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Inter-practice variation in polypharmacy prevalence amongst older patients in primary care

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ABSTRACT

Purpose

Complex medication management in older people with multiple chronic conditions can introduce practice variation in polypharmacy prevalence. This study aimed to determine the inter-practice variation in polypharmacy prevalence and examine how this variation was influenced by patient and practice characteristics.

Methods

This cohort study included 45,731 patients aged 55 years and older with at least one prescribed medication from 126 general practices that participated in NIVEL Primary Care Database in the Netherlands. Medication dispensing data of the year 2012 were used to determine polypharmacy. Polypharmacy was defined as the chronic and simultaneous use of at least five different medications. Multilevel logistic regression models were constructed to quantify the polypharmacy prevalence variation between practices. Patient characteristics (age, gender, socioeconomic status, number, and type of chronic conditions) and practice characteristics (practice location and practice population) were added to the models.

Results

After accounting for differences in patient and practice characteristics, polypharmacy rates varied with a factor of 2.4 between practices (from 12.4% to 30.1%) and an overall mean of 19.8%. Age and type of conditions were highly positively associated with polypharmacy, and to a lesser extent a lower socioeconomic status.

Conclusions

Considerable variation in polypharmacy rates existed between general practices, even after accounting for patient and practice characteristics, which suggests that there is not much agreement concerning medication management in this complex patient group. Initiatives that could reduce inappropriate heterogeneity in medication management can add value to the care delivered to these patients.

INTRODUCTION

In older people, who are frequently diagnosed with multiple (chronic) conditions,[1] regular use of multiple different medications is common.[2] As a consequence, appropriate prescribing is often not that simple or apparent for physicians.[3-5] On the one hand, prescribing according to recommendations stated in practice guidelines may result in an excessive amount of medications which, in turn, may lead to poor adherence and adverse effects.[6-8] On the other hand, when deciding not to prescribe an additional medication, uncertainty remains about potential benefits of the omitted medication to the patient.[9, 10] Overall, for patients with multiple chronic conditions, who are usually treated in primary care, several pharmaceutical treatment options seem possible and adequate, influenced by the physician's and the patient's perspective, which may lead to variation in medical behavior and practice variation.[11, 12] More focused on the number of medications prescribed for a patient, complex medication management might result into practice variation as regards the number of patients with multiple medications or polypharmacy. Polypharmacy is the simultaneous use of several medications and is often defined as the chronic use of at least five different medications.[2, 13, 14] Polypharmacy has been associated with reduced medication adherence, an increased risk for potentially inappropriate medication use, adverse drug reactions, and unplanned hospitalizations.[6-8] Studies have demonstrated that a higher age, lower socioeconomic status (SES), a higher number, and the type of diagnosed conditions are suggested to be positively associated with polypharmacy. Findings of a gender effect are inconsistent.[2, 6, 15]

When variation in medication prescribing, and polypharmacy, cannot be justified or explained by differences in the patient population and their clinical characteristics,[16-18] this points towards other factors involved in decision-making on a higher level (practice level), for instance, contextual factors, or a lack of consensus about the chosen pharmaceutical treatment.[11, 12] Available studies on practice variation and medication prescribing focused on the use of potentially inappropriate medications in older patients,[8, 19, 20] and to our knowledge, only one study examined the broader concept of polypharmacy in relation to practice variation.[21] They found a sixfold variation between practices in the prevalence rate of polypharmacy; part of this variation could be explained by practice structure, workload, and prescribing profile. Although they adjusted for age and gender, other assuming relevant patient characteristics were not included in this study.[21] Quantifying and understanding practice variation as regards polypharmacy prevalence is relevant, as it can highlight the complexity in managing these patients and may provide clues to facilitate prescribing medications in this patient group. Therefore, the aim of this study was to examine the inter-practice variation of the prevalence of polypharmacy amongst older patients in primary care and how this is influenced by patient and practice characteristics. Based on previous studies,[2, 6, 15, 17, 22, 23] our hypothesis was that patient characteristics (age, gender, SES, and chronic conditions) were associated with polypharmacy and could explain part of the variation between practices, and we hypothesized that some of the practice variation could be explained by differences in practice population. In some general practices, physicians might be more experienced with managing older complex patients with polypharmacy, which could result in less uncertainty in management. In previous studies,[8, 17, 20] it was found that the type of practice or practice size and the

practice location were associated with (high risk) prescribing. Our hypothesis was that practice size could explain some practice variation because in larger practices, several physicians share work environment and cultural aspects and can therefore have a more similar prescribing behavior than physicians from different practices.[12]

