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Neighbourhood characteristics and use of benzodiazepines in The Netherlands

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ABSTRACT

This paper analyses the relationship between individual and neighbourhood characteristics and the use of benzodiazepines within a Dutch city. It is hypothesized that the proportion of users is lower in more socially integrated and less deprived neighbourhoods. Hypotheses have been tested by using multi-level analysis to distinguish between composition and context effects. Age and gender have a clear relation to the use of benzodiazepines and neighbourhood differences in the proportion of users are partly the effect of population composition by age and gender. The proportion of users is higher in neighbourhoods with a higher percentage of one-parent families, with a lower percentage of social rented housing and with a larger number of rooms per person. The strength of the relation between age and use is influenced by neighbourhood characteristics. Neighbourhood variation in the amount used only depends on population composition.

INTRODUCTION

The impact of factors such as age, gender and socio-economic status on the prescribing and use of drugs is well recognized (Leufkens and Urquhart, 1994b). Decisions related to drug therapy are influenced by the social and cultural environment of prescribers and patients alike (Denig, 1994). It is useful to recognize and understand the great variability in drug treatment and patient outcomes caused by these non-pharmacological factors.

The use of benzodiazepines has been controversial for many years (Cooperstock; Gabe and van). Benzodiazepines are considered safe and effective in short-term therapy, but long-term use is far from recommended therapy and a clear risk factor for abuse and dependency (Olfson and Pincus, 1994). For several reasons they are both widely used and prone to a high variability in patterns of prescribing and use (Lagro and Markovitz): they are being prescribed for a large spectrum of indications; therapeutic alternatives, such as counselling and psychotherapy, are very time-consuming and probably stigmatizing; there is controversy over their long-run safety.

Chronic use of benzodiazepines, in particular in elderly patients, is a well-recognized risk factor for health problems. Users of benzodiazepines are most often in a high-risk position,

both socio-economically and as regards health and mental well-being (Lagro-Janssen and Liberton, 1993). In particular elderly patients have a higher prevalence of clinically significant insomnia than younger patients. These symptoms are usually comorbid with depression, chronic disease, dementia or personality disorders and all of these factors impact on treatment.

Physicians differ in the volume and kind of (psychotropic) drugs they prescribe (Haaijer, 1984 and Denig, 1994). The variation in the use of benzodiazepines may partly be related to greater psychiatric morbidity and more psychosocial problems, but different prescribing habits among physicians are also important (Cormack and Howells, 1992). In the Netherlands, most prescriptions are repeat prescriptions, handled by the practice secretary at the request of the patient (Van der Waals et al., 1993).

Geographical variations in use

In the literature a number of studies have been reported on geographical variations in benzodiazepine use between countries and regions (Balter and Pariente). For instance, the difference between Denmark (highest) and Sweden (lowest) is almost twofold (Ekedahl et al., 1993). There are also large within-country variations, e.g. benzodiazepine utilization in the Swedish city of Helsingborg (close to Denmark) was at the average Danish level but the highest in Sweden (Balter et al., 1974). Other studies have shown that the use of benzodiazepines is more prevalent in urban areas than in rural areas (Gabe and Williams, 1986).

Potential explanations for these geographic variations are twofold. The first line of reasoning states that socio-demographic characteristics that are related to benzodiazepine use at the level of individuals are unevenly distributed across rural and urban areas. Differences in the composition of the population, e.g. in terms of age or socio-economic status, that cluster spatially, explain geographical variations in use. Williams and Gabe (1987) call this a minimalist position from a social science point of view because only individual characteristics are taken into account. The second line of reasoning states that apart from this explanation there are also differences at the level of the social and geographical context that contribute to the explanation of differences in benzodiazepine use. The tranquility of rural life or the social integration in rural communities, as an example, might influence tranquilizer use apart from individual characteristics of the users. This might be called the 'place matters' position (Duncan et al., 1993).

Socio-demographic patterns of benzodiazepine use

Several pharmaco-epidemiologic studies have addressed the widespread use of benzodiazepines and the importance of demographic and socio-economic factors (Cormack and Howells, 1992). Users of benzodiazepines are more often female than male. The number of users increases with age (Van der Waals et al., 1993). Age and gender at the individual level can be regarded as proxies of the 'risk' of having (mental) health problems for which benzodiazepines are usually prescribed, such as sleeping disorders, nervous complaints and pain and associated insomnia in chronic illness. Long-term use of benzodiazepines is highly prevalent; a Dutch study showed 89% of prescriptions in a three-month period to be repeat prescription (Van der Waals et al., 1993).

Context aspects of use of benzodiazepines

Apart from individual characteristics, aspects of the social environment and people's relations to their social environment could influence the use of tranquilizers. This influence might be conceived of in two ways. First, some social environments might coincide with a greater occurrence of the kind of social or psychological problems for which benzodiazepines are being prescribed (Giggs; Curtis and Thornicroft). Secondly, given that social or psychological problems occur, some social environments might provide people with more resources to cope with these problems without using benzodiazepines or with smaller amounts (Tijhuis et al., 1995).

For each of these two ways different characteristics of social environment are relevant. For the first one characteristics of social deprivation seem to be relevant. If people live in deprived areas, they will experience more social and psychological problems and hence more people will be 'at risk' for benzodiazepine use. For the second one characteristics of social integration are more relevant. If people live in socially integrated areas and if they happen to experience social or psychological problems, they have more resources to cope with these problems. Hence, fewer people will use benzodiazepines and if they use them, they will do so more often in smaller amounts.

