

Establishment of the nationwide Norwegian Prescription Database (NorPD) – new opportunities for research in pharmacoepidemiology in Norway

Kari Furu

Division of Epidemiology, Norwegian Institute of Public Health, P.O. Box 4404 Nydalen, N-0403 Oslo, Norway

E-mail: kari.furu@fhi.no

ABSTRACT

Objectives: To give an overview of the data collection and content of the Norwegian Prescription Database (NorPD). In addition, key figures and results from different studies using data from NorPD are presented.

Methods: From 1st January 2004 the Norwegian Institute of Public Health receives monthly data on prescriptions dispensed and collected at all Norwegian pharmacies.

Results: Overall, during the four year period (2004-2007) over 4.2 million unique individuals have been recorded in NorPD with at least one prescription medication dispensed from a pharmacy. In each year about two-third of the entire Norwegian population had at least one prescription dispensed, 75% of the women and 61% of the men. The age-specific prevalence was lowest in both genders in those aged 10-14 years. Among 0-17 years old children and adolescents 45% had one or more prescriptions issued in 2007. About 30% of the girls and 38% of the boys had a prescription issued before they were 1 year old. About 90% of individuals aged 70 years and older received prescription medications.

Conclusion: NorPD covers the entire nation, 4.75 million inhabitants, and is a valid and reliable data source for studying use of prescription drugs. New areas for pharmacoepidemiological research in Norway are made possible with NorPD, like doing longitudinal studies and record-linkage studies with health surveys and other registers in Norway. It also clearly offers a sound basis of knowledge for national decision-making in the field of drug utilisation.

INTRODUCTION

The proposal to establish a national prescription register in Norway has been mentioned in official documents since 1996. In 2000, the Royal Ministry of Health decided to start a project to facilitate the establishment of a population-based pharmacoepidemiological database to be used for research and drug surveillance. In May 2001, the first article about the new prescription database in Norway was published in the Norwegian Journal of Epidemiology (1). The article "Drug utilisation in a public health perspective: establishing a national prescription register in Norway" focused on the process of planning and the necessary steps needed to establish a nationwide prescription database in Norway. What has happened since May 2001?

A general hearing among all the concerned parties was completed in autumn 2001. The Norwegian government handled the case further during 2002 (2). In October 2002 the Royal Ministry of Health proposed the establishment of "Reseptbasert legemiddelregister" as one of ten important target areas in the National Budget of 2003 (3). In December 2002, the main milestone was achieved: the Norwegian Parliament (Stortinget) passed a resolution to establish a register based on prescriptions dispensed at all Norwegian pharmacies. Stortinget decided to grant 10 million NOK to the Norwegian Institute of Public Health (NIPH), established in January 2002, to build up the Norwegian Pre-

scription Database as the first pseudonymous health register in Norway. Stortinget decided also to establish a unit for pharmacoepidemiological research connected to the register (3).

Due to changes in the drug market in Norway the Norwegian government had already decided to move the centre of expertise of drug statistics, the WHO Collaborating Centre for Drug Statistics Methodology and the Norwegian Drug Wholesalers Database (NorDWD), from the Norwegian Medicinal Depot to NIPH. The Department of Pharmacoepidemiology as a part of the Division of Epidemiology was established in autumn 2002 after the Royal Ministry of Health had proposed the establishment of "Reseptbasert legemiddelregister". The department includes the two entities from the Norwegian Medicinal Depot together with the new Norwegian Prescription Database and the research unit in pharmacoepidemiology.

The competence in drug statistics of the staff of the WHO Collaborating Centre for Drug Statistics Methodology and the Norwegian Drug Wholesalers Database (NorDWD) was very important and decisive for the successful process during the establishment of NorPD (4).

The aim of this article is to give an overview of the data collection and content of the Norwegian Prescription Database (NorPD). In addition, key figures and results from different studies using data from NorPD are presented.

