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ORIGINAL REPORT

Prescribing potentially inappropriate medication (PIM) in Germany's elderly as indicated by the PRISCUS list. An analysis based on regional claims data

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ABSTRACT

Purpose The aim of this study was to estimate the prevalence of potentially inappropriate medication (PIM) in the elderly as indicated by Germany's recently published list (PRISCUS) and to assess factors independently associated with PIM prescribing, both overall and separately for therapeutic groups.

Methods Claims data analysis (Health Insurance Sample AOK Hesse/KV Hesse, 18.75% random sample of insurants from AOK Hesse, Germany) is used in the study. The study population is composed of 73 665 insurants >64 years of age continuously insured in the last quarter of 2009 and either continuously insured or deceased in 2010. Prevalence estimates are standardized to the population of Germany (31 December 2010). The variables age, sex, polypharmacy, hospital stay and nursing care are assessed for their independent association with general PIM prescription and among 11 therapeutic subgroups using multivariate logistic regression analysis.

Results In 2010, 22.0% of the elderly received at least one PIM prescription (men: 18.3%, women: 24.8%). The highest PIM prevalence was observed for antidepressants (6.5%), antihypertensives (3.8%) and antiarrhythmic drugs (3.5%). Amitriptyline, tetrazepam, doxepin, acetyldigoxin, doxazosin and etoricoxib were the most frequently prescribed PIMs. Multivariate analyses indicate that women (OR 1.39; 95% CI: 1.34–1.44) and persons with extreme polypharmacy (≥10 vs. <5 drugs: OR 5.16; 95% CI: 4.87–5.47) were at higher risk for receiving a PRISCUS-PIM. Risk analysis for therapeutic groups shows divergent associations.

Conclusion PRISCUS-PIMs are widely used. Educational programs should focus on drugs with high treatment prevalence and call professionals' attention to those elderly patients who are at special risk for inappropriate medication. Copyright © 2013 John Wiley & Sons, Ltd.

KEY WORDS—potentially inappropriate medication; elderly; prevalence; risk factors; claims data; pharmacoepidemiology

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INTRODUCTION

Since publication of the first compilation of potentially inappropriate medications (PIMs) for the elderly in the USA in 1991—the Beers list[1] and its later updates[2–4]—there is an ongoing discussion about the benefits and usefulness of such lists. Prevalence estimations of PIM use, mostly referring to the Beers list, have been reported for many countries, settings and patient groups[5–18] with wide variations from, for example, 15% in a non-institutionalized population in Finland[14] to 48% in long-term residents in the region of Umbria in Italy.[13] Many studies found that the listed drugs are not up to date or not marketed in their respective countries.[7,9,13,14] Country specific PIM lists or criteria for assessing PIM prescriptions were developed.[19–25] For Germany, a specific PIM list, the so-called PRISCUS list, was developed by a council of 27 experts with eight different specialist backgrounds. The list consists of 83 PIMs together with recommendations for possible therapeutic alternatives and precautions in the case of application.[26]

The first prerequisite for the improvement of prescribing habits is transparency about PIM use. Hence, one aim of the study was to analyze overall PIM prevalence as indicated by the PRISCUS list and to identify the most frequently prescribed PIM drugs by using regional health insurance data. A further aim was to provide the first-ever assessment of risk factors for prescribing PRISCUS-PIM in general and for 11 therapeutic drug classes.

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METHODS

Data source

The analysis is based on claims data, the "AOK Hesse/KV Hesse Statutory Health Insurance Sample", an 18.75% random sample of all subjects insured by AOK Hesse, a local statutory health insurance provider.[27] The observation period is the year 2010. In 2010, the German federal state of Hesse had a population of about 6.1 million people, 1.5 million of whom were insured by the AOK. The data were provided by the AOK Hesse and the KV Hesse, the association of SHI-accredited physicians in Hesse. The utilization of the database for research purposes was approved by the Ministry of Social Affairs of Hesse.

For the purpose of the study, the following information of each insured person was used: age, gender, time insured, German modification of the International Classification of Diseases 10th edition (ICD-10-GM) coded diagnoses (ambulatory care), hospital stay, nursing care and prescribed drugs. The database comprises all prescription data for ambulatory care for drugs being reimbursed by the SHI. Because of the nature of the administrative database, information on over-the-counter drugs and other clinical data like body mass index or blood pressure are not included. Several health care research studies have been conducted with this database.[28–31]

PRISCUS-PIM

For the analysis, we included all drugs on the PRISCUS list classified with "1" (drugs to avoid) or "2" (indicating formulations that are not recommended). Drugs rated as PIM for higher doses (e.g., Haloperidol >2 mg, in total nine drugs on the PRISCUS-list) were not included, as calculation of actually used doses is hampered by the defined daily dose (DDD)-methodology. The PRISCUS list contains PIMs out of 15 therapeutic subgroups (cf. Holt *et al.* [26]).

Study populations

The study population for prevalence estimates comprised all insurants >64 years of age continuously insured in the last quarter of 2009 and either continuously insured or deceased in 2010 ($n = 73\,665$, Figure 1). Definition of PIM user: receiving at least one prescription of an explicit PRISCUS-drug in 2010 that was reimbursed by the sickness fund.

When comparing PIM recipients to recipients without any PIM drug and for the analysis of risk factors for PIM prescribing, only persons receiving at least one prescription from the 15 therapeutic subgroups (PIM or no PIM) were included. Risk factors for PIM use are analyzed according to 11 of the 15 therapeutic subgroups only, because, in four subgroups (antithrombotic drugs, antibiotics, ergotamine and laxatives), the sample size was too low (proportion of PIM < 5%). The study population for risk analysis comprised 41 808 persons.

