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**Statistics on local drug sales:  
A tool to identify problem areas and  
to follow effects of education on  
drug use**

**Anders Ekedahl**

**Malmö 2002**

## Abstract

*Aims:* 1) To assess if drug sales data indicate differences in morbidity, mortality, socio-economic conditions and deviating prescribing habits among physicians; 2) to identify areas for educational interventions and to analyse changes in prescribing after educational activities. In addition, an effort was made to estimate differences between pharmacy sales and purchases by the population, and the amount and value of unused drugs returned to pharmacies.

*Method:* Information on drug sales was gathered from three Swedish and one Nordic drug registers, namely, Sales Statistics on Drugs, Nordic Statistics on Medicines, The National Prescription Survey and The Diagnosis-Prescription Survey, as well as from local prescription studies, copies of prescriptions processed at pharmacies, copies of issued prescriptions and computerised patient records at a health care centre.

*Results:* There was a significant correlation between sales of tranquillizers and hypnotics/sedatives, on the one hand, and mortality, suicides and UnderPrivileged Area score, on the other, in the 33 municipalities of Skåne County.

Benzodiazepine sales in the city of Helsingborg were the highest in the country and higher than the national average to all age groups and both genders. A minority of the physicians, <5%, had issued about 10 times as many benzodiazepine prescriptions as the average physician in Helsingborg.

High compliance rates among district physicians after information by pharmacists, to brands recommended by the Drugs and Therapeutics Committee, attributed to cost savings several times the costs of the information campaign.

Repeated verbal producer-independent education produced significant changes in attitudes towards drugs, drug treatment and drug information. Both this programme and a local educational programme at a health care centre resulted in an overall and sustained reduction in antibiotic prescribing.

There was a substantial difference between sales at the local pharmacy and the purchases on prescription by the local population. Less than 4% of the purchased drugs were returned unused to pharmacies for destruction.

*Conclusion:* There are large differences in sales of drugs between municipalities within the same county. The results show that local drug sales covariates with, and hence may indicate, socio-economic conditions, morbidity and mortality. This information may be used to identify areas where there is a need of information and education activities to promote rational prescribing. Local sales data are reasonably well suited to follow effects of such information and educational activities.

However, local sales of drugs do not fully correspond to purchases and drug use by the local population, neither to prescribing by the local physicians. In order to identify target groups for information and education, there is a need for additional information, as deviant prescribing habits among a minority of doctors may be influential.

Nevertheless, successively improved quality and accessibility of local sales data may provide a useful and cost-effective means to analyse and improve prescribing and use of drugs.

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Till Ingrid, Jonas och Sara

## Abbreviations

<b>ATC</b>	Anatomical Therapeutic Chemical (Classification System)
<b>DDD</b>	Defined Daily Dose(s)
<b>DDD/TID</b>	Defined Daily Doses per 1000 inhabitants and day
<b>PDD</b>	Prescribed Daily Dose(s)
<b>UPA</b>	UnderPrivileged Area

## List of publications

This thesis is based on the following papers, which are referred to by Roman numerals I to VI. In addition, some previously unpublished data are presented, concerning the effects of commuting on drug sales statistics

I. Ekedahl A, Lidbeck J, Lithman T, Noreen D and Melander A:  
**Benzodiazepine prescribing patterns in a high-prescribing Scandinavian community.** Eur J Clin Pharmacol 1993; 44:141-6.

II. Sundquist J, Ekedahl A, Johansson S-E:  
**Sales of tranquillizers, hypnotics/sedatives and antidepressants and their relationship with underprivileged area score and mortality and suicide rates.** Eur J Clin Pharmacol 1996; 51:105-9.

III. Ekedahl A, Wergeman L, Rydberg T:  
**Unused drugs in Sweden measured by returns to pharmacies.**  
Manuscript.

IV. Ekedahl A, Petersson BÅ, Eklund P, Rametsteiner G and Melander A:  
**Prescribing patterns and drug costs: Effects of formulary recommendations and community pharmacists' information campaigns.**  
Int J Pharm Pract 1994; 2:194-8.

V. Ekedahl A, Andersson SI, Hovelius B, Mölsted S, Liedholm H and Melander A:  
**Drug prescription attitudes and behaviour of general practitioners. Effects of a problem-oriented educational programme.**  
Eur J Clin Pharmacol 1995; 47:381-7.

VI. Mölsted S, Ekedahl A, Hovelius B and Thimansson H:  
**Antibiotics Prescription in Primary Care: A 5-Year Follow-up of an Educational Programme.** Family Practice 1994; 11:282-6.

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# Contents

Abstract.....	ii
Abbreviations .....	iv
List of publications .....	v
Introduction .....	1
Background .....	1
General information of drug utilisation data in Sweden.....	1
The Diagnosis-Prescription Survey.....	3
The National Prescription Survey .....	3
Sales statistics on drugs .....	4
Nordic Statistics on Medicines .....	4
Local prescription studies .....	4
Computerised patient records.....	4
Collection and copies of prescriptions .....	4
General information about drug classification systems used in Sweden .....	4
General information about units of measurement.....	5
Defined Daily Dose (DDD) .....	5
Prescribed Daily Dose (PDD) .....	5
Units of comparison and exposure .....	5
Rational Drug Therapy .....	6
Problem areas .....	6
Focus of thesis .....	7
Aims.....	8
Material and methods .....	9
Paper I.....	9
Paper II.....	10
Paper III.....	10
Paper IV .....	11
Paper V .....	11

Paper VI .....	12
Unpublished data .....	12
Statistics .....	12
Results .....	13
Crude sales data on drugs – indication on differences in morbidity, mortality and socio-economic conditions (papers I and II).....	13
Crude sales data on drugs – indication on deviating prescribing habits among physicians (paper I) .....	13
Areas for educational interventions in order to promote rational drug prescribing (paper I) .....	14
Changes in prescribing after information and educational activities (papers IV, V and VI) .....	14
Effects of commuting (unpublished data).....	15
Amounts and value of unused drugs returned to pharmacies (paper III).....	17
Discussion .....	18
Crude sales data – indication on differences in morbidity, mortality and socio-economic status.....	18
Crude sales data - indication on deviating prescribing habits among physicians.....	22
Areas for educational interventions .....	23
Changes in prescribing after information and educational activities .....	23
Effects of commuting.....	27
Amounts and value of unused drugs returned to the pharmacies.....	28
Variability in the units of measurements DDD, DDD/TID, PDD and prescriptions .....	31
Considerations of ecologic studies.....	31
Conclusions .....	33
Sammanfattning på svenska .....	34
Acknowledgements.....	36
References .....	37







## Introduction

### Background

Sales statistics indicate a large variation in drug utilisation between different countries – e.g. the Nordic countries (Nordic Statistics on Medicines 1975-1992). There are also large differences within countries, between regions and counties, and between municipalities within the same county. To some extent, the variation may be related to differences in the prevalence of the disease in question (Olsson et al 1994, Larsson et al 1994), but the variation largely seems to lack rational explanations (Hjort et al 1982).

