previously developed by the French health insurance, which identifies a list of 58 diseases based on various information reported in the SNDS (hospital diagnoses, declaration of long-term disease, dispensed drugs, and medical



**FIGURE 1** Study population selection, community-dwelling older adults (CDOAs) and nursing home residents (NHRs) aged 75 years or over, France, second quarter 2019

procedures).<sup>22,23</sup> A 17 binary variables corresponding to diseases or groups of diseases were defined in this study, covering cardioneurovascular diseases, diabetes, cancer (active or under surveillance), psychiatric disorders, neurological or degenerative diseases (including Alzheimer's and Parkinson's diseases), chronic respiratory diseases, inflammatory diseases, and other chronic diseases.

## 2.5 | Analyses

Prevalence of PIMs was described according to the place of residence (NH or the community) in numbers and percentages.

The prevalence ratio (PR) and 95% confidence interval (CI) for PIMs between NHRs and CDOAs were assessed using a

multivariable robust Poisson regression model adjusted for age category (75–79 years; 80–84 years; 85–89 years;  $\geq$ 90 years), sex, the 17 disease variables, and polypharmacy.<sup>24</sup> A significant interaction was found between sex and place of residence, and between age and place of residence. As a result, we also provide PR stratified by sex and age categories (75–89 years and  $\geq$ 90 years).

Patient-related factors (age, sex, diseases, and polypharmacy) associated with the dispensing of at least one PIM were explored in multivariable robust Poisson regression models separately for NHRs and CDOAs.

Since many of the PIM indicators are related to CNS drugs, complementary analyses restricted to people with psychiatric disorders, dementia, and Parkinson's disease were conducted. **TABLE 1** Characteristics of community-dwelling older adults (CDOAs) and nursing home residents (NHRs) aged 75 years or over on April 1st, 2019, France.

	CDOAs (N = 4 893 721) n (%)	NHRs (N = 274 971) n (%)	All (N = 5 168 692) n (%)
Sex			
Men	1 963 766 (40.1)	57 511 (20.9)	2 021 277 (39.1)
Women	2 929 955 (59.9)	217 460 (79.1)	3 147 415 (60.9)
Age, in years (mean ± std)	82.5 ± 5.4	89.2 ± 5.9	82.9 ± 5.6
75-79	1 898 459 (38.8)	21 128 (7.7)	1 919 587 (37.1)
80-84	1 506 361 (30.8)	43 939 (16.0)	1 550 300 (30.0)
85-89	984 149 (20.1)	79 833 (29.0)	1 063 982 (20.6)
≥90	504 752 (10.3)	130 071 (47.3)	634 823 (12.3)
Deceased during the quarter	48 421 (1.0)	15 735 (5.7)	64 156 (1.2)
Cardio-neurovascular diseases	1 489 541 (30.4)	123 251 (44.8)	1 612 792 (31.2)
Coronary heart disease	589 454 (12.1)	33 837 (12.3)	623 291 (12.1)
Heart failure	282 075 (5.8)	37 919 (13.8)	319 994 (6.2)
Stroke	250 443 (5.1)	36 875 (13.4)	287 318 (5.6)
Arrhythmia or conduction disorders	615 502 (12.6)	55 257 (20.1)	670 759 (13.0)
Valvular heart disease	154 850 (3.2)	11 092 (4.0)	165 942 (3.2)
Peripheral arterial occlusive disease	203 855 (4.2)	14 281 (5.2)	218 136 (4.2)
Other cardiovascular disease	97 884 (2.0)	6299 (2.3)	104 183 (2.0)
Hypertension without other cardio-neurovascular disease	1 691 387 (34.6)	78 750 (28.6)	1 770 137 (34.3)
Diabetes	849 321 (17.4)	42 110 (15.3)	891 431 (17.3)
Cancer <sup>a</sup>	794 303 (16.2)	38 709 (14.1)	833 012 (16.1)
Psychiatric disorders <sup>b</sup>	237 589 (4.9)	60 257 (21.9)	297 846 (5.8)
Neurological or degenerative diseases	366 680 (7.5)	147 270 (53.6)	513 950 (9.9)
Dementia (including Alzheimer's disease)	237 244 (4.9)	132 399 (48.2)	369 643 (7.2)
Parkinson's disease	89 963 (1.8)	18 013 (6.6)	107 976 (2.1)
Other	64 088 (1.3)	9991 (3.6)	74 079 (1.4)
Chronic respiratory diseases	509 212 (10.4)	30 021 (10.9)	539 233 (10.4)
Inflammatory diseases	132 682 (2.7)	7597 (2.8)	140 279 (2.7)
Other chronic diseases <sup>c</sup>	101 242 (2.1)	5472 (2.0)	106 714 (2.1)
Polypharmacy (mean ± std)	7.0 ± 4.4	8.0 ± 4.1	7.0 ± 4.4
Use of 0 to 4 drugs	1 488 957 (30.4)	51 815 (18.8)	1 540 772 (29.8)
Polypharmacy (5 to 9 drugs)	2 117 099 (43.3)	131 177 (47.7)	2 248 276 (43.5)
Hyper-polypharmacy (≥ 10 drugs)	1 287 665 (26.3)	91 979 (33.5)	1 379 644 (26.7)