Based on these ideas, both deprivation and social integration of the neighbourhood people live in might be related to the level of use of benzodiazepines and to the age-specific use rates. It is anticipated that in more deprived and less socially integrated neighbourhoods the level of use will be higher. Moreover, use will especially be higher in the lower age brackets. The reason is that according to the literature there is a fairly strong relation between age and the use of benzodiazepines (irrespective of neighbourhood context). Adverse neighbourhood characteristics will therefore also affect older people who already would use benzodiazepines for other (chronic disease-related) reasons. In contrast, in younger age groups the level of use is generally low and the effects of adverse neighbourhood context will be more easily visible. This means that in regressions of age on use of benzodiazepines, the slopes will differ between neighbourhoods and that these differences will be related to neighbourhood characteristics (so-called cross-level interactions).

Research questions

Put in general terms the question is 'does place matter?' In this paper we elaborate this question in two ways. We look at differences in the use of benzodiazepines between neighbourhoods in one city. If rural-urban differences exist that relate not only to differences in socio-demographic composition, but also to contextual differences, they might as well exist between neighbourhoods. In this way the application of the minimalist and 'place matters' positions is broadened to the study of differences within cities.

Furthermore, we elaborate the question from a methodological point of view. Recent developments in the methodology of multi-level models will be used to study the effects of characteristics at the individual level and at the neighbourhood level (Jones; DiPrete and Westert). Until recently this kind of data was usually analysed by aggregating all data to neighbourhood level or by distributing neighbourhood characteristics over individual cases. Both strategies have serious drawbacks. Aggregating means loss of information on individual level variation and the risk of ecological fallacy. Distributing leads to underestimating the standard errors of the higher-level regression coefficients, increasing the probability of statistically significant, but non-existent relationships. Moreover, the coefficients and standard errors may be erroneous owing to an unbalanced design (Bryk and Raudenbush, 1992).

The aim of the study is to evaluate whether or not differences in benzodiazepine use exist between neighbourhoods within one urban area. If these differences do exist, we want to analyse to what extent they are related to neighbourhood characteristics and to the interaction of individual and neighbourhood characteristics.

Hypotheses

We have no specific hypotheses on the relative weight of indicators of deprivation and social integration as far as the number of recipients of prescriptions of benzodiazepines is concerned. Hence we state them as separate hypotheses.

The more the living environment of people is characterized by social deprivation, the greater will be the number of people who receive a prescription of benzodiazepines. The less the living environment of people is characterized by social integration, the greater will be the number of people who receive a prescription of benzodiazepines. If people use benzodiazepines, we expect them to use smaller amounts the more their living environment is characterized by social integration. Finally we expect that the relation at the individual

level between age and use of benzodiazepines is weaker with more social deprivation or less social integration at the neighbourhood level.

DATA AND METHODS

The study area consists of a new town in the area reclaimed from the former Zuiderzee (Van de Ven, 1993). The total population was 58,000 people at the time of the study. The city is approximately 50 km from Amsterdam. It was founded in 1965. Most of its inhabitants migrated from Amsterdam. It functions largely as a satellite suburb of Amsterdam with little employment opportunities of its own.

Over a three-month period in 1989 (August–October) computerized pharmacy records in the study area were searched for prescriptions of benzodiazepines. In the Netherlands computerization of pharmacy records, and thus the compilation of prescription drug histories, is almost universal. These records contain data elements (drug product code, prescribing physician, date of dispensing, projected stop date of therapy and prescribed daily dose (PDD)) on all dispensed medicines. A patient identifier that enables one to link all records to the same individual is an essential element in these virtually complete drug use profiles. Completeness is based on the system that people frequent a single pharmacy for their prescription drugs in the place where they live (obligatory for the publicly insured) (Leufkens and Leufkens). In this paper we use information on the binary variable of whether benzodiazepines were prescribed or not and, if prescribed, the defined daily doses, computed on the basis of the PDD. The population of non-users has been reconstructed by subtracting the number of users in each age-gender category from the total number of inhabitants of each neighbourhood.

The city consists of 23 administrative areal units, the neighbourhoods. With respect to these neighbourhoods characteristics have been provided by the city's statistical service. We have classified the available neighbourhood characteristics as indicators of social deprivation and integration respectively (Table 1). Unfortunately, data on income and social security dependence were not available at neighbourhood level. It turned out that the correlations between the percentage of people living alone, the total migration rate of a neighbourhood, and the percentage of one-family housing are too high to use in one analysis (Table 2). Although they do not all refer to the same concept, according to our initial classification of neighbourhood characteristics as indicators either of social deprivation or of social integration, the highly related variables have been factor analysed using LISREL (Long, 1983) and combined into one factor (eigen value 2.7; bounded variance 90%) which is higher in the case of more people living alone, a higher migration rate and a lower percentage of one-family housing (referred to as 'level of integration' in Table 3 to follow). Factor analysis over all neighbourhood characteristics did not show a clear or interpretable factor structure. The other variables are therefore used as separate variables as presented in

[TABLE 1.]

[TABLE 2.]

[TABLE 3.]

