

# Polypharmacy in general practice

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## ABSTRACT

**INTRODUCTION:** Polypharmacy increases the risk of side effects and interactions. We quantified the prevalence of major polypharmacy (MPP) in a Danish county with 236,000 inhabitants, invited general practitioners (GPs) to participate in a quality improvement project and discussed the medication of 10-20 MPP patients selected by the participating GPs.

**MATERIAL AND METHODS:** This was a prospective registry study of all prescriptions of subsidized drugs in the third quarter of 2005 for all inhabitants living in Roskilde County, Denmark. An audit was performed of the prescriptions of 220 MPP patients selected by the GPs based on a list of each MPP patient's medications.

**RESULTS:** MPP patients constituted 2.1% of the county's population. GPs demonstrated a strong interest in auditing prescriptions. A large share of the patients selected by the GPs was treated with drugs which were no longer indicated, or with drugs with a doubtful indication.

**CONCLUSIONS:** MPP compromises the GP's ability to manage medication of individual patients. Systematic audit of the total medication of patients should be introduced.

Polypharmacy (PP), concomitant use of multiple drugs, is common in elderly patients. PP patients are at increased risk of adverse drug reactions, potential drug interactions and insufficient treatment outcomes [1-3]. Frequently, the general practitioner (GP) responsible for a patient is unaware of all the drugs that form part of the patient's treatment because some of the drugs have been prescribed by other physicians [2, 4] or by the GP's assistants [4]. Many patients require treatment with several drugs for each diagnosis, and PP is therefore often indicated [5]. The term *major polypharmacy* (MPP) was coined to characterize situations of drug overuse.

Prescription data may be used to improve GPs' prescription patterns [2]. We quantified MPP in the former Roskilde County (236,000 inhabitants) and investigated GPs' PP cases via an inter-disciplinary review of the treatment of 10-20 PP patients selected by each participant. Furthermore, we checked whether each prescription for each patient was warranted.

## MATERIAL AND METHODS

There is no broadly accepted operational definition of MPP. Concomitant use of a minimum of five [6], six [7],

nine [8] or ten [9] drugs was previously used to define MPP. Concomitant use of four drugs is often indicated for treatment, e.g. in diabetes [5]. We therefore defined MPP as the use of six or more prescription drugs during a three-month period.

## Registry study of major polypharmacy

By law, pharmacies shall report data on each prescription dispensed. Reporting requirements include the Anatomical Therapeutic Chemical (ATC) classification code, number of defined daily doses, costs and the GP's General Medical Council Registration Number. The data are reported to a national administrative database. If a patient picks up prescription drugs at a pharmacy outside his or her county, the prescription data are also reported to the database. From the database we obtained a dataset on citizens registered with a GP in Roskilde County in the third quarter of 2005. The database included information on each GP's General Medical Council Registration Number, the patients' sex and age, and all subsidized prescription drugs dispensed to the patients during the third quarter of 2005. Drugs sold over-the-counter, non-subsidized prescription drugs (e.g. benzodiazepines) and prescriptions which were not picked up by the patients were not included in the database.

Our dataset included data for each individual patient on sex, age and the number of different drugs dispensed at ATC level five. The trademark was not included in the registry, and generic substitution was not registered. We calculated the number of MPP patients in the county in the third quarter of 2005 and their sex, age and number of drugs.

## Analyses performed in cooperation with the general practitioner

At end of 2005 and 2006, the 150 GPs practising in Roskilde County received an invitation to participate in a quality assurance project concerning PP in their practice. The invitation included a description of the project.

The county's drugs consultant (a pharmacist) identified all patients who were in treatment with more than five drugs during the third quarter of 2005 (recruitment period one) or 2006 (recruitment period two) and made a list of all the prescription drugs bought by the patient during the three-month period. Participants in the study

## ORIGINAL ARTICLE

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received a list of their MPP patients and were asked to select 10-20 patients, whose medications they would like to discuss, and to fill in a questionnaire for each patient. In the questionnaire the GPs were asked to indicate for each prescription:

- What was the treatment indication?
- Was the prescription indicated at the time of the prescription?
- Whether treatment targets were defined for the drug and known by the GP and the patient?
- Whether treatment targets were reviewed regularly by the GP?
- Whether a treatment duration target had been defined?
- Whether a date for review of the prescription had been scheduled?
- Whether the risk of interactions between the drug and other prescriptions were considered at the time of referral?

The medication of the selected patients was discussed in the general practice by the GP, an internal medicine consultant and two drug consultants (a GP working part-time for the county and a pharmacist working full-time for the county). The GPs were reimbursed for their lost income during the visit which was scheduled to take two hours.

## RESULTS

### The registry study

In the third quarter of 2005, a total of 236,445 citizens were registered with a GP in Roskilde County. During the study period, 4,996 patients (2.1%) were treated with six or more (range: 6-32) drugs (**Figure 1**). 2.4% of the female and 1.6% of the male patients were MPP patients. A total of 92% of the MPP patients were 50+ years old, and 76% were 60+ years old. These two age groups constituted 36% and 21% of the county's population, respectively [10] (**Figure 2**).