<sup>a</sup>Active or under surveillance.

<sup>b</sup>Psychotic disorders, neurotic and mood disorders, and other psychiatric disorders.

<sup>c</sup>HIV, diseases of the liver or pancreas, end-stage renal failure, and hereditary metabolic diseases or amyloidosis.

A sensitivity analysis excluding individuals who died during the study period was performed to assess their weight in the main analysis, although they did not contribute to the full observation period.

## 3 | RESULTS

## 3.1 | Characteristics of study population

Analyses were performed using SAS version 9.4 software (SAS Institute, Inc).

# The selection of the study population is presented in Figure 1. The final study sample included 274 971 NHRs and 4 893 721 CDOAs

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	<b>CDOAs</b> (4,893,721) %	NHRs (274,971) %	aPR [95% CI]	aPR [95% CI]
At least one PIM	28.9	54.3	•	1.33 [1.33-1.34]
Phenothiazine	0.4	2.2		2.56 [2.46-2.65]
Concurrent use of BZD and Z-drugs	1.7	5.6		1.78 [1.74-1.81]
Short and intermediate-acting BZDs	11.4	36	•	1.67 [1.66-1.69]
Hypnotic Z-drugs	7.2	14.6	•	1.43 [1.42-1.45]
Concurrent use of at least two BZD	0.8	2		1.37 [1.32-1.41]
Concurrent use of opioids and BZD	2.7	5.1	•	1.27 [1.25-1.30]
Anti-H1	2.4	3.7	-	1.22 [1.19-1.25]
CCB* immediate release	2.5	3.7	•	1.16 [1.14-1.19]
Tricyclic antidepressants	1.6	2	•	0.94 [0.92-0.97]
Long-acting BZDs	5.8	5.4	•	0.84 [0.82-0.85]
Chronic use of oral NSAIDs	1.4	0.8	•	0.71 [0.68-0.75]
Concurrent use of BB and CCB**	0.2	0.1	-	0.69 [0.60-0.78]
Central alpha-blockers	2.2	1.1	•	0.59 [0.56-0.61]
Concurrent use of NSAIDs and OAC	0.2	0.1	+	0.36 [0.32-0.42]
Concurrent use of NSAIDs and APT	1.1	0.2	•	0.28 [0.26-0.31]
Concurrent use of 2 or more NSAIDs	0.1	0.01		0.16 [0.12-0.23]
			0.4 1 2	2

**FIGURE 2** Adjusted Prevalence Ratio (aPR) for potentially inappropriate medications (PIMs) by place of residence (nursing home vs. community), second quarter of 2019, France. ANTI-H1, first-generation Antihistamine; APT, anti-platelet agent; BB, β-blocker; BZD, benzodiazepine; CCB, selective calcium channel blocker; NSAID, nonsteroidal anti-inflammatory drug; OACs, oral anticoagulants. \*Nifedipine or nicardipine, \*\*Verapamil or diltiazem.

