Sales of tranquillizers, hypnotics/sedatives and antidepressants and their relationship with underpriviliged area score and mortality and suicide rates.

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Abstract *Objective*: This study analyses the correlation between the Swedish underprivileged area score and sales of tranquillizers, hypnotics/sedatives, neuroleptics and antidepressants, and the correlation between these sales and mortality and suicide rates, with the aim of using sales data to identify areas with poor socioeconomic conditions.
Setting: Southern Sweden, 33 municipalities in Skåne, 1987 and 1994.
Design: Ecological study. Determined and undetermined cases of suicide were taken from the local death register for the years 1987–1993. Suicide rates (determined and undetermined cases) were calculated as the ratio between observed and expected number of suicides. Mortality for people aged 20–64 years was calculated from life tables for the decade 1981–1990. The underprivileged area score was calculated for municipalities using the proportion of persons in the following groups: elderly living alone, under 5 years of age, one-parent families, unskilled, unemployed, living in crowded households, those moving house in the previous year, and ethnic groups. After transformation ($\sqrt{}$arc sine) and standardization, each of the eight variables was weighted by the British general practitioners average weighting and added to give the underprivileged area score. The selection of the eight variables was based on general practitioners' perceptions of the effect of the social characteristics of the populations in their respective residential areas on their workload or pressure on services. The total drug sales figures for tranquillizers, hypnotics/sedatives, neuroleptics and antidepressants are expressed in Defined Daily Doses per 1000 inhabitants per day. The relationship between these variables was analysed using Pearson's correlation coefficient.
Results: There was a moderate correlation (0.41–0.68) between the sales expressed as in Defined Daily Doses per 1000 inhabitants per day of tranquillizers and hypnotics/sedatives and underprivileged area score. Furthermore, the sales of tranquillizers and hypnotics/sedatives seemed to be moderately correlated with both mortality (0.44–0.67) and suicide (0.47–0.58).
Conclusion: Sales of tranquillizers or hypnotics/sedatives could be used with caution as markers for socioeconomic conditions on the basis of their moderate ecological correlation with a composite socioeconomic index such as the Swedish underprivileged area score and their moderate correlation with mortality and suicide.

Key words Drug prescription, Hypnotics, Neuroleptics, Antidepressants; pharmacoepidemiology, socioeconomic conditions, mortality, suicide

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Introduction

The present ecological study focuses firstly on the extent to which medical practice, in particular the prescription of tranquillizers, hypnotics/sedatives, neuroleptics and antidepressants, may correlate with age- and sex-standardized mortality rates and suicide rates, and the Swedish underprivileged area score, for 33 municipalities in the province of Skåne, the southernmost part of Sweden. Secondly, it investigates whether sales data could be used to identify areas with poor socioeconomic conditions that may be prone to high rates of suicide or mortality.

In Sweden it is well known that there are differences between counties and municipalities in the sales of tranquillizers and hypnotics/sedatives [1–3]. The use of tranquillizers and hypnotics/sedatives seems to be less associated with morbidity differences than with demographic and socioeconomic differences.

To explain possible differences in sale patterns and standardized mortality rates between the 33

municipalities in Skåne, we used a composite index, the underprivileged area score that has recently been introduced in Sweden [4]. This score includes proxy markers of material deprivation in a residential area (such as levels of unemployment, belonging to a low social class or not, owning a home, and living in overcrowded conditions) and, in addition, factors relating to breakdown of family structures (such as elderly living alone and single-parent families), lack of social networks and instability (as measured by the variable "moved house"), cultural needs (ethnic groups), and children under 5 years of age; all of which impact directly on both the frequency and complexity of consultation in a primary care setting. It is based on general practitioners' perceptions regarding the effect of social characteristics of the populations in their respective residential areas on their workload or pressure on services, which are used to guide the choice of variables and their relative weightings in the calculation. Secondly, the index provides a measure of increased relative need over and above that relating to the most important determinants of health need — namely the total size of the population and its age distribution. Ethnicity, single-parent family status, low socioeconomic status and geographical mobility and other similar sociodemographic variables included in the underprivileged area score in Sweden have a significant influence on the pressure on primary health care services [5, 6]. In a 10% random survey of all British general practitioners it was shown that the socioeconomic characteristics of a population, as reflected in its underprivileged area score, correlate well with the level of workload as perceived by general practitioners serving that population [7].