THE DATA COLLECTION AND CONTENT OF NORPD

In October 2003, the King in the Council of State (Kongen i Statsråd), passed the final Regulation on the Norwegian Prescription Database (5). The regulation set the aims and thereby the application of NorPD. The main objectives of NorPD, as defined in authoritative regulations, are to collect and prepare data on drug use in individuals in order to:

- describe drug use patterns, including changes over time
- promote and form a basis for research and review of the safety and effectiveness of drug use
- serve as a management tool for the authorities in order to assure quality of prescribing, in addition to general surveillance, control and planning
- give the prescribing doctors a basis for internal control, as part of an audit method to improve quality of prescribing practices

All use of data from NorPD has to be in accordance with these objectives. The regulation also determines what kind of data we may collect from the pharmacies and administrative registers. Each record in NorPD contains the following variables:

- **Patient:** Person-identifier (encrypted), month/year of birth, month/year of death, gender, place of residence (municipality & county)
- **Prescriber:** Person-identifier (encrypted), month/year of birth, gender, profession, speciality
- **Drug:** Nordic article number (brand name, strength, package size), number of packages, ATC code, Defined Daily Dose (DDD), category of prescription, code of reimbursement (from March 2008: ICD10 or ICPC codes), area of application & prescribed dose (free-text), dispensing date, price (Pharmacy retail price)
- **Pharmacy:** Name, licence number, municipality & county

The Nordic article number is a unique identifier for each drug formulation and package format providing detailed information on the dispensed drugs. Area of application and the prescribed dosage are recorded in free-text and therefore more difficult to use for research. The indication for prescribing is not yet recorded in the database. However, the code of reimbursement is recorded and may in some cases function as a proxy of diagnosis. From March 2008 the prescribers have to use either the International Classification of Diseases version 10 (ICD10) or the International Classification of Primary Care codes (ICPC) as the code of reimbursement on the prescriptions.

From 1st January 2004 the Norwegian Institute of Public Health receives monthly data on prescriptions from all the Norwegian pharmacies (figure 1). All the Norwegian pharmacies have computerised the dispensing of prescription drugs. NAF Data (owned by the

Norwegian Pharmacy Association) is responsible for the IT-system FarmaPro, which is used by all the Norwegian pharmacies. NorPD contains information from all drugs prescribed (reimbursed or not) and dispensed at pharmacies to individual patients living outside institutions, i.e. ambulant care. Unlicensed drugs are also included, but drugs sold over-the-counter (OTC) are not recorded in NorPD. However, if the OTC drugs are prescribed by a physician and dispensed, then they will be recorded in the database. Although NorPD is named a "Prescription" database, there are also other kinds of data collected. The main data are prescriptions to individual humans, but also prescribed drugs by veterinarians to animals and prescribing to the physicians' offices are collected in NorPD. Regarding patients in nursing homes and hospitals, the register receives figures on drug use at the level of the institution or the department, i.e. on an aggregate level.

Data protection

As illustrated in figure 1 the pharmacy records of dispensed drugs are electronically and automated transferred through Statistics Norway before they arrive at NIPH and included in NorPD. Statistics Norway is acting as a so-called trusted third party centre and is a part of the data protection to ensure confidentiality of personal information. Statistics Norway has access to only the patient personal identification number and the prescriber's health personnel number and replaces both with a pseudonymised identifier. Statistics Norway can not read any of the other prescription data because this information is encrypted by NAF Data before Statistics Norway receives the data. When Statistics Norway sends the data included the pseudonymised identifiers to NIPH, NIPH is allowed to decrypt the prescription information again. The term "Pseudonymous health data" is defined in the Personal Health Data Filing System Act (in Norwegian: Helseregisterloven): "*personal health data in which the identity has been encrypted or otherwise concealed, but nonetheless individualized so that it is possible to follow each person through the health system without his identity being revealed*" (6). This means that the identity of patients and prescribers has been encrypted according to Norwegian legislation, but nonetheless individualized so that it is possible to follow individuals over time and do record-linkage studies. Data linkage is based on the unique identification number system which is available in all the Nordic countries. To do record-linkage, the current dataset, e.g. The Medical Birth Registry, has to be transformed to XML-format and encrypted and then sent by NIPH to the trusted third party centre, Statistics Norway. Statistics Norway encrypts the data further according to the pseudonymous process, and the data may then be linked to files from NorPD. According to the current Norwegian law, it is necessary to receive approval by the Data Inspectorate before these kind of data-linkage studies are performed.