Data analysis

To analyse individual level variation directly in relation to variation at the level of neighbourhoods we use multi-level models in the statistical package MLn (Rasbash and Woodhouse, 1995). In the analysis of the use or non-use of benzodiazepines we used logistic regression (partial quasi-likelihood estimators with second-order approximation (Goldstein, 1995)). To distinguish between individual level and neighbourhood level effects it is

important that the individual level model fits rather well, because of potential spatial clustering of individual characteristics. Because the age effect is not perfectly linear, at the individual level the first- and second-order polynomials of age and the interaction between age and gender have also been added. This did not alter the main effect of age.

In our study we have two dependent variables: whether or not a person has received a prescription of benzodiazepines in the three-month recording period and the amount that has been prescribed for those with a prescription. This means that two equations have to be estimated simultaneously, a logistic version for the binary dependent variable and a linear version for the continuous dependent variable.

To find out whether or not a relation exists between the number of users of benzodiazepines and the amount used, we utilize a special application of multilevel models, the mixed multivariate response model (Duncan et al., 1996). This model uses an extra level, the response level, below the individual level and the neighbourhood level. The response vector is modelled as a combination of a logit equation for the binary response and linear equation for the continuous response. This model allows us to estimate the relation between the chance of being a user and the amount used.

We were not able to analyse the influence of prescriber behaviour. This is due to data availability. However, the implication is that utilization patterns of neighbouring areas might not be independent of each other, because in part the same physicians are prescribing. Consequently we expect to find some degree of spatial autocorrelation in neighbourhood residuals. The usual way of testing for spatial autocorrelation is by using Moran's coefficient I (Ebdon, 1977). If Moran's I differs significantly from zero (tested against the Chi-square distribution (Cliff and Ord, 1973)), this confirms the existence of spatial autocorrelation, which might actually be due to differences in prescribing behaviour of physicians.

RESULTS

We shall start the description of the results with an analysis of the proportion of users of benzodiazepines. At the individual level the dependent variable is whether or not someone is a user. The second part of the results section analyses the amount used by those who have one or more prescriptions in the three-month period. Here, the relation between both dependent variables will also be discussed.

Users and non-users of benzodiazepines

During the observation period close to 6% of the study population received one or more prescriptions for benzodiazepines. 40% of the users were 60 years and older, while 65% were females. Diazepam was the most prescribed agent, with 23% of prescription volume, followed by oxazepam (19%), temazepam (14%), lorazepam (12%) and nitrazepam (9%). Diazepam and oxazepam recipients tended to be younger than 60 years, while temazepam, lorazepam and nitrazepam were popular with people 60 years and older.

In Fig. 1 the percentage of users of benzodiazepines is mapped for each neighbourhood. The map shows substantial differences between neighbourhoods, with the highest values for the central district and adjacent districts. However, in this map it is impossible to distinguish between differences resulting from the composition of neighbourhoods and differences resulting from the neighbourhood context. By using multilevel analysis we are able to distinguish between both sources of variation.

[FIGURE. 1.]

Table 3 shows the parameters of the different models that have been estimated. The overall percentage of benzodiazepines users is 5.6%, with confidence interval between 4.7 and 6.7%. With individual level variance constrained to one (Goldstein, 1995), the neighbourhood level variance is 0.20 and differs significantly from zero (model A), using the chi-square significance test for random contrasts (Woodhouse, 1995).

Age and gender have a strong influence on the use of benzodiazepines (model B). The possibly non-linear character of the relation between age and use of benzodiazepines has been modelled by adding first- and second-order polynomials, both of which are significant. There is no statistically significant interaction between age and gender. The neighbourhood level variance decreases to 0.11 (but is still significantly different from zero). Hence, some of the differences between neighbourhoods are the result of differences in age and gender composition of the population.

In Model C the neighbourhood level variables are included. Of the indicators of social integration, only the percentage of single-parent families has a (borderline) significant coefficient. The coefficients of two of the indicators of social deprivation are significant and show, contrary to our hypothesis, that use of benzodiazepines is higher in neighbourhoods with less social deprivation. The decrease of neighbourhood level variance from 0.11 to 0.04 suggests that there is an influence of the neighbourhood context on the use of benzodiazepines.

Until now we have assumed that age has the same influence on use in all neighbourhoods. However, the hypothesis is that the effect of age is stronger in neighbourhoods with lower levels of deprivation and higher levels of integration. For the lower age groups the amount of variation between neighbourhoods is higher than for older age groups, as is shown by the neighbourhood-specific regression lines of age on use of benzodiazepines with use plotted on a logit scale (Fig. 2 and Table 4). To explore the random effect of gender, this variable was coded as two dummy variables to prevent variance estimates from becoming negative. The variance of the intercept for females does not significantly differ from zero. However, there is significant covariance between the intercepts for males and females and there is significant variance between neighbourhoods in the intercepts for males. This means that there is significant variation in the use of benzodiazepines between neighbourhoods among males (Table 4).

[FIGURE. 2]

[TABLE 4]

To test the hypothesis on the varying relation between age and use, we have added cross-level interactions between age and neighbourhood characteristics (model D). There are three cross-level interactions with coefficients that differ significantly from zero. The effect of age on use of benzodiazepines is less strong in neighbourhoods with a higher percentage of one-parent families and with a higher percentage of people with no religious affiliation (i.e. in less integrated areas). The effect of age is stronger in neighbourhoods with a higher internal migration surplus (i.e. in more attractive areas). In this final model the coefficient of the percentage of one-parent families differs significantly from zero, but the one for the percentage of social rented housing decreased to just below the conventional level of significance.