METHODS

Database and study population

In this cohort study, we used linked data from routine electronic medical records (EMR) of general practices that participate in a network of a representative sample of practices in the Netherlands, the NIVEL Primary Care Database (NIVEL-PCD),[24] and from dispensing data of a sample of public pharmacies that supplied data to a pharmacy-dispensing registration database (i.e., the Foundation for Pharmaceutical Statistics, SFK).[25] The general practitioner (GP) in the Netherlands, and several other countries, has a gatekeeper role for access to specialized care.[26] As a result, EMR records from the GP are likely to be most complete, hold information from other health professionals like the medical specialists, who manage the patient as well, and include the total population as all Dutch inhabitants are obligatory listed to a GP. The sample of participating pharmacies in NIVEL-PCD is representative as regards the age and gender, compared with the total sample of pharmacies in the Netherlands.[27] Linkage was based on matching records from variables available in both data sources, namely, gender, year of birth, four-digit postal code, date of dispensing/prescribing, and the Anatomic Therapeutic Classification code (ATC) of a medication (i.e., A10BA02 metformin). Linkage was accepted if at least half of the prescriptions (NIVEL-PCD) matched with the dispensed medications (SFK) within a lag period of 0–6 days.[28] We included older patients, specified as those aged 55 years and older, who were registered on the full calendar year of 2012 in a participating general practice. From NIVEL-PCD, we extracted demographic information and morbidity data from patients' EMRs. To determine polypharmacy, information about the chronic usage of patients' prescribed medications was needed. Accurate information about the duration of a prescription and its daily dosage was available in the SFK database. Dispensed data from SFK was also considered more complete as regards the medications prescribed in specialized care, rather than prescription data from NIVEL-PCD. Moreover, dispensed data represent actual usage of medications more closely than prescription data as the medications were actually distributed from the pharmacy to the patient. Therefore, from SFK, we extracted data of patients' dispensed medications. Of the population aged 55 years and older with at least one prescription (117,232 patients) 45,731 patients from 126 general practices participating in NIVEL-PCD were identified in 120 pharmacies that supplied data to SFK (mean number of prescriptions linked population vs. non-linked population 22.3 and 22.8, respectively).

Measures

Polypharmacy

The definition of polypharmacy (no/yes) was derived from the Dutch multidisciplinary guideline of Polypharmacy in the elderly[29]; five or more chronically used medications with different ATC codes at the third level (e.g.,

R03B), which were used simultaneously for at least 1 day in 2012. Chronic usage was defined as four or more prescriptions of a medication (i.e., similar ATC codes at the third level) or a medication prescribed for at least 90 days.[29] See Box 1 for more information.

Box 1. Additional information related to the operationalization of the outcome variable polypharmacy

For the prescription duration period, recorded information about the amount of doses dispensed by the pharmacist and about the daily defined dose for the patient was applied. The prescribed periods of all chronically used medications determined whether five or more different medications were used simultaneously for at least 1 day in 2012 (i.e., polypharmacy). Dermatologicals for topical usage were excluded of the count because these medications usually do not interact with other (systemic) medications.[29] Antibiotics (i.e., ATC codes "J01") were also not taken into account because they are almost exclusively prescribed for acute infections. For some dispensed prescriptions, there was no or incorrect information about the dispensed dosage or daily prescribed dosage. For these prescriptions (11% of all prescriptions in the dataset), the prescribed period was considered the period between the first and last dispensing date of that medication. We have set 120 days between two dates as the maximum number of days to be considered as a consecutive period. If there were more than 120 days between two dates, this was considered as a gap in using.