Risk assessment for PIM prescribing

The following factors possibly influencing the prescribing of a PRISCUS drug were assessed: (i) sex; (ii) age; (iii) number of different drugs according to Anatomical Therapeutic Chemical (ATC) classification system (5th level, chemical substance) prescribed in the year 2010 (less than five different drugs, five to nine different drugs, and 10 and more different drugs); (iv) hospital stay in the last quarter of 2009 (yes/no); and (v) nursing care status (at least one documented nursing care service in the last quarter of 2009, yes/no), place of nursing care (ambulatory nursing care and institutionalized nursing care). In cases where different places of care were documented, the person was assigned to institutionalized care. We did not consider the number of different diagnoses as risk factors for PIM prescription because multicollinearity has been shown in other studies.[7]

Statistics

Treatment prevalence was standardized according to age and sex distribution of the population of Germany on 31 December 2010. Confidence intervals (95%) were computed for proportions. Differences between the populations receiving a PRISCUS drug or no PRISCUS drug were assessed by chi square test for categorical variables. Multivariate logistic regression was performed to determine independent risk factors for PIM prescribing. Odds ratios (ORs) and 95% confidence intervals were calculated. For all tests, a p-value <0.05 was considered to be statistically significant. All analyses were performed using SAS for Windows Version 9.2 (SAS Institute Inc, Cary, NC, USA). Database software was MS-SQL-Server 2008 for Windows Server 2003.

Sensitivity analysis

To further assess the robustness of our findings regarding risk factors for PIM use in therapeutic subgroups, a sensitivity analysis on exposure was performed. In the therapeutic groups with a wide range of indications (analgesics/anti-inflammatory drugs, anticholinergic drugs, antihypertensives and neuroleptics), the three main diagnoses for receiving a prescription for the respective indication were included in the regression model to control for confounding by indication. To evaluate the diagnoses in 2010, we compared the PIM recipients with sex and age-matched controls. The first three diagnoses with

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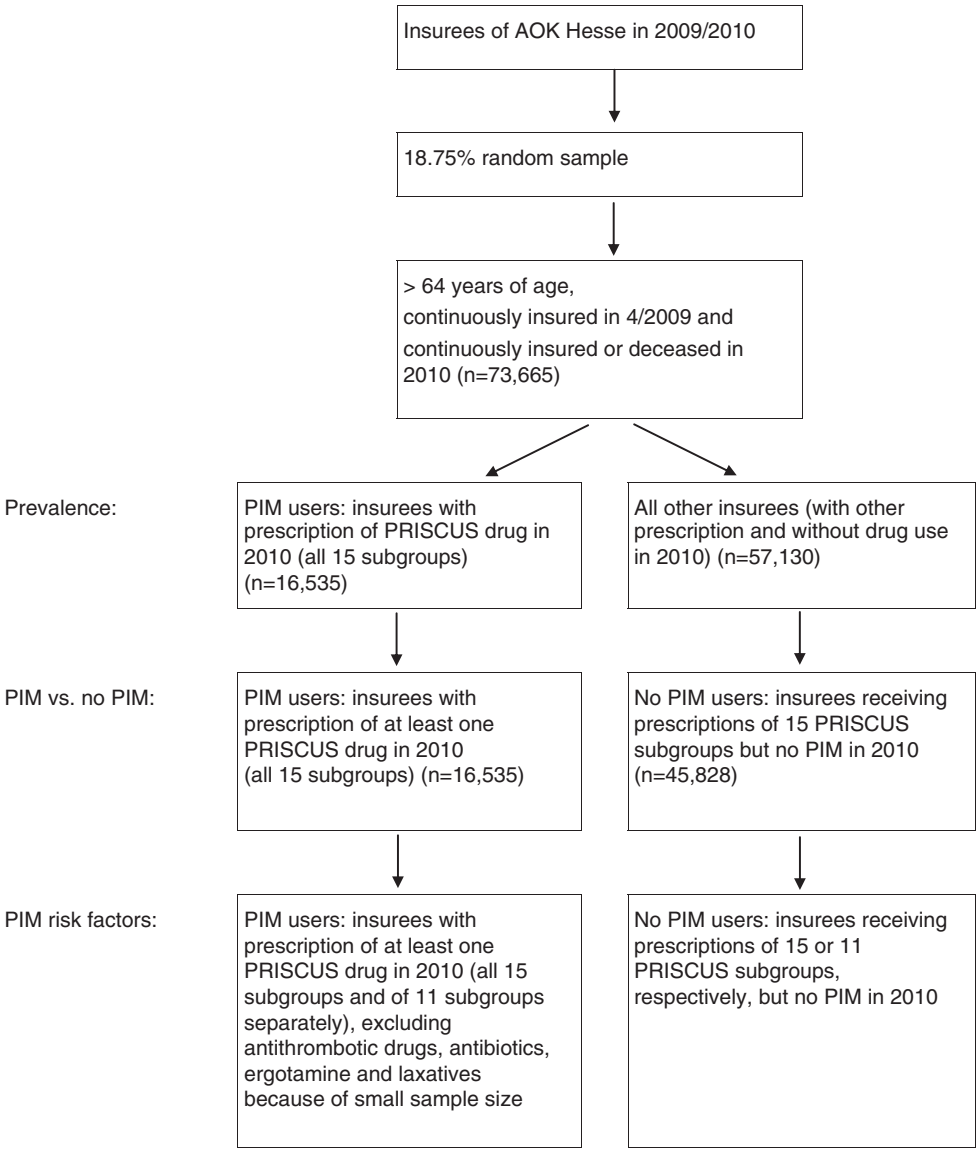

Figure 1. Study population

higher prevalence in patients with PIM compared with controls were rated as specific for PIM-recipients, and they accounted for (yes/no) influencing factors in the regression analysis. For the diagnoses, see e-Table 1.

