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ORIGINAL REPORT

Polypharmacy in primary care practices: an analysis using a large health insurance database†

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SUMMARY

Purpose To ascertain the rate and range of continuous polypharmacy in German general practices and compare practice characteristics and prescribing profiles in practices with a high rate of polypharmacy patients (HPP) and a low rate of polypharmacy patients (LPP), respectively.
Methods This observational study used a database composed of prescription data from a large German statutory health insurance. We defined polypharmacy as the continuous prescription of five or more drugs and calculated the percentage of polypharmacy patients for each practice to identify HPP and LPP.
Results A total of 136 521 patients in 730 general practices received continuous medication. About 10% of these patients (14 293/136 521) received five or more different drugs. HPP had, on average, 15.1% polypharmacy patients compared to 4.2% in LPP. The total number of patients attending either a HPP or LPP was comparable (437 vs. 416; $p = 0.102$), but HPP had a higher number of patients with prescriptions (76.9% vs. 70.8%; $p < 0.0001$). The patients' age distribution was similar (68.0 in LPP vs. 68.8 in HPP) and there were slightly more female patients in LPP. Doctors in HPP prescribed proton pump inhibitors and NSAIDs more frequently than doctors in LPP, but there was no difference in the prescription of *me-too* drugs.
Conclusion The absolute differences in age and gender distribution between HPP and LPP were modest. Prescribing quality, as measured by the rate of *me-too* drug prescriptions, was similar across all practices. Therefore, differences in the rate of polypharmacy in general practice cannot sufficiently be explained by these factors. Copyright © 2009 John Wiley & Sons, Ltd.

KEY WORDS — polypharmacy; prescriptions; drug utilisation review; databases; family practice

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INTRODUCTION

Polypharmacy has been a major concern in recent decades.[1] It is associated with adverse drug reactions, an increased risk of hospitalisation, decreased medication adherence and unnecessary costs.[2-4] Polypharmacy has been studied especially with respect to gender (with women more prone to polypharmacy), increasing age[5-7] and socioeconomic status.[7]

More recently, there has been a shift towards a more balanced view[8] and the use of different drugs to treat one condition or multi-morbidity has been promoted especially in elderly people.[9,10] Some authors are even concerned about under-treatment of patients using five or more drugs.[11]

The degree and variation of polypharmacy in general practices has only been studied by a few authors. Junius-Walker[12] and colleagues found more than a quarter of older patients in 67 German general practices taking in excess of five drugs. Bjerrum and colleagues[13] have studied prevalence rates of polypharmacy in 173 practices in a defined region of Denmark and found a 6-fold variation; more than half of this variation could be explained by practice structure, workload and prescribing profile.

The definition of polypharmacy is crucial and often seems to be a mix of cumulative polypharmacy (the number of different medications during a particular

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time window),[14] simultaneous polypharmacy (number of medications at any given time) and continuous polypharmacy (chronic medication). Studying the latter is the major challenge. Moreover, characteristics of practices or doctors with a high rate of polypharmacy prescriptions could also be proxies for other factors such as the practice patient age profile that might be the underlying reason for polypharmacy.

The present study takes advantage of an impressive data set comprising every prescription for all those insured by one major statutory health insurance (SHI) in a large region of Germany. With this data, it was possible to identify all patients (1) for whom a provider (general practitioner) prescribed one or more drugs and (2) over what time period these drugs were prescribed. Utilising this information, one aim of the study was to reliably ascertain the rate and range of continuous polypharmacy in all general practices encompassed by this SHI. The major aim, however, was to identify general practices with a high rate of polypharmacy patients ('high' polypharmacy practices, HPP) and to compare their prescribing behaviour with those with a low rate of polypharmacy patients ('low' polypharmacy practices, LPP). Five hypotheses were investigated to determine whether:

(1) Patients in a HPP, compared to those in LPP, receive fewer drugs from other doctors than their general practitioner, so that, a higher rate of polypharmacy may not be a characteristic of some general practices but an artefact caused by prescriptions from specialists.
(2) There is a positive correlation between the rate of patients with continuous polypharmacy and practice size.
(3) The rates of polypharmacy in different practices are due to practice patient age or gender profile.
(4) Practices with a high rate of polypharmacy patients also prescribe *me-too* drugs more often, suggesting non-rational prescribing.
(5) Practices with a high rate of polypharmacy patients differ from the remainder in their drug profile, e.g. they prescribe significantly more or fewer drugs in certain drug classes.