The aim of this study was to analyse the correlation between the underprivileged area score and the sales of tranquillizers, hypnotics/sedatives, neuroleptics and antidepressants of 33 municipalities in Skåne in 1987 and 1994 with the objective of finding a single simple marker, i.e. to identify poor socioeconomic conditions and proneness to high suicide rates and mortality, expressed by the Swedish underprivileged area score.

Methods

Suicides, determined and undetermined cases (E950-959 and E980-989 according to ICD-9), were taken from the local death register in Skåne for the years 1987–1993. Suicide rates (determined and undetermined cases), for the age group 20–79 years for 33 municipalities in Skåne, were calculated. Unless otherwise stated, the term "suicides" in this article refers to "suicides and undetermined deaths". The total suicide rates for Skåne in 1987–1993 were used as a standard. The number of suicides for the 7 years was summed for 10-year age classes, separately for males and females. Suicide rates were calculated as the ratio between observed and expected number of suicides.

Mortality for all causes, for people aged 20–64 years for 33 Swedish municipalities, was calculated from life tables for the decade 1981–1990 with Sweden as a standard [8].

The underprivileged area score was calculated for municipalities using six variables from the Swedish census of 1990, one variable from the unemployment registry for 1992 and one variable, "moved house" 1992, as previously described [4]. The eight variables are the proportions of persons in the following groups: elderly living alone, under 5 years of age, one-parent families, unskilled (SEI 1), unemployed, living in crowded households, those who have moved house in the last year, and ethnic groups. After transformation ($\sqrt{\text{arc sine}}$) and standardization, each of the eight variables was weighted by the British general practitioners average weighting and added to give the underprivileged area score [4].

Pearson's correlation coefficient was calculated between the sales (total sales – deliveries for hospital "in care" use) of tranquillizers, hypnotics/sedatives, neuroleptics, and antidepressants, and the underprivileged area score in all the municipalities in Skåne and mortality and suicide rates (SAS/STAT guide for personal computers, 6th edn. SAS Institute Inc. 1987, Cary, NC). Sample size was always 33.

Total drug sales figures in number of Defined Daily Doses per 1000 inhabitants per day of the anatomical-therapeutic-chemical (ATC) classification of subgroups: N05A — neuroleptics; N05B — minor tranquillizers/anxiolytic agents; N05C — hypnotics/sedatives; and N06A — antidepressants were calculated for the 33 municipalities in Skåne. Total drug sales figures, which are based on the monitoring of drug sales to pharmacies by wholesalers, closely reflect the drug sales in the area in question. The data on drug utilization were obtained from the Apoteksbolaget. The Defined Daily Doses per 1000 inhabitants per day is a technical unit of measurement and was established as the average recommended maintenance dose of the drug for its major indication [9].

Results

There was a decrease in sales of tranquillizers and hypnotics/sedatives between 1987 and 1994 in Skåne from 22.3 and 37.9 Defined Daily Doses per 1000 inhabitants per day, respectively, to 17.4 and 34.9, respectively (Table 1). In the same period there was a more than twofold increase in sales of antidepressants with an increase from 7.6 in 1987 to 16.1 Defined Daily Doses per 1000 inhabitants per day in mean sales. The sales of neuroleptics decreased by 8% during the 7-year period. The distribution of underprivileged area score ranged from −38.8, in the most affluent municipalities, to 17.0 in the most deprived areas (Table 1). The distributions of mortality and suicide rates are presented in Table 1.

There was a significant correlation between sales of tranquillizers in 1987 and 1994 and the underprivileged area score for the 33 municipalities in Skåne (Table 2). Sales for hypnotics/sedatives in 1994 showed a moderate association with underprivileged area score ($r = 0.68$; $P = 0.0001$). There was no significant correlation between sales of antidepressants, neuroleptics and the underprivileged area score.

