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## Benzodiazepine prescribing patterns in a high-prescribing Scandinavian community

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**Summary.** Sales statistics indicate large variations in benzodiazepine consumption between the Scandinavian countries; the current difference between Denmark (highest) and Sweden (lowest) is almost two-fold. There are also large within-country variations; e.g. benzodiazepine sales in the Swedish city of Helsingborg, which is close to Denmark, were at the average Danish level and were the highest in Sweden.

Repeated prescription analyses were carried out in Helsingborg, and register data were used to compare the extent of psychiatric morbidity and psychosocial problems in this city with those in neighbouring cities.

Benzodiazepine consumption was higher than the national average in all age groups. However, neither the choice of the predominant benzodiazepine agents nor the dose size or number of doses per prescription showed any major deviation. Hence, Helsingborg may have a larger proportion of benzodiazepine users or longer exposure periods among users. The latter is supported by the fact that about 40% of all benzodiazepine prescriptions were repeated. Psychiatric morbidity, suicide rate, alcohol-related diseases, unemployment and the proportion of socially isolated subjects were higher than the county average. On the other hand, within the county, there were cities that despite lower benzodiazepine sales had an equal or higher rate of suicide, unemployment and alcohol-related diseases. Of all benzodiazepine prescriptions processed in Helsingborg, > 30% were issued by < 5% of the prescribers ( $\geq 15$  prescriptions per prescriber and per week).

Thus, the higher usage of benzodiazepines in Helsingborg may partly be related to higher psychiatric morbidity and more psychosocial problems, but deviant prescribing habits among a minority of physicians are also important.

**Key words:** Benzodiazepines, Prescribing habits; pharmacoepidemiology, psychiatric morbidity, psychosocial problems, Sweden, Denmark

Benzodiazepines may cause dependence [1–5], and reduced use is associated with reduced abuse [6, 7]. It is of interest, therefore, to analyse between- and within-country differences in benzodiazepine consumption. The current study has compared 1981–90 benzodiazepine sales in Denmark, Finland, Norway and Sweden, and in certain Swedish counties and cities. Repeated prescription analyses were made in a high-prescribing Swedish city, and attempts were made to assess whether different prescriber habits or differences in demographics, psychiatric morbidity or psychosocial aspects could help to account for the differences in benzodiazepine consumption.

### Material and methods

#### *Drug sales*

The yearly numbers of defined daily doses (DDD)/1000 inhabitants/day<sup>1</sup> of all benzodiazepines under ATC<sup>2</sup> codes N05 BA (tranquillizers or anxiolytics) and N05 CD (hypnotics/sedatives) sold in the four major Nordic countries<sup>3</sup> (Denmark, Finland, Norway and Sweden) were obtained from the Nordic Council of Medicines [8]. The data for Swedish counties and municipalities were obtained from the (Swedish) National Corporation of Pharmacies. The latter figures are based on the monitoring of drug sales by the wholesalers to community and hospital pharmacies, and closely reflect drug sales by pharmacies in the county or municipality in question [9].

#### *Demographic and geographical data*

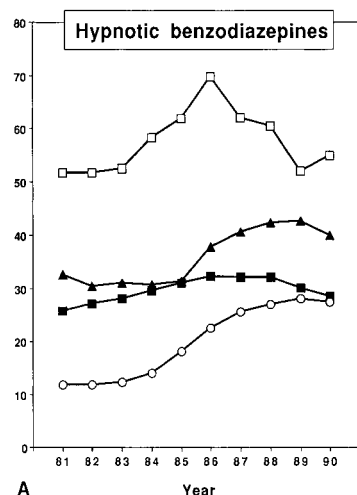
Helsingborg is the second most populous municipality of the 20 municipalities in the southernmost county of Sweden, Malmöhus. It comprises the city of Helsingborg and some surrounding rural di-

<sup>1</sup> DDD is a technical unit of comparison, based upon international agreement (8, 9). It is not synonymous (but may coincide) with the recommended dose

<sup>2</sup> Anatomical Therapeutic Chemical system (cf. 1, 7)

<sup>3</sup> Data from the fifth Nordic country, Iceland, were not included as the population is small (about 200 000) compared to those of the other four countries, which range between 8.5 and 4.5 million

