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# Studies of Drug-treated Diabetes in the County of Jämtland, Sweden, Based on Prescription of Insulin and Oral Antidiabetic Drugs

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ABSRACT

Epidemiological data on drug-treated diabetes mellitus was obtained by analyzing prescriptions of insulin and oral antidiabetics in the county of Jämtland Sweden. During a 12-year period, from 1971 to 1982, the prevalence of diabetes increased from 1.5% to 2.2%, while there was no significant change in the annual incidence of around 2.7/1000 inhabitants.

Women displayed a considerable higher prevalence and incidence than men in the over 70 age-group, while in the 50 - 69 age-group there was a male dominance. A significant change in the prescription pattern with an increased use of insulin and decreased use of oral antidiabetics was observed during the period. More patients were started on oral antidiabetics during the first part of the year than during the latter.

## INTRODUCTION

By recording drug prescription data valuable information can be obtained concerning the morbidity of a certain disease, provided the drugs are prescribed on one well defined indication (2). This is the case for antidiabetic drugs and therefore prescription of insulin and oral antidiabetics should reflect the morbidity of drug-treated diabetes. In the county of Jämtland, Sweden, an individual-based drug prescription project has been in operation since 1970. At the start of this project about 2% of the county inhabitants were prescribed antidiabetic drugs (3,4). Here we report data on prescription of antidiabetic drugs and diabetes morbidity during the following 12-year period from 1971 to 1982.

## METHODS

Jämtland has a relatively stable population of around 135000 inhabitants. The age distribution differs from that of Sweden as a whole, in so far that the

county has relatively more people in the older age groups. In 1982, 13.3% of the population was over 70 years of age compared to 11.5% in the whole of Sweden.

Since 1970 all drug prescriptions to inhabitants of the county born on four certain days of the month have been recorded. Thirteen per cent of the inhabitants of the county, i.e. about 17000 inhabitants, have thus been continuously monitored. Drugs dispensed to occasional visitors to the county have not been registered. The recording concerns, inter alia, the patient's identity number, the year and week of dispensation, the prescribing physician, total amount of the drug and the dosage. A detailed presentation of the method was given by Boethius and Wiman (5).

Prescriptions of insulin and oral antidiabetics were analyzed retrospectively for the 12-year period, from 1971 to 1982. The prevalence of drug-treated diabetes was obtained by counting the number of individuals prescribed antidiabetic drugs during one particular year. The incidence was calculated from the number of individuals who obtained their first prescription of antidiabetic drugs during that year. Patients who changed to insulin within six months after the start of oral treatment have been regarded as inuslin-treated. A few patients, who started on insulin but changed to tablets within six months, were considered tablet-treated.

The population at risk was the average population of the county at the end of each year according to vital statistics. The figures thus obtained somewhat underestimate the real prevalence and incidence of drug-treated diabetes since the drugs used by diabetics at geriatric clinics are not recorded.

Defined daily dose (DDD) is the average dose for a particular drug (2). Recommended doses for insulin are 40 IE and oral antidiabetics, e.g. glibenclamide 5 mg. Data concerning sale figures were obtained from the National Corporation of Swedish Pharmacies.

## RESULTS

### Prevalence and incidence

The prevalence of drug-treated diabetes increased gradually from 1.5% in 1971 to 2.2% in 1982 (Table 1). Women displayed a higher prevalence than men throughout the whole period. After correcting the figures according to sex and age of the total Swedish population, the prevalence for 1982 was 1.9% for men and 2.2% for women.

Table 1.
Prevalence of drug-treated diabetes in the county of Jämtland.

| | Men % | Women % | Total % |
|---|---|---|---|
| 1971 | 1.3 | 1.6 | 1.5 |
| -73 | 1.6 | 1.7 | 1.6 |
| -75 | 1.7 | 1.9 | 1.8 |
| -77 | 1.8 | 2.0 | 1.9 |
| -79 | 1.9 | 2.2 | 2.1 |
| -81 | 1.9 | 2.4 | 2.1 |
| -82 | 2.1 | 2.3 | 2.2 |

During the observation period, the prevalence was fairly constant in the age groups below 60 years, but over this age there was a gradual increase (Fig 1). In the youngest age-group (0-19 years), the average prevalence was 0.11%. In the age group between 50 and 69 years the prevalence was higher for men than for women, while the reverse was seen in the over 70 age group. In women a rapid increase in diabetes prevalence occurred after the age of 70. At the end of the observation period the prevalence was about 3 % in women aged 60 to 69 years, whereas in women over 70 years the corresponding figure was about 9%.

