Promoting Rational Drug Prescribing in General Practice

KELD VÆGTER
Abstract

Aims: To introduce the concepts “quality assurance”, “rational drug prescribing” and “outreach visits” in general practice in Storstrøm County, Denmark and study the effect of unsolicited mailed feedback and outreach visits on drug prescribing.

Methods: The first step was to generate standardised charts displaying the county variations of drug volume prescribing within 13 major drug groups at the second ATC-level. The charts were mailed unsolicited to the 94 general practices in the county. Each practice could identify its position within the county prescribing variation. This procedure was repeated every six months from 1992 to 1998. In 1998 annual outreach visit were offered to general practice and 88 of 94 practices accepted. The awareness of prescribing profiles was monitored during the visits in 1998 and 1999. In 2000 a randomised controlled trial allocating practices into two parallel arms was launched. Effects of two desk guides on rational drug prescribing promoted during outreach visits were evaluated.

Results: During the period of mailed feedback, there was a large variation in drug prescribing volumes between practices but little within-practice variation over time. No significant change was detected. Practitioners’ assessment of their own prescribing profiles improved significantly through the outreach visits. The prescribing of antibiotics was significantly affected by the desk guide whereas no effect was detected on the prescribing of non-steroid anti-inflammatory drugs.

Conclusions: Semi-annually mailed feedback over a seven-year period had no significant effect on prescribing volumes or variations in prescribing volumes, but some effect on the practitioners’ awareness of their own prescribing profiles. Outreach visits significantly improved the awareness. A randomised controlled trial using outreach visits combined with a simple desk guide affected the prescribing of some antibacterial drugs as intended whereas the similar intervention had no detectable effect on the prescribing of non-steroid anti-inflammatory drugs.

Keywords: rational drug prescribing, family medicine, general practice, postal feedback, outreach visits, randomised controlled trial

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To my grandmother Nora
List of Papers

This thesis is based on the following papers, which are referred to in the text by their Roman numerals.


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## Abbreviations

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<tbody>
<tr>
<td>ATC</td>
<td>Anatomical Therapeutic Classification</td>
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<tr>
<td>CME</td>
<td>Continuous Medical Education</td>
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<tr>
<td>DDD</td>
<td>Defined daily doses</td>
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<tr>
<td>DDD/1000</td>
<td>Defined daily doses prescribed per 1000 listed patients</td>
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<tr>
<td>DNHS</td>
<td>Danish National Health Service</td>
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<td>DURG</td>
<td>Drug Utilization Research Group</td>
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<td>EQiuP</td>
<td>European Working Party on Quality in Family Medicine</td>
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<tr>
<td>FUAP</td>
<td>Professional Development in General Practice (Faglig Udvikling i Almen Praksis)</td>
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<tr>
<td>GP</td>
<td>General Practitioner</td>
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<tr>
<td>KLAP</td>
<td>Quality Assurance of Drug prescribing in General Practice (Kvalitetssikring af Lægemiddelordinationer i Almen Praksis)</td>
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<tr>
<td>NLN</td>
<td>Nordic Council on Medicines (Nordisk Läkemedelsnämnd)</td>
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<td>NMD</td>
<td>Norwegian Medicinal Depot</td>
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<tr>
<td>QI</td>
<td>Quality improvement</td>
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<tr>
<td>PIN</td>
<td>Practice Identification Number</td>
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<tr>
<td>WHO</td>
<td>World Health Organization</td>
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<tr>
<td>WONCA</td>
<td>World Organization of National Colleges, Academies and Academic Associations of General Practitioners/Family Physicians</td>
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How does a country boy from the remote Danish island of Falster end up writing a PhD thesis at Uppsala University, Sweden, on drug prescribing in primary health care in Denmark? Chance, coincidence and faith certainly plays a role in the process. However, an important step was my graduation at the School of Medicine at Copenhagen University in 1990 rather than becoming a blacksmith in my home town.

My great grandfather was the local blacksmith in the small town of Nørre Vedby located in the rural northern part of the island Falster, Denmark, where farming has been the main occupation for centuries. His oldest daughter Nora was my grandmother. She was a very bright person who never got the chance to develop her intellectual skills in the educational system because of limitations by social class, tradition and economy. After finalising seven years of primary and secondary school she was sent off to work as a farm maid like most young girls in rural areas in those days.

That was how she met my grandfather Hans Adolf Vægter, who worked as farm labourer. They married at young age and bought a tiny house with a small piece of land in my grandmother’s hometown. They spent their entire life in this small town, grandfather working in road constructions in the summer and at the local sugar mill in the winter. Grandmother took care of the household, their two children, and the small piece of land. Their son Knud, my father, became a carpenter and later a construction foreman and married my mother, Christa, who worked as a clerk at the local grocery store, and they too settled in Nørre Vedby.

Growing up I spent much time in the smithy, but also many evenings at the kitchen table in my grandparents’ house, where many great stories of life and much wisdom was distributed unsolicited. It was my intention to become a blacksmith following the family tradition, but foremost grandmother urged me to study and challenged me intellectually in many ways to stimulate my appetite of learning. She encouraged me to become a physician and during my first year in high school I took an optional course in Latin, which at that time was mandatory to enter medical school.

Grandmother came to our house several evenings every week to help me with the Latin rhymes and grammatical inflections. Although she could not understand a word of the language, she would check the textbook while I was practicing Latin grammar, being very enthusiastic about my progress and we found a great mutual pleasure in the process. No one was happier and
prouder than grandmother, when I graduated from high school with grades good enough to allow me direct access to medical school in Copenhagen, being the first member of the family ever to enter university studies.

Before entering my last year in medical school I worked during the summer leave as a doctor’s assistant in Northern Sweden, where many Danish medical students traditionally have been most welcomed and gained great practical and clinical skills because of local shortage of doctors. After graduating from medical school, adventurousness and great pleasure in the magnificent scenery of Northern Sweden made me accept an offer of an internship at Kalix Hospital and later on I entered the specialist programme to become a general practitioner.

This programme included several mandatory courses, and one of them was “Research and Development in General Practice” at the Department of Family Medicine, later a section within the Department of Public Health and Caring Sciences at Uppsala University, Sweden, where I first met professor Kurt Svärdssudd in 1994. This course was my major inspiration to enter research in parallel to working as a general practitioner.

In 1997 I moved back to Denmark and became responsible for establishing a County Drug Facilitator service in general practice in Storstrøm County on a one-year project basis. The project turned out well and was consolidated as a permanent service. During the following three years I worked as County Drug Facilitator performing annual outreach visits to the general practitioners in the county.

In the fall of 2000 our family moved to Nyköping, Sweden and I started working as a general practitioner at Ekensberg Health Care Centre. In 2001 the Centre for Development and Research in Primary Care in Sörmland (AmC) led by Dr. Rolf Wahlström offered an “Introduction to research” course in collaboration with the Family Medicine and Clinical Epidemiology Section, Uppsala University. Among the teachers were Dr. Rolf Wahlström and professor Kurt Svärdssudd. During the course I presented data and results from the drug facilitator programme in Storstrøm County, and was encouraged to enter the PhD programme at the Department of Public Health and Caring Sciences at Uppsala University. The present PhD thesis is based on data collected during my time as County Drug Facilitator in Storstrøm County, Denmark.
Introduction

Quality improvement in General Practice

Physicians are required to maintain a high level of continuous medical education (CME) within all fields of importance to their work. Drug therapy is one the most significant therapeutic assets of the medical treatment options. The field is constantly expanding, and it is difficult and demanding to keep up with the latest treatment innovations and recommendations. The pharmaceutical industry is marketing its products while government funded health care systems try to keep the ever-growing expenses at a minimum, demanding best value for money.

In the ideal case, research, CME and quality improvement are tightly connected. All three fields are needed for professional development. The research provides knowledge, the CME improves competence and the quality improvement incorporates this knowledge and competence into daily clinical work. During the last three decades of the 20th century research, CME, and quality improvement gradually gained foothold in general practice. This development was in many ways the result of the activities of the World Organization of Family Doctors (Wonca) founded in 1972 and the European Working Party on Quality in Family Medicine (EQuIP) founded in 1989 [1].

Wonca is an acronym for the World Organization of National Colleges, Academies and Academic Associations of General Practitioners/Family Physicians, or World Organization of Family Doctors for short [2]. Wonca Europe is the European regional branch of Wonca [3]. It has more than 40 member organisations representing more than 45,000 family physicians in Europe. The society is the academic and scientific society for general practitioners in Europe. Its objective is to improve the quality of life of people of the world through fostering and maintaining high standards of care in general practice/family medicine by providing a forum for exchange of knowledge and information; encouraging and supporting the development of academic organisations of general practitioners/family physicians; and representing the educational, research and service provision activities of general practitioners/family physicians in relation to other world organizations and forums concerned with health and medical care.

The aim of EQuIP is to contribute to the achievement of high levels of quality and safety of care for patients in European general practice [1].
EQuiP endeavours to achieve this goal by offering a structured collaboration and exchange of expertise and methodology and by initiating projects on development and evaluation with regard to quality improvement (QI) and quality management and development.

Quality and safety development for general practice is a continuous process of planned activities based on performance review and setting of explicit targets for good clinical practice with the aim of improving the actual quality of patient care. This understanding of quality development focuses on a critical view of the actual performance of general practitioners and their practices rather than on competence alone. The members of EQuiP assume that this quality development should be the responsibility of the medical profession.

Measuring drug utilisation— a historical view

The field of drug utilisation research has attracted increasing interest since the early 1960s. The pioneering work was done by two consultants (Engel and Siderius) at the WHO Regional Office for Europe [4]. Their early studies of drug utilisation in six European countries showed great differences between population groups. A symposium held in Oslo in 1969 led to the establishment of the Drug Utilization Research Group (DURG) with the objective to promote the development of internationally applicable methods for drug utilisation research.

In order to measure drug use, it is essential to have a classification system as well as a unit of measurement. The Anatomical Therapeutic Chemical (ATC) classification system was developed by the Norwegian Medicinal Depot (NMD) [5, 6]. NMD also developed a technical unit of measurement called the Defined Daily Dose (DDD). The Nordic Council on Medicines (NLN), established in 1975, collaborated with the NMD to further develop the ATC/DDD system. The NLN published the Nordic Statistics on Medicines using the ATC/DDD methodology for the first time in 1976. At the same time, international interest in the ATC/DDD system for drug utilisation research expanded beyond the Nordic countries largely through the activities of the DURG, that recommended the ATC/DDD methodology for international drug utilisation studies.

