Variation in prescribing of hypnotics, anxiolytics and antidepressants between 61 general practices

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SUMMARY

Background. *Although the desirability of reducing prescribing of hypnotics and anxiolytics has long been recognized, variation between practices in patterns of psychotropic drug prescribing has received little attention; factors underlying such variation are poorly understood.*

Aim. *The study aimed to describe the extent of variation between general practices in the prescribing of hypnotics, anxiolytics and antidepressants; it also aimed to analyse the influence of measures of practice population and general practice and general practitioner characteristics on any variation in prescribing volumes.*

Method. *Routinely collected prescribing data and practice population data, from April 1992 to March 1993, from all 61 practices in the Cambridge and Huntingdon Health Commission were analysed. Prescribing was measured as annual defined daily doses per 1000 practice population for each drug class. Data on variables relating to practice structure and general practitioner characteristics were obtained and analysed. Potentially influencing variables were investigated by multiple regression.*

Results. *Between the highest and lowest prescribing practices there was an 11-fold difference, a 13-fold difference and an eightfold difference in the annual defined daily doses per 1000 practice population prescribed for hypnotics, for anxiolytics and for antidepressants, respectively. Strong positive correlations existed between volumes of prescribing of each drug class. The drugs prescribed in the greatest volumes were hypnotics. Practice population structure had some influence on psychotropic drug prescribing with high prescribing being associated with the proportions of temporary residents and women aged 65 years and over in the practice for all three classes of drug. Other factors, including presence of a practice counsellor, were not found to have a significant influence on psychotropic drug prescribing.*

Conclusion. *The degree of variation in prescribing volumes of psychotropic drugs between practices raises serious concerns. Further study is needed, but progress will be hampered until there is more clarity over the effectiveness and appropriateness of using these substances in the various illness, symptom and life-stress presentations seen in primary care.*

Keywords: psychotropic agents; anti-anxiety agents; hypnotic agents; antidepressant agents; prescribing rates.

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Introduction

PATTERNS of psychotropic drug prescribing in general practice have raised serious concerns for many years. In 1975 Trethowan, reviewing trends for prescribing of anxiolytics and hypnotics, drew attention to what he called 'the relentless march of the psychotropic drug juggernaut', pointing to the use of these drugs to solve non-specific personal problems.[1] In 1984, by which time the widespread use of barbiturate hypnotics had disappeared, benzodiazepines were declared to be 'on trial',[2] as evidence for pharmacological dependence on benzodiazepines accumulated.[3] In that year, 27 million prescriptions were written in England for drugs classified as hypnotics, sedatives and tranquillizers in official statistics.[4] These drugs include the hypnotic and anxiolytic benzodiazepines and other minor and major tranquillizers. Although prescriptions for these drugs fell to 21 million in 1990,[5] benzodiazepines still warranted a specific mention in the government's *Health of the nation* initiative, with a goal set to further reduce the prescribing of benzodiazepines.[6]

On the other hand, antidepressants may be underprescribed, and evidence has accumulated of a failure to recognize and treat depression appropriately in general practice. Studies have suggested that half of the patients consulting who have depression are not recognized on initial consultation[7] and that of these, 40% remain undiagnosed as depressed six months later.[8]

Despite this disquiet over trends in prescribing, variation between practices in patterns of psychotropic drug prescribing has attracted little attention. A wide variation in total prescribing of all classes of drugs between individual general practitioners and between practices has long been recognized,[9] but the causes of this variation are poorly understood.[10,11] A number of studies have described the prescribing patterns for certain psychotropic agents in individual general practices,[12-15] but few have described variation in prescribing between general practitioners or between practices.[16,17] Holm and Olesen, using the defined daily dose as a measure of prescribing, found a 100-fold range in the prescribing of psychotropic drugs between 227 general practitioners in Denmark.[16] They found a greater rate of prescribing by general practitioners from rural areas and small towns compared with those from larger towns and cities, but no differences in rate of prescribing in relation to the size and type of practice or to the age and sex of the general practitioner. McGavock used the prescription item as a measure of prescribing and found a sevenfold range between urban general practices in Belfast in the prescribing of anxiolytics and hypnotics combined.[17]

The aim of this study was to describe the extent of variation between general practices in the prescribing of hypnotics, anxiolytics and antidepressants. It also aimed to analyse the influence of measures of practice population and general practice and general practitioner characteristics on any variation. The traditionally quoted prescription item is an unsuitable measure of prescribing volume[18] and so this study used the 'defined daily dose' system, which was designed to be a valid measure of the quantity of prescribing.