Patient characteristics

We included age, gender, SES, the number of chronic diseases, and the type of chronic diseases in the analyses. Age was divided in seven 5-year categories (55 to ≥85 years). For SES, a 'status score' was applied, based on patients' four-digit postal codes (neighborhood level), developed by the Netherlands Institute for Social Research.[30] It was established in 2010 with four indicators (mean income, the proportion of people with a low education level, low income, and unemployed). Similar to previous studies,[30, 31] we divided the scores into quintiles, and patients with a score in the highest and lowest quintile indicated patients living in a neighborhood with a high and low SES, respectively. Scores of patients within the middle three quintiles indicated patients living in a neighborhood with a medium SES. Based on previous studies, we selected 29 chronic diseases using constructed disease episodes of recorded morbidity data from GPs' EMRs.[32, 33] The number of chronic diseases was divided into three categories (0–1 chronic disease, 2–4 diseases, and ≥5 diseases). Multimorbidity was defined as two or more chronic diseases (no/yes).

Practice characteristics

Three measures on GPs' experience with managing complex patients were studied. The measures were "proportion elderly patients" operationalized as the proportion patients of ≥70 years in a practice from the total practice population, "proportion patients from a low SES neighborhood" and "proportion multimorbid patients." The variable "proportion patients from a low SES neighborhood" was divided in three categories (i.e., 0–10%, 10–50%, and ≥50%) because of the skewness of the data. We also analyzed the practice type (i.e., solo, duo, and group), the practice's degree of urbanization in three categories (highly, moderate, and not urbanized) and practice

size (i.e., small, medium, and large), based on the practices' number of listed patients divided into tertiles.

Statistical analysis

Descriptive statistics described the study population. To examine inter-practice variation in polypharmacy prevalence, we constructed multilevel logistic multivariate regression models with patients (level 1) clustered within general practices (level 2), polypharmacy as the dependent variable, the patient and practice variables as determinants, and the practice level as random effect. In order to test our hypotheses, the first model included the patient-related variables gender, age, SES, and number of chronic conditions as determinants. In model 2, we added 29 types of chronic conditions, and it considered the full model as regards the patient-related variables. In model 3, the practice population variable "proportion patients with multimorbidity" was added, as well as the variable concerning the practices' degree of urbanization. The other variables on practice level were not included into the multivariate model because their p-values were ≥0.20 when adding them to model 2 separately. All determinants were centered on their mean to make the results more interpretable. In all models, we adjusted for the practice's type of electronic medical record software system to account for possible differences in registration methods. Only patients with complete data were included in the multilevel analysis, and practices with a minimum number of 50 patients to estimate robust models. Besides the odds ratio (OR), 95% confidence interval (CI), and p-value indicating the association between polypharmacy and the determinants, we reported the practice variance component as an estimation of the variance of the polypharmacy rate between practices (i.e., a decrease in value between the models indicated a decrease in the inter-practice variation). Further, we reported the proportion change in variance, indicating the proportion of variance explained by adding explanatory variables. The 95% coverage interval of the practice variance components indicated the range in the practices' difference in the proportion polypharmacy patients that cannot be explained by the covariates. This coverage interval was calculated in the following way: Intercept ± 1.97 sqrt (between practice variance), which was transformed back to the probability scale. The average polypharmacy prevalence per general practice was also estimated by using an empirical Bayes estimator.[34] All analyses were performed using STATA SE version 13.0 and MLwiN version 2.30. A p-value below 0.05 was considered statistically significant.

RESULTS

Population characteristics

Of the patients, 27% had polypharmacy, and they were on average 5 years older than those without polypharmacy (72 vs. 67 years), lived more often in a neighborhood with a low SES (20% compared with 16%), and showed more multimorbidity (90% vs. 46%; Table 1). The number of medications used in the polypharmacy group was on average 11.2 of which 6.9 was used chronically. Information about the practice characteristics is shown in Table 2.

[TABLE 1][TABLE 2]

Inter-practice variation

For the multilevel analyses, data of 44,917 patients from 86 practices (mean no. of patients per practice (SD); 525 (464)) were studied because for 235 patients data on SES was missing and 40 practices (with 579 patients) had less than the required number of patients.

