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The influence of patient variables on polypharmacy and combined high dose of antipsychotic drugs prescribed for in-patients†

AIMS AND METHOD
A 1-day census, involving 3576 psychiatric in-patients prescribed antipsychotic medication, was conducted as a prelude to a multi-centre audit. The aim was to explore the extent to which a number of patient variables explain antipsychotic polypharmacy and the use of high doses of these drugs.

RESULTS
Prescriptions of more than one type of antipsychotic drug were made for 50.5% of patients. Patient factors that influenced the probability of polypharmacy were: younger age, being male, detained under the Mental Health Act and on a rehabilitation or forensic ward, and a diagnosis of schizophrenia. The effect of ethnicity was not significant. Polypharmacy was the most powerful factor influencing the probability of being prescribed a high dose. Identified patient variables accounted for only 18% of the variance in dose prescribed.

CLINICAL IMPLICATIONS
The patient and clinician factors that account for the unexplained variance need to be identified.

A large multi-centre audit (Harrington *et al*, 2002*a*, this issue) found that psychiatric in-patients in the UK are often prescribed more than one antipsychotic drug concurrently (polypharmacy). Furthermore, the effect of polypharmacy is that patients are often also prescribed a high dose of antipsychotic medication. A 1-day census of prescribing, conducted as a prelude to the multi-centre audit, was large enough to examine the extent to which these prescribing practices can be explained by a number of patient variables.

Method

The sample and data collection

Forty-nine mental health services volunteered to participate in the initial census. All the psychiatric wards concerned specialised in the care of people aged 18–65. However, patients outside of this age range were included if they occupied a bed in one of these wards on the census day.

All patients prescribed an antipsychotic drug between midnight 20 July and midnight 21 July 1998 were included. Data were collected from prescription charts about the type, dose and route of administration of all antipsychotic drugs administered and/or prescribed during the census period. In addition, the age, gender, ethnicity, diagnosis (according to ICD–10; World Health Organization, 1992) and Mental Health Act (MHA) status of all 3576 patients were recorded together with the type of psychiatric bed that they occupied (acute, rehabilitation or forensic).

Data management

Data were returned to the Royal College of Psychiatrists' Research Unit and analysed using SPSS for Windows, version 8.

Missing data

Age was not recorded for 55 subjects (1.5%), gender for 20 (0.6%), ethnicity for 372 (10.4%), MHA status for 22 (0.6%) and diagnosis for 111 (3.1%). All valid cases were included in each analysis.

Data analysis

Thirty-one different antipsychotic drugs were prescribed for the patient sample (22 oral preparations, 4 drugs in aqueous solution to be given parenterally and 5 in longer-acting preparations to be given intramuscularly). Furthermore, many patients were prescribed more than one antipsychotic drug concurrently (see Results). For the regression analysis, the doses of these antipsychotic drugs had to be standardised and summed. The method used is described in an accompanying paper (Harrington *et al*, 2002*a*, this issue).

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The probability of a subject being prescribed polypharmacy was modelled using logistic regression. The dependent variable was whether more than one antipsychotic drug was prescribed to be given during the 24-hour census period (yes/no). The independent variables (age, gender, ethnicity, MHA status, diagnosis and ward type) were entered individually and then in combination.

A second set of logistic regressions was performed with the dose of antipsychotic prescribed as the dependent variable (high dose/standard dose) and polypharmacy (yes/no) as a further independent variable. Linear regression was also carried out with the dose prescribed expressed as a continuous variable (percentage of *British National Formulary* (*BNF*; British Medical Association & Royal Pharmaceutical Society of Great Britain, 1999) maximum) and using the same explanatory variables.

Finally, the regression analyses were repeated using dose of antipsychotic medication actually administered as the dependent variable. That is, medication that was prescribed but not given during the census period was excluded from the analysis.

Results

Description of the sample

A total of 3576 patients were prescribed at least one antipsychotic drug during the census period. Sixty-one per cent (n=2169) were men; their mean age was 40 years (range 15–96; median 38). Eighty-four per cent were White (n=2691), 10% Black (n=310), 4% Asian (n=142) and 2% from another ethnic minority group (n=61). Nearly a half (49%; n=1757) were detained under the MHA. Sixty-two per cent (n=2202) were on an acute ward, 27% (n=969) on a rehabilitation ward and 11% (n=405) on a forensic ward. The majority of patients (62%, n=2158) had a primary ICD–10 diagnosis of schizophrenic or delusional disorder (F2); 22% (n=758) of mood disorder (F3); 5% (n=188) of personality disorder (F6); 4% (n=134) of organic mental disorder (F1); and 3% (n=113) of neurotic, stress-related or somatoform disorder (F4). The remainder (n=113) had a variety of other diagnoses.

