

# Relationship between polypharmacy and underprescribing

Mascha A. J. Kuijpers,<sup>1</sup> Rob J. van Marum,<sup>1</sup> Antoine C. G. Egberts,<sup>2</sup>  
Paul A. F. Jansen<sup>1</sup> & The OLDY (OLd people Drugs & dYsregulations)  
study group

<sup>1</sup>Department of Geriatric Medicine, University Medical Centre, Utrecht and <sup>2</sup>Department of Clinical Pharmacy, University Medical Centre, Utrecht and Division of Pharmaco-epidemiology and Pharmacotherapy, Utrecht Institute of Pharmaceutical Sciences, Faculty of Science, Utrecht University, Utrecht, the Netherlands

## WHAT IS ALREADY KNOWN ABOUT THIS SUBJECT

- Polypharmacy is common among the elderly.
- Underprescribing is also frequent.
- Optimizing polypharmacy includes avoiding underprescription.

## WHAT THIS STUDY ADDS

- The probability of underprescription increases with the number of drugs used.
- Forty-three % of patients who used five or more medicines are undertreated.
- In undertreated patients a mean of 1.4 medicines were lacking.

## Correspondence

P.A.F. Jansen, MD/PhD, Department of Geriatric Medicine, B05.256, PO Box 85500 3508 GA Utrecht, the Netherlands.  
E-mail: p.a.f.jansen@umcutrecht.nl

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## AIMS

Underprescribing is increasingly recognized as an important problem. The aim of this study was to determine the relationship between polypharmacy and underprescribing.

## METHODS

Treatment of current medical problems in geriatric patients was compared with general practitioner and national guidelines. Underprescription was defined as lack of an indicated drug, while no reason could be found for not prescribing it. Polypharmacy was defined as five or more drugs.

## RESULTS

Polypharmacy was present in 61% of 150 patients. Underprescription was found in 47 (31%). Of patients with polypharmacy 42.9% were undertreated, in contrast to 13.5% of patients using four medicines or less (OR 4.8, 95% CI 2.0, 11.2). The estimated probability of underprescription increased significantly with the number of drugs.

## CONCLUSIONS

We found a clear relationship between polypharmacy and underprescribing.

## Introduction

Research on polypharmacy is mainly aimed at reducing inappropriate prescription of drugs, drug–drug and drug–disease interactions. However, despite of the use of many medicines, undertreatment is also frequent present in the elderly [1, 2]. The objective of this study was to investigate the relationship between polypharmacy and underprescribing in a geriatric population.

## Methods

### Setting, study population and data collection

We asked permission from all patients, consecutively admitted between October 2004 and February 2005 to the Department of Geriatric Medicine of the University Medical Centre Utrecht, to study their general practitioner (GP) and pharmacy records.

We collected data concerning past medical history, current medical problems, and medication use to evaluate the applied therapy.

### Endpoint

The primary endpoint was the frequency of underprescription. Underprescription was defined as lack of drug treatment for a present disease, for which drug therapy is indicated according to clinical practice guidelines (CPGs) in the Netherlands, and for which no contra-indication, therapy failure or relevant adverse effects, for which the drug was stopped, was found in the GP record. The patients were questioned about present diseases and examined. The conditions were evaluated using biometric, for example blood pressure, and laboratory data. Actual treatment was compared with the pharmacological treatment according to the following CPGs:

*General Practitioner Guidelines* [3]: Hypertension, acute coronary syndrome, angina pectoris, heart failure, atrial fibrillation, peripheral arterial vascular disease, TIA, CVA, diabetes mellitus type 2, cholesterol, osteoporosis, stomach problems, COPD treatment, urinary tract infections, pain treatment.

*National Interdisciplinary Guidelines* [4]: Hypertension, heart failure, peripheral artery disease, CVA, cholesterol, osteoporosis, stomach complaints, NSAID use and prevention of stomach injury, deep venous thrombosis and pulmonary embolus, and urinary tract infections.

In the case of differences between both used guidelines, the GP guidelines were followed because most patients were referred by GPs. In three situations lack of pharmacotherapy, indicated according to the guidelines, was not considered as underprescription: 1) when there was no pharmacotherapy for a disease for which the patient was primarily referred, 2) when the indicated drug had been prescribed for a sufficient time period in the past, for example a bisphosphonate and 3) when a patient had stopped using a prescription on his own initiative.

Three researchers (MK, RM, PJ) determined the indicated drugs for the present conditions and then decided, independently of each other, if a drug was lacking. In a case of disagreement consensus was reached.

### Determinant

Determinant of interest was polypharmacy defined as the concomitant use of five or more drugs. Actual drug prescription was determined from the GPs' and pharmacy's records.

### Statistical analysis

The number of patients with lack of an indicated drug was calculated as a percentage of the total number with an indication for this drug. The percentage of patients with lack of one or more medications was calculated per number of drugs. The relationship between the risk of underprescription and number of drugs used was estimated using logistic

regression analysis with adjustment for age and gender. A Chi-square test was used to calculate the relationship between undertreatment and polypharmacy. Statistical analyses were performed in SPSS, version 11.5.