Table 3 (bottom line) shows that the null model comes close to showing significant spatial autocorrelation. However, when individual characteristics are introduced, the value of Moran's I decreases, indicating that the similarity of neighbouring areas is caused by differences in population composition.

Amount of benzodiazepines used

The users of benzodiazepines have, in the three-month recording period, received a varying number of prescriptions for different agents. To have a comparable measure of the amount prescribed, the Defined Daily Doses (DDDs) have been computed. The DDD is the daily dose for the main indication for an adult and has been developed as a unit of measurement in drug utilization research as a normalization technique, to facilitate comparisons on drug

usage (World Health Organisation, 1993). On average, for those who received a prescription 66 DDDs were prescribed.

The amount of benzodiazepines used shows less neighbourhood variance than the mere fact of being a user (Table 5, models A). The neighbourhood variance for the continuous response variable is relatively low compared to its standard error and not significant. However, there is a significant covariance between the binary and continuous responses, suggesting that, in those neighbourhoods where more people use benzodiazepines, the amounts used are also higher. The individual level variables (model B continuous response variable) explain a large share of the neighbourhood variance in the amount used. Hence, neighbourhood variation in the amount of benzodiazepines used, given the fact that one is a user, is due to the composition of the population by age and gender. In model B, the covariance of the binary and continuous response is not significant. In the equation for the amount of benzodiazepines used, the second-order polynomial of age is not significant and excluded from the analysis. The first-order polynomial has a significant, negative coefficient. This is congruent with the clinically relevant observation that the amounts prescribed should be lower for older people, but in contrast to some of the empirical literature (Isacson et al., 1993). In conclusion, the joint analysis of use or non-use and amount of benzodiazepines used shows that the initial relation between both is most probably due to composition effects and not context effects.

[TABLE 5.]

DISCUSSION

The results only partly confirm our hypotheses. Of the indicators of social integration, only the percentage of one-parent families in the neighbourhood has a clear relation to the use of benzodiazepines in the hypothesized direction. Of the indicators of deprivation, two have a clear relation to use, but neither of them in the hypothesized direction. In contrast to the hypothesis, the percentage of benzodiazepines users is higher in neighbourhoods with a lower percentage of social rented housing and with a higher number of rooms per person. However, the significant cross-level interactions are according to the hypothesis: in neighbourhoods with more one-parent families and more people with no religious affiliation the relation between age and use of benzodiazepines is weaker, and in neighbourhoods with a higher internal migration surplus the relation between age and use is stronger. The neighbourhood level relation between use or non-use of benzodiazepines and the amounts used and the neighbourhood level variation in the amounts used, seem to be caused by the composition by age and gender. The implication is that the hypotheses on the relations between social integration and deprivation and the amounts used are not relevant. A possible explanation is that prescriber behaviour is (even) more important here than in the decision whether or not benzodiazepines are being used.

At both the individual and the neighbourhood level we would rather have had better data and indicators, for slightly different reasons. At the neighbourhood level the number of units is relatively small, they are heterogeneous and the indicators of social integration and deprivation are probably not the only, nor the best indicators. In the literature too other indicators are being used, such as car ownership and unemployment (Davey Smith et al., 1998). In health policy, indicators of deprivation are used in the UK to compensate family physicians who work in 'underprivileged areas' (Majeed et al., 1996). In the Netherlands compensation payment for family physicians' patients from deprived areas was introduced in 1996, but is used only in highly urbanized areas (Van der Velden et al., 1997).

The unexpected sign of the coefficient of the rooms per person variable is probably due to the fact that this indicator favours small households (and consequently lower social integration). The possibility of lower access to primary care services in more deprived areas in the Netherlands can be ruled out as an explanation for the unexpected results; the use of

family physician services even slightly higher in deprived areas (Verheij et al., 1998) and for people with lower socio-economic status (Van der Meer, 1998).

The absence of census data in the Netherlands (the last census was held in 1971) makes it impossible to use the richer census data at census tract level, rather than being dependent on the information a city's statistical office collects and on what a city defines as its administrative units.

At the individual level the problem is different and related to the basic question of this study. Is the spatial variation in the use of benzodiazepines only the result of spatial differences in composition of the population or is there a contextual influence of the environment people live in? That is the basic question we started this research with. The answer is that place does indeed matter in the case of use of benzodiazepines. However, we have to keep one proviso. The fit of the individual level model, with only age and gender as variables, is far from perfect. There are numerous other individual level influences on the use of benzodiazepines that we do not have information about. Especially the lack of data on individual level indicators of socio-economic status, such as income or education, is problematic. If these variables cluster in some neighbourhoods and less in others, part of the variation at neighbourhood level might in reality be due to compositional effects and not to contextual effects.