(Figure 1). NHRs came from 5380 NHs (out of about 8100 NHs in 2019 in France). As reported in Table 1, NHRs were older (89.2  $\pm$  5.9 vs. 82.5  $\pm$  5.4 years) and more likely to be female (79% vs. 60%) than CDOAs. The proportion of neurological or degenerative diseases was seven times higher in NHRs than in CDOAs; specifically, 48% of NHRs had dementia versus 5% of CDOAs. Among NHRs, hyper-polypharmacy frequency was 33% compared with 26% among CDOAs.

# 3.2 | Prevalence of PIMs in NHs and in the community

In the second quarter of 2019, 54% of NHRs and 29% of CDOAs received at least one PIM. After adjustment for confounders, the prevalence of PIMs was 33% higher among NHRs compared to CDOAs (aPR [95% CI] = 1.33 [1.33-1.34]) (Table 1). The most frequent PIMs in NHRs were short- and intermediate-acting BZDs (36%), followed by concomitant use of CNS-active drugs (18%) and hypnotic Z-drugs (14.6%) (Figure 2). In CDOAs, the most frequent PIMs were short- and intermediate-acting BZDs (11.4%), hypnotic

Z-drugs (7.2%), and long-acting BZDs (5.8%) (Figure 2). Compared to CDOAs, NHRs received BZD-related PIMs (aPR [95% CI] = 1.43 [1.42–1.43]) and ACH drug-related PIMs (aPR [95% CI] = 1.29 [1.27–1.31]) more frequently (Table 2). The prevalence of concomitant use of CNS-active drugs was almost two times greater in NHRs than in CDOAs. On the other hand, the prevalence of NSAID-related PIMs was 50% lower in NHs compared to the community. NHRs and CDOAs had a similar prevalence of AHT drug-related PIMs.

Figure 2 illustrates the differences in PIM prevalence for each individual indicator. The most significant difference in PIM prevalence was observed for phenothiazines, with NHRs being more exposed than CDOAs (aPR [95% CI] = 2.56 [2.46-2.65]). NHRs also received BZDs more frequently, except for longacting BZDs, for which the prevalence was 15% lower than in the community. The prevalence of concurrent use of two or more NSAIDs was also lower among NHRs (aPR [95% CI] = 0.16 [0.12-0.23]).

Table 2 shows that the magnitude of the difference varies between men and women (results are also presented graphically for each indicator in Figure S1). Indeed, the differences between NHRs

**TABLE 2** Prevalence ratio (PR) for potentially inappropriate medications (PIMs) between nursing home residents (NHRs) and communitydwelling older adults (CDOAs) and stratified by sex and age category, second quarter of 2019, France.