RESULTS

Treatment prevalence

Raw and standardized prevalence estimates for PIM use in 2010 are given in Table 1. Overall, 22.0% of the elderly received at least one PIM prescription (men: 18.3%, women: 24.8%). Extrapolated to the population of Germany in 2010, this equals about 3.7 million persons. PIM use increased with age. For those with nursing care, the standardized treatment prevalence with PIM was 36.6% (32.9% ambulatory, 34.6% institutionalized).

In Table 2, the treatment prevalence for therapeutic subgroups is presented. The highest PIM treatment prevalence was observed for antidepressants, with 6.5% of all insured persons (65 years and older) receiving a PIM-prescription of this indication group. A total of 3.8% of all insured individuals received at least one PIM prescription with an antihypertensive drug.

Overall, the most frequently prescribed drugs were amitriptyline (2.8%), tetrazepam (2.3%), doxepin (2.2%), acetyldigoxin (1.7%), doxazosin (1.3%) and etoricoxib (1.3%). Among patients with a PIM prescription ($n = 16\,535$), 48.7% received one of these drugs (prevalence estimates for PIM $\geq 0.5\%$, see Table 3; for each active

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Table 1. Treatment prevalence of insured elderly with drugs of the PRISCUS list (PIM) according to gender and age groups in 2010

	Men		Women		Total	
Age (years)	*n*	% (95% CI)	*n*	% (95% CI)	*n*	% (95% CI)
65–69	1178	15.6 (14.8–16.5)	1598	21.2 (20.3–22.2)	2776	18.4 (17.8–19.0)
70–74	1638	17.4 (16.7–18.2)	2614	24.3 (23.5–25.1)	4252	21.1 (20.6–21.7)
75–79	1340	20.0 (19.1–21.0)	2442	27.0 (26.1–27.9)	3782	24.0 (23.3–24.7)
80–84	927	22.0 (20.8–23.3)	2042	27.1 (26.1–28.1)	2969	25.3 (24.5–26.1)
≥85	548	21.3 (19.8–23.0)	2208	26.4 (25.5–27.4)	2756	25.2 (24.4–26.0)
Total	5631	18.5 (18.1–19.0)	10904	25.2 (24.8–25.6)	16535	22.4 (22.1–22.8)
Standardized*		18.3		24.8		22.0

PIM, potentially inappropriate medication.
Study population 1: $n = 73\,665$ persons age 65 years and older.
*Standardized to the population of Germany (31 December 2010).

Table 2. Prevalence of PIM prescriptions according to different therapeutic subgroups in 2010

	Men		Women		Total	
PIM within	*n*	%	*n*	%	*n*	%
Antidepressants (N06A, N06C)	1215	4.0	3577	8.3	4792	6.5
Antihypertensives (C02, C08, N07BB06)	1201	3.9	1591	3.7	2792	3.8
Antiarrhythmic drugs (C01A, C01B, C07A, C07B, C08D)	888	2.9	1686	3.9	2574	3.5
Sedatives/anxiolytic drugs (N05B, N05C, N01BX06)	715	2.3	1776	4.1	2491	3.4
Analgesics/antiinfl. drugs (M01, N02 excl. N02C; R05XA10)	787	2.6	1421	3.3	2208	3.0
Muscle relaxants (M03)	674	2.2	1237	2.9	1911	2.6
Anticholinergic drugs (G04, R06)	513	1.7	891	2.1	1404	1.9
Antidementia drugs (C04, N06B, N06D)	353	1.2	431	1.0	784	1.1
Antibiotics (J01)	206	0.7	554	1.3	760	1.0
Antiepileptics (N03, N05C)	116	0.4	285	0.7	401	0.5
Neuroleptics (N05A excl. N05AD01, N05AH03)	127	0.4	167	0.4	294	0.4
Antiemetics (A04)	10	0.0	26	0.1	36	0.0

PIM, potentially inappropriate medication.

Table 3. Treatment prevalence of the insured population (≥ 0.5%) and of PIM recipients in 2010

ATC	Substance	% Insured	% PIM-recipients
N06AA09	Amitriptyline	2.8	12.6
M03BX07	Tetrazepam	2.3	10.1
N06AA12	Doxepin	2.2	9.8
C01AA02	Acetyldigoxin	1.7	8.4
C02CA04	Doxazosin	1.3	5.8
M01AH05	Etoricoxib	1.3	5.7
N05BA08	Bromazepam	1.2	5.5
N06AA06	Trimipramine	1.1	4.9
C08CA05	Nifedipine	1.0	4.6
N05BA01	Diazepam	1.0	4.5
J01XE01	Nitrofurantoin	0.9	4.5
C07AA07	Sotalol	0.8	3.9
C02AC01	Clonidine	0.7	3.2
G04BD04	Oxybutynin	0.7	3.4
M01AC06	Meloxicam	0.6	2.5
G04BD08	Solifenacin	0.5	2.4

PIM, potentially inappropriate medication.

substance, see e-Table 2). The mean number of PIM prescriptions per year was 3.5 for men and 3.7 for women.

Factors associated with PIM prescribing

A description of the study population according to PIM drug use is given in Table 4. Of all 16 535 persons with a PIM prescription, 34% were men and 66% were women with a mean age of 75.3 years (SD: 6.6 years) and 77.7 years (SD: 7.6 years), respectively. Unadjusted, a higher percentage of PIM users than non-users received 10 or more different drugs. For PIM recipients, a higher number of hospital stays and a significantly higher percentage of nursing care receipt were documented.

To identify factors associated with PIM prescription in prevalent users, multivariate logistic regression analysis was conducted for all PIM prescriptions (Table 5) and for selected indication subgroups (Table 6). When mutually adjusting for all variables presented in the table, female gender and receiving more than five different drugs were associated with PIM prescribing.

