

Diagnosis-prescription studies – Important steps towards a national drug prescription statistics in Norway

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ABSTRACT

In the first part of this article, drug utilization and prescribing practice is discussed as seen from a Norwegian general practice perspective. Which are the data sources available? What kind of studies have been performed? Prescription-diagnosis studies are reviewed, in particular the Møre & Romsdal Prescription Study (MRPS). Because the wholesales drug statistics do not include information about neither patients, prescribers or diagnoses, there is a current need for establishing a more comprehensive statistics giving wider and deeper insights into the prescribing and utilization of drugs in the Norwegian society. The proposed Norwegian prescription statistics is discussed in relation to previous experiences from prescription-diagnosis studies and current needs for research and statistics in the field. Some examples are given illustrating why the 11-digit person number probably should be included in the database. Lack of diagnostic information may to some extent be compensated for by introducing a more differentiated list of diagnoses for the drugs reimbursed. The use of data from this statistics for quality assurance in e.g. general practice is discussed. Finally, some suggestions are given for how the Norwegian prescription statistics may be organised.

STUDYING GPs' PRESCRIBING PRACTICE

First we need baseline data

"It is hard to evaluate or to improve the quality of something that you do not know how look like. Most physicians know remarkably little about their own practice. Simple things like the distribution of own patients according to gender and age groups, how many patients on treatment for hypertension, or how many who are regular users of benzodiazepines or strong analgesics, remains obscure guesswork."

O. Rutle (1995)¹

If we want to do something better (e.g. prescribing), we first need to know what the baseline is. The patterns of prescribing and utilization of drugs are also important because they to some extent reflect what the community needs and wants when it comes to drugs.² Descriptive studies serve to profile the present situation and to pinpoint possible problems.

Not so many studies have been undertaken to make comprehensive descriptions of drug prescribing practice in general practice. Most studies focus on selected therapeutic areas, specific drugs, or on selected patient groups. Most studies are not limited to general practice, they are rather examining the total drug use as reported by patients in selected populations or districts. With few exceptions, diagnostic information (reason for encounter; diagnosis for prescribing) is

generally *not* available. On the other hand, morbidity statistics from general practice have traditionally been recorded during separate surveys not paying particular attention to the content of prescribing.³⁻⁵

Data for describing drug utilization or prescribing studies can principally be obtained in two different ways: using routine data that otherwise would have been collected (e.g. for administrative purposes) or the gathering of data within frameworks of specific studies employed to address specific scientific questions.

There are both advantages and disadvantages with respect to the kind of data available depending on from where the information is collected. The different data sources for drug utilization studies are listed in Table 1.

Table 1. Different sources for drug prescription data.

Prescribers (physicians in different settings)
Dispensers (pharmacies)
Seller of drugs (pharmacies, wholesaler)
Payers (owner of institution, reimbursement company)
Health authorities (Norwegian Board of Health, County Chief Medical Officer)
Other health personnel than the prescriber (e.g. home nurse)
Patients

The most comprehensive single source for prescription information is directly from the prescribers. This may allow information about diagnoses, comorbidity, co-prescribing as well as information about the setting during prescribing, e.g. the kind of encounter. It is important to notice that medical records also may provide information about encounters during which drug prescriptions are not issued. The introduction this year of the patient-list system in Norwegian general practice, will probably for the first time provide a reliable population denominator for each practice. However, to get access to the prescribers' data demands both goodwill and a close collaboration with the prescribers. Such studies are therefore often run by the general practitioners (GPs) themselves, sometimes as a part of a prescribing audit.⁶ Almost all Norwegian GPs today have computerised record systems and make prescriptions by the computer. The quality of the data may nevertheless be impaired by bad quality recording by the GPs.

Research by making copies of prescriptions

Some of the first drug prescription studies in general practice were undertaken by aggregating data based on photocopied prescription sheets.