In 1981, the WHO Regional Office for Europe adopted the ATC/DDD system for international drug utilisation studies. In connection with this process, and to make the methodology more widely used, there was a need for a central body responsible for coordinating the methodology. The WHO Collaborating Centre for Drug Statistics Methodology was accordingly established in Oslo in 1982. In 1996, WHO recognised the need to develop use of the ATC/DDD system as an international standard for studies of drug utilisation.
tion. The Centre was therefore linked directly to WHO Headquarters in Geneva.

Structure of the ATC classification system

In the ATC classification system, the active substances are divided into groups according to the organ or organ system on which they are intended to act, and their therapeutic, pharmacological and chemical properties. The classification code has five levels. Level 1 is the organ or organ system for which the drug is intended, level 2 represents a main sub-grouping, levels 3 and 4 represent chemical, pharmacological, or therapeutic subgroups and level 5 represents the chemical substance.

Rational drug prescribing

The Hippocratic oath, formulated in the third century B.C, is one of the oldest binding documents in history [7]. Doctors to this very day hold its principles sacred. The central obligations for doctors in relation to their patients are: cure when possible, aim to relieve, always comfort, and above all never cause harm (primum non nocere).

When it comes to pharmacotherapy, it is important to remember, that there are no absolutely safe drugs. All drugs have some kind of side effects. Many of those side effects may be considered relatively harmless, others more severe and some may even be lethal. Pharmacotherapy is a balance between the desired and expected effects against a medical condition and the potential and actual side effects. The concept “rational pharmacotherapy” developed during the 1980s and presupposes the following criteria: It must be efficient, safe, economical and appropriate for patients [8]. Earlier, drug prescribing overall was considered the doctor’s own affair, a privilege and right with no outer interference and this is still a common attitude in the USA and many countries in southern Europe. WHO has defined rational pharmacotherapy as being a therapeutically sound and cost-effective use of medicines by professionals and consumers [8].

Previous research on rational drug prescribing

A prerequisite when addressing rational drug prescribing is a stable prescribing pattern, i.e., that the levels prescribed persist over time and are not swinging up and down. Few authors have addressed the issue of stability of prescribing habits in general practice. One of the main reasons may be the lack of comprehensive long-term prescription data registers at prescribing
physician level. In a New Zealand study from 1992-94 [9], based on reimbursement data, a 9% median intra-GP variability was found in both volume and total costs from year to year in a regional GP sample (305 GPs), and a 16% variation in total costs and 17% in total volume in a national GP sample (74 GPs). Since the data on stability was scarce it was decided to analyse this issue in Paper I of this study.

At the time of the planning of this study little was known about the effects of mailed feedback about prescribed levels of drugs in general practice. In this study it was anticipated that practices that were ‘outliers’, i.e., had a considerably higher or lower prescribing level of the specific drug as compared to the mean of all practices, would contemplate over this situation and think of possible reasons for it. Later, when the data collection for this part of the study was concluded, a number of studies reported no effect of mailed feedback on GPs’ prescribing levels [10-12].

However, a number of studies demonstrated effects [13-15]. In a 2006 Cochrane review it was concluded that the combination of audit and feedback had a small to moderate effect on professional practice [16]. Although mailed feedback only has shown a modest or no effect on doctors' drug prescribing, it is still widely used in continuing medical education (CME), and in quality assurance and improvement. The method is easy to apply on a large scale and relatively cheap. However, the approach appears to be more effective if combined with other strategies [17], such as audit-feedback with peer discussions [18, 19].

Various methods have been used to promote rational drug prescribing. Among these, outreach visits have been documented to be one of the more effective methods to obtain a specific goal. Later they have been shown to affect prescribing habits in several studies [11-13, 15, 16, 20].

Outreach visits, or academic detailing, represent university or non-commercial-based educational outreach involving face-to-face education of prescribers by trained health care professionals. The method has been applied since the early 1980ies [21]. Traditionally, the trained health care professional who performs the outreach visit is a physician, a clinical pharmacist or a nurse [22]. The primary goal of academic detailing is to influence the prescriber to prescribe drugs consistent with the latest updated recommendations according to the principles of rational pharmacotherapy.

Outreach visits have been used in order to affect prescribing habits, but the effects are at variance. In a randomized controlled trial performed in Leicestershire, England, with the intention of reducing the prescribing of broad-spectrum antibiotics, no effect was found [23]. In a three-year randomised controlled trial using outreach visits in Denmark no effect on the prescribing level of asthma medication was found [24], and similar lack of effect was found in another Danish study [12]. In contrast, effects on prescribing of analgesics were shown in a Canadian trial [15]. Similar effects were found in a Norwegian study [13] and in another Canadian study [14].
In a 2007 Cochrane review [20] outreach visits were identified as an intervention that may improve the practice of health care professionals.

Setting for the present study

Denmark has a tax-financed government run public health care system. Today five regions are responsible for providing hospital care, and own and run hospitals and prenatal care centres. The regions also finance general and specialist practice, physiotherapy, dentistry (to some extent) and pharmaceuticals.

At the time of the present study, the former Storstrøm County (since 2007 part of Region Sjælland), was served by 166 general practitioners, distributed across 94 practices. In Denmark general practitioners are private contractors within the National Health Insurance system, each taking care of approximately 1500 listed patients. All citizens are listed with a practice and the practitioners are paid through a combination of capitation (30%) and fee-for-service by the National Health Insurance (Sygesikringen) through the Regional Health Departments.

Traditionally most practices in primary health care in Denmark have been solo practices (run by one GP), but over the last decades the formation of group practices has become increasingly common. Each practice is given a specific practice identification number (PIN). All relevant information related to administration and fees in the practices, such as patient demographics, prescriptions, referrals and specific services and treatments performed in the practice, is registered by the PIN in the Regional (former County) Health Insurance Unit of Statistics for Primary Health Care.

Registration of purchased prescriptions in Denmark

The analyses in this study are based on information from the local section of the Danish National Health Service (DNHS) in Storstrøm county. At the time of the study, each community pharmacy collected data on all handled prescriptions and forwarded data on reimbursable drugs to their local DNHS section on a monthly basis. The registration was almost complete since the reimbursement system provided a powerful economic incentive for both the pharmacies and the health care providers to handle data correctly. Several studies has shown a very high coverage (97,5%-99%) for the register data [25-27].

In 1994 the Register of Medicinal Product Statistics was established at the Medicines Division of the National Board of Health. The register contains data on the total sales of drugs in Denmark on individual level regardless of reimbursement. The information in the register is derived from Danish
community pharmacies, hospital pharmacies and the Danish State Serum Institute, which register any dispatch or delivery of medicines in Denmark. Since 1 October 2001, new distributors selling over-the-counter medicines have also reported their sales to the register.

Quality development in General Practice in Storstrøm County

In 1991, increasing drug costs and large variation in prescribing habits among general practitioners (GPs) in Storstrøm County led to the formation of a local task force to promote quality development of drug prescribing. The task force was named KLAP (Kvalitetssikring af Lægemiddelordination I Almen Praksis, or in English ‘Quality Improvement of Drug Prescribing in General Practice’) and consisted of representatives from dedicated local GPs, and representatives from the County Health Department, the local division of the Danish National Health Service and the political and professional level of the organisation of general practitioners in the county. Initially, the initiative was considered provoking and an intrusion into personal professional matters by a majority of the GP community. Historically, the relation between the County Health authorities and the general practitioners in Denmark has been characterised by difficulties and disagreements due to mutual scepticism in conjunction with collective bargaining relations as opponents. The County Health authorities have for many years been regarded as “Big Brother watching you”. Nevertheless, local negotiations led to a breakthrough and the project was finally accepted.

In 1995 KLAP transformed to FUAP (Faglig Udvikling I Almen Praksis, or in English Professional Development in General Practice) with a broader mandate to handle not just quality improvement in drug prescribing, but all aspects of quality improvement and continuous medical education (CME) in general practice. Two GPs were part time employed to run the FUAP office.

Before KLAP, there had been no formal collaboration between the health administrators and the GP community addressing drug prescribing. KLAP’s first initiative was to launch a quality improvement project in 1992, focusing on rational drug prescribing. The first step of the project meant introducing postal feedbacks (standardised charts) on the volumes and costs of prescribed drugs, as described in Paper I. This activity was performed from 1992 to 1998.

When the first step, using postal feedbacks, was finalised, the second step, introducing academic detailing through outreach visits in general practice, was launched in 1998. The decision to incorporate academic detailing in the project was strongly influenced by a publication from The Danish Institute for Health Services Research in 1996 [28]. For this purpose a GP (KV) was
employed as facilitator, who performed two rounds of outreach visits, one in 1998 and one in 1999, as described in Paper II. The two first reports were published in 1998 and 1999 [29, 30].

Since the two outreach visit rounds were successfully completed and the GP community had become accustomed to the facilitator and the visits, a third step in the project, two parallel randomised controlled trials using outreach visits to promote the intervention message, was launched in 2000, as described in Papers III and IV.

This thesis is focused on the three steps of the rational prescribing project in Storstrøm County on drug prescribing habits, how they were performed, how they were received by the GP community, and what their impact on prescribing habits were.
Aims of the study

The aims of this thesis were to test the possibilities of promoting rational
drug prescribing in primary health care. The specific aims were:

- to assess whether prescribing levels in general practice are affected by
  long-term, unsolicited, systematically repeated, mailed feedback,
- to analyse awareness among general practitioners of their drug prescrib-
ing profile following six years of mailed feedback and during two out-
reach visits one year apart,
- to study the effects of outreach visits and a simple desk guide on the
  prescribing in general practice of antibacterial agents intended for sys-
temic use,
- to study the effects of outreach visits and a simple desk guide on the
  prescribing in general practice of non-steroid anti-inflammatory drugs.
Study populations and methods

Study populations

Papers I and II

The study area included the southern part of island Sjælland, the islands of Falster and Lolland, and a few other minor islands, and had 257,000 residents. The area is mainly rural with a few small towns, and was served by 166 general practitioners distributed across 94 practices.

In Denmark the general practitioners are private contractors to the County Health Authority, each taking care of approximately 1,500 listed patients. Each practice has a specific identification number (PIN) within the National Health Insurance system. All relevant information related to administration and fees in the practices, such as patient demographics, prescriptions (obtained from the Danish Medicines Agency), referrals and specific services and treatments performed in the practice is registered in the local County Health Insurance database.