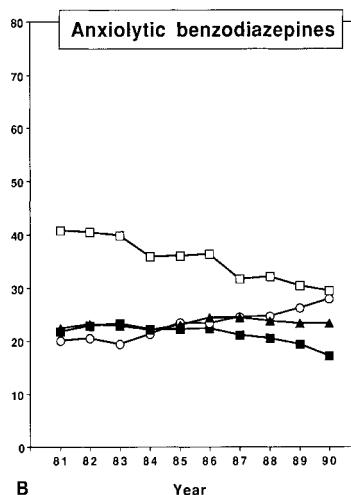
DDD/1,000 inhabitants/day



A

Year

DDD/1,000 inhabitants/day



B

Year

Fig. 1 A, B. Benzodiazepine sales (DDD/1000 inhabitants/day) 1981–1990 in Denmark –□–, Finland –○–, Norway –▲–, and Sweden –■–. A hypnotic, B anxiolytic benzodiazepines

stricts. The number of inhabitants is just below 110 000. In 1985, 1987, 1989 and 1990, the proportion of elderly (> 65 years old) subjects was 19.1, 19.7, 19.8 and 19.9%, respectively, being higher than the Swedish average (17.1, 17.6, 17.8 and 17.8%, respectively) [10]. The major occupations are manufacturing industries, commerce, shipping, and various service activities. Tourism and communications are socially and economically important, particularly because much of the traffic to and from Sweden, Norway and Finland passes through Helsingborg by ferries to and from Helsingør (Elsinore) in Denmark, only 4 km across the dividing sound.

### Structure of medical care

Malmöhus County Council is responsible for public medical care in 19 of the 20 municipalities in Malmöhus county, including Helsingborg. The 20th and largest municipality, Malmö, has its own medical administration. The public medical care in Helsingborg comprises in- and out-patient care in Helsingborg Hospital, and outpatient care at 8 primary health care centres in 5 primary health care districts. Private medical care at a number of out-patient clinics is offered by one or a group of doctors, and there are small clinics for somatic short-term care. In 1985 (1987 figures in brackets) the number of active doctors in Helsingborg was 338 (423). Of them, 254 (305) were full-time or part-time hospital doctors, 57 (68) full-time or part-time district physicians (specialists in general medicine/family medicine, employed at primary health care centres by the county council), 47 (44, i.e. < 15%) full-time private practitioners, 45 (16) were part-time private practitioners with their main occupation within the public medical service, and 18 (16) were occupational health care doctors. There were 37 (43) psychiatrists, 32 (36) of whom were in the public service and 5 (7) were in private practice [11]. There were 8 pharmacies in Helsingborg in 1985, and 9 in 1987.

### Prescriptions, prescribers and recipients

All N05 BA and N05 CD benzodiazepine prescriptions purchased at any of the pharmacies in Helsingborg during Weeks 10 in 1985 and 1987 were copied and recorded. Week 10 was selected to represent a "normal" week, not including a major holiday or vacation time. The analysis involved prescribed benzodiazepine, dosage, strength and number of doses, number of refills, identify and specialty of pre-

scriber, and age and sex of the recipients. It was also noted whether the prescription was issued from a unit within or outside Helsingborg. The distributions of prescriptions and benzodiazepines were analysed, as well as the amounts prescribed per prescription and the size of prescribed daily doses (PDD). Similar data were also obtained from a pilot study performed during Week 10 in 1984 (Eke-dahl and Lidbeck, unpublished).

The pharmacies in Helsingborg also conducted prescription studies throughout March 1989 and 1990, by a technique reported in a corresponding analysis in Stockholm [12]. Permission was obtained to use data from those studies about prescribed benzodiazepine, strength and number of doses, number of DDD prescribed, and the sex and age distribution of recipients.

Age (5-year classes) and sex distributions of the recipients of benzodiazepine prescribing in Sweden and mean PDD for various benzodiazepines were obtained from the National Corporation of Pharmacies [9]. Yearly demographic data for Helsingborg (sex and age in 5-year classes) were obtained from the municipality council of Helsingborg.

Indirect standardization of national prescription figures to the population in Helsingborg was made in 5-year classes.

