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Comparison of Long-Term Benzodiazepine Users in Three Settings

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Background. Most studies of chronic benzodiazepine users consider selected populations which may be unrepresentative. This study was undertaken to examine possible differences between groups.
Method. Subjects chosen were benzodiazepine users in general practice, a hospital clinic, and attending TRANX trials. Descriptive data were collected on characteristics and outcome.
Results. TRANX trial patients had the best outcome ($P=0.027$). Hospital cases used high doses of anxiolytic benzodiazepines; concomitant mental disorder, including schizophrenia, was common. General practice cases were older and mainly used hypnotics ($P<0.05$).
Conclusions. Because groups of benzodiazepine users are different, there cannot be one single management approach. Cases require individual medical assessment.

Approximately 8–10% of the general population take a benzodiazepine each year, although the prescribing rate has apparently fallen by 20% over the last eight years (Mellinger *et al*, 1971; Balter *et al*, 1984; Koenig *et al*, 1987; Dunbar *et al*, 1989). This reduction has been mainly in anxiolytic prescribing, while prescribing rates for hypnotics have remained constant.

Dependence and withdrawal syndromes are recognised complications of benzodiazepine use (Hallstrom & Lader, 1982; Owen & Tyrer, 1983). These may impair psychomotor performance and represent a particular hazard for the elderly (Hendler *et al*, 1980; Golombok *et al*, 1988). The long-term use of benzodiazepines is discouraged (Committee on Safety of Medicine, 1988; Department of Health, 1992; British Medical Association, 1993).

Our knowledge of the characteristics of benzodiazepine users and how they respond to treatment is based largely on patients treated in hospitals. Response to intervention is generally reported as being good. However, patients treated in specialist units may be unrepresentative of the wider population of benzodiazepine users in general practice. For example, hospital studies tend to comprise relatively young, female, anxiolytic users who are presumably strongly motivated towards treatment (Ashton, 1987; Golombok *et al*, 1987; Crouch *et al*, 1988). Those recruited to controlled studies may differ greatly from patients who are not eligible to enter a study, or who refuse to do so. In community and general practice studies, the drug used is more commonly a hypnotic, the patients are on average older, and prescribing rates rise with increasing age. There also appears to be an association with poor physical health, and the preponderance of female cases is less marked (Cummins *et al*, 1982; Morgan *et al*, 1988; Simpson *et al*, 1990). Although one study showed that minimal intervention by a general practitioner (GP) can help patients to stop drug use (Cormack *et al*, 1989), another study of group therapy in general practice showed that most patients either declined the offer or dropped out after two sessions (O'Leary, 1989). Thus one must doubt the validity of extrapolating findings based on hospital studies to general practice (King *et al*, 1990).

Another important difference between populations of chronic benzodiazepine users could be the degree of preexisting psychopathology. Both Tyrer (1989) and Ashton (1989) focused attention on this issue rather than on the properties of the drugs. They cite personality disorder, mood disorder and neurotic traits as strong predisposing factors to drug dependence. It would be reasonable to hypothesise that patients treated by psychiatrists would have the greatest comorbidity, compared with those treated by self-help groups or GPs. If such variations do exist, any attempt to employ a uniform treatment approach is likely to be misguided.

Method

The three settings for the study were: (a) the Benzodiazepine Dependence Clinic at Charing Cross Hospital, London; (b) TRANX; and (c) general practice.

The clinic at Charing Cross Hospital provides both a national and a district service, and receives over 100 referrals a year. Patients are referred by GPs, psychiatrists and clinical psychologists, and self referrals are also accepted. It is a research clinic staffed principally by a psychiatrist of senior registrar grade who has at his disposal the resources of an academic teaching hospital department (Crouch *et al*, 1988).

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TRANX (Tranquilliser Recovery and New Existence) is the largest and best known of the self-help organisations. It provides education, advice and counselling to benzodiazepine users. Its approach is rigorously non-medical, and the central philosophy of the organisation is that tranquilliser use is unhealthy and abstinence can be facilitated by peer group support. Further details of this component of the study are reported by Tattersall & Hallstrom (1992).

The general practice patients were drawn from a clinic close to the hospital. The practice was chosen as the GP has an interest in research and an established computerised patient database. The list size was 4780, of whom 54.2% were male.

Data collection

Hospital clinic

At first consultation, patients were given a standard psychiatric interview supplemented by a standard research schedule. All patients were interviewed by the same researcher (CJH). Data for all patients were included in the series, whether or not they elected to undertake a treatment programme. Patients were followed up for between 6 and 18 months. For patients who completed or dropped out of treatment before six months, outcome data was taken as that recorded at the last contact.