Traditionally, most practices in primary health care in Denmark have been "solo" practices (run by one GP), but in recent decades the formation of group practices has become increasingly common. In group practices it is not possible to identify the individual GP's contribution to the common prescribing profile, since the PIN refers to the practice as a whole. The population of listed patients in the practice system is stable, with an average annual change between practices of less than 10%. The differences between practice patient populations in terms of age and gender were small (personal communication from the Pharmaco-economic Division, Danish Medicines Agency).

Papers III and IV

All 94 general practices participating in the first step (the postal feedback study) were invited in the next, second, step of the rational drug prescribing project, of which 88 practices accepted. The practices were divided into six groups according to geographical location, continuing medical education (CME) groups, and on-call affiliation. The groups were geographically lo-
Figure 1. Map of the intervention and control areas. Green areas were antibiotic intervention areas and yellow areas were NSAID intervention areas.

cated in a line from south to north, Figure 1. The first group was randomly allocated to NSAID intervention and the remaining groups were allocated in alternating order to antibiotic or to NSAID intervention. Thus, three groups received intervention regarding the rational prescribing of antibiotics, and three groups intervention regarding rational prescribing of NSAID.

Data collection

Paper I
All prescriptions filled at Danish pharmacies, reimbursed as well as non-reimbursed, are registered in a database at the Danish Medicines Agency by
practice PIN code and Anatomical Therapeutic Chemical (ATC) code [5]. The registration is almost 100% complete. All prescriptions analysed in this report were fully reimbursed.

In 1991 the first steps were taken to establish a ‘GP Quality Unit’ by collaboration between representatives from general practice and officials from the health administration within the Health Department of Storstrøm County. The aim was to encourage a review among GPs of their prescribing habits in order to improve and enhance rational drug therapy. To visualise differences in prescribing habits and to trigger the awareness of the GPs, prescribing data on reimbursed pharmaceuticals with the ATC-codes A02 (antacids), A10 (anti-diabetes drugs), C01 (cardiac drugs), C03 (diuretics), C07 (beta blockers), C08 (calcium channel blockers), G03 (reproduction hormones), J01 (antibacterial drugs for systemic use), M01 (non-steroid anti-inflammatory drugs), N02 (analgesics), N05 (neuroleptic drugs), N06 (psycho-analeptic drugs), and R03 (anti-asthma drugs), were extracted from the County Health Insurance database, presented in charts, and mailed to each practice every six months. No intervention other than the mailed feedback was made.

The feedback diagrams illustrated the prescribing levels of each of the 13 drug groups as number of defined daily doses (DDD) per 1000 listed patients and the practice's percentile position within the distribution across all practices in the county. The corresponding information on costs per DDD prescribed by the practice was presented in a similar way. An example of the feedback diagrams is shown in Figure 2. Every six months new data was added to the charts and mailed to the practices.

If this type of feedback works, the anticipated effect would be a clustering of prescribed DDDs towards the mean, i.e., a smaller dispersion between practices and a tendency towards instability of individual practice prescribing patterns over time owing to changing habits. Since the initiative for political reasons was launched full scale simultaneously in all practices throughout the county, no control group was available. Therefore, the prescribing habits of all practices were followed through the study period.

Paper II

In 1998, all the 94 practices participating in the postal feedback study in 1992-1998 were invited to participate in an outreach visits programme, involving a one-hour visit from a GP (KV, programme facilitator, linked to the programme), of which 88 practices agreed to participate. The outreach visits were performed in two rounds, the first in 1998 and the second in 1999, and followed a predetermined general protocol. First, the programme facilitator gave a brief introduction of the programme and presented a pools coupon-like form, showing the 13 major ATC groups used in the postal feedback.
The GPs were asked to fill in the form regarding their perception of actual prescribing levels in the practice during the preceding year for each of the 13 ATC groups. Possible responses were the lowest quartile, the top quartile, or the two mid-quartiles of the prescribing distribution across all practices. Solo practices gave individual responses while group practices gave a joint response.

The estimates on the form were then compared with the actual prescribing levels based on register data, and the number of accurate answers registered. During this process rational drug prescribing regarding the drug group in question was discussed in general terms as an important element of the outreach visit. All GPs in the practice participated in the discussions. Certain general rules of rational prescribing were stated, such as using generic drug brands when possible, avoiding overuse or underuse of medications, and being generally restrictive about antibiotic prescriptions, and especially regarding the amounts of broad spectrum antibiotics.

GP’s age and gender, seniority as a GP, number of GPs per practice, access to electronic patient record system, and duration of the outreach visit were recorded. At the end of the session, the GPs filled in an evaluation form regarding the visit, which included their rating of the outreach visit concept in general, rating of the present outreach visit, rating of outreach visits as a quality tool, and their attitude to an new outreach visit the following year. In addition, the GP facilitator rated the participating GPs’ attitudes to the out-

Figure 2. Levels of prescribed defined daily doses (DDDs) per 1000 population per 6 months by drug group.
reach visit concept, and their involvement in the present visit. In the second round of outreach visits the same 88 practices participated. Updated prescribing data was used but otherwise the procedure was the same.

Paper III

For Paper III a third outreach visit round was performed in the spring of 2000. The main objective of the first two outreach rounds was to introduce and implement the concept of outreach visits to general practice, to establish a professional contact between the GPs and the facilitator, and to collect data for Paper II, as described above.

Prior to the 2000 outreach visit round a desk guide, containing four short messages about rational prescribing of antibiotics, was developed in cooperation with the newly established Institute for Rational Pharmacotherapy at the Danish Medicines Agency, Copenhagen. The messages were 1) be generally restrictive with the use of antibiotics, 2) phenylmetoxypenicilin (penicillin V) is still the drug of choice in most infections in general practice, 3) be restrictive prescribing macrolides, 4) use sulfamethizol and not mecillamin/pivmecillinam as the first drug of choice in uncomplicated lower urinary tract infections.

The hypotheses tested in this study were accordingly: the prescribing of all antibiotic drugs together, macrolids, and mecillamin/pivmecillinam will decrease, while penicillin V will increase or be stable in the intervention area as compared with the control area.

The same facilitator as in 1998 and 1999 performed the 2000 outreach visit round. The desk guide was handed out to all the GPs in the practices in the antibiotic intervention area and was thoroughly discussed. GPs in practices in the control area received a similar desk guide regarding rational prescribing of NSAID.

The year 1999 was used as the run-in period during which no intervention was performed, 2000 was the intervention year, and the spring of 2001 was used as the post-trial period where no active intervention was performed. Information on practice characteristics (number of GPs and of female GPs, GP age, experience as GP, and size of listed population) and on the prescribing level of broad spectrum penicillins (ATC code J01CA), pivmecillinam (ATC code J01CA08), betalaktamase sensitive penicillin (ATC code J01CE), macrolids (ATC code J01FA), and all antibacterial agents for systemic use (ATC code J01) was obtained from the County Health Insurance database and was almost 100% complete. Data was extracted as number of daily defined doses (DDD) per 1000 listed patients for each of the participating practices per six-month-period, i.e., January to June and July to December in 1999 and in 2000, and January to June in 2001.
Paper IV

The same 88 practices as used in Paper III were used also in Paper IV, but in this case the practices in the area receiving intervention regarding rational NSAID prescribing were used as the intervention area and practices in the area receiving intervention regarding antibiotics were used as control area.

Prior to the year 2000 outreach visit round a desk-guide, containing six short messages about the prescribing of NSAIDs, was developed in cooperation with the newly established Institute for Rational Pharmacotherapy at the Danish Medicines Agency, Copenhagen. The messages were 1) be generally restrictive with the use of NSAIDs, 2) reduce prescribing of NSAID to patients with cardiovascular diseases, 3) scrutinize patients’ medicine lists and clear NSAIDs if possible, especially if poly-pharmacy is at hand, 4) NSAIDs should not be first drug of choice in pain of non-inflammatory origin, 5) avoid long-term NSAID use, and 6) when prescribing NSAID use a low price alternative.

The same facilitator as in 1998 and 1999 performed the outreach visit round in the spring of 2000. The desk guide was handed out to practices in the intervention area and was thoroughly discussed. Practices in the control area received a similar desk guide regarding rational prescribing of antibiotics.

As in Paper III the year 1999 was used as a run-in period during which no intervention was performed, and the year 2000 was the intervention year. Information on practice characteristics (number of GPs and of female GPs, GP age, experience as GP, and size of listed population) and on the prescribing level of non-steroid anti-inflammatory drugs (ATC code M01A), and its subgroups acetic acid derivatives (ATC code M01AB), oxicames (M01AC), propionic acid derivatives (M01AE), coxibes (M01AH), and other non-steroid anti-inflammatory drugs (M01AX) was obtained from the County Health Insurance database. Data was extracted as number of daily defined doses (DDD) per 1000 listed patients for each of the participating practices per six-month-period, i.e., January to June and July to December in 1999 and in 2000.

Ethical approval

Approval from an ethics committee was not needed since the project did not include any direct patient involvement, and no classified information that could reveal patient identity was handled.
Statistical considerations

Statistical analyses were performed using the SAS software, version 9.1 for Paper I, version 9.2 for Paper II, and version 9.3 for Papers III and IV [31]. Data was complete. Simple (crude) differences between groups regarding continuous variables were tested with Student's t-test and differences in proportions with the chi-square test. All tests were two-tailed. The level of significance was set at p<0.05.

Paper I

During the observation period 1992-1998 a few new practices were established. This might have given rise to false low values regarding the numbers of prescribed DDD/1000 patients in the opening period. To avoid this problem, data from the first six-month period of new practices were excluded.

In order to discover and test changing prescribing habits, four methods were employed. The first focussed on intra-practice variation of prescribing habits, where variation would increase in case of changing habits. The prescribing data constitute a time series of prescriptions issued by the same GP population. The resulting DDDs may therefore be auto-correlated, i.e., the value for a specific six-month period predicts, to a certain extent, the value of the next period. To overcome this problem the SAS procedure "autoreg" was used to diagnose and to adjust for auto-correlation. The adjustment included the nearest three six-months periods, as these were significantly auto-correlated. The resulting adjusted measure of variability, mean square error (MSE), may be regarded as a variance adjusted for prescribing trend across time. We used the square root of this measure, which is equivalent to a standard deviation unit, as a measure of prescribing variability within practices over time.

The second method was based on the so called "folding rule" regression analysis. The study period was divided in two sub periods and a regression line of prescribed DDDs per 1000 listed patients over time were calculated for each practice and for each sub period, much like a folding rule. The meeting point, or intersection, between the lines was successively moved across the study period. A significant difference in regression coefficient ("leaning") between the two lines would then indicate a change of prescribing habit. In this way the existence of a systematic deviation towards the central part of the prescribing distribution might be detected.