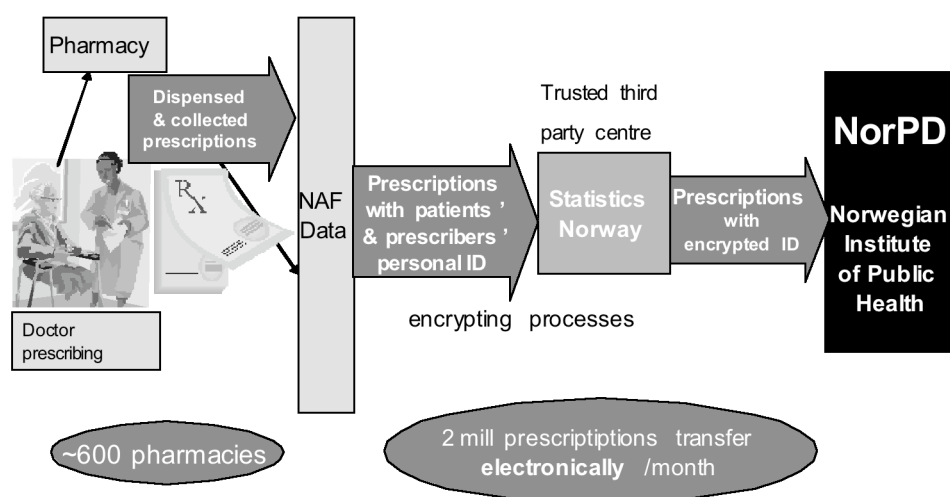


Figure 1. Data flow into the Norwegian Prescription Database.

Quality checks

For quality assurance, a number of queries are carried out monthly or half-yearly to identify possible errors or inconsistencies. NIPH do different routine checks on the data before they are transferred to the NorPD. During transfer of the data the ATC code and the Nordic article number are checked. In NorPD, the Nordic article number is linked to the national register of medicinal products with validated ATC codes and DDD values (7). This register is updated monthly. NIPH also checks if the data deliveries from each pharmacy are of reasonable size. The total number of prescription records, the total number of patients and prescribers are checked every month. Every half year routine statistics for pharmacies, which show great variations in size of data deliveries from month to month, are controlled. This will catch up missing deliveries of special data types, for example reimbursement prescriptions, or if a data delivery from one pharmacy is empty in one month due to technical error at the pharmacy or at the trusted third party. The administrative unit at NorPD has close contact with the pharmacies and those who are responsible for the IT-system FarmaPro in the Norwegian pharmacies (NAF Data). The Personal Identification Number is checked in Statistics Norway against the Central Population Registry. When the Personal Identification Number is invalid or missing Statistics Norway create a special pseudonym, but these individuals are not possible to follow or to be linked to other data sources. However, the reported number of prescriptions and DDDs will be included in the total statistics.

WHAT HAS BEEN FOUND?

KEY FINDINGS AND PUBLICATIONS

Each year 35 million records have been collected, including both prescriptions to individual patients and

deliveries to institutions. NorPD has been operative for more than four years and contains now about 150 million records. Overall, during the four year period (2004-2007) over 4.2 million unique individuals have been recorded in NorPD with at least one prescription medication dispensed from a pharmacy. In each year about two-third of the entire Norwegian population had at least one prescription dispensed, 75% of the women and 61% of the men (table 1). The age-specific one year prevalence in 2007 was lowest in both genders at about 10-14 years of age (figure 2). About 90% of individuals aged 70 years and older received prescription medications. When excluding women who received no other prescribed drugs than prescription of hormonal contraception for systemic use (ATC code G03A), the prevalence of drug use was reduced with about 10-15% in women aged 15-29, but the proportion of drug users among women over 15 years is still higher than in men. Among those 0-17 years ($N_{2007}=1\ 066\ 367$), 45% had one or more prescriptions issued in 2007. About 30% of the girls and 38% of the boys had a prescription issued before they were 1 year old. The proportion of boys receiving at least one drug is slightly higher than in girls until the early teens (figure 3). From the age of 14 the proportion of girls receiving drugs are increasing steeply, while the boys are quite stable. Table 2 shows children aged 0-17 years who received at least one prescription in each of the main ATC groups. The increase in girls is mainly due to the use of contraceptive pills (table 2). About 220 000 individuals used drugs for diseases in the respiratory system (ATC code R), the drug group most used in children. The second most used drug group was anti-infectives which were prescribed and dispensed to over 195 000 children aged 0-17 years in 2007.

In our research activities at the Department of Pharmacoepidemiology we have used NorPD 1) alone or 2) linked data from NorPD to other national registers and population-based health surveys.