In a Danish provincial town (21 000 inhabitants), Frølund and Nyrop-Larsen surveyed the prescription practice of nine GPs during two 3-month periods (in 1975 and 1976).⁷ This was done by self copying prescription notes and by photocopying the telephone prescriptions. Altogether about 35 000 prescriptions for 14 100 patients were recorded.⁷

During four weeks, Damsgaard and associates photocopied all prescriptions made by the five GPs in their local community in Denmark.^{8,9} During the 4228 GP-patient encounters, 1876 prescription notes were filled in including prescriptions for altogether 3177 drug items.

In the 70s, Sweden established three long-term prescription studies including diagnostic information. They include the Tierp community project and the Jämtland study, which are both presented in more detail elsewhere in this issue of the *Journal*.^{10,11} A third Swedish survey is the Diagnosis and Therapy Survey which now has collected prescription data on a regular basis from representative samples of prescribers since 1978.^{12,13} Each week about 30 randomly selected physicians are asked to participate in the study for one week. During the week, the participating doctors record all (direct) encounters with patients using a self-copying prescription form, the second part of which includes a carbon copy of the prescription (if any), and where the doctor fills in additional information: age and sex of the patient, initial or follow-up consultation, the diagnosis or the symptom causing the prescription, and the reason if no drug was prescribed. The results are analysed and published according to the standards of the International Medical Statistics

(IMS), and published yearly (Medical Index of Sweden) by the National Corporation of Pharmacies and Sweden Pharmaceutical Data Ltd.^{12,13} In this Swedish Diagnosis and Therapy Survey, neither patients nor prescribers can be identified in the database, which is available for researchers, but unfortunately, most data remain scientifically unpublished.^{13,14}

THE MØRE & ROMSDAL PRESCRIPTION STUDY (MRPS)

The most comprehensive pharmacoepidemiologic study conducted so far in Norway, is the Møre & Romsdal Prescription Study (MRPS). This was a prospective, multipractice study in general practice in the county of Møre & Romsdal.^{15,16} The aims of the MRPS were:

- to form a comprehensive, descriptive basis for describing GPs' contacts with patients as well as their drug prescribing patterns during various contact types (house calls, office consultations, indirect contacts) and for particular patient groups (children, elderly)
- to analyse prescriptions patterns and make brief assessments of the appropriateness of prescribing within selected areas (hypnotics, diuretics, antibiotics, pain-killers)
- to meet the methodological challenges in presenting drug prescription data, e.g., ATC/DDD data, more relevant to a general practice perspective
- to perform a controlled intervention trial to examine if prescribing feedback mailed to GPs along with therapeutic recommendations might improve their prescribing practice for insomnia and acute cystitis.

More than 95% of the 156 GPs in the county participated in the study during which they recorded all contacts (90 458) with patients as well as drug prescriptions (74 079 prescriptions) issued during the two study periods (November 1988 and November 1989). The MRPS was not a prevalence-study investigating drug utilization patterns for the population in the county. The denominator was rather the number of GP-patient contacts in general practice.

By the means of self copying prescription pads with a questionnaire to be filled in for each contact (also for indirect contacts and for contacts where drug treatment was not issued) with a patient, the GPs themselves provided the data for the MRPS. The data recorded during the MRPS are listed in Table 2. The particular prescription pad/questionnaire was developed based on corresponding questionnaires used by the Swedish Diagnosis and Therapy Survey (*Diagnos-Recept-undersökningen*).¹²

The main results from this study are published in about thirty publications listed elsewhere,¹⁶ plus a final manuscript prepared for this theme issue of the *Journal*.¹⁷

Table 2. Data recorded for all contacts in general practice during the Møre & Romsdal Prescription Study.