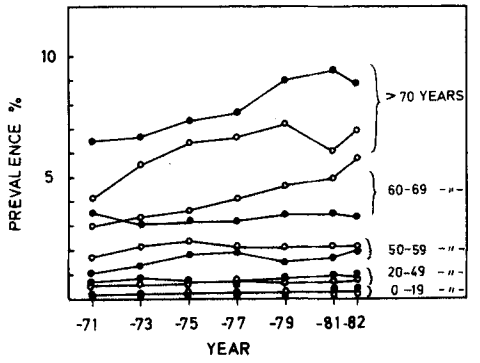


Fig 1.
Prevalence of diabetes mellitus, treated with insulin or oral antidiabetics in various age groups during the period 1971 - 1982 (O—O men; ●—● women).

No significant change in the annual incidence was observed during the period (Fig 2). The incidence of diabetes treated with oral drugs was somewhat higher in women than in men (2.4 and 2.1/1000 respectively). This tendency was also noted for insulin-treated diabetes (0.39 and 0.35/1000).

The annual incidence was low in all age groups given insulin (Fig 3). In the age group 0 - 19 years it was 0.16/1000. For those treated with oral antidiabetics, there was a considerable increase with age. The highest incidence (12.5/1000) was found in females over 80 years of age. During the period no significant change in incidence was observed in any of the age groups.

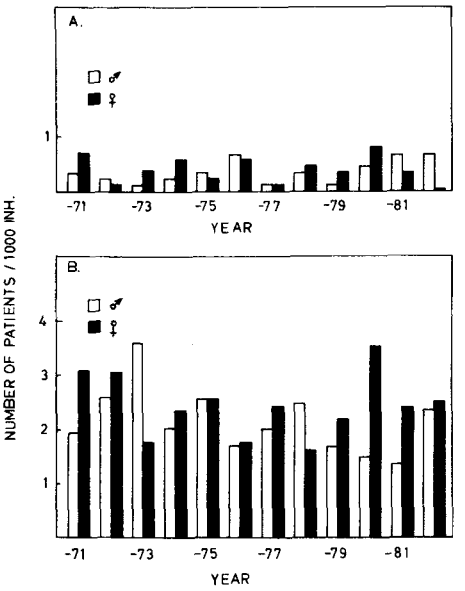


Fig.2.

Annual incidence of diabetes mellitus treated with insulin (A) or oral antidiabetics (B) during the period 1971-1982.

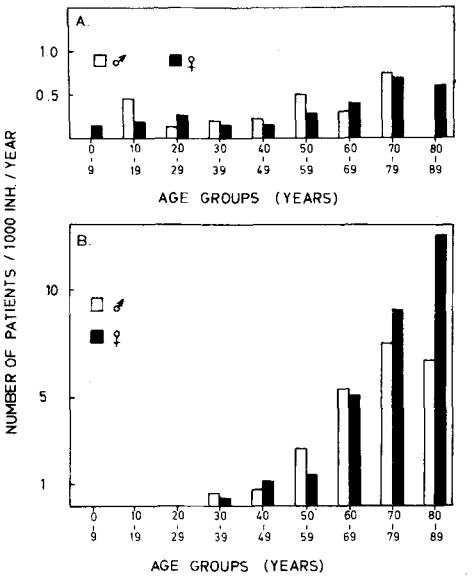


Fig. 3.

Average annual incidence of diabetes mellitus treated with insulin (A) or oral antidiabetics (B) in various age groups during the period 1971 - 1982.

Sales of insulin and oral antidiabetics (excluding hospitals)

Sales of insulin (excluding hospitals) were higher in the county of Jämtland than in Sweden as a whole and increased slowly during the period (Fig.4). Sales of oral antidiabetic drugs declined in the county in the middle of the 70's and have since then been somewhat lower than in the rest of Sweden (Fig.5).

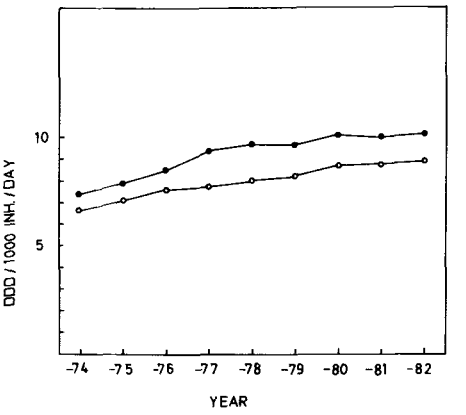


Fig.4.