Table 1. Number of individuals and one-year prevalence (% of the entire Norwegian population) who had at least one prescription dispensed at Norwegian pharmacies. Norwegian Prescription Database 2004-2007.

	Women n (%)	Men n (%)	Both genders n (%)
2004	1 685 636 (72.8)	1 331 140 (58.5)	3 016 776 (65.7)
2005	1 730 324 (74.3)	1 381 385 (60.2)	3 111 709 (67.3)
2006	1 756 444 (74.8)	1 412 436 (61.0)	3 168 880 (68.0)
2007	1 774 710 (75.0)	1 440 136 (61.5)	3 214 846 (68.3)

Table 2. Number of individuals and one-year prevalence (% of Norwegian children and adolescents aged 0-17 years) who had at least one prescription dispensed in each main ATC group at a pharmacy in 2007. Norwegian Prescription Database 2007.

ATC	Female n (%)	Male n (%)
A. Alimentary tract and metabolism	9 682 (1.9)	9 138 (1.7)
B. Blood and blood forming organs	1 979 (0.4)	1 520 (0.3)
C. Cardiovascular system	2 083 (0.4)	2 620 (0.5)
D. Dermatologicals	45 041 (8.7)	43 818 (8.0)
G. Genitourinary system and sex hormones	36 649 (7.1)	575 (0.1)
H. Systemical hormonal preparations, excl. sex hormones and insulins	7 668 (1.5)	11 685 (2.1)
J. Antiinfectives	102 355 (19.7)	94 007 (17.2)
L. Antineoplastic and immunomodulating agents	871 (0.2)	611 (0.1)
M. Musculoskeletal system	15 827 (3.0)	10 943 (2.0)
N. Nervous system	23 088 (4.4)	29 296 (5.4)
P. Antiparasitic products, insecticides and repellants	2 532 (0.5)	1 699 (0.3)
R. Respiratory system	98 760 (19.0)	122 261 (22.4)
S. Sensory organs	58 506 (11.3)	70 304 (12.9)
V. Various	1 082 (0.2)	1 896 (0.3)

1) Using data from NorPD alone

Prescriptions in NorPD may be used as a proxy for a diagnosis in some occasions. For example, an assessment of the asthma prevalence in an entire population is challenging as no single instrument can be used to identify asthma with certainty. Most reports on asthma prevalence among children and adolescents are based on surveys in which parents were asked about asthma symptoms in their children and/or the asthma was diagnosed by a doctor. We have used data from NorPD as a proxy for asthma in young individuals. We argue that the prevalence of reimbursed, inhaled anti-asthmatics dispensed at pharmacies to all Norwegians aged 0–19 may be a valid prevalence estimate for ongoing and clinically important asthma. On this basis it was estimated that about 1 in 20 Norwegian children/adolescents have ongoing asthma (8).

Carisoprodol was developed to create a drug with less potential for abuse than meprobamate. However, case reports have established carisoprodol as a drug of abuse and by using NorPD we explored the extent of potential abuse of this drug in Norway. Our analyses demonstrated that carisoprodol was widely used and

the skewedness in use indicated that it was a potential drug of abuse (9). A large number of patients used more carisoprodol than recommended in the guidelines. Based on these findings, and some other studies, both the Norwegian Medicines Agency and the European Medicines Agency (EMA) have concluded that the benefit/risk ratio for carisoprodol was negative. This has led to a suspension of the marketing authorisation for all carisoprodol containing products in EU/EØS countries, and this was implemented from 1 May 2008.

NorPD may be used for evaluating introduction of new reimbursement regulations. In June 2005, the Norwegian Medicines Agency introduced new reimbursement regulations for lipid-modifying agents to improve cost containment further. All new users of statins should be prescribed simvastatin and present statin users switched to simvastatin at their first medical visit and latest within a 1-year transition period. Our study showed that nearly 40% of the atorvastatin users switched to simvastatin during the 13-month period after implementation of the new regulations (10). Among the new users of statins the proportion receiving simvastatin increased from 48% in May 2005 to