	CDOAs (N = 4 893 721)	NHRs (N = 274 971)	PR [95% CI]	
	n (%)	n (%)	Unadjusted	Adjusted <sup>a</sup>
At least one PIM during the quarter	1 412 225 (28.9)	149 245 (54.3)	1.88 [1.87 to 1.89]	1.33 [1.33 to 1.34]
Men	436 816 (22.2)	29 635 (51.5)	2.32 [2.30 to 2.34]	1.51 [1.50 to 1.53]
Women	975 409 (33.3)	119 610 (55.0)	1.65 [1.65 to 1.66]	1.30 [1.29 to 1.30]
(75–90)	1 244 363 (28.4)	83 008 (57.3)	2.02 [2.01 to 2.03]	1.38 [1.37 to 1.38]
≥90	167 862 (33.3)	66 237 (50.9)	1.53 [1.52 to 1.54]	1.31 [1.30 to 1.32]
Anticholinergic drug-related PIMs	205 637 (4.2)	20 646 (7.5)	1.79 [1.76 to 1.81]	1.29 [1.27 to 1.31]
Men	60 969 (3.1)	4338 (7.5)	2.43 [2.36 to 2.50]	1.45 [1.40 to 1.50]
Women	144 668 (4.9)	16 308 (7.5)	1.52 [1.50 to 1.54]	1.27 [1.25 to 1.29]
(75–90)	187 169 (4.3)	12 796 (8.8)	2.07 [2.04 to 2.11]	1.24 [1.21 to 1.26]
≥90	18 468 (3.7)	7850 (6.0)	1.65 [1.61 to 1.69]	1.34 [1.30 to 1.38]
Non-steroidal anti-inflammatory drug-related PIMs	122 433 (2.5)	2627 (1.0)	0.38 [0.37 to 0.40]	0.50 [0.48 to 0.52]
Men	46 666 (2.4)	587 (1.0)	0.43 [0.40 to 0.47]	0.54 [0.50 to 0.59]
Women	75 767 (2.6)	2040 (0.9)	0.36 [0.35 to 0.38]	0.49 [0.47 to 0.51]
(75–90)	113 913 (2.6)	1409 (1.0)	0.37 [0.36 to 0.39]	0.42 [0.40 to 0.44]
≥90	8520 (1.7)	1218 (0.9)	0.55 [0.52 to 0.59]	0.59 [0.55 to 0.63]
Benzodiazepine-related PIMs	1 054 221 (21.5)	130 909 (47.6)	2.21 [2.20 to 2.22]	1.43 [1.42 to 1.43]
Men	298 171 (15.2)	25 557 (44.4)	2.93 [2.90 to 2.96]	1.68 [1.66 to 1.70]
Women	756 050 (25.8)	105 352 (48.5)	1.88 [1.87 to 1.89]	1.38 [1.38 to 1.39]
(75–90)	921 098 (21.0)	72 640 (50.1)	2.39 [2.38 to 2.40]	1.48 [1.47 to 1.49]
≥90	133 123 (26.4)	58 269 (44.8)	1.70 [1.69 to 1.71]	1.41 [1.40 to 1.42]
≥ 3 CNS-active drugs	205 663 (4.2)	49 377 (18.0)	4.27 [4.23 to 4.31]	1.94 [1.92 to 1.96]
Men	48 381 (2.5)	9707 (16.9)	6.85 [6.71 to 6.99]	2.39 [2.33 to 2.46]
Women	157 282 (5.4)	39 670 (18.2)	3.40 [3.36 to 3.43]	1.86 [1.83 to 1.88]
(75–90)	184 535 (4.2)	32 596 (22.5)	5.35 [5.29 to 5.41]	1.90 [1.88 to 1.92]
≥90	21 128 (4.2)	16 781 (12.9)	3.08 [3.02 to 3.14]	1.96 [1.92 to 2.01]
Antihypertensive drug-related PIMs	227 724 (4.7)	13 210 (4.8)	1.03 [1.01 to 1.05]	0.94 [0.92 to 0.96]
Men	82 124 (4.2)	2252 (3.9)	0.94 [0.90 to 0.98]	0.87 [0.84 to 0.91]
Women	145 600 (5.0)	10 958 (5.0)	1.01 [1.00 to 1.03]	0.94 [0.92 to 0.96]
(75-90)	199 437 (4.5)	6534 (4.5)	0.99 [0.97 to 1.02]	0.98 [0.95 to 1.00]
≥90	28 287 (5.6)	6676 (5.1)	0.92 [0.89 to 0.94]	0.94 [0.91 to 0.96]

<sup>a</sup>Adjusted for chronic diseases, polypharmacy, and mutually adjusted for age and sex.

and CDOAs were more significant among men than women for most criteria. No major difference between age groups was observed. The stratified analyses according to the presence of psychiatric disorders, dementia or Alzheimer's disease and, Parkinson's disease are presented in Table S2. Of note, the difference in the prevalence of PIMs between NHs and the community was attenuated in people having psychiatric disorders (aPR [95% CI] = 1.16 [1.15-1.17]), whereas it was in line with the main analysis for those having Parkinson's disease (aPR [95% CI] = 1.25 [1.23-1.27]) or dementia (aPR [95% CI] = 1.39 [1.38-1.40]).

During the second quarter of 2019, the death rate was 1% in the community and 6% in NHs. There was no difference in the prevalence

of PIMs when people who had died were excluded from the analysis (Table S3).