Sales of insulin (excluding hospitals) in the county of Jämtland ( ●—● ) and in Sweden as a whole ( o—o ) during the

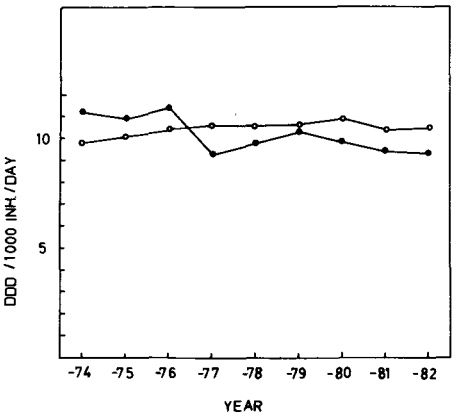


Fig.5.

Sales of oral antidiabetics (excluding hospitals) in the county of Jämtland ( ●—● ) and in Sweden as

period 1974 - 1982. Number of defined daily doses (DDD) per 1000 inhabitants and day.

as a whole ( o—o ) during the period 1974 - 1982. Number of DDD per 1000 inhabitants and day.

Change in prescription pattern

The prescribing of various types of insulin from 1970 to 1982 is shown in Fig.6. A steady increase was observed during the period for medium-acting insulin, while there was a decline in the use of long-term and regular insulin. Amongst the oral antidiabetic drugs chlorpropamide was largely replaced by glibenclamide (Fig.7). The prescribing of phenformin diminished after 1973 and it was withdrawn from the Swedish market in 1978.

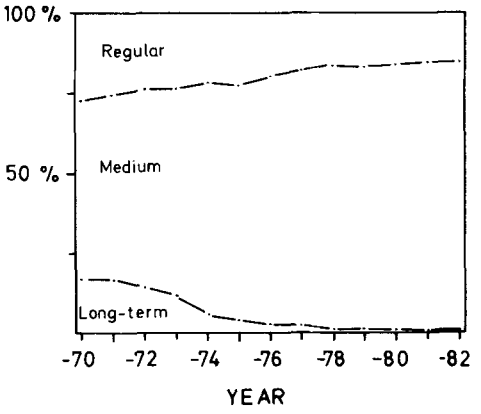


Fig.6.

Prescription of various types of insulin in the county of Jämtland 1970-1982. Percentage distribution based on the number of DDD.

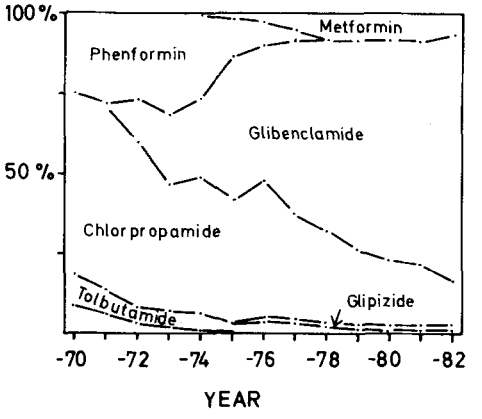


Fig.7.

Prescription of various types of oral antidiabetics in the county of Jämtland 1970 - 1982. Percentage distribution based on the number of DDD.

The relation between prescription of insulin and oral antidiabetics varied with age and with time (Fig.8). At the beginning of the 70's combined antidiabetic therapy (insulin + oral drugs, sulfonyl urea + biguanid drugs) was frequently adopted. At the end of the period hardly any patients were prescribed insulin in combination with oral drugs and very few used combinations of oral drugs. In 1982 40% of drug-treated diabetics were prescribed insulin and 60% oral drugs.

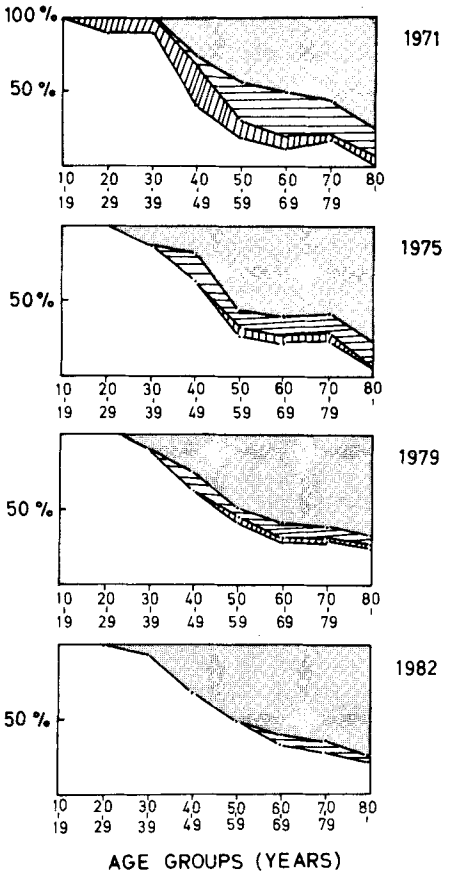


Fig. 8.
Prescription in various age groups; insulin (□), oral antidiabetics (▦), insulin + oral drugs (▥), and sulfonyl urea + biguanid (▤). Percentage distribution of patients.