METHODS

Design

This was an observational study, analysing prescription data from general practices during a 3-month time period. The term 'general practice' or 'general practitioner' refers to general practitioners, general internists and physicians without specialisation. These doctors are regularly consulted in Germany by more than 90% of the population for medical problems or health advice.[15]

Database

The database for the study comprised prescription data of members insured by the Local Health Care Funds (AOK) in the German federal state of Mecklenburg-Vorpommern.[16] This SHI is by far the largest in Mecklenburg-Vorpommern covering about one third of this state's entire population (about 520 000 from 1.7 million people).

The study covered all patients with a prescription by a general practitioner in the first 3 months of 2007. For each patient record, the following data were available:

- Pseudonymised identification number of the insured person, including age and sex.
- Identification number for the practice including the information if the practice is a general practice.
- Central pharmaceutical number, an identification number providing every detail of the finished drug, including an ATC-classification for the active substance.
- Number and the date of each prescription.
- Prescription data from October 2006 to June 2007, providing the information whether a drug was also prescribed 3 months before and after the actual 3-month study time period from January to March 2007—as the marker of continuous medication.

We had access to the total number of AOK-patients for each practice, but only in an aggregated form.

Definition of polypharmacy, me-too drugs and data analysis

Polypharmacy. We defined polypharmacy as the prescription of five or more drugs—defined by the ATC-Code—for at least 3 months. Changes in brand name or dosage had therefore no effect on our results. In addition, all active substances must have been prescribed to the patients in a 3-month period both before and after the actual 3-month study time—which represents continuous polypharmacy in contrast to cumulative or simultaneous polypharmacy.[14]

Unless otherwise noted, the drugs had to be prescribed continuously by the same general practice to the same patient. In particular for the definition of HPP and LPP (see below) only prescriptions made by the corresponding general practice were taken into account.

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Polypharmacy practices. As one major aim of our study was to characterise practices with a high rate of polypharmacy practices we needed an appropriate comparator. As described in the Result section of this paper, some general practices in our dataset supplied only very few patients with a continuous medication. To rule out a comparison of HPP with general practices with a focus in non-pharmacological therapy, we decided to exclude very small practices. We calculated the percentage of polypharmacy patients for each included general practice. The sample of practices was split into quartiles, according to the polypharmacy rate of their patients, with the top quartile representing high polypharmacy practices (HPP) and the lowest quartile defined as low polypharmacy practices (LPP).

Me-too drugs. These drugs are defined as novel drugs with no advantage over, but more expensive than, drugs already on the market.[17] In Germany, a list of these drugs[18] was developed on behalf of the North Rhine Association of Statutory Health Insurance Physicians and the North-Rhine Health Insurance Funds. This is also valid for other German regions.

Statistical analysis. Prevalence ratios (PR) and corresponding 95%confidence intervals (CIs) were calculated to define the probability of receiving a drug from a certain ATC-class in HPP compared to patients in LPP.[19] To compare differences between HPP and LPP, the t-test or the Mann–Whitney U-test were used, as appropriate.

RESULTS

Patients, practices and prescriptions

During the first 3 months of 2007, a total of 243 246 patients (47% of all insured by the SHI) received at least one drug prescription from one of the region's 1028 general practitioners. Of these patients, 140 796 had taken at least 1 active substance continuously, i.e. also within the 3 months both before and after the actual study period (on average, 166 patients per practice; standard error [SE]: 99). Patients with at least one continuous prescription made up 57.9% of the patients who received a prescription and 27% of all patients insured by this SHI.

Some practices studied were rather small and many of them obviously had a non-pharmacological treatment focus. Since these practices did not represent the average primary care practice, we decided to exclude small practices with not more than 67 patients (mean per practice [166] minus SE [99]) receiving at least one prescription continuously from their general practitioners over the 3-month study period. This analysis generated a sample of 124 practices with 4275 patients that were excluded, so that the study sample consisted of 730 general practices with 136 521 patients prescribed at least one active substance continuously. The mean number of prescriptions per patient was 2.4. About 10% of these patients (14 293/136 521) received five or more different drugs from their general practitioner and 640 (0.5%) received nine drugs or more (Table 1). A total of 664 patients received continuous medication from two different general practitioners, another seven from three and one patient from four general practitioners. If the prescriptions from doctors other than general practitioners were also considered, the mean number of continuous prescriptions per patient rose, on average, by 12.6% from 2.4 to 2.7, and the percentage of patients who were prescribed five or more drugs then was 14.7%.