In model 1 (Table 3), the overall mean polypharmacy rate was 21.4%. The practice variance component was 0.07 (SE = 0.01), which corresponds to a 95% coverage interval of 14.1–31.0, meaning that the polypharmacy prevalence ranged from 14% to 31% between practices. The number of chronic conditions was most strongly positively associated with polypharmacy (OR 36.4, 95%CI 32.8 − 40.3, for ≥5 chronic conditions). After including the type of chronic conditions into the model (model 2), only having 2–4 conditions compared with 0 or 1 condition was still significantly associated with polypharmacy. Nearly all chronic conditions were positively associated with polypharmacy, most strongly cardiac conditions (heart failure: OR 5.25, 95%CI 4.59–6.00; coronary artery disease: OR 6.50, 95%CI 6.02–7.02). The practices' difference (95% coverage interval) in adjusted polypharmacy prevalence ranged from 12.1% to 31.6%. For model 2, the average proportion of patients with polypharmacy in each practice separately is presented in Figure 1. After accounting for the patient population, in some practices, there were still at least twice as many patients with polypharmacy than in other practices (a factor 2.6 difference). In model 3, including the practice variables, the practices' range (95% coverage interval) in polypharmacy prevalence varied from 12.4% to 30.1%, indicating that there was a factor 2.4 difference as regards the polypharmacy prevalence between practices after including all explanatory variables, with an overall mean of 19.8%. Practices located in moderately and low urbanized areas had a significantly lower odds ratio of polypharmacy than practices located in very strong or strong urbanized areas.

[TABLE 3][FIGURE 1]

DISCUSSION

Although polypharmacy is common in primary care, this is one of the first studies examining the variation in polypharmacy prevalence between general practices. It was shown that after accounting for differences in patient and practice characteristics, practice variation existed in the polypharmacy rate between practices (factor 2.4). Higher age and most prevalent chronic conditions were highly positively associated with polypharmacy, and to a lesser extent, a lower SES. Further, practices located in lower urbanized areas had a lower odds ratio of polypharmacy than (very) strong urbanized located practices.

One study from 1995 examined inter-practice variation in relation to polypharmacy rates in general practices.[21] They showed lower rates of polypharmacy and more inter-practice variation, that is, a sixfold variation. The discrepancy in findings might be due to the increasing prevalence of polypharmacy in recent years[13] or to changes in regulation and the rise in the development of disease guidelines.[35, 36] Furthermore, the introduction of electronic health record systems, electronic

prescription systems, and guidelines that recommend uniformity in recording are also likely to contribute to reduced variation between practices.[37]

Recently conducted studies on polypharmacy found prevalence rates comparable with our findings.[2, 14] In accordance with our hypothesis, and similar with other studies, we found that higher age and number of chronic conditions were highly positively associated with polypharmacy.[2, 6, 13-15, 38] It was also found that the type of chronic conditions was associated with the number of medications.[2, 38] Our current study underlined that especially the type of diseases, rather than the number of diseases, was related to the number of medications prescribed. The strong association between the number of conditions and polypharmacy decreased when including the type of chronic conditions. Remarkably, an increase in the number of prevalent chronic conditions is not directly accompanied by an increase in prescribed medications. In patients with five or more conditions, it seems that other factors start to play an important role, for instance, interactions between medications, other treatment options like surgery, or perhaps maintaining the status quo.[9] Some diseases are associated with a high number of prescribed medications,[2, 38] and especially as—not unlikely in this age group—other diseases are involved as well, this could lead to several eligible treatment options and practice variation in the number of prescribed medications. Nevertheless, after accounting for the type of chronic conditions, still considerable variation between practices remained.

The finding that practices located in the lowest and moderately urbanized areas had a significantly lower odds ratio of polypharmacy than very strong urbanized located practices cannot be confirmed in literature. Guthrie et al.[20] found that practices located in moderately urbanized areas were more likely to have patients with a high-risk prescription than practices in primary cities; however, the clinical significance of the associations were marginal.[20] In contrary to our hypothesis, practice size did not significantly affect polypharmacy prevalence as had been shown in other studies. Yet, in these studies, those factors could hardly explain any variance in prescribing (high risk) medication.[18, 20]

