

THE NITHSDALE SCHIZOPHRENIA SURVEYS

ROBIN GRAEME McCREADIE

Submitted for the Degree of DSc in Science

August 1992

Department of Clinical Research  
Crichton Royal Hospital  
DUMFRIES DG1 3TG

© Robin McCreadie  
1992

ProQuest Number: 13834112

All rights reserved

INFORMATION TO ALL USERS

The quality of this reproduction is dependent upon the quality of the copy submitted.

In the unlikely event that the author did not send a complete manuscript and there are missing pages, these will be noted. Also, if material had to be removed, a note will indicate the deletion.



ProQuest 13834112

Published by ProQuest LLC (2019). Copyright of the Dissertation is held by the Author.

All rights reserved.

This work is protected against unauthorized copying under Title 17, United States Code  
Microform Edition © ProQuest LLC.

ProQuest LLC.  
789 East Eisenhower Parkway  
P.O. Box 1346  
Ann Arbor, MI 48106 – 1346

Thesis  
9444  
Copy 1



## ACKNOWLEDGEMENTS

My principal acknowledgement is to the patients of Nithsdale and their relatives whose willing co-operation over many years made the project possible. The surveys also depended on the enthusiasm and energy of trainee psychiatrists at Crichton Royal Hospital, Dumfries. Not only did they help collect the data, but contributed to many of the discussions: Drs Barron, Berry, Crorie, Ewing, Hall, Phillips, Robertson, Robinson, Stewart, Waldron and Winslow.

Mr David Wiles, Principal Biochemist, The Laboratory, Crichton Royal was responsible for assaying plasma neuroleptic levels; Dr Michael Geals, Consultant Obstetrician, Cresswell Hospital, Dumfries, gave advice about the development of a semistructured interview for use with the Obstetric Complications Scale; and Ms Jackie Harvey and Mr David Baird, Mental Health Officers, participated in the treatment programme for patients and their relatives.

Finally, invaluable secretarial and other support has been given throughout the project by Mrs Marion McCormick, Research Assistant.

## CONTENTS

	Page
Acknowledgements	2
Summary	5
1. Introduction.	8
2. The Patient	
2.1 Psychiatric and social handicaps.	18
2.2 Social adjustment by self report.	32
3. The Family	
3.1 Relatives' expressed emotion: prevalence, patterns and clinical assessment.	45
3.2 Does relatives' high expressed emotion predict relapse?	62
3.3 Do relatives want family intervention - and does it help?	74
3.4 Stability of relatives' expressed emotion over five years and its relation to relapse.	85
4. Movement Disorders	
4.1 Abnormal movements.	100
4.2 Handedness and tardive dyskinesia.	110
4.3 Follow-up of tardive dyskinesia at 3½ years.	120
4.4 Akathisia, parkinsonism, tardive dyskinesia and plasma neuroleptic levels.	129

5.	Obstetric Complications	
5.1	Obstetric complications, movement disorders and family history.	150
	REFERENCES	168

## SUMMARY

A generation of schizophrenic patients has grown up since the introduction in the 1950's of community care and antipsychotic medication, and over the past two decades many have been exposed to long term maintenance antipsychotic drug treatment. However, there have been very few studies describing the impact of these developments on a community of schizophrenic patients. The Nithsdale surveys over a 10 year period have tried to do this. The studies fall into three broad groups: the mental state, behaviour and social adjustment of the patient; the family life of the patient, with special reference to relatives' expressed emotion; and the motor disorders produced by antipsychotic medication. Most recently, the frequency of obstetric complications in schizophrenic patients has been examined.

### THE PATIENT

The first census in 1981 of all known schizophrenic patients in Nithsdale, Dumfries and Galloway Region, Scotland identified 133 patients, a point prevalence of 2.38 per 1,000 of the total population. Only three percent of the cohort had no abnormality in mental state or behaviour; negative schizophrenic symptoms were prominent. Only one quarter were inpatients. Patients' and their relatives' assessment of the patient's overall social adjustment correlated very closely, thus suggesting a schizophrenic patient can satisfactorily describe his own adjustment. The patients were less well adjusted than a normal community population in all areas except the parental role.

### FAMILY LIFE

A repeat census in 1985 found that 50 percent of patients were living with relatives or friends. The family atmosphere, that is, the relatives' level of expressed emotion (EE), was assessed through the Camberwell Family Interview. Thirty two percent of patients

living with relatives or friends had high face-to-face contact with a relative showing high EE; put another way, 87% of all Nithsdale schizophrenic patients were not living in a high contact/high EE family. Parents were more critical than spouses, and more showed emotional overinvolvement. A prospective 12 month follow-up identified relapsing patients. There was no difference in relapse rates in patients living on their own, with low EE or with high EE relatives. Amount of contact with high EE relatives did not affect relapse rates.

A further census in 1987 identified 77 patients living at home with relatives or friends. Sixty three relatives of 52 of these patients were offered a package of treatments by professionals working in an everyday NHS setting: educational seminars, relatives' groups and family meetings. Thirty two relatives refused intervention. Of the 31 relatives who agreed, 14 attended neither the educational seminars nor the relatives' groups. Seventeen relatives had a mean of 10 treatment sessions but there was little change in their level of EE after intervention. The number of patients who relapsed was the same in the 18 months before and after intervention, although the total number of relapses fell after intervention.

By 1990 30 relatives and 30 schizophrenic patients had lived together continuously for five years. The relatives had had their level of EE assessed on three separate occasions over the five years, namely in 1985, 1987 and 1990. In the majority of relatives (63%) the level of EE was stable over time. Patients who relapsed were evenly spread throughout those living in a consistently high, consistently low or fluctuating EE home. However, patients living in low EE homes who did relapse did so significantly less often than those who relapsed and were living in high or fluctuating EE homes.



## MOTOR DISORDERS

The prevalence of abnormal movements, side effects of the antipsychotic drugs, was examined in the 1981 cohort. Thirty one percent of patients had parkinsonism and 31% tardive dyskinesia (TD). Patients with TD were significantly older than those without TD and more showed flattening of affect and social withdrawal. A repeat census in 1989 identified 161 patients, 146 of whom were assessed for the presence of akathisia (18%), pseudoakathisia (5%), TD (29%) and parkinsonism (27%). Forty four percent had no movement disorder, 36% one and 20% more than one movement disorder. The presence of TD had also been assessed in 61 of the 146 patients in 1981 and 1984. Only 8% showed TD on all three occasions. There was no relationship between plasma antipsychotic drug levels and akathisia, parkinsonism or TD. More non-right-handed than right-handed patients showed TD. Patients with parkinsonism or receiving an antiparkinsonian drug more often had a history of at least one definite obstetric complication.

## OBSTETRIC COMPLICATIONS

Fifty one mothers of 54 patients of the 1989 cohort were interviewed to obtain obstetric histories of patients and their sibs. There was no statistically significant difference in the proportion of schizophrenic patients (35%) and sibs (29%) who had at least one definite obstetric complication. There was also no evidence that patients with a history of obstetric complications were less likely to have a first degree relative with a history of psychiatric illness leading to inpatient care. There was a trend for TD to be more common in those patients with no obstetric complications, but a family history of schizophrenia.

## 1 INTRODUCTION

## INTRODUCTION

Over the past 30 years there have been two radical changes in the management of the schizophrenic patient. Firstly, although the mean length of a schizophrenic illness is approximately 15 years (Cooper, 1978), most patients now spend most of their time outside hospital - so called 'community care'. This is illustrated in Tables 1.1 and 1.2. The total number of residents in Scottish mental illness hospitals and psychiatric units has fallen between 1970 and 1990 from 18,297 to 13,229, a fall of 28%. The principal reason for this fall is the reduction in the number of schizophrenic inpatients, from 5,109 to 2,742, a fall of 46%. In contrast, changes in the number of patients suffering from the second most common psychiatric diagnosis leading to admission in 1970, namely senile and presenile organic psychotic conditions, have been in the opposite direction. The number has increased over the 20 years from 3,006 to 4,724, an increase of 57%.

Part of the reduction in the number of residents with schizophrenia may be due to a falling incidence of the disease (Der et al, 1990). As it is probable that almost all patients with schizophrenia will have at least one inpatient admission, first admission rates will reflect incidence. Table 1.3 shows that first admissions between 1975 to 1990 dropped from 495 to 399, a fall of 19%.

However, a more important reason for the reduction in the number of residents with schizophrenia, and the second radical change in the management of schizophrenia, was the introduction in the 1950's of antipsychotic medication. Such drugs in placebo-controlled studies were found to be effective in the treatment of the acute episode (e.g. NIMH Psychopharmacology Service Centre Collaborative Study Group, 1964) and as maintenance therapy (Hogarty and Ullrich, 1977). Antipsychotic drugs have improved

and maintained the patient's mental state so that life outside hospital has become possible. Antipsychotic drugs do not prevent relapse, they postpone it. Thus readmission(s) to hospital will prove necessary for most patients (Scottish Schizophrenia Research Group, 1992). This is illustrated in Table 1.3. Although patients are spending less total time in hospital the ratio of readmissions to first admission of schizophrenic patients has increased between 1975 and 1990 from 2,124: 495 (4.3:1) to 3,215: 399(8.1:1).

In summary, a generation of schizophrenic patients has grown up since the introduction in the 1950's of antipsychotic medication and community care, and over the past two decades many have been exposed to long-term maintenance antipsychotic treatment. However, there have been very few studies describing the impact of these developments on a community of schizophrenic patients. The Nithsdale surveys over a ten year period have tried to do this.

Nithsdale (see map) is one of the four local authority districts of Dumfries and Galloway Region in South West Scotland and is historically ancient and geographically discrete. The author has had clinical responsibility for most schizophrenic patients in Nithsdale throughout the years of the Nithsdale project.

The studies fall into three broad groups. Firstly, patients have been examined to determine psychiatric and social handicaps, and to assess the social adjustment of those living outside hospital. Secondly, the family life of the patient is described: this includes an assessment of the prevalence of relatives' high 'expressed emotion', the effect of family life on schizophrenic relapse, the effectiveness of family treatment, and the stability of attitudes of relatives towards patients over five years. Thirdly, the principal side effects of antipsychotic drugs, namely motor disorders, have been

assessed: prevalence, persistence and relationship to plasma neuroleptic levels are described, and their relationship to obstetric complications.

Finally, in view of the current interest in schizophrenia as an organic illness (Roberts, 1991), the Nithsdale project has examined the relationship between obstetric complications and schizophrenia.

The following 11 papers all have, or are about to be, published in the British Journal of Psychiatry.

### THE NITHSDALE SURVEYS

McCREADIE, R.G. (1982) The Nithsdale Schizophrenia Survey I: Psychiatric and social handicaps. British Journal of Psychiatry, 140, 597-6.

McCREADIE, R.G., BARRON, E.T. and WINSLOW, G.S. (1982) The Nithsdale Schizophrenia Survey II. Abnormal movements. British Journal of Psychiatry, 140, 587-90.

McCREADIE, R.G., CRORIE, J., BARRON, E.T. and WINSLOW, G.S. (1982) The Nithsdale Schizophrenia Survey III: Handedness and tardive dyskinesia. British Journal of Psychiatry, 140, 591-4.

McCREADIE, R.G. and BARRON, E.T. (1984) The Nithsdale Schizophrenia Survey IV Social adjustment by self-report. British Journal of Psychiatry, 144, 547-50.

ROBINSON, A.D.T. and McCREADIE, R.G. (1986) The Nithsdale Schizophrenia Survey V: Follow-up of tardive dyskinesia at 3½ years. British Journal of Psychiatry, 149, 621-623.

McCREADIE, R.G. and ROBINSON, A.D.T. (1987) The Nithsdale Schizophrenia Survey VI. Relatives' expressed emotion: prevalence, patterns and clinical assessment. British Journal of Psychiatry, 150, 640-644.

McCREADIE, R.G. and PHILLIPS, K. (1988) The Nithsdale Schizophrenia Survey VII. Does relatives high expressed emotion predict relapse? British Journal of Psychiatry, 152, 477-481.

McCREADIE, R.G., PHILLIPS, K., HARVEY, J.A., WALDRON, G., STEWART, M. and BAIRD, D. (1991) The Nithsdale Schizophrenia Surveys VIII. Do relatives want family intervention - and does it help? British Journal of Psychiatry, 158, 110-113.

McCREADIE, R.G., ROBERTSON, L.J. and WILES, D. (1992) The Nithsdale Schizophrenia Surveys IX. Akathisia, parkinsonism, tardive dyskinesia and plasma neuroleptic levels. British Journal of Psychiatry, 161, 793-799.

McCREADIE, R.G., HALL, D.J., BERRY, I.J., ROBERTSON, L.J., EWING, J.I. and GEALS, M.F. (1992) The Nithsdale Schizophrenia Surveys X. Obstetric complications, family history and abnormal movements. British Journal of Psychiatry, 161, 799-805.

McCREADIE, R.G., ROBERTSON, L.J., HALL, D.J. and BERRY, I.J. (1992) The Nithsdale Schizophrenia Surveys XI. Relatives' expressed emotion: stability over five years and its relation to relapse. British Journal of Psychiatry. In Press.

TABLE 1.1  
MENTAL ILLNESS HOSPITALS AND PSYCHIATRIC UNITS.  
RESIDENTS, BY SEX

	1970	1975	1980	1985	1990
Number of residents					
TOTAL	18297	16841	15164	14094	13229
Male	8433	7521	6547	5745	5431
Female	9864	9320	8617	8349	7798
Rate per 100,000 population					
TOTAL	351	323	294	274	259
Male	336	300	264	232	220
Female	364	345	322	314	296

Taken from Scottish Health Statistics 1991. Edinburgh: Information and Statistics Division, Common Services Agency for the Scottish Health Service.

TABLE 1.2  
 MENTAL ILLNESS HOSPITALS AND PSYCHIATRIC UNITS.  
 RESIDENTS BY SEX AND DIAGNOSIS

<u>RESIDENTS</u>	MALE				FEMALE			
	1975	1980	1985	1990	1975	1980	1985	1990
Senile and presenile organic psychotic conditions	673	803	1110	1218	2333	2686	3418	3506
Schizophrenic psychoses	3013	2470	2013	1655	2096	1692	1387	1087

Taken from Scottish Health Statistics 1991. Edinburgh:  
 Information and Statistics Division, Common Services  
 Agency for the Scottish Health Service.



TABLE 1.3  
 MENTAL ILLNESS HOSPITALS AND PSYCHIATRIC UNITS.  
 INPATIENT ADMISSIONS (ALL, FIRST AND READMISSIONS) BY SEX AND DIAGNOSIS

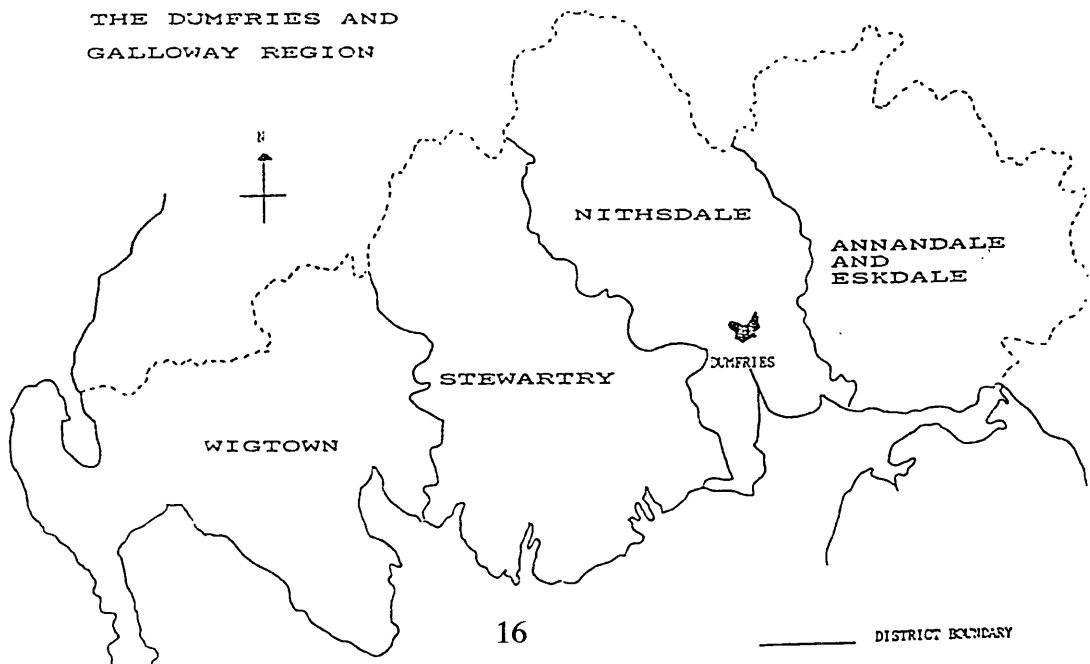
<u>ADMISSIONS</u>		MALE				FEMALE			
		<u>1975</u>	<u>1980</u>	<u>1985</u>	<u>1990</u>	<u>1975</u>	<u>1980</u>	<u>1985</u>	<u>1990</u>
Senile and presenile organic psychotic conditions	ALL	545	916	1480	1955	1271	1975	3271	3698
	FIRST	404	567	743	844	888	1163	1512	1425
	READMISSIONS	141	346	721	1088	373	802	1734	2248
Schizophrenic psychoses	ALL	1358	1589	1843	2189	1261	1417	1433	1446
	FIRST	264	253	204	238	231	235	177	161
	READMISSIONS	1094	1330	1637	1937	1030	1177	1252	1278

Taken from Scottish Health Statistics 1991. Edinburgh: Information and Statistics Division,  
 Common Services Agency for the Scottish Health Service.

# SCOTLAND



THE DUMFRIES AND  
GALLOWAY REGION



## 2 THE PATIENT

## **2.1 PSYCHIATRIC AND SOCIAL HANDICAPS**

**R G McCREADIE**

## SUMMARY

A review of all known schizophrenic patients from a discrete geographical area, Nithsdale in Dumfries and Galloway Region, found a point prevalence of 2.38 per 1000 of the total population; this figure fell to 1.73 when only Feighner positive schizophrenic patients were considered. Only three percent of the population interviewed had no abnormality in mental state or behaviour; negative schizophrenic symptoms were prominent, positive symptoms uncommon. Approximately one quarter were in-patients, who were an atypical group, showing much more obvious social and psychiatric disability. In- and day patient care and state benefits for schizophrenic patients cost each member of the Nithsdale community approximately £12 a year.

A generation of schizophrenic patients has grown up since the introduction in the 1950s of neuroleptics and community care, and in the past decade they have been exposed to long-term maintenance anti-psychotic drugs. However, there have been very few community studies describing the impact of these developments. A recent detailed description of schizophrenic in-patients (Owens and Johnstone, 1980) showed many such patients continuing to have multiple social and clinical handicaps, while a review of patients in the community (Cheadle *et al*, 1978) found such handicaps were moderately severe. No recent study in the United Kingdom, however, has identified all schizophrenic patients from a discrete geographical area and described their handicaps. The present study has attempted this.

## METHOD

### Area

Nithsdale, an historically ancient and geographically discrete part of Dumfries and Galloway Region, has an area of 550 square miles and a population of 56,000 (General Registrar Office, Scotland, 1981). It is largely rural, but contains the market town of Dumfries (population 31,000) and three other small towns along the banks of the River Nith. Psychiatric services are provided by Crichton Royal Hospital. It is probable that very few patients from Nithsdale receive treatment elsewhere, especially as the Crichton has had amenity beds for many years and the two nearest psychiatric hospitals are 35 and 60 miles from Dumfries.

### Patient identification

Patients included in the survey were all the in-patients, day patients, and out-patients of Crichton Royal Hospital who, on 1 March 1981, had a firm case record diagnosis of

schizophrenia and whose home address was in Nithsdale. All general practitioners (n = 32) in Nithsdale were sent a list of schizophrenic patients in their practice currently in contact with the Crichton. They were asked if there were any other schizophrenic patients known to the practice and receiving treatment. The Feighner criteria for schizophrenia (Feighner *et al*, 1972) were then applied to each patient, using information obtained from the case record and the clinical assessment (see below).

The following demographic, social, financial and clinical information was recorded: age, sex, marital status, number of children, place of birth, domiciliary and employment status, value of all financial benefits (including free prescriptions, if any), length of illness (as estimated from first hospital admission), length of total in-patient stay and current medication.

### Assessment

Over the four weeks following the census date the mental state of patients was assessed by the author using the Manchester Scale for chronic psychotics (Krawiecka *et al*, 1977); a 10 percent sample was assessed independently by a second psychiatrist to estimate inter-rater agreement. In-patient and day patient behaviour was assessed by senior nurses using the Wing Ward Behaviour Scale (Wing, 1961); the behaviour at home of patients living with relatives was assessed by community nurses through interviews with the relatives, also using the Wing Scale, with minor modifications. Parkinsonism and tardive dyskinesia were assessed using the Targeting Abnormal Kinetic Effects scale (TAKE) and the Abnormal Involuntary Movements Scale (AIMS) (Wojcik *et al*, 1980; US Department of Health, Education and Welfare, 1976); results of these assessments are reported separately (McCreadie *et al*, 1982a) as is an assessment of handedness (McCreadie *et al*, 1982b), determined by a series of tests (Annett, 1970).

### Statistics

Differences between groups were tested by the chi-square test (two-tailed tests throughout).

## RESULTS

This study identified 133 schizophrenic patients, of whom 38 were in-patients (28 percent), 23 daypatients (17 percent) and 42 out-patients (32 percent). All general practitioners replied to the questionnaire. This identified a further 30 patients (23 percent) of whom all except one had had contact with Crichton Royal at some time in the past. The figures gave a point prevalence of 2.38 per 1000 of the total population. When the Feighner criteria were applied, there were 97 'definite' or 'probable' schizophrenics, a point prevalence of 1.73 per 1000.

Three general practitioners refused access to eight patients but supplied some demographic and social information. A further seven patients attending only their general practitioner refused to be assessed clinically.

### Demographic and social findings

Fifty-two percent of probands were male, 48 percent female; their mean age was 48 years, range 20 to 94 years. Half had been born in Nithsdale, a further 11 percent in other parts of Dumfries and Galloway Region, 23 percent elsewhere in Scotland. Seventy-eight percent were from the town of Dumfries, where 55 percent of the general population of Nithsdale lives. Fifty-nine percent were single, 22 percent married, 14 percent divorced or separated and 5 percent widowed; this compares with 40 percent single, 51 percent married and 9 percent widowed, divorced or separated for the general



population of Dumfriesshire aged over 16 years (General Registrar Office, Scotland, 1971). Sixty-eight percent had no offspring.

The following information excludes in-patients. Twenty-five percent lived with their spouse, 30 percent with parents and 27 percent alone. Seventy-five percent (68 percent of males) were unemployed, compared with 12 percent (13 percent of males) of the general population in Dumfries and Galloway Region (personal communication, Employment Service Agency); 18 percent of this group attended the hospital's industrial or occupational therapy department.

### Financial findings

Ninety-five percent of in-patients were receiving state benefits (mainly non-contributory invalidity payments), the average weekly value of which was £7.50. Seventy percent of other patients were also receiving benefits (invalidity, unemployment or supplementary benefit or retirement pension), the average value of which was £31.80. Thirty-eight percent of non-in-patients received free prescriptions and a further 14 percent had a prescription 'season ticket'. The assessed cost of in-patient care at Crichton Royal at the time of the survey was £182 per patient per week (Dumfries and Galloway Health Board, 1981). This is a slight overestimate as the figure of £182 includes the cost of running the day hospital and the salaries and very considerable travelling expenses of community nurses, two of whom work mainly in Nithsdale with chronic schizophrenic patients. It is likely that the cost of day care is not far short of the cost of in-patient care. When only the cost of in- and day patient care and state benefits are considered, then, with 56,000 people in Nithsdale, the cost of caring for schizophrenic patients is approximately £12 per year to each member of the Nithsdale community. Taxes and national insurance and pension contributions paid by the small number of schizophrenic patients in open employment will slightly offset this cost.

### Clinical findings

The mean length of illness was 18 years, the median 14 years (range two months to 60 years), the mean total length of in-patient stay eight years and the median one year (range one week to 60 years). Twenty-four percent of patients were receiving no anti-psychotic medication; 30 percent were receiving oral, 31 percent intra-muscular and 15 percent both oral and intra-muscular neuroleptics. Thirty-two percent were receiving anti-parkinsonian medication and 25 percent other psychotropic drugs, mainly benzodiazepines (15 percent) or anti-depressants (9 percent).