Table 1. Number of drugs continuously prescribed per patient*

Drugs (*n*)	Prescribed drugs for patients†	
	In general practice only (%)	In all practices (%)
1	37.5	30.5
2	26.3	25.8
3	16.3	17.9
4	9.5	11.3
5	5.3	6.8
6	2.7	3.8
7	1.3	2.0
8	0.6	1.0
9	0.3	0.5
10	0.1	0.2
>10	0.1	0.2

*Included were patients who received 1 or more drugs continuously throughout the study period.
†$n = 136\,521$.

Figure 1 shows the nearly Gaussian distribution of the rate of polypharmacy patients (five or more drugs from the general practitioner) in the 730 practices. Seventy percent (509/730) of the practices had a rate of polypharmacy patients between 6 and 13% and 13% of the practices had 5% or less polypharmacy patients.

High polypharmacy practices (HPP) and low polypharmacy practices (LPP)

The 730 general practices were ranked according to the relative frequency of patients receiving at least five or more prescription drugs continuously. The 183 practices in the upper quartile (HPP) had, on average, 15.1% polypharmacy patients compared to 4.2%

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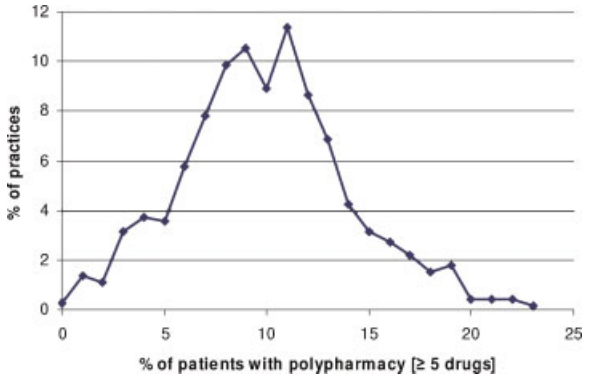

Figure 1. Distribution of polypharmacy in general practices ($n = 730$ practices)

patients in the lowest quartile (LPP); general practitioners in the second and third quartile had 7.9% and 10.7% patients with polypharmacy, respectively. The average number of different continuous prescribed drugs per patient in the LPP was 2.1, compared to 2.7 in the HPP. Interestingly, doctors other than the general practitioners supply patients in LPP with a higher rate of prescriptions (0.4 per patient) than patients in HPP (0.3 per patient). Consequently, the increase of prescriptions per patient, given by these other doctors, was significantly higher in LPP (from 2.1 to 2.5; 18.4%) than in HPP (from 2.7 to 3.0; 10.6%; $p < 0.001$).

Compared to LPP, HPP had a somewhat higher number of patients in the 3-month study period (437 vs. 416; $p = 0.102$). This small difference was due to a significantly higher number of patients with prescriptions in HPP (76.9% vs. 70.8%; $p < 0.001$).

The patients' age distribution in all four quartiles was similar and the mean age in LPP and HPP was 68.0 years (SD 6.5 years) and 68.8 years (SD 3.9 years), respectively ($p = 0.988$). There was a more or less linear increase across all quartiles in the number of prescribed drugs with patient age (Table 2). The only difference was that HPP started at a higher level in younger patients (2.1 drugs per patient compared to 1.7 of LPP) and maintained this higher level with an average number of 3.0 drugs for the oldest patients (compared to 2.3 in LPP).

In all four quartiles, female patients received, on average, more drugs than male patients (2.42 vs. 2.34 over all quartiles; $p < 0.001$). The majority in all quartiles were female (61% over all quartiles) with a slightly higher rate of female patients in LPP than HPP (62% vs. 60%, $p < 0.001$).

According to the list of *me-too* drugs, there were only small differences between the four quartiles of practices. The rate of *me-too* drugs prescribed by LPP and HPP was, on average, 8.1% (SD 5.8) and 7.2% (5.1), respectively ($p = 0.18$).

In a last step, we analysed—on a patient level—prescribing differences between HPP and LPP, to determine whether HPP not only prescribed more drugs than LPP in general, but also certain drug classes significantly more often. Since doctors in HPP prescribed 1.3 times more drugs per patient than those in LPP, we only considered strong differences in prescriptions between both groups of practices. Especially four drug groups were prescribed with a prevalence ratio of >1.3 for the lower 95%CI: drugs for acid related disorders, lipid reducing agents, diuretics and antiinflammatory and antirheumatic products (Table 3). In both LPP and HPP, 88% of the patients with drugs for acid related disorders (ATC class A02) received a proton pump inhibitors (PPI), and 98% of all patients with anti-inflammatory agents (ATC class M01) had a prescription of NSAIDs (data not shown).