Prescriber behaviour is a source of variation in the use of benzodiazepines that could influence spatial patterns. In the city where we did this research, general practitioners mainly work in health centres. Although the health centres have their patients usually within the neighbourhood, there is also neighbourhood border crossing utilization. We could not assess prescriber behaviour directly. The reason is that although we have information on the prescribing physician for each prescription of benzodiazepines, we do not have access to the patient list of these physicians. Hence we do not know to which physician's list the non-users belong. The influence of prescriber behaviour on the spatial pattern of utilization was indirectly taken into account by analysing spatial autocorrelation. There was only weak spatial autocorrelation and this was most probably due to composition of the population. With more complete data cross-classified models could be used, defining the physicians' practice population as an additional level.

The fact that physicians' lists extend over neighbourhood borders raises the issue of the most appropriate scale level. The districts we used are administrative units that are possibly not the most homogeneous spatial units. However, earlier research on spatial aspects of tranquilizer use focused on rural-urban differences or differences at even higher scale levels. The neighbourhood is a relevant level of scale in the explanation of behaviour that is (also) influenced by people's direct living circumstances. It might be more so for people who are more dependent on the neighbourhood, such as children, women and elderly people. However, we did not find significant variation between neighbourhoods in the percentage of female users of benzodiazepines, but we did, unexpectedly, for males. A possible explanation could be differences between neighbourhoods in male unemployment rates; unfortunately we do not have data on unemployment by neighbourhood.

Neighbourhoods as units of analysis are to a certain extent artificial and the question is whether results would be different with another division of the city into areal units. Here, we followed (and had to follow, owing to restrictions of available information) the usual assumption that spatial units are given, meaningful and fixed (Openshaw, 1984). The problem of the more or less artificial nature of spatial units, the so-called 'modifiable areal unit problem' (Openshaw and Wrigley), has to our knowledge been discussed only briefly in the context of multi-level analysis with special reference to the scale problem (Jones, 1993). It seems to us that, within a multi-level context, the zoning problem depends on whether the neighbourhood characteristics can be seen as genuine context characteristics or rather as proxies for individual characteristics. Assuming that the relation between a context variable and the (individual level) dependent variable is linear, there is no 'modifiable areal unit problem': if another zoning of the area is used, that would only mean that the

neighbourhoods are somewhere else on the same underlying regression line. However, if neighbourhood variables essentially represent aggregated individual characteristics and are only proxies for unmeasured individual characteristics, the results might indeed depend on the zoning of the area.

Although there are a number of drawbacks to this study, it shows that both individual characteristics and social or spatial characteristics influence the use of tranquilizers such as benzodiazepenes. Furthermore, this paper shows the possibilities of multilevel modelling in testing these hypotheses. The substantial issues raised in this paper could be taken further by combining survey data to collect individual characteristics, with a richer set of administrative and qualitative data on neighbourhood characteristics.

REFERENCES

- Balter, M.B., Levine, J. and Manheimer, D.I., 1974. Cross-national study of the extent of antianxiety/sedative use. *New England Journal of Medicine* 290, pp. 769–774.
- Bryk, A.S. and Raudenbush, S.W., 1992. *Hierarchical Linear Models* Sage, Newbury Park.
- Cliff, A. and Ord, J., 1973. *Spatial Autocorrelation* Pion, London.
- Cooperstock, R. and Parnell, P., 1982. Research on psychotropic drug use: a review of findings and methods. *Social Science & Medicine* 16, pp. 1179–1196.
- Cormack, M.A. and Howells, E., 1992. Factors linked to the prescribing of benzodiazepines by general practice principals and trainees. *Family Practice* 9, pp. 466–471.
- Curtis, S.E., 1990. Use of survey data and small area statistics to assess the link between individual morbidity and neighbourhood deprivation. *Journal of Epidemiology and Community Health* 44, pp. 62–68.
- Davey Smith, G., Hart, C., Watt, G., Hole, D. and Hawthorne, V., 1998. Individual social class, area-based deprivation, cardiovascular disease risk factors, and mortality: the Renfrew and Paisley study. *Journal of Epidemiology and Community Health* 52, pp. 399–405.)
- Denig, P., 1994. Drug choice in medical practice: rationales, routines, and remedies. Dissertation, University of Groningen, Groningen..
- DiPrete, T.A. and Forrestal, J.D., 1994. Multilevel models: methods and substance. *Annual Review of Sociology* 20, pp. 331–357.
- Duncan, C., Jones, K. and Moon, G., 1993. Do places matter? A multi-level analysis of regional variations in health-related behaviour in Britain. *Social Science & Medicine* 37, pp. 725–733.
- Duncan, C., Jones, K. and Moon, G., 1996. Health-related behaviour in context: a multilevel modelling approach. *Social Science & Medicine* 42, pp. 817–830.
- Ekedahl, A., Lidbeck, J., Lithman, T., Noreen, D. and Melander, A., 1993. Benzodiazepine prescribing patterns in a high-prescribing Scandinavian community. *European Journal of Clinical Pharmacology* 44, pp. 141–146.
- Ebdon, D., 1977. *Statistics in Geography; a Practical Approach* Blackwell, Oxford.
- Gabe, J. and Bury, M., 1991. Tranquilisers and health care in crisis. *Social Science & Medicine* 32, pp. 449–454.
- Gabe, J. and Williams, P., 1986. Rural tranquility? Urban–rural differences in tranquiliser prescribing. *Social Science & Medicine* 22, pp. 1059–1066.
- Giggs, J., 1986. Mental disorders and ecological structure in Nottingham. *Social Science & Medicine* 23, pp. 945–961.
- Goldstein, H., 1995. *Multilevel Statistical Models* Edward Arnold, London.
- Haaijer, F.M., 1984. Het voorschrijfgedrag van de huisarts. Dissertation, University of Groningen, Groningen..
- van Hulst, R., Leufkens, H.G. and Bakker, A., 1998. Usage patterns of benzodiazepines in a Dutch community: a ten-year follow-up. *Pharmacy World and Science* 20, pp. 78–82.
- Isacson, D., Bingefors, K., Wennberg, M. and Dahlström, M., 1993. Factors associated with high-quantity prescriptions of benzodiazepines in Sweden. *Social Science & Medicine* 36, pp. 343–351.