Drug utilisation has become a research tool

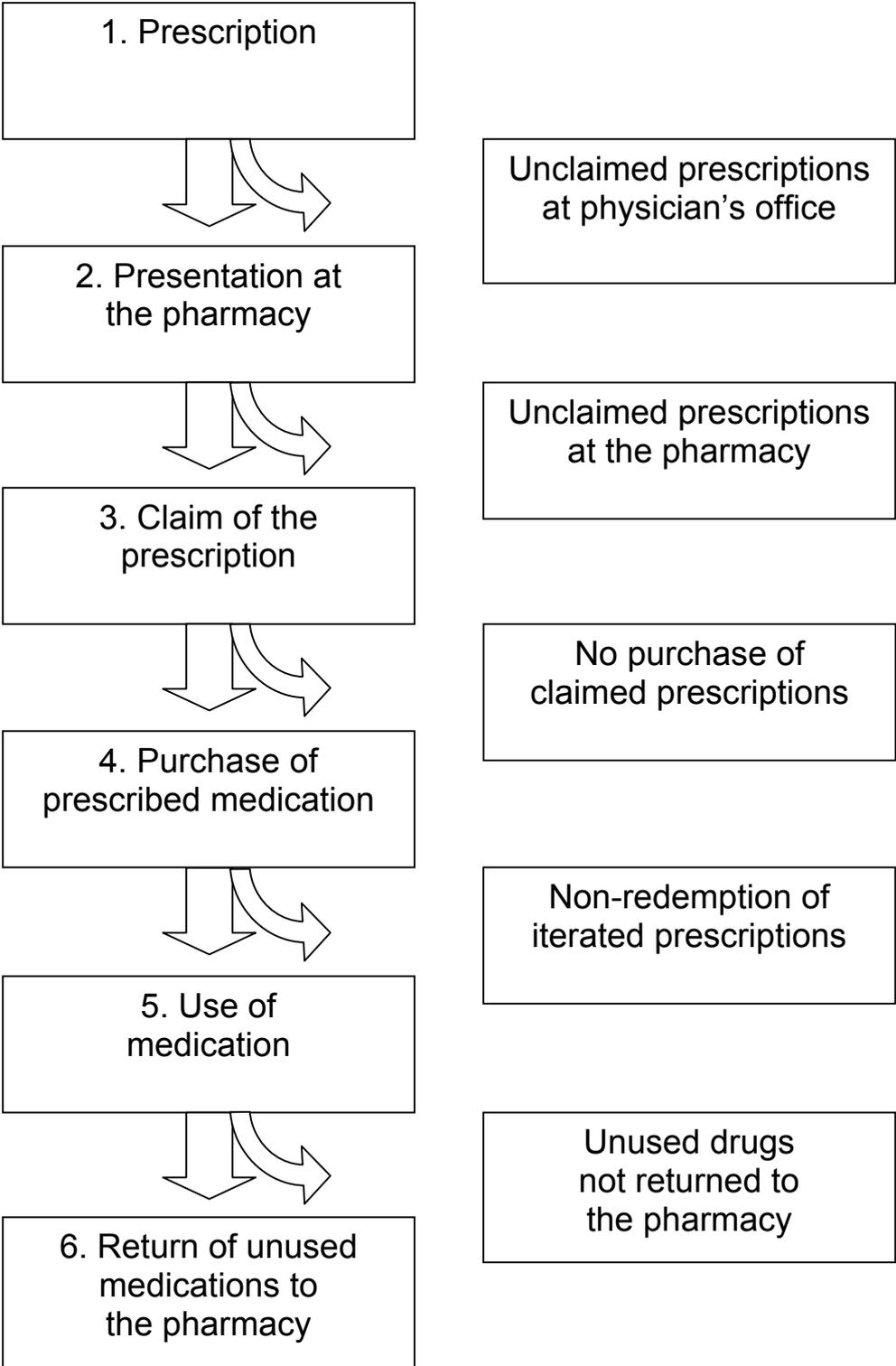
- to measure drug exposure in the population over time
- to measure the effects of information, education, regulatory enforcements and pricing policies
- to obtain indications on under- and over-treatment, misuse and abuse of drugs
- to identify areas for investigation of the rationale behind a certain drug treatment
- to relate data on drug utilisation to patterns of morbidity
- as proxy-variable of morbidity
- to give feed-back to physicians on prescribing and drug sales (Wade et al).

### General information of drug utilisation data in Sweden

In Sweden every drug purchased is registered (prescribed as well as over-the-counter) at every pharmacy in the country. The sales data (both volumes and costs) are collected and compiled by the National Corporation of Swedish Pharmacies. Accordingly, there is a very good basis for drug utilisation studies. However, only ecologic (aggregated) data are available for research, as no identification of the drug purchases of an individual patient (record-linkage) is allowed.

Drug utilisation data may be collected at various collecting points (figure 1). There are differences in the data frame and data quality, depending on how, when and where data are collected. All prescriptions are not redeemed and all

Figure 1. *The prescription flow*



purchased drugs are not consumed. Prescriptions may also be redeemed at a pharmacy outside the home municipality.

There are three main data sources on drug prescribing and sales in Sweden:

- the Diagnosis-Prescription Survey
- the National Prescription Survey
- the Sales Statistics on Drugs

The National Prescription Survey and the Diagnosis-Prescription Survey were originally designed to provide information on drug prescribing and utilisation, i.e. sales on prescription, at the national level. At the local level, only crude sales data from the Sales Statistics on Drugs were available. As computer aided prescription processing successively was introduced at the pharmacies, the sample size and the data collecting of the National Prescription Survey have changed to permit use and analyses also at the regional and local levels.

### **The Diagnosis-Prescription Survey**

Prescribing of drugs to outpatients is followed since October 1978 (Agenäs et al 1980). Data are captured at the prescribing physician's office. The survey is based on a running sample – 1/8th - of Swedish physicians, who are asked to participate each year.

### **The National Prescription Survey**

Since 1974, the sales on prescription in Sweden are continuously recorded in the National Prescription Survey (Wessling 1990). Data are collected following purchases at the pharmacies. The collecting of data has varied over the years:

1974-1982	Sample size 1/288th of all processed prescriptions, i.e. ~0.35%
1983-1986	Sample size increased to 1/25 at computer-equipped pharmacies; 1/288 at all others
1987-1995	Sample size 1/25 at all pharmacies, i.e. 4%
1996	Sample size increased to 100% except for pharmacy dose dispensed drugs (not included)
1997	Purchases by the population at the parish level are provided. (civil registration numbers, including date of birth and gender, are used in the processing of prescriptions at the pharmacies from 1996).
1999	Sales of pharmacy dose dispensed drugs are included

### **Sales statistics on drugs**

Sales statistics on drugs have been available since 1975. Data are captured at the wholesalers. Data are based on deliveries, i.e. invoices of the sales from the wholesalers to individual pharmacies minus returns of unsold drugs from the pharmacies to the wholesalers.

### **Nordic Statistics on Medicines**

Data on drug sales in the five Nordic countries, Denmark, Finland, Iceland, Norway and Sweden, are available from 1975. The Nordic Council on Medicines publishes data covering 3-year periods.

### **Local prescription studies**

From 1989, the National Corporation of Swedish Pharmacies has offered physicians (individually or as a group) to follow their drug prescribing by local prescription studies, i.e. local auditing. In these studies, when a prescription has been processed at the pharmacy, the identity of the prescriber or clinic has been recorded (Wessling 1992).

### **Computerised patient records**

The primary health care centres in the Swedish county of Skåne use computerised patient records to a high extent (>90%). Patient records contain details of consultations, diagnoses, and prescriptions.

### **Collection and copies of prescriptions**

The prescription forms used in the Diagnosis Prescription Survey may be used to produce copies of issued prescriptions.

Copies of prescriptions processed at the pharmacies may be produced for special studies.

### **General information about drug classification systems used in Sweden**

Until 1987, drugs were classified according to the Swedish drug classification system, a mixed pharmacological and chemical system. The classification was governed by its presumed principal use. Since 1988, Sweden uses the Anatomical Therapeutic Chemical (ATC) Classification System for classification of drugs (WHO Collaborating Centre for Drug Statistics Methodology).

## **General information about units of measurement**

Statistics on drug sales may be presented by economic or some other quantity specification, e.g. number of solid doses, volume or weight. However, different active substances used on the same indication may have different potencies. In such cases comparisons cannot be based on weight or volume.

### **Defined Daily Dose (DDD)**

The Defined Daily Dose (DDD) is a technical unit of measurement defined as the assumed average dose per day for the drug used on its main indication in adults. (Baksaas Aasen et al 1975; Lunde et al 1979).

Alterations in DDDs or ATC-codes are decided by the WHO International Working Group for Drug Statistics Methodology. The WHO Collaborating Centre for Drug Statistics Methodology issues an updated version of the ATC index in January each year.

### **Prescribed Daily Dose (PDD)**

The Prescribed Daily Dose (PDD) is the mean actually prescribed dose of a drug. PDD is not synonymous with DDD. PDD may vary with indication, patient characteristics (e.g. age or reduced renal function) and therapy traditions.

### **Units of comparison and exposure**

Drug exposure is often expressed in number of prescriptions per 1000 individuals and year or DDDs per thousand individuals and day (DDD/TID), with the population figures as denominator. DDD/TID gives a rough estimate of the exposure to drugs and the proportion of the population that may daily receive treatment with a particular drug.

The units DDD and DDD/TID have to be used cautiously. DDD is a convention of the average daily dose to adults. Due to lower actual dosages used (PDDs), DDD and DDD/TID data may cause a substantial underestimation of exposure among children and adolescents. For children, the units “prescriptions” and “prescriptions per thousand individuals and year” are often preferred.