Thirdly, the change in the distribution of DDD per 1000 listed patients across the 14 six-month periods was tested. If a change of habit had occurred, the distribution would be narrower towards the end of the study period than in the beginning. Fourthly, scatter plots of the prescription volumes for each practice over time were produced and scrutinized for change of trend.
Univariate and multivariate linear regression analyses were used to analyse the influence of various potential determinants, such as age and sex of the listed patients ("case mix"), age and sex of the GPs, practice type, and number of years of experience as a GP, on prescribing variation, measured as mean error, or on practice regression coefficients.

**Paper II**
The assessment of the accuracy of the GPs’ estimates of their prescribing profiles poses an analytical problem, since the a priori probability of an accurate estimate varies with the prescribing level. Those who had an actual prescribing level in the two central quartiles had twice as high probability of an accurate assessment (50% chance) than those in the lowest and highest quartiles (25% chance each). To overcome this problem the form data, where the responses were given as lowest, two middle, or highest quartile, were cross tabulated with the actual prescribing levels across all 88 practices graded in the same way. The resulting three-by-three tables were then analysed with the chi-square test, which provided the actual proportion of accurate assessments, the proportion that would be provided by chance only, and the probability that the actual proportions would be better or worse than those provided by chance alone. The same procedure was used for the first and second rounds of outreach visits.

Multivariate linear regression analysis was used to analyse the influence of potential determinants on the change of assessments from the first to the second rounds, using the second assessment as the dependent variable and the assessment during the first round, GP’s age and sex, practice type (solo or group practice), number of years of experience as a GP, number of GPs in the practice, access to electronic patient record system, duration of the outreach visit, the GPs’ ratings of the outreach visits and the GP facilitator’s ratings of the participating GPs’ attitudes, as independent variables. The multivariate analysis was performed with backward elimination of non-significant variables to avoid model overload.

**Paper III**
Multiple linear regression analysis with the SAS ‘general linear model’ procedure was used to analyse differences in trends between the intervention and control areas of prescription levels for each drug group. The prescription level during each six-month-period was entered as the dependent variable and the variable measuring whether the practice was in the intervention or control area was entered as an independent variable, controlling for between-area and within-area effects. There were fairly large differences between the intervention and control area in prescription level during the run-in-period,
which could have caused a bias in the analyses. For this reason the initial level of prescribing was entered as a covariat.

In a first analysis variables measuring whether the practice was a solo or group practice and the size of the listed patient population were also entered as covariats, but none had any effect and they were therefore not used in the final analyses. The information in Figure 4 was obtained from the analysis model using the SAS ‘general linear model’ procedure and its ‘lsmeans’ statement.

Paper IV
Multiple linear regression analysis with the SAS ‘general linear model’ procedure was used to analyse differences in trends between the intervention and control areas of prescribing levels for each of the drug group. The prescribing level during each six-month-period was entered as the dependent variable and the variable measuring whether the practice was in the intervention or control area was entered as an independent variable, controlling for between-area and within-area effects. There were fairly large differences in prescribing level during the run-in-period, which might cause a bias in the analyses. For this reason the prescribing level during the first six-month-period was entered as a covariat in addition to whether the practice was a solo or group practice and the size of the listed patient population to account for effects due to time available for consultation and number of GPs in the practice. The information in Figure 5 was obtained from the analysis model using the SAS ‘general linear model’ procedure and its ‘lsmeans’ statement.
Results

Paper I

Characteristics of the study population

Study population characteristics are shown in Table 1. Fifty-four practices were solo practices, and 40 were group practices with an average of 2.8 GPs per practice. The 166 GPs were on average 50 years old (interquartile range 46-54 years), 81% were men, mean number of years as a GP was 14.5 (interquartile range 8-20 years). There were no significant differences in the distribution of age, sex and GP experience between GPs in solo versus group practices.

Prescribing habits over time

The overall prescribing rate of the 13 drug groups studied increased from 64,870 DDDs/1000 patients in the first six months of 1992 to 70,360 DDD/1000 listed subjects in the last six months of 1998, an annual increase rate of 915 DDD/1000 listed subjects. The trends in prescribing rate for the various drug groups are shown in Figure 2. The number of DDDs per 1000 listed subjects prescribed during the study period increased significantly for antacids (A02), anti-diabetes drugs (A10), beta blockers (C07), calcium channel blockers (C08), reproduction hormones (G03), analgesics (N02), psycho-analeptic drugs (N06) and anti-asthma drugs (R03), while it decreased for cardiac drugs (C01), and diuretics (C03), and remained unchanged for antibiotics (J01), non-steroid anti-inflammatory drugs (M01) and neuroleptic drugs (N05).

Prescribing variation among practices

The variations between practices in amount of prescribed drugs within the various ATC groups are presented in Table 2 as semi-annual mean DDD/1000 listed patients, the 95th and the 5th percentile of the DDD distribution across practices, and the ratio of these two. There were fairly large variations in prescribing level between the practices, as reflected by the 95th
Table 1. Characteristics of the study population.

<table>
<thead>
<tr>
<th></th>
<th>Solo practices</th>
<th>Group practices</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>mean or %</td>
<td>95% CI(^a)</td>
</tr>
<tr>
<td>n</td>
<td>54</td>
<td>57.4</td>
<td>48.7-51.9</td>
</tr>
<tr>
<td>Age, years</td>
<td>54</td>
<td>50.3</td>
<td>48.7-51.1</td>
</tr>
<tr>
<td>Male physicians, %</td>
<td>46</td>
<td>85.2</td>
<td>75.4-95.0</td>
</tr>
<tr>
<td>No. of GPs in practice</td>
<td>54</td>
<td>1.0</td>
<td></td>
</tr>
<tr>
<td>No. of years as a GP(^b)</td>
<td>54</td>
<td>15.1</td>
<td>13.0-17.1</td>
</tr>
</tbody>
</table>

\(^a\) 95% CI = 95% confidence interval  
\(^b\) GP = general practitioner
to 5th percentile ratios. The largest differences were seen for neuroleptic drugs (ratio 6.0) and the smallest for anti-asthma drugs (ratio 2.5).

There was little variation over time within prescribing practices, as reflected by the root of the MSE, a measure of the mean prescribing standard deviation adjusted for the increasing or decreasing trend line over the fourteen six-month periods Table 2. The root MSE was 0.20 units, one fifth of a standard deviation, with 95% confidence interval 0.18-0.23 for all drug groups combined after adjustment for auto-correlation, indicating only minute deviations from the trend line. Among the individual drug groups, analgesics (N02) and calcium channel blockers (C08) had the lowest variability and anti-diabetes drugs (A10) the highest. The within practice deviation range was 0.01-1.08 for individual ATC-groups.

In the folding rule regression analysis across all practices there was no evidence of a deviation of high or low prescribers towards the mean for all GP practices, nor was there any significant change in the DDD per 1000 listed subjects distribution across time when adjusting for the increasing mean. Scrutiny of practice specific trend lines for the prescribing levels of the various ATC-groups, gave no evidence that high or low prescribing practices tended to change their course (data not shown).

The solo practices had larger prescribing variation than group practices (0.30 SD units, 95% CI 0.24-0.35, versus 0.19, 95% CI 0.15-0.23, p<0.005).
Table 2. Variation of drug prescribing habits, measured as mean standard deviation of prescribed DDD/1000 patients across the follow-up period.

<table>
<thead>
<tr>
<th>Drug group</th>
<th>ATC code</th>
<th>Semi-annual mean 1)</th>
<th>Percentiles</th>
<th>Ratio 95th/5th</th>
<th>Root MSE 2)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>95th</td>
<td>5th</td>
<td>mean</td>
</tr>
<tr>
<td>Antacids</td>
<td>A02</td>
<td>2475.59</td>
<td>4377.0</td>
<td>1137.4</td>
<td>3.8</td>
</tr>
<tr>
<td>Anti-diabetes drugs</td>
<td>A10</td>
<td>2460.11</td>
<td>3889.0</td>
<td>1304.4</td>
<td>3.0</td>
</tr>
<tr>
<td>Cardiac disease drugs</td>
<td>C01</td>
<td>4689.73</td>
<td>8289.7</td>
<td>1981.4</td>
<td>4.2</td>
</tr>
<tr>
<td>Diuretics</td>
<td>C03</td>
<td>19315.90</td>
<td>31723.8</td>
<td>10143.7</td>
<td>3.1</td>
</tr>
<tr>
<td>Betablockers</td>
<td>C07</td>
<td>2845.88</td>
<td>4695.4</td>
<td>1366.0</td>
<td>3.4</td>
</tr>
<tr>
<td>Calcium channel blockers</td>
<td>C08</td>
<td>6123.94</td>
<td>10276.1</td>
<td>2747.2</td>
<td>3.7</td>
</tr>
<tr>
<td>Sex hormones</td>
<td>G03</td>
<td>4642.50</td>
<td>7545.8</td>
<td>2089.0</td>
<td>3.6</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>J01</td>
<td>1433.18</td>
<td>2481.2</td>
<td>645.8</td>
<td>3.8</td>
</tr>
<tr>
<td>NSAIDS 3)</td>
<td>M01</td>
<td>5107.58</td>
<td>8171.3</td>
<td>2854.1</td>
<td>2.9</td>
</tr>
<tr>
<td>Analgesics</td>
<td>N02</td>
<td>5374.84</td>
<td>9979.6</td>
<td>2416.6</td>
<td>4.1</td>
</tr>
<tr>
<td>Neuroleptics</td>
<td>N05</td>
<td>1321.11</td>
<td>2852.4</td>
<td>474.5</td>
<td>6.0</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>N06</td>
<td>3139.88</td>
<td>4501.1</td>
<td>1494.0</td>
<td>3.6</td>
</tr>
<tr>
<td>Anti-asthma drugs</td>
<td>R03</td>
<td>9851.54</td>
<td>14575.7</td>
<td>5900.0</td>
<td>2.5</td>
</tr>
</tbody>
</table>

1) DDD/1000 patients  2) Root Mean Square Error  3) Non-Steroid Anti Inflammatory Drugs
Among the solo practices there was no difference in prescribing variation between male and female GPs, but the variation decreased with 0.02 SD units by year of GP age. There were no significant relationships between age, sex, and number of years as GP on the one hand and prescribing volume over time on the other (data not shown).