Patient data	- gender - date of birth
Date	- date and weekday
Place	- postal code
Type of GP-patient contact	- office consultation - house call - telephone consultation - letter or via a third person (e.g. practice nurse)
Principal diagnosis for the contact	
First time or follow-up contact for the diagnosis	
Drug prescriptions (if any)	- name of drug - amount prescribed - daily dose - initial or repeat prescription - labelling information - diagnostic indication for each prescription
If no drug prescription	- reason for not prescribing - <i>patient has drugs issued before</i> - <i>patient admitted (to hospital)</i> - <i>others</i>
Physician data	- age and gender - speciality - number of years in practice - kind of practice - <i>group practice or single handed</i> - <i>urban or rural</i> - kind of salary (fixed salary or fee for service)

An advantage with the MRPS was that the survey included diagnostic information and data regarding both the GPs and the (kind of) encounters. However, for patients only gender and age were included. Due to lack of a unique person identifying code, we were not able to trace multiple prescriptions issued during several occasions to the same person.

The results were mainly analysed at an aggregated level as a cross sectional study.

Data presented from the prescribers' perspective

For the physicians, it is usually more relevant to show prescribed drugs as single compounds or therapeutic groups rather than as ATC-main groups. The drug amount unit, the Defined Daily Dose (DDD), is most commonly expressed as DDDs/1000inhabitants per day. This denominator is tailored for a population perspective and does therefore often not fit for showing how individual patients use various drugs. However, a simple transformation to numbers of DDDs per person or patient per year, may sometimes be more relevant

e.g. for the uses of benzodiazepine hypnotics. Sometimes it may also be relevant to show the actually prescribed doses (i.e., prescribed daily dose, PDD), which may differ significantly from the DDD. In the case of antibiotics the mean amount issued per prescription event may correspond to the duration of a cure.

In the MRPS, we did large efforts in setting up tables linking much of the information available (e.g. patients, drugs, diagnoses, encounters). The challenge was to make the presentation clinically relevant, keeping in mind the patient perspective rather than the population perspective. This work is discussed in more detail elsewhere.¹⁶

Prescribing feedback with recommendations

In the intervention study, the intervention was only sent to the GPs in one of the districts (i.e. Romsdal) between the two data-recording periods.¹⁸ The GPs in the other districts (i.e. the Møre districts) comprised the control group. The intervention included prescribing feedback showing own, individual prescribing patterns for the diagnoses insomnia and acute cystitis (as recorded during the first period). Average figures for all GPs in the county were given for comparison. Along with the prescribing feedback were therapeutic recommendations on how to improve the quality of the prescribing for insomnia and acute cystitis (Table 3). Among others, the intervention study revealed that GPs in the intervention group prescribed significantly less DDDs of sleeping pills per ordination than before the intervention. In the case of medium- and long-acting benzodiazepine hypnotics, the patients in the intervention group received on average 11 DDDs less on each ordination in 1989 than in 1988. For these substances, the prescribing of small packages (containing ≤ 30 DDDs) increased by 37% whereas the prescribing of large packages (containing ≥ 100 DDDs) decreased by 20%. Corresponding changes were not seen in the control group. Regarding treatment for acute cystitis, GPs in the intervention group increased the number of prescriptions (and DDDs) for trimethoprim, whereas the corresponding figures for trimethoprim-sulfa decreased. Also on line with the intervention, the number of DDDs per ordination decreased significantly which indicate more frequent use of shorter antibiotic courses for cystitis. On the other hand, GPs in the control group increased their uses of trimethoprim-sulfa, and they did not reduce the amount of DDDs per ordination.¹⁸

This intervention study substantiated that it is in fact possible to improve the GPs' prescribing habits through mailed feedback on prescribing profiles combined with recommendations concerning treatment for specific diagnoses. The non-governmental and anti-control profile of the study, giving priority to confidentiality and voluntary quality assurance, may to some extent also explain the GPs' willingness to change their prescribing habits.

Table 3. The recommendations for treatment of insomnia and acute cystitis given to the general practitioners in Romsdal (intervention group).