The change in diabetes treatment in individual patients during the period is illustrated in Table 2. Several patients changed from oral drugs to insulin while the reverse was less common. A change from one to two oral drugs was instituted fairly frequently at the earliest part of the observation period but then became less common.

Table 2. Changes of treatment in individual patients.

| Change over | -72 | -73 | -74 | -75 | -76 | -77 | -78 | -79 | -80 | -81 | -82 |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Oral drug→ insulin | 7 | 11 | 8 | 13 | 11 | 12 | 16 | 4 | 15 | 11 | 13 |
| Insulin→ oral drug | 3 | 2 | 3 | 1 | 0 | 1 | 2 | 2 | 0 | 1 | 1 |
| One oral drug→ two | 4 | 8 | 5 | 11 | 5 | 4 | 5 | 5 | 1 | 4 | 3 |
| Newly diagnosed diabetics | 52 | 51 | 45 | 60 | 41 | 41 | 43 | 38 | 55 | 42 | 49 |
| Diabetics registered | | 287 | | 318 | | 335 | | 365 | | 378 | |

Seasonal variation

There was no significant seasonal variation in the total sales of insulin or oral antidiabetics during the period studied (Fig.9). However, when considering each patient's first purchase of antidiabetic drugs, more patients were found to start therapy with oral antidiabetics during the first half of the year than during the latter (Fig.10). This difference was statistically significant ($p<0.01$, Chi-square test).

Patients starting treatment with insulin were too few to permit any valid conclusions.

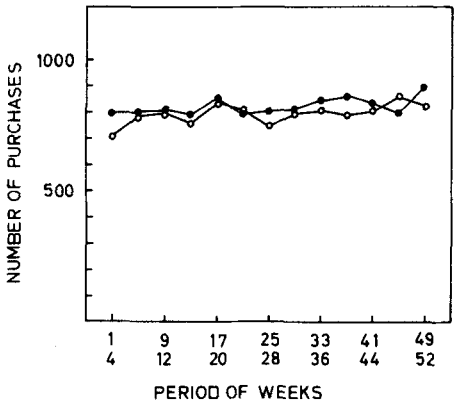


Fig.9.
Seasonal distribution in the total purchases of insulin (●—●) and oral antidiabetics (○—○) during the period 1971-1982.

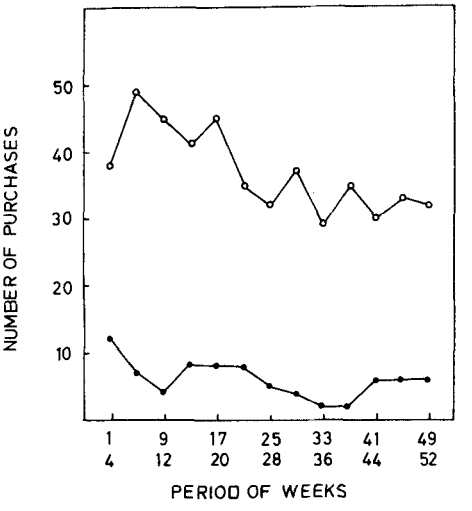


Fig.10.
Seasonal distribution for the start of medication with insulin (●—●) and oral antidiabetics (○—○) during the period 1971 - 1982.

## DISCUSSION

In this study a continual increase in the prevalence of drug-treated diabetes was observed from 1.5% in 1972 to 2.2% in 1982. This was due to an increase in diabetes prevalence in the over 60 age groups, whilst no change was observed below 60 years of age. Few other reports on the change in diabetes prevalence over such a long period of time are available. In a study on drug utilization in the county of Gotland, Sweden, 1.7% of the population used such drugs in 1972 compared to 2.5% in 1981 (9). In Czechoslovakia annual reports on the total number of diabetics have been available for several years. An increase in diabetes prevalence from 1.9% in 1972 to 3.1% in 1980 was observed (14).