# 3.3 | Factors associated with PIMs in NHs and in the community

The factors most associated with PIMs were polypharmacy, psychiatric disorders, and neurological or degenerative diseases in both NHs and the community (Table 3). It is worth noting that being aged 90 years or older was associated with an increased prevalence of PIMs in the community (aPR = 1.06; 95% CI [1.06–1.07]), whereas in

	CDOAs (N = 4 893 721)		NHRs (N = 274 971)	
	Unadjusted PR [95% CI]	Adjusted PR <sup>a</sup> [95% CI]	Unadjusted PR [95% CI]	Adjusted PR [95% CI]
Age, in years				
75-89	1.0	1.0	1.0	1.0
≥90	1.17 [1.17-1.18]*	1.06 [1.06-1.07]*	0.89 [0.88-0.90]*	0.93 [0.92-0.93]*
Sex				
Men	1.0	1.0	1.0	1.0
Women	1.50 [1.49-1.50]*	1.17 [1.17-1.17]*	1.07 [1.06-1.08]*	1.04 [1.03-1.04]*
Cardio-neurovascular diseases				
No	1.0	1.0	1.0	1.0
Yes	1.19 [1.19-1.19]*	0.89 [0.89-0.90]*	0.99 [0.99-1.00]	0.87 [0.86-0.88]*
Diabetes				
No	1.0	1.0	1.0	1.0
Yes	1.14 [1.14-1.15]*	0.86 [0.86-0.87]*	1.00 [0.99-1.01]	0.87 [0.87-0.88]*
Cancer				
No	1.0	1.0	1.0	1.0
Yes	1.06 [1.06-1.07]*	1.01 [1.01-1.02]*	1.02 [1.01-1.03]*	0.99 [0.98-1.00]
Psychiatric disorders				
No	1.0	1.0	1.0	1.0
Yes	2.22 [2.21-2.23]*	1.66 [1.65-1.67]*	1.37 [1.36-1.38]*	1.25 [1.24-1.25]*
Neurological or degenerative diseases				
No	1.0	1.0	1.0	1.0
Yes	1.30 [1.30-1.31]*	1.10 [1.10-1.11]*	1.00 [0.99-1.00]	1.06 [1.05-1.06]*
Dementia (including Alzheimer's)				
No	1.0	1.0	1.0	1.0
Yes	1.28 [1.27-1.29]*	1.13 [1.12-1.13]*	0.99 [0.98-1.00]	1.08 [1.07-1.08]*
Parkinson's disease				
No	1.0	1.0	1.0	1.0
Yes	1.32 [1.31-1.33]*	1.03 [1.02-1.03]*	1.02 [1.01-1.04]*	0.93 [0.92-0.94]*
Chronic respiratory diseases				
No	1.0	1.0	1.0	1.0
Yes	1.30 [1.29-1.30]*	0.94 [0.94-0.95]*	1.06 [1.05-1.07]*	0.94 [0.93-0.95]*
Inflammatory diseases				
No	1.0	1.0	1.0	1.0
Yes	1.21 [1.20-1.22]*	0.92 [0.91-0.92]*	1.04 [1.02-1.07]*	0.94 [0.92-0.95]*
Polypharmacy				
Use of 0 to 4 drugs	1.0	1.0	1.0	1.0
Polypharmacy (5 to 9 drugs)	3.57 [3.55-3.59]*	3.57 [3.55-3.59]*	2.29 [2.26-2.33]*	2.34 [2.30-2.38]*
Hyper-polypharmacy (≥ 10 drugs)	6.32 [6.28-6.35]*	6.47 [6.43-6.50]*	3.15 [3.10-3.20]*	3.35 [3.29-3.40]*

**TABLE 3** Factors associated with receiving at least one potentially inappropriate medication (PIM) in community-dwelling older adults (CDOAs) and in nursing home residents (NHRs) during the second quarter of 2019, France.

<sup>a</sup>Mutually adjusted for age, sex, chronic diseases, and polypharmacy.

\*P-value for Chi-square test <0.05.