Strengths of the study are the number of data; 86 practices with, on average, 500 older patients, which contributes to stable and robust multilevel models. A second strength concerned the analyses of actually distributed medications from the pharmacist to the patient instead of just prescription data. A possible limitation is that due to the fact that not all pharmacies agreed to share their data with the NIVEL-PCD, the study population covered a subpopulation of the total general practice sample. Nevertheless, it was found that the studied patients were comparable as regards the mean age and gender with a larger sample of eligible patients only available in NIVEL-PCD. Further, the proportion of patients with polypharmacy may be slightly overestimated as patients with one or two prescriptions were less likely to be included in the analyses because of the applied linkage method. Yet, the majority of the study population (90%) did receive more than two prescriptions, and as it applies to all practices in the same order, it is not likely to affect the results of our main question, namely, practice variation. The identified variation in polypharmacy prevalence might not only be due to the GPs, or physicians working in the general practice. Our dispensed medication data could also hold medications prescribed by medical specialists. Besides, also the pharmacist could have a role in the medications dispensed as he/she checks whether the patients' prescribed medications can be combined.

Because evidence for effective treatment is mostly gathered in younger adults without multimorbidity, it seems logical that for older patients with multiple chronic conditions, physicians more often rely on their own experiences and reasoning when prescribing medications. This is not necessarily worrisome if it is justified, for instance, when accounting for the patient's preferences and priorities.[39] However, because considerable variation between practices existed after accounting for differences in patient and practice characteristics, the results indicate that physicians from different practices have different prescribing behaviors, and it suggests that there might be professional uncertainty about the best treatment. However, next to the GP, also the medical specialist and pharmacist play an important role in medication therapy management. It is likely that part of the unexplained variation is due to pharmacy-related factors or by factors that indicate the level of cooperation between the GP and pharmacist. Several strategies and activities exist to reduce unnecessary medication use, involving different health professionals such as the GP and pharmacist.[29, 40-46] For instance, when contemplating on complex patients and medication combinations, this could turn differences in management views into a common view. It seems valuable to further investigate possible explanations for the variance in polypharmacy prevalence, such as differences in physician-related characteristics, such as their clinical experience, and in the level of cooperation between the various professionals involved in medication prescribing.
In conclusion, because numerous inter-practice variations in polypharmacy prevalence exist, attention for medication management is important, especially in complex older patients with multiple chronic conditions. Physician initiatives to achieve a more shared vision about the best therapeutic treatment add to the patient's value of care.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.
Key Points

- Considerable variation in polypharmacy prevalence exists between general practices (from 12% to 30%);
- The type, rather than the number, of prevalent chronic conditions was highly associated with polypharmacy, especially in patients with many diagnosed diseases, but it hardly explained inter-practice variation.
- The variation in polypharmacy prevalence could only, for a small part, be explained by differences in the patient population and by practice characteristics;
- The results of this study suggest that there might be professional uncertainty about the best treatment for this complex patient group;
- Because different health professionals play a role in medication management, initiatives to achieve a more shared vision about the best therapeutic treatment for this patient group can be valuable.

ETHICS STATEMENT

This study was executed according to the precepts of the Dutch legislation on privacy and the regulations of the Dutch Data Protection Authority. According to Dutch

legislation, studies using this type of observational data do not require medical ethical approval nor informed consent.

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TABLES AND FIGURES

Table 1. Descriptive characteristics of the study population: patients aged ≥ 55 years with at least one prescribed medication in 2012, divided by patients with and without polypharmacy

	No polypharmacy ($N = 33,449$)		Polypharmacy ($N = 12,282$)		p-value*
	N	%	N	%	
Male	15,279	45.7	5,702	46.4	0.155
Female	18,170	54.3	6,580	53.6	
Age, mean (SD)	66.6 (8.7)		72.4 (9.5)		<0.001
Age groups					<0.001
55–59 years	8,220	24.6	1,214	9.9	
60–64 years	7,859	23.5	1,664	13.5	
65–69 years	6,583	19.7	2,134	17.4	
70–74 years	4,467	13.3	2,088	17.0	
75–79 years	3,105	9.3	2,108	17.2	
80–84 years	1,900	5.7	1,677	13.6	
≥85 years	1,315	3.9	1,397	11.4	
SES categories†					<0.001
High	5,044	15.2	1,477	12.1	
Medium	22,772	68.4	8,275	67.8	
Low	5,472	16.4	2,456	20.1	
Mean no. of chronic conditions (SD) ‡	1.6 (1.3)		3.4 (1.6)		<0.001
Number of chronic conditions					
0	6,916	20.7	133	1.1	<0.001
1	11,054	33.0	1,118	9.1	
2	8,516	25.5	2,738	22.3	
3	4,341	13.0	3,166	25.8	
4	1,770	5.3	2,468	20.1	
5	636	1.9	1,459	11.9	
≥6	216	0.6	1,200	9.7	
Multimorbidity§	15,479	46.3	11,031	89.8	<0.001
Mean no. of medications (SD)¶	4.5 (2.9)		11.2 (4.2)		<0.001
Mean no. chronically used medications (SD)‖	1.7 (1.4)		6.9 (2.1)		<0.001
Number of chronically used medications					
0	8,424	25.2	0	0.0	<0.001
1–4	24,715	73.9	0	0.0	
5–9	310	0.9	10,838	88.2	
10–14	0	0.0	1,377	11.2	
≥15	0	0.0	67	0.6	