There were differences between groups within the sample. The mean age of women was significantly higher than that of men (42.9 *v.* 39.0 years, 95%; CI of the difference=3.1–4.8; t-test, t=8.7, $P<0.001$). Men were more likely to be formally detained than women (54% *v.* 43%; χ^2=37, $P<0.001$). Black and Asian people and those from other ethnic minorities were younger than the White people (36.1, 36.0 and 33.5 *v.* 41.0; Kruskal–Wallis, χ^2=71, $P<0.001$). A higher proportion of those from the three ethnic minority groups were detained under the MHA than those who were White (78%, 61% and 66% *v.* 47%; χ^2=120, $P<0.001$).

Polypharmacy

Half of patients were prescribed more than one antipsychotic drug concurrently (50.5%; n=1807). The results of the logistic regression for polypharmacy can be summarised as follows:

(a) the odds for a person to be prescribed more than one antipsychotic drug decreased by about 12% for an age increase of 10 years; the great majority of this sample were aged 18–65
(b) the odds for men were 1.4 times those for women
(c) the odds for a person detained under the MHA were 1.9 times those for a person with informal MHA status
(d) the odds for a person on a rehabilitation ward or forensic ward were 1.3 times those for a person on an acute ward
(e) a person with schizophrenic or delusional disorder was more likely to be on polypharmacy than a person suffering from another type of disorder
(f) the effect of ethnicity was not significant.

Doses of antipsychotics

Although 23.3% (n=832) of patients were prescribed a high dose, this was actually administered to only 10.4% (n=371) during the 24-hour census period. The difference was almost entirely accounted for by 'as required' medication that was written on the prescription chart but not given during the census period.

Effects of variables on dose of antipsychotics

Fewer than 1% of patients (n=34) were prescribed a single antipsychotic drug at a dose that exceeded *BNF* limits. For the remainder, high dose was owing to the effect of the concurrent prescription of more than one antipsychotic. Thus, only 2% of the 1769 subjects prescribed a single antipsychotic drug were prescribed a high dose compared with 44% of the 1807 subjects who were prescribed more than one antipsychotic drug. This difference was highly significant (χ^2=900, $P<0.0001$).

The effects identified by the regression involving high dose can be summarised as follows:

(a) polypharmacy is by far the most powerful factor influencing the probability of a subject being prescribed a high dose. For a patient prescribed more than one antipsychotic drug, the odds of also being prescribed a high dose were 41 times those for a patient who was prescribed a single drug
(b) for this patient sample, the great majority of whom were aged 18–65, the odds of a person being prescribed a high dose decreased by 11.9% for every 10-year increase in age
(c) the odds for a man were 1.7 times those for a woman
(d) the odds for a person detained under the MHA were 2.4 times those for an informal patient
(e) the odds for a person on a rehabilitation or forensic ward were about 1.6 times those for a person on an acute ward

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Table 1. High-dose prescribing and polypharmacy by bed type

Prescription	Bed type		
	Acute	Rehabilitation	Forensic
Total high dose (*n*)	434	278	120
High dose plus polypharmacy (*n*, %)	412 (95)	270 (97)	116 (97)
High dose with depot drugs[1] (*n*, %)	185 (43)	126 (45)	80 (67)
High dose with 'as required' drugs[2] (*n*, %)	379 (87)	214 (77)	90 (75)

1. χ^2=22.3; d.f.=2; $P<0.0001$.
2. χ^2=17.1; d.f.=2; $P<0.0001$.

(f) a person with a diagnosis of schizophrenic or delusional disorder (F2) was much more likely to be prescribed a high dose than a person with another diagnosis

(g) the effect of ethnicity was not significant.

The effects of each explanatory variable changed little after controlling for all the others, apart from age and gender, which became insignificant.

Using dose of antipsychotic actually administered as the dependent variable in the regression gave very similar results to that which used dose prescribed.

The linear regression, using prescribed dose expressed as a percentage of *BNF* maximum, yielded very similar results to the logistic regression analysis. Age, gender, ethnicity, MHA status, diagnosis and ward type in combination explained only 18% of the variance in high-dose prescribing. However, 40% of the variation was explained when polypharmacy entered the linear regression model along with these six other explanatory variables.

Differences between patients in different types of beds

Patterns of prescribing by bed type are given in Table 1. Compared with acute and rehabilitation wards, forensic wards had a higher proportion of patients receiving high-dose antipsychotic medication, who were on depot medications.