However, also PDD to adults may differ substantially from the DDD. The relation between DDD and PDD may even vary for drugs belonging to the same ATC-group, making comparisons difficult.

## Rational Drug Therapy

The concept of Rational Drug Therapy has been defined in different ways, but has mainly been focussed on rational prescribing – i.e. that

- *the drug prescribed should be effective for the symptom/disease in question*
- *the drug prescribed should be safe with as few adverse drug reactions as possible*
- *the drug should be prescribed in the correct dosage and with correct duration for the indication*
- *the drug chosen should be cost-effective compared with alternative drugs*

Rational drug therapy is in the best interest of both patients and third party payors. Hence, initiatives to promote rational use of drugs are important. It is also important to follow the effects of educational and information efforts and to measure if these efforts are effective and efficient.

## Problem areas

There has been a continuous debate on the use, misuse, abuse and adverse reactions of tranquillizer-sedative/hypnotic drugs for several decades. In Sweden, there has been a 2-3-fold variation between counties in sales of benzodiazepines. Very high sales of barbiturates in Malmö were recorded in 1978 and an information campaign was initiated which reduced prescribing, abuse and suicide (Melander et al 1991). This was followed by activities concerning the subsequently predominant agents, the benzodiazepines. In 1984 it was recognised that Helsingborg had even higher sales of benzodiazepines than Malmö, and this led to studies in Helsingborg (paper I).

The emergence and rapid increase of antibiotic resistant strains of pathogens causing respiratory tract infections, especially in regions with a high utilisation of antibiotics has been the cause of much concern (Zackrisson et al 1988; Stjernquist-Desatnik et al 1994). There has been a 1.5-fold variation between Swedish counties in the sales of antibiotics, and the former county of Malmöhus (now part of Skåne County) had the highest sales figures of antibiotics in Sweden, 25 - 40% above the country average. Different approaches for the purpose of modifying the prescription patterns of antibiotics in the primary care sector have been tested. However, an overall and enduring reduction in antibiotic prescription rates has been difficult to achieve (Midtvedt, Bruusgaard 1983; Harvey et al 1986; Friis 1988; Needham et al 1988) (papers VI, V and VI).

Local Drugs and Therapeutics Committees have since the 60s produced formularies and recommendations to promote effective, safe and economic use of drugs. However, the effects of informational and educational activities on prescribing had varied (paper IV).

### **Focus of thesis**

This study addresses various aspects on the usefulness of available statistics on local drug prescribing and sales in order to promote rational drug therapy, i.e. prescribing, by

- identifying areas for interventions and educational efforts
- analysing the effects on drug utilisation of these interventions

## Aims

The aims of this study has been

- to test if crude sales data on drugs may indicate differences in morbidity, mortality and socio-economic conditions
- to assess if crude sales data on drugs may indicate deviating prescribing habits among physicians
- to use drug sales data to identify areas for educational interventions in order to promote rational drug prescribing
- to use drug sales data to analyse changes in prescribing after information and educational activities
- to use drug sales data to estimate differences between pharmacy sales and purchases by the population
- to estimate the amount and value of unused drugs returned to pharmacies for destruction

## Material and methods

**Table 1.** Sources on drug prescriptions and sales used in the studies

Data sources used in the studies	Sales statistics on drugs	National Prescription Survey	Diagnosis Prescription Survey	Local prescription studies	Copies of prescriptions	Patient records
Paper I	x	x	x	x	x	
Paper II	x					
Paper III	x	x				
Paper IV	x			x		
Paper V	x			x	x	
Paper VI	x	x		x	x	x
Unpublished data		x				

### Paper I

This study was planned in late 1984 and early 1985.

- The *Sales Statistics on Drugs* was used to collect data on sales of benzodiazepines in Helsingborg and five other cities in Sweden
- *Copies of prescriptions on benzodiazepines* (ATC codes N05BA and N05CD), collected when processed at the pharmacies in Helsingborg during one week in 1985 and one week in 1987, were used to obtain data on individual prescribing physician (identity and office location), age and gender of patients, prescribed drug, brand, preparation, strength, number of doses, PDD and number of fills
- *Local prescription studies* in 1989 and 1990 were used to obtain data on category of physicians, age and gender of patients, purchased drug, preparation, strength, number of doses

- The *National Prescription Survey* was used to obtain national data on sales of different benzodiazepines with respect to patient age and gender
- The *Diagnosis-Prescription Survey* was used to obtain national data on PDDs of different benzodiazepines
- *Nordic Statistics on Medicines* was used to collect data on benzodiazepine sales in the Nordic countries

*Considerations of sample size.* It was estimated that the capture of processed prescriptions for benzodiazepines would yield about 1000 prescriptions with an average of 25 prescriptions of the 4 main products in a matrix with 5 age groups and gender ( $4 \times 2 \times 5 = 40$ -field matrix).

## **Paper II**

This study was planned in 1995.

*Sales Statistics on Drugs* were used to obtain crude sales data on tranquillizers (ATC-code N05B), hypnotics/sedatives (N05C), neuroleptics (N05A) and antidepressants (N06A) for each of the 33 municipalities in Skåne in 1987 and 1994;

the *local death register* in Skåne was used to obtain data on suicides;

mortality was calculated from life tables;

UnderPrivileged Area (UPA) score was calculated on eight variables (Sundquist 1993; Sundquist et al 1994; Bajekal et al 1996).

## **Paper III**

This study was planned in 1999.

All drugs returned during 2 weeks in 1999 to the 100 pharmacies in Skåne were collected and the following data were recorded:

pharmacy the drugs were returned to;

from the package: barcode or product number or brand name, dosage form, strength, package size and expiry date;

from the pharmacy label: birth year of patient and purchase date;

The remaining contents in the packages were estimated.

The *Medical Product Register in Sweden* was used to obtain data for each package (i.e. product, ATC-code, packages size, number of doses, DDD, retail price).

The *Sales Statistics on Drugs* was used to obtain data on crude drug sales per pharmacy.

The *National Prescription Survey* was used to obtain regional data on drug

sales with respect to age and gender.

#### *Considerations of sample size*

The study period and the size of the material were based on data from a prior study in 1996 (Isacsson, Olofsson 1999), and the extent of totally returned goods for disposal in south Sweden during 1998. About 12500 packages were returned to the pharmacies in Skåne during an ordinary week. A two-week study period was considered appropriate to obtain about 25000 packages, on average 60 packages per field in a 400 field-matrix (5 age groups and 3-digit ATC-code - 5x80).

### **Paper IV**

This study was planned in 1989.

*Local prescription studies* were used to obtain data on prescriber (i.e. specialty and/or clinic) and prescribed drug.

The *Sales Statistics on Drugs* was used to obtain data on secular trends for sales of drugs on prescription in the health care districts.

### **Paper V**

The initial programme, a controlled experimental study, was planned in 1983 (part one).

The subsequent study, an observational study, was planned in 1989 (part two).

#### **Part one - controlled experimental study**

Copies of prescriptions issued by the participants were used to obtain information on prescribed drugs from two weeks prior to and two weeks after the educational programme.

A statement test comprising 96 items was used to measure attitudes towards drugs, drug treatment in general and the reliability of various sources of drug information, before and after the seminars.

#### **Part two - observational study**

Copies of prescriptions issued by the participants were used to obtain data on prescribed drugs during one month prior to, one month immediately after, and one month one year after the seminar.

Anders Ekedahl

Local prescription studies were used to obtain data on secular trends in prescribing (i.e. purchases of prescribed drugs) by district physicians and other doctors.

*Sales Statistics on Drugs* was used to obtain data on secular trends.

## **Paper VI**

This study was planned in 1991.

Computerised patient records at a health care centre were used to obtain information on physicians, diagnoses and prescribed antibiotics.

A local prescription study was used to obtain data on prescribing of antibiotics by district physicians in three municipalities and *Sales Statistics on Drugs* was used to obtain data on secular trends in sales of antibiotics at the pharmacies.

## **Unpublished data**

The National Prescription Survey was used to obtain data for the 33 municipalities in Skåne County on all antibiotic and benzodiazepine prescriptions in 1998 processed at the pharmacies within the municipalities, purchased by the populations at the pharmacies in the same municipalities and purchased by the populations irrespective of the location of the pharmacy.