Table 6 presents the results of the multivariate analysis for 11 indications groups. For most of these indications (analgesics/anti-inflammatory drugs, antidementia drugs, antidepressants, neuroleptic drugs, muscle relaxants and sedatives/anxiolytic drugs), age is inversely related to PIM prescribing when adjusted for all other variables in the table. But people >70 years of age with a prescription of antiarrhythmic drugs had a higher risk for PIM compared with persons younger than 70 years.

Overall, a higher percentage of women received PIM drugs (Table 5). With respect to drug classes, women have a higher risk to receive PIM drugs out of the groups of analgesics, anticholinergics, antidepressants,

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Table 4. Description of study population according to PIM drug use in 2010

	Recipient of PIM ($n = 16535$)		Recipient of no PIM ($n = 45828$)		
	n	%	*n*	%	*p*-value
Age (years)					
65 to <70	2776	16.8	8885	19.4	
≥70 to <75	4252	25.7	12421	27.1	
≥75 to <80	3782	22.9	9912	21.6	
≥80 to <85	2969	18.0	7550	16.5	
≥85	2756	16.7	7060	15.4	<0.0001
Sex					
Male	5631	34.1	19361	42.2	
Female	10904	65.9	26467	57.8	<0.0001
Number of different drugs					
<5 drugs	1796	10.9	13298	29.0	
≥5–<10 drugs	6286	38.0	20632	45.0	
≥10 drugs	8453	51.1	11898	26.0	<0.0001
Hospital stay					
No	14268	86.3	41096	89.7	
Yes	2267	13.7	4736	10.3	<0.0001
Nursing care					
No	12815	77.5	37833	82.6	
Yes	3720	22.5	7995	17.4	<0.0001

PIM, potentially inappropriate medication.

Table 5. Association of prevalent PIM prescription and risk factors

	OR	95%-CI
Age (years)		
65 to <70	1.00	
≥70 to <75	1.02	0.96–1.08
≥75 to <80	1.04	0.98–1.11
≥80 to <85	1.01	0.95–1.07
≥85	0.97	0.91–1.04
Sex		
Male	1.00	
Female	1.39	1.34–1.44
Number of different drugs		
<5 drugs	1.00	
≥5 to <10 drugs	2.23	2.10–2.36
≥10 drugs	5.16	4.87–5.47
Hospital stay		
No	1.00	
Yes	1.03	0.97–1.09
Nursing care		
No	1.00	
Yes	1.03	0.98–1.08

PIM, potentially inappropriate medication.

antiepileptics, antiarrhythmics and sedatives (Table 6), whereas men are at a higher risk to receive an antihypertensive, antidementia or neuroleptic PIM drug. Within the group of antiemetics and muscle relaxants, no sex-related differences in odds ratios were observed.

With the exception of antiepileptic drugs, neuroleptic drugs, antiemetic drugs, muscle relaxants and sedatives, the number of different drugs prescribed in 2010 is significantly associated with PIM prescribing. For patients treated with analgesics, antidementia drugs, antidepressants, antihypertensives or sedatives, those with nursing care are at lower risk for PIM prescription and among patients treated with antiepileptic drugs, antiarrhythmics or sedatives, those with hospital stay are at lower risk for PIM prescription.

Including the three main indications for receiving analgesics, anticholinergic drugs, antihypertensives or neuroleptic drugs into the logistic regression model does not change the estimates substantially (see e-Table 3).

DISCUSSION

We determined an annual PIM prevalence of about 22% in an elderly population on the basis of the claims data for one sickness fund (AOK) and one region (Hesse) of Germany. The annual prevalence increased with age and was higher in persons receiving nursing care. Our results are in line with the analysis of Thuermann *et al*. (2012)[32] who, using a nation-wide AOK database, reported a PIM prevalence of 24% for Germany and 23.3% for Hesse in 2010. The higher percentage of their study might be due to different inclusion criteria for PRISCUS drugs (allowing for drugs rated as PIM in higher dosage). Amann *et al*. (2012),[33] applying nationwide and regional health insurance data of Germany for the year 2007, reported a much higher PIM prevalence of 28%. Here too, discrepancies can be attributed to methodological differences (year of observance, kind of insurance and inclusion of PIM drugs). International studies investigating PIM have also addressed the difficulties of comparing results from multiple studies.[7,9,12,14]

In our study, the highest PIM prevalence was observed for antidepressants and antihypertensives followed by PIMs for antiarrhythmic drugs. This result—a small set of drug groups accounting for a high percentage of PIM—is not astonishing as these therapeutic groups are prominent in the elderly, and many PIM drugs were identified in these classes. Psychotropic PIMs are the most frequently prescribed PIM drugs in other countries as well.[5,10,14,34] The prevalence of bromazepam and other benzodiazepines might be underestimated in our study, as there are hints that prescriptions are also issued for out-of-pocket payment.[35] Moreover, a considerable number of benzodiazepines and so-called Z-drugs (e.g. zolpidem) are dose-specified on the PRISCUS-list and therefore not considered in this analysis.