Method

Data relating to all 61 general practices in the Cambridge and Huntingdon Health Commission were used in this study. This

area is characterized by relatively low levels of social deprivation, rural and urban districts, and relatively high primary care staffing levels and expenditure on primary care compared with other areas in England.

Prescribing data

Routinely published general practice statistics analyse prescribing in terms of numbers of prescriptions and total costs. As these measures give little indication of the volume of therapeutic prescribing,[18] the World Health Organization's 'defined daily dose' system was adopted for this study. This system allows conversion of each prescribed substance into equivalent units of a standard volume.[19] The method codes different formulations, strengths and quantities on each prescription into a standardized daily drug dose. Defined daily doses can be aggregated to measure notional days of treatment prescribed for each drug or for a group of drugs in a therapeutic class.

Detailed data from the Prescription Pricing Authority on the contents of each prescription were used to calculate the defined daily doses[20] prescribed by each of the 61 practices, covering the 12 months from April 1992 to March 1993. The total number of defined daily doses for each drug prescribed was calculated. These were then aggregated into therapeutic classes using *British national formulary* classifications for hypnotics, anxiolytics and antidepressants.[21] Most of the drugs classified as hypnotics and anxiolytics are benzodiazepines, but these classes also include non-benzodiazepine minor tranquillizers. In order to compare psychotropic drug prescribing with total prescribing, prescribing analyses and cost (PACT) data were used to obtain the total number of prescription items for all classes of drugs in the same period for each practice.

Practice population data

For each of the 61 practices, the practice list size, the number of temporary residents and the numbers of patients in eight age–sex bands were obtained from the Cambridgeshire Family Health Services Authority register. The age–sex bands were of males and of females in the age ranges: up to 14 years, 15 to 44 years, 45 to 64 years and 65 years and over. Family health services authority records were also used to identify practices that cared for residents of nursing homes for people with learning difficulty, elderly people and elderly mentally infirm people. For each practice, the standardized mortality ratio for men and women aged under 75 years and the Townsend deprivation index were obtained from the health and environment research group of the University of East Anglia (unpublished). They used patients' postcode addresses to allocate patients to census wards and thus determined the ward distribution of patients registered with each practice. This information was then combined with the 1991 census ward indicators to calculate a patient-weighted average of the ward values for each practice.

Practice structure variables

For each practice, the following data relating to practice structure and organization were obtained from family health services authority records: number of general practitioner partners; administrative and clerical costs per 1000 practice population; nursing costs per 1000 practice population; whether or not the practice was a dispensing practice; whether or not the practice had a computerized repeat prescribing system; and whether or not the practice employed a counsellor. The proportion of the patients on the practice list who were defined as living in a rural area (that is, living more than three miles from the surgery) was used as a measure of urban–rural differences between practices.

General practitioner characteristic variables

Little routine data are available that might be used to characterize individual general practitioners. Data that were available from family health services authority records were general practitioners' ages and their self-declared special interests. The mean age of the general practitioners in each practice was calculated. The special interests of the general practitioners were assigned to one of three categories: the highest category was an interest in psychiatry; an interest in psychotherapy/counselling was the middle category; and no special interest in psychiatry/psychology was the lowest category. The practice was then assigned to the category of the partner with the highest category special interest.

Analysis

The aim of the analysis was to identify the combination of the variables that would best explain any variation in prescribing between general practices. In order to eliminate variation caused by the practice list sizes, the output variables used were the annual defined daily doses prescribed per 1000 practice population, for each of the three classes of drugs — hypnotics, anxiolytics and antidepressants.