Paper II

Characteristics of the study population

Forty-eight practices were solo and 40 were group practices with an average of 2.8 GPs per practice. The 160 GPs were on average 49.9 years old, inter-quartile range 46-54 years, 81% were men, mean GP experience was 15.1 year, inter-quartile range 11-19 years. There were no significant differences in the distribution of age, sex and GP experience between GPs in solo versus group practices.

Results of first and second round of outreach visits

The results of the assessments during the first round of outreach visits are shown in Table 3, left hand panel. Regarding antacids (A02) 45 out of 88 (51.1%) practice made an accurate estimate as compared to the 37 (42.0%) expected to provide a accurate estimate by chance only, yielding a significant difference between accurate estimate and estimate by chance (p<0.01). The difference between actual estimate and chance were significant for all drug groups, except anti-diabetes drugs. Across all drug groups, the difference between actual estimate and chance was highly significant (χ²=337, 4df, r=0.37, both p<0.0001). Practices in the lowest and highest quartiles generally made accurate assessments more often (47% accurate versus 24% expected by chance) than those in the middle two quartiles (58% accurate versus 52% expected by chance).

The corresponding data for the second round is shown in the right hand panel of Table 3. The assessments generally showed a higher degree of accuracy in relation to what could be expected by chance than those from the first round. The assessment accuracy improved especially for anti-diabetes drugs, now highly significant. Not only the assessments in the extreme quartile practices improved (60% accurate versus 22% expected by chance), but also those in the combined middle two quartiles (69% accurate versus 56% expected by chance). Overall, the estimations during round 2 were better than those during round 1 (χ²=724, 4df, r=0.48, both p<0.0001).
Table 3. Accurate estimates of general practitioners’ own prescribing level in relation to that of all practices in Storstrom County, Denmark, during the first and second outreach visit round.

<table>
<thead>
<tr>
<th>Drug group</th>
<th>ATC code</th>
<th>Observed First outreach visit round</th>
<th>Expected First outreach visit round</th>
<th>χ²</th>
<th>p&lt;sup&gt;e)</th>
<th>Observed Second outreach visit round</th>
<th>Expected Second outreach visit round</th>
<th>χ²</th>
<th>p&lt;sup&gt;e)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antacids</td>
<td>A02</td>
<td>n&lt;sup&gt;a)&lt;/sup&gt; 45/88, %&lt;sup&gt;b)&lt;/sup&gt; 51.1</td>
<td>n&lt;sup&gt;c)&lt;/sup&gt; 37/88, %&lt;sup&gt;d)&lt;/sup&gt; 42.0</td>
<td>14</td>
<td>&lt;0.01</td>
<td>n&lt;sup&gt;a)&lt;/sup&gt; 59/87, %&lt;sup&gt;b)&lt;/sup&gt; 67.8</td>
<td>n&lt;sup&gt;c)&lt;/sup&gt; 43/87, %&lt;sup&gt;d)&lt;/sup&gt; 49.4</td>
<td>32</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Anti-diabetes drugs</td>
<td>A10</td>
<td>n&lt;sup&gt;a)&lt;/sup&gt; 41/88, %&lt;sup&gt;b)&lt;/sup&gt; 46.6</td>
<td>n&lt;sup&gt;c)&lt;/sup&gt; 37/88, %&lt;sup&gt;d)&lt;/sup&gt; 42.0</td>
<td>5</td>
<td>0.27</td>
<td>n&lt;sup&gt;a)&lt;/sup&gt; 58/87, %&lt;sup&gt;b)&lt;/sup&gt; 66.7</td>
<td>n&lt;sup&gt;c)&lt;/sup&gt; 40/87, %&lt;sup&gt;d)&lt;/sup&gt; 46.0</td>
<td>30</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Cardiac disease drugs</td>
<td>C01</td>
<td>n&lt;sup&gt;a)&lt;/sup&gt; 51/88, %&lt;sup&gt;b)&lt;/sup&gt; 58.0</td>
<td>n&lt;sup&gt;c)&lt;/sup&gt; 35/88, %&lt;sup&gt;d)&lt;/sup&gt; 39.8</td>
<td>21</td>
<td>&lt;0.0005</td>
<td>n&lt;sup&gt;a)&lt;/sup&gt; 54/87, %&lt;sup&gt;b)&lt;/sup&gt; 62.1</td>
<td>n&lt;sup&gt;c)&lt;/sup&gt; 41/87, %&lt;sup&gt;d)&lt;/sup&gt; 47.1</td>
<td>22</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>Diuretics</td>
<td>C03</td>
<td>n&lt;sup&gt;a)&lt;/sup&gt; 43/88, %&lt;sup&gt;b)&lt;/sup&gt; 48.9</td>
<td>n&lt;sup&gt;c)&lt;/sup&gt; 33/88, %&lt;sup&gt;d)&lt;/sup&gt; 37.5</td>
<td>18</td>
<td>&lt;0.005</td>
<td>n&lt;sup&gt;a)&lt;/sup&gt; 61/87, %&lt;sup&gt;b)&lt;/sup&gt; 70.1</td>
<td>n&lt;sup&gt;c)&lt;/sup&gt; 40/87, %&lt;sup&gt;d)&lt;/sup&gt; 46.0</td>
<td>43</td>
<td>&lt;0.0001</td>
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<td>Betablockers</td>
<td>C07</td>
<td>n&lt;sup&gt;a)&lt;/sup&gt; 38/88, %&lt;sup&gt;b)&lt;/sup&gt; 43.2</td>
<td>n&lt;sup&gt;c)&lt;/sup&gt; 31/88, %&lt;sup&gt;d)&lt;/sup&gt; 35.2</td>
<td>12</td>
<td>&lt;0.05</td>
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<td>n&lt;sup&gt;c)&lt;/sup&gt; 35/87, %&lt;sup&gt;d)&lt;/sup&gt; 40.2</td>
<td>12</td>
<td>&lt;0.05</td>
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<td>Calcium channel blockers</td>
<td>C08</td>
<td>n&lt;sup&gt;a)&lt;/sup&gt; 48/88, %&lt;sup&gt;b)&lt;/sup&gt; 54.6</td>
<td>n&lt;sup&gt;c)&lt;/sup&gt; 36/88, %&lt;sup&gt;d)&lt;/sup&gt; 40.9</td>
<td>15</td>
<td>&lt;0.005</td>
<td>n&lt;sup&gt;a)&lt;/sup&gt; 52/87, %&lt;sup&gt;b)&lt;/sup&gt; 59.8</td>
<td>n&lt;sup&gt;c)&lt;/sup&gt; 36/87, %&lt;sup&gt;d)&lt;/sup&gt; 41.4</td>
<td>20</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Reproduction hormones</td>
<td>G03</td>
<td>n&lt;sup&gt;a)&lt;/sup&gt; 51/88, %&lt;sup&gt;b)&lt;/sup&gt; 58.0</td>
<td>n&lt;sup&gt;c)&lt;/sup&gt; 33/88, %&lt;sup&gt;d)&lt;/sup&gt; 37.5</td>
<td>27</td>
<td>&lt;0.0001</td>
<td>n&lt;sup&gt;a)&lt;/sup&gt; 62/87, %&lt;sup&gt;b)&lt;/sup&gt; 71.3</td>
<td>n&lt;sup&gt;c)&lt;/sup&gt; 37/87, %&lt;sup&gt;d)&lt;/sup&gt; 42.5</td>
<td>51</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Antibiotics</td>
<td>J01</td>
<td>n&lt;sup&gt;a)&lt;/sup&gt; 46/88, %&lt;sup&gt;b)&lt;/sup&gt; 52.3</td>
<td>n&lt;sup&gt;c)&lt;/sup&gt; 32/88, %&lt;sup&gt;d)&lt;/sup&gt; 36.4</td>
<td>24</td>
<td>&lt;0.0001</td>
<td>n&lt;sup&gt;a)&lt;/sup&gt; 58/87, %&lt;sup&gt;b)&lt;/sup&gt; 66.7</td>
<td>n&lt;sup&gt;c)&lt;/sup&gt; 34/87, %&lt;sup&gt;d)&lt;/sup&gt; 39.1</td>
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<td>&lt;0.0001</td>
</tr>
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<td>NSAIDs&lt;sup&gt;f)&lt;/sup&gt;</td>
<td>M01</td>
<td>n&lt;sup&gt;a)&lt;/sup&gt; 54/88, %&lt;sup&gt;b)&lt;/sup&gt; 61.4</td>
<td>n&lt;sup&gt;c)&lt;/sup&gt; 34/88, %&lt;sup&gt;d)&lt;/sup&gt; 38.6</td>
<td>39</td>
<td>&lt;0.0001</td>
<td>n&lt;sup&gt;a)&lt;/sup&gt; 59/87, %&lt;sup&gt;b)&lt;/sup&gt; 67.8</td>
<td>n&lt;sup&gt;c)&lt;/sup&gt; 36/87, %&lt;sup&gt;d)&lt;/sup&gt; 41.4</td>
<td>44</td>
<td>&lt;0.0001</td>
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<td>Analgesics</td>
<td>N02</td>
<td>n&lt;sup&gt;a)&lt;/sup&gt; 52/88, %&lt;sup&gt;b)&lt;/sup&gt; 59.1</td>
<td>n&lt;sup&gt;c)&lt;/sup&gt; 34/88, %&lt;sup&gt;d)&lt;/sup&gt; 38.6</td>
<td>29</td>
<td>&lt;0.0001</td>
<td>n&lt;sup&gt;a)&lt;/sup&gt; 54/87, %&lt;sup&gt;b)&lt;/sup&gt; 62.1</td>
<td>n&lt;sup&gt;c)&lt;/sup&gt; 40/87, %&lt;sup&gt;d)&lt;/sup&gt; 46.0</td>
<td>20</td>
<td>&lt;0.0001</td>
</tr>
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<td>Neuroleptics</td>
<td>N05</td>
<td>n&lt;sup&gt;a)&lt;/sup&gt; 41/88, %&lt;sup&gt;b)&lt;/sup&gt; 46.6</td>
<td>n&lt;sup&gt;c)&lt;/sup&gt; 30/88, %&lt;sup&gt;d)&lt;/sup&gt; 34.1</td>
<td>13</td>
<td>&lt;0.01</td>
<td>n&lt;sup&gt;a)&lt;/sup&gt; 51/87, %&lt;sup&gt;b)&lt;/sup&gt; 58.6</td>
<td>n&lt;sup&gt;c)&lt;/sup&gt; 29/87, %&lt;sup&gt;d)&lt;/sup&gt; 33.3</td>
<td>42</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>N06</td>
<td>n&lt;sup&gt;a)&lt;/sup&gt; 46/88, %&lt;sup&gt;b)&lt;/sup&gt; 52.3</td>
<td>n&lt;sup&gt;c)&lt;/sup&gt; 34/88, %&lt;sup&gt;d)&lt;/sup&gt; 38.6</td>
<td>18</td>
<td>&lt;0.001</td>
<td>n&lt;sup&gt;a)&lt;/sup&gt; 65/87, %&lt;sup&gt;b)&lt;/sup&gt; 74.7</td>
<td>n&lt;sup&gt;c)&lt;/sup&gt; 35/87, %&lt;sup&gt;d)&lt;/sup&gt; 40.2</td>
<td>66</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Anti-asthma drugs</td>
<td>R03</td>
<td>n&lt;sup&gt;a)&lt;/sup&gt; 48/88, %&lt;sup&gt;b)&lt;/sup&gt; 54.6</td>
<td>n&lt;sup&gt;c)&lt;/sup&gt; 32/88, %&lt;sup&gt;d)&lt;/sup&gt; 36.4</td>
<td>17</td>
<td>&lt;0.005</td>
<td>n&lt;sup&gt;a)&lt;/sup&gt; 62/87, %&lt;sup&gt;b)&lt;/sup&gt; 71.3</td>
<td>n&lt;sup&gt;c)&lt;/sup&gt; 40/87, %&lt;sup&gt;d)&lt;/sup&gt; 46.0</td>
<td>51</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>All drug groups</td>
<td></td>
<td>604/1144, % 52.8</td>
<td>438/1144, % 32.3</td>
<td>197</td>
<td>&lt;0.0001</td>
<td>741/1131, % 65.5</td>
<td>485/1131, % 42.9</td>
<td>417</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