NHs older residents were less likely to receive PIMs compared to their younger counterparts (aPR = 0.93; 95% CI [0.92-0.93]). Whether in NHs or the community, women were more likely to receive PIMs than

men, although differences were more pronounced in the community. Regarding other diseases, similar associations were found in NHs and the community (Table 3).

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## 4 | DISCUSSION

Our study shows that 54% of NHRs and 29% of CDOAs received at least one PIM over three months in 2019. After accounting for differences in age, sex, and diseases between these two populations, the prevalence rate of PIMs was still 33% higher in NHs compared to the community. This result confirms that NHRs are particularly exposed to PIMs, while they may be more vulnerable to ADRs. However, disparities underlie this overall result. While NHRs received PIMs related to BZDs, ACH drugs, and concomitant use of CNS-active drugs more frequently than CDOAs, long-acting BZDs and NSAID-related PIMs were used less among NHRs. In both settings, dispensing at least one PIM was strongly associated with polypharmacy and psychiatric disorders.

Previous studies using the French national health insurance database estimated the prevalence of PIMs to be 53% in people aged 75 years or over in 2007 (annual prevalence) and 32% in people aged 75 years or over in 2014 (three-month prevalence).<sup>17,25</sup> Aside from some methodological variations, we can say that our result of 29% is in line with these results and is part of a downward trend.<sup>26</sup> In NHRs, the level we observed is within the wide range of PIM prevalence reported in previous studies in France (30%-77%).<sup>25,27-30</sup> In this context, our study provides an updated estimate of PIM prevalence in NHRs based on large-scale and reliable data. Furthermore, as we used the same definition and measurement methods to assess PIMs among NHRs and CDOAs, we were able to compare PIM prevalence between the two settings.

Our findings show that NHRs were more exposed to PIMs than CDOAs. Previous studies have reported a positive association between institutionalization and PIMs.<sup>31,32</sup> In contrast, a study based on claims data in Ontario, Canada in 2001 has shown that NHRs had a 50% lower risk of exposure to PIMs.<sup>33</sup> This result may be explained by the practice of 3-monthly medication reviews by the pharmacy department of the NHs included in this study, while there was no equivalent in the community at the time of the study. In Belgium, a cluster-randomized control trial has shown that a complex multifaceted intervention (including training programs, interdisciplinary meetings, and medication reviews) improved the appropriateness of prescribing practices in NHs.<sup>34</sup> These results raise the question of the role of organizational factors in NHs to help prevent ADRs. In France, the presence of a coordinating physician within NHs could help organize actions to prevent ADRs among the residents. However, the current organization of NHs is not yet tailored to implement medication reviews on a systematic basis. In CDOAs, randomized controlled trials have also demonstrated that pharmacist intervention, computerized clinical decision support information, and multifaceted interventions were effective in reducing PIMs.<sup>35</sup> However, as ADRs are multifactorial, the direct impact of these interventions on clinical outcomes (such as hospitalization, quality of life, and ADRs) and the feasibility of their large-scale implementation are not well established.35,36

As previously reported, the pattern of individual PIM indicators differed according to the place of residence.<sup>25,37</sup> This difference could

be related to distinct goals and organization of care between the community and NH. For instance, the highest difference in prevalence was reported for phenothiazines, which may be explained by their use for sedative purposes in end-of-life care (chlorpromazine) in NH. The use of three or more CNS-active drugs was almost twice more frequent in NHRs compared to CDOAs. Differences in severity and intensity of behavioral symptoms could partly explain the higher use of CNS-active drugs, especially BZDs, in NHRs. Another partial explanation could be the higher rate of prescriptions "to be given if needed" in NHRs, although we could not verify this hypothesis. On the other hand, our study also shows a lower use of long-acting BZDs in NHRs compared to CDOAs. The lower level of exposure to long-acting BZDs and NSAIDs-related PIMs in NHRs could reflect the awareness of physicians working in NHs of the risks of these medications in old age. Indeed, a recent study in France reported a decrease in the use of long-acting BZDs and NSAIDs after admission to NHs, suggesting the role of institutionalization in medication changes.<sup>38</sup>