### Mental state

The mental state of all in-patients, day patients and out-patients and of 50 percent of the general practice patients was assessed (n = 118, i.e., 89 percent of the total group). The nine items on the Manchester Scale assess four positive schizophrenic symptoms (incongruity of affect, delusions, hallucinations and incoherence of speech), two negative schizophrenic symptoms (flattening of affect, poverty of speech) and three non-schizophrenic symptoms (depression, anxiety and retardation), each on five-point scale (0 = absent to 4 = severe). Affect was separated in the present study into 'incongruous' and 'flat'. Inter-rater agreement, complete or partial (a difference of one point), ranged from 91 to 100 percent on eight items; it was 73 percent on the ninth, incoherence of speech.

In 18 percent of patients there was no abnormality in the mental state. Table 2.1.1 lists the symptoms in order of prevalence. The negative symptoms were most prominent, the positive least. Almost half the patients showed flatness of affect while less than 15 percent exhibited hallucinations, incoherence of speech or incongruity of affect.

### Behaviour

The behaviour of all in-patients and day patients, 74 percent of out-patients, and 13 percent of general practice patients (n = 96, 72 percent of the total group) was assessed.

The Wing Behaviour Scale assesses behaviour in the previous week. In 21 percent of patients no abnormality was detected. Table 2.1.2 lists the symptoms in order of prevalence. Social withdrawal, lack of leisure interests and limited conversation were found in about half of the patients. Socially embarrassing behaviour such as threatening behaviour or overactivity was uncommon.

Only three percent of patients whose mental state and behaviour were both examined had no abnormality on either assessment.

### Differences between groups

Various groups were compared on the basis of demographic, social and clinical findings. Unless specified, differences stated below were significant at least at the 1 percent level.

#### Feighner positive versus negative schizophrenics

Feighner positive schizophrenic patients ('definite' or 'probable') were older ( $P < 0.05$ ), more of them were single, fewer had children, and more were unemployed. They had been ill longer ( $P < 0.02$ ) and had spent a longer total time as in-patients.

#### Male versus female

More males were single ( $P < 0.05$ ), more lived with their parents and fewer were unemployed ( $P < 0.02$ ).

#### In-patients versus other groups

More in-patients had been born in Dumfries and Galloway Region ( $P < 0.05$ ), they were older, more were single, fewer had children and more were unemployed. In-patients had been ill longer ( $P < 0.02$ ) and had a longer total in-patient stay. More were on both oral and intra-muscular neuroleptics ( $P < 0.02$ ). Flattening of affect ( $P < 0.02$ ), poverty of speech and retardation of movement ( $P < 0.02$ ) were more common in in-patients and ordinary conversation, social mixing, spontaneous interests and pride in personal appearance were less common.

#### Out-patients versus general practice patients

Out-patients had had a longer total in-patient stay than general practice patients and more of them exhibited flatness of affect and retardation ( $P < 0.05$ ).

### DISCUSSION

The point prevalence which we found, 2.38 per 1000 of the total population, lies between the 1.98 found in 1974 in Camberwell, and the 2.77 found in Salford (Wing and Fryers, 1976). The Camberwell and Salford prevalence figures were obtained from case registers and did not include patients attending only their general practitioners. When Feighner positive schizophrenic patients only are considered, the prevalence in Nithsdale falls to 1.73. The Nithsdale figure must be an underestimate, as inevitably some schizophrenic patients have nothing to do with their general practitioner but continue to have symptoms. However, there are likely to be fewer such patients in Nithsdale than in urban areas, as it is a heavily doctored district where practitioners are

very much part of the community in which they live. The results will also be effected by some schizophrenic patients having drifted away from Nithsdale to such cities as Glasgow and Edinburgh; indeed, there seems to have been a drift from rural Nithsdale to Dumfries.

The application of the Feighner criteria distinguish two groups of patients, who differ mainly in age and length of illness. However, there are no differences between the groups on the basis of the patients' mental state or behaviour. The Feighner criteria tend to identify chronic patients (Overall and Hollister, 1979) as a main requirement is that a patient must have had symptoms for at least six months without a return to the premorbid level of psychological adjustment.

Approximately one quarter of schizophrenic patients in our survey were in-patients; this contrasts with both Camberwell and Salford, where in 1974 about two-thirds were in-patients. No doubt the shift to community care over the past seven years would now produce different figures in both these urban areas.

Although almost three-quarters of the schizophrenic patients were living out of hospital, social and psychiatric disability was still considerable. When compared with the general population fewer had married, and among those who had more marriages had ended in separation or divorce. The vast majority were unemployed. Only three percent of schizophrenic patients examined had no abnormality in either mental state or behaviour. Psychiatric disability, however, was 'quiet'. Flattening of affect and social withdrawal were most prominent; florid positive symptoms and embarrassing behaviour were uncommon. The latter symptoms are effectively controlled by neuroleptics (Crow, 1980); the former are much more difficult to manage.

The finding that most schizophrenic patients are likely to be out of hospital means that the burden of their care has been transferred to the community. In many instances the 'community' is the patient's family, and the stresses produced by the schizophrenic patient living at home have already been well documented (Creer and Wing, 1974). To relieve the burden on the family and to give support to patients living on their own, day care is offered to all Nithsdale schizophrenic patients without employment, but distances and problems with transport in a rural area dictate that only those living in or around Dumfries can reasonably be expected to attend. A subgroup likely to need considerable support in the future are those currently living with ageing parents; indeed, males in this category form 15 percent of the total schizophrenic population.

The most striking differences found were between in-patients and other groups. The former were older, had been ill longer and in terms of both mental state and behaviour were more disabled. Studies which nowadays confine themselves to in-patients are likely, therefore, to be examining a small and atypical group of schizophrenic patients. The number of patients examined who were attending only their general practitioner was small and, perhaps, not typical of the group as some refused to be interviewed. However, those who were assessed were less disabled than out-patients, a finding reported in another study (Leff and Vaughn, 1972). In Nithsdale this probably reflects willingness among general practitioners to care for less seriously disabled schizophrenic patients.

Although the majority of schizophrenic patients in Nithsdale are no longer living in hospital, the financial cost is still considerable. Such costs are extremely hard to estimate (Cheadle and Morgan, 1974), but when only readily identifiable costs were taken into account, £12 per person per year was the approximate cost to the Nithsdale community of caring for schizophrenic patients. If these findings are typical

throughout the United Kingdom (which admittedly is highly speculative) then the cost of caring for schizophrenic patients nationwide must be approximately £650-700 m per year.

**TABLE 2.1.1**  
**MENTAL STATE: PREVALENCE OF SYMPTOMS**

<b>SYMPTOM</b>	<b>PERCENTAGE OF PATIENTS SHOWING SYMPTOM</b>
Flatness of affect	45
Retardation	33
Poverty of speech	29
Anxiety	28
Delusions	26
Depression	23
Incoherence of speech	14
Hallucinations	10
Incongruity of affect	8



**TABLE 2.1.2**  
**BEHAVIOUR: PREVALENCE OF ABNORMALITIES**

<b>BEHAVIOUR</b>	<b>PERCENTAGE OF PATIENTS SHOWING ABNORMALITY</b>
Social withdrawal	61
Leisure interests	50
Conversation	48
Slowness of movement	33
Underactivity	30
Personal appearance	24
Laughing and talking to self	12
Posturing and mannerisms	9
Threatening or violent behaviour	8
Overactivity	7
Behaviour at meal times	3
Personal hygiene	2

## 2.2 SOCIAL ADJUSTMENT BY SELF-REPORT

R G McCREADIE

E T BARRON

## SUMMARY

The Social Adjustment Scale Self-report (SAS-SR) was completed by chronic schizophrenic patients (N = 82) living in Nithsdale, in Dumfries and Galloway Region. Relatives also assessed patients' adjustment. The questionnaire response indicated that scrutiny of the form by a professional immediately after completion is necessary. Patients' and relatives' assessment of the patients' overall adjustment correlated very closely, thus suggesting a schizophrenic patient can satisfactorily describe his own adjustment. The patients were less well adjusted than a normal community population in all areas except the parental role. The SAS-SR highlights for each individual where many of his problems lie, and therefore may act as a guide to specific rehabilitative measures.

A recent community survey has shown that at any given time, approximately three-quarters of all known schizophrenic patients are probably living outside hospital (McCreadie, 1982a). As many patients continue to have psychiatric and social handicaps, further rehabilitation is usually necessary after discharge from in-patient care. The efficacy of such rehabilitation needs to be evaluated and any assessment should include a measure of social adjustment. In a busy community psychiatric service a short, simple, inexpensive assessment is required. The present study reports the use by chronic schizophrenic patients of the Social Adjustment Scale Self-Report (SAS-SR) (Weissman and Bothwell, 1976). Previous studies suggest the scale can be used successfully with non-psychiatric patients and with different psychiatric populations (Weissman *et al*, 1978). There have been no reported studies, however, on the use of the scale by both a schizophrenic patient and a relative, although when a modification of the original scale (Weissman and Paykel, 1974) was used by trained interviewers, agreement between schizophrenic patients and 'significant others' about the patient's social adjustment was found to be satisfactory (Glazer *et al*, 1980).

The present study aims firstly to determine the acceptability to patients of the self-report, secondly to compare patients' and relatives' assessment of the patient, and thirdly to compare patients' social adjustment with that of a normal population.

## METHOD

### Patients

The patients were drawn from the 1982 cohort of schizophrenic patients in Nithsdale, an historically ancient and geographically discrete part of Dumfries and Galloway Region. The original census (1.3.81) of all known schizophrenic patients in the area, in-patients, day-patients, out-patients, and patients known only to their general

practitioner has been fully described elsewhere (McCreadie, 1982a) and identified 133 schizophrenic patients. A repeat census on 1.3.82 identified 136 patients; of the original cohort five had died, four had moved away from the district, and three no longer had a diagnosis of schizophrenia. Fifteen patients had been added to the cohort during the intervening year; six had developed the illness *de novo*, four had moved into the district and five had either experienced a fresh episode of schizophrenia or had their diagnosis changed to schizophrenia. Of the 136 patients 28 were day-patients, 42 out-patients, and 30 were known only to their general practitioner (total N = 100). These non-inpatients were the subject of the present study.

### Assessment

The SAS-SR, which takes 10-15 minutes to complete, is a 54 item questionnaire examining adjustment during the previous two weeks. It yields an overall adjustment score and a rating of six role areas: work as a worker, housewife or student; social and leisure activities; relationships with extended family; and marital roles as a spouse, parent and member of the family unit. A final question asks about economic circumstances. The scale also has four descriptive categories: performance at expected tasks; amount of friction with others; finer aspects of interpersonal relations; and inner feelings and satisfactions. Each question is rated on a five point scale, with a higher score indicating greater impairment.

The SAS-SR was administered during the four weeks following the census date. The form was explained to patients and relatives and on return checked for completion. Patients were requested to complete the questionnaire at the hospital (Crichton Royal, Dumfries); some asked to take it home and a stamped addressed envelope was provided. Where patients who answered the questionnaire stayed with a relative (N = 50), he also was asked to complete a questionnaire describing the patient's adjustment.

The form was either given to the relative at the out-patient department if he accompanied the patient or delivered to his home by a community psychiatric nurse. Again, where necessary, a stamped addressed envelope was provided.

## RESULTS

### Questionnaire response

Of the 100 patients, 82 answered the questionnaire. It was read to four because of illiteracy. Of the 18 who did not answer, one day-patient was in a general hospital at the time of the survey, two out-patients took the questionnaire home and never returned it, one out-patient did not understand it because of language difficulties, and 14 general practice patients did not attend for interview. Demographic and social data on the 82 patients are shown in Table 2.2.1. All had a firm case record diagnosis of schizophrenia and 73 percent fulfilled the Feighner criteria for 'definite' or 'probable' schizophrenia (Feighner et al, 1972).

Questionnaires were returned by 41 out of 50 relatives (15 spouses, 21 parents, one child, and four more distant relatives). With the nine relatives who did not answer, the questionnaire had been delivered to their home and a stamped addressed envelope provided.

In 82 percent of questionnaires returned by patients and 71 percent by relatives, more than 90 percent of relevant questions had been answered; these formed the basis of the results. In almost all cases where less than 90 percent of questions had been answered, the questionnaire had been completed at home and returned by post.

### Patients' and relatives' assessment

In 24 pairs, both patients and relatives answered more than 90 percent of relevant questions. Correlations between patients' and relatives' scores for overall adjustment, five role areas, and four descriptive areas were measured by the product moment correlation coefficient (Table 2.2.2). The sixth role area, as a parent, is excluded as only three of the 24 patients were parents. Correlations were positive and high in overall adjustment and role areas except relationships with the extended and immediate family. In descriptive categories, correlations were high in performance and interpersonal behaviour, but negligible in friction.

To determine whether relatives consistently under or over-estimated patients' adjustment when compared with the patients' own assessment, means of scores obtained by patients and relatives in the various areas were compared using Students t-test. No significant differences were found.

### Patients' assessment

Patients' assessment of themselves (N = 67) was compared with the self-assessment of a normal community sample (Weissman *et al*, 1978) (Table 2.2.3). The patients were significantly more handicapped in overall adjustment and all role areas except the parental role. There are no normative data for descriptive categories. The overall social adjustment of Feighner positive patients ('definite' or 'probable' schizophrenia) was less than in Feighner negative patients ( $P < 0.02$ ). The following factors were not associated with differences in overall adjustment: sex, age, length of illness or stay in hospital, and domiciliary status.

Replies to individual questions help to describe the patients' adjustment. Only 27 percent worked in open employment and 24 percent were married. Thirty-nine percent

either had no friends or had met none in the previous two weeks, 34 percent had not gone out socially in the past two weeks, and 33 percent of the unmarried said they were completely uninterested in going out with a member of the opposite sex. Fifty-two percent had spent no time in the previous two weeks on interests or hobbies except watching television. Although most depended on social security benefits, 79 percent said they had enough money for their needs.

## DISCUSSION

The study suggests that SAS-SR can be used reasonably successfully with chronic schizophrenic patients. The nature of the questionnaire was readily understood by most patients and relatives and when returned, more than 80 percent of patients and 70 percent of relatives satisfactorily answered at least 90 percent of questions. In the majority of cases, both with patients and relatives, where the form was not returned or inadequately completed, the patient or relative had said he would return it by post. It would therefore seem advisable for the questionnaire to be scrutinised by a professional immediately after completion. There has recently appeared a British version of the SAS-SR (Cooper *et al*, 1982). The language has been modified somewhat and the rating scale simplified. However, there are as yet no normative data for a community population.

The assessment of overall adjustment by a patient corresponded very closely with that by his relative. Within various sub-scales, however, there were some differences in how the patient and relative saw the patient functioning, especially within both the immediate and extended family. It was also clear, and perhaps to be expected, that relatives and patients assessed friction differently; patients sensed friction where the relatives did not and vice versa.



The findings in the present study extend previous work (Glazer et al, 1980) which used a modification of the SAS in schizophrenic patients and showed that with trained interviewers, correlations between patients and relatives were high. The present study suggests that an accurate assessment of overall adjustment can probably be made by the patient himself. This is an advantage, as many schizophrenic patients in the community live alone and their adjustment can not readily be assessed by anyone else. It may be, of course, there was collusion between the patient and his relative. Such collusion would presumably lead to an over-estimate of the patient's social adjustment. In this context, it is noteworthy that when the patients were compared with a normal American community sample (as stated above, there are no normative United Kingdom data), the patients' adjustment was less satisfactory in all areas, with the exception of the parental role.

The only factor which differentiated patients was whether or not they fulfilled the Feighner criteria for schizophrenia; Feighner positive schizophrenic patients were less well adjusted. This is understandable, as an essential requirement to fulfil the Feighner criteria is that the patient must have had symptoms for at least six months without a return to the premorbid level of psychological adjustment.

The study of Nithsdale schizophrenic patients reported previously (McCreadie, 1982a) showed that although the vast majority of patients in the community continued to have many psychiatric and social handicaps, the disability was 'quiet'. Flattening of affect and social withdrawal were prominent; florid positive symptoms and embarrassing behaviour were uncommon. The more detailed assessment in this study of patients' social adjustment confirms their withdrawal. Many had no friends, did not go out socially, and were completely uninterested in members of the opposite sex. The majority spent no time on interests other than television. Few perceived any unmet

financial needs, although social security benefits were the main source of income. In short, they lead a quiet life and probably the majority cause little disturbance to most people in the community.

SAS-SR results highlight for each individual where many of his problems lie. An individual's score could act as a guide to specific rehabilitative measures, described in detail elsewhere (McCreadie, 1982b). Reassessment using the same scale might determine what improvements, if any, had been brought about by these measures. Care, though, must be taken in interpretation of such data. For example, if an unemployed patient subsequently finds work but performs poorly in this area, the overall adjustment score might fall. However, knowledge of each individual patient would prevent the clinician from falling into the trap of believing such a patient had deteriorated.

TABLE 2.2.1

## SOCIAL AND DEMOGRAPHIC DATA

		N = 82 %
Sex	Male	49
	Female	51
Marital status	Single	55
	Married	23
	Widowed	2
	Divorced/separated	20
Hospitalisation status	Out-patient	48
	Day-patient	33
	General practice patient	19
Age	< 25 years	4
	25-44 years	50
	45-64 years	44
	65 + years	2
Length of illness	< 2 years	4
	2 < 10 years	34
	10 < 20 years	38
	20 + years	24

TABLE 2.2.2

CORRELATIONS BETWEEN PATIENTS' AND RELATIVES' ASSESSMENT  
OF PATIENTS' ADJUSTMENT

Rating	Number of Pairs	'r'	P
Overall adjustment	24	+0.89	<0.001
Role areas			
Work	19	+0.77	<0.01
Social/leisure	24	+0.77	<0.001
Extended family	24	+0.44	<0.05
Marital	10	+0.79	<0.01
Family unit	23	+0.02	NS
Descriptive areas			
Performance	24	+0.91	<0.001
Interpersonal behaviour	23	+0.79	<0.001
Friction	23	-0.01	NS
Feelings	24	+0.54	<0.01

TABLE 2.2.3  
COMPARISON BETWEEN ADJUSTMENT OF PATIENTS  
AND NORMAL COMMUNITY POPULATION +

Rating	Patients		Normals	
	N	Mean score (SD)	N	Mean Score (SD)
Overall adjustment	67	2.00 (0.46)	482	1.59 (0.33)
Role areas				
Work ***	62	1.59 (0.66)	399	1.40 (0.46)
Social/leisure *	67	2.64 (0.71)	482	1.83 (0.52)
Extended family*	16	1.62 (0.69)	475	1.34 (0.33)
Marital ***	12	2.10 (0.64)	361	1.75 (0.48)
Parental	24	1.54 (0.71)	276	1.40 (0.42)
Family unit **	67	1.86 (0.71)	464	1.46 (0.58)

Difference between groups      \* P < 0.001  
    \*\* P < 0.01  
    \*\*\* P < 0.05

+ Taken from Weissman et al, 1978

### 3. THE FAMILY

### **3.1 RELATIVES' EXPRESSED EMOTION: PREVALENCE, PATTERNS AND CLINICAL ASSESSMENT**

**R G McCREADIE**

**A D T ROBINSON**

## SUMMARY

A review of all known schizophrenic patients (N = 142) in Nithsdale, Scotland, found 50% were living with relatives or friends. Of these, 32% had high contact with a relative showing high expressed emotion (EE); put another way, 87% of all Nithsdale schizophrenic patients were not living in a high contact/high EE family. Parents were more critical than spouses, and more showed emotional over-involvement. A retrospective review showed a trend, not of statistical significance, towards a higher admission rate to in-patient care in patients from high EE homes. Of relatives believed by a consultant psychiatrist to be neither critical nor hostile, 80% fell into the low EE category, but only 55% thought hostile or critical belonged to the high EE category; that is, the clinician had a wider view of high EE than the Camberwell Family Interview. Relatives' scores on a short patient-rejection scale were higher in high EE than in low EE relatives, but the wide scatter of scores suggested the scale could not be used to identify an individual relative with high EE.



Reports over 25 years from the MRC Social Psychiatry Unit in London have suggested the prognosis of schizophrenic patients discharged from hospital may depend on their living arrangements. Patients living with relatives who show high expressed emotion (EE) are more likely to relapse, especially if face-to-face contact between patient and relative is high and the patient is unprotected by maintenance antipsychotic medication (Brown *et al*, 1962, 1972; Vaughn & Leff, 1976a). These findings have become of increasing clinical relevance in recent years as in both the UK and USA family therapy which includes education, relatives' groups and family sessions has been shown to reduce contact and lower EE, and thus substantially reduce relapse rates (Leff *et al*, 1982, 1985; Falloon *et al*, 1982, 1985).

Both the UK and USA studies examined patients in an urban setting. A study in Chandigarh, Northern India found different levels of expressed emotion (Leff, 1986); whether this was due to rural or cultural factors is not certain. The present study is the first to examine schizophrenic patients living in a rural area in the West. It is also the first to assess the prevalence of high EE in a community; in contrast with previous studies it does not confine itself to patients recently admitted to in-patient care. By assessing prevalence the amount of work likely to face a NHS clinician willing to embark on prophylactic family therapy can be estimated. The study also describes patterns of EE in different types of relative, and examines, retrospectively, rates of admission to in-patient care in patients living on their own, and with different categories of relative.

If clinicians are prepared to carry out family therapy they must be able to recognise high EE. EE is currently assessed by the Camberwell Family Interview (CFI), which cannot be used without specialised training and is time consuming; it is therefore not suitable for use in everyday clinical practice. Are there any shortcuts

in the assessment of EE? The present study examines two possibilities, firstly an experienced clinician's hunch, and secondly a short 'patient rejection' scale administered to relatives by a community psychiatric nurse.

## METHOD

### Patients

Patients were drawn from Nithsdale, a rural, historically ancient and geographically discrete part of Dumfries and Galloway Region, Scotland. Those included were all in-patients, day-patients and out-patients of Crichton Royal Hospital, Dumfries, who on the census date (1 July 1985) had a firm case record diagnosis of schizophrenia and whose home address was in Nithsdale. Also, all general practitioners in the area replied to a questionnaire which identified other schizophrenic patients known to the practice and receiving treatment but not known to the hospital. The census identified 142 schizophrenic patients; as the population of Nithsdale is 56,000, this gives a point prevalence of 2.53 per 1000 of the total population. Sixty-eight percent fulfilled the Feighner criteria for 'definite' or 'probable' schizophrenia (Feighner et al, 1972).

At the time of the census 20% were long-stay in-patients, 28% lived alone or in lodgings, and 2% lived with relatives under 18 years of age. Fifty percent (N = 72) were living with adult relatives or significant others and it was these on whom the present study focused. Forty nine percent of such patients were male (mean age 42 years, s.d. 12 years, range 21-66 years; mean length of illness, as estimated from first psychiatric hospital contact, 14 years, s.d. 10 years, range 1-40 years) and 51% female (mean age 50 years, s.d. 13 years, range 27-79 years; mean length of illness 18 years, s.d. 12 years, range 2-48 years).

Scrutiny of case records identified all Nithsdale schizophrenic patients admitted to psychiatric in-patient care in the year preceding the census, 1 July 1984 - 30 June 1985.

### Relatives

The type of relative with whom the 72 patients were living is shown in Table 3.1.1. More males than females were living with parents ( $\chi^2$  6.75,  $P < 0.01$ ). Relatives of 12 patients were not interviewed; six patients had refused to take part in any of the previous Nithsdale surveys; a general practitioner refused access to a seventh patient; three patients refused access to relatives; and two relatives refused to be interviewed. Of the 12 patients, two had had no previous psychiatric admissions and the mean time from the census to the previous admission in the remaining ten was 12 years (s.d. 8 years, range 2-26 years).

### Assessment

One of us (A.D.T.R.), trained in the use of the CFI by Dr Christine Vaughn, carried out all interviews which on all but three occasions took place in the patients' homes over a three month period following the census. Interviews were taped and an assessment made from the recordings of the five main components of EE, namely criticism, hostility, emotional over-involvement, warmth and positive comments. The amount of face-to-face contact between relative and patient during a typical week was also assessed through the construction of a time budget; more than 35 hours per week indicates high contact (Vaughn & Leff, 1976a). The husband or wife of a married patient was always seen; where an unmarried patient lived with both parents, both mother and father were interviewed. In all, 70 relatives or friends were seen. A relative fell in the high EE category if he had a score of 6 or more critical comments, any degree of hostility, or a rating of 3 or more on emotional over-involvement (EOI) (Leff *et al*, 1982).