TRANX

Initial contact information was recorded by an experienced, but non-professional, receptionist using a standard data collection schedule. A research psychiatrist (MT) followed up the clients nine months later by telephone. Telephone interviews lasted 15–20 minutes. Details of data collection in this setting are reported by Tattersall & Hallstrom (1992).

General practice

The computer database was used to identify all patients who had been prescribed benzodiazepines continuously for 12 months or more. The point prevalence of chronic use was 1.5% for this GP's list. This is a relatively low figure (Cummins *et al*, 1982; Morgan *et al*, 1988). The patients' case notes were scrutinised to obtain further information. The patients' computer records and case notes were reexamined after nine months to establish outcome.

Results

The patients' age and sex characteristics are summarised in Table 1. Among the TRANX clients, 14% ($n = 16$) were over the age of 65. In the hospital clinic, only five patients (4%) were over 65. The highest proportion of older patients was found in general practice; 27 (36%) were aged 65 years or more ($\chi^2 = 36$, d.f. = 2, $P < 0.01$).

Table 1
Age, sex and marital status in the three groups

	Clinic	TRANX	General practice
n	117	117	74
Sex m : f	3 : 1	5 : 1	1.3 : 1*
Mean age (years)**	44.4	47.0	62.9
s.d.	11.4	12.6	18
% married	39%	77%	67%***

*$\chi^2 = 18.4$, $P < 0.01$.
**F test: clinic v. GP = 18.6, $P < 0.05$; TRANX v. GP = 4.3, $P < 0.05$; clinic v. TRANX = 2.6, $P > 0.05$.
***$\chi^2 = 47$, $P < 0.01$.

Drug use

The mean duration of drug use was similar in all three settings, at a mean of around 9.5 years. The drug used was classified either as a hypnotic or an anxiolytic, based on whether the drug was listed under section 4.1.1. or 4.1.2 in the *British National Formulary* (BMA, 1992). The clinic patients and TRANX clients principally used anxiolytics, typically diazepam or lorazepam. The converse applied to the general practice patients, the majority of whom used a hypnotic (Table 2).

Doses of the various benzodiazepines taken were expressed as milligram equivalents of diazepam (Higgitt *et al*, 1985). Expressing the daily dose in milligram equivalents of diazepam, it was found that the mean daily intake for the clinic patients was 37.9 mg, while the TRANX and GP patients were

Table 2
Drug use by dose, duration and type

	Clinic	TRANX	General practice
Duration of drug use			
years	9.6	10.0	8.6*
s.d.	6.8	7.6	6.6
Type of drug:			
anxiolytic	60%	71%	22%**
hypnotic	14%	16%	70%
both	26%	13%	8%
Mean dose/day			
(mg DEquiv)	37.9	8.8	14.7
s.d.	42.4	8.5	16.8
range	1–300	1–41	1–100

*F test, $P > 0.05$.
**$\chi^2 = 90$, $P < 0.001$.

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taking 8.8 mg and 14.7 mg a day respectively ($F=22.9$, $P<0.05$).

Psychiatric history

Forty-six per cent of the clinic patients, 25% of the TRANX clients and 20% of the GP patients had been admitted as psychiatric in-patients at some point in their adult lives ($P<0.01$). These admissions were not simply for help with the addiction problem. For example, in over half of the clinic patients with a history of in-patient psychiatric treatment, this had antedated the long-term use of benzodiazepines.

Outcome

The outcome was judged according to the following criteria. A 'good' outcome was represented by cessation of drug use or reduction to less than 25% of the initial dose, with continuing progress and little disability. Those who reduced the dose by less than 25%, made no reduction, or increased the dose, were considered to have a bad outcome. Dose reduction by 25–75%, or reduction by more than this amount but only at the expense of other problems (e.g. anxiety symptoms, relapse of alcoholism or depression), was considered as a moderate outcome.

All patients attending the clinic were offered treatment. Some made only half-hearted attempts at compliance, and others had such severe psychiatric disorder that the prognosis appeared hopeless from the start. However, as all patients were referred for treatment, not merely advice, the whole series is analysed.

The outcome is summarised in Table 3. Of the GP patients, eight had died or moved away, leaving a sample of 66 cases. The outcome was much better for the TRANX clients than the other two groups. The principal is the excess of good outcomes versus moderate or poor outcomes between the TRANX and clinic groups (d.f. = 1, $\chi^2=4.8$, $P=0.027$).

There were within-group differences in the outcomes. In the TRANX group, a poor outcome was associated with higher initial dose ($P=0.01$), longer duration of use ($P<0.01$) and the use of lorazepam rather than diazepam ($P=0.03$). These associations were not found in the other patients.