INSOMNIA

Non-pharmacological treatment with general advice should be tried more often

When prescribing a drug for insomnia, give the lowest effective dosage for the shortest possible time

When prescribing benzodiazepines:

- short-acting benzodiazepine hypnotics should be preferred to medium- and long-acting
- avoid benzodiazepine tranquillisers

Avoid barbiturates

Use antihistamines more often

ACUTE CYSTITIS

Pharmacological treatment is always recommended

As first choice:

- prescribe three days treatment with either trimethoprim or sulfonamides
 - it is not recommended to prescribe trimethoprim-sulfa
 - avoid penicillines with extended spectrum
 - avoid nitrofurantoin
-

During the data analysis we made an interesting observation. A substantial increase was observed in the control group for the uses of mecillinam, a drug approved for urinary tract infections, but which was not among the drugs recommended as a part of our intervention.¹⁸ This increase from one year to the next was probably caused by a heavy marketing during 1989 of this particular drug. However, our figures suggest that the intervention given in the Romsdal district in fact counteracted the effects of this drug promotion by the industry.

It should be noticed that the therapeutic recommendations (Table 3) rather reflected the opinions of the experts at that time than evidence based medicine of today.

It has later been substantiated that the impact of this kind of intervention strategy may be significantly enforced by involving the GPs more in the development of the standards applied, and to include discussions on own prescribing profiles in educational groups of peers. This has been shown by e.g. Lagerløv et al. who used a group based intervention strategy to improve the quality of GPs' prescribing.¹⁹

DRUG CONSUMPTION IN NORWAY

Each year about 20 million prescriptions are dispensed at Norwegian pharmacies to a total cost of about 11 billion NOK (about 110 mill USD). The vast majority, around 90%, of all prescriptions are issued by general practitioners (GPs).

Norwegian Prescription Statistics (1990-1996)

The MRPS may be regarded as a pilot study for the national survey, Norwegian Prescription Statistics (*Norsk Reseptstatistikk*), which was established in 1990. This survey was run by the Norwegian Medicinal Depot (NMD) in collaboration with The International Medical Statistics (IMS) and was based on data collected from about 250 physicians (mainly GPs).²⁰ The objective for this survey was to establish a representative and annual prescription statistics. Some results from this ongoing survey have been published along with the annual wholesales statistics report from the Norwegian Medicinal Depot, but apart from this, the data has generally not been reported scientifically (i.e. original publications in peer reviewed journals). The external validity of this diagnosis-therapy survey has also been questioned due to a low, and decreasing, participation rate.²⁰ When the IMS in 1996 took over the full responsibility for this statistics in Norway, the data collecting came to a standstill and no data from later than 1996 are available.

The sales statistics

During the 1970s, Norway was one of the pioneering nations in the world with respect to pharmacoepidemiology. For example, Norwegian researchers (e.g., Andrew M, Baksaas I, Lunde PKM, and Øydvinn K) made important contributions in the field of drug utilization studies, in particular by the development of the ATC/DDD-methodology.²¹ The current national and international status for the ATC/DDD methodology is given elsewhere in this issue of the *Journal*.²² Norway was one of the first nations to establish a national wholesales statistics.²³ In the annual wholesales statistics report, *Drug consumption in Norway*, the total sales of drugs are given for the various drugs in terms of volume (DDDs) sold (both per county and for the nation) in relation to a population unit (1000 inhabitants) per a given time unit (day). Furthermore, the costs (pharmacy retail price) for the various drugs are given.

Major limitations with the sales statistics are, however, the complete lack of information regarding what is really going on out there when patients encounter physicians for some illnesses which subsequently make them show up in pharmacies with prescription notes for some drugs. The sales statistics do not include any information about neither patients, prescribers, the kind of encounter during prescribing, nor the diagnoses for prescribing.