We repeated this analysis for only those patients who received five or more drugs. Some of the above-mentioned differences could be still detected but the PR was much lower (Table 3). Significantly, PR above 1.0 could again be detected in drugs for acid related disorders, lipid reducing agents, diuretics and antiinflammatory and antirheumatic products with highest ratios for antiinflammatory and antirheumatic products/NSAIDs and drugs for acid related disorders/PPI. We also analysed associations in the prescriptions of

Table 2. Patient age and average number of drugs, prescribed by the patient's general practitioner

General practices	Age group								All	
	<60		60–69		70–79		≥80			
	Patients (%)	Drugs (n)*	Patients (%)	Drugs (n)*	Patients (%)	Drugs (n)*	Patients (%)	Drugs (n)*	Patients (%)	Drugs (n)*
1st quartile (=LPP)	22	1.7	21	2.0	36	2.2	21	2.3	100	2.1
2nd quartile	22	1.8	21	2.3	37	2.4	20	2.6	100	2.3
3rd quartile	22	1.9	21	2.4	36	2.6	21	2.7	100	2.4
4th quartile (=HPP)	21	2.1	21	2.6	37	2.9	21	3.0	100	2.7
All	22	1.9	21	2.3	37	2.5	20	2.7	100	2.4

*Average number of active substances prescribed per patient.

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Table 3. Top 10 prescribed ATC classes in low and high polypharmacy practices

Rank	ATC-Code	Therapeutic subgroup	All patients ($n = 136\,521$)							Patients with at least five drugs ($n = 14\,293$)						
			Patients		LPP*	HPP*	PR†	95% CI		Patients		LPP*	HPP*	PR†	95% CI	
			n	(%)	(%)	(%)				*n*	(%)	(%)	(%)			
1	C09	Agents acting on the renin-angiotensin system	50.184	36.6	34.2	40.5	1.19	1.16	1.21	9.290	65.0	63.8	66.1	1.04	0.99	1.08
2	C07	Beta-blocking agents	35.742	26.1	23.8	27.9	1.17	1.14	1.20	6.568	46.0	44.7	46.5	1.04	0.98	1.11
3	A10	Drugs used in diabetes	27.692	20.2	18.5	21.7	1.17	1.14	1.21	6.834	47.8	46.6	48.1	1.03	0.97	1.09
4	C08	Calcium channel blockers	23.367	17.0	15.8	18.9	1.19	1.15	1.23	5.371	37.6	36.7	38.3	1.04	0.97	1.12
5	C01	Cardiac therapy	21.029	15.3	14.2	16.4	1.15	1.11	1.19	5.496	38.5	40.5	38.0	0.94	0.88	1.00
6	C03	Diuretics	20.211	14.7	11.4	17.7	**1.54**	**1.49**	**1.60**	6.794	47.5	44.2	48.7	**1.10**	**1.03**	**1.17**
7	N02	Analgesics	12.299	9.0	7.5	9.9	1.32	1.25	1.39	3.438	24.1	22.0	23.4	1.06	0.96	1.18
8	A02	Drugs for acid related disorders‡	12.248	8.9	6.8	10.8	**1.58**	**1.50**	**1.67**	3.450	24.1	21.0	25.6	**1.22**	**1.10**	**1.36**
9	C10	Serum lipid reducing agents	11.217	8.2	6.1	10.2	**1.66**	**1.57**	**1.75**	3.339	23.4	21.3	24.9	**1.17**	**1.05**	**1.30**
10	M01	Antiinflammatory and antirheumatic prod.§	10.332	7.5	6.0	8.7	**1.44**	**1.36**	**1.53**	2.307	16.1	13.7	16.9	**1.24**	**1.08**	**1.42**

*HPP = high polypharmacy practices; LPP = low polypharmacy practices.
†Prevalence ratio (95%confidence interval) for patients in HPP, compared to LPP, for receiving a drug in the corresponding subgroups; PR for all patients in bold type, if the lower 95%CI exceeds 1.3.
‡Mostly PPI.
§Mostly NSAIDSs.

two drug groups, especially PPI and NSAIDs. Doctors in HPP prescribed this combination significantly more often than those in LPP (RR: 1.5; 95%CI 1.1–2.1).