<sup>a)</sup> number of accurate estimates of all estimates made. <sup>b)</sup> proportion of accurate estimates.
<sup>c)</sup> number of accurate estimates expected by chance only of all estimates made. <sup>d)</sup> proportion of accurate estimates expected by chance only.
<sup>e)</sup> p for difference observed-expected. <sup>f)</sup> non-steroid anti-inflammatory drugs
Change from the first to the second outreach visit

The improvement of accurate assessments from the first to the second outreach visits across all participating practices and across all drug groups is shown in the bar graph in Figure 3. There was a clear shift in the distribution of number of accurate assessments from round 1 to round 2. The scatter plot in Figure 4 shows the results based on individual practices. The number of accurate assessments during round 1 is shown on the vertical axis and those from round 2 on the horizontal. The diagonal line indicates no change. A shift of dots from the upper left half of the graph to the lower right one indicates a movement towards more accurate assessments.

To find determinants of the difference in accurate assessments between the two rounds a multivariate linear regression was performed, with the proportion of accurate assessments in the second round as the dependent variable and the proportion of accurate estimates from the first round, GP’s age and sex, practice type (solo or group practice), number of GPs in the practice, number of years of experience as a GP, access to electronic patient record system, duration of the outreach visits, GPs’ ratings of the outreach visits, and the GP facilitator’s ratings of the participating GPs’ attitudes as the independent variables. The only significant determinants affecting the degree of accurate assessments during round 2 were the degree of accurate assessments during round 1 (regression coefficient=0.41, F=22.72, p<0.0001), and the number of GPs in the practice (regression coefficient=0.42, F=7.35, p<0.01), both increasing the degree of accuracy in the second round.

Paper III

Characteristics of the study population

The distribution of solo and group practices between the intervention and control areas was similar, Table 4. There were somewhat more GPs in the intervention than in the control area, small differences in GP age and proportion of women, and GP experience in terms of number of years, and small differences between the intervention and control areas in number of listed patients. None of these differences were statistically significant.
Figure 3. Distribution of number of accurate estimates of practices’ prescribing position (lowest quartile, the top quartile, or the two mid-quartiles in the prescribing level distribution across all practices and across all drug groups) during the first and second round of outreach visits.

Table 4. Characteristics of the study population.

<table>
<thead>
<tr>
<th></th>
<th>Intervention area</th>
<th>Control area</th>
<th>p *)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>Mean (SD) or %</td>
<td>N</td>
</tr>
<tr>
<td><strong>Practices</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Solo</td>
<td>24</td>
<td>51.1</td>
<td>25</td>
</tr>
<tr>
<td>Group</td>
<td>23</td>
<td>48.9</td>
<td>16</td>
</tr>
<tr>
<td><strong>General practitioners</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>90</td>
<td>57.0</td>
<td>67</td>
</tr>
<tr>
<td>Mean age, years (SD)</td>
<td></td>
<td>51.1 (6.3)</td>
<td>50.5 (5.6)</td>
</tr>
<tr>
<td>Women, %</td>
<td>17</td>
<td>19.1</td>
<td>15</td>
</tr>
<tr>
<td>GP experience, years (SD)</td>
<td></td>
<td>15.6 (7.8)</td>
<td>14.9 (7.5)</td>
</tr>
<tr>
<td><strong>Listed patients per practice</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>2,829 (1,981)</td>
<td>2,517 (1,796)</td>
<td></td>
</tr>
<tr>
<td>Median</td>
<td>1,885</td>
<td>1,791</td>
<td></td>
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<tr>
<td>Inter quartile range</td>
<td>1,410-3,666</td>
<td>1,544-2,960</td>
<td></td>
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</tbody>
</table>

*) p for difference between intervention and control areas.
Figure 4. Change of accurate estimates of individual practices’ prescribing position (lowest quartile, the top quartile, or the two mid-quartiles in the prescribing level distribution across all practices and across all drug groups) from the first to the second round of outreach visits.

Effects of intervention

The crude prescription levels of the five antibiotics groups are given in Table 5. It is obvious that the initial prescription levels differed between the two areas, which might have caused a bias in the analysis. For this reason initial prescription level was taken into account when comparing the prescribing trends in the two areas.

Prescription levels for broad-spectrum penicillin (ATC code J01CA), adjusted for differences in initial prescription levels are shown in Figure 5a. During the trial the prescription level in the intervention area was significantly lower than in the control area (p<0.01). For the specific broad-spectrum penicillin Pivmecillinam (ATC code J01CA08) there was a non-significant trend towards lower prescription levels during the trial period. The difference between the areas across the whole trial period was non-significant (p=0.91), Figure 5b.
Table 5. Mean crude prescribed DDD per 1,000 listed patients and practice in the intervention area and in the control area for broad spectrum penicillins (ATC code J01CA), Pymecillinam (ATC code J01CA08), beta-lactamase sensitive penicillin (ATC code J01CE), macrolids (ATC code J01FA), and all antibacterial agents for systemic use (ATC code J01).

<table>
<thead>
<tr>
<th>ATC Code</th>
<th>Intervention Area</th>
<th>Control Area</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-intervention period</td>
<td>Post-intervention period</td>
</tr>
<tr>
<td>J01CA</td>
<td>Jan-June</td>
<td>Jan-June</td>
</tr>
<tr>
<td>320.2</td>
<td>280.4</td>
<td>275.4</td>
</tr>
<tr>
<td>J01CA08</td>
<td>63.8</td>
<td>83.8</td>
</tr>
<tr>
<td>J01CE</td>
<td>654.4</td>
<td>634.9</td>
</tr>
<tr>
<td>J01FA</td>
<td>345.6</td>
<td>252.6</td>
</tr>
<tr>
<td>J01</td>
<td>1,514</td>
<td>1,340.5</td>
</tr>
</tbody>
</table>

Note: DDD = Defined Daily Dose.
Figure 5a-c. Trends in the prescribing of broad spectrum penicillins, pivmecillinam, and betalactamase sensitive penicillin across the study period in general practices in the intervention and control areas.
Figure 5d-e. Trends in the prescribing of macrolids and all antibiotics for systemic use across the study period in general practices in the intervention and control areas.

The corresponding data for betalaktamase sensitive penicillin (ATC code J01CE) is shown in Figure 5c. The prescription levels in the intervention area were slightly higher than in the control area, but the difference was non-significant (p=0.09). Regarding macrolids (ATC code J01FA), Figure 5d, the prescription levels tended to decrease more in the invention area than in the control area, (p=0.81). For all antibacterial agents for systemic use combined, the intervention area had a significantly lower prescription level than the control area (p<0.03), Figure 5e.
Paper IV

Characteristics of the study population

The distribution of solo and group practices between the intervention and control area was similar, Table 6. There were somewhat fewer GPs in the intervention than in the control area, small differences in age, proportion of women, and GP experience in terms of number of years, and small differences between the intervention and control group in number of listed patients. None of these differences were statistically significant.

Effects of intervention

The crude prescribing levels of the six NSAID groups are given in Table 7. It is obvious that the initial prescribing levels differed between the two areas, which might cause a bias in the analysis. For this reason initial prescribing level was taken into account when comparing the prescribing trends in the two areas.

Prescribing levels for acetic acid derivatives, adjusted for differences in initial prescribing levels are shown in Figure 6a. During the trial the prescribing level in the intervention area was slightly and non-significantly higher than in the control area (p=0.13), and the same was true for the oxycames (p=0.11), Figure 6b, the propionic acid derivatives (p=0.10),

Table 6. Characteristics of the study population.

<table>
<thead>
<tr>
<th></th>
<th>Control area</th>
<th>Intervention area</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N Mean (SD)</td>
<td>N Mean (SD)</td>
</tr>
<tr>
<td></td>
<td>or %</td>
<td>or %</td>
</tr>
<tr>
<td>Practices</td>
<td></td>
<td>p *)</td>
</tr>
<tr>
<td>Solo</td>
<td>24 51.1</td>
<td>25 61.0</td>
</tr>
<tr>
<td>Group</td>
<td>23 48.9</td>
<td>16 39.0</td>
</tr>
<tr>
<td>General practitioners</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N</td>
<td>90 57.0</td>
<td>67 43.0</td>
</tr>
<tr>
<td>Mean age, years (SD)</td>
<td>51.1 (6.3)</td>
<td>50.5 (5.6)</td>
</tr>
<tr>
<td>Women, %</td>
<td>17 19.1</td>
<td>15 22.4</td>
</tr>
<tr>
<td>GP experience, years (SD)</td>
<td>15.6 (7.8)</td>
<td>14.9 (7.5)</td>
</tr>
<tr>
<td>Listed patients per practice</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>2829 (1981)</td>
<td>2517 (1796)</td>
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<tr>
<td>Median</td>
<td>1885</td>
<td>1791</td>
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<tr>
<td>Inter quartile range</td>
<td>1410-3666</td>
<td>1544-2960</td>
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</tbody>
</table>

*) p for difference between intervention and control area.
Table 7. Mean crude prescribed DDD per 1000 listed patients and practice in the intervention area and in the control area for acetic acid derivatives (ATC code M01AB), oxicames (ATC code M01AC), propionic acid derivatives (ATC code M01AE), coxibes (ATC code M01AH), other non-steroid anti-inflammatory drugs (ATC code M01AX), and all non-steroid anti-inflammatory drugs combined (ATC code M01A).