For each potentially influencing variable, the univariate linear regression equation was derived. Variables that were not significant at the 20% level were discarded. Stepwise multiple regression was then used to model the effect of the remaining explanatory variables. The adequacy of the final models in meeting the assumptions underlying multiple regression was assessed using standard diagnostic plots (a plot of residual against observed values, a histogram of residual values, and a normal plot of regression standardized residuals). Association between variables was measured using Spearman's rank correlation. Partial correlation was used to measure association between variables while controlling for potentially confounding factors.

All data were analysed using the *SPSS for Windows* statistical package.

Results

Figure 1 shows the frequency histograms for different levels of prescribing (measured as annual defined daily doses per 1000 practice population) of hypnotics, anxiolytics and antidepressants over the 61 practices. For hypnotics, the median prescribing volume was 6043 defined daily doses per 1000 practice population (interquartile range 3525 to 7471), with an 11-fold difference between the highest and lowest prescribing practices. The median prescribing volume for anxiolytics was 1714 defined daily doses per 1000 population (interquartile range 991 to 2229), with a 13-fold difference between the highest and lowest prescribing practices. For antidepressants, the median prescribing volume was 4651 defined daily doses per 1000 practice population (interquartile range 3401 to 5363), with an eightfold difference in the extremes.

Variables that were found to be significant at the 20% level in the univariate analyses, for hypnotics, anxiolytics and antidepressants, are shown, with the regression correlation coefficients, in Table 1. On subsequent stepwise multiple regression two variables were found to influence the volume of prescribing of all three classes of drug: the proportion of temporary residents on the practice list and the proportion of women aged 65 years and over on the practice list. These two variables explained 25% of the variation in the volume of prescribing of hypnotics ($F = 10.9$, 2,58 degrees of freedom (df), $P<0.001$), 19% of the variation in volume of anxiolytic prescribing ($F = 8.18$, 2,58 df, $P<0.001$), and 34% of the variation in volume of antidepressant prescribing ($F = 16.7$, 2,58 df, $P<0.001$). The final multiple regression equations are shown in Appendix 1.

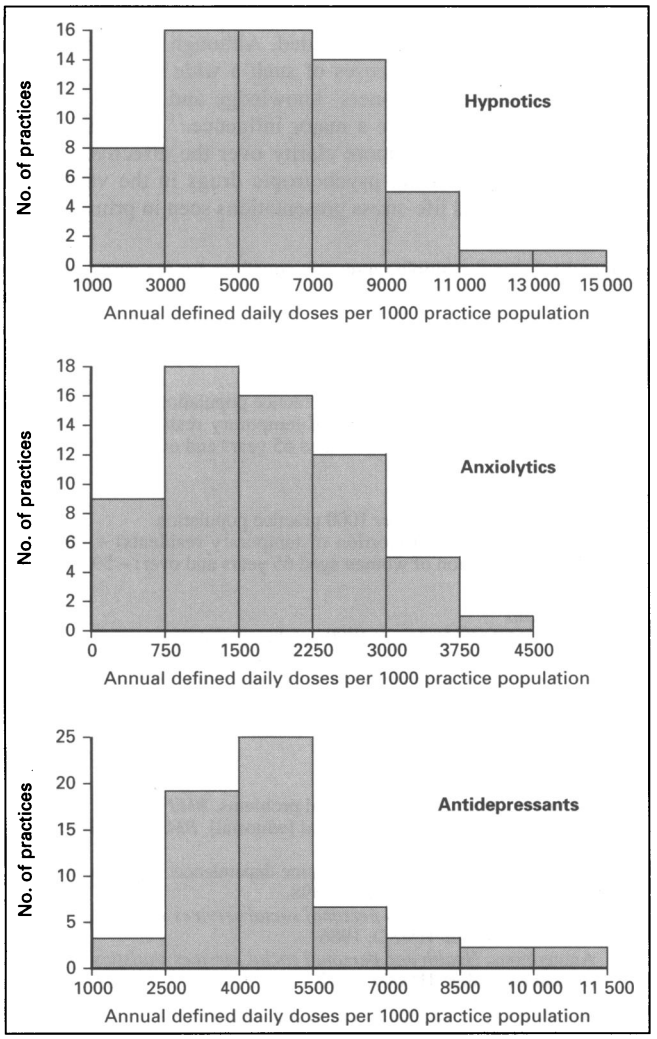

Figure 1. *Frequency histograms for different volumes of prescribing over 61 practices for hypnotics, anxiolytics and antidepressants.*