The correlation between sales of tranquillizers in 1987 and 1994 and total mortality in the 33 municipalities was moderate, $r = 0.53$; $P = 0.002$ and $r = 0.60$; $P = 0.0002$, respectively (Table 2). Sales of hypnotics/sedatives in 1994 were also moderately correlated with mortality ($r = 0.67$; $P = 0.0001$). Sales of antidepressants were weakly but significantly correlated with mortality in 1987 but not in 1994. There was no

Table 1 Sales of tranquillizers, hypnotics/sedatives, antidepressants and neuroleptics in 1987 and 1994 in Defined Daily Doses per 1000 inhabitants per day, underprivileged area score (in units), mortality, and suicide (means, SD, minimum and maximum values) in 33 municipalities in Skåne, Sweden

Variable	Mean sales, Defined Daily Doses per 1000 inhabitants per day	SD	Minimum	Maximum
Tranquillizers 1987	22.3	6.9	11.3	35.0
Tranquillizers 1994	17.4	5.4	7.4	30.7
Hypnotics/sedatives 1987	37.9	11.5	15.4	63.7
Hypnotics/sedatives 1994	34.9	10.1	14.7	60.6
Neuroleptics 1987	7.2	4.4	2.5	20.0
Neuroleptics 1994	6.6	3.9	2.2	19.3
Antidepressants 1987	7.6	2.3	4.1	13.3
Antidepressants 1994	16.1	5.4	7.4	26.0
	Scores, mortality and suicide rates in units			
Underprivileged area score	−5.6	13.7	−38.8	17.0
Mortality	0.92	0.14	0.64	1.20
Suicide rates	0.88	0.21	0.45	1.30

significant association between sales of neuroleptics and mortality.

There was a moderate correlation between sales of tranquillizers and hypnotics/sedatives in 1987 and 1994 and suicide (Table 2). The sales of antidepressants and neuroleptics were not significantly associated with suicide. However, the correlation between antidepressants and mortality was twice as high in 1987 as in 1994.

Discussion

The main finding in this paper was the moderate correlation between sales of tranquillizers and hypnotics/sedatives and underprivileged area score. Furthermore, the sales of tranquillizers and hypnotics/sedatives seemed to correlate with both total mortality and suicide (determined and undetermined) in the 33 municipalities in the province of Skåne. This finding implies that, with caution, sales of tranquillizers and hypnotics/sedatives could be used as a marker for poor socioeconomic conditions.

Socioeconomic deprivation was strongly associated with psychiatric morbidity and mortality and a strong ecological association existed between socioeconomic deprivation and suicide [10]. Mental disorder, particularly depression, is a risk factor for suicide, with rates varying between 1/4 [11] and 1/2 [12] among the patients who later commit suicide.

We argue that the underprivileged area score, based on data from 1990–1992, reflects socioeconomic and social conditions in residential areas for the 1980s and the 1990s. The English underprivileged area score is based on data from the 1970 census [13] and has been used for at least 2 decades for the distribution of economic resources to general practice in the United Kingdom. It is based on general practitioners' perceptions regarding the effect of social characteristics of the populations in their respective residential areas on their workload or pressure on services, which are used to guide the choice of variables and their relative weightings in the calculation. The underprivileged area 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 underprivileged area score. The former study focused on calculations of the Swedish underprivileged area score, not on the validation of the score [4]. The Swedish underprivileged area score will be validated by a survey among Swedish general practitioners about the variables included in the index for Sweden as well

Table 2 Pearson's correlation coefficients calculated for the association between tranquillizers, hypnotics/sedatives, antidepressants, neuroleptics and the underprivileged area score, mortality and suicide (determined and undetermined)

	Correlation with underprivileged area score	Correlation with mortality	Correlation with suicide
Tranquillizers1987	0.41 ($P = 0.02$)	0.53 ($P = 0.002$)	0.49 ($P = 0.004$)
Tranquillizers 1994	0.42 ($P = 0.02$)	0.60 ($P = 0.0002$)	0.47 ($P = 0.007$)
Hypnotics/sedatives 1987	0.44 ($P = 0.01$)	0.44 ($P = 0.01$)	0.58 ($P = 0.0004$)
Hypnotics/sedatives 1994	0.68 ($P = 0.0001$)	0.67 ($P = 0.0001$)	0.52 (0.002)
Antidepressants 1987	0.11 ($P = 0.54$)	0.37 ($P = 0.03$)	0.30 (0.09)
Antidepressants 1994	0.08 ($P = 0.65$)	0.20 ($P = 0.25$)	0.15 (0.40)
Neuroleptics 1987	0.23 ($P = 0.20$)	0.12 ($P = 0.52$)	0.26 (0.14)
Neuroleptics 1994	0.24 ($P = 0.18$)	0.13 ($P = 0.47$)	0.33 (0.06)

as the weights attached to each variable. Furthermore, the index has to be validated against mortality, suicide rates and primary health care utilization.