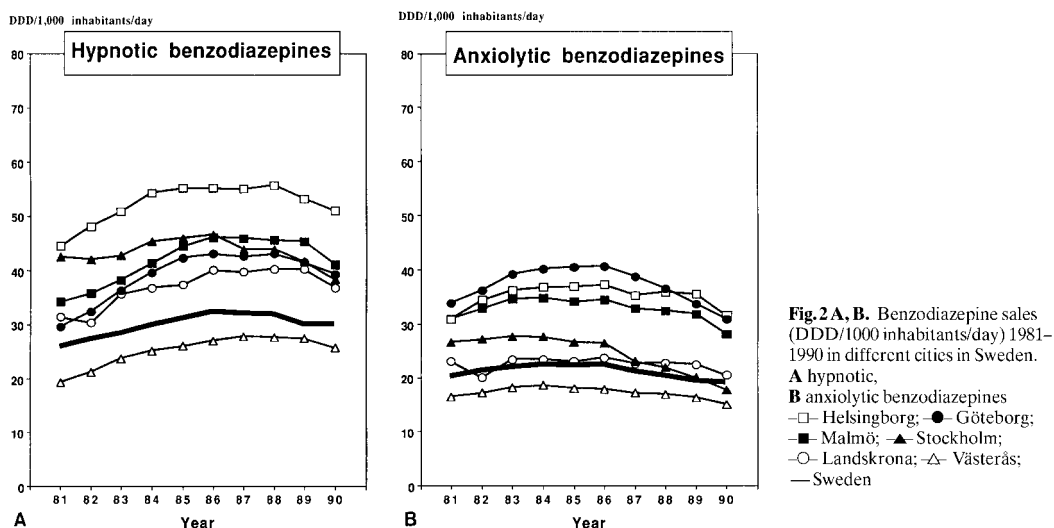
### Register studies

In an attempt to assess relative differences in psychiatric morbidity and psychosocial problems between Helsingborg and other cities in Malmöhus county, the registers of Malmöhus County Council and the Swedish Central Bureau of Statistics were used to obtain frequencies of in-patient and out-patient psychiatric care, suicide rate, alcohol-related diseases, unemployment rate, and numbers of subjects experiencing social isolation.

## Results

### Benzodiazepine sales in Nordic countries

The 1981–90 benzodiazepine sales in Denmark, Finland, Norway and Sweden, expressed in numbers of DDD/1000 inhabitants/day, are shown in Fig. 1. Denmark consistently



had the highest sales, while those in Sweden decreased from 1986 onwards to be the lowest in the four countries in 1989–90, when they were only about half those in Denmark. Except in Finland, hypnotic benzodiazepines have constituted about two thirds of the total benzodiazepine sales.

#### Benzodiazepine sales in Swedish counties

The mean 1981–90 benzodiazepine sales were much higher in the west (Göteborg and Bohus county: 63.4 DDD/1000 inhabitants/day) and the south (Malmöhus county: 62.0) of Sweden than in the east (Stockholm county: 46.2) and the north (Norrbotten county: 30.3). The highest (Göteborg and Bohus) and lowest (Norrbotten) sales of anxiolytic benzodiazepines differed three-fold, while those of hypnotic benzodiazepines differed less, (being about two thirds higher in Malmöhus than in Norrbotten).

#### Benzodiazepine sales in Swedish cities

In most Swedish counties benzodiazepine sales were highest in the major cities. The 1981–90 benzodiazepine sales in several Swedish cities are shown in Fig. 2. Sales in Helsingborg were higher than in other Swedish cities during the entire decade. The higher sales in Helsingborg relate particularly to hypnotic benzodiazepines (Fig. 2a). Except for Göteborg (Fig. 2b), sales of hypnotic benzodiazepines were higher than those of the anxiolytic types both in Helsingborg and elsewhere. The benzodiazepine sales figures in Helsingborg's three immediate neighbouring municipalities, Landskrona, Höganäs and Bjuv, were all above the Swedish average (1990: 57.2, 68.2 and 45.1 DDD/1000 inhabitants/day, respectively).

#### Distribution by category of doctor of prescriptions processed in Helsingborg

Only 6% (1985) and 7% (1987) of all benzodiazepine prescriptions processed in Helsingborg emanated from doctors outside the city. Of all doctors within Helsingborg, 62% (1985) and 48% (1987) had prescribed benzodiazepines during Week 10. Private practitioners prescribed the largest proportion (38 and 34%, respectively) followed by district physicians (23 and 25%) and hospital doctors (20 and 15%).