## **Statistics**

### **Standardisation**

Standardisation of sales data was performed using the sales data concerning the entire population in Sweden as standard (by age, 5-year classes, and gender) in paper I.

Standardisation of suicide rates and UPA score for the 33 municipalities in Skåne County were calculated using the population of this county as standard (by age, 10-year classes and gender) in paper II.

### **Calculations**

*Pearson's correlation coefficients* were calculated for the associations in paper II. A correlation coefficient of 0.5 to 0.7 was considered moderate, <0.5 as weak. The significance level was set at  $P < 0.05$ .

Student's t-test was used in the validation of the method in paper III.

Analysis of variance was used in Paper IV.

Chi-square tests were used in Paper IV.

Two-tailed Fisher's exact probability tests were used in paper III and paper IV.

## Results

### **Crude sales data on drugs – indication on differences in morbidity, mortality and socio-economic conditions (papers I and II)**

Based on data in the National Prescription Study in 1987, the estimate of the average volume of prescriptions processed an ordinary week in Helsingborg was 1080 prescriptions. The capture during week 10 in 1987 was 1069 prescriptions, close to the estimate.

The sales of benzodiazepines were higher in Helsingborg than the national average and also than those in five other major Swedish cities throughout 1981 - 1990. Psychiatric morbidity, suicide rate, alcohol-related diseases, unemployment and the proportion of socially isolated subjects were higher than the county average, but cities within the county with equal or higher rates had lower benzodiazepine sales.

The correlations in 1987 and in 1994 between sales of tranquillizers and hypnotics/sedatives in DDD/TID, on the one hand, and the UPA score, on the other, varied from 0.41 to 0.68. Moreover, the correlations between the sales of tranquillizers and hypnotics/sedatives in 1987 and in 1994, on the one hand, and mortality and suicide rate, on the other, varied from 0.44 to 0.67. All correlations were statistically significant.

There was no significant correlation between sales of antidepressants or antipsychotics, on the one hand, and the UPA score or suicide, on the other. Sales of antidepressants showed a moderate positive correlation with overall mortality in 1987 (before the introduction of SSRIs) but not in 1994.

### **Crude sales data on drugs – indication on deviating prescribing habits among physicians (paper I)**

There were 338 active doctors in Helsingborg in 1985 and 423 in 1987. The mean numbers of benzodiazepine prescriptions per physician processed at the pharmacies was 3 in 1985 and 2,2 in 1987. Two prescriptions or less were processed for the majority of the prescribers. Nine physicians were high prescribers; i.e. they had issued about 10 times as many prescriptions of

benzodiazepines as the average Helsingborg physician, signifying >30% of all processed benzodiazepine prescriptions.

### **Areas for educational interventions in order to promote rational drug prescribing (paper I)**

Benzodiazepine sales in Helsingborg were higher than the national average in all age groups and for both genders. Neither the choice of benzodiazepine agent nor the dose size or number of doses per prescription showed any major deviation from the national average. Prescriptions were iterated in 37% (1985) and 49% (1987) of the cases.

### **Changes in prescribing after information and educational activities (papers IV, V and VI)**

Compared with other physicians, the district physicians in the intervention group had greater increases in prescription volume of the four recommended low-price brands, and they had higher rates of compliance with the recommendations by the local Drugs and Therapeutics Committee. The consequent overall cost reduction in the Lund-Orup health care district in 1989 through 1991 was approximately MSEK 3, of which almost SEK 700000 was attributable to the higher compliance rates among district physicians. Reduced costs were seven times greater than the costs of the information campaign (paper IV).

There were significant changes ( $P < 0.05$ ) in the intervention group for 36 out of 96 items in the attitude test, all in the direction actively propagated for in the programme. These 36 items were all included in the 40 items concerning issues on which the lecturers had been particularly specific. The number of new or changed prescriptions in this part of the study was too small to allow statistical calculations (paper V, part 1).

Ninety (60%) of the 150 district physicians attending the seminars on "Antibiotics in Primary Health Care" participated in the prescription analyses, and 70 also took part in the study period one year after the seminars. There were consistent and sustained changes in the prescribing of antibiotics in the intended direction, both immediately after and one year after the meetings. Already before the meetings, the participants in the study had an antibiotic prescription profile that was more in the intended direction than had the entire population of district physicians. Despite this, the proportions of prescribed

antibiotics changed further in the intended direction both in the exposed group and in the entire group of district physicians (the target group) as compared to the secular trends among all other prescribers (paper V, part 2).

The comparisons are based on numbers of consultations in October 1984 (212), October through December in 1985 (472); entire 1989 (3050) and entire 1990 (3478). There was an overall reduction in prescriptions for antibiotics, particularly broad-spectrum antibiotics among the district physicians in the intervention group (Höör). Forty-four per cent of the patients with respiratory tract infections were prescribed antibiotics in 1990, a similar proportion as immediately after the programme. During a five-year follow-up period, 1986 through 1990, antibiotics dispensed at the pharmacy in Höör decreased from 16.6 DDD/TID in 1985 to 13.2 DDD/TID in 1990. Both in the county and in the whole of Sweden, there was instead an increase during the same period. The district physicians in Höör, compared with district physicians at other municipality health centres in three adjacent municipalities in the Lund-Orup health care district, prescribed more penicillin V and less tetracyclines, erythromycin and cephalosporins (paper VI).

### Effects of commuting (unpublished data)

The possible distortion by commuting on the interpretation of sales data on municipality level was examined by analyses of data on processed prescriptions on antibiotics and benzodiazepines in the 33 municipalities in Skåne County.

**Table 2.** Benzodiazepine prescription items in Helsingborg 1998

Purchases by the population			
Total purchases (1)	At the pharmacies in Helsingborg	Total sales at the pharmacies in Helsingborg (2)	Total sales (2) / total purchases (1)
35327	33334	36895	104.4%

The population in Helsingborg made 94% of their purchases of benzodiazepines in 1998 within Helsingborg, constituting 89% and 92%, respectively, (tranquillizers and sedatives/ hypnotics) of all benzodiazepine prescription items processed at the pharmacies in Helsingborg. Exposure based on prescriptions on benzodiazepines processed at the pharmacies in 1998 apparently gave a small overestimation (+ 4.4%).

For all 33 municipalities in Skåne in 1998, the populations made 82.9% (mean; range 70.4 98.7) of their purchases of prescribed benzodiazepines within the municipality. Of the prescriptions processed at the pharmacies, on average 85.6% were prescriptions to the local population.

The estimates of drug exposure, based on prescription items processed at pharmacies compared with purchases by the populations in the 33 municipalities, was 97.8% (mean; range 77.3 130.8). For 15 of the 33 municipalities (46%), pharmacy sales figures gave an underestimation of  $\geq 5\%$  and for 7 (21%) of the municipalities there was an overestimation of  $\geq 5\%$ . The difference was larger in the small municipalities. For the 12 municipalities with the largest populations, i.e. cities, the difference was small.

**Table 3.** Prescription items on antibiotics in Höör, Hörby and Eslöv in 1998

Municipality	Purchases by the population in the municipality		Total sales at the pharmacies in the municipality (2)	Total sales (2) / total purchases (1)
	Total purchases (1)	At the pharmacies in the municipality		
Höör	6280	4955	6007	95.7%
Hörby	7221	5829	6440	89.2%
Eslöv	14225	11725	13271	93.3%

The population in Höör made 79% of their purchases of prescribed antibiotics at the local pharmacy in Höör. These prescription items constituted only 82% of all antibiotic prescription items processed at the local pharmacy. Exposure based on the prescription items, processed at the pharmacy in Höör, appeared

to give a small underestimation (-4%) compared to exposure based on purchases by the population.

In Hörby, 81% of the prescriptions to the population were purchased at the local pharmacy in Hörby. These prescriptions constituted 91% of all prescriptions on antibiotics dispensed at the local pharmacy. Exposure based on these prescription items processed at the pharmacy gave a moderate underestimation (-11%).

In Eslöv, 82% of the prescription items on antibiotics to the population were purchased at the pharmacies in the municipality, constituting 88% of the prescription items processed. Exposure based on sales at the pharmacies in Eslöv gave a moderate underestimation (-7%).