Drugs classified as PIM might be in contradiction with other prescribing recommendations.[36] This is the case for amitriptyline, which is recommended as the drug of choice for non-selective monoamine

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Table 6. Association of prevalent PIM prescription and risk factors

	Analgesics/Anti-inflamm. drugs		Anticholinergic drugs		Antidementia drugs		Antidepressants		Antiepileptic drugs	
	OR	95%-CI	OR	95%-CI	OR	95%-CI	OR	95%-CI	OR	95%-CI
Age (years)										
65 to <70	1.00		1.00		1.00		1.00		1.00	
≥70 to <75	1.02	0.90–1.16	0.99	0.81–1.22	0.65	0.44–0.94	0.96	0.85–1.09	1.01	0.71–1.43
≥75 to <80	0.97	0.85–1.11	1.12	0.91–1.37	0.46	0.32–0.65	0.84	0.74–0.95	1.08	0.71–1.54
≥80 to <85	0.86	0.74–1.00	1.13	0.91–1.40	0.33	0.23–0.48	0.81	0.71–0.93	1.09	0.76–1.58
≥85	0.80	0.68–0.95	0.99	0.78–1.25	0.47	0.33–0.68	0.73	0.63–0.84	1.57	1.09–2.24
Sex										
Male	1.00		1.00		1.00		1.00		1.00	
Female	1.11	1.01–1.21	5.81	5.11–6.61	0.78	0.64–0.95	1.14	1.05–1.22	1.37	1.09–1.72
Number of different drugs										
<5	1.00		1.00		1.00		1.00		1.00	
≥5 to <10	1.26	1.09–1.46	1.29	1.03–1.63	1.39	1.03–1.89	1.07	0.93–1.23	1.21	0.77–1.90
≥10	1.86	1.62–2.15	1.37	1.09–1.72	1.59	1.17–2.15	1.19	1.04–1.37	1.18	0.76–1.82
Hospital stay										
No	1.00		1.00		1.00		1.00		1.00	
Yes	0.97	0.85–1.10	1.10	0.92–1.32	0.89	0.66–1.19	0.94	0.85–1.05	0.73	0.54–0.97
Nursing care										
No	1.00		1.00		1.00		1.00		1.00	
Yes	0.52	0.45–0.59	1.21	1.03–1.43	0.20	0.16–0.25	0.55	0.50–0.60	0.92	0.74–1.16

PIM, potentially inappropriate medication.

reuptake inhibitors in a budgetary agreement between sickness funds and the associations of SHI-accredited physicians. Amitriptyline is also frequently used as a co-analgesic in pain treatment. However, this drug is included in all PIM-lists, irrespective of the indication.[1–4,23–25] Another issue is the inclusion of nitrofurantoin on the PRISCUS-list, which is currently the recommended drug for short-term and long-term treatment of lower urinary tract infection according to the German College of General Practitioners and Family Physicians.[37] Nevertheless, nitrofurantoin is also included on the most recently updated Beers list in the USA.[4]

Most studies analyzing PIM versus non-PIM use assess several factors independently associated with the prescribing of PIM[5–7,9–13,16,18,21,38–41] (for an overview, see Liu[34]). All studies include age and sex, and most studies assess the number of drugs and/or morbidity, hospitalization and nursing care. Some studies include patient characteristics such as ethnicity, marital status, income, geographic region, referral status, self-reported health[6,7,21,42] and physician characteristics.[5,6,43] The analyzed variables are closely related to the setting of the study and the data available. Therefore, no clear picture concerning risk factors for PIM prescribing can be generated.

In our analysis, women were at higher risk for PIM prescribing. Most studies report female sex as an independent factor for PIM use,[6,11,21,39,40] others do not.[9,41] Yet the results of the latter two have to be evaluated against the prevalence of the most frequently prescribed PIMs, as in both studies doxazosin was the most frequently prescribed PIM, which can be used as an antihypertensive drug and for the treatment of benign prostatic hyperplasia. Furthermore, Maio *et al*.[9] were not able to assess benzodiazepines in their prescription claims database—a drug group that is more frequently used by women than men and is included in PIM lists. The contradicting results with regard to the influence of sex on PIM prescription may be due to the substantial difference between the compositions of the study populations.

In the multivariate analysis, we could not observe a statistically lower risk for the highest age group to receive a PIM prescription, which has been reported in several studies from other countries[6,7,13,17,40,44] and in the study of Költzsch *et al*.[38] for nursing homes in Germany. By contrast, some other studies report higher prevalences for older age groups even when adjusting for sex and number of prescriptions.[9,16]

A high number of prescriptions (>5, >10) was identified to be independently positively associated with PIM prescribing in our study. This, again, is in line with many other studies.[6,7,9,11,13,34,39–41]

Drugs classified as PIM are not equally distributed between indication groups. Thus, predictors for total PIM prescribing are likely to characterize mostly patients receiving psychotropic or cardiovascular drugs, as most PIMs are identified in these drug groups. We therefore performed separate risk analysis restricted to single indication groups in order to

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Table 6. (Continued)

	Neuroleptic drugs		Antiarrhythmic drugs		Antiemetic drugs		Antihypertensives		Muscle relaxants		Sedatives	
	OR	95%-CI	OR	95%-CI	OR	95%-CI	OR	95%-CI	OR	95%-CI	OR	95%-CI
Age (years)												
65 to <70	1.00		1.00		1.00		1.00		1.00		1.00	
≥70 to <75	0.86	0.59–1.24	1.25	1.07–1.45	0.34	0.10–1.10	1.10	0.96–1.27	0.88	0.69–1.11	1.04	0.88–1.24
≥75 to <80	0.71	0.49–1.04	1.65	1.42–1.91	0.90	0.34–2.37	1.14	0.99–1.32	0.75	0.59–0.97	1.01	0.85–1.19
≥80 to <85	0.41	0.27–0.63	1.87	1.60–2.18	1.38	0.49–3.93	1.09	0.93–1.27	0.74	0.55–0.98	0.87	0.73–1.04
≥85	0.26	0.17–0.40	2.47	2.11-2.89	0.90	0.20–4.00	1.15	0.97–1.36	0.77	0.55–1.08	0.76	0.63–0.91
Sex												
Male	1.00		1.00		1.00		1.00		1.00		1.00	
Female	0.70	0.55–0.89	1.10	1.01–1.20	2.03	0.92–4.48	0.78	0.71–0.85	0.97	0.81–1.16	1.16	1.04–1.30
Number of different drugs												
<5	1.00		1.00		1.00		1.00		1.00		1.00	
≥5 to <10	0.81	0.55–1.20	1.54	1.34–1.77	0.08	0.01–0.73	1.00	0.86–1.17	0.80	0.57–1.13	0.97	0.79–1.19
≥10	0.75	0.52–1.10	1.88	1.63–2.16	0.25	0.04–1.38	1.60	1.38–1.85	0.74	0.53-1.04	0.98	0.80–1.19
Hospital stay												
No	1.00		1.00		1.00		1.00		1.00		1.00	
Yes	1.21	0.90–1.62	0.86	0.76–0.97	0.43	0.18–1.06	1.02	0.89–1.16	1.14	0.87–1.50	0.80	0.70–0.92
Nursing care												
No	1.00		1.00		1.00		1.00		1.00		1.00	
Yes	1.28	0.99–1.66	1.06	0.96–1.18	3.84	1.79–8.23	0.86	0.76–0.97	1.13	0.90–1.41	0.79	0.70–0.89