- Jones, K., 1993. . 'Everywhere is Nowhere': Multilevel Perspectives on the Importance of Place The University of Portsmouth Inaugural Lectures, Portsmouth.
- Lagro-Janssen, A.L. and Liberton, I., 1993. Profiles of regular consumers of benzodiazepines in a family practice. *Nederlands Tijdschrift voor Geneeskunde* 137, pp. 1969–1973 (in Dutch).
- Leufkens, H.G. and Bakker, A., 1992. Netherlands. In: Spivey, R.N., Wertheimer, A.I. and Rucker, T.D. Editors, 1992. *International Pharmaceutical Services; the Drug Industry and Pharmacy Practice in Twenty-three Major Countries of the World* Pharmaceutical Products Press, New York.
- Leufkens, H.G. and Urquhart, J., 1994. Automated record linkage and other approaches to pharmaco-epidemiology in the Netherlands. In: Strom, B.L. Editor, , 1994. *Pharmacoepidemiology* (2nd ed. ed.), Wiley, London.
- Leufkens, H.G. and Urquhart, J., 1994. Variability in patterns of drug usage. *Journal of Pharmacy and Pharmacology* 46 suppl 1, pp. 433–437.
- Long, J.S., 1983. . *Confirmatory Factor Analysis; a Preface to LISREL* Sage, Beverly Hills.
- Majeed, F.A., Martin, D. and Crayford, T., 1996. Deprivation payments to general practitioners: limitations of census data. *British Medical Journal* 313, pp. 669–670.
- Markovitz, P.J., 1993. Treatment of anxiety in the elderly. *Journal of Clinical Psychiatry* 54 Suppl, pp. 64–68.
- van der Meer, J.B.W., 1998. Equal care, equal cure? Socio-economic differences in use of health services and the course of health problems. Dissertation, Erasmus University, Rotterdam..
- Olfson, M. and Pincus, H.A., 1994. Use of benzodiazepines in the community. *Archives of Internal Medicine* 154, pp. 1235–1240.
- Openshaw, S., 1984. . *The Modifiable Areal Unit Problem* Geobooks, Catmog 38, Norwich.
- Pariente, P., Lepine, J.P. and Lellouch, J., 1992. Self-reported psychotropic drug use and associated factors in a French community sample. *Psychological Medicine* 22, pp. 181–190.
- Rasbash, J. and Woodhouse, G., 1995. . *MLn Command Reference* Institute of Education, University of London, London.
- Thornicroft, G., Bisofi, G., De Salvia, D. and Tansella, M., 1993. Urban–rural differences in the associations between social deprivation and psychiatric service utilization in schizophrenia and all diagnoses: a case-register study in Northern Italy. *Psychological Medicine* 23, pp. 487–496.
- Tijhuis, M.A.R., Flap, H.D., Foets, M. and Groenewegen, P.P., 1995. Social support and stressful events in two dimensions: life events and illness as an event. *Social Science & Medicine* 40, pp. 1513–1526.
- van der Velden, J., Rasch, P. and Reijneveld, S.A., 1997. Identification of deprived areas: an allocation model of extra payments to general practitioners. *Nederlands Tijdschrift voor Geneeskunde* 141, pp. 693–697 (in Dutch).
- van de Ven, G.P. Editor, , 1993. *Man-made Lowlands; History of Water Management and Land Reclamation in the Netherlands* Matrijs, Utrecht.
- Verheij, R.A., Reijneveld, S.A. and De Bakker, D.H., 1998. . *Identification of Deprived Urban Areas: Evaluation of the Allocation Model of Extra Payments to General Practitioners* NIVEL/TNO-PG, Utrecht/Leiden (in Dutch).
- van der Waals, F.W., Mohrs, J. and Foets, M., 1993. Sex differences among recipients of benzodiazepines in Dutch general practice. *British Medical Journal* 307, pp. 363–366.
- Westert, G.P. and Verhoeff, R.N. Editors, 1997. *Places and People: Multilevel Modelling in Geographical Research* Netherlands Geographical Studies, Utrecht.
- Williams, P. and Gabe, J., 1987. Research note: urban–rural differences in tranquiliser prescribing: a critique of the 'minimalist' position. *Sociology of Health and Illness* 9, pp. 318–324.
- Woodhouse, G. Editor, , 1995. *A Guide to MLn for New Users* University of London, London.
- World Health Organisation Collaborating Centre for Drug Statistics Methodology, , 1993. . *Guidelines for Defined Daily Doses* World Health Organisation, Oslo.
- Wrigley, N., 1995. Revisiting the modifiable areal unit problem and the ecological fallacy. In: Cliff, A.D., Gould, P.R., Hoare, A.G. and Thrift, N.G. (eds). Editors, 1995. *Diffusing Geography: Essays for Peter Haggett* Blackwell, Oxford.