There was a strong positive correlation between the level of prescribing of the different classes of drug over all practices: antidepressant prescribing (annual defined daily doses per 1000 practice population) was positively correlated with prescribing of hypnotics (Spearman's rho (ρ) = 0.68, $P<0.001$) and with prescribing of anxiolytics (ρ = 0.51, $P<0.001$); and hypnotic prescribing was positively correlated with prescribing of anxiolytics (ρ = 0.65, $P<0.001$). When the four highest prescribing practices were excluded as outliers, the correlation remained significant between prescribing of antidepressants and prescribing of hypnotics (ρ = 0.63, $P<0.001$) and of anxiolytics (ρ = 0.39, $P<0.01$).

The partial correlation coefficient for defined daily doses per 1000 practice population with total prescription items (for all classes of drugs) per 1000 practice population, after controlling for age–sex structure, was 0.38 ($P<0.01$) for hypnotics, 0.26 ($P<0.05$) for anxiolytics and 0.43 ($P<0.01$) for antidepressants.

Discussion

This study demonstrated that there were large variations between the 61 practices in the prescribing of hypnotics, anxiolytics and antidepressants; these variations exceed the 2.5-fold differences in referral rates to surgical outpatient departments between a similar number of practices from the same geographical area as in this study.[22]

Table 1. Variables that significantly (at 20% level in univariate analyses) influenced the variation in prescribing of hypnotics, anxiolytics and antidepressants between 61 practices.

	R^2	F
Hypnotics		
Proportion of practice population:		
Women aged 65+ years	0.071	5.61*
Men aged 65+ years	0.004	2.64
Temporary residents	0.138	10.57**
Anxiolytics		
Proportion of practice population:		
Women aged 45–64 years	0.025	2.57
Women aged 65+ years	0.041	3.58
Men aged 45–64 years	0.033	3.05
Men aged 65+ years	0.034	3.10
Temporary residents	0.122	9.32**
Standardized mortality ratio		
for men aged under 75 years	0.029	2.82
Antidepressants		
Proportion of practice population:		
Women aged 15–44 years	0.056	4.54*
Women aged 45–64 years	0.064	5.08*
Women aged 65+ years	0.138	10.57**
Men aged 45–64 years	0.039	3.44
Men aged 65+ years	0.102	7.82**
Temporary residents	0.153	11.83**
Living in rural area	0.046	3.92

R^2 = regression correlation coefficient. F = variance ratio. *$P<0.05$, **$P<0.01$.

In reviewing the results of the present study, several potential errors need to be considered. Small errors in practice population estimates are possible but could not explain more than a small fraction of the variation found. The prescribing analyses and cost data, which form part of a payments system, are unlikely to contain important inaccuracies. The traditionally quoted prescription item is an unsuitable measure of prescribing volume[18] and so this study has used the defined daily doses system, which was designed to provide a valid measure of the quantity of prescribing.

General practices vary in several respects which may explain some of the variation in prescribing between practices. First, factors relating to the practice population vary. Such factors include practice list size and age–sex structure and characteristics such as morbidity, mortality and level of deprivation. Secondly, practices vary in terms of their structure and organization. These factors include the number of general practitioners and the quantity and type of resources in the practice. Thirdly, practices vary in terms of factors relating to the general practitioners themselves, such as their ages, training and attitudes to prescribing in general and to mental illness.