Discussion

The finding that most high-dose prescribing is strongly associated with polypharmacy replicates the conclusion of one small-scale survey in the UK (Chaplin & McGuigan, 1996) and a much larger one in Italy (Tibaldi *et al*, 1997). That high-dose prescribing is more common for younger people and for those with a diagnosis of schizophrenic or delusional disorder has also been reported for patients in Italy (Muscettola *et al*, 1991; Tibaldi *et al*, 1997) and in the US (Benson, 1983). A recent study in the US has reported that African American patients with schizophrenia are more likely than White patients to be treated with higher doses of antipsychotic medication (Walkup *et al*, 2000). The absence of any effect of ethnicity on either polypharmacy or high-dose prescribing in this UK sample is striking, given the concern commonly expressed that psychiatric services respond differently to patients of different ethnic origin (Bhui, 1998).

Being detained under the MHA approximately doubled the odds of being prescribed or receiving either more than one antipsychotic drug or a high dose. It could be argued that patients admitted compulsorily are more disturbed than those admitted informally. However, this argument is uncertain, given the current pressure on in-patient beds (Harrington *et al*, 2002*b*, this issue).

The results of this study highlight the need for further and more detailed examination of the patient characteristics that influence prescribing practice. Despite the significant contributions found for the explanatory variables measured in this study, together they explained less than a fifth of the variance in the combined dose of antipsychotic medication. Other characteristics of the patient that might account for some of this unexplained variance include: length of illness, history of relapse, level of disturbance, resistance of symptoms to antipsychotic medication and pharmacokinetic differences between individuals. Some of the variance might also be due to differences between clinicians (Wilkie *et al*, 2001) and/or the characteristics of the treatment setting. These factors are considered more fully elsewhere (Harrington *et al*, 2002*b*, this issue).

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Declaration of interest

C.P. has very occasionally received speaker fees from Eli Lilly and Pfizer. Over the past year she has been involved with research projects funded by Novartis, Eli Lilly and Janssen-Cilag, but has not received any personal income from those projects. T.S. has been paid honoraria by numerous pharmaceutical companies for contributing to educational events. In 2000 he attended a meeting as a participant in an advisory board for Pfizer. The views expressed do not necessarily reflect those of the Royal College of Psychiatrists.

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The results of a multi-centre audit of the prescribing of antipsychotic drugs for in-patients in the UK†

AIMS AND METHOD

Forty-seven UK mental health services participated in a 1-day audit of prescribing of antipsychotic drugs. Audit standards were derived from national guidelines and consensus statements.

RESULTS

Of the 3132 patients, 20% were prescribed a total dose of antipsychotic medication above that recommended by the *British National Formulary*. The majority of case notes failed to record an indication for high-dose prescribing or that the patient had been informed; only 8% had undergone an electrocardiogram. Forty-eight per cent of patients were prescribed more than one antipsychotic drug.

CLINICAL IMPLICATIONS

Antipsychotic prescribing for in-patients often runs counter to existing guideline recommendations. It is likely that many patients who are prescribed high doses or polypharmacy are unaware that their prescription is out of line with guideline recommendations and is inadequately monitored.

In the UK, 23 antipsychotic drugs are available on prescription, many by more than one route. Most side-effects of these drugs are dose related, cause substantial morbidity and may contribute to poor treatment adherence (American Psychiatric Association, 1997). It remains unclear whether the risk of sudden death, acknowledged to occur with antipsychotic drugs, is dose related (Royal College of Psychiatrists, 1997). Existing research offers limited guidance on optimal prescribing in individual circumstances. However, reviews have concluded that, in general, the use of high doses or of polypharmacy (simultaneous use of more than one antipsychotic drug) offers little, if any, benefit over moderate doses of a single drug, in relation to the disadvantages (Royal College of Psychiatrists, 1993). This evidence has influenced the development of national guidelines and consensus statements.

Method

Development of the audit standards

Five English-speaking countries have published national guidelines or consensus statements that refer to the prescribing of antipsychotic drugs (American Psychiatric Association, 1997; EPPIC Statewide Services, 1999; New Zealand Ministry of Health, 1996; Royal College of Psychiatrists, 1993, 1997; Working Group for the Canadian Psychiatric Association and the Canadian Alliance for Research on Schizophrenia, 1998). All advise against the use of high doses other than in exceptional circumstances. Four make a similar, explicit recommendation in respect of polypharmacy. Audit standards were derived from these documents and were presented to, and agreed by, a separate 'expert panel' of psychiatric pharmacists and psychopharmacologists. The standards audited, and the measures used to audit them, are shown in Table 1.

Dose

The *British National Formulary* (*BNF*; British Medical Association & Royal Pharmaceutical Society of Great Britain, 1999) states a maximum recommended dose, or a dose range for all antipsychotic drugs except trifluoperazine. The Royal College of Psychiatrists' consensus statement (Royal College of Psychiatrists, 1993) recommends that, when an antipsychotic is given at a dose above the

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