#### Age and sex distribution of benzodiazepine recipients in Helsingborg

The age and sex distribution of benzodiazepine recipients in Helsingborg during Week 10 in 1985 and 1987, and during March 1989 and 1990, are shown in Table 1, which also relates the Helsingborg figures to average national figures in the different age groups. Benzodiazepine prescribing in Helsingborg was higher in both sexes and in all age groups.

#### Types and doses of benzodiazepines prescribed in Helsingborg

Oxazepam, diazepam, nitrazepam and flunitrazepam constituted about 90% of all benzodiazepines prescribed, as well as of all DDD sold (Table 2a and b). The relative distribution of the sales (in DDD) of these benzodiazepines in Helsingborg was similar to that of the national average during the corresponding years (Table 2b). Except for oxazepam, the mean PDD were very close to the DDD (Table 3a). The mean numbers of DDD per prescription were similar in Helsingborg and in Sweden in

**Table 1.** Age and sex distribution of recipients of benzodiazepine prescriptions in Helsingborg (a), and ratios of observed vs expected benzodiazepine prescribing in Helsingborg after standardization in 5-year classes for age and sex based on national prescription figures (b)

a	Week 10 1985		Week 10 1987		March 1989		March 1990	
	M	F	M	F	M	F	M	F
Age group (y)								
0-14	4	—	2	3	5	6	4	6
15-24	7	11	7	7	12	25	16	11
25-44	85	163	76	146	302	572	267	421
45-64	130	273	119	237	662	1333	601	1098
> 65	136	358	119	344	880	2042	795	1923
Unknown	6		9		1	6	0	4
Total	362	805	323	737	1862	3984	1683	3464
Total	1173		1069		5935		5253	
Ratios								
b	Week 10 1985		Week 10 1987		March 1989		March 1990	
Total age group (y)	1.48		1.37		1.79		1.73	
25-44	1.78		1.62		1.72		1.51	
45-64	1.58		1.46		1.98		1.88	
> 65	1.28		1.18		1.69		1.66	

**Table 2.** Proportions of different benzodiazepines as percentages of total numbers of benzodiazepine prescriptions in Helsingborg (a); and percentage of total benzodiazepine sales (in DDD) of the four most commonly prescribed benzodiazepines in Helsingborg (H) and in Sweden (S) (b)

a	Week 10 1985		Week 10 1987		March 1989		March 1990	
agent								
Oxazepam	29.1		25.6		25.2		25.0	
Nitrazepam	25.1		17.8		18.1		18.4	
Diazepam	23.0		22.3		20.2		19.8	
Flunitrazepam	14.4		22.9		22.9		23.0	
Chlorazepate	3.0		2.2		1.8		2.0	
Chlordiazepoxide	2.8		1.1		1.2		0.8	
Lorazepam	2.7		3.9		3.9		3.3	
Alprazolam	—		4.3		5.0		4.9	
Triazolam	—		—		1.8		3.0	
Total	100		100		100		100	
b								
Agent	1985		1987		1989		1990	
	H	S	H	S	H	S	H	S
Nitrazepam	37.7	37.2	31.3	30.8	28.5	26.3	27.8	25.7
Flunitrazepam	22.2	21.5	29.3	29.1	29.7	32.8	30.9	32.3
Diazepam	20.1	19.6	17.9	17.8	16.7	17.4	16.3	16.6
Oxazepam	13.5	16.2	12.4	14.3	12.2	13.6	11.5	12.7

general during 1985 and 1987, and were only slightly higher in Helsingborg during 1989 and 1990 (Table 3b). The proportions of alprazolam, lorazepam and triazolam were low at only about 10% of the entire volume (Table 2).

### Repeat prescriptions

Prescriptions were iterated (one or more refills per prescription) in 37 % (1985) and 49 % (1987) of all cases.

### Number of prescriptions per prescriber

The mean number of benzodiazepine prescriptions per prescriber was 3.0 (1985) and 2.2 (1987). A majority of the prescribers – 68 % (1985) and 76 % (1987) – had issued two or fewer benzodiazepine prescriptions. Only 5 % (1985) and 3 % (1987) of the Helsingborg doctors were high prescribers ( $\geq 15$  benzodiazepine prescriptions/week), but they were responsible for 39 % (1985) and 31 % (1987) of all benzodiazepine prescriptions.