The estimates of exposure to antibiotics in the 33 municipalities in Skåne in 1998, based on prescription items processed at pharmacies as compared to drug exposure based on the purchases on prescription by the populations, was 94.8% (mean; range 63.3 122.2). For 17 of the 33 municipalities (52%), pharmacy sales figures gave an underestimation of  $\geq 5\%$  and for 11 (33%) of them there was an overestimation of  $\geq 5\%$ . However, the most pronounced overestimation for antibiotics, +22%, appeared in Lund, one of the large municipalities in Skåne.

### **Amounts and value of unused drugs returned to pharmacies (paper III)**

The volume of unused drugs returned to the pharmacies in Skåne during two weeks in 1999 corresponded to 3.8% (2.4% in packages and 1.4% in single doses) of sales of drugs during two average weeks. Pharmacy labels with information on birth year of the patient and date of purchase were present on 57% of the packages. Fifty-one percent of the packages were returned within two years after purchase and thirty-eight percent of the returned packages were unbroken. The value of the drugs returned in packages was 1.35 MSEK and the value of only unbroken packages, which had not passed expiry date, was 0.73 MSEK, corresponding to 0.7% of sales.

Two thirds of all and 70% of unbroken packages were prescribed to elderly patients (>65 years of age). The proportion of unbroken packages that had not passed expiry date was significantly higher among elderly patients.

## Discussion

In Sweden there are accurate data on all drug sales at pharmacies, but only ecologic studies can be performed, as record-linkage is not allowed on a general basis. Individual data may only be used if the patient has agreed to such use. Use of individual data and linkage of prescription to diagnosis and health care consumption are hence only possible in specially designed studies with special permissions. The current studies are based on ecologic data, with the limitations this signifies. They have aimed to evaluate the usefulness and drawbacks of available drug statistics in Sweden.

### **Crude sales data – indication on differences in morbidity, mortality and socio-economic status**

As shown in paper I, there were large variations in benzodiazepine consumption between the four Nordic countries both in volume and over time, but there are no data to support the view that there are major differences in psychiatric morbidity between these countries. The overall per capita consumption not only of benzodiazepines but also of alcohol is almost twice as high in Denmark as in Sweden (Yearbook of Nordic Statistics 1991). Similarly, Helsingborg and Malmö, which are geographically and culturally close to Denmark, show a higher consumption both of benzodiazepines and alcohol than most Swedish cities (Yearbook of Nordic Statistics 1991). This might reflect different attitudes towards agents that may cause habituation and dependence. Accordingly, it is likely that the between-country differences relate to variations in attitudes towards drug use.

The study further confirmed the higher consumption of benzodiazepines in southern and western Sweden than in the eastern and northern parts (Wessling et al 1991), and it seems likely that also these differences relate to within-country attitude variations rather than to differences in psychiatric morbidity.

The importance of demographic and socio-economic factors in relation to psychotropic drug use has been emphasized in previous studies (Isacsson, Haglund 1988; King et al 1982). Benzodiazepine consumption increases with age but this can hardly explain the fluctuations over time. Furthermore, the Swedish population had the highest mean age but lowest benzodiazepine

consumption. Helsingborg has a high proportion of elderly subjects, but this could account for only a small fraction of the high sales in Helsingborg.

The gender distribution of benzodiazepine recipients in Helsingborg did not differ from the national average (Svensk Läkemedelsstatistik); neither did the choice of benzodiazepine agents nor the mean dose sizes or number of doses per prescription. Moreover, with the exception of oxazepam, which in Sweden is used both as low-dose tranquillizer and low-dose hypnotic in elderly subjects, the mean PDD of benzodiazepines was very close to the DDD both in Helsingborg and Sweden in general. Hence it appears that Helsingborg either had an unusually large proportion of benzodiazepine users or that the users had unusually long treatment periods. Moreover, benzodiazepine prescribing to younger and middle-aged subjects in Helsingborg was notably higher than the national average. This is noteworthy, as most reports on benzodiazepine dependence and abstinence have concerned young and middle-aged subjects (Peturson, Lader 1981; Ashton 1984; Roy-Byrne, Hommer 1988; Wolf et al 1989; Ashton 1991). Long-term exposure seems to be the main risk factor in the development of benzodiazepine dependence (Peturson, Lader 1981; Ashton 1984; Ashton 1991; Roy-Byrne, Hommer 1988; Wolf et al 1989). In addition there is little evidence for the maintenance of therapeutic efficacy on long-term treatment (Committee on the review of medicines 1980; Shapiro et al 1983; Tyrer 1984).

Helsingborg had more psychiatric in-patients and outpatient visits, and a higher suicide rate than average. This may indicate higher psychiatric morbidity as a partial cause of the higher consumption in Helsingborg. An additional explanation may be a greater extent of psychosocial problems related to higher unemployment, to a greater number of socially isolated subjects and to more cases of alcohol-related diseases. On the other hand, there were cities with lower benzodiazepine sales and equal or higher suicide rates (Lund), unemployment (Landskrona) or alcohol-related diseases (Ystad), indicating that other factors also influence benzodiazepine prescribing.

The major finding in paper II, comparing the 33 municipalities in the county of Skåne, was the moderate correlation between sales of tranquillizers and

hypnotic/sedatives\* and underprivileged area (UPA) score. The sales of these drugs seemed to correlate with both total mortality and suicide rates. Socio-economic deprivation was strongly associated with psychiatric morbidity and mortality, and a strong ecological association existed between socio-economic deprivation and suicide (Gunnell et al 1995). Mental disorder, particularly depression, is a risk factor for suicide with rates between 0.25 and 0.5 among patients who later commit suicide (Henriksson et al 1993; Milne et al 1994). The UPA score provides a measure of increased relative need in addition to the size and age distribution of the local population. In this context the index might be considered useful for analysing the correlation between sales and UPA score.

Geographical correlation studies by themselves do not provide a firm basis for information about individual health, or its relation to lifestyle and socio-economic circumstances in units of large geographical areas (Fox et al 1985). However, in this study the problem of cross-level bias was not relevant because no inferences from group to individual were needed.

The association between sales of tranquillizers and hypnotics/sedatives and UPA score supports the generally accepted view that social inequalities are associated with higher sales of tranquillizers and hypnotic/sedatives. This in turn implies that sales rates of these drugs could be used as markers of socio-economic conditions. Thus, sales data for tranquillizers and hypnotic/sedatives might be used to identify areas of low socio-economic status that may be prone to high rates of mortality and suicide. This finding also concurs with an Irish study in which 95% of the variance in hypnotic benzodiazepine prescribing could be explained by demographic and socio-economic factors (King, Griffiths 1984). A possible additional explanation of the fact that Malmö and Helsingborg, the two largest cities in Skåne, had the highest sales of tranquillizers and hypnotics/sedatives is that they are densely populated areas with a large number of prescribing doctors.

Reduced prescribing is associated with reduced abuse (Brahams 1990; Melander et al 1991). The reduction in mean sales of tranquillizers by 20% and by hypnotics/sedatives by 10% between 1987 and 1994 in Skåne should reflect a degree of abuse reduction. Benzodiazepines are generally thought to

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\* benzodiazepines constituted >80% in 1987 and 70% in 1994 of total sales of tranquillizers and sedatives/hypnotics in Sweden

be safe in overdose, but toxicological screenings of 73 fatal poisonings in southern Sweden showed that benzodiazepines (55%) were the most common agents present followed by analgesics (38%) and antidepressants (30%). Amitriptyline and diazepam were more commonly detected in suicides than expected from prescription data (Alsén et al 1994).

Prospective data from the American Cancer Society with a random sample of about 800000 persons revealed that males and females who reported sleeping 10 h or more had about 1.8 times the mortality compared with those who reported 7.0 – 7.9 h of sleep. Furthermore, those using sleeping pills “often” had a 1.5 times higher 6-year mortality than those who had “never” used sleeping pills; controls were made for self-reported stroke, heart disease, high blood pressure and diabetes (Kripke et al 1979). An Australian prospective study of people over 65 found an increased 5-year mortality rate among those taking some form of medication for sleep (Rumble, Morgan 1992). However, when sleep medication users were categorized as being either users of drugs with hypnotic or sedative action or other users (including analgesics and over-the-counter medicines), only “other users” showed excess mortality (Rumble, Morgan 1992). A study on elderly men in Malmö indicated excess mortality in those using both analgesics and hypnotics/sedatives (Merlo et al 1996).