identify patient groups whose prescriptions should be reviewed in particular. Some risk factors differ among indication groups. Female sex was inversely associated with the risk of receiving a potentially inappropriate antidementia, antihypertensive or neuroleptic drug. Previous nursing care was identified as risk factor for the prescribing of only two PIM groups, that is, anticholinergic and antiemetic PIM drugs.

The issue of unequally distributed PIM drugs within the indication groups has rarely been addressed by other studies. We are only aware of the study by Carey *et al.*,[21] who presented risk estimates for analgesic, antidepressants and sedatives/anxiolytic drugs for patients receiving a PIM drug from the respective pharmacological subgroup adjusted for age, sex, practices and number of drugs prescribed. Much like our findings, they report a lower risk among older age groups for analgesic and antidepressants and found no age dependency for sedatives or anxiolytic drugs. Again, comparison is hampered by differing PIM lists and methodologies.

Limitations and strengths of the study

Our study has several limitations. First of all, we analyzed data of one sickness fund in one region of Germany. This has to be kept in mind when trying to generalize our results to the whole population of Germany. In the light of other German studies,[32,33] however, we feel confident that our results are transferable to other funds and regions in Germany. The prevalence of PIM use in the population might be higher, as we used claims data analyzing reimbursed drugs only, we did not include data on drugs administered during a hospital stay, over-the-counter drugs or drugs on private prescription. The latter two might affect the estimates for antihistamines and benzodiazepines in particular, whereas the PRISCUS-list does not include OTC-drugs. Like other studies applying claims data, we have no information on whether the drugs were taken. Furthermore, we could only assess a limited number of variables associated with PIM prescribing, as other factors of interest such as other patient or physician characteristics are not available in our database. We also were unable to evaluate the inappropriateness of the treatment for the individual patient and to assess the reasons for the choice of the drug.

The strength of our study is that it includes insured people independently of their living situation, mental and health status or capacity to understand German. Selection and recall bias are not issues. As the data are related to individual persons, both administrative prevalence for each single PIM and percentages related to those receiving a PIM can be estimated. Moreover, our data allowed for analyzing drug groups controlled for confounding by indication.

Conclusion and perspective

In our study, women and persons with polypharmacy were at higher risk for receiving a PIM on the PRISCUS list. To improve the ability to address risk groups, we

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recommend the analysis of indication groups and the inclusion of additional risk factors.

Our claims-data analysis can be updated for subsequent years in order to evaluate the impact of the implementation of the PRISCUS list on prescribing habits.

Yet one has to remember that drugs not included on the list might be inappropriate as well. To enhance patient safety, multifaceted interventions involving different professions will be necessary.[45] Besides list distribution and electronic tools, training to evaluate the appropriateness of prescribing by applying review tools,[45,46] the Medication Appropriateness Index[47] or other comprehensive protocols[22] and chart reviews by pharmacists and physicians can be useful. However, feedback to physicians on their prescribing practices and a discussion about frequently prescribed substances are the first steps for optimizing therapy. We recommend focusing on the most frequently prescribed PIM drug groups: psychotropic drugs and—for Germany—acetyldigoxin. But following a warning of Gurwitz and Rochon,[48] we have to be cautious not to reduce the quality of medication use to an easy-to-assess single measure of "drugs to avoid", as we could miss other (perhaps more relevant) problems such as the underuse of evidence-based therapies or problems related to polypharmacy.

CONFLICT OF INTEREST

P. A. Thuermann is one of the authors of the PRISCUS list, which has been supported by the Ministry of Education and Research, project number 01ET0721; P. A. Thürmann received lecture honoraria from Rottapharm Madaus GmbH. I. Schubert, J. Kuepper-Nybelen, and P. Ihle have declared no conflict of interest

KEY POINTS

- Nearly one quarter of the elderly (22.0%) received at least one potentially inappropriate medication (PIM) defined by the German PRISCUS list in ambulatory care during an observation period of 1 year.
- The highest PIM prevalence was observed for antidepressants followed by antihypertensives and antiarrhythmic drugs.
- Most PIMs are used for long-term treatment.
- To improve prescribing, professionals involved in the care of the elderly should focus on alternatives for the most frequently prescribed PIMs: amitriptyline, tetrazepam, doxepin, acetyldigoxin, doxazosin and etoricoxib.
- Women and persons with polypharmacy are at higher risk for PIM prescription.

SUPPORTING INFORMATION

Additional supporting information may be found in the online version of this article.

e-Table 1: First three higher prevalence diagnoses in PIM recipients compared to sex and aged matched controls, accounted for in sensitivity analysis.

e-Table 2: Annual treatment prevalence of the insured population (≥ 0,1%) and of PIM recipients (2010).

e-Table 3: Association of prevalent PIM prescription and risk factors adjusting for indications.