The effect of practice list size on the volume of prescribing was eliminated by using annual defined daily doses per 1000 practice population to measure prescribing volume. In describing the effects of practice population structure on psychotropic drug prescribing it would be desirable to have specific prescribing rates for different age–sex bands. Such data are not yet available either at a national or local level. The use of multiple regression with the practice population proportions in different age–sex bands would be a potential problem if all the bands were included in the analysis, as the proportions would be mutually constrained (they must by definition add up to one). By excluding those age–sex bands that were not found to be important as uni-

variate factors, this constraint was removed, enabling the influence of population structure to be described.

The prescribing of psychotropic drugs has been shown to be more common for women and elderly people than for men and younger age groups, and the duration of use is longer among women and elderly people;[12-15] the results of this study confirm the association with the number of women aged 65 years and over in the practice population.

The association between psychotropic drug prescribing and the number of temporary residents registered with the practice requires further analysis. Practices with higher proportions of these patients tend to be situated in large urban areas, echoing findings elsewhere that general practitioners in urban areas prescribe psychotropic drugs more frequently than their rural counterparts.[16,23] It may, however, confirm a clinical impression that general practitioners are likely not to change existing prescriptions of temporary residents and that some temporary residents or visiting patients register in order to get prescriptions for psychotropic drugs.

Although differences in the age–sex structures of the practice populations explained some of the variation in psychotropic drug prescribing between practices, mortality rates and deprivation in the practice population did not influence prescribing significantly. Because the practices in this study were in a district without local areas of severe deprivation, these particular findings may not hold in other districts, for example in inner cities. Prescribing was also not significantly influenced by the variables relating to the structure and organization of the practice or relating to the general practitioners themselves. However, the routine data that is available can only be a crude measure of general practitioners' psychological skills and attitudes, and further research is needed to establish the extent to which factors such as these might influence psychotropic drug prescribing.

The finding that the presence of a practice counsellor had no detectable effect on the prescribing of hypnotics, anxiolytics or antidepressants is not encouraging. Government efforts to reduce the use of benzodiazepines have centred on the use of alternatives for the treatment of anxiety.[6] Although the prescribing of benzodiazepines as anxiolytics has received much attention, it should be noted that in this study hypnotics (almost exclusively benzodiazepines) were prescribed in greater volumes than anxiolytics. The finding that prescribing of psychotropic drugs was associated with the number of women aged 65 years and over registered with practices should raise concerns. Several authors have expressed doubts about the efficacy and desirability of the use of benzodiazepines in chronic insomnia,[24,25] and any impact of the well-documented side effects are likely to be particularly disabling in elderly people.

Campaigns aimed at reducing the use of benzodiazepines and improving the recognition and treatment of depression might have been thought to have resulted in a negative correlation between the volumes of prescribing of antidepressants and hypnotics and/or antidepressants and anxiolytics. However, results from this study show strong positive correlations, suggesting that there is little substitution of these therapeutic approaches. The finding here and in other studies that high prescribers of psychotropic drugs tend to be high prescribers overall[17,23,26] suggests that factors determining this behaviour are general and not specific to prescribing for mental illness.

The results presented in this study imply that campaigns aimed at reducing benzodiazepine use should probably concentrate on their use as hypnotics and on those general practices with a high level of benzodiazepine prescribing. Simple methods are available to help general practitioners reduce benzodiazepine prescribing in general practice[27] and other ways to facilitate a change to more rational prescribing of psychotropic drugs in general practice are urgently needed. Although more research is needed to establish the causes of such a wide variation, differences in general practitioners' knowledge and attitudes to prescribing are likely to have a major influence.[11] Progress will be hampered until there is more clarity over the effectiveness and appropriateness of using psychotropic drugs in the various illness, symptom and life-stress presentations seen in primary care.

Appendix 1. Final multiple regression equations for the variation in prescribing volume between 61 practices, for hypnotics, anxiolytics and antidepressants.