Sales of antidepressants in Skåne more than doubled between 1987 and 1994 and were accompanied by a diminished correlation between sales of antidepressants and mortality and suicide. Low compliance and therapeutic failure could be one explanation for the non-significant association between antidepressants and mortality. Another explanation could be that the newer antidepressants may be used on other indications than depressive disorders. Yet another explanation could be that the differences in DDD and PDD for antidepressants (Ekedahl, Wessling 1996) and “commuting” distort the figures of antidepressant exposure in the Skåne municipalities and may weaken apparent correlations. Early optimism regarding the newer antidepressants seems to be justified as there is a significant change in the rate of suicides which coincides with the introduction of the selective serotonin reuptake inhibitors in Sweden (Carlsten et al 2001).

## **Crude sales data - indication on deviating prescribing habits among physicians**

Data from Sales Statistics on Drugs showed that Helsingborg had the highest sales of benzodiazepines of all examined municipalities in 1983. However, as sales data do not contain any information on individual prescriber or patient, this had to be explored in special prescription studies.

Only few benzodiazepine prescriptions purchased at the pharmacies in Helsingborg emanated from doctors outside Helsingborg. This indicates that the large benzodiazepine sales in Helsingborg reflect higher prescribing by doctors in Helsingborg. It is noteworthy that the majority of doctors had issued  $\leq 2$  prescriptions dispensed per week during the investigational periods. A minority of doctors, fewer than 5%, were responsible for >30% of all prescriptions on benzodiazepines and for about 10 times as many as the average Helsingborg physician. Obviously, deviant prescribing habits among a minority of doctors contributed considerably. Most doctors of this minority were private practitioners. Private practitioners were also the group that had the highest overall prescribing. This agrees with findings in Malmö (Melander et al 1991).

It may be argued that an observation period of only a week is insufficient for a prescription survey. However, week 10 represented a “normal” week, and the prescriptions by the different categories of doctors in Helsingborg were similar in 1985 and 1987. A study in Malmö showed a close relation between yearly sales figures and weekly prescription purchase figures (Melander et al 1991). Furthermore, the capture of prescriptions in 1987 was close to the estimated average of processed prescriptions during one ordinary week.

Commuting seems to play a minor role, as benzodiazepine sales in the adjacent municipalities were not exceptionally low, and these municipalities are much less populous than Helsingborg. Similarly, the data from the National Prescription Survey in 1998 showed that the estimate of benzodiazepine exposure based on pharmacy sales in Helsingborg was only slightly higher than the data on purchases by the population.

Attitudes towards benzodiazepine drugs and prescribing among a limited group of physicians seem to be an important contribution to the high sales in Helsingborg.

## **Areas for educational interventions**

Sales statistics on antibiotics and benzodiazepines indicate large differences in drug sales between municipalities in Skåne (Svensk Läkemedelsstatistik). Demographic variables, differences in prevalence of diseases in question (Olsson et al 1994; Larsson et al 1994) and commuting do influence sales data. It appears that in Helsingborg either more patients were treated with benzodiazepines or treated for longer time periods or both. As this hardly seems rational, the data formed a basis for educational intervention (Lidbeck 1987).

However, local sales data do not necessarily equal the purchases by the local population or the prescribing by the local physicians. Further exploration is needed via information on prescribing by other data. Individual data on prescriber and patient could provide such information but are only allowed in Sweden if the patients in question have permitted use.

As stated, the high sales of benzodiazepines in Helsingborg were not due to high prescribing volumes among all physicians, but merely a small group of them. Targeting had not been possible if sales statistics had been used as the sole basis for an intervention programme.

## **Changes in prescribing after information and educational activities**

The objectives of the studies in papers IV, V and VI were to influence physicians' decisions to prescribe antibiotics and choice of antibiotics prescribed (V and VI) and prescribing of brands recommended by the local Drugs and Therapeutics Committees (IV and V).

Most studies dealing with the prescribing patterns of general practitioners have focussed on inappropriate prescribing, i.e. they have tried to establish changes in therapy (Avorn, Soumerai 1983; Schaffner et al 1983; Ray et al 1985; Newton-Syms et al 1992). Few studies have aimed at changing brand choice. Harris et al found that feedback to the prescriber with written analyses of their prescribing habits and a group discussion after 18 months increased generic prescribing (Harris et al 1985). Similarly, education of a small group of physicians by a clinical pharmacist increased their generic prescribing (Erramouspe 1989).

It appears that campaigns based solely on printed material have not been very effective but, when combined with other measures, such material may become more useful (Avorn, Soumerai 1983; Harvey et al 1986; Denig et al 1990; Needham et al 1988). The effects of printed material alone may differ depending on the topic and the kind of printed material (Freemantle et al 2001; Denig et al 1990). Well-known drug bulletins, widely recognised as reliable sources of information, had significant impact on prescribing habits (Denig et al 1990; Mersey Regional Drug Information 1983).

In contrast, verbal information, “academic detailing”, to individuals or groups, seems more effective than printed material in influencing the prescribing patterns in office practice and has had a significant impact on prescribing habits in some studies (Avorn, Soumerai 1983; Diwan et al 1995; Schaffner et al 1983; Ray et al 1985; Newton-Syms et al 1992; Erramouspe 1989; van de Poel et al 1991). There are also reports that the influence of a pharmacist is no different from that of printed material (Thomson O’Brien et al 2001; Schaffner et al 1983; Ray et al 1985). Credibility seems to be the key factor in explaining differences in outcome.

As reported in paper IV, not only did combined verbal and printed information, including feed-back information, significantly promote higher compliance rates than did written information alone, but the compliance rates also continued to increase during the study period. Furthermore, the effects were the same for erythromycin, which is mainly used for short-time treatment based on new prescriptions, and for naproxen, which is predominantly used for long-term treatment based on repeat prescriptions. It is assumed that combined verbal and printed information, including feedback information from the community pharmacists, was effective in both the short and the long term. This, in turn, may indicate that these pharmacists had achieved a high degree of credibility during their interchange with the district physicians.

The initial study in paper V, which involved a limited number of doctors, indicated that verbal “face-to-face”, producer-independent educational model was effective in changing both general and specific attitudes towards drugs and drug treatment. There was a considerable change following the educational programme. All these attitude changes were in accordance with the intentions of the meetings.

Due to the high proportion of prescription renewals in the initial study, it was not possible to measure any changes in drug prescribing, although the results suggested that even the prescribing of chronic medication could be influenced, at least when such prescriptions were made for the first time. However, the subsequent study, which only dealt with antibiotics and involved a large number of doctors, indicated that the educational model was effective in changing drug prescribing by general practitioners in a rather large scale.

Admittedly, only 50% of the entire target group of 550 district physicians in the southern health care region of Sweden participated in the programme, and those who participated in the antibiotic prescription study had a different pre-education prescription profile than that of the whole population of district physicians. This implies that the positive results may not be wholly representative. However, monitoring of the prescribing on "Intention to treat" basis, showed that prescribing of penicillin V and tetracyclines by the entire target group of district physicians altered in the desired directions (penicillin increase, tetracycline decrease), whereas prescribing of these antibiotics by all other physicians in the same region developed in the opposite direction. It is assumed that the repeated use of small groups with an interactive teamwork approach was instrumental in bringing about the positive and apparently long-lasting results.

The results are in accordance with those of others (Avorn, Soumerai 1983; Schaffner et al 1983; Ray et al 1985; Newton-Syms et al 1992; Erramouspe 1989; van de Poel et al 1991; Thomson O'Brien et al 2001). However, a difference between our study and those of others is that we measured the prescribing behaviour of all prescribers, as our material included all prescriptions processed at the pharmacies in the study period. Also, estimates were based on all prescribers in the area being included in the analyses, irrespective of whether or not they were present at the information meetings. In addition, as no individual prescriber could be identified it may be assumed that their prescribing was not influenced by feelings of being personally surveyed.

In the study of paper VI, antibiotic prescription patterns at the Community Health Care Centre in Höör were monitored over a 5-year period after an educational programme focussed on the use of antibiotics for respiratory tract infections (RTI). In 1985, 68% of patients with RTIs consulting at the Health

Centre were prescribed an antibiotic but only 44% in 1986 (after the educational programme; Mölsted, Hovelius 1989). Similar figures were recorded in 1989 and 1990. Changes in the choice of antibiotics with an increase in the rate of penicillin V prescriptions and a decrease in those of broad-spectrum antibiotics were confirmed by the results of the local prescription study.