COMING SOON (?) – A NORWEGIAN DRUG PRESCRIPTION STATISTICS

Efforts are currently being undertaken to establish a national prescription statistics in Norway. Rogaland Research have provided two background reports among others outlining which data should be included

in a prescription database, and how prescription data may be used for individual prescribing feedback to the prescribers as an ongoing audit.^{24,25}

For reasons of completeness, data quality and feasibility it has been concluded that a National Drug Prescription Statistics should be based on data gathered from the pharmacies.²⁴ All prescription drugs, irrespective of their reimbursement status, should be included in the statistics.²⁴

Linking multiple prescriptions to right individuals

A unique code linking prescriptions issued over time to the same individual is a prerequisite for doing longitudinal studies, e.g., in the study of inappropriate drug combinations²⁶ and polypharmacy.²⁷

For example, in the MRPS we were only able to study multiple ordinations when they were written on the same prescription sheet (up to three ordinations were possible on each prescription sheet). Nevertheless, our figures revealed that about one of six elderly patients who received a benzodiazepine tranquillizer was concurrently prescribed another benzodiazepine for sleeping problems.²⁶ Furthermore, 13.5% of all prescriptions for elderly patients met at least one of the listed criteria for pharmacological inappropriateness. However, our figures regarding inappropriate co-prescribing did only show the tip of the iceberg because we were not able to link prescriptions issued on different prescription sheets or that were made at different occasions.²⁶

The only feasible method for linking multiple prescriptions made over time to right individuals seem to be by including the 11-digit person number in the dataset. This is at the same time the key for linking prescription data (exposure) to databases with health outcome data. This may e.g. be data from microbiological databases showing antibacterial resistance. For example in Finland, it has been shown that increased prevalence of resistance to erythromycin among group A streptococci was directly caused by overuse of macrolide antibiotics.²⁸

Another example illustrating the need for linking prescription data with health outcome is drug induced ulcer in the gastrointestinal tract. It has recently been shown that the risk for a bleeding ulcer increases substantially when a non-steroidal antiinflammatory drug is used concurrently with a selective serotonin reuptake inhibitor.²⁹

Some drugs may also cause serious pathology like cancer which may appear long time after the drug exposure. Another potential threat are congenital malformations in babies when mothers take a particular drug during pregnancy. The thalidomide tragedy was in fact one of the main reasons why The Medical Birth Registry was established in Norway about thirty years ago. Finally, the need for having a longitudinal prescription statistics where prescription data may be linked to health outcome, is underlined by the fact that new drugs now in general are launched on the market

before their safety and efficacy are fully established in common practice in large populations. During the last years several new drugs therefore have been dispelled from the market because their safety had not been established.

A population based prescription statistics which when needed may be linked to relevant morbidity statistics can become an extremely useful tool for investigating relationships between drug use and adverse drug reactions in the population.

Lessons from Denmark

In Denmark, relatively large prescription databases were established in Odense and in Aarhus during the 1990s aimed for pharmacoepidemiological research.³⁰ The databases are based on data recorded at the pharmacies for reimbursed prescriptions in the county. One particular feature with these pharmacoepidemiological databases is that they include a unique person identifying code which makes it possible to identify all prescriptions over time for individual patients.^{30,31} This opens up for a new dimension in pharmacoepidemiological research, like doing longitudinal studies and to perform record linkage with other health data registries. The research undertaken by these databases have now substantiated that the included person identifying number is *the* key to clinically relevant and successful research.^{31,32}

At least in theory, there may be a conflict between protecting the confidentiality of the patients and research issues when it comes to prescription- and morbidity statistics. This potential conflict may increase if the database also may be used by the authorities to identify individual patients or prescribers using or prescribing drugs inappropriately. The Danish databases are therefore strictly restricted to research issues. An important lesson from Denmark in this respect is that they have managed to organise the practical data handling in a way that does give the patients a reasonable confidentiality protection even if the person identification numbers are accessible.³²

However, two limitations with the Danish regional pharmacoepidemiologic research databases are that they do not have access to diagnostic information, and that they only cover drugs that are reimbursed by the Danish Social Service. Not included are for example, sedatives, hypnotics, oral contraceptives, a large share of NSAIDs, and analgesics.²⁷

What about diagnostic information?