At the same time as the CFI ratings were made the consultant psychiatrist (R.G.McC), responsible for the patients' clinical management and blind to the ratings, made his own assessment of expressed emotion through the use of a simple 4-point global scale:

I think this relative (i) is probably neither critical nor hostile (group 1 relatives), (ii) is possibly neither critical nor hostile (group 2), (iii) is possibly critical and/or hostile (group 3), (iv) is probably critical and/or hostile (group 4).

To make the assessment as simple as possible, no attempt was made to rate EOI. Over the same period, community psychiatric nurses visited relatives in their homes and asked them to complete a patient rejection scale (PRS) (Kreisman et al, 1979\*). This is a 24-item questionnaire containing such statements as "I am very disappointed in my.....", "I wish my..... had never been born". The relative is invited to respond to each statement in one of seven ways ranging from "I feel this way 'always'" through 'sometimes' to 'never'. Each item is scored 1-7 and a grand total obtained (range 24-168); a lower score indicates less hostility.

---

\* The questionnaire has been expanded somewhat since the first version was published (full details on request to Dr D Kreisman, New York State Psychiatric Institute, New York, 10032).

## RESULTS

### Prevalence and patterns of high EE

At the time of the survey 58% (n = 35) of the 60 patients were living with low EE relatives, 42% (n = 25) with at least one high EE relative, and 32% (n = 19) with at least one high EE relative with whom they were in face-to-face contact for more than 35 hours each week. Thirty relatives showed high EE. The breakdown by type of EE was as follows: criticism, as evidenced by a score of 6 or more critical comments, without EOI, as evidenced by a rating of less than 3, was shown by 10% of relatives (n = 7), criticism and EOI by 21% (n = 15) and EOI alone by 11% (n = 8). Hostility, as evidenced by a score of 1 or more, shown by 8% (n = 6) was never found without criticism. Sixteen of 21 mothers (76%) interviewed showed high EE, three of six fathers (50%) (that is, 70% of parents showed high EE); one of nine wives (11%), four of 14 husbands (29%) (that is, 22% of spouses); four of nine other first degree relatives (44%); two of three more distant relatives (67%); none of eight friends showed high EE. Parents had significantly higher scores when compared with spouses in mean number of critical comments (5.67 (s.d. 4.79) vs 2.82 (2.29): t-test,  $t = 2.60$ ,  $P < 0.02$ ), and also more showed EOI (63% vs 13%:  $\chi^2 = 10.89$ ;  $P < 0.001$ ). There were no statistically significant differences in the percentage showing hostility (11% parents (n = 3) vs 4% (n = 1)) but the numbers in each group were very small.

Patients living in high EE homes, in low EE homes or on their own did not differ in: sex distribution, length of illness, and number of previous admissions. Patients living on their own were older than those living in high EE homes (mean 51 years vs 43 years; t-test:  $t = 2.65$ ,  $P < 0.02$ ). More patients in high than in low EE homes lived with parents (68% vs 14%;  $\chi^2 = 15.88$ ;  $P < 0.001$ ).

### Admissions to in-patient care

Scrutiny of case records showed that all Nithsdale schizophrenic patients admitted to in-patient care in the year preceding the census ( $n = 27$ , 24% of all non long-stay in-patients) did so as a result of an exacerbation of a chronic schizophrenic illness or a fresh episode. There was no difference between admissions and non-admissions in: age, sex distribution, marital status and length of illness. Admissions had had more previous admissions than non-admissions (mean 7.3 vs 4.9;  $t$ -test:  $t = 2.12$ ,  $P < 0.05$ ).

Patients were then grouped on the basis of domiciliary status and whether they had received maintenance antipsychotic medication in the year preceding the census or at least until the time of hospital admission (Table 3.1.2). Admission rates for the three main groups (patients living on their own, in low EE homes and in high EE homes) ranged from 22% to 36%; the trend, not statistically significant, was towards a higher admission rate in patients from high EE homes. Admission rates for patients in high and low contact with high EE relatives were virtually the same. There were no significant differences between relatives of patients admitted and not admitted in mean number of hours face-to-face contact with patients and mean scores on criticism, hostility, emotional over-involvement, warmth and positive comments sub-scales. A trend in patients living on their own or in low EE homes was that admission rates were lower in patients on antipsychotic medication (Table 3.1.2) in contrast the trend in high EE patients was that admission rates were higher in patients on medication. No trend, however, reached statistical significance.

### Comparison of CFI with consultant's assessment and PRS

The consultant psychiatrist rated 54 of the 70 relatives; he believed his knowledge of the remainder was so slight that an assessment could not be attempted. He assigned 17 relatives to group 1 ("probably neither critical nor hostile"), 12 to group

2, 14 to group 3 and 11 to group 4 ("probably critical and/or hostile"). When groups 1 and 2 were combined, it was found that 23 out of 29 relatives (80%) fell into the low EE category as assessed by the CFI; when groups 3 and 4 were combined, 11 out of 25 (44%) fell into the high EE category. Concordance rates were only marginally or not improved when relatives in groups 1 and 4 were compared respectively with those in low and high EE categories, and when groups were compared with relatives categorised by the criticism and EOI sub-scales of EE. The number of relatives showing hostility on the CFI ( $n = 4$ ) was too small to warrant examination of concordance rates but two fell into group 3 and two into group 4.

Fifty-eight relatives completed the PRS; the remainder were not known to the community psychiatric nurse. Mean scores on the hostility questionnaire for different categories of relative as determined by the CFI are shown in Table 3.1.3. Although there were statistically significant differences between mean scores in different EE categories, there was such a wide scatter of scores in high EE relatives (see standard deviations in Table 3.1.3) that it was not possible to determine a cut-off point on the PRS above which most high EE but few low EE relatives would be found.

## DISCUSSION

Relatives of 12 patients were not interviewed and some might belong to the high EE category. However, either patients had no history of admission to a psychiatric hospital or had not been admitted for many years. If there is a relationship between high EE, relapse and subsequent in-patient care it is likely few of these relatives fell into the high EE category.

The study, the first prevalence survey of high EE, found that in a community of schizophrenic patients 50% were living with relatives or friends and of these, 32% lived in high contact with high EE relatives, the family structure believed by Leff and colleagues to be most conducive to schizophrenic relapse. However, put another way, 87% of all Nithsdale schizophrenic patients were not living in a high contact/high EE family. In terms of absolute numbers, therefore, it is unlikely that at any given time many Nithsdale schizophrenic patients have to face this sort of family life. If these results obtain in other parts of the country, and if NHS clinicians wish to embark on prophylactic family therapy with schizophrenic patients at risk, then the amount of work involved is not likely to be great. It is possible of course that within an individual the level of EE fluctuates over time and that a higher or lower prevalence of high EE might have been found on another date. However, with highly enmeshed families (high EE, high contact), EOI in one study barely changed in relatives where no therapeutic intervention took place, at least over a 9-month period (Leff et al, 1982). Criticism appears less stable; a considerable reduction occurred over 9 months in some relatives where patients markedly improved (Brown et al, 1972).

A common family structure in Nithsdale is the male schizophrenic patient living with elderly parents (McCreadie, 1982a); such a patient may be at high risk as the present survey found parents were more critical and over-involved than spouses. Why this should be so is not clear. It has previously been suggested that more emotion is expressed by those with low rates of contact with friends and relatives (Brown et al, 1972). Perhaps parents are more isolated than spouses, most of whom were born and brought up in Nithsdale and possibly had other supportive contacts more readily available outside the nuclear family.

Comparison of the present findings with other studies is very difficult, firstly



because the Nithsdale survey examines prevalence while the others examined relatives of patients recently admitted to in-patient care, and secondly because different cut-off points in the subscales of criticism and EOI were used at different times to determine the presence or absence of high EE. At the suggestion of Dr Leff (personal communication), the fairest comparison is to use a cut-off of 6 for criticism and 4 for EOI (although 3 has been used in this and later studies); and to consider only relatives of Nithsdale schizophrenic patients recently admitted to in-patient care, that is, during the previous year. The recalculation of results suggests the prevalence of high EE in rural Nithsdale (50%) might be similar to that in urban London (57%) but much higher than in Chandigarh, (23%; cut-off of 3 for EOI) and lower than in California (67%).

The results of the retrospective review must be treated very cautiously because, as discussed above, EE may in some cases fluctuate over time and if relatives had been assessed at the time of the patients' admission more might have shown high EE than in the prevalence survey. Nonetheless the retrospective results are of some interest. Although in the year previous to the survey there was a trend towards increased admission rates among schizophrenic patients living in high EE families there were no statistically significant differences in admission rates between patients living on their own or with relatives, between patients living with high and low EE relatives and between patients having little or much contact with high EE relatives. This contrasts sharply with relapse rates over 9 months in the prospective studies reported by Vaughn & Leff (1976a). In these studies, 13% of patients discharged to low EE homes but 51% of patients discharged to high EE homes relapsed. Also, medication in the present study did not appear to exert a prophylactic effect in patients living with high EE relatives; in contrast, in the studies of Vaughn & Leff, 92% of patients discharged on no medication to high contact/high EE homes relapsed. However, the numbers of patients in the different Nithsdale subgroups

are perhaps too small to warrant serious statistical analysis (for example there were only four patients in the high contact/high EE/no medication group).

It may be that other more important determinants of relapse swamp the contribution of family life in a community of schizophrenic patients. Patients admitted over the preceding year had had more previous admissions than patients who were not admitted; this may simply reflect severity of illness. Also, life events which are not assessed by the CFI can affect relapse rates (Leff & Vaughn, 1980). Alternatively, might there be protective factors in a rural community such as Nithsdale which do not exist in an inner-city area such as Camberwell? Most schizophrenic patients in Nithsdale were born and brought up in the area and many still have some contact with acquaintances, friends and more distant relatives outside the nuclear family home. Also, there is a well developed community psychiatric nursing service, a considerable number of patients are regular attenders at the day hospital, and most attend out-patient clinics. Perhaps such contributions outside the home are more widespread and better developed than in an urban area; advice, encouragement and support from these people may help to protect against the hostility, criticism and over-involvement of close relatives.

Neither the clinician's hunch nor the PRS proved to be an adequate shortcut to the assessment of high EE. If the consultant believed a relative was neither hostile nor critical, then it was highly likely that the relative fell into the low EE category as determined by the CFI. However, he had less success in determining which relatives had high EE. He appeared to have a much wider concept of hostility and criticism than that determined by the CFI and thus assigned many low EE relatives to the high EE category. If on the basis of his clinical hunch he and his team were to embark on family therapy for schizophrenic patients living with high EE relatives a substantial number of low EE families would find themselves in treatment - perhaps no bad thing.

The PRS completed by relatives certainly distinguished in a statistical sense between high and low EE categories. However, because of the wide scatter of scores on the questionnaire in the high EE category, there was no clear cut-off point above which the clinician could confidently assert most high EE but few low EE relatives would be found. The PRS, therefore, may be of use for research purposes but not appropriate in an everyday clinical setting where the purpose is to identify an individual relative with high EE. Statistical probability does not yield precise prediction.

As an important by-product of the study, valuable insights were gained into the families of the Nithsdale schizophrenic patients and we would like to conclude by recording some of our more vivid impressions. Interviewing the family and friends of a given patient was a dialogue about the lives of the people who have taken on a considerable burden of care with varying degrees of willingness. The impression left was of people struggling, but often succeeding in coming to terms with a major change in a child or spouse, a change that left that person unpredictable, sometimes dangerous. One father said that his world had shrunk to the small but chaotic world of his daughter. The most contented homes were often the group homes; it is surprising that in place of the expected emotional blunting there was warmth and positive regard. While many experiences were adverse, humour was not lacking, which was to be expected from a couthie people such as live in Nithsdale. Where a schizophrenic patient was married, the overall impression of the marriages was of stability with the offspring well cared for. Maybe the stigma helps to draw a family together to withstand any external threat. Any adverse effect of caring for schizophrenic children did not seem to be reflected in the mothers either. Two were aged over 90; both gave vivid interviews.

To see people in their homes gives an insight rarely gained in the out-patient

department and a willingness by a doctor ('busy people') to take an interest in home life was remarked on favourably many times. Advice is needed for next-of-kin and must be greatly helped by knowing home circumstances (Kuipers & Bebbington, 1985).

TABLE 3.1.1  
PATIENTS' LIVING ARRANGEMENTS

Patient lives with: %	Total (n = 72)	Male (n = 35)	Female (n = 37)
Parents	41	57	24
Spouse	42	34	49
Child(ren)	4	0	8
Other relative	6	6	5
Friend	7	3	14

TABLE 3.1.2  
ADMISSION OF NITHSDALE SCHIZOPHRENIC PATIENTS TO IN-PATIENT  
CARE IN PREVIOUS YEAR

	TOTAL NUMBER OF PATIENTS	NUMBER OF PATIENTS ADMITTED	PERCENTAGE OF PATIENTS ADMITTED
Lives alone	42	9	22
No medication	14	4	29
Receiving medication	27	5	28
Low EE family	35	9	26
No medication	14	6	43
Receiving medication	21	3	14
High EE family	25	9	36
No medication	6	1	17
Receiving medication	19	8	42
High EE/high contact family	19	7	37
No medication	4	1	25
Receiving medication	15	6	40

1. Medication unknown in one patient.
2. More than 35 hours per week in face-to-face contact.

TABLE 3.1.3  
SCORES ON PATIENT REJECTION SCALE

TYPE OF RELATIVE AS DETERMINED BY CAMBERWELL FAMILY INTERVIEW	NUMBER OF RELATIVES	REJECTION SCORE		
		MEAN SCORE(SD)	STUDENT'S 't'	P
High expressed emotion	25	68 (27)	} 2.05	<0.05
Low expressed emotion	33	56 (18)		
Hostile	5	93 (11)	} 3.61	<0.001
Not hostile	53	58 (21)		
Critical	17	76 (25)	} 3.40	<0.01
Not critical	41	55 (19)		

- 1 Any degree of hostility on CFI  
2 Six or more critical comments on CFI

### **3.2 DOES RELATIVES' HIGH EXPRESSED EMOTION PREDICT RELAPSE?**

**R G McCREADIE**

**K PHILLIPS**



## SUMMARY

A review of all known schizophrenic patients living in Nithsdale in South-West Scotland identified long-stay in-patients, patients living on their own and those living with relatives showing low or high expressed emotion (EE). A prospective 12-month follow-up identified relapsing patients, defined as those readmitted to hospital with exacerbation of schizophrenic symptoms or a fresh episode of illness, or, if not readmitted, with a significant increase in antipsychotic medication. There was no difference in relapse rates in patients living on their own, with low-EE, or with high-EE relatives. Amount of contact with high-EE relatives did not affect relapse rates. The different results obtained from the Nithsdale group compared with one from Camberwell are discussed.

Reports over 25 years from the MRC Social Psychiatry Unit in London have suggested that schizophrenic patients living with relatives who show high expressed emotion (EE) are more likely to relapse, especially if face-to-face contact between patient and relative is high, and the patient is unprotected by antipsychotic medication (Brown *et al*, 1962, 1972; Vaughn & Leff, 1976a). However, a retrospective review of all known schizophrenic patients living in Nithsdale found only a trend, not of statistical significance, towards a higher admission rate to in-patient care in patients from high-EE homes (McCreadie & Robinson, 1987). We report now a 12-month prospective study of relapse rates among Nithsdale schizophrenic patients living in long-stay in-patient wards, and living in the community on their own, or with low-EE or high-EE relatives. We believe the study is unique, in that the rating of EE was made when patients were not in a state of relapse. If high EE is causally important in schizophrenic relapse, then the relapse rate over the months following assessment might be expected to be higher in the high than in the low-EE group.

## METHOD

The identification of schizophrenic patients and the rating of EE in their relatives have been described in detail elsewhere (McCreadie & Robinson, 1987). Briefly, a census on 1 July 1985 of all known schizophrenic patients ( $n = 142$ ) in Nithsdale, an historically ancient and geographically discrete part of Dumfries and Galloway Region in south-west Scotland, found 20% were long-stay in-patients; 30% lived alone, in digs, or only with relatives aged under 18 years; 50% were living with adult relatives or friends, and it was these on whom the present study focused. Forty-nine percent were males (mean age 42 years), of whom 57% lived with parents, and 51% female (mean age 50 years) of whom 49% lived with a spouse. A psychiatrist trained in the use of the Camberwell Family Interview (Vaughn & Leff, 1976b) rated EE in relatives and friends of 60 patients, and assessed the amount of face-to-face contact between

patient and relative during a typical week. The husband or wife of a married patient was always seen; where an unmarried patient lived with both parents, both mother and father were interviewed. In all, 70 patients or friends were seen. A relative fell into the high-EE category if he made six or more critical comments, showed any degree of hostility, or had a rating of 3 or more on emotional over-involvement (EOI) (Leff *et al*, 1982). The interviews took place over a 3-month period following the census. The results showed that 58% of patients were living with low-EE relatives and 42% with at least one high-EE relative; parents were more critical and over-involved than spouses.

Relapse over 12 months after assessment, or following the census date in the case of in-patients and patients living on their own was determined in two ways. Firstly, if a patient was readmitted to in-patient care, his or her case-records were scrutinised, and a decision made as to whether that admission was the result of an exacerbation of a chronic schizophrenic illness, or a fresh episode. Secondly, as not all patients who relapse are necessarily readmitted to in-patient care, medication prescribed to all schizophrenic patients over the 12 months was determined through examination of medication charts and out-patient records, and discussion with community psychiatric nurses and general practitioners. A relapse was deemed to have occurred where the dose of an antipsychotic drug was increased by at least 100%, where a patient on no antipsychotic medication was then prescribed such a drug, or where another antipsychotic drug was added to the pre-existing antipsychotic regime. Both assessments of relapse were made by psychiatrists blind to the EE ratings. Finally, as part of routine ward practice, the social problems of all schizophrenic patients admitted to in-patient care over the 12 months were assessed by the Nithsdale team social worker using the National Institute for Social Work Case Review System (Goldberg & Warburton, 1979).

## RESULTS

Table 3.2.1 shows relapse rates over 6 and 12 months as defined by readmission, increase in medication, and by readmission and/or increase in medication ('total relapse rate'). Results are given separately for long-stay in-patients and for patients living on their own, in low-EE homes, and in high-EE homes. Results are also given for patients living in high contact with high-EE relatives (more than 35 h per week face-to-face contact). The results for patients living with relatives excluded 12 whose relatives were not rated for level of EE and one who was in a state of relapse at the time of EE assessment.

The following results refer to 'total relapse rates'. The relapse rate in all Nithsdale schizophrenic patients (excluding the one patient in a state of relapse at EE assessment) over 6 months was 13 out of 141 (9%) and over 12 months, 23 of 141 (16%). The relapse rate in patients from different settings ranged, over 6 months, from 7% (patients living on their own) to 13% (patients living with high-EE relatives) and over 12 months from 14% (patients living on their own) to 21% (in-patients). When measured by chi-squared tests, there were no statistically significant between-group differences in relapse rates; for example, the relapse rate over 12 months in patients living in high contact with high-EE relatives was 17% and the corresponding figure for patients living with low-EE relatives was 20%. Two of 32 patients (6%) who received no medication relapsed over 6 months, and 3 (9%) over 12 months; the corresponding percentages for patients receiving medication were 10% and 14%. In patients living on their own, only one of 11 (9%) on no medication relapsed over 12 months while five of 31 on medication did so (16%). In patients in low-EE homes, two of seven on no medication (29%) relapsed over 12 months, while five of 28 (18%) on medication did so. In high-EE homes, none of four patients on no medication relapsed, while four out of 20 (20%) on medication did so over 12 months.

The above results refer to the total Nithsdale schizophrenic population, all of which has a firm case-record diagnosis of schizophrenia. The data were reanalysed for only those fulfilling the Feighner criteria for 'definite' or 'probable' schizophrenia (Feighner *et al*, 1972). Relapse rates in 'Feighner positive' patients with different living arrangements were essentially the same as for the total Nithsdale group. However, more Feighner positive than Feighner negative patients lived with high-EE relatives (80% of patients living with high-EE relatives were Feighner positive:  $\chi^2 = 3.96$ ;  $P < 0.05$ ).

When patients (excluding long-stay in-patients) who relapsed over 12 months were compared on social and demographic data with those who did not relapse, there were no statistically significant between-group differences in age, sex distribution, marital status, and length of illness; however, those who relapsed had more previous admissions (mean 8.8 vs 4.9). When tested by the Mann-Whitney U-test, this difference was significant ( $P < 0.001$ ). There were no statistically significant differences between relatives of patients who relapsed and did not relapse in mean number of hours of face-to-face contact with patients, and mean scores on criticism, hostility, emotional over-involvement, warmth, and positive comment sub-scales of the EE rating.

Thirteen patients were admitted to in-patient care over 12 months. When rated by the National Institute for Social Work Assessment Schedule (Goldberg & Warburton, 1979), the mean number of social problems at the time of admission was found to be 4.4. The problems ranged from severe physical illness of a relative to a relative's increasing and excessive drinking to a serious debt of £1000. Numbers in each group were small, but there were no statistically significant differences in the mean number of problems in patients living on their own (3.8), with low-EE relatives (5.4), or with high-EE relatives (3.8).

## DISCUSSION

The present, unique, 12-month prospective study of schizophrenic patients living in a discrete geographical area has shown that relapse rates, as defined by readmission to in-patient care because of schizophrenic symptoms or a fresh episode of illness, or a significant increase in medication, were no greater in patients living with high-EE relatives than in those living with low-EE relatives or on their own. The findings therefore do not support the Camberwell findings (Vaughn & Leff, 1976a) that high EE is an important aetiological factor in schizophrenic relapse.

However, the differences between the Nithsdale and Camberwell results must be treated with caution, as the two studies methodologically approached the problem from very different angles. The first major difference was that the Nithsdale study was naturalistic, while Camberwell was a controlled trial. In Nithsdale, patients had a firm clinical diagnosis of schizophrenia, and the majority (68%) fulfilled the Feighner criteria for definite or probable schizophrenia; in Camberwell, the diagnosis was made using the Present State Examination (PSE; Wing *et al*, 1974). In Nithsdale, relapse was defined by readmission and/or increase in medication, in Camberwell by a recurrence of schizophrenic symptoms as detected by the PSE. A second major difference was the timing of patient recruitment and EE assessment. In Nithsdale, patients living in the community were recruited when they were not in a state of relapse, and relatives assessed over the following 3 months; in Camberwell, patients entered the study and relatives were assessed at the time of in-patient admission for relapse. The finding in Nithsdale that relapse rates were no greater in high- than in low-EE homes assumes that EE levels did not change over the months after assessment. Is this assumption valid? We know of no study that has examined serially relatives identified initially as low EE, whether or not this assessment was made at the time of relapse.

Previous work on high EE has suggested that in highly enmeshed families (high EE, high contact) EOI rated at the time of relapse barely changed in relatives where no therapeutic intervention took place, at least over a 9-month period (Leff et al, 1982). The same study found a small non-significant reduction in the number of critical comments made by untreated relatives, a reduction entirely accounted for by two relatives. However, another study found criticism to be less stable; a considerable reduction occurred over 9 months in some relatives where patients markedly improved (Brown et al, 1972).

The most convincing evidence in a prospective and naturalistic study, such as the Nithsdale review, that EE is not causally related to schizophrenic relapse, would be that the relapse rate in patients living in consistently low-EE homes (low EE both at initial assessment and at time of relapse) is as great as in consistently high-EE homes. A switch from low EE to high EE at relapse could be interpreted as relapse raising the level of EE, or vice-versa. It is the case in the present study, however, that over the 3 months after assessment (a period of time too short to allow much change in the level of EE?), only one of 24 patients living in a high-EE family relapsed. If high EE is of major causal importance, then it is probable that more than one patient would have relapsed in this period.

If the methodological drawbacks in the present study are more apparent than real, what possible reasons could explain the difference between the Nithsdale and Camberwell results? Firstly the Camberwell sample, patients identified on admission to hospital, is biased towards relapse and chronicity. The Nithsdale schizophrenic population is not biased in this way and consequently might contain a high proportion of individuals with a good prognosis, some of whom might rarely be seen by hospital psychiatrists. This interpretation is supported by the low relapse rate of 16% over 1 year. Other studies of chronic schizophrenic patients in the community maintained on antipsychotic

medication found relapse rates of 20% over 9 months, 26-29% over 15 months (Hirsch et al, 1973), and 17-20% over 6 months (Johnson, 1979). The effect of high EE may not be demonstrable in such a geographically based sample of individuals with an overall good prognosis in the same way that drug effects are hard to show in a good-prognostic group (Leff, 1973). The low relapse rate in Nithsdale complements the very long-term outcome studies of Bleuler (1983) and Ciompi (1980) which also revealed a much better prognosis for schizophrenic patients than is conventionally accepted.