<table>
<thead>
<tr>
<th></th>
<th>Intervention area</th>
<th>Control area</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-intervention period</td>
<td>Intervention period</td>
</tr>
<tr>
<td></td>
<td>Jan-June</td>
<td>July-Dec</td>
</tr>
<tr>
<td>M01AB</td>
<td>1683</td>
<td>1507</td>
</tr>
<tr>
<td>M01AC</td>
<td>530</td>
<td>442</td>
</tr>
<tr>
<td>M01AE</td>
<td>3998</td>
<td>3341</td>
</tr>
<tr>
<td>M01AH</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>M01AX</td>
<td>95</td>
<td>74</td>
</tr>
<tr>
<td>M01A</td>
<td>6338</td>
<td>5398</td>
</tr>
</tbody>
</table>
Figure 6 a-c. Trends in the prescribing of acetic acid derivatives, propionic acid derivatives, oxicames and across the study period in general practices in the intervention and control areas.
Figure 6 d-f. Trends in the prescribing of coxibes, other non-steroid anti-inflammatory drugs, and all non-steroid anti-inflammatory drugs across the study period in general practices in the intervention and control areas.
Figure 6c, the coxibes (p=0.09), Figure 6d, and other non-steroid anti-inflammatory drugs (p=0.09), Figure 6e. For all NSAIDs combined the intervention area had a non-significantly higher prescribing level than the control area (p=0.12), Figure 6f.
Discussion

Summary of results
There was a considerable variation in prescribing levels between practices, but a considerable stability in the variation of prescribing behaviour over the study period for individual practices, irrespective of analysis method. The mailed feedback had no detectable effect on prescribing behaviour. As expected, there was slightly more variation within solo practices than within group practices because of the counter balancing effect of accumulated prescribing by of two or more GPs' in the group practices. The variation decreased somewhat with GP age, and there were no statistically significant gender effects.

GPs’ assessments of their prescribing profiles were generally better than chance during the first round of outreach visits, and were even better during the second. The majority of the practices improved their assessment accuracy, a minority had no change or had fewer accurate assessments during round 2. The two most important determinants of an improvement from the first to the second round were good results during the first round and the number of GPs in the practice.

The prescription level of all antibacterial agents for systemic use decreased in the intervention area as compared with the control area after a single outreach visit and provision of a desk guide with emphasis on the key message. Moreover, the prescribing of broad-spectrum antibiotics decreased, and the prescribing of penicillin V tended to increase, while that of macrolids tended to decrease, all in line with the hypothesis.

The prescribing level of NSAIDs remained higher in the intervention area as compared to the control area after a single outreach visit and provision of a desk guide with emphasis on the key message. No change of prescribing of the drug subgroups was in line with the hypothesis.

Paper I
The strengths of Paper I include that the analyses were performed on official data, based on filled prescriptions, with little or no data loss. The same authority registered all filled prescriptions, minimising handling variation. Potential disturbing factors, such as auto-correlation, were eliminated during data
processing. It was not possible to establish a control group within the county, as the quality improvement initiative ('GP Quality Unit') aimed at covering all practices. Comparison with other county or counties was not possible, since data were not available for areas other than Storstrøm County. Therefore, the practices served as their own controls over time. Data refer to prescribing habits during the 1990s. However, the problem of rational prescribing habits is still prevalent [14].

Few authors have addressed the issue of stability of prescribing habits in general practice. One of the main reasons may be the lack of comprehensive long-term prescription data registers at prescribing physician level. In a New Zealand study from 1992-94 [9], based on reimbursement data, a 9% median intra-GP variability was found in both volume and total costs from year to year in a regional GP sample (305 GPs), and a 16% variation in total costs and 17% in total volume in a national GP sample (74 GPs).

Our finding of no effects of mailed feedback on GPs' prescribing behaviour conforms with what has been shown in a comprehensive 2000 Cochrane review [32]. Similar results have also been shown in the few studies where large data registers were used to collect outcome measures. In a randomised controlled trial in Australia [10], no effects were found of unsolicited, posted government-sponsored feedback based on centralised aggregated data on prescribing levels of general practitioners. In a Danish randomized, controlled trial it was concluded that postal prescribing feedback in addition to clinical guidelines on the diagnosis and treatment of asthma did not influence GPs' prescribing patterns [11, 12].

However, there are studies that demonstrate some effects. In a Canadian trial 54 GPs whose prescribing of analgesics was more than two standard deviations above average, were randomly allocated to receiving a note on their prescribing volume and a 1-day group education activity, or to receive a written notification only, or to no intervention [15]. Those in the first group decreased their prescribing volume by 33%, and those in the second group by 25%, while there was no change in the third group. Similar but smaller effects were found in a Norwegian study [13] and in a Canadian study [14] when written feedback of prescribing profiles was combined with treatment recommendations. In a 2006 Cochrane review it was found that the combination of audit and feedback had a small to moderate effect on professional practice [16].

Although mailed feedback only has shown a modest or no effect on doctors' drug prescribing, it is still widely used in continuing medical education (CME), and in quality assurance and improvement. The method is easy to apply on a large scale and relatively cheap. However, the approach appears to be more effective if combined with other strategies [17], such as audit-feedback with peer discussions [18, 19].

Some possible explanations for the lack of success with mailed feedback only in this study might be that he GPs may not have paid attention to the
diagrams, or they may not have understood the diagrams, or they may have taken the diagrams into consideration but found no reason to chance their prescribing habits. Moreover, too much information with poor explanation may have been provided.

It is important to note, that the establishing of the "GP Quality Unit", the development of the feedback charts, and the semi annual mailed prescribing feedback, were some of the first, but important, steps in the process of establishing a formal local quality improvement culture within the general practice community of Storstrøm County in the early 1990s. The main purpose of the initiative was to initiate reflections on variations in prescribing behaviour and raise awareness about prescribing patterns. The feedback diagrams were not accompanied by any clinically relevant information and they were based on aggregated prescribing data at the second ATC level with no chance of identifying specific substances at the fifth ATC level. On the other hand, too detailed prescribing information at this early stage in the quality assurance process might possibly have impeded the overall ambition of starting a debate about rational drug prescribing in a broader sense.

**Paper II**

The strengths of Paper II include that the actual prescribing levels were based on register data with a high degree of completeness and reliability, and that the response form might be regarded as having high face validity. All practices within a geographically defined area were invited to participate, the non-participation rate, 6 out of 94 practices (6.4%) was low and is unlikely to have affected the results. A limitation might be that the data referred to prescribing habits during the 1990s and not today. However, the problems regarding rational prescribing habits are still prevalent [14]. We therefore have no reason to believe that the results are biased to such an extent that the conclusions would be affected.

In Paper I it was found that postal feedback of prescribing profiles regarding the same 13 drug groups as used in this study had no effect on prescribing volumes, in spite of the fact that the project was initiated by the local GP community and that the information was updated and sent out every six months for seven years. We speculated on possible reasons for the lack of effect on prescribing habits, for instance that the feedback information was not read, or was read but ignored, or was read but no action taken.

The results from the present study indicate that the first option, that the feedback was not read, probably does not apply. Since the GP assessments during the first round were generally more accurate than chance, they most probably read the feedback information. However, this information did not constitute a sufficiently strong argument for the GPs to take action. More of
the same would probably not have made any difference, since a total of 14 semi-annual feedback sheets had no effect on prescribing habits.

Other means appear to be necessary to achieve changes in prescribing habits. In this study, outreach visits were used. There was a clear effect of the visits during the second round. The improved results were most probably caused by the discussions during the first round, since neither we nor anyone else made any other intervention. The content of these discussions focussed on the prime purpose of the project, to promote rational drug prescribing.

The two rounds of outreach visits in this study thus appear to have had an effect on the GPs’ awareness of their prescribing habits. Whether it also affected the prescribing habits is not known. However, outreach visits have been shown to affect prescribing habits in other studies. In a Canadian trial, 54 GPs whose prescribing of analgesics was more than two standard deviations above average were randomly allocated to receiving notification of their prescribing volume and a 1-day group education activity, or to receiving written notification only, or to no intervention [14]. Those in the first group decreased their prescribing volume by 33%, and those in the second group by 25%, while there was no change in the third group. Similar but smaller effects were found in a Norwegian study [11] and in another Canadian study [15], when written feedback of prescribing profiles was combined with treatment recommendations. A 2006 Cochrane review stated that the combination of audit and feedback only had a small to moderate effect on professional practice [16].

In this study the outreach visit with discussion of general guidelines for rational drug prescribing may be regarded from the individual practice point of view as an isolated educational opportunity. More long-term educational efforts are probably needed to achieve larger, more sustainable effects.

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**Paper III**

The strengths of Paper III include that the study population of general practices was highly representative of all practices in the county. Furthermore, data on practice characteristics and on prescribed drugs was complete. Moreover, the study was performed in Denmark, where the patient load on the practices is moderate, thanks to the primary health care structure, which means that GPs probably had time to consider drug prescribing to a greater extent than in other settings, where practices might have a heavier patient load.

The limitations include that the number of practices was moderate. The non-significant trends in the desired direction seen in the study might have been significant with a larger number of practices. On the other hand, the relatively small numbers of practices made it possible to have a thorough discussion of the prescribing message at the outreach visits.

50
Another possible limitation might have been that the allocation of practices to the intervention or control area was not fully random. However, in the considerations of allocation method it was regarded as essential to avoid ‘contamination’ of the intervention message from intervention to control practices. Since several of the practices cooperated in CME and other activities it was regarded as essential that such practices were allocated to the same geographical practice group. All things considered, the allocation method used in the study was deemed to have the most advantages and least disadvantages.

Outreach visits have previously been used in order to affect prescribing habits in other studies, but the effects are at variance. In a randomized controlled trial performed in Leicestershire, England, with the intention of reducing the prescribing of broad-spectrum antibiotics (amoxicillin with clavulanic acid and quinolone antibiotics), involving 14 practices, no effect of outreach visits on the prescribing of these drugs was found [23]. In a three-year randomized controlled trial using outreach visits with 12-monthly follow-ups carried out in general practice in Denmark no effect on prescription level of asthma medication was found, either in the short-term or long-term follow up [24].