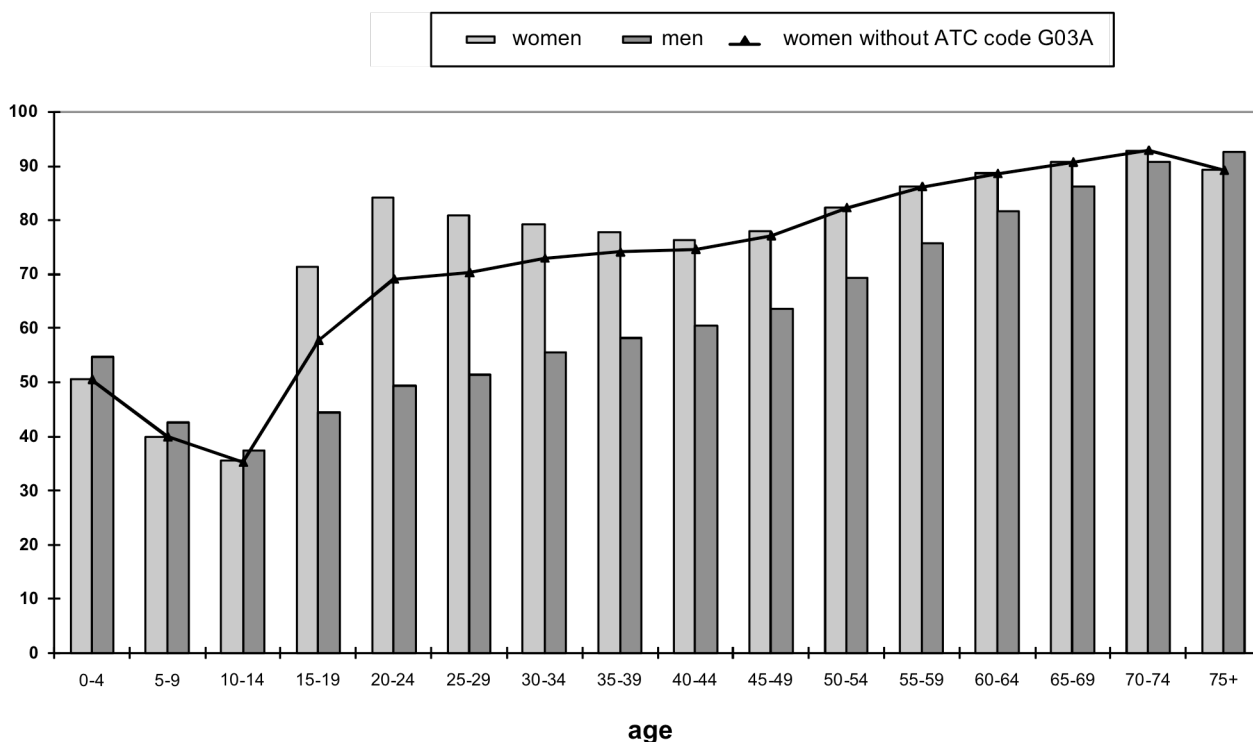


Figure 2. Age- and sex-specific one-year prevalence (%) of the entire Norwegian population who had at least one prescription of medication dispensed in 2007. N=3 214 846 (Excluding those women receiving no other prescribed drugs than hormonal contraceptives for systemic use (ATC code G03A), results in the prevalences shown by the black line).