Eight of the 9 prescribers who were responsible for most benzodiazepine prescribing in 1984 also had very high prescribing rates in 1985 and 1987. The mean number of their benzodiazepine prescriptions was 28/week, with ranges of 16–42 (1984), 19–57 (1985) and 12–39 (1987). Seven of them were private practitioners and 2 were hospital physicians (one of them was in part-time in private practice as well). Six of those 9 prescribers had obtained a licence to practise in 1960 or earlier.

### Psychiatric morbidity

The number of out-patient psychiatric care visits (per 100 inhabitants) in 1990 was 6.0 in Helsingborg, 4.5 in Landskrona, 3.9 in Lund, 2.9 in Ystad and 3.6 in Malmöhus county overall. The number of in-patient discharges from psychiatric care (per 100 inhabitants) was higher in Helsingborg (1.6) than in Lund (1.4), Landskrona (1.3), Ystad (0.9), and than the Malmöhus county average (1.1). Similarly, the mean number of bed-days in psychiatric care was higher: Helsingborg 80, Landskrona 57, Lund 53, Ystad 35, and county mean 46.

### Suicide rates

The age-standardized 1979–86 indices (1–74 years) of definite suicides (ICD8 E950–959) and o deaths probably but not definitely due to suicide (ICD8 E980–989) in the cities of Helsingborg, Landskrona, Lund and Ystad, relative to the mean of the 19 municipalities of Malmöhus County Council are shown in Table 4. Definite suicide was more frequent in Lund and Landskrona, whereas deaths probably but not definitely due to suicide were more frequent in Helsingborg.

### Alcohol-related diseases

The age- and sex-standardized frequency (% of mean of the 19 municipalities of Malmöhus County Council) of alcohol-related diseases (in-patients; ICD9 291, 303, 571 A–D; (ICD8 57100–57101) and 980) in the cities of Helsingborg, Landskrona, Lund and Ystad in 1986–87 are

**Table 3.** Mean Prescribed Daily Doses (PDD) of the 4 most commonly prescribed benzodiazepines in Helsingborg during Week 10 in 1985 and 1987, and in Sweden 1986. DDD for each agent in brackets (a); mean numbers of DDD per prescription in Helsingborg (H) and in Sweden (S) of the four most commonly prescribed benzodiazepines (b)

	DDD	Helsingborg		Sweden
		PDD 1985	PDD 1987	PDD 1986
Diazepam	(10 mg)	9.9 mg	9.4 mg	8.8 mg
Oxazepam	(50 mg)	24.8 mg	26.3 mg	23.9 mg
Nitrazepam	(5 mg)	5.2 mg	5.2 mg	4.4 mg
Flunitrazepam	(1 mg)	1.0 mg	1.1 mg	0.9 mg

Agent	1985		1987		1989		1990	
	H	S	H	S	H	S	H	S
Diazepam	38.4	38.5	42.0	38.9	43.6	38.0	42.4	38.3
Oxazepam	25.2	23.7	26.2	23.3	25.7	22.5	25.9	22.2
Nitrazepam	74.8	76.2	74.8	76.1	82.8	75.8	85.8	75.9
Flunitrazepam	73.8	71.5	74.5	70.8	78.0	66.1	77.8	66.3
Difference (%)								
H vs S	+ 0.8 %		+ 3.9 %		+ 12.1 %		+ 12.6 %	

**Table 4.** Age-standardized (vs county average) suicide index (age 1–74 y) in four cities in Malmöhus County, Sweden

City	Suicide index	
	Suicide definite cause of death	Suicide probable cause of death
Helsingborg	1.11	1.86
Landskrona	1.15	1.74
Lund	1.28	0.78
Ystad	0.91	0.84
County	1.00	1.00

**Table 5.** Age-standardized (vs county average) index of alcohol-related diseases (all ages) in four cities (1986–87) in Malmöhus County, Sweden

City	Index of alcohol-related diseases
Helsingborg	1.39
Landskrona	1.76
Lund	0.72
Ystad	1.54
County	1.00

shown in Table 5. It appears that alcohol-related diseases in Helsingborg were more common than average, but also that they were even more common in Landskrona and Ystad.