A second explanation of the difference between Nithsdale and Camberwell might be that the association in Camberwell between high EE (rated at the time of relapse) and relapse was due to the relapsing patient who raised the level of EE in the relative. Leff et al, 1982, 1985) have argued that this is not so; they have shown that lowering EE in relatives through a package of social interventions including family sessions, a group for relatives, and an educational programme, was associated with a lower relapse rate in schizophrenic patients living in high contact with high-EE relatives. Thus high EE appears to be causally important. However, it is possible that such social interventions may have lowered also the relapse rate in schizophrenic patients living with low-EE relatives (not examined by Leff et al), and that lowering EE is merely a by-product of treatment which produces its effect in other ways. It is noteworthy that a recent American study (Hogarty et al, 1986), which found that no patient relapsed where EE changed from high to low, also found that a treatment package which included both social-skills training and family treatment could lower relapse rates in patients living with high-EE relatives without lowering the level of EE itself. That study also found that the amount of face-to-face contact between patient and relative did not affect relapse rates, as did the Nithsdale study.



A third explanation of the Nithsdale results might be that factors more important than high EE precipitate relapse in schizophrenic patients, and thus swamp the effect of high EE. For example, patients who relapsed had significantly more previous admissions; this may simply reflect severity of illness. Also, life events are important in schizophrenic relapse (Brown & Birley, 1968), and in the present study, assessment by a social worker of stresses schizophrenic patients were experiencing at the time of admission to in-patient care found most patients had many pressing problems. Physical illness in a relative, developing alcoholism, and severe financial problems may be more important causes of stress than a critical relative. Such stresses were found as commonly in patients living on their own as with those living with relatives.

A fourth explanation might be that in a rural community such as Nithsdale, factors not found in an inner-city area such as Camberwell protect against high-EE relatives. Such possible factors have been discussed elsewhere (McCreadie & Robinson, 1987) but are worth summarising. Most Nithsdale schizophrenic patients have been born and brought up in Nithsdale, and many still have contact with more distant relatives and friends outside the nuclear home. Most patients are supervised at home by community psychiatric nurses who themselves have worked for many years in the area, most attend an out-patient clinic, and a significant minority attend a day hospital. Some patients also have contact with other consistent agencies such as social workers and voluntary organisations. Such relatives, friends and professionals might well provide sufficient long-standing and consistent warmth, support, and encouragement to protect against criticism and hostility within the home. It is possible that such long-term support is not found in an inner-city area such as Camberwell with its more rapid turnover of both patients and professionals. The low overall relapse rate in Nithsdale, 16% over 12 months, may be due to a high proportion of good-prognosis patients (see above), and possibly these protective factors contribute to the good prognosis.

Previous work has suggested that maintenance antipsychotic medication is especially useful in protecting patients living with high-EE relatives (Vaughn & Leff, 1976a). Although numbers were small, no such effect was found in the present study; indeed, in high-EE homes, none of the patients on no medication relapsed. The Nithsdale findings are not surprising, as the study was in no sense controlled, but simply an examination of clinical practice. It is the policy in Nithsdale to give as little antipsychotic medication to schizophrenic patients as possible, and efforts have been made over the years to reduce cautiously and discontinue medication. Also, the 'protective factors' discussed above may protect non-medicated patients against relapse.

More Feighner positive than negative patients lived with high-EE relatives. The main criterion which determines if a schizophrenic patient is Feighner positive is length of illness - the patient must have experienced at least 6 months of symptoms without a return to the previous level of functioning. Thus, the more chronically ill patients are to be found in high-EE homes. It is possible that high-EE relatives have a more damaging long-term effect on patients, but on the face of it, it is more probable that patients with longstanding deficits produce more hostility and criticism in relatives.

Our tentative conclusion in this naturalistic study is that there is no clear association between high EE measured when patients are in remission and relapse rates of schizophrenic patients over a 12-month period. Methodological drawbacks in the present study cannot be ignored, but the results suggest that there is not necessarily a causal relationship between high EE and relapse. More studies of the present naturalistic kind, which rate EE serially, are urgently needed.

TABLE 3.2.1  
RELAPSES OVER 6 AND 12 MONTHS

Living arrangement	Relapses over 6 months						Relapses over 12 months					
	Relapses by admission		Relapses by increase in medication		Relapses by admission and/or increase in medication		Relapses by admission		Relapses by increase in medication		Relapses by admission and/or increase in medication	
	N	%	N	%	N	%	N	%	N	%	N	%
Lives alone (n=42)	3	7	3	7	3	7	4	10	6	14	6	14
Lives with low-EE relative (n=35)	2	6	4	11	4	11	5	17	6	18	7	20
Lives with high-EE relative (n=24)	2	8	1	4	3	13	4	17	2	8	4	17
Lives in high contact with high-EE relative (n=18)	2	11	0	0	2	11	3	17	1	6	3	17
Long-stay in-patients (n=28)	-	-	3	11	-	-	-	-	6	21	-	-
Total	-	-	-	-	13	9	-	-	-	-	23	16

The table excludes one patient in relapse at time of EE assessment.

**3.3 DO RELATIVES WANT FAMILY INTERVENTION -  
AND DOES IT HELP?**

**R G McCREADIE**

**K PHILLIPS**

**J A HARVEY**

**G WALDRON**

**M STEWART**

**D BAIRD**

## SUMMARY

Sixty three relatives of 52 schizophrenic patients living at home in Nithsdale in South West Scotland were offered a package of treatments by professionals working in an everyday NHS setting: educational seminars, relatives groups, and family meetings. Thirty-two relatives refused intervention; the commonest reason was "things are fine at the moment". Of the 31 relatives who agreed, 14 attended neither the educational seminars nor the relatives' groups, both of which were held in the local psychiatric hospital. These findings demonstrate the difficulty in engaging relatives in treatment. Seventeen relatives had a mean of 10 treatment sessions and formed the intervention group. There was little change in relatives' level of expressed emotion after intervention. The number of patients who relapsed was the same in the 18 months before and after intervention, but the total number of relapses fell after intervention.

A recent consistent finding in schizophrenia research is the impact family intervention has on relapse rates. Different forms of intervention in the United Kingdom (Leff et al 1982, 1985, 1989; Tarrier et al 1988, 1989), and in the United States (Falloon et al 1982, 1985; Hogarty et al 1986) have produced a reduction in relapse rates which may be associated with a reduction in the level of relatives' expressed emotion (EE).

The reported studies have involved research teams in addition to clinicians responsible for patient care. "The application of the results in a routine way to the work of the busy clinical team must be the next phase" (Kuipers and Bebbington, 1988). The present study attempts to answer the following questions: in an everyday NHS setting, do relatives want intervention; does such intervention lower relatives' EE; and is there a reduction in relapse rates?

## METHOD

The identification of schizophrenic patients has been described elsewhere (McCreadie, 1982a; McCreadie and Robinson, 1987). Briefly, repeat censuses since 1981 in Nithsdale, an historically ancient and geographically discrete part of Dumfries and Galloway Region in South West Scotland, have identified all known schizophrenic patients - inpatients, daypatients, outpatients and patients known only to their family doctor. A repeat census on 1.1.87 identified 77 patients living at home with relatives or friends: it was these on whom the present study focused. The patient was informed of the purpose of the study by the consultant responsible for his care (RGMCC) and if consent was given an approach was made by the consultant to the relatives with whom the patient was living. Frequently both these interviews were lengthy. If relatives then consented a psychiatrist (KP) trained in the use of the Camberwell Family Interview rated EE in relatives and assessed the amount of face to face contact between patient and relative during a typical week. A relative fell into the high EE category if he made

six or more critical comments, showed any degree of hostility or had a rating of three or more on emotional overinvolvement (Leff *et al* 1982); more than 35 hours a week indicated high contact (Vaughn and Leff, 1976).

Relatives were offered a package of treatments: educational seminars, relatives discussion groups, and family meetings. The seminars, held weekly at the hospital, lasted approximately one hour, and were led by a psychiatrist of four years' experience (GW). They covered the main areas of aetiology, symptoms, treatment and prognosis. Relatives were encouraged to ask questions. The relatives groups, also held weekly at the hospital and lasting one to one and a half hours, were led by two social workers who had been qualified for seven and six years, and were both Mental Health Officers (JH and DB). One had attended a one year course on family therapy on a day release basis at the Scottish Institute of Human Relations, Edinburgh. The groups focused on the day-to-day problems of coping with a schizophrenic relative. One principal aim was to bring high and low EE relatives together, and encourage low EE relatives to offer their solutions. Family meetings which included the patient were held weekly or fortnightly, and were led by a social worker in the patient's home (JH or DB). They focused on everyday problems of living.

Relatives' EE and amount of contact with the patient were reassessed at the end of treatment. The interviewer was not told if the relative had in fact taken part in the intervention programme (see below), nor did he ask the relative; inevitably, however, the topic cropped up on occasion during interviews.

Patients were followed for 18 months after intervention. The number of relapses for that 18 month period, and an equivalent 18 months before intervention was determined. As in a previous study (McCreadie and Phillips, 1988), relapse was defined in two ways. Firstly, if a patient had been readmitted to inpatient care his or her case records

were scrutinised, and a decision made as to whether that admission was the result of an exacerbation of a chronic schizophrenic illness or a fresh episode. Secondly, as not all patients who relapse are necessarily readmitted to inpatient care, medication prescribed to the patients over the 18 months was determined through examination of medication charts and outpatient records. A relapse was deemed to have occurred where the dose of an antipsychotic drug was increased by at least 100 %, where a patient on no antipsychotic medication was then prescribed such a drug, or where another antipsychotic drug was added to the pre-existing antipsychotic regime. Assessment of relapse was made by a psychiatrist (MS) blind both to the EE ratings and whether or not the patients' relatives had had the intervention programme.

## RESULTS

All 77 patients had a firm clinical diagnosis of schizophrenia, and 62% fulfilled the Feighner criteria for "definite" or "probable" schizophrenia (Feighner *et al* 1972). There were 35 males (mean age 43 years (range 21 - 68), mean length of illness 13 years (< 1 year - 42 years) and mean time since last hospital admission 5 years (< 1 - 21); and 42 females (mean age 44 years (18 - 78), mean length of illness 15 years (< 1 - 50) and mean time since last hospital admission 6 years (< 1 - 30)). Relatives and/or friends of 25 patients were not interviewed: 10 patients lived with other schizophrenic patients and/or in a group home, six patients had made no contact in any of the previous Nithsdale surveys, three patients did not attend interview when consent was sought to approach relatives, one patient refused an approach to relatives, two relatives failed to keep appointments, a family doctor refused an approach to either a patient or her relatives, and two patients were not seen for administrative reasons. Thus 63 relatives of 52 patients were interviewed. Thirty one relatives agreed to intervention, 32 did not. There were no differences between those who did and did not agree in sex distribution, relationship to patient and numbers with low EE (Table 3.3.1); and in the following



patient characteristics: sex, age and length of illness. In the refusal group, relatives with high EE and those who declined an assessment of their EE status equalled the number with high EE in the group agreeing to intervention. Eight out of 12 patients whose relatives agreed to and took part in the intervention programme (see below) had been admitted to hospital during the previous year compared with 4 of 27 patients whose relatives refused intervention ( $\chi^2 = 8.19$ ,  $P < 0.01$ ). The principal reasons for refusing intervention were: "things are fine at the moment" ( $N = 12$ ); "it's (the patient) who needs help, not me" ( $N = 6$ ); "(the patient) doesn't want anyone else to know he has been ill" ( $N = 5$ ). Other reasons given by a single relative included "I'm too busy", "I've coped all these years", "it's too late now".

Although 14 of 31 relatives agreed to intervention they failed to appear at the educational seminars and relatives groups; they only had one or two family meetings in their homes. The remaining 17 relatives were designated the intervention group. They had a mean of 10 treatment sessions (range 3 - 20: viz. educational seminars: mean 2 (range 0 - 4); relatives groups: mean 3 (0 - 8); family meetings: mean 5 (0 - 14)). At least one member of each family had a minimum of 8 sessions (mean 12, range 8 - 20).

Sixteen of the 17 relatives had their level of EE and amount of contact with the patient measured before intervention. Five had high EE/high contact, 4 high EE/low contact, 2 low EE/high contact and 5 low EE/low contact. Thirteen relatives were reassessed at the end of intervention. One high EE relative was now low EE, and one low EE high EE; the remaining 11 (6 high EE, 5 low EE) were unchanged. Two relatives in high contact were now low, two in low contact high.

Nine of the 12 patients whose relatives had intervention relapsed at least once in the 18 months before intervention; six relapsed in the 18 months after intervention. Between them the 12 patients had 17 relapses over the 18 months before intervention and 8

relapses in the 18 months after intervention. Readmission to hospital defined 23 of the relapses, a 100% increase in medication defined two. The number of relapses in the 7 patients from high EE homes fell from 13 to 4 (sign test,  $P < 0.06$ ).

### General Comments

The relatives who took part in the intervention programme were in the main pleased with the results. They were initially nervous about attending the group, and needed encouragement from the group leader. They appreciated the educational seminars most and believed at the end they knew more about the illness, treatments available and prognosis. They were pleased that 'for a change' interest was being shown in relatives. They thought the relatives' groups were most useful if there was a crisis at home. They were relieved their experiences were not unique. Topics frequently discussed included violence, loneliness, childlike behaviour, withdrawal, refusal to take medication, and anxiety over suicide attempts. Both in the relatives groups and in the family meetings means of overcoming these problems were examined. Practical help through for example holidays and financial advice was appreciated.

During the 18 month follow up period most relatives believed that 'things were easier at home'. Also, a loose network amongst relatives continued after formal intervention stopped. The network was strengthened when many relatives and patients joined either the local recently established Mental Health Association or National Schizophrenia Fellowship. Thus education and support, organised by and for patients and relatives themselves continued. Relatives who refused intervention did not join either organisation.

## DISCUSSION

The present study is "different" (Bebbington, 1988) in that it examined schizophrenic patients in remission living in the community. Other studies of EE and family intervention have examined patients admitted to hospital after a relapse. Great caution must therefore be taken when results in this study are compared with others.

Perhaps the most important finding was the difficulty experienced in engaging relatives in treatment. Most relatives did not want to participate in the family intervention programme. Many reasons were given, but the statement "things are fine at the moment" occurred repeatedly. It was our subjective impression that in many cases this statement was accompanied by a mixture of resignation, pride and resentment. It is not surprising therefore that most relatives who did eventually agree to intervention were living with a patient who had been readmitted to hospital the previous year. A number of relatives said they would join an intervention programme, but did not then attend the educational seminars or relatives groups. Both these activities took place during the day at the hospital and this might have mitigated against attendance. In another recent study (Leff *et al*, 1989) 5 of 11 families failed to attend a relatives group carried out in central London. Leff and colleagues now believe it is particularly important to offer home visits to families who are unable or refuse to attend the relatives groups. It is clear therefore that vigorous outreach is necessary in order to enable relatives to accept an offer of help, particularly if they feel other offers have been unhelpful.

Although relatives who did participate in the intervention programme had a considerable number of sessions in one of the three treatment areas, there was virtually no change in their level of EE after intervention. There are three possible reasons for this. Firstly, the intervention may have been inadequate or did not continue long enough. Treatment was given by professionals who were experienced practitioners,

but who did not have special skills in family intervention in schizophrenia. They were aware of the principles behind the intervention of Leff and colleagues, but had received no specific training from his group. The intervention in the present study is therefore an approximation of what was achieved in other studies; however, this probably reflects clinical reality as it is unlikely in the foreseeable future that many professionals working in hard pressed NHS psychiatric facilities will be seconded for specialised training. A second possibility is that after family intervention the level of EE falls only gradually, and that if a reassessment of EE had been carried out at the end of the 18 month follow-up period results might have been different. However, a previous study (Tarrier *et al*, 1988) found EE status had changed by four and a half months after intervention. Thirdly, it may be that the level of EE is robust, and is a stable dimension. Even in intensive intervention settings (Leff *et al*, 1982, 1985, 1989) 6 of 12 and 10 of 16 relatives did not move from high to low EE. As the years pass in Nithsdale a considerable number of relatives have had their level of EE rated on a number of occasions, separated by many months. This will be the subject of a separate enquiry, but there is tentative evidence that the level of EE changes little over the years. In this context it is again necessary to emphasise that relatives were assessed when patients were not in a state of relapse.

Relapse was used as the outcome measure of intervention firstly because it allows easy comparison with most other previous studies, and secondly because it is readily understandable to clinicians. It might have been possible to use broader outcome measures such as family burden, problem solving, and role performance of patients. However, these more sophisticated measurements are not routinely applied in an everyday NHS situation. Although intervention did not alter greatly the number of patients who had at least one relapse, there was a fall in the total number of relapses over the subsequent 18 months, a fall which just failed to reach statistical significance at the 5% level in patients living in high EE homes (the sample size was small).

Consideration of the total number of relapses is probably realistic and of importance to relatives. Other studies have shown that relapse rates can fall without a corresponding fall in high EE. In an American study (Hogarty et al, 1986) this happened when social therapy and family intervention were combined; in a United Kingdom study (Leff et al, 1989) it happened when face-to-face contact was reduced. If the finding in the present study is genuine, that there has been a fall in the total number of relapses, what factors in Nithsdale might be important? It is possible that an improved ability amongst families to solve problems has reduced both the patient's vulnerability and his environmental stress. In addition the much greater interest in relatives shown by doctors and social workers already well known to schizophrenic patients might have increased the family's sense of worth and support. Finally the continuing network amongst relatives during the follow-up period provided continuing mutual support. It is noteworthy that although relatives believed the educational seminars to be most helpful, a previous study (Tarrier et al, 1988) found education alone had no effect on relapse rates.

In conclusion, if professionals working in everyday NHS facilities wish to embark on family intervention they should probably offer such help to relatives living with patients who have recently been readmitted to hospital.

TABLE 3.3.1 CHARACTERISTICS OF RELATIVES

	Relatives who agreed to intervention % (N = 31)	Relatives who did not agree to intervention % (N = 32)
<u>Sex</u>		
Male	48	41
Female	52	59
<u>Relationship to Patient</u>		
Father	23	12
Mother	32	41
Husband	13	25
Wife	10	16
Child	16	3
Other	6	3
<u>Level of Expressed Emotion</u>		
High	48	28
Low	48	47
Refused	-	22
Not known	4	3

### **3.4 RELATIVES' EXPRESSED EMOTION: STABILITY OVER FIVE YEARS AND ITS RELATION TO RELAPSE**

**R G McCREADIE**

**L J ROBERTSON**

**D J HALL**

**I BERRY**

## SUMMARY

The level of expressed emotion (EE) in 30 relatives of 30 schizophrenic patients was assessed on three separate occasions over five years. EE was high on all three occasions in 25% of relatives, low on all three in 38% and fluctuating in 38%; that is, in the majority of relatives (63%) the level of EE was stable over time. Three relatives who had previously shown high EE had evidence of dementia at the time of the third assessment, and showed low EE. Forty-seven percent of patients relapsed at least once over five years; patients who relapsed were evenly spread throughout those living in a consistently high, consistently low or fluctuating EE home. However, patients living in low EE homes who did relapse did so significantly less often than those who relapsed and were living in high or fluctuating EE homes. A number of patients in consistently high EE homes did not relapse at all over five years. Assessment of EE at the time of relapse did not show consistently high EE ratings.



The relationship between relatives' expressed emotion (EE) and schizophrenic relapse has been examined over a thirty year period (e.g. Brown et al, 1962, 1972, Vaughn and Leff, 1976a, Leff et al, 1982, Hogarty et al, 1986, Tarrier et al, 1988, 1989, Leff et al, 1990). In all such studies, the level of EE has been assessed at the time of relapse. However, it is not clear whether in the absence of family therapy the level of EE shown at the time of relapse persists over a long time. That is, is the level of EE constant, reflecting the relatives' fixed set of attitudes or is it a temporary state waxing and waning in association with the patient's mental state?

There has been some work on the stability of EE over a short period. For example, Brown and colleagues (1972) found that the proportion of relatives who expressed criticism fell from 30% to 14%, over nine months, but that emotional overinvolvement (EOI) showed 'less of a tendency' to fall. Leff and colleagues (1982) found that two of eight relatives changed spontaneously over nine months from high to low EE, as measured by criticism, but there was no change in EOI. Hogarty and colleagues (1986) found that 11 of 44 households moved from high to low EE over one year without family treatment. Tarrier and colleagues (1988) found that seven of 16 relatives changed from high to low EE over nine months. Finally, Leff and colleagues (1990) in a study in Chandigarh in India found that 79% dropped from high to low EE over one year. All this work has examined changes in high EE. With regard to low EE, Tarrier and colleagues (1988) found one of 18 relatives moved from low to high EE over nine months. We know of no study which has examined the stability of EE over longer periods, nor of any studies, apart from our own (McCreadie and Robinson, 1987, McCreadie and Phillips, 1988, McCreadie et al, 1991), which have examined the level of EE before relapse.

It may well be that relatives show a variety of attitudes. Some may show persistently high and some persistently low EE over many years, and others a fluctuating level of EE. It has been suggested (Kuipers and Bebbington, 1988) that very low EE relatives

cope well whatever the circumstances and very high EE relatives have multiple problems, and cope badly with most of them, including the patients. The third 'vacillating' group may change category depending on their ability to learn new coping skills, spontaneously or through the intervention of others, and in their ability to use these new skills to manage crises. If the new skills are insufficient they may display reduced EE at one assessment, but revert back when they are unable to manage.

If high EE is causal in patient relapse, as argued by Leff and colleagues, then it might be expected that patients living in a persistently high EE environment would be more likely to relapse than those living in a persistently low EE environment. Those relatives in whom EE fluctuates might be expected to show such fluctuations in the high direction at the time of relapse.

The present study, by taking advantage of our naturalistic review, aims therefore to answer the following questions. How stable is the level of EE over a five year period? What are the relapse rates in patients who live in a consistently high, consistently low and fluctuating EE environment? What is the pattern of EE at the time of relapse?

## METHOD

The identification of schizophrenic patients has been described in detail elsewhere (McCreadie, 1982a, McCreadie et al, 1991). Briefly, repeat censuses have identified all known schizophrenic patients living in Nithsdale, an historically ancient and geographically discrete part of Dumfries and Galloway Region in South West Scotland. One such census on 1.8.85 identified 142 schizophrenic patients, all of whom had a firm case record diagnosis of schizophrenia, and of whom 68% fulfilled the Feighner criteria for probable or definite schizophrenia (Feighner et al, 1972). Fifty percent (N = 72) were living with relatives or significant others. Forty nine

percent of such patients were male (mean age 42 years, standard deviation (SD) 12 years, range 21-66 years; mean length of illness, as estimated from first hospital contact, 14 years, SD 10 years, range 1-40 years) and 51% female (mean age 50 years, SD 13 years, range 27-79 years; mean length of illness 18 years, SD 12 years, range 2-48 years). Forty one percent were living with parents, 42% with a spouse, 4% with a child (or children), 6% with an other relative and 7% with a friend. More males than females were living with parents. It was 60 such patients and their 70 relatives on whom the first of the Nithsdale EE studies focused (McCreadie and Robinson, 1987). This examined the prevalence of high EE. A second review of EE took place in 1987 as part of a screening procedure for a family therapy project (McCreadie *et al*, 1991). By 1990, 34 of the original 60 patients had lived continuously with the same relatives in Nithsdale over five years, and had had a firm clinical diagnosis of schizophrenia throughout that period. The remainder of the patients no longer fulfilled these criteria for various reasons: eight relatives and six patients had died, nine relatives were no longer living with the patient, six patients were no longer considered to be schizophrenic, and one family had moved away from Nithsdale. Thirty of the 34 patients had 30 relatives who agreed to be assessed for a third time. The age and length of illness of the 30 patients in 1985 were similar to the original cohort of patients living with relatives (11 males: mean age 39 years (SD7), mean length of illness 11 years (SD7); 19 females: mean age 52 years (SD14), mean length of illness 18 years (SD12)). The male but not female patients were younger than the total Nithsdale cohort. In the latter the mean age of males was 48 years (SD14) and females 51 years (SD13). The total cohort included 28 long stay inpatients, 19 of whom were male.