Because interventions to reduce PIMs are not easily implementable across the entire older population, identifying patientrelated factors associated with PIM exposure could help target older people at a higher risk of receiving PIMs. As observed in previous studies, our results suggest that specific attention should be paid to patients with polypharmacy, as well as patients with psychiatric or neurological disorders consistently in NHs and the community.<sup>13,39,40</sup>

This is the largest study to compare the frequency of PIMs between NHRs and CDOAs based on the French Health Insurance databases. Indeed, the study was carried out on more than 200 000 NHRs, while there was a capacity of about 600 000 beds in France in 2019. The set of PIM criteria used in this study can be easily measured and used to monitor prescribing practices in older adults living in NHs and the community at a national level. Another strength of this study is that we adjusted the comparison of PIM prevalence between NHs and the community for age, sex, polypharmacy, and a number of diseases. However, our study faces several limitations. First, the use of claims data restricted the assessment of medications to reimbursed drugs dispensed in community pharmacies. In this way, NSAIDs and ACH drugs taken without a prescription could not be considered, although self-medication may be limited in NHRs. Second, residents of NHs with a pharmacy department were excluded. Third, we lacked information on some potential residual confounding factors, such as frailty, severity of diseases, and disability. NHRs are potentially less healthy and have more advanced diseases such as dementia or Parkinson's disease, which could partly explain a higher use of psychoactive drugs in NHRs. Finally, we did not assess all the criteria included in the Beers and STOPP lists.

## 5 | CONCLUSION

About half of NHRs and one-third of CDOAs were exposed to at least one PIM over three months in 2019. Although NHRs had a 33%

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increased risk of receiving PIMs compared to CDOAs, we observed different patterns of PIMs according to the place of residence, with more sparing use of long-acting BZD and NSAIDs in NHRs. All these results together may help to refine priorities for intervention in NHs and the community.

#### AUTHOR CONTRIBUTIONS

This study is a part of Solene Drusch's PhD thesis supervised by Marie Herr and Mahmoud Zureik Marie Herr and Mahmoud Zureik conceptualized the study. Marie Herr, Mahmoud Zureik, Joel Ankri and Solene Drusch designed the methodology, Solene Drusch and Thien Le Tri extracted and managed the data, Solene Drusch performed the analyses under the supervision of Marie Herr, Solene Drusch wrote the manuscript, Marie Herr, Mahmoud Zureik, Joel Ankri and H.M. reviewed and edited the manuscript. Thien Le Tri reviewed the manuscript. Mahmoud Zureik. Solene Drusch and Thien Le Tri have full access to the data.

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#### CONFLICT OF INTEREST

The authors have no competing interests to declare that are relevant to the content of this article.

### DATA AVAILABILITY STATEMENT

In accordance with data protection legislation and French regulations, the authors cannot publicly release data from the French National Health Data System (SNDS). However, any person or structure, public or private, for-profit or non-profit, is entitled to access SNDS data upon authorization from the French Data Protection Office (CNIL), for the purposes of carrying out a study, research or an evaluation in the public interest (https://www.snds.gouv.fr/ SNDS/Processus-d-acces-aux-donnees and https://www.indsante. fr/). EPI-PHARE has permanent regulatory access to data from the French National Health Data System (SNDS) via its constitutive bodies ANSM and CNAM. This permanent access is given in accordance with French Decree No. 2016-1871 of December 26, 2016 relating to personal data processing under the French National Health Data System (SNDS), and French law articles Art. R. 1461-13 and 14. All requests in the database were made by duly authorized people. In accordance with the permanent regulatory access granted to EPI-PHARE via ANSM and CNAM, this work did not require the approval of the French Data Protection Authority (CNIL). The study was registered on the study register of EPI-PHARE for studies based on SNDS data.

#### **ETHICS STATEMENT**

This study has been authorized and conducted according to decree 2016-1871 of December 26, 2016 relating to personal data processing under the French National Health Data System (SNDS), and French law articles Art. R. 1461-1323 and 1424(5). As permanent user of SNDS, the authors team is exempted from Institutional Review Board approval. Given that data are anonymous, informed consent to participate is not required.

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## SUPPORTING INFORMATION

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

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