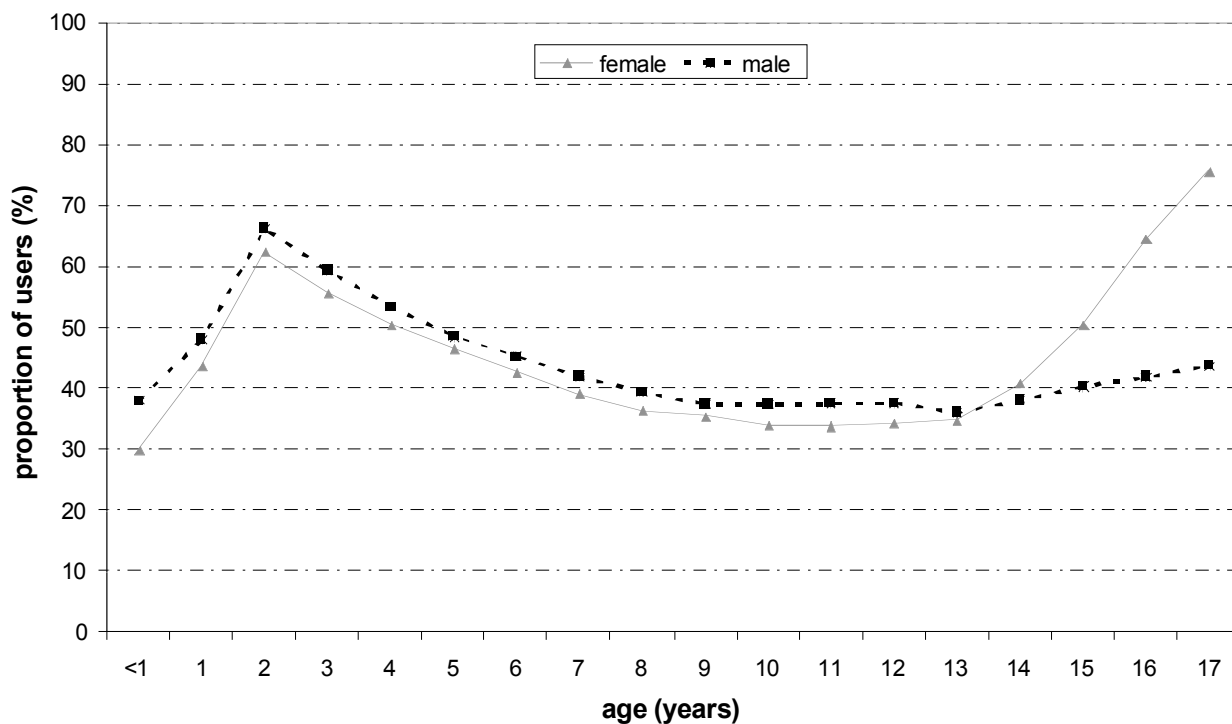


Figure 3. Children and adolescents (aged 0-17 years) who had at least one prescription of medication dispensed at a pharmacy in 2007. N=477 071.

Record-linkage

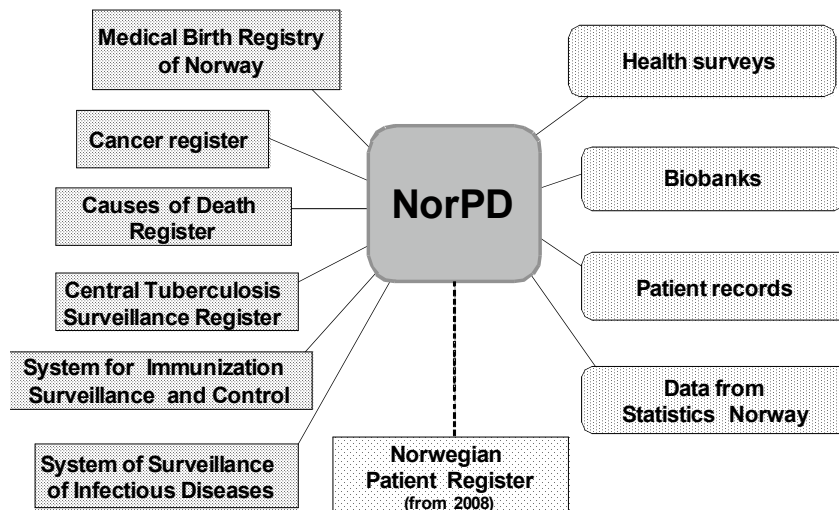


Figure 4. Linkage of Norwegian Prescription Database to other registers and data sources.

92% in June 2006. Our study demonstrated that the new reimbursement policy for statins had a great impact on physicians' prescribing of statins in Norway.

2) *NorPD linked to other data sources*

Figure 4 illustrates a model based on existing data sources in Norway and shows some of the possibilities to link NorPD to health surveys, other registers and data sources. One example of drug use during pregnancy is presented. There is still very limited information about the risk and safety of prescription drugs during pregnancy. However, pregnant women do not differ dramatically from other populations in their use of drugs. It is therefore important to know which drugs are most commonly used during or around pregnancy, because the potential risks of these drugs may have major clinical and public health impact. By linking the Medical Birth Registry of Norway and the Norwegian Prescription Database we were able to describe the use of prescribed drugs in both mothers and fathers before and during pregnancy in Norway. In a register-based study which covered the entire population of Norway, we examined more than 100 000 Norwegian pregnancies and described the drug prescription pattern of both fathers and mothers around conception and during pregnancy (mothers). During pregnancy, 57% were prescribed drugs. In the first trimester, 33% of mothers were dispensed drugs, while the figure was 29% for mothers in the last trimester. Among fathers, 25% used prescribed drugs during the 3 months prior to conception (11). An editorial comment referred to our study and called attention to the creditable and unusual inclusion of data on drug use by fathers 3 months before conception. The editorial concluded that “*More countries should follow Norway's example in their data collection strategies*” (12).