A psychiatrist (LJR), trained in the use of the Camberwell Family Interview (CFI), interviewed relatives in their homes over a five month period (April - August 1990). Interviews were taped and an assessment made from the recordings. A relative fell

into the high EE category if he/she made six or more critical comments, showed any degree of hostility or had a rating of three or more on emotional overinvolvement (EOI) (Leff et al, 1982).

Inter-rater agreement was examined between the three raters of EE in 1985, 1987 and 1990, all of whom had all been trained in the CFI. The third rater (LJR) assessed 21 audiotapes, 10 from the 1985 and 11 from the 1987 studies. The tapes were of interviews with relatives not assessed in the present study, and of whom 10 had originally been assessed as showing high EE, and 11 low EE.

As the current study proceeded it was clear to the psychiatrist that one or two elderly relatives appeared to be dementing. A brief test of intellectual functioning was therefore given to relatives over 65 years of age by one of two psychiatrists (DJH and IB) blind to the EE ratings (Hodkinson, 1972).

Relapses over the five year period were determined in two ways as in previous studies. Firstly, if a patient was readmitted to inpatient care, his or her case notes were scrutinised by a psychiatrist (DJH) blind to the relative's EE rating, and a decision made as to whether that admission was the result of an exacerbation of a chronic schizophrenic illness or a fresh episode. Secondly, as not all patients who relapse are necessarily readmitted to inpatient care, medication prescribed to all schizophrenic patients over the five years was determined through examination of medication charts and outpatient records. A relapse was deemed to have occurred where the dose of an antipsychotic drug was increased by at least 100%, where a patient on no antipsychotic medication was then prescribed such a drug, or where another antipsychotic drug was added to the pre-existing antipsychotic regime.

## RESULTS

### Inter-rater agreement

In 19 of 21 tapes there was agreement as to whether a relative showed high or low EE. There was agreement in all tapes about high or low criticism, in 20 tapes about the presence or absence of hostility and in 18 tapes about high or low EOI. The coefficients  $r$ , for the correlation between the two pairs of raters for raw scores were +0.78 and +0.87 for criticism and +0.74 and +0.92 for EOI. It was not possible to estimate correlation coefficients with regard to hostility as in 17 of the 21 tapes both raters gave a score of 0, that is, no evidence of hostility.

### Stability of EE over five years

Thirty relatives and friends of 30 patients were re-assessed; two fathers, seven mothers, eight husbands, five wives, one son, two daughters, two aunts and three friends. Included was the assessment of the level of EE in two relatives towards the same patient. Also, the level of EE in a mother towards two schizophrenic sons was assessed. Thus there were in all 32 EE ratings. EE was high on all three occasions (1985, 1987 and 1990) in eight relatives (25%) and low on all three occasions in 12 relatives (38%). Of the remaining 12 (38%) EE was low in eight relatives on two occasions and high on one; in four it was high on two occasions and low on one.

The stability of EE was further examined by considering only those ratings made outwith a patient's relapse (see below). Twenty nine relatives had at least two such ratings; the ratings showed consistently high EE in seven relatives (24%), consistently low in 13 (45%) and fluctuating EE in nine (31%). The corresponding results for criticism were high throughout in three relatives (10%) low in 18 (62%) and fluctuating in 8 (28%); for hostility 2 (7%), 24 (83%), and 3 (10%); and for EOI

3 (10%), 16(55%) and 10 (35%). There was no significant difference in the mean number of critical comments or degree of EOI in those who had consistently high EE when compared with those who showed high but other times low EE.

Two relatives aged over 65 years of age were rated by the mental test score as dementing and a third died before formal testing could be carried out. However, she had been interviewed for another study at the time of EE assessment by a psychiatrist blind to EE status; his clinical opinion was that she had a significant degree of dementia. All three had previously been rated as showing high EE (two overinvolved, and one both overinvolved and critical). At the third assessment all were rated as showing low EE.

Three of the 30 'relatives' were in fact three schizophrenic patients living together, namely two sisters and a daughter of one of the sisters. EE relationships on the three occasions are shown in Table 3.4.1. Sister (1) and her daughter had relapses over the five year period. Both had their level of EE assessed on one occasion at the time of their own relapse. Sister (2) had no relapses.

### Relapses and EE

Fourteen of the 30 patients (47%) relapsed on 33 separate occasions over five years: three of seven patients in a consistently high EE home (mean number of relapses 3.7), five of 12 in a fluctuating EE home (mean 3.2) and six of 11 in a consistently low EE home (mean 1.1). The eight patients living in a high or fluctuating EE home who relapsed did so significantly more frequently than the six living in a consistently low EE home (Mann Whitney U test;  $p < 0.02$ ). The amount of contact between patients and relatives was assessed in 1985 and 1987 but not in 1990. Of the seven patients living with relatives with consistently high EE, contact between patient and relative was high (more than 35 hours per week) in six of the patients on both occasions.

By chance a rating of a relative's EE was carried out within two months of relapse in 10 patients (13 relapses in all and thus 13 ratings) (Figure 3.4.1). Three of the 10 patients were in a consistently high EE home, three in a consistently low EE home and four in a fluctuating EE home. Relative's EE was high at the time of eight relapses and low at the time of five. As indicated in the introduction, previous research assessed patients and relatives only at the acute episode and at follow-up. In order to provide a point of contact with this research, results (shown in figure 3.4.1) were extracted for six patients and relatives assessed at the time of relapse and at follow-up when not in relapse. Three relatives showed low EE on both occasions, two high EE on both occasions, and one relative moved from high to low EE. The figure also shows three patients and their relatives who were assessed before, at the time of, and after relapse. The EE ratings in the first patient were low before, low during and low after; in the second, low, high, high; and in the third, low, high, low. In three patients, EE was assessed in a relative at the time of two separate relapses. In one patient the relative showed high EE on both occasions; in the other two the relative showed high, then low EE.

## DISCUSSION

As this review was part of a long term project it meant that EE was assessed on the three occasions over five years by three different psychiatrists. All three raters, however, had been trained in the use of the CFI and an examination of inter-rater agreement showed it to be satisfactory. In only two of 21 joint assessments (5%) was there disagreement as to whether EE was high or low. A strength of having three raters, as opposed to one, was that each was blind to the other ratings; ratings therefore were not influenced by previous results.

Some comment is necessary about the sample of patients and relatives assessed. Seventy two of the original 142 schizophrenic patients were living with relatives or friends. Sixty of these participated in the first study. At five year follow-up only 34 of the original 60 patients were still living with the same relatives, and of these four patients had relatives who refused to participate further. The study therefore focused on 30 of 142 patients (21%) who had lived continuously with the same relatives and friends for five years and whose relatives co-operated with detailed interviews. The sample is therefore not typical of the Nithsdale schizophrenic cohort; a bare majority of Nithsdale patients live with relatives or friends and a bare majority of those live with them for lengthy periods of time.

The level of EE was stable in the majority of relatives when assessed at any time (63%) or only outwith patients' relapse periods (69%). It seems therefore that EE in most relatives reflects a fixed set of attitudes. On the one hand there are low EE relatives who are probably supportive of the patient whatever the circumstances; on the other there are high EE relatives who are persistently critical, hostile or overinvolved. It is impossible to know of course for how long this fixed set of attitudes existed before the first EE assessment. Patients at the time of first assessment were in the main in or approaching middle age and had been ill for many years. The relative's fixed attitude may be a trait or the outcome of a developmental process. If the latter, EE might be less stable during the early years of a schizophrenic patient's illness.

In a minority of relatives the level of EE fluctuated and not necessarily only at the time of relapse. Such changes may have occurred spontaneously or in reaction to changed family circumstances not necessarily involving the patient. The number of patients and relatives in this fluctuating category is too small to warrant detailed discussion of the possibilities outlined in the introduction and by Kuipers and Bebbington (1988).



However, relatives could be found to fit most categories; for example, low EE before and after relapse, but high at relapse; low before relapse, but high at two subsequent relapses; and low before relapse, high at one subsequent relapse, but low at the next.

It has been suggested (Favre *et al*, 1989) that relatives who show fluctuating EE may make fewer critical comments when showing high EE than those who show consistently high EE. This was not the case in the present study. It has previously been found that even with vigorous family treatment it may not be possible to lower a relative's high EE (Leff *et al*, 1982, 1985, 1989). Perhaps many such relatives would fall into the consistently high EE group in the present study. Family treatment may be effective in lowering EE mainly in those where spontaneous fluctuations also occur.

It is noteworthy that the onset of dementia was associated in three relatives with a shift from high to low EE. Studies of the family life of dementing patients focus especially on the damaging effect dementia and its sequelae have on carers; in one respect at least the family atmosphere may well have improved in those three families, at least from the schizophrenic patients' point of view.

Those schizophrenic patients living together allowed an examination of the level of EE in schizophrenics as relatives, not as patients. The complexity of emotional expression is illustrated by sister(1), a paranoid schizophrenic patient who showed fluctuating levels of EE over time towards both her sister and daughter. At the time of her own relapse with a florid delusional and hallucinatory state she showed low EE towards her sister and high EE towards her daughter. Sister (2) who had a defect state showed consistently low EE towards her niece.

Forty seven percent of patients had at least one relapse over five years. This relapse rate is less than in other studies but a community survey such as that carried out in

Nithsdale is likely to include those with a better prognosis (McCreadie and Phillips, 1988). Numbers are small but patients who relapsed were divided evenly into those living in a consistently high, consistently low or fluctuating EE home. This finding over five years is broadly similar to that over one year, described previously (McCreadie and Phillips, 1988). However, when patients who did relapse were considered separately, those living in a consistently low EE home did so significantly less often than those who relapsed and were living in a high or fluctuating EE home. This supports the link between relapse and level of EE described elsewhere (Leff et al, 1982). Those seven living in a consistently high EE environment fell into two groups - four did not relapse at all and three relapsed many times. The former are of interest; if high EE is causal in precipitating relapse, then perhaps these patients have developed strategies to cope with consistent criticism, hostility or overinvolvement. In this context it is noteworthy that Hogarty and colleagues (1986) found that relapse rates in patients whose relatives received social therapy and family intervention fell without a corresponding fall in high EE. Also, it has been suggested (Leff et al, 1989) that diminishing contact between patient and relative might reduce relapse in those living with high EE relatives. However, in the present study, six of the seven patients who lived in a consistently high EE home were also in high contact with relatives, at least over the first two years of the project.

Where the level of EE was assessed at the time of relapse, it was low on five out of 13 occasions. If EE is causal, other factors must have been operating at the time of relapse. Perhaps in these patients life events may be important precipitants of relapse (Leff et al, 1973).

We conclude that EE in most relatives is stable over a five year period, and that a consistently low level of EE is associated in those patients who do relapse with a fewer number of relapses.

Figure 3.4.1                      Pattern of relapse in 10 patients and level of expressed emotion in their relatives over five years.

Legend

Boxes indicate inpatient admission, vertical lines relapses not leading to inpatient admission. Broken horizontal lines connecting boxes or vertical lines indicate a clinical judgement that a single relapse has occurred. H=high expressed emotion shown by relative; L=low expressed emotion shown by relative.

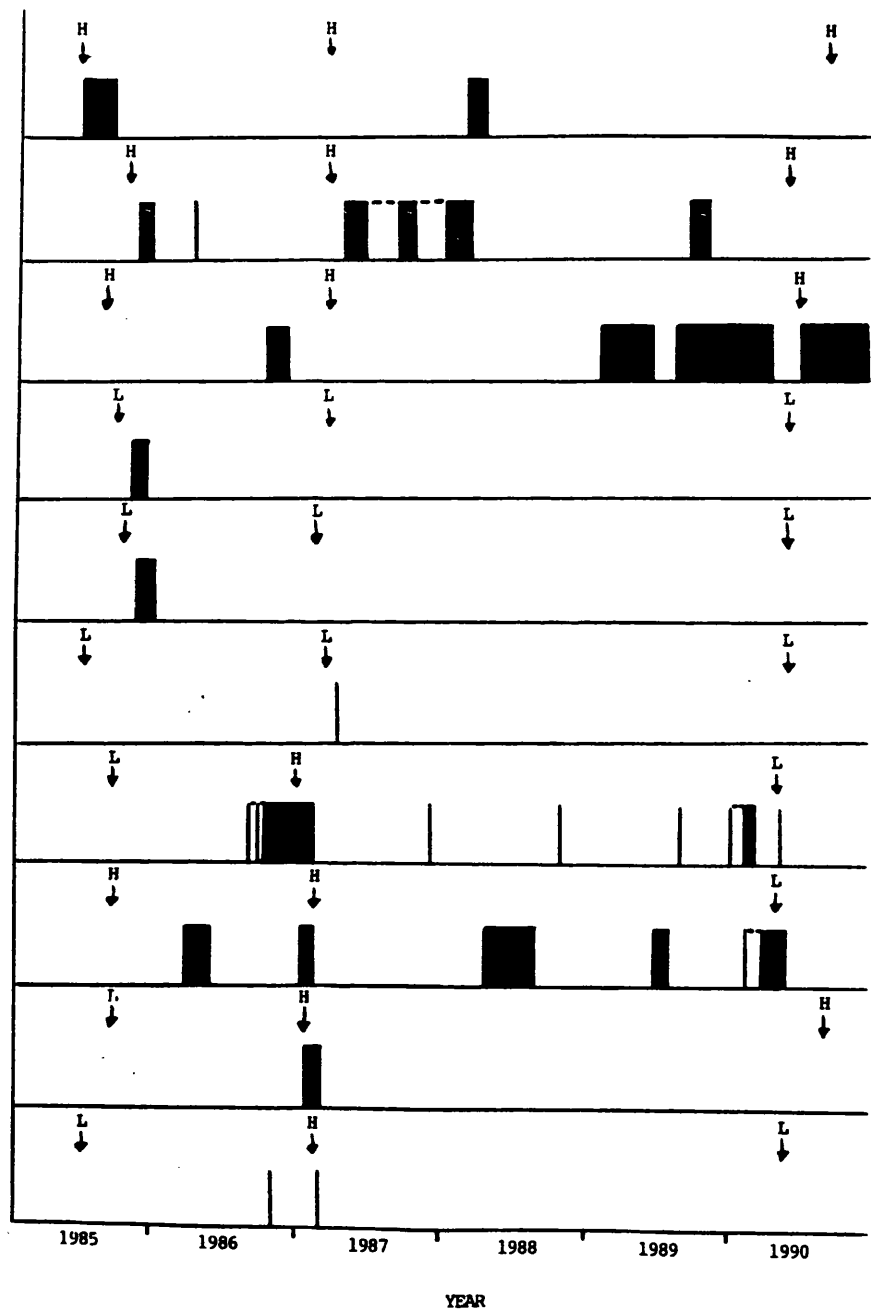
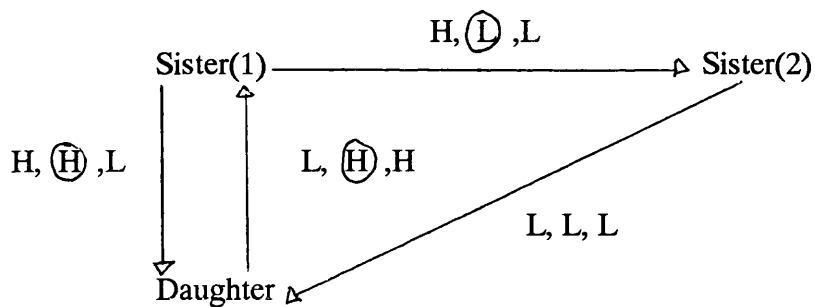


TABLE 3.4.1  
LEVELS OF EXPRESSED EMOTION  
IN A FAMILY OF SCHIZOPHRENIC PATIENTS



Legend EE has been assessed on three occasions over five years.  
H = high EE; L = low EE; arrow indicates direction of EE; circled letter indicates that EE was assessed at time of the relative's own relapse.

MOVEMENT DISORDERS

#### 4.1 ABNORMAL MOVEMENTS

R G McCREADIE

ELIZABETH T BARRON

G S WINSLOW

## SUMMARY

In a review of all known schizophrenic patients (n = 133) from a discrete geographical area, Nithsdale in Dumfries and Galloway Region, 88 percent were examined for evidence of tardive dyskinesia (TD) and parkinsonism. The prevalence of both TD and parkinsonism was 31 percent. The TD group was older and more often showed negative schizophrenic symptoms than the non-TD group. The trend was towards a higher prevalence among in-patients and Feighner positive schizophrenic patients. Parkinsonism was common in patients receiving antiparkinsonian drugs. Ten percent of patients had both TD and parkinsonism. The findings will act as a baseline for regular reassessments of the population.

Tardive dyskinesia (TD) is now widely believed to be an important side effect of neuroleptics (Anonymous, Lancet, 1979) which are used especially in the treatment of schizophrenia. In a recent comprehensive review (Jeste and Wyatt, 1981) the prevalence of TD among chronically ill neuroleptic-treated adult psychiatric in-patients was estimated at 25.7 percent from studies published between 1976 and 1980. However, due to the impact of community care, in-patients probably now form a small atypical group of schizophrenic patients (McCreadie, 1982a). To assess the magnitude of the problem, community reviews would be more valuable. Out-patient studies of TD in schizophrenia are very few; such studies suggest a prevalence of 30-40 percent (Chouinard et al, 1979; Smith et al, 1979; Ezrin-Waters et al, 1981).

Parkinsonism, the other principal side effect of neuroleptics has been recognised for many years but has recently attracted little attention. One study (Johnson, 1978) found the three-monthly prevalence of parkinsonism in patients treated with depot neuroleptics to be 24-29 percent.

To further our knowledge about prevalence rates for both these movement disorders and to obtain a baseline for follow-up studies, a review of such side effects in the vast majority of all known schizophrenic patients, including in-patients, from a discrete geographical area has been carried out.



## METHOD

The geographical area from which the patients were drawn, Nithsdale in Dumfries and Galloway Region, the identification of such patients, and the social, demographic and clinical information obtained have been described elsewhere (McCreadie, 1982a). On 1 March 1981 there were 133 schizophrenics, of whom 28 percent were in-patients, 17 percent day patients and 32 percent out-patients; 23 percent were attending only their general practitioner. All in-patients, day patients and out-patients, and 46 percent of general practice patients ( $n = 117$ , 88 percent of the total population) were examined for evidence of TD using the Abnormal Involuntary Movements Scale (AIMS) (US Department of Health, Education and Welfare, 1976) and of parkinsonism, using the Targeting Abnormal Kinetic Effects (TAKE) scale (Wojcik *et al*, 1980); both examine individual areas of the body, following which a global assessment is made. The assessments were made during a four-week period by three psychiatrists who took part in several practice sessions before the study began. Forty-one percent of the subjects were examined independently by different combinations of two of the three psychiatrists to assess inter-rater agreement.

Of those examined, 20 percent were not currently receiving neuroleptics, but in only seven patients (6 percent) was there no record of such drugs being prescribed in the past. Thirty-three percent were receiving anti-parkinsonian drugs. No attempt was made to assess for how long patients had received neuroleptics or how much had been prescribed throughout the course of the illness; such information would probably have been inaccurate, especially for out-patients and patients attending only their general practitioner.

Differences between groups were tested by the chi-square test (two-tailed tests throughout).

## RESULTS

Inter-rater agreement on the five-point global scales (0 = none to 4 = severe) was complete or partial (a difference of only one point) in 90 percent of assessments for TD and 94 percent for parkinsonism.

### Tardive dyskinesia

The prevalence and severity of TD as shown by the global and individual scales are given in Table 4.1.1. If patients with at least a rating of 'mild' on the global scale are considered to have definite TD, then the prevalence is 31 percent. The areas affected most were the lips, jaw and tongue.

When patients with and without definite TD were compared on the basis of demographic, social and clinical data only the following statistically significant differences were found. Patients with TD were older ( $P < 0.001$ ), had been ill longer ( $P < 0.02$ ) and spent a longer time as in-patients ( $P < 0.02$ ). These three factors are no doubt intimately related. More of them showed flattening of affect ( $P < 0.05$ ), were socially withdrawn ( $P < 0.05$ ) and needed supervision of their personal appearance ( $P < 0.05$ ). Trends, which failed to reach statistical significance, were that TD was more common in in-patients than in other groups (45 percent versus 25 percent), and in Feighner positive (Feighner *et al*, 1972) than Feighner negative schizophrenic patients (38 percent versus 13 percent).

### Parkinsonism

The prevalence and severity of parkinsonism are shown in Table 4.1.2. When a rating of at least 'mild' on the global severity scale is taken as evidence of definite parkinsonism the prevalence is 31 percent. Prevalence rates for bradykinesia, rigidity

and tremor were broadly similar. When patients with and without definite parkinsonism were compared the only statistically significant difference was that patients with parkinsonism were aware of such side effects ( $P < 0.001$ ).

Twelve patients (33 percent of both the TD and parkinsonism groups) had symptoms of at least mild TD and parkinsonism. This proportion was similar to that found in the parent group.

Among variables which did not help to differentiate patients with either TD or parkinsonism from others were the patient's sex and current neuroleptic or anti-parkinsonian medication. Thirty-eight percent of patients receiving anti-parkinsonian drugs had parkinsonism. Seven patients with TD and six with parkinsonism were not receiving neuroleptics; the mean age of the TD group was 75 years, the parkinsonian group 76 years. There was no record of two patients in the TD group and four in the parkinsonian group ever having received neuroleptics.

## DISCUSSION

Although the prevalence figure we obtained for tardive dyskinesia, 31 percent, compares broadly with findings in other studies, the plethora of rating scales used to assess TD (Gardos *et al*, 1977) makes an accurate comparison impossible. In the present study, patients with tardive dyskinesia include those with withdrawal dyskinesia and those with spontaneous non-drug-related dyskinesia, estimated to be present in one quarter of patients with persistent dyskinesia (Jeste and Wyatt, 1981). Spontaneous dyskinesia is said to be more common in the aged, and it is noteworthy that the mean age of patients in the present study with TD, but not currently receiving neuroleptics was 75 years.

The findings that the prevalence of TD in in-patients tended to be higher than in other groups suggests that the examination of only in-patients may paint an unduly pessimistic picture. The difference in prevalence rates is probably due to the fact that in-patients are significantly older (McCreadie, 1982a); advancing age is one of the few factors shown consistently to produce an increased risk of TD (Smith and Baldessarini, 1980). Also, in-patients are more disabled in terms of the negative symptoms of schizophrenia such as flattening of affect (McCreadie, 1982a) which, in turn, were more commonly found in patients with TD. This association between TD and negative schizophrenic symptoms has been reported previously where the factors of age and sex were controlled (Ital et al, 1981). The patients with prominent negative symptoms belong to the Type 2 syndrome of schizophrenia (Crow, 1980) where organic brain damage may be an important aetiological factor. Perhaps these patients run a greater risk of developing TD.

The trend towards TD being more common in Feighner positive than in Feighner negative schizophrenic patients may also be due to the fact that the former were older and had been ill longer (McCreadie, 1982a).

Parkinsonism was common in patients receiving anti-parkinsonian drugs. The value of such medication given continuously to patients receiving neuroleptics has long been questioned (Mindham et al, 1972). It may be, of course, that the prevalence and severity of parkinsonism would have been even greater if the patients had not been receiving such drugs. Also, parkinsonism was found in a small number of aged patients (average age 76 years) not receiving neuroleptics. It is possible some of these patients had developed idiopathic parkinsonism.

In a small group of patients, parkinsonism and TD co-existed. If parkinsonism is due to dopamine receptor blockade and TD to dopamine receptor supersensitivity (Marsden and Jenner, 1980) it is hard to understand how both conditions can exist in the same patient at the same time, unless the two processes are mediated through different dopamine systems.

The present study will act as a baseline for regular reassessment of the population. The members of the population will change as new patients develop the illness or move to Nithsdale, while others move away from the area or die. It will be valuable to learn whether tardive dyskinesia and parkinsonism will increase further in the community or whether, now that neuroleptics have been available to a generation of schizophrenic patients, the prevalence of these side effects has reached a plateau.

In conclusion this community survey, the first of its kind has identified a high prevalence of both TD and parkinsonism. This illustrates well the cost to schizophrenic patients of taking neuroleptics. Such drugs are effective in controlling the positive symptoms of the disorder (Crow, 1980), but the price to be paid is considerable.