In contrast, in a Canadian trial, 54 GPs whose prescribing of analgesics was more than two standard deviations above average were randomly allocated to three groups: receiving notification of their prescription volumes and a 1-day group training activity, or to receiving written notifications only, or no intervention [14]. GPs in the first group decreased their prescribing volume by 33%, and those in the second group by 25%, while there was no change in the third group. Similar but smaller effects were found in a Norwegian study [11] and in another Canadian study [15], when written feedback concerning prescribing profiles was combined with treatment recommendations, an intervention similar to the outreach visits used in the present study. Prescribing practices in line with national guideline recommendations were shown in a randomized controlled clinical trial using academic detailing in groups of GPs [33, 34].

A 2006 Cochrane review stated that the combination of audit and feedback only had a small to moderate effect on professional practice [20]. A large number of studies on the effect of outreach visits in various setting have been performed [17, 35-49]. In a 2007 Cochrane review [16] these studies were evaluated. Outreach visits were identified as an intervention that may improve the practice of health care professionals. The median adjusted risk difference in compliance with desired practice was highly consistent regarding prescribing.

There may be several reasons why some trials using outreach visits have failed while others have been successful. First, statistical power seems to be a crucial factor. In the trial performed by Witt et al. in Denmark only 14 practices participated [24]. In the present study 88 practices participated.
Second, the circumstances around the outreach visits may be important. In the present study, the randomized controlled intervention took place during the third year of annual outreach visits in general practice. The barriers to change according to the delivered message may therefore have been low, since the outreach visit concept was well established in the study population. For the participating GP, it may be easier to focus on the facilitator’s core message when the setup is familiar.

Paper IV

The strengths of Paper IV were similar to those of Paper III. The limitations include that the number of practices was moderate. However, this circumstance most probably had no or very little influence on the outcome of the study, since the differences between the intervention and control are were consistent. Moreover, the rather few practices made it possible to have a thorough discussion of the prescribing message during the outreach visits.

Another possible limitation might have been that the allocation of practices to the intervention or control was not fully at random. However, in the considerations of allocation method it was regarded essential to avoid ‘contamination’ of the intervention message from intervention to control practices. Since several of the practices cooperated in CME and other activities it was regarded essential that such practices were allocated to the same geographical practice group. All things considered, the allocation method used in the study was considered the most advantageous and least disadvantageous.

Outreach visits have previously been used in order to affect prescribing habits in other studies, but the effects are at variance. In a randomized controlled trial performed in Leicestershire, England, with the intention to reduce the prescribing of broad-spectrum antibiotics (amoxicillin with clavulanic acid and quinolone antibiotics) involving 14 practices no effect of outreach visits on the prescribing of these drugs was found [23]. In a 3-year randomized controlled trial using outreach visits with 12-monthly follow-ups carried out in general practice in Denmark no effect on prescribing level of asthma medication was found, neither in the short-term nor long-term follow up [12].

In contrast, in a previous study from this project of the effects of outreach visits on the prescribing of antibiotic drugs a clear effect towards less prescribing was shown [50]. As mentioned previously, in a Canadian trial, 54 GPs whose prescribing of analgesics was more than two standard deviations above average were randomly allocated to receiving notification of their prescribing volume and a 1-day group education activity, or to receiving written notification only, or to no intervention [15]. Those in the first group decreased their prescribing volume by 33%, and those in the second group...
by 25%, while there was no change in the third group. Similar but smaller effects were found in a Norwegian study [13] and in another Canadian study [15], when written feedback of prescribing profiles was combined with treatment recommendations, an intervention similar to the outreach visits used in the present study. The postal feedback model has been further developed into an internet based presentation tool (WOPS 2000), where the Storstrøm County GPs can follow their prescribing profiles [51, 52]. Later on, the concept was extended to a national device in the early 2000, available for all Danish GPs [53].

In a 2006 Cochrane review it was stated that the combination of audit and feedback only had a small to moderate effect on professional practice [20]. In a 2007 Cochrane review [16] outreach visits were identified as an intervention that may improve the practice of health care professionals. The median adjusted risk difference in compliance with desired practice was highly consistent for prescribing.

There may have been several reasons why some trials using outreach visits failed while others were successful. First, the statistical power seems to be a crucial factor. In the trial performed by Witt et al. in Denmark only 14 practices were used. In the present study 88 practices were used.

Second, the circumstances around the outreach visits may be important. In the present study, the randomized controlled intervention took place during the third year of annual outreach visits in general practice. The barriers for change according to the delivered message may therefore have been low, since the outreach visit concept was well established in the study population. For the participating GP, it may be easier to focus on the facilitator’s core message, when the setup is familiar.

Third, the type of drug prescribed may be of importance. It appears that intervention against a drug usually prescribed as first, new prescription, such as antibiotic drugs, probably is easier to affect then drugs usually prescribed as an iteration (prolongation) prescription. In a situation when the patient needs a new type of drug the GP may be more free to follow recommendations than in a situation where the patient comes for an iteration, where the patient requests the same type of drug or the drug prescribed is a result of a process, trying various drug with best effects and least drawbacks of this specific drug, even if prescribing the drug is going against recommendations (“you should not change a winning team”).
Conclusions

There was a considerable variation in prescribing levels between practices, but a considerable stability in the variation of prescribing behaviour of 13 drug groups over the study period for individual practices, irrespective of analysis method. After seven years of semi-annual mailed feedback there was no detectable effect on prescribing behaviour, irrespective of analysis method.

During outreach visits GPs assessed their levels of prescribing in relation to the prescribing level distribution across all practices better than chance. After a single educational session during an outreach visit, their knowledge of their own prescribing levels was further improved.

A simple intervention in the form of outreach visits to general practices with discussions of the key message, and provision of desk guides with the same message resulted in a change of prescribing habits of antibiotic drugs for systemic use in line with the key message in the intervention group as compared with the control group.

A simple intervention in the form of outreach visits to general practices with discussions of the key message, and provision of desk guides with the same message did not result in a change of prescribing habits in line with the key message when it comes to NSAIDs.
Läkemedel är ett centralet element i läkarens terapeutiska arsenal och utgör en väsentlig del av förebyggande, lindring och behandling i sjukvårdsystemet. Läkemedelskostnaderna upptar en betydande och ökande del av hälso- och sjukvårdens budget och det tillkommer kontinuerligt nya, dyrare och i några fall betydligt bättre och effektivare läkemedel. Sjukvården och sjukvårdens huvudmän har begränsade ekonomiska resurser och möts från patienthåll och från politiskt håll av ökande krav om behandling och bot parallellt med att läkemedelsindustrin driver sin marknadsföring över en bred front. Läkemedelsområdet har således föga förvånande blivit föremål för ökande politisk, massmedial och inte minst professionell uppmärksamhet under de senare decennierna.

I länder med ett välutbyggt offentligt hälso-och sjukvårdsystem är primärvårdsläkaren en viktig nyckelperson i förmedlingen av en rad behandlingsåtgärder, däribland, och inte minst, läkemedelsbehandling. Detta gäller oavsett om sjukvårdssystemet tilldelar allmänmedicinaren rollen av "grindvakt", som i Danmark, Storbritannien och delar av övriga Västeuropa där man har personlig listning av patienter hos den enskilde läkaren, eller om man har ett mer öppet sjukvårdsystem, som till exempel primärvården i Sverige. Sedan början av 1990-talet har man i Danmark lagt ned mycket arbete på att introducera, etablera och förankra konceptet "rationell farmakoterapi" inom allmänläkarkåren. Tidigare ansågs läkemedelsförskrivning vara läkarens ensak, men stora variationer i preparatval, och därmed kostnader och förskrivningsvolym inom i övrigt jämnförbara patientpopulationer ledde till politisk och professionell vilja att agera på området. Rationell farmakoterapi innebär

1. att läkemedelförskrivningen är ändamålsenlig i förhållande till icke-farmakologisk behandling
2. att läkemedlets effekt är väldokumenterad vid den aktuelle indikationen
3. att det finns ett gynnsamt förhållande mellan önskat och oönskad effekt
4. att dosering och duration är välgrundad – speciellt med tanke på patientens följsamhet
5. att förskriva billigaste läkemedel med den/de önskade effekter

Hur marknadsför man konceptet "rationell läkemedelsförskrivning" till en allmänläkarkår, som är stolta yrkesmän/kvinnor, som är egna självständiga
företagare och fria entreprenörer med stor personlig integritet och ansvar samt god vana att fatta egna beslut, som inte har något eget incitament till att ändra sina förskrivningsvanor och som framför allt är trötta på ’storebrors’ ständiga och otidiga inblandning i läkarverksamheten?


Därefter gick informationsläkaren igenom förskrivningsstatistiken med läkarna och inhämtade samtidigt information, som användes vid de senare statistiska analyserna. Det visade sig att utskicken hade haft en viss effekt på kännedomen om den egna praktikens förskrivningsprofil, i genomsnitt 7 rätt av 13 möjliga, alltså något bättre än slumpen. Vid besöken 1999 fyllde praktikerna återigen i samma typ av tipskupong som vid förra besöket. Denna gång uppvisade praktikerna en klart bättre kännedom om den egna förskrivningsprofilen, i genomsnitt 9 rätt av 13 möjliga.


Hypotesen bakom studien kunde bekräftas. Interventionsområdet reducerade sin förskrivning av hela antibiotika-läkemedelsgruppen, och speciellt förskrivningen av bredspektrumanitibiotika jämfört med förskrivningen i kontrollgruppen.


Syftet med delarbete 4 var att testa om samma enkla och överskådliga typ av behandlingsrekommendation som i delarbete 3 men gällande smärtstillande läkemedel kunde tänkas påverka förskrivningen. Samma uppsättning av mottagningar som deltog i delarbete 3 deltog även här, men med ombytta
roller. Kontrollgruppen i delarbete 3 blev interventionsgrupp i delarbete 4, och interventionsgruppen i delarbete 3 blev nu kontrollgrupp. I övrigt var designen och genomförandet identiskt för de två delarbetena.

I motsats till delarbete 3 fann vi ingen effekt av informationsläkarbesöket på förskrivning av smärtstillande läkemedel. En förklaring kan vara att antibiotika ofta är förstagångsförskrivningar, där man mera fritt kan välja läkemedel, medan förskrivningen av smärtstillande ofta är receptförnyelser, där man i högre grad är bunden av tidigare preparatval.
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