A full list of the publications of studies (per May 2008) which have used data from NorPD, is given on page 208 of this issue of the Norwegian Journal of Epidemiology.

Where can I find out more about NorPD?

The database is held by the Department of Pharmacoepidemiology, Division of Epidemiology at NIPH. Our website is: www.norpd.no (English version) or www.resseptregisteret.no (Norwegian version). Information about the users of a particular drug or drug category split by sex, age and geography are accessible online. Data are currently available from 2004 with an annual update in March for the preceding year. In addition, researchers may apply for research data files to be used according to the objectives of NorPD. Researchers will find the application form on our website and all applications for access to data from NIPH should be sent to Datatilgang@fhi.no. The data is free of charge, but costs in connection with the administrative handling and file processing have to be paid for: 815 NOK exl VAT/hour (~ 100 Euro/hour).

MAIN STRENGTHS AND WEAKNESSES WITH NORPD

Strengths

The database makes it possible to do continuous post-marketing surveillance of drug dispersion in society and of drug effects, the two core elements in the definition of pharmacoepidemiology. In pharmacoepidemiological research it is essential to have complete and valid information on drug exposure (13). Drug use can be measured in great detail in pharmacy records and may give information on the specific drug used, the indication for use, the prescribed dose, and duration of

use. Pharmacy records are considered more complete than medical records. Only those prescriptions which is dispensed and collected by the patients are entered into NorPD. This means that primary non-compliance will be eliminated and thereby the validity of the data will improve (14). The prescription data are also without the potential recall bias that may arise from survey data (15,16). Completeness is good due to the law implemented in January 2004, which makes it clear that all Norwegian pharmacies are legally required to send electronic data to this database on all prescription drugs dispensed and collected. It is also a strength that NorPD was created by and is hosted within a research organisation, which is to say in a scientific setting.

Weaknesses

Unfortunately, drugs dispensed to individuals during a hospital stay or in nursing homes are not recorded in NorPD. This will underestimate the total drug use in the population, especially among the elderly people. The demand to put the patients' 11-digit personal identification number on the prescription was obliged by law from 2003. In 2004, the first operational year of NorPD, the proportion of prescriptions (not individuals) having invalid or missing personal identification number reached 6%. Therefore, the prevalence figures from 2004 will be too low, and the real number of individuals receiving at least one prescription during the year should be higher this year. The proportion of prescriptions having invalid personal identification number has declined further to about 2% in 2007.

Every month the individuals who die are automatically updated in NorPD. However, to keep an overview also of those who emigrate, we have to link the data with the Central Population Registry. Norway has several health registers, such as the Norwegian Medical Birth Registry, the Causes of Deaths Register and the Cancer Register, but unfortunately until 2007 the nationwide register on discharges from hospitals has not been available for linkage studies. However, from 2008 the Norwegian Patient Register is established and will be available for linkage studies in the future.

Future challenges

The population required detecting a particular drug and event association depends upon the background of the event, the proportion of people using the drug, and the magnitude of the risk. Skegg and Doll pointed out already in 1981 that when setting up record linkage for

drug monitoring, one should include a population of at least half a million to detect the commonest hazards, and preferably as many as five million to detect rare events (17). The Norwegian Prescription Database (NorPD) will cover the entire nation, 4.75 million inhabitants, but in some cases it still will be too small to detect rare events. The Nordic countries have a long tradition for register-based epidemiological studies due to the existence of various population-based health registers since 1960s. A driving force is the ubiquitous use of unique person identifiers in these registers making linkage possible. All countries have full-coverage tax supported public health service independent of socioeconomic status. National prescription databases based on drugs dispensed at pharmacies (exposure data), and with potential for outcome linkage, have been available since 1994 in Finland and Denmark, 2002 in Iceland, 2004 in Norway and 2005 in Sweden. The databases cover all the 25 million inhabitants (Denmark: 5.5, Finland: 5.3, Iceland: 0.3, Norway: 4.7, Sweden 9.1 million). There are both similarities and differences in methodology, coverage, validity and access to data which will require close collaboration between the Nordic countries. Therefore it has been taken initiatives to establish a Nordic Pharmacoepidemiological Network for knowledge exchange, research and research training. The number of useful epidemiological techniques and methodologies for drug safety research is large and in 2003 Professor Stricker reminded us in a commentary: "*It is about time for Europe to start using this instrument for a more systematic approach to drug safety*" (18). The Nordic countries have unique potential for collaborative high-quality pharmacoepidemiological studies with large populations. They may contribute to resolving safety issues of international interest and thus to protect society from either over-reaction or under-reaction to drug safety issues.