TABLES AND FIGURES

Table 1
 Descriptive statistics of neighbourhood characteristics

No. of inhabitants	Minimum (507)	Maximum (5151)	Average (2488)
<i>Social integration</i>			
Percent of people living alone	3.7	43.4	15.2
Percent one parent families	3.3	32.4	16.7
Percent no religious affiliation	45.2	69.2	59.4
Total migration	15.8	66.5	32.9
<i>Social deprivation</i>			
Percent social renting	0	56.5	11.4
Percent one family homes	20.6	100	84.0
Rooms per person	0.83	2.12	1.56
Internal migration surplus ^a	0	1	0.70

^a This variable is 1 for neighbourhoods with an internal migration surplus and 0 otherwise.

Table 2
 Correlation between neighbourhood characteristics (Pearson correlation)

	1	2	3	4	5	6	7	8
(1) Percent living alone	1.00	0.60	-0.10	0.91	0.24	-0.83	0.72	-0.09
(2) Percent one parent		1.00	-0.02	0.68	0.41	0.38	0.63	-0.24
(3) No re. affil.			1.00	-0.27	-0.39	0.22	0.00	0.32
(4) Tot. migration				1.00	0.39	-0.81	0.73	-0.24
(5) Percent soc. rent					1.00	-0.39	0.49	-0.49
(6) Percent one fam. home						1.00	-0.54	0.14
(7) No. rooms per person							1.00	-0.19
(8) Int. migr. surpl.								1.00

Table 3
 Logistic regression coefficients (and standard errors) of four two level models with user (1) or non-user (0) of benzodiazepines as dependent variable. *Significant at $p < 0.05$

	A	B	C	D
<i>Individual level</i>				
Intercept	-2.82 (0.096)	-3.22 (0.083)	-3.23 (0.06)	-3.27 (0.059)
Gender		0.52* (0.07)	0.52* (0.07)	0.52* (0.07)
Age		0.44* (0.018)	0.44* (0.018)	0.44* (0.019)
Age ^a		-0.06* (0.006)	-0.06* (0.006)	-0.06* (0.006)
Age ^a		0.004* (0.0008)	0.004* (0.0008)	0.004* (0.0008)
Gender*age		0.02 (0.015)	0.02 (0.015)	0.02 (0.015)
<i>Neighbourhood level</i>				
Social integration				
Level of integration ^a			0.01 (0.071)	-0.06 (0.079)
Percent one parent family			0.13 (0.066)	0.25* (0.073)
No religious affiliation			-0.06 (0.056)	0.02 (0.06)
Social deprivation				
Percent social renting			-0.16* (0.066)	-0.14 (0.071)
No. rooms per person			0.24* (0.082)	0.25* (0.094)
Internal migration surplus			0.10 (0.058)	0.02 (0.063)
<i>Cross-level interactions</i>				
Age*level of integration				0.01 (0.01)
Age*percent one parent				-0.03* (0.011)
Age*no religious affiliation				-0.02* (0.008)
Age*percent social renting				-0.006 (0.011)
Age*No. rooms per person				-0.008 (0.014)
Age*internal migration surplus				0.02* (0.01)
<i>Variance</i>				
Individual level	1.00	1.16 (0.007)	1.16 (0.007)	1.18 (0.007)
Neighbourhood level	0.20 (0.063)	0.11 (0.038)	0.04 (0.015)	0.03 (0.013)
<i>Contrast test neighbourhood variance</i>				
Chi-square (df=1)	10.23 ($p=0.001$)	9.09 ($p=0.0025$)	6.55 ($p=0.01$)	6.01 ($p=0.014$)
Moran's I	-0.245 ($p=0.09$)	-0.119 ($p=0.31$)	-0.149 ($p=0.24$)	0.10 ($p=0.16$)

^a Higher score indicates lower levels of integration.

Fig. 1. Percentage of users of benzodiazepines per neighbourhood.

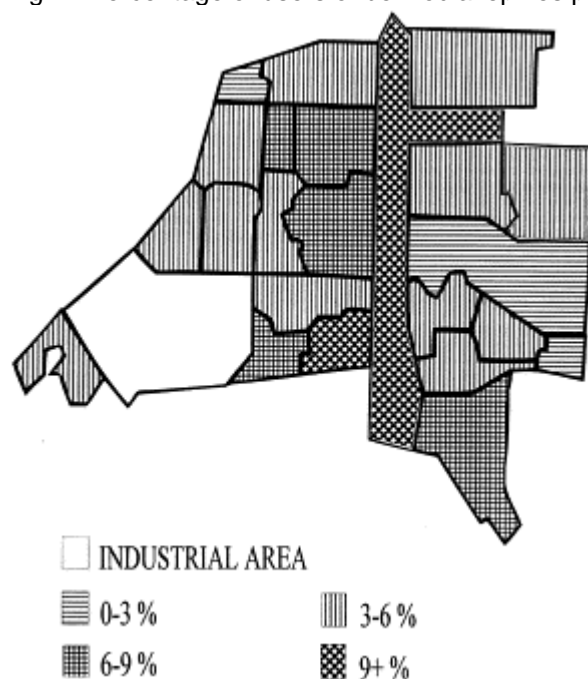


Fig. 2. Neighbourhood specific regression lines of age (in 14 categories) on use of benzodiazepines (with use of benzodiazepines on a logit scale).