Prescription statistics based on the data files in Norwegian pharmacies, do not include diagnostic information except the relatively wide diagnostic categories for drugs that are reimbursed according to the "blue prescription list". However, by elaborating this list so that the various reimbursement codes better correspond to clinical diagnoses, this information may be more useful than the situation of today. Table 4 presents a preliminary suggestion as to how the reim-

bursement codes may be differentiated for the present reimbursement paragraph numbers 12 (cardiovascular disease) and 18 (long-term psychiatric disease). Such minor changes can probably be implemented at an administrative level. Introducing mandatory diagnostic codes on all prescriptions will probably be opposed by both physicians and patients for reasons of confidentiality and workload. For not-reimbursed drugs it is therefore probably best today to collect relevant diagnostic information during research projects or audit, e.g. for antibiotic prescriptions.

In Finland, the reimbursement system is organised differently from in Norway. In their system they get access to more detailed diagnostic information, which is described in more details by Dr. Timo Klaukka in this issue of the *Journal*.

Table 4. A preliminary suggestion on how the present reimbursement paragraphs numbers 12 (cardiovascular disease) and 18 (long-term psychiatric disease) can be differentiated into more clinically relevant categories.

Present code	Suggestion for new categories
§9 p. 12 Cardiovascular disease	Hypertension Coronary heart disease Heart failure Cardiac arrhythmias Elevated blood lipids Increased risk for trombosis Other chronic cardiovascular disease
§9 p. 18 Long term psychiatric disease	Psychosis Depression Generalized/panic anxiety Other severe psychiatric disease

Data for quality assurance

Drugs are now comprising the fastest increasing segment of the health care costs, which substantiate that the health authorities need appropriate statistics for monitoring this segment of our health care system.

A national prescription statistics should not only focus on research. The data should also be published as an annual statistics report in addition to, or integrated with, the current "Drug consumption in Norway".

A prescription statistics should also include unique identification codes for the prescribers. Not for "arresting" poor prescribers, but for being able to provide

data for prescribing feedback to individual physicians. This may e.g. be GPs participating in audit groups on prescribing. This kind of system may be established based on previous national experiences, e.g. MRPS,²¹ the DEP-study²² and the pilots ran by Rogaland Research²⁵ last year. Also here are important lessons to be learned from abroad, e.g. the advanced routines developed for prescribing feedback implemented by the Institute for Rational Pharmacotherapy in the Danish County, Storetøms Amt.³³

A National Institute for Public Health Research

The Norwegian Ministry of Social Welfare and Health has just suggested that most national epidemiological registries should be located within one independent unit, a National Institute for Public Health Research. The Danish experience of having one national and two regional prescription databases may also be considered for the Norwegian context. However, if we choose *not* to build up regional databases, the national database must have as one of its explicit obligations to deliver requested prescription data for research purposes to researchers located elsewhere in the country.

Experiences from both Aarhus and Odense have demonstrated some of the advantages of establishing a pharmacoepidemiological research database as independent units within the university system.^{30,32,34} Based on these Danish experiences and The Medical Birth Registry in Bergen, it seems appropriate to rule out if the suggested National Institute for Public Health Research should be established as an independent unit, but scientifically integrated with relevant academic units of the university. This was in fact what the University of Oslo proposed in its comments recently sent to the Ministry in response to the proposed National Institute for Public Health Research.³⁵

"Some of the most successful examples of epidemiological registries with high scientific output have been undertaken by placing the research registry within, not outside, the universities. The planning (of a National Public Health Research Institute) should take these experiences into consideration."

A national prescription statistics may become an extremely useful tool for research and quality assurance to the benefits of the population. However, it may also end up as a "data graveyard". The difference between the two scenarios will to a large extent depend on which data that will be included, and how the database will be organised and funded.

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