REFERENCES

1. Beers MH, Ouslander JG, Rollingher I, *et al*.. Explicit criteria for determining inappropriate medication use in nursing home residents. *Arch Intern Med* 1991; **151**: 1825–1831.
2. Beers MH. Explicit criteria for determining inappropriate medication use in nursing home residents. *Arch Intern Med* 1997; **157**: 1531–1536.
3. Fick DM, Cooper JW, Wade WE *et al*.. Updating Beers criteria for potentially inappropriate medication use in older adults. Results of a US consensus panel of experts. *Arch Intern Med* 2003; **163**: 2716–2724.
4. The American Geriatrics Society. Beers criteria update expert panel. American Geriatrics Society updated Beers criteria for potentially inappropriate medication use in older adults. *JAGS* 2012; **60**: 616–631. doi: 10.1111/j.1532-5415.2012.03923x
5. Howard M, Dolvich L, Kaczorowski J, Sellors C, Sellor J. Prescribing of potentially inappropriate medications to elderly people. *Fam Pract* 2004; **21**: 244–247.
6. Goulding MR. Inappropriate medication prescribing for elderly ambulatory care patients. *Arch Intern Med* 2004; **164**: 305–312.
7. Fialová D, Topkinová E, Gambassi G, *et al*.. Potentially inappropriate medication use among elderly home care patients in Europe. *JAMA* 2005; **293**: 1348–1358.
8. Van der Hooft CS, Jong GW, Dielemann JP, *et al*. Inappropriate drug prescribing in older adults: the updated 2002 Beers criteria – a population based cohort study. *Br J Clin Pharmacol* 2005; **60**: 137–144.
9. Maio V, Yuen EJ, Novielli K, *et al*.. Potentially inappropriate medication prescribing for elderly outpatients in Emilia Romagna, Italy: a population-based cohort study. *Drugs Aging* 2006; **23**: 915–924.
10. Rothberg M, Pekow P, Liu F, *et al*.. Potentially Inappropriate Medication Use in Hospitalized Elders. *J Hosp Med* 2008; **3**: 91–102. DOI: 10.1002/jhm.2909
11. Bongue B, Naudin F, Laroche M-L, *et al*.. Trends of the potentially inappropriate consumption over 10 years in older adults in the East of France. *Pharmacoepidemiol Drug Saf* 2009; **18**: 1125–1133.
12. Bongue B, Laroche ML, Sutton S, *et al*.. Potentially inappropriate drug prescribing in the elderly in France: a population-based study from the French National Insurance Healthcare system. *Eur J Clin Pharmacol* 2011; **67**: 1291–1299.
13. Ruggiero C, Dell'Aquila G, Gasperini B, *et al*.. Potentially inappropriate drug prescriptions and risk of hospitalization among older, Italian, nursing home residents: the ULISSE project. *Drugs Aging* 2010; **27**: 747–758.
14. Leikola S, Dimitrow M, Lyles A, *et al*.. Potentially inappropriate medication use among Finnish non-institutionalized people aged ≥65 years: a register-based, cross-sectional, national study. *Drugs Aging* 2011; **28**: 227–236.
15. Barnett K, McCowan C, Evans JM, *et al*.. Prevalence and outcomes of use of potentially inappropriate medicines in older people: cohort study stratified by residence in nursing home or in the community. *BMJ Qual Saf* 2011; **20**: 275–281.
16. Lin YJ, Peng L-N, Chen LK, Lin M-H, Hwang S-J. Risk factors of potentially inappropriate medications among older patients visiting the community health center in rural Taiwan. *Arch Gerontol Geriatr* 2011; **53**: 225–228.
17. Sakuma M, Morimoto T, Matsui K, *et al*.. Epidemiology of potentially inappropriate medication use in elderly patients in Japanese acute care hospitals. *Pharmacoepidemiol Drug Saf* 2011; **20**: 386–392. DOI: 10.1002/pds.2110
18. Rigler S, Jachna CM, Perera S, Shireman TI, Emg ML. Patterns of potentially inappropriate medication use across three cohorts of older Medicaid recipients. *Ann Pharmacother* 2005; **39**: 1175–1181. DOI: 10.1345/aph.1E581
19. Hamilton H, Gallagher P, Ryan C, *et al*. Potentially inappropriate medications defined by STOPP criteria and the risk of adverse drug events in older hospitalized patients. *Arch Intern Med* 2011; **171**: 1013–1019. DOI: 10.1001/archinternmed.2011.215
20. de Wilde S, Carey I, Harris T, *et al.* Trends in potentially inappropriate prescribing amongst older UK primary care patients. *Pharmacoepidemiol Drug Saf* 2007; **16**: 658–667. DOI: 10.1002/pds.1306