Eighteen patients in the clinic group were enrolled in a placebo-controlled trial of withdrawal under antidepressant cover. They did much better than the other 99 patients; 77% of cases had a good or moderate outcome, compared with 40% of the rest of the clinic population ($\chi^2=9.3$, $P<0.01$).

Table 3
Outcomes for the three groups after nine months follow-up

Outcome	Clinic ($n=117$)	TRANX ($n=117$)	General practice ($n=66$)
Good	19 (16%)	33 (28%)	11 (17%)
Moderate	35 (30%)	25 (21%)	7 (11%)
Poor	63 (54%)	59 (51%)	48 (72%)

Psychiatric state of the clinic patients

Detailed examination of the clinic patients gave further valuable information about their psychiatric state. Although strictly comparable data is not available for the chronic benzodiazepine users in the other settings, it is presented here as it appears to illustrate differences between the groups.

Diagnosis of any concomitant psychiatric illness was made according to DSM-III-R criteria (American Psychiatric Association, 1987) (Table 4). More than half the patients were suffering from anxiety or depressive disorders, in addition to benzodiazepine dependence. A small but important group were suffering from schizophrenia, and it is noteworthy that three of these had not been previously diagnosed. The patients suffering major depression were rated on the Montgomery-Åsberg Depression Rating Scale (1979). The mean score was 27.1 (range 14–45). Five patients scored greater than 40, suggesting severe illness.

Discussion

The characteristics of the chronic benzodiazepine users in the three settings show important differences. The patients in general practice were relatively old and mainly took hypnotics in normal doses. This group exhibited a conspicuous lack of interest in having any help with their chronic drug use. In order to validate the data available from the computerised records and the doctors' notes, half of the group were approached by telephone. Most did not consider

Table 4
DSM-III-R diagnoses in the clinic sample (single preferred diagnosis)

Axis 1 diagnosis	*n*
None	21 (18%)
Panic disorder and/or generalised anxiety disorder	30 (26%)
Other neuroses	6 (5%)
Depressive disorders	30 (26%)
Alcohol abuse and/or dependence	12 (10%)
Multiple drug abuse	6 (5%)
Schizophrenia	7 (6%)
Other	5 (4%)
Total	117 (100%)

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they had a "problem" and less than a fifth were prepared to be interviewed in person.

The TRANX clients comprised predominantly young married women, typically taking modest doses of anxiolytic drugs. They were seemingly highly motivated and do well even without intensive intervention. The principal characteristics of the group (good motivation, low dose dependence on a single agent, and only moderate psychiatric comorbidity) could be taken to indicate an inherently good prognosis at the outset.

The group referred to the hospital clinic had the greatest problems. Their mean daily dose was three times greater than the other two groups, and they were more likely to be taking both an hypnotic and an anxiolytic. Over half had a history of psychiatric treatment, and the majority received psychiatric diagnosis in addition to that of benzodiazepine dependence. For many patients, the main focus of treatment was the concomitant psychiatric disorder rather than the benzodiazepine dependence. Of particular concern were those suffering from schizophrenia or severe major depression. These patients received intensive interventions, including admission to hospital and electroconvulsive therapy. Treatment within the TRANX model, which denies the use of any psychoactive drugs, could be considered at least hazardous, and at worst potentially fatal, for such patients.

The TRANX approach could not be considered a viable alternative even for the less severely ill patients attending the hospital clinic. Psychiatric expertise was of great importance in identifying and treating the concomitant neurosis, depression and substance misuse. The treatment necessary could not have been undertaken by a GP. This underlines the need for proper assessment of long-term tranquilliser users, and for treating any concomitant psychopathology before contemplating tranquilliser withdrawal.

The situation in general practice is interesting. The advanced age and seeming absence of motivation militates against any strategy, pharmacological or psychological, being effective. We suggest that belated attempts at treatment in this group will do little good and create more problems than are solved. Injunction towards abstinence may be resisted by the patients.

Conclusions

Major differences may exist between populations of benzodiazepine users. The differences between the groups are validated by the difference in outcomes. Extrapolation of the results of treatment and outcome from studies in one setting to another may well be erroneous.

In summary, the authors would contend that: (a) the evaluation of treatment studies for benzodiazepine dependence should take into consideration the context of the patient population to which they are applied; (b) there is no uniform management strategy that represents the 'best' way to treat benzodiazepine dependence; and (c) medical assessment is required to detect and treat comorbid illness.

The greatest success will be achieved by having a diversity of response, catering for the various needs of different groups.

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