TABLE 4.1.1  
PERCENTAGE OF PATIENTS SHOWING TARDIVE DYSKINESIA (N = 117)

	Absent	Doubtful	Mild	Moderate	Severe
Global rating	48	21	26	4	1
Face	92	4	4	0	0
Lips	69	14	16	1	0
Jaw	71	15	10	4	0
Tongue	67	14	18	1	0
Upper limbs	84	7	8	0	1
Lower limbs	85	9	6	0	0
Trunk	94	2	3	1	0

TABLE 4.1.2  
PERCENTAGE OF PATIENTS SHOWING PARKINSONISM (N = 117)

	Absent	Doubtful	Mild	Moderate	Severe
Global rating	39	30	29	2	0
Bradykinesia	54	17	27	2	0
Rigidity	68	11	20	1	0
Tremor	62	15	21	2	0
Akathisia	96	2	2	0	0
Autonomic symptoms (e.g. salivation)	92	4	4	0	0

## **4.2 HANDEDNESS AND TARDIVE DYSKINESIA**

**R G McCREADIE**

**J CRORIE**

**ELIZABETH T BARRON**

**G S WINSLOW**



## SUMMARY

Handedness was assessed in 87 percent ( $n = 116$ ) of all known schizophrenic patients from a discrete geographical area, Nithsdale in Dumfries and Galloway Region. Seventy-three percent were right-handed, a proportion greater than that found in a normal population. It was especially Feighner positive schizophrenics and non-in-patients who produced the excess of right-handers. Within the Feighner positive group, 68 percent of mixed or left-handers, but only 29 percent of right-handers had tardive dyskinesia.

There have recently been several conflicting reports about whether there is an excess of right or left-handedness amongst schizophrenic patients, or whether the distribution is similar to that found in the general population (e.g. Lishman and McMeekan, 1976; Taylor *et al*, 1980; Chaugule and Master, 1981). Different ways of classifying handedness and defining schizophrenia may have given rise to some of the confusion. Also, former studies have examined only in-patients, who now probably form a small atypical group of schizophrenic patients (McCreadie, 1982a). The present study reports, firstly, handedness patterns in the vast majority of all known schizophrenic patients from a discrete geographical area, and secondly, an association between handedness and tardive dyskinesia (TD).

## METHOD

The geographical area from which patients were drawn, Nithsdale in Dumfries and Galloway Region, the identification of such patients, and the demographic, social and clinical information obtained have been described elsewhere (McCreadie, 1982a). On 1 March 1981 there were 133 schizophrenic patients, of whom 28 percent were in-patients, 17 percent day patients, and 32 percent out-patients; 23 percent attended only their general practitioners. All in-patients (except one who was uncooperative), day patients and out-patients and 46 percent of general practice patients ( $n = 116$ ) were assessed for handedness using the Annett Questionnaire (Annett, 1970). Patients were asked to perform 11 tasks: writing, throwing a ball, holding a tennis racket, holding a match to strike it, hammering, using a toothbrush, using scissors, guiding thread through the eye of a needle, holding a broom, dealing cards, and unscrewing a lid from a jar. A twelfth task, using a shovel, was omitted as it is interchangeable with holding a broom (Annett, 1970). The necessary equipment to perform each task was placed in front of the patient equidistant from his hands. The broad classification of handedness of Fleming and his colleagues (1977) was used. A patient was defined as right-

handed if the right-hand was used for all activities, mixed-handed if the right-hand was used for writing and the left-hand for one or more of the other activities, and left-handed if the left-hand was used for writing.

Full details of the assessment of TD are given elsewhere (McCreadie et al, 1982a). Briefly, TD was assessed by the Abnormal Involuntary Movements Scale (AIMS) (US Department of Health, Education and Welfare, 1976), and a patient was defined as having TD if he or she had a rating of at least 'mild' on the global scale.

The psychiatrist who examined the patients for TD were different from the ones who carried out the handedness test, except in the case of general practice patients (n = 14), all assessments on whom were carried out by the senior psychiatrist (R.G.McC).

Differences between groups were tested by the chi-square test (two-tailed tests throughout).

## RESULTS

Table 4.2.1 shows the distribution of handedness for the total population, and also according to age and whether the patients belonged to the Feighner positive ('definite' or 'probable') or negative category (Feighner et al, 1972). It also includes the distribution of handedness in a large normal population aged 16-64 years (Fleminger et al, 1977). Seventy-three percent of the schizophrenic patients were right-handed, 23 percent mixed-handed, and 4 percent left-handed. When compared with the normal population, there were significantly more right-handers in the Feighner positive group in both the under 40 years and the 40-64 years age groups (86 percent versus 44 percent, P

< 0.001; 78 percent versus 56 percent,  $P < 0.02$ ). Statistically significant differences were not found between the Feighner negative schizophrenic patients and normal subjects.

When a comparison was made of the distribution of handedness in in-patients and non-in-patients (Table 4.2.2) within the Feighner positive group, there were significantly more right-handers among the non-in-patient population (Table 4.2.2; 85 percent versus 64 percent,  $P < 0.05$ ).

Right-handers (dextrals) were compared on the basis of demographic, social and clinical data with those who were left-handed or of mixed-handedness (non-dextrals). An analysis was carried out separately for the Feighner positive and negative groups. The only statistically significant difference was in the proportion of patients in the two groups with TD (Table 4.2.3). Sixty-eight percent of Feighner positive non-dextrals, but only 29 percent of dextrals, had TD ( $P < 0.01$ ). The difference was not apparent in the Feighner negative group. A trend, not statistically significant, was that within the Feighner positive group, non-dextrals showed more flatness of affect and poverty of thought.

## DISCUSSION

The decision to compare handedness patterns between Nithsdale schizophrenic patients and normal subjects needs further comment. It may be argued that cultural differences between Nithsdale and London (from which the normal subjects were taken) might explain some of the results. Child rearing practices in a largely rural, conservative area might have been directed towards the use of the right-hand in all activities. However,

only one half of the schizophrenic patients were born in Nithsdale and there were no differences in handedness patterns between schizophrenic patients born in Nithsdale and those born elsewhere. It must also be pointed out that, in the survey of normals, subjects completed a questionnaire but were not asked to perform any of the items. Self-reports of handedness can lead to over-reporting of left-handedness (Satz *et al*, 1967). Furthermore, in the study of normals, the option of 'either hand' was given; an 'either' response was grouped with the left responses. In the present study the hand used to carry out the action was taken to be the preferred hand. Thus there might be a small bias in the present study towards finding a greater number of dextrals. It is most unlikely, however, that this bias would explain the marked difference found in the proportion of dextrals in the Feighner positive group compared with the normal subjects. The proportion in the Feighner positive population, 78 percent, is somewhat greater than that found in another study which also found an excess of right-handers, 64 percent (Taylor *et al*, 1980). That study, which also examined Feighner positive patients but confined itself to in-patients, asked only some patients to perform all tasks, and included 'either' responses.

A recent study (Chaugule and Master, 1981) which used the same classification of handedness as in the present study but which used a different definition of schizophrenia (ICD-8; WHO, 1974) found an excess of non-dextrals. Other studies (e.g. Gur, 1977; Nasraliah *et al*, 1981) which found an excess of non-dextrals among schizophrenic patients examined only in-patients and did not use either the classification of handedness or the definition of schizophrenia employed in the present study. The way in which schizophrenia is defined is probably crucial. This is shown in the present study by the fact that in Feighner negative schizophrenic patients, who nonetheless had a firm case record diagnosis of schizophrenia, the distribution of handedness patterns was not significantly different from that in normal subjects. It

appears that the excess of right-handers is to be found especially among the more chronically ill patients.

Possible reasons for an excess of dextrals in a schizophrenic population have been discussed fully elsewhere (Taylor *et al*, 1980). Briefly, Taylor and her colleagues postulate that the more dominant one hemisphere is, the more vulnerable that individual will be to disease or injury. Full right-handedness correlates with strong left hemisphere dominance for language skills, while mixed or left-handedness is more likely to be associated with bilateral, albeit still unequal, representation of language function.

One possible explanation of the excess of right handers among Feighner positive non-in-patients suggests itself if the results are looked at from another direction, namely, that relatively more non-dextrals were found among in-patients. In-patients who have a greater prevalence of negative symptoms (McCreadie, 1982a) belong especially to the Type 2 Group of schizophrenic patients (Crow, 1980) where organic brain disease is thought to be an important aetiological factor. Could it be that some cerebral insult has both shifted natural dextrals towards non-dextrality and predisposed schizophrenic patients to the development of negative symptoms? Might this also explain the high prevalence of tardive dyskinesia amongst non-dextrals, as brain damage might render patients more susceptible to the side effects of prolonged administration of neuroleptics, now widely accepted as the main aetiological factor in tardive dyskinesia (Anonymous, Lancet, 1979)? This interpretation of the data is highly speculative and, as yet, we have no convincing explanations of our results.

If the unexpected association between tardive dyskinesia and non-dextrality can be confirmed in other, larger studies, then assessment of handedness may be a useful predictive test of tardive dyskinesia in schizophrenic patients. If a patient is non-dextral, caution in the prescription of neuroleptics may be necessary.

TABLE 4.2.1

## DISTRIBUTION OF HANDEDNESS

Nithsdale schizophrenic patients								
	Total		Feighner positive schizophrenic patients		Feighner negative schizophrenic patients		Normal subjects*	
	N	%	N	%	N	%	N	%
Under 40 years of age:								
Right	35	78	30	86	5	50	189	44
Mixed	9	20	4	11	5	50	195	46
Left	1	2	1	3	0	0	44	10
Total	45	100	35	100	10	100	428	100
40 - 64 years of age:								
Right	41	75	28	78	13	68	207	56
Mixed	10	18	6	17	4	21	139	37
Left	4	7	2	5	2	11	26	7
Total	55	100	36	100	19	100	372	100
65 years and over:								
Right	9	56	8	57	1	50	-	-
Mixed	7	44	6	43	1	50	-	-
Left	0	0	0	0	0	0	-	-
Total	16	100	14	100	2	100	-	-
All ages:								
Right	85	73	66	78	19	61	392	49
Mixed	26	23	16	19	10	32	336	42
Left	5	4	3	3	2	7	72	9
Total	116	100	85	100	31	100	800	100

\* Taken from Fleminger et al (1977)

TABLE 4.2.2

HANDEDNESS IN IN-PATIENTS AND NON-IN-PATIENTS

Handedness	Feighner positive schizophrenic patients				Feighner negative schizophrenic patients			
	In-patients		Non-in-patients		In-patients		Non-in-patients	
	n	%	n	%	n	%	n	%
Right	19	64	47	85	4	57	15	63
Mixed	10	33	6	11	3	43	7	29
Left	1	3	2	4	0	0	2	8
Total	30	100	55	100	7	100	24	100



TABLE 4.2.3

HANDEDNESS AND TARDIVE DYSKINESIA

	Feighner positive schizophrenic patients				Feighner negative schizophrenic patients			
	Dextrals		Non-dextrals		Dextrals		Non-dextrals	
	n	%	n	%	n	%	n	%
Tardive dyskinesia	19	29	13	68	3	16	1	8
No tardive dyskinesia	47	71	6	32	16	84	11	92
Total	66	100	19	100	19	100	12	100

#### **4.3 FOLLOW-UP OF TARDIVE DYSKINESIA AT 3½ YEARS**

**A D T ROBINSON**

**R G McCREADIE**

## SUMMARY

The point-prevalence of tardive dyskinesia in schizophrenic patients from a discrete geographical area (Nithsdale, in Dumfries and Galloway Region) in 1981, 1982, and 1984 was 31%, 27% , and 33% respectively. This suggests that the prevalence of tardive dyskinesia in a community of schizophrenic patients has reached a plateau. In 12% of patients there was persistent dyskinesia, i.e. abnormal involuntary movements were present at all three assessments. Persistent dyskinesia was more common in older patients. The severity of tardive dyskinesia fluctuated between assessments in 41% of patients, indicting that it is only a transient feature in some cases.

A previous study of tardive dyskinesia (TD) in all known schizophrenic patients in Nithsdale, an historically ancient and geographically discrete part of Dumfries and Galloway Region, found a point-prevalence of 31% (McCreadie *et al*, 1982a); an interim review one year later found a prevalence of 27% (Barron & McCreadie, 1983). It was suggested that as a generation of schizophrenic patients has now been exposed to neuroleptics, which are thought to be the main aetiological factor in TD (Anonymous, Lancet, 1979), the community prevalence might have reached a plateau. To determine whether this may be so, the present study examined Nithsdale schizophrenic patients 3½ years after the initial census. It also identified and described patients with persistent dyskinesia.

## METHOD

### The 1981 census

The original census, carried out in March 1981, identified all known schizophrenic patients in Nithsdale. Included in the survey were all in-patients, day-patients, and out-patients of Crichton Royal Hospital who on 1 March 1981 had a firm case-record diagnosis of schizophrenia and whose home address was in Nithsdale. In addition, all the general practitioners in the area replied to our questionnaire and identified schizophrenic patients known to the practice and receiving treatment. The Feighner criteria for schizophrenia (Feighner *et al*, 1972) were applied to each patient. The census identified 133 schizophrenic patients, 117 of whom were examined for tardive dyskinesia.

### 3½ year follow-up

The repeat census was carried out 3½ years later (20 August, 1984) in a similar way to

the initial survey. It identified 145 schizophrenic patients, of whom 70% fulfilled the Feighner criteria for definite or probable schizophrenia, and 88 (61%) were members of the original cohort: 17% were in-patients, 24% day-patients, 39% out-patients or supervised by a community psychiatric nurse (CPN), and 20% were attending only their family doctor.

We examined 130 of the schizophrenic patients (90%) for evidence of tardive dyskinesia - all the in-patients, all the day-patients except one, all the out-patients except one, all the CPN patients and 57% of the general-practice patients. To assess TD, we used the Abnormal Involuntary Movements Scale (AIMS) (US Department of Health, Education and Welfare, 1976), in which individual areas of the body are examined and then a global assessment is made: this ranges from 0 (no movements) through 1 (minimal), 2 (mild), and 3 (moderate), to 4, 'severe movements'. The assessments exclude tremor, akathisia, and dystonia. Our assessments were made during a 6 week period by two psychiatrists, and 12% of patients were examined independently by both psychiatrists to assess inter-rater reliability.

Of those examined, 16% were not currently receiving neuroleptics, but only 5 patients (4%) had no record of such drugs having been prescribed in the past; 27% were receiving anti-parkinsonian drugs. The length of time for which patients had been receiving neuroleptics since the initial census and the route of drug administration were determined; no attempt was made to estimate the total quantity of medication prescribed, as such information would probably have been inaccurate, especially for out-patients and general-practice patients.

Differences between groups were tested by the chi-square test.

## RESULTS

Inter-rater reliability on the 5-point global AIMS scale was high (Spearman rank correlation coefficient  $r = +0.82$ ,  $P < 0.01$ ).

### 1984 prevalence of abnormal movements

If patients with a rating of at least 'mild' on the global AIMS scale are considered to have definite TD, then the prevalence is 30% (Table 4.3.1): 18% with only oro-facial movements, 3% with trunk and/or limb movements, and 9% with both oro-facial and distal movements.

### Persistent dyskinesia

Of the 145 patients, 88 (61%) had been examined on all three occasions. The prevalence figures for definite TD in this subgroup in 1981, 1982, and 1984 were 35%, 32%, and 30% respectively (Table 4.3.1). Almost half (47%) of the subgroup had never shown signs of dyskinesia; 12% had dyskinesia on all three occasions ('persistent dyskinesia'); and 41% had dyskinesia on at least one but not three occasions ('fluctuating dyskinesia'). In the 'fluctuating' group, the severity of dyskinesia increased over time in 11% of cases, decreased in 17%, and showed no trend in 13%. The details of these changes are presented in Table 4.3.2.

Patients with persistent dyskinesia were compared with those who had never had abnormal movements, on the basis of sex, age, hospitalisation status, Feighner categorisation, and medication (current and previous, antipsychotic and anti-parkinsonian). There were no statistically significant differences between the two groups, although the trend was that patients in the persistent dyskinesia group were older (mean age 51 years vs 45 years) and more often in-patients or day patients (73% vs 44%).

In the group with fluctuating dyskinesia, when those with worsening TD were compared with patients showing decreasing TD, there were no statistically significant differences in the clinical, social, and demographic characteristics outlined above. In particular, there was no clear relationship between the starting or stopping of anti-psychotic or anti-parkinsonian medication and fluctuation in dyskinesia. However, the trend was that patients with worsening TD were younger (mean age 51 years vs 61 years).

Of those with persistent dyskinesia, 9% had only oro-facial movements and 91% both oro-facial and distal movements.

## DISCUSSION

The point-prevalence of TD in all known schizophrenic patients from a given geographical area, assessed on three separate occasions spread over 3½ years, has remained fairly constant between 27% and 31%. It is probable, therefore, that the community prevalence has indeed reached a plateau, and is not likely to increase further with time. As new patients develop schizophrenia and are given neuroleptics, some will develop dyskinesia. These will be balanced in numbers by others dying or recovering from the illness; in the latter group, medication will probably be stopped. The plateau in the present series of studies contrasts sharply with the reported increase in prevalence during the 1970s. As anti-psychotic medication was widely prescribed at that time, the supposed increase in prevalence probably reflects clinicians' increasing awareness of the condition: the true prevalence may well have been essentially unchanged throughout.

Interpretation of our results is complicated by the finding that although about a third of the patients had TD at any given time, only 12% of those patients rated on all three occasions had persistent dyskinesia. This latter figure is probably a more accurate assessment of the severity of the problem: point-prevalence figures include mild and reversible TD, and paint too gloomy a picture. Schizophrenic patients with persistent dyskinesia tended to be older than those with no TD: age is the only factor consistently found to be associated with TD (Smith et al, 1979; Seeman, 1981; Kane & Smith, 1982; Barnes et al, 1983).

Forty one percent of patients examined on all three occasions had TD on one or two, but not all three occasions. There are no doubt several reasons for fluctuating dyskinesia (reviewed by Bergen et al, 1984). Deficiencies in assessment, such as within-rater variability (Bergen et al, 1984), lack of sensitivity of the rating scale (Barnes, 1984), or lack of standardisation of rating schedules in relation to time of depot neuroleptic administration (Barnes & Wiles, 1983) may be important. It is unlikely, however, that these methodological problems can entirely explain fluctuating dyskinesia: the present findings therefore emphasise the transient nature of TD in some patients. In the present study, worsening dyskinesia over time was more common in young patients. Such patients had probably had a shorter exposure to neuroleptics, which had not yet produced their maximum effect; as the years go by, dyskinesia may be expected to worsen in them.



TABLE 4.3.1

POINT PREVALENCE OF ABNORMAL INVOLUNTARY MOVEMENTS  
AMONG SCHIZOPHRENIC PATIENTS IN NITHSDALE (1981, 1982, 1984)

Abnormal movements (AIMS score)	1981		1982		1984	
	All patients (N = 117)	Subgroup* (N = 88)	All patients (N = 122)	Subgroup* (N = 88)	All patients (N = 130)	Subgroup* (N = 88)
Mild/moderate/severe	31%	35%	27%	32%	30%	30%
Nil/minimal	69%	65%	73%	68%	70%	70%

\* Subgroup: patients rated on all three occasions

TABLE 4.3.2

PATTERNS OF PRESENCE/ABSENCE OF ABNORMAL INVOLUNTARY  
MOVEMENTS IN A GROUP OF 88 SCHIZOPHRENIC PATIENTS ALL OF WHOM  
WERE ASSESSED IN 1981, 1982 AND 1984

1981	1982	1984	n (%)
Absent	Absent	Absent	41 (47)
Absent	Absent	Present	4 (4)
Absent	Present	Present	6 (7)
Absent	Present	Absent	6 (7)
Present	Absent	Present	5 (6)
Present	Absent	Absent	10 (11)
Present	Present	Absent	5 (6)
Present	Present	Present	11 (12)
			88(100)

#### 4.4 AKATHISIA, PARKINSONISM, TARDIVE DYSKINESIA

#### AND PLASMA NEUROLEPTIC LEVELS

ROBIN G McCREADIE

LESLEY J ROBERTSON

DAVID H WILES

## SUMMARY

Eighty eight percent (N = 146) of all known schizophrenic patients living in Nithsdale, South-West Scotland were examined for the presence of the three principal movement disorders secondary to antipsychotic medication, namely akathisia, tardive dyskinesia and parkinsonism. Eighteen percent had akathisia, 5% pseudoakathisia, 29% tardive dyskinesia, 8% persistent tardive dyskinesia, and 27% parkinsonism. Forty four percent had no movement disorder, 36% had one and 20% more than one movement disorder. Plasma neuroleptic levels at the time of clinical assessment were measured by the radioreceptor technique. Correlations between dose and plasma level were low; the ratio mean plasma concentration: mean dose was greatest with fluphenazine decanoate and lowest for sulpiride. The concentration:dose ratio was higher in the elderly. There was no relationship between neuroleptic levels and akathisia, parkinsonism or tardive dyskinesia. Additional psychotropic medication influenced neuroleptic levels. In 9% of patients receiving oral antipsychotic medication no drug was detected in plasma.

At any given time the majority of schizophrenic patients are living outside hospital. Such 'community care' has been made possible especially by the use of maintenance antipsychotic drug therapy. Such drugs however can produce marked side effects, especially movement disorders. A previous survey (McCreadie *et al*, 1982a) estimated the community prevalence of both drug-induced parkinsonism and tardive dyskinesia (TD) to be 31%. However, a third movement disorder secondary to antipsychotic medication, namely akathisia, has been little studied.

Akathisia is a long recognised side effect (Steck, 1954), is distressing and can lead to poor drug compliance (Van Putten, 1974). Its incidence in patients prescribed neuroleptics was initially reported as 21% (Ayd, 1961) but this study included patients now recognised as having orofacial dyskinesia. Two more recent studies (Van Putten, 1975, Braude *et al*, 1983) found incidences of 45% and 25%, the latter in patients admitted to acute admission wards. Individual neuroleptics may cause different rates of incidence; for example haloperidol produced akathisia in 75% of patients (Van Putten *et al*, 1984). Satisfactory prevalence studies are even fewer. 'Motor restlessness' was found in 30% of chronic hospitalised schizophrenic patients receiving trifluoperazine (Kennedy *et al*, 1971) but this study did not assess subjective restlessness, considered to be a cardinal feature of the disorder. Thirty-five and 41% of chronic schizophrenic patients attending outpatient clinics and receiving intra- muscular antipsychotic drugs (Barnes and Braude, 1985, Gibb and Lees, 1986) and 19% of chronic schizophrenic inpatients (Barnes, 1989) had akathisia.

We report the findings of what is to our knowledge the first community survey of the prevalence of akathisia in schizophrenic patients. The relationship between akathisia, TD and parkinsonism is also examined. The survey thus assesses the prevalence of the three principal movement disorders and quantifies the 'cost' to the patient, in terms of side effects, of antipsychotic drug treatment.

It has also been suggested that high plasma neuroleptic levels are associated with the three movement disorders (e.g. Hansen *et al*, 1982). The present study examines further the relationship between akathisia, parkinsonism and TD and plasma neuroleptic levels.

## METHOD

The identification of schizophrenic patients has been described elsewhere (McCreadie, 1982a). Briefly, repeat censuses since 1981 in Nithsdale, an historically ancient and geographically discrete part of Dumfries and Galloway Region in South-west Scotland, have identified all known schizophrenic patients - inpatients, daypatients, outpatients, patients supervised by community psychiatric nurses and patients known only to their family doctor. A repeat census on 11 September 1989 identified 165 patients, it was these on whom the present study focussed.

Patients were examined in three ways: firstly for the presence of akathisia through the use of the Barnes akathisia scale (Barnes, 1989); secondly for TD through the Abnormal Involuntary Movements Scale (AIMS) (US Department of Health, Education and Welfare, 1976) and thirdly for parkinsonism through the Simpson and Angus scale (Simpson and Angus, 1970). Assessments were made over the three months following the census date by two psychiatrists who took part in several practice sessions before the study began. Twenty patients were assessed by both psychiatrists to measure inter-rater agreement.

A blood sample was also taken to measure the plasma neuroleptic level by the radio-receptor technique (Krska *et al*, 1986), using sheep caudate instead of calf. Samples were assayed in duplicate and individual sample blanks were subtracted.