### Analyses made in cooperation with general practitioners

In recruitment period one, eight practices joined the study (7% of the GPs in the county); in recruitment period two, 15 practices (10% of the GPs) joined the study. In all, 55,841 citizens (24% of the total county population) were registered with the 23 practices. On average, 2.9% of the registered citizens in the participating practices were MPP patients (median: 2.9%; range: 1.3-5.7%) compared with 2.1% in all the county's practices. In 18 of the 23 participating practices, the share of MPP patients was above the county average.

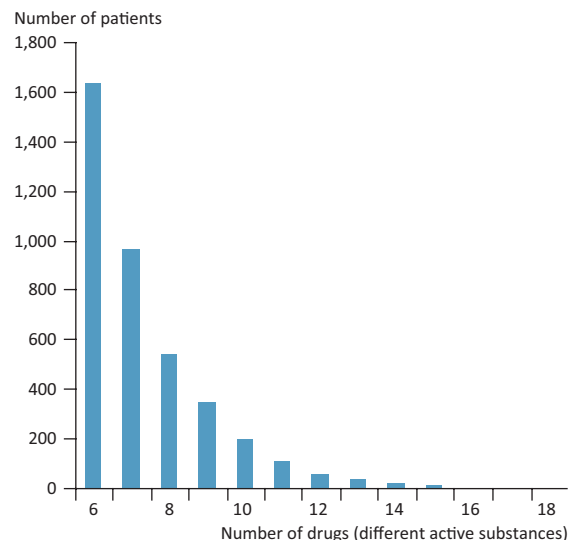
Twenty-three practices, 29 GPs (12 in single-handed

practices and 17 in 11 partnerships) and 1,809 MPP patients were included in the study.

Only a few GPs responded to the questions regarding medical treatment, thereby indicating that treatment objectives had not been defined; that targets for treatment time had not been set and that no date for review of prescriptions had been scheduled. However, the GPs may have found that collecting data from the patients' records would be too time-consuming. The findings also applied to MPP patients for whom the GPs retrospectively found indication for review of the prescription. A major share of the MPP patients was in treatment with one or more drugs, whose indication the

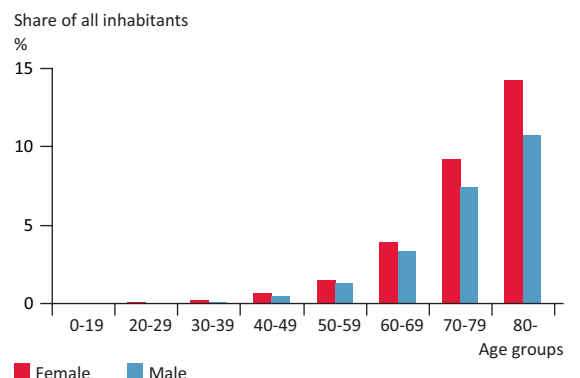
**FIGURE 1**

Polypharmacy patients in Roskilde County July-September 2005.



**FIGURE 2**

Polypharmacy patients share by age group. July-September 2005 – Roskilde County.



GP and reviewers agreed was doubtful at the time of review or was already doubtful when the drug was prescribed. Significant interactions were only found in a few patients.

The medication of 220 MPP patients (arithmetic mean: 10.0 patients; range: 6-18 patients) was discussed. On average, 1.9 medication changes were proposed for each patient (range: 0-6). The reason for the majority of these recommendations was that a prescription was no longer indicated or that the effect of a drug was doubtful. Many recommendations were similar within each practice and between various practices. On average, there were 12.8 (range: 6-28) different recommendations or comments regarding the prescriptions at each practice. Common recommendations concerned:

*Drug dose:* E.g. patients were treated with too high doses of proton-pump inhibitors (PPIs), non-steroidal anti-inflammatory drugs (NSAIDs) or the thrombosis inhibitor acetylsalicylic acid, e.g. with 150 mg acetylsalicylic acid instead of 75 mg.

*Patients treated with too high doses of NSAIDs and for a longer time than recommended* in the guidelines from the national Danish Institute for Rational Pharmacotherapy [11].

*Discontinuation:* E.g. treatment with PPIs or antirheumatic drugs continued beyond its indication. Treatment with glucosamine continued after exceeding a time limit as determined in a national guideline on treatment with the drug.

*Risk of adverse drug reactions or interactions:* E.g. NSAIDs were prescribed in cases where paracetamol was considered sufficient for effective treatment.

*Financial considerations:* Relatively expensive drugs such as the NSAID Todolac could have been substituted by less expensive analogues. Cipralex could have been substituted by the less expensive Citalopram or Mirtazapine in accordance with the county's recommendations. Patients were prescribed angiotensin II-antagonists as the GP's first choice instead of equally effective, but less expensive angiotensin-converting enzyme inhibitors in accordance with the county's recommendations.

*Prescription of obsolete drugs or drugs without documented effect:* E.g. quinine against leg cramps.