21. Carey IM, De Wilde S, Harris T, *et al*. What factors predict potentially inappropriate primary care prescribing in older people? Analysis of UK primary care patient record database. *Drugs Aging* 2008; **25**: 693–706.
22. Matanovic SM, Vlahovic-Palcevski V. Potentially inappropriate medications in the elderly: a comprehensive protocol. *Eur J Clin Pharmacol* 2012; **68**:1123–1139. DOI:10.1007/s00228-012-1238-1
23. McLeod PJ, Huang A, Tamblyn RM, Gayton DC. Defining inappropriate practices in prescribing for elderly people: a national consensus panel. *Can Med Assoc J* 1997; **156**: 385–391.
24. Laroche ML, Charmes JP, Merle L. Potentially inappropriate medications in elderly: a French consensus panel list. *Eur J Clin Pharmacol* 2007; **63**: 725–731.
25. Rognstadt S, Brekke M, Fetveit A, *et al*.. The Norwegian General Practice (NORGEP) criteria for assessing potentially inappropriate prescription to elderly patients. A modified Delphy study. *Scand J Prim Health Care* 2009; **27**: 153–159.
26. Holt A, Schmiedl S, Thuermann PA. Potentially inappropriate medications in elderly. The Priscus list. *Dtsch Arztebl Int* 2010; **107**(31–32): 543–551. DOI: 10.3238/aerztebl.2010.0543
27. Ihle P, Köster I, Herholz H, Rambow-Bertram P, Schardt T, Schubert I. Versichertenstichprobe AOK Hessen/KV Hessen – Konzeption und Umsetzung einer personenbezogenen Datenbasis aus der Gesetzlichen Krankenversicherung. [Sample survey of persons insured in statutory health insurance institutions in Hesse – concept and realisation of a personalized data base.] *Gesundheitswesen* 2005; **67**: 638–645.
28. Köster I, Ferber Lv, Ihle P, Schubert I, Hauner H. The cost burden of diabetes mellitus: the evidence from Germany – the CoDiM Study. *Diabetologia* 2006; **49**: 1498–1504.
29. Köster I, Huppert E, Hauner H, Schubert I. Direct costs of diabetes mellitus in Germany. CoDiM 2000–2007. *Exp Clin Endocrinol Diabetes* 2011; **119**: 377–385.
30. Schubert I, Köster I, Lehmkuhl G. The changing prevalence of attention-deficit/hyperactivity disorder and methylphenidate prescriptions: a study of data from a random sample of insurees of the AOK Health Insurance Company in the German State of Hesse, 2000–2007. *Dtsch Arztebl Int* 2010; **107**: 615–621.
31. Kuepper-Nybelen J, Hellmich M, Abbas S *et al*.. Association of long-term adherence to evidence-based combination drug therapy after acute myocardial infarction with all-cause mortality. A prospective cohort study based on claims data. *Eur J Clin Pharmacol* 2012; **68**: 1451–1460.
32. Thuermann PA, Holt S, Nink K, Zawinell A. Arzneimittelversorgung älterer Patienten. In Günster C, Klose J, Schmacke N. Versorgungs-Report 2012. Schattauer Verlag Stuttgart 2012; 111–130.
33. Amann U, Schmedt N, Garbe E. Prescribing of potentially inappropriate medications for the elderly: an analysis based on the PRISCUS list. *Dtsch Arztebl Int* 2012; **109**: 69–75. DOI:10.3238/arztebl.2012.0069
34. Liu GG and Christensen DB. The continuing challenge of inappropriate prescribing in the elderly. An update of the evidence. *J Am Pharm Assc* 2002; **42**: 847–857.
35. Hoffmann F, Glaeske G, Scharffetter W. Zunehmender Hypnotikaverbrauch auf Privatrezepten in Deutschland. [Increasing use of hypnotics on private prescriptions in Germany]. *SUCHT* 2006; **52**: 360–366.
36. Fiss T, Dreier A, Meinke C, van den Berg N, *et al*.. Frequency of inappropriate drugs in primary care: analysis of a sample of immobile patients who received periodic home visits. *Age Ageing* 2011; **40**: 66–71.
37. Deutsche Gesellschaft für Allgemeinmedizin und Familienmedizin (editor). Brennen beim Wasserlassen. DEGAM Leitlinie Nr. 1. Düsseldorf 2009 [http://leitlinien.degam.de/uploads/media/Brennen-beim-Wasserlassen-Langfassung.pdf]
38. Költzsch M, Kopke K, Fischer T, *et al*.. Prescribing of inappropriate medication in nursing home residents in Germany according to a French consensus list: a cross-sectional cohort study. *Pharmacoepidemiol Drug Saf* 2011; **20**: 12–19.
39. Buck MD, Atreja A, Brunker C, *et al*.. Potentially inappropriate medication prescribing in outpatient practices: prevalence and patient characteristics based on electronic health records. *Am J Geriatr Pharmacother* 2009; **7**: 84–92.
40. Pugh MJ, Rosen AK, Montez-Rath M, *et al*.. Potentially inappropriate prescribing for the elderly: effects of geriatric care at the patient and health care system level. *Med Care* 2008; **46**: 167–173.
41. Ma HM, Lum CM, Dai LK, *et al*.. Potentially inappropriate medication in elderly patients in outpatients clinics. *Asian H Gerontol Geriatr* 2008; **3**: 27–33.
42. Dedhiya SD, Hancock E, Craig BA, *et al*. Incident use and outcomes associated with potentially inappropriate medication use in older adults. *Am J Geriatr Pharmacother* 2010; **8**: 562–570.
43. Imai H, Fick DM, Waller JL, Maclean JR. Physician characteristics associated with prescription of inappropriate medications using Beers criteria. *Geriatr Gerontol Int* 2007; **7**: 380–387. DOI: 10.1111/j.1447-0594.2007.00428.x
44. Piecoro LT, Browning SR, Prince ST, *et al*.. A database analysis of potentially inappropriate drug use in an elderly Medicaid population. *Pharmacotherapy* 2000; **20**: 221–228.
45. Page RL, Linnebur SA, Bryant L, Ruscin JM. Inappropriate prescribing in the hospitalized elderly patient. Defining the problem, evaluation tools, and possible solutions. *Clin Interv Aging* 2010; **5**: 75–87.
46. Gallagher P, Ryan B, Byrne S, *et al*.. STOPP (screening tool of older persons' prescriptions) and START (screening tool to alert doctors to right treatment). Consensus validation. *Int J Clin Pharmacol Ther* 2008; **37**: 673–679.
47. Hanlon JT, Schmader KE, Samsa GP, *et al*.. A method for assessing drug therapy appropriateness. *J Clin Epidemiol* 1992; **45**: 1045–1051. DOI: 10.1016/0895-4356(92)90144-C
48. Gurwitz JH, Rochon P. Food and Drug Administration (U.S.). Improving the quality of medication use in elderly patients: a not-so-simple prescription. *Arch Intern Med* 2002; **162**: 1670–1672.