The most recent diabetes epidemiological study performed in Sweden is that from the community of Ystad, based on both in- and out-patient registers and

thus includes all types of diabetes (10). When the figures were standardized against the total Swedish population, the diabetes prevalence was 2.01% for men and 1.95% for women. In a study from Tierp, Sweden, also including all types of diabetes, the prevalence was 2.3% after age-adjustment as above (8). In the present study corresponding values were 1.9% for men and 2.2% for women at the end of the observation period. However, these figures only comprise drug-treated diabetes, no estimation is available on the prevalence of diet-treated diabetes in Jämtland. Probably this figure is similar to that obtained for Gotland (20%) and Tierp (25%) but regional differences may exist depending on the availability of dietitians.

As expected the use of antidiabetic drugs increased rapidly with age. Eight per cent of the inhabitants in Jämtland over 70 years of age were prescribed such drugs at the end of the observation period. For the age group above 75 years the corresponding figure was 7.3% in Tierp (8) and 11% in Gotland (9).

Women displayed a higher prevalence for diabetes than men throughout the whole period. This is in accord with other Swedish studies (8,9) and was due to a high prescription of oral antidiabetics to women over 70 years of age. Thus, at the end of the period, the use of antidiabetics was almost three times higher in women over 70 years compared to those in the lower age group (60 - 69 years).

The prevalence and incidence of diabetes in the youngest age group (0 - 19 years) was 0.11% and 0.16/1000 inhabitants and year. These values are lower than those reported by Dahlquist et al (7) for the age group 0 - 15 years in Jämtland (prevalence 0.175%, incidence 0.21/1000). Our values should however be considered as approximate, since the number of patients is few.

We have not been able to trace data on the incidence of adult diabetes in Sweden. In a study from Finland (13) the annual incidence of type II diabetes was estimated at 4/1000 inhabitants. The figure for diabetes treated with oral drugs was approximately 2/1000, which is in good agreement with that reported here (2.3/1000). By comparison, the Rochester study (12), including all types of diabetes, reported an annual incidence of 1.7/1000.

Very few (0.4/1000 inhabitants and year) of those with newly diagnosed diabetes were treated with insulin from the start. However, a high proportion of those (2.3/1000) treated with oral antidiabetics changed over to insulin therapy. The reason for this was probably secondary failure after some years of treatment with oral drugs. At the end of the period, as many as 40% of the drug-treated patients had insulin prescribed while 60% had oral drugs. In the studies from Tierp and Gotland, 22% and 31% respectively of the drug-treated patients used insulin (8.9). Thus the proportion of insulin-treated patients seemed to be fairly high in Jämtland.

During the first part of the period combination therapy was frequently used. Similarly in the Gotland survey 1982, 28% of the patients were receiving a combination therapy. At the end of the period very few patients in Jämtland used this therapy. However, in Gotland combination therapy was as common in 1982 as in 1972 (9).

Considerable changes also occurred during the period with respect to the type of antidiabetic drugs prescribed. Thus glibenclamide, introduced in 1971, was soon the dominating oral antidiabetic drug in Jämtland. The rapid fall in prescriptions of phenformin in the middle of the 70's and its withdrawal from the Swedish market in 1978 was due to the potential risk of lactic acidosis. The prescription of long-term insulin steadily decreased during the period in favour of medium-acting insulin. These changes in prescription pattern are in accordance with revised principles for diabetes treatment in general and with recommendations issued by the local drug committee.

During the observation period, there was a steady increase in sales of insulin and an increased prescription of insulin compared to oral drugs, which was especially evident in older patients. There was a corresponding decrease in sales of oral drugs. These changes are also in accord with modern principles for diabetes therapy, which favour insulin above oral drugs in adult diabetes (11). The decline in the sale of oral drugs probably also reflects the appointment of dietitians in the county in the middle of the 70's. Many diabetics could then be treated by diet alone, or a reduced dose of antidiabetic drugs. Information from Northern Ireland, Czechoslovakia and Sweden suggests that there may be a reciprocal relationship between dietery and oral treatment (1).

The total number of prescriptions of antidiabetic drugs dispensed to county inhabitants during the period studied did not show any seasonal variation. This is in accord with the previous study in Jämtland by Boethius (6). However, more patients started oral antidiabetic therapy during the first part of the year than during the latter. This fact indicates a seasonal variation in the start of oral therapy for diabetes and possibly also for the detection of type II diabetes. A similar seasonal variation, with high incidence during the winter months, is well-known for childhood diabetes in Sweden and several other countries (7). It shows the importance of environmental factors, such as virus infections, for the pathogenesis of type I diabetes. Such factors have not been considered of importance for the onset of type II diabetes. Thus, our finding was unexpected and will be the subject of further investigations.

ACKNOWLEDGEMENTS

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