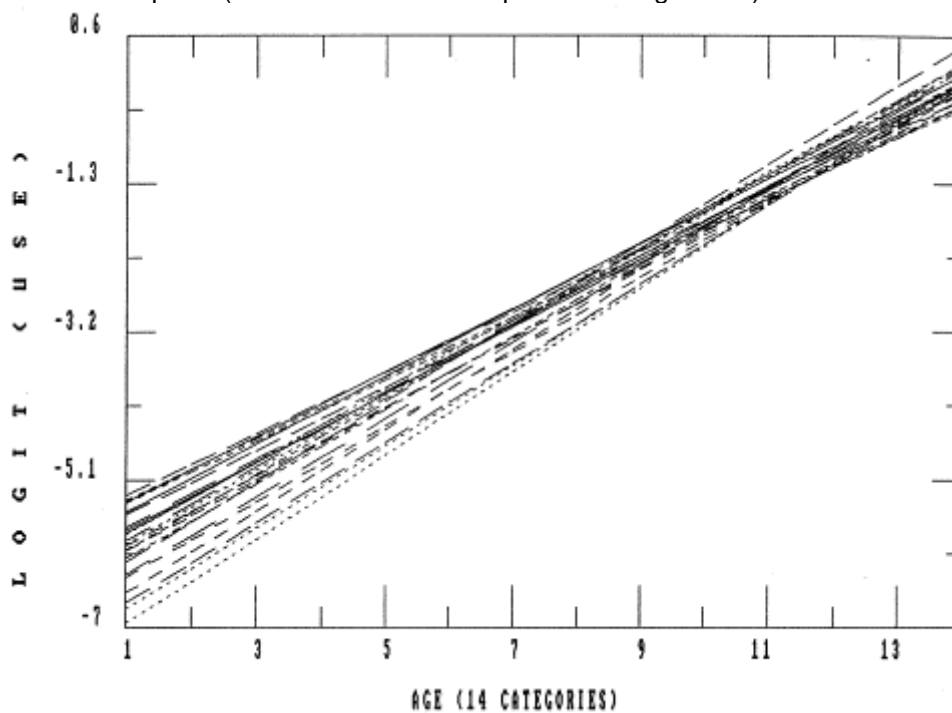


Table 4
 (Co-)variance components (and standard errors) of two-level models with random effects with user (1) or non-user (0) of benzodiazepines as dependent variable

	Model C + gender random	Model C + age random	Model D
<i>(Co-)variance components</i>			
Variance of intercepts for females	0.011 (0.01)		
Variance of intercepts for males	0.063 (0.024)		
Co-variance of intercepts for males and females	0.035 (0.014)		
Variance in age categories		0.003 (0.001)	0.001 (0.001)
Co-variance of age and use of benzodiazepines		-0.011 (0.0057)	-0.004 (0.003)
Variance of use of benzodiazepines		0.076 (0.032)	0.048 (0.023)
<i>Contrast test for neighbourhood (co-)variances</i>			
Chi-square (df = 1) female	1.22 ($p = 0.269$)		
Chi-square (df = 1) male	6.78 ($p = 0.009$)		
Chi-square (df = 1) male/female	6.47 ($p = 0.011$)		
Chi-square (df = 1) age		5.04 ($p = 0.025$)	1.70 ($p = 0.192$)
Chi-square (df = 1) age/intercept		3.96 ($p = 0.047$)	1.50 ($p = 0.221$)
Chi-square (df = 1) intercept		5.71 ($p = 0.017$)	4.33 ($p = 0.037$)

Table 5

Regression coefficients (and standard errors) for two level, mixed model regression with user (1) and non-user (0) as binary dependent variable and amount of benzodiazepines prescribed as continuous dependent variables. *Significant at $p=0.05$

	A (binary)	A (continuous)	B (binary)	B (continuous)
<i>Individual level</i>				
Intercept	-2.92 (0.100)	63.08 (2.416)	-3.22 (0.084)	163.5 (25.37)
Gender			0.52* (0.069)	17.06 (12.33)
Age			0.44* (0.018)	20.71* (4.036)
Age ²			-0.06* (0.006)	-0.72* (0.194)
Age ³			0.004* (0.0008)	
Gender*age			0.02 (0.015)	-1.34 (1.112)
<i>Variance</i>				
Individual level	1.00 (0.006)	7418 (186.6)	1.13 (0.007)	7173 (180.5)
Neighbourhood level	0.22 (0.068)	73.9 (38.43)	0.12 (0.039)	43.58 (28.49)
<i>Covariance</i>				
Binary-continuous response	3.23 (1.343)		1.37 (0.813)	
<i>Contrast test neighbourhood variance</i>				
Chi-square (df= 1) binary	10.28 ($p=0.001$)		9.18 ($p=0.002$)	
Chi-square (df= 1) continuous		3.70 ($p=0.054$)		2.34 ($p=0.126$)
Chi-square (df= 1) binary/continuous		5.50 ($p=0.019$)		2.84 ($p=0.092$)