Cough and cold preparations (ATC R05) were 1.7 times more frequently prescribed in HPP than LPP (95%CI: 1.4–2.0); for polypharmacy patients this ratio was 2.8 (95%CI 1.2–6.3; data not shown). This drug group, however, comprised only 973 patients (0.7%) and 165 polypharmacy patients (2.3%).

DISCUSSION

Summary of main findings

Our first important result is a valid estimate of the rate of continuous polypharmacy in primary care practice. Of those patients who received at least one continuous prescription, the polypharmacy rate was about 10%. This rate is lower than in many other studies and would be even lower if we had also included those patients who received a non-continuous prescription or no prescription at all. Our second important result was that we detected significant differences between practices with either a high or low percentage of polypharmacy patients, such as the numbers of patients receiving drug prescriptions or the frequency of PPI or NSAID prescriptions. HPP and LPP also differed in the rate of prescriptions issued by doctors other than the patient's general practitioner. However, the absolute differences were modest. Moreover, differences in polyphamacy rates between general practices could not be explained by differences in the practice patient age or gender profile. LPP and HPP did not differ significantly in one relevant indicator for the quality of prescribing performance, the prescription rate for *me-too* drugs.

Strengths and limitations of the study

One major advantage of this study is the large data set analysed, covering all prescriptions to every member of one large SHI. This identified patients with continuous polypharmacy reliably which, as opposed to cumulative or simultaneous polypharmacy,[14] poses a major challenge for general practitioners and clinical pharmacologists.

We had only access to prescription data and the patient's gender and age but neither to diagnoses nor further details of the doctors. So, on principle, it was not possible to determine the appropriateness of any prescriptions and especially of five or more drugs. However, the data in this study provide a reliable basis for a rational debate about the real rate and range of polypharmacy in primary care.

We excluded some practices since they had only a small number of patients and prescribed only very few drugs so that they did not seem to represent typical primary care practices and were not suited for an adequate comparison with HPP. Of course, this decision might have excluded some practices with typical general practitioners who prescribed, for whatever reasons, only few drugs, but we think it would increase a possible bias to include all small practices. Moreover, in a few practices several doctors used the same practice ID, so that these practices were less likely to be excluded.

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We should be aware that doctors in Germany can prescribe, or recommend, drugs without using prescriptions that are forwarded to the SHIs. This happens especially in cough and cold medications or NSAIDs so that patients' real medication use may be underestimated in our study. This is also true for *over-the-counter* (OTC) medicines.

Comparison with the literature

Data in the literature about the prevalence of polypharmacy varies strongly depending upon how polypharmacy is defined. It is not only the number of drugs (usually >4 or >5) that matters, but also the time window and the continuity of prescriptions, which influence prevalence rates. Many studies have chosen 'simultaneous' polypharmacy,[14] i.e. several drugs prescribed at any time, as the criterion for polypharmacy. Since care of the chronically ill—especially the elderly with multiple problems—is a core activity in primary care, we decided to analyse 'continuous polypharmacy',[14] i.e. five or more drugs prescribed continuously over at least a 3-month time period, which seems to mirror a general practitioner's typical challenge in the prescribing process.

Due to differing definitions of polypharmacy, a wide spectrum of prevalence rates is, therefore, not astonishing. For example, Junis-Walker *et al*.[12] found a 25% rate of patients in general practice receiving more than five drugs, and this frequency rose to about 50% when OTC medicines were also included. The prevalence of polypharmacy was 19% in a Danish study of frequent attenders in general practice[20] and even over 75% in a recently published study of Swedish people aged 75–89.[7] At least two studies have reported polypharmacy prevalence frequencies similar to those we have detailed here: a longitudinal study from the Netherlands[5] and a large pharmacoepidemiological study from Denmark[13] reported rates around 4%. Like many other studies, we could also show an increase in polypharmacy in older patients although this increase may be less prominent than other studies have recorded.[2,21] Due to the fact that we considered polypharmacy in patients with at least one continuous prescription, younger patients in our cohort with a chronic disease may have been overrepresented.