Inter-assay accuracy and precision (percent of known concentration + CV) obtained by repeated analysis of known concentrations of haloperidol were: 106.6 + 10.3, 99.9 + 23.7, 96.8 + 17.1, 100.9 + 8.3 and 98.0 + 7.1 for 20, 50, 100, 200 and 500 nM solutions respectively. Results are expressed as Units of Neuroleptic Activity (UNA) where one UNA is equivalent to the activity of a 1 nM solution of haloperidol.

In some cases it was possible to take the blood sample immediately before the morning dose if the patient was receiving oral medication or immediately before a depot injection if the patient was receiving intra-muscular medication. In others the blood sample was random in relation to medication, but in all cases samples were taken at the time of clinical assessment. A record of all current psychotropic medication was made. Doses of neuroleptics were converted to chlorpromazine equivalents, through published tables (Davis, 1985) and estimates (100mg chlorpromazine, 1.6mg pimozide, 2mg oral flupenthixol, 10mg oral clopenthixol, 200mg sulpiride, 75mg remoxipride).

## RESULTS

All 165 patients had a firm case record diagnosis of schizophrenia. Nineteen patients (12%) were not examined: 12 refused (2 inpatients, 1 daypatient, 3 outpatients, 2 patients supported by community psychiatric nurses and 4 others); access in a further three was refused by general practitioners; and four were not approached (one patient was in a terminal care ward and three patients known only to their general practitioner had refused to take part in previous Nithsdale surveys). Thus 146 patients (88%) were assessed. Their mean age was 50 years (standard deviation (SD) 15, range 20-82). Social and demographic data are shown in Table 4.4.1.

When DSM-III-R criteria (American Psychiatric Association, 1987) were applied to case records 74% were schizophrenic, 8% had delusional disorder, 3% schizophreniform disorder and 6% schizoaffective disorder; 9% could not be categorised. At the time of clinical assessment 88% were receiving antipsychotic medication; of these, 50% were receiving oral, 34% longacting intra-muscular and 16% both oral and intra-muscular medication. Six percent of in- and day-patients and 14% of others were not receiving antipsychotic medication.

### Akathisia

The Barnes scale gives a global rating of akathisia ranging from absent through questionable, mild, moderate and marked to severe. Observation of movements characteristic of akathisia in the absence of a subjective report of inner restlessness or compulsive desire to move the legs is classified as pseudoakathisia. In 19 of the 20 patients rated by both psychiatrists there was complete agreement on the global scale. If a rating of mild or more is taken as definite akathisia, then 18% had akathisia and a further 5% pseudoakathisia (Table 4.4.2). Those with definite akathisia (N = 27) were compared on social, demographic and clinical data with those with no akathisia (N = 98) (the 'questionable' and pseudoakathisic groups were excluded). The only statistically significant difference was that those with akathisia were more often inpatients or daypatients ( $\chi^2 = 8.75$ ,  $P < 0.01$ ).

There was a trend, not statistically significant, for parkinsonism to be more common in akathisic patients (41% vs 22%).

### Tardive dyskinesia

Probable TD was diagnosed if there were at least "moderate" abnormal involuntary movements in one or more body areas or at least "mild" movements in two or more



areas (Schooler and Kane, 1982). In 17 of the 20 patients rated by both psychiatrists there was agreement as to whether TD was absent or probable. Probable TD was diagnosed in 42 (29%) patients (Table II). Those with probable TD when compared with those with no TD were older ( $\chi^2 = 7.43$ ,  $P < 0.01$ ), had been ill longer ( $\chi^2 = 4.17$ ,  $P < 0.05$ ) and more often were on long acting intra-muscular antipsychotic medication ( $\chi^2 = 5.00$ ,  $P < 0.05$ ).

Four of the seven patients with pseudoakathisia had at least mild TD of the trunk or extremities.

Sixty one of the 146 patients had been assessed for the presence of TD on two previous occasions, 1981 and 1984 (McCreadie *et al* , 1982a, Robinson and McCreadie, 1986). Of the 61, 32 (53%) had never shown TD, 24 (39%) showed TD on at least one occasion, and 5 (8%) showed TD on all three occasions. Of the 14 patients who had TD in 1981, six had it in 1989.

### Parkinsonism

As recommended by Simpson and Angus (1970) a score of more than 0.3 was taken as evidence of parkinsonism. In 18 of the 20 patients rated by both psychiatrists there was agreement as to the presence or absence of parkinsonism. Of the 146 patients, 39 (27%) had parkinsonism (Table 4.4.2).

Patients who had parkinsonism when compared with those who had not were older ( $\chi^2 = 9.97$ ,  $P < 0.01$ ) were more often inpatients or daypatients ( $\chi^2 = 9.02$ ,  $P < 0.01$ ), had been ill longer ( $\chi^2 = 5.54$ ,  $P < 0.02$ ) and were more often on intra-muscular antipsychotic medication ( $\chi^2 = 4.46$ ,  $P < 0.05$ ). Twenty two percent of patients without, and 34% with parkinsonism, were receiving antiparkinsonian medication.

Of the 146 patients, 64 (44%) had no movement disorder, 52 (36%) had one and 30 (20%) more than one movement disorder (Table II).

Eighteen patients were receiving no antipsychotic medication at the time of assessment. Two (11%) had akathisia, 5 (20%) TD and 2 (11%) parkinsonism. The corresponding percentages for patients receiving antipsychotics were 19%, 29% and 29%. Thus akathisia and parkinsonism but not TD were less common in those receiving no antipsychotics; the differences however were not statistically significant.

In addition to antipsychotic medication 37 patients were receiving antiparkinsonian medication, 18 antidepressants and 24 benzodiazepines. There were no significant differences in the prevalence of the three movement disorders between those who were and were not receiving such drugs.

There were three principal types of neuroleptic prescribed - phenothiazines, thioxanthenes and substituted benzamides. Fewer patients taking benzamides alone had a movement disorder and/or were receiving antiparkinsonian medication (7 of 17, 41%) when compared with those taking phenothiazines (32 of 48, 67%) or thioxanthenes (20 of 27, 74%) alone ( $\chi^2 = 3.94$ ,  $P < 0.05$ ). Similar trends, not statistically significant, were found when benzamides (all oral) were compared with oral phenothiazines (only two patients were receiving an oral thioxanthene).

#### Dosage and plasma neuroleptic levels

The correlation ( $r$ ) between dose and units of neuroleptic activity (UNA) in plasma in the 114 patients who gave a blood sample and who were receiving antipsychotic medication, was +0.43 ( $P < 0.001$ ). The correlation in those receiving less than the equivalent of 1000mg chlorpromazine daily ( $N = 103$ ) was +0.08 (NS); for those receiving more than 1000mg ( $N = 11$ ) it was +0.72 ( $P < 0.01$ ). In 42 patients the

blood sample was taken either before the morning oral dose or the next longacting intra-muscular injection; the correlation between dose and UNA in these cases was  $+0.48$  ( $P < 0.01$ ).

Ninety eight patients who gave a blood sample were receiving a single neuroleptic. Comparisons between individual drugs could therefore be examined in this group. Results for 80 patients receiving the most commonly prescribed antipsychotics are shown in Table 4.4.3. Correlations between dose and UNA varied widely. The range was from  $+0.97$  (chlorpromazine) to  $+0.14$  (pimozide). A drug's potency, that is, its ability to block dopamine D2 receptors, may be estimated by dividing UNA by dose; intra-muscular fluphenazine was the most, sulpiride the least potent (Table 4.4.3).

The UNA: dose ratio was greater in those aged over 60 years (mean  $1.61$  (SD  $3.04$ ) vs  $0.42$  ( $0.60$ )  $t = 2.16$   $P < 0.05$ ) and the correlation between potency and age was  $+0.28$  ( $P < 0.01$ ).

There were no significant differences in mean dose of neuroleptic, UNA and drug potency in those who did or did not have akathisia (patients with questionable and pseudo-akathisia were excluded) and did or did not have parkinsonism (Table 4.4.4). The latter finding also held good when those receiving antiparkinsonian medication were excluded. The mean dose and UNA in those with TD were significantly lower than those without TD (Table 4.4.4). However, the elderly were receiving less medication than younger age groups (eg. mean dose for those aged under 40 years,  $661\text{mg}$  (SD  $791\text{mg}$ ); 40-59 years,  $405\text{mg}$  ( $409\text{mg}$ ); 60 years and over,  $200\text{mg}$  ( $131\text{mg}$ )). When those aged over 60 were considered separately there was no difference between the probable and no TD groups in dosage, UNA and drug potency .

It was possible to match 15 patients with and without akathisia for gender, hospital status and drug; 12 patients with and without parkinsonism for gender, age and drug; and 14 patients with and without TD for gender, age and drug. When the matched pairs were compared there were no significant between group differences in dosage, UNA or drug potency.

#### Additional medication

As reported above, some patients were prescribed other psychotropic medication in addition to neuroleptics; the three principal groups of drugs were antiparkinsonian medication, antidepressants and benzodiazepines. The mean UNA is those receiving and not receiving additional medication is shown in Table 4.4.5. The results suggest lower neuroleptic levels per unit dose when antiparkinsonian medication was added and higher levels when antidepressants were given; benzodiazepines had no effect.

#### Compliance

Below a level of 10 UNA, antipsychotics cannot be detected in plasma with the methods used in the present study. Of the 114 patients receiving antipsychotic medication who gave a blood sample, 55 were taking only oral antipsychotics. In five of these patients (9%) no neuroleptic could be detected in plasma. Although it is likely these five were non-compliant, in 11 patients receiving low doses of long acting intra-muscular medication no neuroleptic was detected. Three of the five patients were female; one was a day patient, two out patients and two were supervised by their general practitioner.

## DISCUSSION

The prevalence of akathisia in Nithsdale schizophrenic patients is 18%; to this figure can be added that for pseudoakathisia, 5%. The former figure is lower than that found in outpatients receiving intra-muscular medication (35 - 41%) (Barnes and Braude, 1985, Gibb and Lees, 1986). However, the present study included patients not receiving antipsychotic medication at the time of assessment. Akathisia was more common in inpatients and daypatients. It is possible that compliance with medication was better in inpatients and daypatients. Four of five patients who were probably non-compliant, as assessed by plasma neuroleptic levels, were outpatients or supervised only by their general practitioner. It may also be that some of the repetitive movements seen in longstay inpatients, such as rocking from foot to foot when standing, represent schizophrenic stereotypies rather than akathisia. However, this would not explain the inner sense of restlessness.

Previous work has found the association between akathisia and other movement disorders to be unclear. Acute akathisia, that is, akathisia occurring in patients where there has been a recent rise in antipsychotic drug dose, may be associated with severe parkinsonism, but not TD (Braude *et al*, 1983). Chronic akathisia, where there has been no recent change in drug dose, may be associated with both parkinsonism and TD (Friis *et al*, 1983, Barnes and Braude, 1985). In the present cross-sectional study, in which most patients probably had chronic akathisia, there was a statistically non-significant association with parkinsonism and no association with TD. Four of the seven patients with pseudo-akathisia had TD of the trunk or extremities. This association may be genuine; however, distinguishing one from the other in an individual patient can be difficult.

The prevalence of TD was 29%. This is broadly similar to that found in a recent survey (23.4%) which included subjects from three psychiatric facilities providing inpatient and outpatient care (Kane et al, 1988). Persistent TD, that is, TD found on all three examinations of 61 patients between 1981 and 1989, was present in only 8%; of 14 patients with TD in 1981, only six had it in 1989. It is now well recognised that the presence and severity of TD can fluctuate over time (Gardos et al, 1988, Yassa and Nair, 1989, Bergen et al, 1989). In the present study TD was associated with increasing age, the most consistent association found in TD research (Kane et al, 1988).

The prevalence of parkinsonism was 27% and it was more commonly found in the elderly. Antiparkinsonian medication was as commonly prescribed in those with parkinsonism as those without; the value of such medication given to patients receiving neuroleptics has long been questioned (Mindham et al, 1972).

Fewer patients receiving benzamides, when compared with those receiving phenothiazines or thioxanthenes had either a movement disorder or were receiving an antiparkinsonian drug.

The correlation between dose and UNA, a measure of plasma drug concentration, although statistically highly significant, was rather weak ( $r = +0.43$ ). When only patients receiving less than the equivalent of 1000mg. chlorpromazine daily were considered, it was negligible. This might be a chance finding, the radioreceptor technique might be less accurate at lower plasma neuroleptic levels, additional psychotropic medication might be a confounding variable (see below) or the conversion to chlorpromazine equivalents might have been inaccurate. The latter is unlikely as when individual drugs were examined, correlations in some drugs

remained low. Lastly, poor or partial drug compliance might have contributed to the lack of correlation. The potency of individual drugs, as expressed by the ratio UNA:dose, in the main corresponded to clinical experience, with fluphenazine decanoate the most potent, and sulpiride the least. Thiordiazine was an exception. It was considerably more potent than chlorpromazine, whereas in clinical practice it is usually taken to be equipotent. Activity in plasma however may not accurately reflect activity in the brain.

Patients with akathisia or parkinsonism did not receive higher doses of antipsychotic drug nor had higher UNA than those without the movement disorder. A previous paper, referred to in the introduction (Hansen et al, 1982), suggested patients who develop extrapyramidal side effects (parkinsonism, akathisia and dystonia) had higher levels. Such patients however were in an acute phase of the illness and 50% had never received neuroleptic treatment before. In the present study probably individual susceptibility and pharmacodynamic changes in patients prescribed neuroleptics over lengthy periods are more important factors than plasma neuroleptic levels in determining whether or not patients develop parkinsonism or akathisia.

It has been suggested that TD is associated with high neuroleptic levels measured by the radioreceptor technique (Jeste et al, 1979) or fluorescence spectrophotometric assay (Yesavage et al, 1987). However, other studies using radioreceptor assay (Jeste et al, 1981, Widerlov et al, 1982) failed to confirm this. Another study suggested a higher ratio of serum concentration to dose was found more often in TD patients (Jeste et al, 1982) and suggested that abnormal metabolism of neuroleptics may be related to the pathophysiology of TD. In the present study, no association between TD and a high UNA or UNA: dose ratio was found when all patients of all ages were examined. On the contrary, patients with TD had a lower mean dose of neuroleptic and UNA. Age however was a confounding variable. The elderly who are more likely to develop TD

were prescribed lower doses of medication. In patients aged over 60 years, the UNA: dose ratio was higher than in the under 60's, but in this age group also there was no relationship between UNA and UNA: dose ratio and TD. The present work therefore lends no support to those who have suggested TD is related to plasma neuroleptic levels.

The results suggest the addition of other psychotropic medication may influence plasma neuroleptic concentrations. In the present study patients receiving antiparkinsonian medication had lower neuroleptic levels. Previous work has produced conflicting results with some supporting the present finding (eg. Rivera-Calimlin *et al*, 1973, Logan *et al*, 1975), others finding no effect (Simpson *et al*, 1980, El-Yousef and Manier, 1974), and others suggesting antiparkinson drugs increase levels (Kolakowska *et al*, 1976). Antidepressants appeared to raise neuroleptic levels. This is to be expected as neuroleptics and tricyclic antidepressants are known to require many of the same liver enzymes for their breakdown (Perel *et al*, 1974). Also, cross reaction of antidepressants in the radio-receptor assay cannot be ruled out. Amitriptyline and imipramine has been shown to cross react in caudate preparations with a potency of  $\frac{1}{4}$   $\frac{1}{2}$  that of thioridazine (Creese *et al*, 1981). Finally, benzodiazepines had no effect. This is in agreement with the finding that benzodiazepines do not affect the pharmacokinetics of the tricyclic nortriptyline (Gram *et al*, 1973); since tricyclics and neuroleptics are degraded by the same metabolic route, benzodiazepines are also unlikely to affect plasma levels of neuroleptics.

Compliance with oral antipsychotic medication was probably high. In only 9% of patients taking oral drugs was antipsychotic medication not detected in plasma. Compliance of course is not an all-or-nothing phenomenon. Some patients may have been taking their medication only intermittently. Others in the community perhaps



only restarted medication a day or two before their assessment; however, they were not aware before their appointment that a blood sample would be requested. Most Nithsdale schizophrenic patients have been in contact with local psychiatric services for many years. Most receive considerable support in the community; professionals from all disciplines stress the importance of maintenance antipsychotic therapy.

We conclude by emphasising the principal clinical finding, namely that only 44% of the 146 patients had no movement disorder. This illustrates the urgent need for neuroleptics with fewer side effects. Seventy seven percent of all Nithsdale schizophrenic patients live outside hospital. Their acceptance by the community, already difficult, will not be improved by the fact that the majority have a disfiguring movement disorder.

TABLE 4.4.1  
NITHSDALE SCHIZOPHRENIC PATIENTS  
DEMOGRAPHIC AND SOCIAL DATA

		NUMBER OF PATIENTS (%)	
SEX	Male	75	(51)
	Female	71	(49)
MARITAL STATUS	Single	91	(62)
	Married	27	(18)
	Widowed	7	(5)
	Divorced/Separated	20	(14)
	Not known	1	(1)
HOSPITAL STATUS	Inpatient	34	(23)
	Daypatient	28	(19)
	Outpatient	32	(22)
	CPN supervision	29	(20)
	GP supervision only	23	(16)
LENGTH OF HOSPITAL STAY: INPATIENTS ONLY	< 6 months	15	(44)
	6 months < 1 year	2	(6)
	1 < 5 years	4	(12)
	5 < 10 years	2	(6)
	10 years +	11	(32)
LENGTH OF ILLNESS	< 1 year	2	(1)
	1 < 5 years	20	(14)
	5 < 10 years	27	(18)
	10 < 20 years	36	(25)
	20 < 30 years	27	(19)
	30 years +	34	(23)

TABLE 4.4.2  
PREVALENCE OF MOVEMENT DISORDERS

	% (N = 146)
<b>AKATHISIA</b>	
Absent	72
Questionable	10
Mild	13
Moderate	5
<b>PSEUDOAKATHISIA</b>	
Absent	95
Present	5
<b>TARDIVE DYSKINESIA</b>	
Absent	71
Probable	29
<b>PARKINSONISM</b>	
Absent	73
Present	27
<b>ANY MOVEMENT DISORDER</b>	
None	44
1	36
> 1	20

TABLE 4.4.3  
DOSAGE, UNITS OF NEUROLEPTIC ACTIVITY (UNA)  
AND POTENCY OF INDIVIDUAL DRUGS

DRUG	NUMBER OF PATIENTS	MEAN DOSE mg/day	MEAN UNA	MEAN UNA/DOSE (potency)	CORRELATION DOSE VS UNA 'r'
<u>ORAL</u>					
THIORIDAZINE	20	194	388	2.46	+0.67
SULPIRIDE	12	567	56	0.10	+0.37
PIMOZIDE	9	8	64	9.18	+0.14
CHLORPROMAZINE	4	475	211	0.43	+0.97
<u>INTRAMUSCULAR</u>					
FLUPENTHIXOL DECANOATE	18	3.5	65	23.16	+0.44
FLUPHENAZINE DECANOATE	11	2.1	56	28.54	+0.23
HALOPERIDOL DECANOATE	6	3.8	29	6.98	+0.81

TABLE 4.4.4  
DOSAGE, UNITS OF NEUROLEPTIC ACTIVITY (UNA)  
AND POTENCY OF DRUGS IN PATIENTS WITH AND  
WITHOUT MOVEMENT DISORDERS

	NUMBER OF PATIENTS	MEAN DOSE,mg (Standard Deviation)	MEAN UNA (Standard Deviation)	MEAN UNA/ DOSE(potency) (Standard Deviation)
AKATHISIA				
Absent	78	365(394)	131(186)	1.09(3.20)
Present	22	374(307)	114(218)	0.54(1.16)
TARDIVE DYKINESIA				
Absent	81	*475(611)	**168(249)	0.74(1.39)
Probable	33	*275(227)	** 66(85)	0.75(2.44)
PARKINSONISM				
Absent	81	376(385)	144(218)	0.86(1.97)
Present	33	517(793)	126(227)	0.45(0.96)

\* P < 0.02

\*\* P < 0.01

TABLE 4.4.5  
DOSAGE, UNITS OF NEUROLEPTIC ACTIVITY (UNA)  
AND POTENCY OF DRUGS IN PATIENTS RECEIVING  
ANTIPSYCHOTIC MEDICATION AND ADDITIONAL  
PSYCHOTROPIC MEDICATION

	NUMBER OF PATIENTS	MEAN DOSE OF NEUROLEPTIC (mg) (Standard Deviation)	MEAN UNA  (Standard Deviation)	MEAN UNA/ DOSE (potency) (Standard Deviation)
Antiparkinsonian medication	37	614(808)	124(201)	0.39(0.83)
No antiparkinsonian medication	90	356(378)	147(229)	0.91(2.02)
Antidepressant medication	18	* 265(174)	157(158)	1.75(3.51)
No antidepressant medication	110	* 459(580)	136(229)	0.58(1.21)
Benzodiazepines	24	459(878)	234(350)	0.80(0.96)
No Benzodiazepines	104	419(443)	119(177)	0.73(1.88)

1 patient not known

\*  $P < 0.01$

**OBSTETRIC COMPLICATIONS**

**5.1 OBSTETRIC COMPLICATIONS, FAMILY HISTORY AND ABNORMAL  
MOVEMENTS**

**ROBIN G McCREADIE**

**DAVID J HALL**

**IAN BERRY**

**LESLEY J ROBERTSON**

**JAMES I EWING**

**MICHAEL F GEALS**



## SUMMARY

Obstetric histories of 54 schizophrenic patients and 114 sibs were obtained from mothers and scored using the Obstetric Complications Scale of Lewis et al (1989). There was no statistically significant difference in the proportion of schizophrenic patients (35%) and sibs (29%) who had at least one definite obstetric complication. There was no evidence that schizophrenic patients with a history of obstetric complications were less likely to have a first degree relative with a history of psychiatric illness leading to inpatient care. Schizophrenic patients with a history of obstetric complications were more likely to have drug induced parkinsonism. There was a trend for tardive dyskinesia to be more common in those schizophrenic patients with no obstetric complications but a family history of schizophrenia.

Most but not all studies have found an excess of obstetric complications in schizophrenic patients when compared with sibs, normal controls, or other patients (reviewed by Lewis, 1989). However, it is difficult to compare one study with another as they have used different control groups and different ways of assessing obstetric complications. For example, studies have compared schizophrenic patients with their sibs (DeLisi et al, 1987, Woerner et al, 1973, Lane and Albee, 1966, Eagles et al, 1990), with other patients (Pollack and Greenberg 1966, Lewis and Murray 1987) and with non-related controls (Jacobsen and Kinney 1980, Gillberg et al, 1986). Studies have obtained obstetric histories from records made at the time of birth (Lane and Albee 1966, Jacobsen and Kinney 1980, Gillberg et al, 1986, Eagles et al, 1990), retrospectively from mothers or other first degree relatives (DeLisi et al, 1987, Pollack and Greenberg 1966), from both (Woerner et al, 1973) or from psychiatric records (Lewis and Murray 1987). All the above studies have shown an excess of obstetric complications in schizophrenic patients compared with the control group; however, the differences were in the main at a low level of statistical significance.

Other studies have not confirmed the excess of obstetric complications in schizophrenic patients. McNeil and Kaij (1978), examining birth records of schizophrenic patients and normal controls, found an excess of obstetric complications in patients with process schizophrenia, but not in those with schizophrenic-like psychosis. Parnas et al (1982), examining birth records of those born to schizophrenic mothers found no statistically significant increase in obstetric complications in those who became schizophrenic when compared with those who did not; those with a diagnosis of borderline schizophrenia had fewer obstetric complications than normal off-spring. Turner et al (1986) in a computerised tomography study obtained histories from a parent or first degree relative and found

no increased frequency of early physical trauma in young schizophrenic patients when compared with normal controls. Done et al (1990), examining birth records of all those born in the United Kingdom during one week in 1958 and tracing psychiatric records, found no excess of obstetric complications in schizophrenic patients when compared with normals. Many of the above studies examined hospitalised and presumably more severely ill schizophrenic patients.

The present study, the first of its kind, takes a broader view and examines obstetric complications in all known schizophrenic patients living within a discrete geographical area.

Tardive dyskinesia (TD) is more commonly found in schizophrenic patients with deficits in a variety of cognitive functions (Waddington et al, 1990). Obstetric complications might be one cause of such cerebral dysfunction and predispose to TD. However, a recent study found patients with TD were less likely to have experienced obstetric complications, and were more likely to have a family history of schizophrenia (O'Callaghan et al, 1990a). The second aim of the present study therefore is to examine further the relationship between obstetric complications, family history and movement disorders secondary to antipsychotic medication.