### Unemployment rate

The age-standardized unemployment index in 1985 (16–64 years of age; Malmöhus county index = 1.0) was 1.25 in Helsingborg, 1.34 in Landskrona, 0.93 in Lund and 1.19 in Ystad.

### Socially isolated subjects

The age-standardized index of social isolation (ages 20–74 y), as revealed by health inquiries in 1989 (Malmöhus county index = 1.0), was 1.15 in Helsingborg, 0.92 in Landskrona, 1.17 in Lund and 1.01 in Ystad.

### Discussion

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. Benzodiazepine consumption increased with age but this can hardly explain the fluctuations over time. Furthermore, the Swedish population has the highest mean age but the lowest benzodiazepine consumption. Accordingly, it is more likely that the between-country differences relate to variation in attitudes towards drug use.

The overall per capita consumption not only of benzodiazepines but also of alcohol is almost twice as high in Denmark as in Sweden [13]. Similarly, Helsingborg and Malmö, which are geographically and culturally close to Denmark, show a higher consumption both of benzodiazepines and alcohol than most other Swedish cities [7, 13]. This might reflect different attitudes toward agents that may cause habituation and dependence.

The current study has confirmed the higher consumption of benzodiazepines in southern and western Sweden than in the eastern and northern parts [7, 14]. The reasons for this are largely unknown [7, 14] but may be illuminated by the prescription analyses in Helsingborg.

It might 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. Furthermore, the same 9 doctors showed similarly high benzodiazepine prescription patterns during 1984, 1985 and 1987. A study in Malmö showed a close relation between yearly sales figures and weekly prescription purchase figures [7]. Even if they were erroneous, however, the weekly figures would under- rather than overestimate benzodiazepine prescribing in Helsingborg, as they gave lower estimates than those obtained during the whole of March 1989 and 1990.

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 for commuters or (other) visitors from neighbour municipalities. However, this would seem to play a minor role, as benzodiazepine sales in the three immediate nearby municipalities were not exceptionally low, and those municipalities are much less populous than Helsingborg. Similarly, a prescription study in Göteborg showed that commuters accounted for only 5 % of prescriptions issued by doctors in Göteborg [A. Carlsten, personal communication].

Benzodiazepine use increases with patient age [9], and Helsingborg has a high proportion of elderly subjects. However, this could account for only a small fraction of the high sales in Helsingborg. Moreover, benzodiazepine prescribing to younger and middle-aged subjects in Helsingborg was notably higher than the national average. This is important, as most reports on benzodiazepine dependence and abstinence have concerned young and middle-aged subjects [1–5].

The sex distribution of benzodiazepine recipients in Helsingborg did not differ from the national average [cf. 9; data not shown], nor 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 a low-dose anxiolytic and a low-dose hypnotic in elderly subjects [9], the mean PDD of benzodiazepines was very close to the DDD both in Helsingborg and in Sweden in general. Hence, it appears that Helsingborg either had an unusually large proportion of benzodiazepine users or unusually long treatment periods by benzodiazepine users. The latter is supported by the large proportion (40%) of repeated prescriptions. This is noteworthy as long-term exposure seems to be the main risk factor in the development of benzodiazepine dependence [1–5]. In addition, there is little evidence for the maintenance of therapeutic efficacy on long-term treatment [15–17]. Reduced prescribing is associated with reduced abuse [6, 7].

Helsingborg had more psychiatric in-patients and out-patient visits, and a higher suicide rate than average. This may indicate higher psychiatric morbidity as a partial cause of the higher benzodiazepine consumption in Helsingborg. An additional explanation may be a greater extent of psychosocial problems related to higher unemployment, to the greater number of socially isolated subjects and to more cases of alcohol-related diseases; the importance of demographic and socioeconomic factors in relation to psychotropic drug use has been emphasized in previous studies [18, 19]. 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.

A minority of fewer than 5% of physicians was responsible for more than 30% of all benzodiazepine prescribing and for about 10-times as many prescriptions as the average Helsingborg doctor. Thus, deviant prescribing habits among a minority of doctors were important. Most doctors in this minority were in private practice, and private practitioners were also the highest-prescribing group. This agrees with previous findings in Malmö [7]. The complexity of factors affecting benzodiazepine prescribing and use warrant further investigation in a larger number of communities.

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