Note: Total $N = 45,731$ patients and 126 practices. SD, standard deviation.
*Statistical significance tested with chi-squared tests (binary variables) or T-tests (continuous variables).
†Socioeconomc status (SES) on neighborhood level (i.e., four-digit postal code)
‡Based on a list of 29 chronic conditions[32].
§≥2 chronic conditions out of the list of 29 chronic conditions[32].
¶Medication on the third Anatomic Therapeutic Classification level.
‖Medication on the third Anatomic Therapeutic Classification level, with at least four prescriptions or those used for minimal 90 days (excluding the dermatologicals and antibiotics).

Table 2. Characteristics of the general practices and the number of patients per practice variable

	Practices ($N=126$)		Patients ($N=45,731$)	
	N	%	*N*	%
Type of practice				
Single-handed practices	69	54.8	20,174	44.1
Duo practices	40	31.7	14,803	32.4
Group practices	17	13.5	10,754	23.5
Practice size*				
Small	76	60.3	15,336	33.5
Medium	33	26.2	16,698	36.5
Large	17	13.5	13,697	30.0
Degree of urbanization (location of the practice)				
(Very) strong	67	53.2	19,185	41.9
Moderate	28	22.2	10,176	22.3
Little or not	31	24.6	16,370	35.8
Practice population characteristics				
Mean % patients ≥70 years (SD)	11.4	(3.92)	—	
Mean % patients living in a low SES neighborhood (SD)†	26.4	(28.8)	—	
Mean % patients with multimorbidity (SD)	20.1	(4.18)	—	
Mean no. of pharmacies per practice (SD)‡	2.28	(1.20)	—	
Electronic medical record software type				
A	63	50.0	22,047	48.2
B	9	7.1	2,783	6.1
C	12	9.5	3,630	7.9
D	34	27.0	12,207	26.7
E	7	5.6	5,063	11.1
F§	1	0.8	1	<0.01

SD, standard deviation.

*Number of registered patients: small, 1819–3408; medium, 3433–6056; large, 6059–15300.

†Estimated by counting the number of patients living in a low socioeconomic status (SES) neighborhood divided by the total practice population for whom SES information was available.

‡The pharmacies that supplied data to Foundation for Pharmaceutical Statistics and Netherlands Institute for Health Services Research.

§Type F electronic medical record software type was not included in the multilevel models because only one practice with one patient of the study population used this type.

Table 3. The association between patient-related and practice-related variables and polypharmacy and the inter-practice variance in proportion patients with polypharmacy with multilevel multivariate regression modeling