## Results

Of 154 consecutive patients, visiting the out-patient clinic, day-hospital, or geriatric ward, 150 gave informed consent. The mean age ( $\pm$ SD) was  $79.6 \pm 7.3$  years (range 65–100 years) and 64% were women. Mean drug use ( $\pm$ SD) was  $6 \pm 3$  (range 0–17) medications. Polypharmacy was present in 61%. Underprescription was found in 47 (31%) patients. Of patients with polypharmacy, 43% were undertreated, in contrast to 13.5% of patients using four or less drugs (adjusted OR 4.8, 95% CI 2.0, 11.2). Of patients who were underprescribed, 83% used five drugs or more. They used on average 7.3 medicines. Correction of underprescribing would augment the medicines in the studied population with 0.4 medicines to a mean of 6.4 and in the 47 undertreated patients with 1.4 medicines to a mean of 8.7. Table 1 shows the most frequently underprescribed conditions. We found the highest percentage of underprescription for laxatives to prevent constipation in patients using morphine and for  $\beta$ -adrenoceptor blockers and ACE inhibitors in the treatment of cardiovascular disease. The probability of underprescription increased significantly with the prescribed number of drugs (Figure 1). Of patients with known cognitive disturbances ( $n = 43$ ), 28% were undertreated in contrast with 33% without cognitive disturbances (NS).

## Discussion

This study shows a clear relationship between polypharmacy and underprescription. The probability of underprescription increased significantly with the number of medicines. Recently Steinman *et al.* [5] found medication underuse in 64% of elderly outpatients. In contrast to our study the frequency of underuse was not related to the number of medicines. The difference from our study is that Steinman *et al.* assessed underuse with the Assessment of Underutilization of Medicine instrument and they only included patients taking five or more medications.

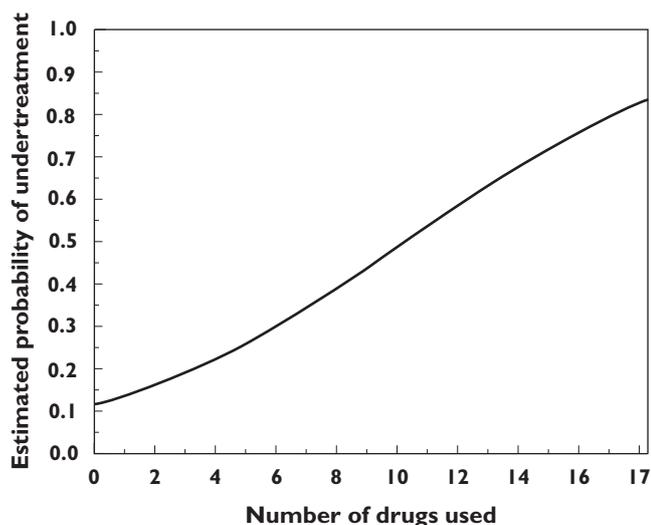
Underprescription can be considered to be an important part of inappropriate prescribing [6]. Undertreatment in middle-aged and elderly patients is reported in a high percentage for cardiovascular diseases, hyperlipidaemia, osteoporosis, COPD, depression and cancer [7–12]. Kuzuya [7] showed that patients with dementia were less likely to be prescribed multiple medications. In our study we found no statistical difference for undertreatment between patients with or without cognitive disturbances.

It can be speculated that GPs are unwilling to prescribe more drugs to patients with polypharmacy (e.g. complex-

**Table 1**

Most frequent underprescribed conditions in a geriatric population

Condition	Missing drug	Total number of patients	Patients not eligible	% of underprescription
Morphine use	Laxative	13	0	61.5%
Myocardial infarction	β-adrenoceptor blocker	15	4	60%
Heart failure	ACE inhibitor	21	4	47%
Atrial fibrillation	Cumarin derivatives	18	2	42%
Osteoporosis	Bisphosphonate or raloxifen	43	9	29%
Hypercholesterolaemia	Statin	13	0	23%
Hypertension	Antihypertensive	56	10	23%
Angina pectoris, CVA, TIA, peripheral arterial vascular disease	Thrombocyte-aggregation inhibitor	53	8	21%
NSAID use	Stomach protection	21	0	21%



**Figure 1**

Estimated probability of underprescription related to the number of drugs

ity of drug regimens, fear of ADRs, interactions and poor adherence). Sometimes a so-called treatment-risk paradox or risk-treatment mismatch exists meaning that patients who are at highest risk for complications, have the lowest probability to receive the recommended pharmacological treatment [9, 11]. Further qualitative research is necessary to establish whether this phenomenon can also explain our observations.

Our study has several limitations. We studied a geriatric population and the results may not be generalized to all community dwelling elderly. We compared the prescriptions of a selection of diseases with guidelines used in the Netherlands. We may have therefore underestimated underprescription. However, GPs were not questioned about the reasons for underprescription. It is also questionable if CPGs can always be used in the treatment of elderly

patients since most CPGs do not take comorbidity, polypharmacy or lack of evidence of efficacy for elderly patients into account [13]. The application of CPGs to the care of older patients with several comorbid diseases may have undesirable effects and GPs may have had reasons not to treat all problems. Also we did not ask patients if they had been offered drugs and declined them. In case of polypharmacy patients might be reluctant to take more drugs. Often adherence decreases as prescriptions increase. Boyd *et al.* [13] showed that if the relevant CPGs were followed, the hypothetical patient would be prescribed 12 medications. In this study correction of underprescribing would augment the medicines in the total studied population by 0.4 medicines to a mean of 6.4 and in the 47 undertreated patients by 1.4 medicines to a mean of 8.7. Because the aim of this study was to determine underprescribing, we did not look at overtreatment. If so, the total amount of appropriate medicines would probably be less. The evidence of the benefit of the application of CPGs in patients with comorbid disease is lacking. However, in optimizing polypharmacy, attention should be directed not only to overtreatment, but also to possible undertreatment. The aim is to prescribe indicated polypharmacy to patients with comorbid diseases.

In conclusion underprescribing is considered an important problem in the elderly with comorbid diseases. This study shows a clear relationship between polypharmacy and underprescription in a geriatric population.

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