The decision to prescribe an antibiotic is subject to a number of factors, medical and non-medical, affecting the physician's evaluation of whether an antibiotic is needed and the type of antibiotic chosen (Howie 1983). In many western countries, ~60% of patients with RTIs consulting in primary care are prescribed antibiotics (Howie et al 1971; Soyka et al 1975). The "drug of choice" has been reported to vary from one country to another (Grassi 1979; McHenry, Weinstein 1983). There is also a wide variation between individual physicians, some of whom might be regarded as "high" or "low" prescribers of drugs in general (Howie et al 1971; McGavock 1988; Cars, Håkansson 1995).

Different approaches have been proposed for the purpose of modifying the prescription patterns of antibiotics in the primary care sector. Both in Denmark (Friis 1988), Australia (Harvey et al 1986) and Sweden (Stålsby Lundborg et al 1999) information campaigns have been successful in moderating the use of various antibiotics. This has also been achieved when antibiotic recommendations have been introduced or formularies to physicians in general practice have been issued (Needham et al 1988). However, overall and enduring reduction in antibiotic prescribing has been difficult to achieve. Since the educational programme at Höör, both antibiotic prescription rates at the community health centre and local consumption, as reflected in sales statistics for the community pharmacy, have manifested good compliance with national recommendations on the use of antibiotics. By contrast, neither statistics for the rest of former Malmöhus county, the major part of Skåne, nor the prescription rates among hospital physicians and private practitioners in the area (as deduced from the local prescriptions study) would seem to manifest compliance with the recommendations. There are no obvious demographic or epidemiological factors that might explain these differences; nor would the high prescription rates for broad-spectrum antibiotics seem to be medically justifiable.

The relatively low antibiotic prescription rates following the educational programme at Höör persisted throughout the five-year follow-up, not only

indicating the programme had an enduring effect, but also showing that monitoring of prescription patterns in primary care is feasible.

Local prescription studies were used to follow changes for the entire target group of prescribers on “Intention to treat” basis in the studies of papers IV and V. Overall prescribing was followed both via sales statistics on drugs and local prescription studies. The data on prescribers in the local prescription studies are not sensitive to distortion by commuting. If the aim of an information or educational activity is to influence the entire target group, registration of category of specialists seems to provide sufficient information. However, if the objective is to audit prescribing on a certain diagnosis or of the individual prescriber, such registration is not sufficient. Data from computerised patient records would then seem more appropriate.

### **Effects of commuting**

The effect of commuting, i.e. to what extent sales figures are influenced by purchases by individuals living outside the municipality, do not seem to have been evaluated previously.

As reported in paper I, only few benzodiazepine prescriptions purchased at pharmacies in Helsingborg emanated from doctors outside Helsingborg. This indicates that the large benzodiazepine sales in Helsingborg reflect high benzodiazepine prescribing by doctors in Helsingborg. Some prescriptions may have been dispensed to commuters or (other) visitors from neighbour municipalities. However, this would seem to play a minor role, as benzodiazepine sales in the three neighbour municipalities were not exceptionally low. Moreover, the neighbour municipalities are much less populous than Helsingborg.

However, when comparing all municipalities in Skåne County, a large variation was observed in the differences between exposures to antibiotics and benzodiazepines based on sales at the local pharmacies or by resident purchases by the population (unpublished data). The results indicate that exposure based on sales at the pharmacies may be considerably distorted. The magnitude of the difference varies depending on municipality and type of drugs. For antibiotics and benzodiazepines, the discrepancies at the municipality level,  $\pm 30\%$ , may reduce or increase the differences between the municipalities twofold and thus should not be ignored. At the regional level, i.e.

Skåne, the difference was small, less than 2% in 1998, and seems to be of minor importance. However, it has been claimed that sales data also at the regional or county level for certain drug groups may cause significant distortion (Hoffmann M 1996).

Accordingly, it seems important to estimate exposure to drugs based on purchases by the population in question rather than on purchases at the pharmacies in the area in question. Analyses of drug exposure at the municipality level based on sales at the pharmacies, as was the rule in Sweden before 1997 in Sweden, may have to be reconsidered.

### **Amounts and value of unused drugs returned to the pharmacies**

As shown in paper III, the volume of returned packages in 1999 had decreased compared with the figures of a 1996 investigation (Isacsson, Olofsson 1999). However, when doses returned without package were included, the volumes were similar, as were the proportions of unopened packages and packages that had not passed expiry date. Accordingly, it seems as if the volume of drugs returned has been stable over a number of years.

Due to the changes in the Swedish drug benefit scheme from January 1997, there was hoarding of prescription drugs late in 1996. The proportions of drugs returned, within 2.25 and 3.25 years after purchase, were unchanged. It was not possible to make any comparison concerning the return of drugs “free of charge” before 1<sup>st</sup> of January 1997, as the original data from the study in 1996 were not available (Isacsson, personal communication). However, returned diabetes drugs (ATC-code A 10) constituted 2.5% of mean sales in 1996 and 2.3% in 1999. The present study was performed almost 3 years after the 1996 hoarding. This may be too late to identify any changes in the patterns. However, sales over an extended period (1<sup>st</sup> of July 1996 until 30<sup>th</sup> of June 1997) were no higher than expected, implying that the main effect of the hoarding may have been that drug purchases were made earlier than otherwise.

Other studies have reported a large variation concerning returned drugs. The proportion of unopened packages has varied from 11 to 36% (Isacsson, Olofsson 1999; Thormodsen et al 1997a; Bronder, Klimpel 2001; Sundin 1989;

Wold, Hunskår 1992), drugs returned within 2 years after purchase from 25 to 89% (Sundin 1989; Henderson 1984; Braybrook et al 1999; Longmore et al 1995), and packages that had passed expiry date from 5 to 75% (Thormodsen et al 1997a; Bronder, Klimpel 2001; Wold, Hunskår 1992; Longmore et al 1995; Hawksworth et al 1996). However, as expected, a consistently large proportion of the returned drugs, 52 to 63%, have been prescribed to individuals >65 years of age (Sundin 1989; Cameron 1996).

The results in the present study are consistent with data from three other Nordic studies (two Swedish - Sundin 1989; Isacsson, Olofsson 1999; and one Norwegian - Thormodsen et al 1997a). However, the results deviate from studies performed in other countries (Bronder, Klimpel 2001; Braybrook et al 1999; Longmore et al 1995; Hawksworth et al 1996; Carter, Coppens 1996; Cameron 1996), indicating different attitudes and behaviour concerning use and non-use of drugs.

The variation between different municipalities in the present study was large. However, the figures for the larger municipalities were close to the mean of the entire region. This indicates that studies performed in non-urban municipalities or only at single pharmacies may not be representative.

Some previous studies have been performed in connection with campaigns directed to stimulate the public to return unused drugs to pharmacies (Longmore et al 1995; Forbes et al 1989). The results from these studies are probably not representative for the average return of unused drugs (to the pharmacies). During April 1999 there was an advertising campaign to return unused drugs within the pharmacies in Skåne. This may have promoted earlier returns than otherwise. However, the campaign took place 6 months before the investigation and the impact during the study period may thus have been minor.

The volume of returned drugs may also vary with season. Therefore, the study period was selected to have a low seasonal variation.

As all pharmacies in the study area, covering 1/8 of the Swedish population, participated in the present study, and as they use the same routines for medical disposals, these results seem representative for the whole of Sweden

and may be representative of returns in general. The results may also be compared with and correlated to total sales of drugs with respect to gender and age. This has, to our knowledge, only been examined in four previous studies (Sundin 1989; Ekedahl 1997; Isacsson, Olofsson 1999; Sörensen 2001). All three Swedish studies have given similar results (Sundin 1989; Ekedahl 1997; Isacsson, Olofsson 1999).

A weakness is the lack of information on how much was disposed of in other ways. Moreover, we do not know how representative the patients are who return drugs to pharmacies. In a recent interview study in Sweden, the proportion of subjects reporting that they would return unused prescription drugs for destruction was as high as 70% (SIFO 2001). If those results are valid, the present study would give a good picture of drugs not consumed. In other countries a small proportion (19 to 27%) of subjects have responded that they would return unused drugs to pharmacies (Wold, Hunskår 1992; Forbes et al 1989). However, how drugs are disposed of may differ with age; elderly subjects may be more prone to return unused drugs to the pharmacies (see also above).