	Model 1			Model 2			Model 3		
	OR	95% CI	*p*-value	OR	95% CI	*p*-value	OR	95% CI	*p*-value
Fixed effects									
Patient characteristics									
Gender (men/women)	0.81	0.77–0.85	<0.001	1.01	0.95–1.06	0.819	1.01	0.95–1.06	0.819
Age groups									
55–59 years	Ref.			Ref.			Ref.		
60–64 years	1.16	1.06–1.26	0.001	1.08	0.98–1.19	0.118	1.08	0.98–1.18	0.120
65–69 years	1.57	1.44–1.71	<0.001	1.39	1.26–1.52	<0.001	1.39	1.26–1.52	<0.001
70–74 years	1.85	1.69–2.02	<0.001	1.60	1.45–1.76	<0.001	1.60	1.45–1.76	<0.001
75–79 years	2.26	2.06–2.47	<0.001	1.94	1.75–2.15	<0.001	1.94	1.75–2.15	<0.001
80–84 years	2.52	2.27–2.78	<0.001	2.08	1.86–2.34	<0.001	2.08	1.86–2.34	<0.001
≥85 years	2.96	2.66–3.31	<0.001	2.44	2.15–2.77	<0.001	2.44	2.15–2.77	<0.001
SES categories									
High	Ref.			Ref.			Ref.		
Medium	1.15	1.05–1.26	0.003	1.12	1.01–1.24	0.028	1.10	1.00–1.22	0.061
Low	1.26	1.12–1.41	<0.001	1.20	1.05–1.36	0.005	1.14	1.00–1.30	0.042
Number of chronic conditions									
0–1 conditions	Ref.			Ref.			Ref.		
2–4 conditions	7.26	6.80–7.76	<0.001	1.37	1.24–1.51	<0.001	1.37	1.24–1.51	<0.001
≥5 conditions	36.4	32.8–40.3	<0.001	0.94	0.77–1.15	0.525	0.94	0.77–1.15	0.527
Type of chronic conditions									
HIV/AIDS	—	—	—	1.25	0.37–4.25	0.130	1.24	0.36–4.19	0.734
Cancer	—	—	—	1.31	1.22–1.41	<0.001	1.31	1.22–1.41	<0.001
Visual disorder	—	—	—	1.14	1.05–1.24	0.002	1.14	1.05–1.24	0.002
Hearing disorder	—	—	—	1.11	1.01–1.21	0.032	1.11	1.01–1.22	0.029
Congenital cardiovascular anomaly	—	—	—	1.88	1.13–3.13	0.014	1.89	1.14–3.14	0.014
Heart valve disorder	—	—	—	2.20	1.85–2.60	<0.001	2.19	1.85–2.60	<0.001
Heart failure	—	—	—	5.25	4.59–6.00	<0.001	5.25	4.59–6.01	<0.001
Coronary artery disease	—	—	—	6.50	6.02–7.02	<0.001	6.51	6.03–7.03	<0.001
Cardiac dysrhythmia	—	—	—	3.06	2.77–3.38	<0.001	3.06	2.77–3.38	<0.001
Hypertension	—	—	—	2.88	2.70–3.08	<0.001	2.89	2.71–3.08	<0.001
Stroke	—	—	—	3.22	2.88–3.60	<0.001	3.22	2.88–3.60	<0.001
Rheumatoid arthritis	—	—	—	3.51	3.06–4.03	<0.001	3.52	3.07–4.04	<0.001
Osteoarthritis	—	—	—	1.18	1.10–1.27	<0.001	1.18	1.10–1.27	<0.001
Chronic back or neck disorder	—	—	—	1.63	1.50–1.79	<0.001	1.63	1.49–1.78	<0.001
Osteoporosis	—	—	—	2.20	1.99–2.43	<0.001	2.20	1.99–2.43	<0.001
Parkinson's disease	—	—	—	2.77	2.13–3.58	<0.001	2.77	2.14–3.59	<0.001
Epilepsy	—	—	—	2.04	1.65–2.52	<0.001	2.04	1.67–2.49	<0.001
Migraine	—	—	—	1.49	1.18–1.87	<0.001	1.49	1.19–1.87	<0.001
Chronic alcohol abuse	—	—	—	2.18	1.67–2.86	<0.001	2.17	1.66–2.84	<0.001
Dementia incl. Alzheimer's disease	—	—	—	1.89	1.55–2.31	<0.001	1.89	1.55–2.31	<0.001
Schizophrenia	—	—	—	3.96	2.47–6.36	<0.001	3.94	2.45–6.34	<0.001
Depression and psychosis	—	—	—	2.71	2.41–3.05	<0.001	2.71	2.41–3.05	<0.001
Anxiety disorder	—	—	—	2.06	1.73–2.45	<0.001	2.06	1.73–2.45	<0.001
Neuraesthenia/surmenage/burn-out	—	—	—	0.85	0.64–1.13	0.159	0.86	0.64–1.14	0.281
Personality disorder	—	—	—	2.17	1.53–3.08	<0.001	2.16	1.52–3.07	<0.001
Intellectual disability	—	—	—	1.76	1.01–3.08	0.048	1.75	1.00–3.07	0.049
COPD	—	—	—	2.46	2.26–2.68	<0.001	2.46	2.26–2.68	<0.001
Asthma	—	—	—	1.82	1.66–2.01	<0.001	1.82	1.66–2.01	<0.001
Diabetes mellitus	—	—	—	4.70	4.38–5.04	<0.001	4.69	4.37–5.04	<0.001
Practice (population) characteristics									
Proportion practice population with multimorbidity*†	—	—	—	—	—	—	1.06	0.95–1.18	0.301
Practice location (urbanization)									
(Very) strong	—	—	—	—	—	—	Ref.		
Moderate	—	—	—	—	—	—	0.78	0.64–0.94	0.008
Little or not	—	—	—	—	—	—	0.81	0.68–0.97	0.025
Random effects									
Practice variance component (SE)	0.066 (0.013)			0.095 (0.018)			0.081 (0.016)		
Mean % polypharmacy	21.4%			20.1%			19.8%		
95% coverage interval polypharmacy ‡	14.1–31.0%			12.1–31.6%			12.4–30.1%		
% variance explained regarding the previous model §	—			−43.9%			14.7%		