CONCLUSION

NorPD covers the entire nation, 4.75 million inhabitants, and is a valid and reliable data source for studying use of prescription drugs. New areas for pharmacoepidemiological research in Norway are made possible with NorPD, like doing longitudinal studies and record-linkage studies with health surveys and other registers in Norway. It also clearly offers a sound basis of knowledge for national decision-making in the field of drug utilisation.

REFERENCES

1. Furu K. Drug utilisation in a public health perspective: Establishing a national prescription register in Norway. *Nor J Epidemiol* 2001; **11** (1): 55-60.
2. Furu K. Etablering av et reseptbasert legemiddelregister. Notat av 30.april 2002. Folkehelseavdelingen, Helsedepartementet, 2002.

3. Stortingsproposisjon 1 (Statsbudsjettet 2002-2003), 2002.
4. Strøm H. Reseptbasert legemiddelregister: Et viktig verktøy for å oppnå detaljert legemiddelstatistikk. *Nor J Epidemiol* 2004; **14** (1): 53-55.
5. [Forskrift om innsamling og behandling av helseopplysninger i Reseptbasert legemiddelregister (Reseptregisteret)], 20-10-2003.
6. Personal Health Data Filing System Act [Helseregisterloven]. Act of 18 May 2001 No. 24, 18-5-2001.
7. Rønning M, Litleskare I, Addis A et al. Recommendations for national registers of medicinal products with validated ATC codes and DDD values. *Ital J Public Health* 2006; **3** (1): 30-35.
8. Furu K, Skurtveit S, Langhammer A, Nafstad P. Use of anti-asthmatic medications as a proxy for prevalence of asthma in children and adolescents in Norway: a nationwide prescription database analysis. *Eur J Clin Pharmacol* 2007; **63** (7): 693-698.
9. Bramness JG, Furu K, Engeland A, Skurtveit S. Carisoprodol use and abuse in Norway: a pharmaco-epidemiological study. *Br J Clin Pharmacol* 2007; **64** (2): 210-218.
10. Sakshaug S, Furu K, Karlstad Ø, Rønning M, Skurtveit S. Switching statins in Norway after new reimbursement policy: a nationwide prescription study. *Br J Clin Pharmacol* 2007; **64** (4): 476-481.
11. Engeland A, Bramness JG, Daltveit AK, Rønning M, Skurtveit S, Furu K. Prescription drug use among fathers and mothers before and during pregnancy. A population-based cohort study of 106,000 pregnancies in Norway 2004-2006. *Br J Clin Pharmacol* 2008; **65** (5): 653-660.
12. Begg EJ. Prescribing in pregnancy and lactation. *Br J Clin Pharmacol* 2008; **65** (5): 627-628.
13. West SL, Strom BL, Poole C. Validity of pharmacoepidemiology drug and diagnosis data. In: Strom BL, ed. *Pharmacoepidemiology*, 3rd edn. John Wiley & Sons, 2000: 661-705.
14. Beardon PH, McGilchrist MM, McKendrick AD, McDevitt DG, MacDonald TM. Primary non-compliance with prescribed medication in primary care. *BMJ* 1993; **307** (6908): 846-848.
15. West SL, Strom BL, Freundlich B, Normand E, Koch G, Savitz DA. Completeness of prescription recording in outpatient medical records from a health maintenance organization. *J Clin Epidemiol* 1994; **47** (2): 165-171.
16. West SL, Savitz DA, Koch G, Strom BL, Guess HA, Hartzema A. Recall accuracy for prescription medications: self-report compared with database information. *Am J Epidemiol* 1995; **142** (10): 1103-1112.
17. Skegg DC, Doll R. Record linkage for drug monitoring. *J Epidemiol Community Health* 1981; **35** (1): 25-31.
18. Stricker BH. Drug safety epidemiology: time for Europe to start using this instrument. *Eur J Epidemiol* 2003; **18** (4): 287-288.