Hypnotics
Annual defined daily doses per 1000 practice population
= (72 745 x proportion of temporary residents) + (39 720 x proportion of women aged 65 years and over) – 237

Anxiolytics
Annual defined daily doses per 1000 practice population
= (22 440 x proportion of temporary residents) + (10 899 x proportion of women aged 65 years and over) – 59

Antidepressants
Annual defined daily doses per 1000 practice population
= (55 184 x proportion of temporary residents) + (36 060 x proportion of women aged 65 years and over) – 418

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Measuring fundal height

THE linchpin of good antenatal care is accurate gestational dating. Traditionally, this is achieved by the estimation of fetal age by the application of Naegele's rule and correlation of this estimate with the fundal height. Unfortunately, this method may often prove fallible since many women are uncertain of their dates or have irregular menstrual cycles. Accurate measurement of fundal height may be confounded by maternal obesity, short stature, a full bladder or even race. Thus, most obstetricians today rely on ultrasound measurement of specific fetal dimensions for gestational dating bearing in mind that ultrasound measurement is most accurate when undertaken before week 20 of pregnancy.

The aim of the study reported by Euans and colleagues was to ascertain whether measurement of fundal height by ultrasonography rather than manually would prove more accurate and would evade the confounding factors mentioned above. They studied 159 consecutive women with singleton pregnancies at between 11 and 42 weeks' gestation, dividing them into two groups, normal and obese, depending on whether or not they were more than 20% above the normal weight for their height. The height of the fundus above the pubic symphysis was then measured both manually and by ultrasonography and fetal age was formally assessed using multiple conventional ultrasound parameters.

In only 12% of the sample did manual and ultrasound fundal values differ by more than two weeks and the authors showed no significant statistical difference between manual and ultrasound techniques. Even in the obese group, the measurements were interchangeable. Race had no influence on the relationship between manual and ultrasound fundal height measurements. Unfortunately, the authors did not assess the effect of a full bladder on either method, so the effect of this was not included in the study.

This paper showed that routine obstetric ultrasound may not be necessary solely for the purpose of determining gestational age and may only be indicated when there is a serial discrepancy between fundal height and calculated dates or where there is suspicion of growth retardation or other anomalies. To quote the authors: 'High technology is most effectively used in combination with good clinical skill.'

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Source: Euans DW, Connor PD, Hahn RG, *et al.* A comparison of manual and ultrasound measurements of fundal height. *J Fam Pract* 1995; **40:** 233-236.

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Educational level of spouses: risk of mortality

THERE is a constant search for new factors that influence cardiovascular disease mortality rates, to enhance current knowledge of associations with hypertension, hyperlipidaemia, obesity, poor nutrition, lack of exercise and psychiatric states. Many studies have concentrated on the prevalence of these factors among the lower social classes. Type A personality has also been highlighted as being disadvantaged with regard to cardiovascular disease mortality.

A recent 9.5 year follow-up study (World Health Organization Kaunas–Rotterdam intervention study, KRIS) comparing two disparate communities in Lithuania and the Netherlands has been able, *inter alia,* to examine the relationship between the educational levels of professional persons and their spouses. It highlights the increased all-cause mortality of professionals who have spouses who are less well educated than themselves. The authors comment on various studies highlighting the fact that professionals with type A personalities fare badly when married to co-professionals of equal or greater educational levels. The study concentrates on a male cohort and, while commenting on higher or lower socioeconomic status, does not eliminate simply marrying across different social classes, where different expectations of behaviour and caring may be of profound importance.

The authors state that, despite the central role of the wife in family matters, little or no research has been conducted into the effects of socioeconomic status of wives upon professional men's mortality. They show a direct relationship between the socioeconomic status and the lower levels of education of wives, highlighting a significant association between a wife's education and all-cause mortality of her husband, even after correcting for increased smoking of the men and all other risk factors.

The conclusion of this study, although at odds with some others, also comments upon the increases in recent years of women in the workforce as well as a number of other factors which may come into play after a latent period, and wonders if professional women may in due course suffer the same problems as men.

Clearly further studies will examine these findings, although human emotions may well confound any changes in behaviour in this field, as has been experienced elsewhere.

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Source: Bosma H, Appels A, Sturmans F, *et al.* Educational level of spouses and risk of mortality: the WHO Kaunas–Rotterdam intervention study (KRIS). *Int J Epidemiol* 1995; **24:** 119-126.

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