Note: Total $N = 44{,}917$ patients in 86 practices. All models were adjusted for the practice's EMR software type. OR, odds ratio; CI, confidence interval; SE, standard error; COPD, chronic obstructive pulmonary disease; SES, socioeconomic status.

*These proportions are based on information of the total practice population.

†Continuous variables.

‡The 95% coverage interval. The range indicates the practices' difference in polypharmacy prevalence.

§This is the proportion variance in polypharmacy between practices explained by including explanatory variables (e.g., $(Var_{practice}model1 - Var_{practice}model2)/Var_{practice}model1$).

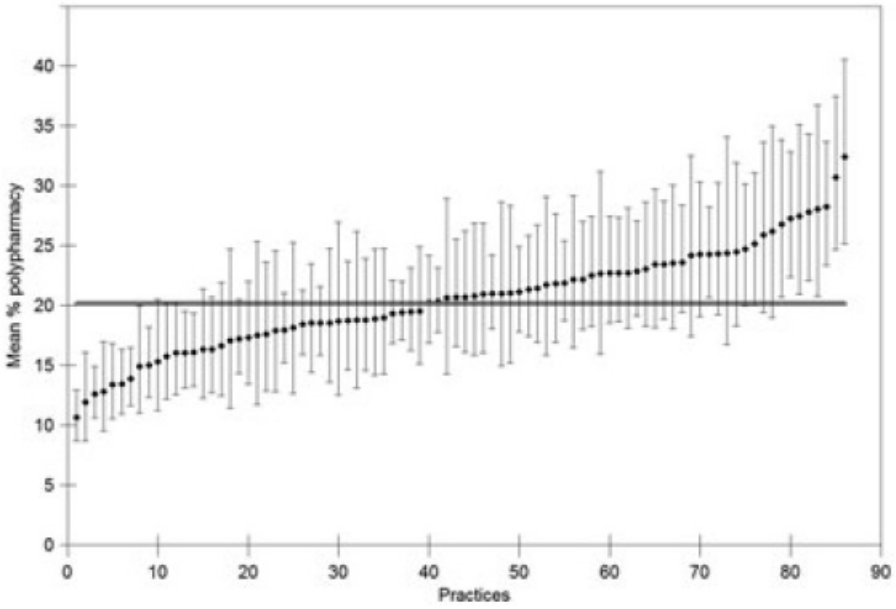

Figure 1. The adjusted average polypharmacy prevalence per practice after accounting for differences in patient characteristics (model 2)
Note: N=44,917 patients in 86 general practices. The thick horizontal grey line at 20.1% represents the overall adjusted proportion of patients with polypharmacy. The black dotted line represents the estimated average proportions of patients with polypharmacy in each practice. The error bars represent the 95% confidence interval around the estimate of that practice. [Correction added on 01 September 2016, after first online publication: The error bars in Figure 1 were previously incorrectly representing 99.9% confidence intervals and should represent 95% confidence intervals. This error has been corrected in this current version of the figure.]