Meaning of the study

Polypharmacy was not, or only to a limited degree, related to those practice characteristics that we investigated in this study. Our five hypotheses therefore explain only partially polypharmacy in primary care:

(1) Compared to HPP, patients in LPP received only slightly more drugs from other doctors. Perhaps doctors in HPP were more self-confident in their prescribing skills; or possibly doctors in LPP tried to restrain pharmacological management by their colleagues to control prescribing costs and the burden for their practice budget. In any case, differences in prescribing behaviour between doctors in HPP and LPP were not completely reflected in the total number of prescriptions that a patient received from all his doctors.
(2) General practitioners in LPP or HPP cared for about the same number of patients, but, on average, about 10% more patients in HPP than in LPP received one or more prescriptions. Some authors believe that a high rate of prescriptions reflects their use to shorten a consultation.[22] However, we should be cautious to draw any conclusions due to the small difference observed between HPP and LPP.
(3) That older patients require more drugs does not simply explain polypharmacy. In all practices, the rate of polypharmacy increased with patient age, but the higher polypharmacy rate in HPP, compared to LPP, could not be traced back to a higher mean patient age in these practices. Likewise we could confirm that female patients were prescribed on average more drugs than male; however the higher rate of polypharmacy patients in HPP was not due to more female patients.
(4) HPP did not prescribe more *me-too* drugs. *Me-too* drugs are taken as an indicator of irrational, or at least economically inefficient, prescribing behaviour,[16,23] reflecting especially the influence of pharmaceutical advertising.
(5) HPP prescribed, on average, 1.3 times more drugs per patient than LPP. This rate was more or less the same for nearly all drug groups. Only drugs for acid related disorders, lipid reducing agents, diuretics and NSAIDs were much more frequently prescribed in HPP.

It is possible that the prescription of multiple drugs itself leads to the need for additional medication, so that polypharmacy may become self-perpetuating, for example, in the case of the prescription of PPI due to adverse gastrointestinal effects from drug intake. However, if we analysed the prescriptions in HPP and LPP only for those patients who received more than five drugs, HPP had, again, higher rates of anti-ulcer agents (mainly PPI) and NSAIDs. In particular overuse of PPI without an appropriate indication is a matter of concern.[24] Some doctors might, therefore, profit from

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interventions to improve their prescribing performance, e.g. by the implementation of a computer-generated feedback system.

There was a striking difference between HPP and LPP in the prescription of cough and cold preparations, although the sample of patients was small. These drugs are considered more or less irrational and can be purchased without a prescription. Obviously, most doctors in both LPP and HPP did not prescribe cough and cold preparations or only to a very limited degree. Similar to general practitioners in a British study,[25] who sometimes prescribed antibiotics without indication because of a perceived patient pressure, doctors in our study may have been aware of the limited value of these drugs but doctors in HPP may have been more prone to responding to patient wishes to prescribe these drugs. Although we did not study the patients' behaviour, this may also be an explanation for the generally higher rate of patients with prescriptions in HPP.

IMPLICATIONS AND CONCLUSIONS

Our analysis may contribute to a more objective consideration of polypharmacy as we show that polypharmacy does not have a simple explanation, such as patient age or gender distribution, and that general practitioners with a high rate of polypharmacy are not a homogeneous group that is characterised by inappropriate prescribing behaviour. The practice variation of polypharmacy may mainly result from the distribution in morbidity, as suggested by the results of a recently published prescription study in the UK where the inclusion of morbidity data explained 80% of the variability in prescribing at the practice level whereas patient age and sex alone explained only 10%.[26] So the higher rate of polypharmacy patients in some of our practices might be a direct consequence of a higher rate of patients with more diseases or more severe diseases. To validate this conclusion, a prescription study with direct data about the patients' health status and more details about the characteristics of the practices and the doctors would be needed.

Although we should avoid stigmatising practices solely because of a high rate of polypharmacy, in some instances such as a high rate of PPI prescriptions in polypharmacy patients, it may be reasonable to inform doctors of possible deficits in their pharmacological management.

KEY POINTS

- The rate of continuous polypharmacy, in general practices, defined as the prescription of five or more drugs for at least 3 months, is lower than usually estimated.
- Even though polypharmacy is more prevalent in the elderly and female patients, age and gender are not relevant factors that discriminate between practices with a high and low percentage of polypharmacy patients.
- General practices with a high percentage of polypharmacy patients had a somewhat higher rate of patients who received a drug prescription and doctors in these practices prescribed significantly more PPIs and NSAIDs.
- Practices with a high percentage of polypharmacy patients did not perform worse in other areas of prescribing performance, such as the rate of *me-too* drugs.

ETHICS

Ethical approval was not necessary due to the nature of the data (secondary data analysis of anonymised data).

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