## DISCUSSION

PP is often associated with treatment of concomitant chronic diseases, providing indication for medical treatment with several drugs for each disease [12] and PP is therefore frequently indicated. However, PP is associated with an increased risk of adverse drug reactions [6] that rises exponentially with the number of concomitant drugs used [13], and interactions may blur the intended effects of the drugs on the disease.



Many polypharmacy patients are treated with drugs which are no longer indicated.

Consequently, the advantages of every prescription must be weighed against its risks, and it is important to quantify and prevent MPP.

Researchers have utilised different definitions of PP and MPP. We defined MPP as the use of six prescription drugs or more during a three-month period. In several previous Danish studies, MPP was defined as concomitant use of five drugs or more [6]. A dynamic definition of MPP may be warranted that takes into account the growing number of drugs available and that admits that concomitant treatment with several drugs is indicated for some of the most common chronic diseases. An MPP limit not exceeding five drugs may, in the current context, therefore exaggerate the importance of MPP as a health problem.

As PP is associated with patient age [2], elderly citizens' growing share of the population will result in a larger share of the population becoming PP patients. MPP is especially problematic in the elderly if prescribers do not consider that their older patients' pharmacokinetics and pharmacodynamics differ from those of their younger patients'. Elderly patients are at increased risk of concomitant chronic diseases, PP and inappropriate prescriptions (drugs which should not be prescribed to the elderly) [6]. A Danish study found that most patients had one or more inappropriate prescriptions, and 12.3% of all prescriptions were not indicated [14].

The present study confirms that the prevalence of MPP is positively correlated with age for both sexes and that female patients are at increased risk of MPP [6]. It is unfortunate that MPP is particularly common in a patient group which often has difficulties in fully understanding their treatment. Surprisingly, a Dutch cohort study of PP found no association between PP and the

number of diseases diagnosed during the study period [12]. Parallel prescription of drugs from several prescribers is a known risk factor for PP [12, 15, 16], but in Denmark each citizen is registered with one general practice, acting as a *gatekeeper*, and this structure probably reduces the PP incidence.

PP may be inappropriate if it reduces compliance, and medication regimens with frequent dosing are associated with a low compliance [17]. PP may be inappropriate due to the risk of interactions, but the actual number of interactions is not necessarily associated with PP [18]. In the present study, we found only few interactions of importance to the patients.

A study of GPs' prescription to MPP patients (defined as patients using five or more drugs concomitantly) found a six-fold inter-practice variation in 173 practices on the Danish island of Funen (range: 16-96 MPP patients for each 1,000 registered citizens, when controlling for patients' sex and age). The prevalence of MPP was positively associated with the GPs' workload (number of consultations and number of telephone consultations), referrals to hospital, number of prescriptions/consultation and the number of different drugs prescribed during a three-month period and was, surprisingly, negatively associated with the number of citizens registered with the practice [6]. The present study indicates that GPs are aware of the risk of adverse drug interactions and attempt to take this risk into account when they choose a drug, but the GPs may fail to gain an overview over an individual patient's medications and the patient's risk of adverse drug interactions. Specialised assistance may be warranted, but the Danish regions' capacity in clinical pharmacology is very limited. Some GPs refer patients to hospital on the assumption that hospital personnel will perform a critical review of the patients' medications, but usually the patients are treated with more drugs at the time of discharge than when they were admitted to hospital [19]. An Irish study found that 90% of all prescriptions performed at hospitals were continued in general practice [20].

Only physicians are allowed to discontinue medications. More than half of all prescriptions in general practice are made by telephone by the GPs' secretaries [4], and the quality of repeat prescriptions is frequently lower than that of the original prescriptions as important topics regarding the medication are often omitted [20]. Politicians at the national and regional levels have expressed great expectations regarding the potential to increase GPs' productivity by transferring some tasks to their assisting personnel. Such transferral may increase the risk of MPP, and patients may mistakenly assume that a repeat prescription reflects a specialist's assessment of their need for the drug.

The GP's interpretation of the patient's expect-

ations regarding prescription of drugs is the strongest predictor of actual medication [21, 22], but GPs may overestimate patients' expectations regarding drug prescription [23]. This phenomenon may contribute to MPP in patients who frequently consult their GP. In the present study, GPs displayed an interest in a facility providing a specialized review of their patients' medications, and such reviews had a strong impact on PP, at least in the short term. These findings confirm Danish, Dutch and Australian experiences [24-26]. GPs' interests were strongest among those who share of MPP patients exceeded the county average.

The present study combines a registry study's high drug data validity and reliability with the opportunities provided by qualitative studies to explain behaviour, but the qualitative study only included self-recruited GPs, which introduced a selection bias. The participants were more likely to have more PP patients than the average GP, but their prescription behaviour and attitude towards change may differ from that of the average GP. We did not study patients' treatment compliance; our recommendations for change could not be divided into clearly defined categories; and the study only included prescription drugs, thereby systematically underestimating MPP.

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**CONFLICTS OF INTEREST:** None

A complete reference list is available from the authors.

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