The reasons for drug returns may be several (Braybrook et al 1999; Hawksworth et al 1996; Carter, Coppens 1996; Cameron 1996; Thormodsen et al 1997b) i.e. that the patient died, the treatment has been changed, adverse drug reactions occurred, hospitalisation has taken place, the expiry date of the package has passed, or the patient did not want to take the drug. The results in the present study are compatible with the assumption that a large proportion of the returned drugs emanate from deceased patients.

From the economic point of view, our study implies that the value of pharmaceutical drugs returned to the pharmacies in Skåne represents 60 million SEK per year, signifying MSEK 500 a year in the whole of Sweden. However, the value of unopened packages that had not passed expiry date (less than 20%) extrapolated to the entire country was MSEK 150, 0.7% of the mean sales.

It has been assumed that non-compliance with prescribed drug therapy is a major reason why pharmaceutical drugs are not used. Initiatives to reduce the "huge volume" of unused drugs have been proposed in Sweden (SOU 2000:86; Prop. 2001/02:63). However, according to our results, the volume of the returned goods to the pharmacies, 3.8% of the corresponding sales

volume, is quite low. Although the proportion of unused drugs disposed of by other means than returning to the pharmacies is not known, it would appear that, in contrast to common belief, the problem of “non-use” of purchased drugs is a minor one in Sweden.

### **Variability in the units of measurements DDD, DDD/TID, PDD and prescriptions**

The term DDD/TID, used to express drug exposure, is sensitive to how well DDDs correspond to PDDs, and is also influenced by the bases of data.

The PDD for oxazepam, a benzodiazepine, has for several years been only 50% of the DDD (Ekedahl et al –92). Prescriptions on oxazepam in Sweden have constituted about 20-30% of the prescriptions on benzodiazepines. This gives an underestimation of the exposure, not only to oxazepam (about 50%), but also to the entire group of benzodiazepines. When comparing areas with different proportions of prescribed drugs, or exposure over time in one area, differences between PDD and DDD ought to be considered. However, the proportions of prescribed benzodiazepines in Helsingborg were the same as in the entire of Sweden (and in the county of Malmöhus). It follows that the results presented in paper I are not distorted.

### **Considerations of ecologic studies**

Ecologic data may be used to evaluate the effectiveness of population interventions. The advantage is that the sales data at different geographical levels are easily accessible, at least in the Nordic countries. Ecologic studies are less expensive and take less time than studies involving individual as the unit of analyses. However, the quality of data differs between different databases, which ought to be considered.

In Sweden, individual prescription data are collected but not stored beyond 3 months, and access to them is as yet prohibited. However, there are abundant ecologic data, which provide good opportunities for studies of certain kinds, if used cautiously.

Susser (1994) considered the salience of ecologic studies in the terms of choices, aptness and convenience and classified them in four groups: 1)

obligate and apt, 2) optional and apt, 3) optional, not apt but convenient and 4) maladroit – neither obligate, apt nor convenient. The “Ecological - Fallacy “ – aggregation bias, specification bias and cross-level bias of ecologic studies - has been discussed since the 1950s (Selvin 1958; Morgenstern 1982; Greenland, Robins 1994; Piantadosi 1994). Morgenstern (1982) states that ecologic studies have two major aims: 1) to generate or test etiological hypotheses and 2) to evaluate the effectiveness of interventions at the population level.

Ecologic analyses may be used to evaluate the effectiveness of population interventions. When we do not wish to make inferences as to individuals but about groups, an ecologic design is not an inferior substitute for a non-ecologic study but is preferable for evaluating the effectiveness of a population intervention (Morgenstern 1982). The information and educational activities in studies IV and V are examples of population interventions for which ecologic analyses may be preferred.

## Conclusions

The studies of this thesis support the following conclusions and assumptions:

- High sales of benzodiazepines in a major Swedish city were associated with higher psychiatric morbidity and more psychosocial problems, but deviant prescribing habits among a minority of physicians were a major contributing factor.
- Sales of tranquillizers and hypnotics/sedatives may be a marker of socio-economic conditions.
- Providing of first-hand verbal information by community pharmacists constitutes a cost-effective means of reducing drug expenditure.
- Repeated involvement of small groups of physicians by an interactive teamwork approach brought about positive changes in attitudes towards drugs, drug prescribing and drug information. The changes in prescribing, i.e. antibiotics, were consistent and long-lasting.
- An educational programme combined with active interest and auditing at the individual level brought about enduring changes in prescribing of antibiotics.
- Estimates of exposure to drugs based on local pharmacy sales may differ substantially from estimates based on purchases by the resident population, especially in smaller municipalities.
- The amount of unused drugs returned to the pharmacies in Skåne was less than 4% of the mean sales, suggesting that the difference between sales and use of drugs may be small. However, the proportion of unused drugs disposed of by other means than returning to the pharmacies is not known.

## Sammanfattning på svenska

### **Lokal läkemedelsstatistik – ett verktyg för att identifiera problemområden och att bedöma effekter av information och utbildning om läkemedel.**

Det finns behov att studera läkemedelsförskrivning och läkemedelsanvändning och dessas samband med och effekter på hälsa, sjuklighet och överdödlighet. Det är också önskvärt att kunna använda individdata. I Sverige är det i allmänhet inte tillåtet att använda individdata avseende läkemedelsanvändning. Det finns däremot god tillgång på befolknings- och områdesbaserade försäljningsdata av god kvalitet.

Syftet med denna studie har varit att undersöka om sådana aggregerade data samvarierar med sjuklighet i befolkningen, att identifiera områden där det finns informations- och utbildningsbehov och att bedöma effekterna av informations- och utbildningsinsatser. Avsikten har också varit att mäta skillnader mellan de lokala apotekens försäljning och den lokala befolkningens inköp av läkemedel mot recept samt att undersöka hur mycket oanvända läkemedel som återlämnas till apoteken för destruktions.

Uppgifterna om den lokala läkemedelsförsäljningen har hämtats från apotekens inleveransstatistik, Receptundersökningen samt lokala förskrivningsstudier. Kompletterande information har inhämtats från kopior av expedierade recept på apotek, kopior av utfärdade recept på vårdcentraler samt ur journaldata på vårdcentral. Dessutom har nationella data om läkemedelsförsäljningen hämtats från apotekens inleveransstatistik och Receptundersökningen samt uppgifter för de nordiska länderna från Nordisk läkemedelsstatistik. Nationella data om förskrivningen har hämtats från Diagnos-Recept-undersökningen. En undersökning har dessutom genomförts om hur mycket läkemedel som under två veckor återlämnades till apoteken i Skåne för destruktions.

Den lokala läkemedelsstatistiken visar stora skillnader i försäljningen av läkemedel mellan kommuner inom samma län. Resultaten från studierna visar att läkemedelsförsäljningen lokalt samvarierar med och indikerar skillnader

mellan kommunerna i socioekonomisk nivå, sjuklighet och överdödlighet. Informationen kan också användas för att identifiera områden där det kan vara motiverat med informations- och utbildningsinsatser för att främja en rationell läkemedelsförskrivning. Lokala data om läkemedelsförsäljningen lämpar sig väl för att bedöma effekterna av informations- och utbildningsinsatser.

Apotekens försäljning av läkemedel lokalt motsvarar dock inte helt den lokala befolkningens läkemedelsinköp eller användning och inte heller receptförskrivningen lokalt. Resultaten i de studier om läkemedelsanvändning som baseras på de lokala apotekens försäljning (t.ex. studier som gjorts före 1997) kan vara missvisande och kan därför behöva revideras.

Försäljningsdata i nuvarande form räcker inte heller för att identifiera vilka målgrupper som informations- och utbildningsaktiviteterna skall riktas till, utan behöver kompletteras med andra informationskällor om receptutfärdare och arbetsplats. Receptundersökningens material kan emellertid komma att få en sådan komplettering, om förslaget i regeringens proposition 2001/02:63; §6 genomförs, dvs. att arbetsplatskod krävs på recepten för att läkemedlet skall ingå i läkemedelsförmånen.

Lokala försäljningsdata, med ökad kvalitet och tillgänglighet, är i många avseenden ett användbart och kostnadseffektivt instrument för att, i kombination med andra tillgängliga data, analysera förskrivning och användning av läkemedel.

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