The use of Defined Daily Dose per 1000 inhabitants per day provides a standardized technical measure of drug use. An advantage of this study could be that the sales data are based only on open care sales at pharmacies in Skåne; drug deliveries for hospital "in care" use are subtracted. If hospital sales had been included the highest sales would have been biased towards municipalities with hospitals. The problem of using ecological data is well known as the ecological fallacy in epidemiological research, according to Morgenstern [14], because it is difficult to control confounding factors in the analysis. Geographical correlational studies by themselves do not, however, provide a strong basis for information about individual health and its relation to lifestyle and socioeconomic circumstances in units of large geographical areas according to Fox et al. [15]. In this study the problem of cross-level bias is not relevant because no inferences from group to individuals were needed.

The finding of a moderate ecological association between the sales of tranquillizers and hypnotics/sedatives and underprivileged area score supports the generally accepted view that social inequalities are associated with higher sales of tranquillizers and hypnotics/sedatives, implying that the sales of these drugs could be used as markers for socioeconomic conditions. Thus, it could be possible to use sales data for tranquillizers and hypnotics/sedatives to identify areas of low socioeconomic 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 benzodiazepine hypnotic prescribing could be explained by demographic and socioeconomic factors [16]. A possible explanation for the fact that Malmö and Helsingborg, two large cities in Skåne, had the highest sales rates of tranquillizers and hypnotics/sedatives in 1978 is that they are densely populated areas with a large number of prescribing doctors, above all a number of private practitioners with a strikingly high number of tranquillizers and hypnotics/sedatives [1]. Socioeconomic factors were not discussed as an explanation for the high sales rates. In another study from Skåne which focused on the city of Helsingborg, with high sales of benzodiazepines and high suicide rates, psychosocial problems related to higher unemployment were stressed as an explanation for high suicide rates [3].

The reduction in mean sales of tranquillizers by 20% and of hypnotics/sedatives by 10% between 1987 and 1994 in Skåne is important for reducing, e.g. abuse. An information campaign in Malmö was accompanied by a 4-year reduction in tranquillizers and hypnotics/sedatives sales and abuse [1]. Benzodiazepines are generally thought to be safe in overdose, but over 10 years in the United Kingdom 1512 fatal poisonings have been attributed to benzodiazepines with or without alcohol [17]. Toxicological screenings of 73 fatal poisonings in southern Sweden showed that benzodiazepines (55%) were most common, followed by analgesics (38%) and antidepressants (30%) [18]. Amitriptyline and diazepam were more commonly detected in completed suicides than expected from prescription data [18].

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 increased 6-year mortality compared with those who had "never" used sleeping pills after controls were made for self-reported stroke, heart disease, high blood pressure, and diabetes [19]. An Australian prospective study of people aged over 65 years found an increased 5-year mortality rate among those taking some form of medication for sleep [20]. However, when sleep medication users were categorized as being either users of drugs with hypnotic or sedative action or other users (including analgesics and other over-the-counter medicines), only "other users" showed an excess mortality [20].

The finding of a more than twofold increase in sales of antidepressants between 1987 and 1994 in Skåne was accompanied by a reduction in the 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 new antidepressants possibly are used for new indications, not depressive disorders. However, this finding implies that sales of antidepressants cannot be used as a proxy or marker for socioeconomic conditions as there was no association with underprivileged area score. In an analysis of fatal toxicities of antidepressant drugs in England, Scotland and Wales in 1985–1989, no decrease in the number of deaths from antidepressant overdose was seen [21]. However, early optimism regarding the newer antidepressants seemed to be justified, since they had a lower fatal toxicity than the other antidepressants. In a Swedish study, less than 16% of 3400 suicide victims had detectable concentrations of antidepressants in their blood and only one-third of them had toxic concentrations [22]. Neuroleptics showed no such association and could not therefore be used as socioeconomic markers. The sales of neuroleptics are probably more concentrated in municipalities with mental hospitals than in municipalities with disadvantaged socioeconomic conditions. We conclude that the sales of tranquillizers and hypnotics/sedatives could be used with some caution as markers of poor socioeconomic conditions.

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