## METHOD

The identification of schizophrenic patients has been described elsewhere (McCreadie, 1982a, McCreadie et al, 1991). Briefly, a repeat census on 11 September 1989 in Nithsdale, South West Scotland, identified all known schizophrenic patients - inpatients, daypatients, outpatients, patients supervised by

community psychiatric nurses and patients known only to their family doctor (N = 165). Nineteen patients (12%) were excluded: 12 refused to participate, general practitioners refused access in a further three, and four were not approached (one patient was in a terminal care ward and three patients known only to their family doctor had refused to take part in previous Nithsdale surveys). Thus the study focused on 146 patients, 74% of whom fulfilled the DSM-III-R criteria for schizophrenia (American Psychiatric Association, 1987). Of these, 51% were male, 49% female. Their mean age was 50 years (standard deviation 15, range 20-82).

Before 1977 birth records at the local maternity hospital were destroyed after seven years. The obstetric history of patients and their sibs was therefore obtained from patients' mothers, who with patients' consent were interviewed at home; such interviews took place as far afield as London and the north of Scotland. The interviews were conducted by one of two psychiatrists (DJH or IB) who at the start of the interview, with the principal exception of eight singletons, was in the majority of instances blind as to who was the patient, and who were his or her sibs. Mothers were asked not to reveal until the end of the interview the identity of the patient. Obstetric histories were obtained through a semi-structured interview developed in collaboration with a consultant obstetrician (MG) (Appendix). A third psychiatrist (JE), blind as to who were patients and sibs, scrutinised written answers to the semi-structured interview. He gave each a score using the Obstetric Complications Scale (Lewis *et al*, 1989). As suggested by Lewis and colleagues a person was categorised as having one or more definite complications, one or more equivocal but no definite complications, or no complications.

Mothers also gave information at the end of the interview about any admissions to psychiatric inpatient care of herself, her children, her childrens' father(s) and her

grandchildren. Case records were then obtained where a schizophrenic patient's sibs, parents or children had been admitted to a psychiatric hospital. References identifying the individual were deleted, and the third psychiatrist (JE) made a case record diagnosis using DSM-III-R criteria. To increase blindness, a number of case records of patients unrelated to the Nithsdale schizophrenic cohort were also included.

As described elsewhere (McCreadie *et al*, 1991) patients were assessed by one of two psychiatrists (RGMcC and LJR) for abnormal movements associated with antipsychotic medication. Both psychiatrists were blind to the obstetric history. TD was measured by the Abnormal Involuntary Movements Scale (US Department of Health, Education and Welfare 1976), parkinsonism by the Simpson and Angus Scale (Simpson and Angus, 1970) and akathisia by the Barnes Scale (Barnes 1989).

## RESULTS

Of the 146 patients identified 61 (42%) had mothers who were alive. Three patients refused access to their mothers, and four mothers declined to be seen. Thus 51 mothers of 54 patients were interviewed - one mother had two and another had three schizophrenic children among the original 146. The 54 patients had 114 sibs. The patients whose mothers were interviewed differed from those whose mothers were dead or were not interviewed in that they were younger ( $\chi^2 = 35.20$ ,  $P < 0.001$ ) and had been ill a shorter time ( $\chi^2 = 24.85$ ,  $P < 0.001$ ); fewer had TD ( $\chi^2 = 4.34$ ,  $P < 0.05$ ) or parkinsonism ( $\chi^2 = 4.43$ ,  $P < 0.05$ ). When the schizophrenic patients about whom an obstetric history was obtained were compared with their sibs there was a trend, not statistically significant, for more of the former to be male (65% versus 48%).

Significantly more were first born (41% vs 26%;  $\chi^2 = 10.36$ ,  $P < 0.01$ ), but this difference disappeared when schizophrenic singletons ( $N = 8$ ) were excluded.

### Obstetric complications

There was no statistically significant difference in the proportion of schizophrenic patients and their sibs who had at least one definite complication (Table 5.1.1: 35% versus 29%); neither was there any difference in the total number of definite complications (Table 5.1.1). Further analyses failed to reveal any differences between schizophrenic patients and their sibs in total number of definite and equivocal complications, antepartum complications alone, intrapartum complications alone, mean maternal age at time of birth, and mean paternal age. There was no significant difference in the mean birth weight of schizophrenic patients whose mothers recalled an actual birth weight ( $N = 52$ ) when compared with sibs ( $N = 106$ ) (3.18kg (SD 0.51) vs 3.15 (0.58)). Inspection of the data showed no differences between schizophrenic patients and sibs in type of individual complication.

When only Nithsdale schizophrenic patients who fulfilled DSM-III-R criteria ( $N = 38$ ) were compared with their sibs, there was again no significant difference in the proportion with at least one definite obstetric complication (32% versus 27%).

A recent study (Eagles *et al*, 1990) compared schizophrenic patients with paired sibs. A paired sib was defined as the other sib in a sibship of two, a sib of the same sex in a sibship greater than two, and the sib closest in age if there were two or more sibs of the same sex. Forty four Nithsdale schizophrenic patients had a paired sib. Again there was no difference in the proportion with at least one definite obstetric complication (34% of schizophrenic patients versus 37% of sibs). The within-pair sign test failed to reveal any statistically significant differences when a comparison

was made of those with and without at least one definite obstetric complication. In eight pairs the patient had an obstetric complication and the sib did not; in 11 pairs the sib had an obstetric complication and the patient did not. A within-pair comparison of those with and without a definite and/or an equivocal complication also failed to reveal any significant difference.

Assessment of family history (see below) identified a further four sibs who did not live in Nithsdale, but were schizophrenic. The figures were reanalysed (58 schizophrenic patients and 110 sibs), but the result was essentially the same; 34% of schizophrenic patients and 29% of sibs had at least one definite obstetric complication. Finally, schizophrenic patients were compared with their sibs who had no history of any psychiatric illness leading to hospitalisation (58 schizophrenic patients and 106 sibs). Again no differences were found: 34% of schizophrenic patients and 28% of sibs had at least one definite obstetric complication.

Nithsdale schizophrenic patients with and without at least one definite obstetric complication were compared. There were no statistically significant differences between the two groups in sex, age, hospital status and age of onset and length of illness.

### Family history

Twenty Nithsdale schizophrenic patients had first degree relatives who mothers said had been admitted to inpatient psychiatric care. Three brothers from one family and two brothers from another belonged to the Nithsdale cohort. The other 15 had relatives, either living outside Nithsdale with a psychiatric admission, or living in Nithsdale with an admission for an illness other than schizophrenia. DSM-III-R criteria applied to hospital case records showed a history of schizophrenia in first

degree relatives of 10 Nithsdale schizophrenics, major depression in six, delusional disorder in two and bipolar disorder in one. One case record could not be traced and therefore 19 were considered to have a broadly defined family history of psychiatric illness. There was no statistically significant difference in sibship size between those who did and did not have a family history (mean 3.8 vs 3.0).

#### Obstetric complications and family history (Table 5.1.2)

There was no statistically significant difference between Nithsdale schizophrenic patients with (N = 19) and without (N = 35) a history of obstetric complications in the proportion with a broadly defined history of psychiatric illness (37% vs 34%). Similarly, when a narrow definition of a family history was used (DSM-III-R schizophrenia in a first degree relative) the proportion with a family history was not significantly different in those with and without a history of obstetric complications (16% vs 20%). A further analysis examined only Nithsdale schizophrenic patients with a DSM-III-R diagnosis of schizophrenia (N = 38). One of 12 patients with a definite obstetric complication (8%) and five of 26 with no complications (19%) had a family history of DSM-III-R schizophrenia leading to psychiatric admission, a statistically non-significant difference.

#### Obstetric complications and movement disorders

Patients, either with parkinsonism, defined as a score of more than 0.3 on the Simpson and Angus Scale (1970), or receiving an antiparkinsonian drug, more often had a history of at least one definite obstetric complication than those with no parkinsonism (58% versus 21%,  $\chi^2 = 5.64$ ,  $P < 0.02$ ). There was a trend, not statistically significant, for fewer patients with TD (defined by the criteria of Schooler and Kane, 1982) to have a history of at least one obstetric complication when compared with those with no TD (1 of 9 (11%) versus 17 of 43 (40%)). There were no differences in obstetric complications in those with and without akathisia.



### Obstetric complications, tardive dyskinesia and family history

None of 13 patients with at least one definite obstetric complication and no family history of psychiatric illness leading to inpatient care had TD; three out of 13 patients with no definite obstetric complication but a family history had TD. One of 16 patients with at least one definite obstetric complication and no family history of DSM-III-R schizophrenia had TD; three of seven patients with no definite obstetric complications but a family history of DSM-III-R schizophrenia had TD. Thus TD was associated with a family history of schizophrenia, but not with obstetric complications.

## DISCUSSION

The present study has failed to demonstrate a difference between schizophrenic patients and their sibs in the proportion with a history of obstetric complications. Three other studies have used the same obstetric complications scale. Only one has used it in interviews with mothers (O'Callaghan *et al*, 1990a). It found a similar proportion of schizophrenic patients with at least one definite obstetric complication (33%); the obstetric history of sibs was not obtained. A second study applied the scale to birth records (Eagles *et al*, 1990 and personal communication); 70% of schizophrenic patients and 59% of normal siblings had at least one definite complication. A statistically significant difference between the two groups was only obtained when a cut-off point of two or more obstetric complications was used. This study probably examined those likely to have a complex or hazardous birth (Owen and McGuffin, 1990). The third study obtained information from psychiatric case records (Lewis and Murray, 1987). Seventeen percent of schizophrenic patients had definite obstetric complications compared with 8% of remaining patients;

information about sibs was not obtained. It is likely information obtained solely from psychiatric records will underestimate the proportion of patients with complications.

In the present study every effort was made to obtain a full and objective history. Mothers were interviewed in the comfort of their own homes; during the interview the interviewers were for the most part blind as to who were patients and who were sibs; the interview was semi-structured, and therefore the same questions were asked about all sibs; and the final assessment of obstetric complications was made using the written replies, with the assessor blind to the patients' and sibs' identity. A criticism of the study might be that obstetric histories were obtained from mothers of patients. It is possible that the mother might have remembered better over the years the obstetric history of the future schizophrenic patient, particularly if there were childhood personality anomalies compared with siblings. If this were so it would magnify the importance of obstetric complications in patients with schizophrenia. This makes the result of the present study the more compelling. However, it has been shown recently, with the rating scale used in the present study, that there is a high level of agreement between mothers' histories and birth records (O'Callaghan et al, 1990b).

The present study has examined a community of schizophrenic patients, that is, all those known to be living in a discrete geographical area at a given moment in time, whether hospitalised or not. The population thus contains a number of patients who have had few admissions, and probably a better prognosis. However there was no difference between inpatients and non-inpatients in the proportion with obstetric complications.

The present study is in agreement with the minority of previous studies (see introduction) which has failed to demonstrate a difference between schizophrenic patients and the comparison group. As stated previously studies which have found a difference have in the main done so at a low level of statistical significance. The most likely conclusion is that if there is an association between obstetric complications and schizophrenia it is a weak one.

It has been suggested that obstetric complications may be over-represented in schizophrenic cases which occur sporadically, and found less often in cases where there is a family history of schizophrenia (Murray et al, 1985); that is, obstetric complications and genetic predisposition are discrete aetiological factors. This view has been challenged (McGuffin et al, 1987) and not confirmed by Murray and colleagues (Nimgaonkar et al, 1988). However, a recent study has provided support for this hypothesis (O'Callaghan et al, 1990a); obstetric complications were more common in schizophrenic patients who did not have a family history of schizophrenia, affective disorder or suicide. In the present study where a rather similar broad definition of psychiatric illness was used, obstetric complications were as frequently found in those with as in those without a family history.

An unexpected finding was the association between obstetric complications and parkinsonism. We know of no other previous study that has reported this. Age was not a confounding factor as although parkinsonism was found more often with increasing age (McCreadie et al, 1991), a history of obstetric complications was not. By no means all patients given antipsychotic drugs develop parkinsonian side effects. Perhaps obstetric complications produce minimal brain damage which renders the brains of some schizophrenic patients more sensitive to neuroleptics.

It has recently been suggested that patients with tardive dyskinesia are more likely to have a family history of psychiatric disorder (O'Callaghan *et al*, 1990a), a finding which suggests that genetic factors contribute not only to the aetiology of schizophrenia, but vulnerability to TD. In the present study numbers are small, but lend no support to this hypothesis when a family history of any psychiatric disorder among first degree relatives leading to inpatient care was considered. When a family history only of DSM-III-R schizophrenia was examined the trend was that TD occurred more often in those patients with no definite obstetric complications but a family history.

In conclusion, the present study has failed to confirm, firstly, an association between obstetric complications and schizophrenia, and, secondly, the separation of schizophrenic patients into those either with a family history or a history of obstetric complications, but not both.

TABLE 5.1.1  
OBSTETRIC COMPLICATIONS

<u>OBSTETRIC COMPLICATIONS</u>	SCHIZOPHRENIC PATIENTS % (N = 54)	SIBS % (N = 114)
Absent	56	53
At least one equivocal but no definite complication	9	18
At least one definite complication	35	29
TOTAL NUMBER OF DEFINITE COMPLICATIONS		
0	65	71
1	18	19
2	9	6
3	8	3
4	-	-
5	-	1

TABLE 5.1.2  
OBSTETRIC COMPLICATIONS AND FAMILY HISTORY

	SCHIZOPHRENIC PATIENTS WITH OBSTETRIC COMPLICATIONS % (N = 19)	SCHIZOPHRENIC PATIENTS WITHOUT OBSTETRIC COMPLICATIONS % (N = 35)
FAMILY HISTORY *	37	34
(broadly defined)		
NO FAMILY HISTORY	63	66
<hr/>		
FAMILY HISTORY **	16	20
(narrowly defined)		
NO FAMILY HISTORY	84	80

\* Family history of schizophrenia (DSM-III-R 295) affective disorder (296) or delusional disorder (297) in first degree relative leading to psychiatric inpatient care.

\*\* Family history of schizophrenia (DSM-III-R 295) in first degree relative leading to psychiatric inpatient care.

## APPENDIX

### OBSTETRIC COMPLICATIONS QUESTIONNAIRE

Numbers in brackets relate to numbered items on Obstetrics Complications Scale  
(Lewis et al, 1989)

#### INTRODUCTION

Thank you for your co-operation. As you know from our letter, the purpose of my visit is to ask you a number of questions about your pregnancies and the births of your children. Although I am aware that member(s) of your family have had psychiatric problems, to allow me to remain completely objective, it would be helpful if you could attempt not to identify explicitly which family member this was.

I would like to work through the questions with you for each child, starting with the oldest.

#### Pregnancy

Firstly, regarding your pregnancy:

- 1.(a) Were there any problems or complications that you remember?  
(1-4)
- (b) Did you have to be admitted to hospital while you were pregnant?
- (c) If so, why and for how long?
- 2.(a) Were any of the tests done at the ante-natal clinic abnormal? (1-2)
- (b) Did they show up any previous infection?
- (c) Did they detect any antibodies? (2)
- (d) Did you have any infections while you were pregnant? (1)
- (e) Did you have German measles or any sexually transmitted disease during pregnancy? (1)
- (f) Did you receive antibiotic treatment? (1)
- 3.(a) Was there a problem with your blood pressure? (3)
- (b) If so, did you have swelling of your ankles/fingers/ face? (3)
- (c) Did you have a fit or fits during pregnancy? (3)
- (d) Were you told that there was protein in your urine? (3)
- (e) Did the problems with your blood pressure mean that you had to come into hospital for a period while you were pregnant? (3)
- (f) Did they have to bring labour on early because of it? (3)

- 4.(a) Did you have any vaginal bleeding during pregnancy?  
(not just "spotting") (4)
- (b) Did you have to go into hospital because of this?
- (c) When, and for how long?

### Delivery

Now, about the birth itself:

- 5.(a) How old were you when the baby was born?
- (b) How old was the father?
- (c) Boy or girl?
- (d) Single or twin?
- 6.(a) If twin - how long was there between the two babies  
being born? (7)
- (b) Who came first? (7)
- (c) More than half an hour between them? (If yes = complicated delivery)
- (d) Were both babies born head first? (7) (If no = complicated delivery)
- 7.(a) Was the baby born on time, early or late?
- (b) Less than 37 weeks? (9)
- (c) More than 42 weeks? (9)
8. Did you go into labour yourself or was the labour induced?
9. Was the baby lying correctly or not? If not, what was the problem? (11)
- 10.(a) How long was it between your waters breaking and the baby being born?
- (b) Was it more than 24 hours? (5)
- 11.(a) How long was the labour?
- (b) Less than 3 hours?
- (c) More than 24 hours?
- (d) More than 36 hours?
12. Would you say that the delivery was easy, normal or difficult? (6E)



- 13.(a) Were forceps used in the delivery? (12)
- (b) If so, did the baby have to be turned with the forceps? (12, if yes = difficult forceps delivery)
- (c) Were you told that it was a difficult forceps delivery? (12)
14. Was the cord around the baby's neck or was it knotted? (8E)
15. Did the cord come down before the baby? (8D)
- 16.(a) Did you have a Caesarean Section? (10)
- (b) Why was that done? (10)
- (c) Was it an emergency or planned? (10)
- 17.(a) How much did the baby weigh? (13)
- (b) Less than 5 lbs?
- (c) Less than 4 lbs?
18. Was the baby all right or did it have to be revived? (probe if necessary) (14)
- 19.(a) Was the baby jaundiced?
- (b) Was the baby treated for this?
- 20.(a) Did the baby have to go to an incubator?
- (b) If so, for how long? More than 4 weeks? (14)
21. Were any physical abnormalities pointed out to you early on? (15)

END

Thank you for your cooperation.

## REFERENCES

## REFERENCES

- AMERICAN PSYCHIATRIC ASSOCIATION (1987) Diagnostic and Statistical Manual of Mental Disorders. (Third Edition - Revised) Washington: American Psychiatric Association.
- ANNETT, M. (1970) A classification of hand preference by association analysis. British Journal of Psychology, 61 303-21.
- ANONYMOUS (1979) Tardive dyskinesia, Lancet, ii, 447-448.
- AYD, F.J. (1961) A survey of drug-induced extrapyramidal reactions. Journal of the American Medical Association, 175, 1054-1060.
- BARNES, T.R.E. (1984) Rating tardive dyskinesia. British Journal of Psychiatry, 145, 338.
- BARNES, T.R.E. (1989) A rating scale for drug-induced akathisia. British Journal of Psychiatry, 154, 672-676.
- BARNES, T.R.E. and WILES, D.H. (1983) Variation in oro-facial tardive dyskinesia during depot anti-psychotic drug treatment. Psychopharmacology, 81, 359-362.
- BARNES, T.R.E., KIDGER, T. and GORE, S.M. (1983) Tardive dyskinesia: a 3-year follow-up study. Psychological Medicine, 13, 71-81.
- BARNES, T.R.E. and BRAUDE, W.M. (1985) Akathisia variants and tardive dyskinesia. Archives of General Psychiatry, 42, 874-878.
- BARRON, E.T. and McCREADIE, R.G. (1983) One year follow-up of tardive dyskinesia. British Journal of Psychiatry, 143, 423-424.
- BEBBINGTON, P.E. (1988) Review of the Nithsdale Schizophrenia Survey. Transmission, 1 (5) 14-15.
- BERGEN, J.A., EYLAND, E.A., CAMPBELL, J.A., JENKINGS, P., KELLEHEAR, K., RICHARDS, A. and BEUMONT, P.J.V. (1989) The course of tardive dyskinesia in patients on longterm neuroleptics. British Journal of Psychiatry, 154, 523-528.
- BERGEN, J.A., GRIFFITHS, D.A., REY, J.M. and BEUMONT, P.J.V. (1984) Tardive dyskinesia: fluctuating patient or fluctuating rater. British Journal of Psychiatry, 144, 498-502.
- BLEULER, M. (1983) Schizophrenic deterioration. British Journal of Psychiatry, 143, 78-79.
- BRAUDE, W.M., BARNES, T.R.E. and GORE, S.M. (1983) Clinical characteristics of akathisia. A systematic investigation of acute psychiatric inpatient admissions. British Journal of Psychiatry, 143, 139-150.
- BROWN, G.W. and BIRLEY, J.L.T. (1968) Crises and life changes and the onset of schizophrenia. Journal of Health and Social Behaviour, 9, 203-214.

BROWN, G.W., BIRLEY, J.L.T. and WING, J.K. (1972) Influence of family life on the course of schizophrenic disorders: a replication. British Journal of Psychiatry, 121, 241-258.

BROWN, G.W., MONCK, E.M., CARSTAIRS, G.M. and WING, J.K. (1962) The influence of family life on the course of schizophrenic illness. British Journal of Preventive and Social Medicine, 16, 55-68.

CHAUGULE, V.B. and MASTER, R.S. (1981) Impaired cerebral dominance and schizophrenia. British Journal of Psychiatry, 139, 23-24.

CHEADLE, A.J., FREEMAN, H.L. and KORER, J.R. (1978) Chronic schizophrenic patients in the community. British Journal of Psychiatry, 132, 221-7.

CHEADLE, A.J., and MORGAN, R. (1974) The economics of rehabilitation. British Journal of Psychiatry, 125, 193-201.

CHOUINARD, G., ANNABLE, L., ROSS-CHOUINARD, A. and NESTOROS, J.N. (1979) Factors related to tardive dyskinesia. American Journal of Psychiatry, 136, 79-83.

CIOMPI, L. (1980) The natural history of schizophrenia in the long term. British Journal of Psychiatry, 136, 413-420.

COOPER, B. (1978) Epidemiology. In: Schizophrenia. Towards a New Synthesis. (e.g. J.K. Wing) London: Academic Press.

COOPER, P., OSBORN, M., GATH, D. and FEGETTER, G. (1982) Evaluation of a modified self-report measure of social adjustment. British Journal of Psychiatry, 141, 68-75.

CREER, C. and WING, J.K. (1974) Schizophrenia at Home. Surbiton, Surrey: National Schizophrenia Fellowship.

CREESE, I., LADER, S. and ROSENBERG, B. (1981) Radioreceptor assay for neuroleptic drugs. In: Clinical Pharmacology in Psychiatry: Neuroleptic and Antidepressant Research (eds. E. Usdin, S.G. Dane, L. Gram and D. Lingjaerde). London: Macmillan.

CROW, T.J. (1980) Molecular pathology of schizophrenia: More than one disease process. British Medical Journal, i, 66-68.

DAVIS, J.M. (1985) Antipsychotic drugs. In: Comprehensive Textbook of Psychiatry (eds. H.I. Kaplan and B.J. Sadock) Baltimore: Williams & Williams.

DeLISI, L.E., GOLDIN, L.R., MAXWELL, E., KAZUBA, D.M., GERSHON, E.S. (1987) Clinical features of illness in siblings with schizophrenic or schizoaffective disorder. Archives of General Psychiatry, 44, 891-896.

DER, G., GUPTA, S. and MURRAY, R.M. (1990) Is schizophrenia disappearing? Lancet, 335, 513-516.

DONE, J., CROW, T.J., FRITH, C.D. and JOHNSTONE, E.C. (1990) Pregnancy and birth complications as causes of psychiatric illness in adult life: a study utilising the perinatal morbidity study (1958). Schizophrenia Research, 3, 91.

DUMFRIES AND GALLOWAY HEALTH BOARD (1981) Summary of Accounts for year ended 31 March 1981.

EAGLES, J.M., GIBSON, I., BREMNER, M.H., CLUNIE, F., EBMEIER, K. and SMITH, N.C. (1990) Obstetric complications in DSM-III schizophrenics and their siblings. Lancet, 335, 1139-41.

EL-YOUSEF, K.M. and MANIER, D.H. (1974) The effect of benztropine mesylate on plasma levels of butaperazine maleate. American Journal of Psychiatry, 131, 471-472.

EZRIN-WATERS, C., SEEMAN, M.V. and SEEMAN, P. (1981) Tardive dyskinesia in schizophrenic out-patients: Prevalence and significant variables. Journal of Clinical Psychiatry, 42, 16-22.

FALLOON, I.R.H., BOYD, J.L., MCGILL, C.W., RAZANI, J., MOSS, H.B. and GILDERMAN, A.M. (1982) Family management in the prevention of exacerbations of schizophrenia: a controlled study. New England Journal of Medicine, 306, 1437-1440.

FALLOON, I.R.H., BOYD, J.L., MCGILL, C.W., WILLIAMSON, M., RAZANI, J., MOSS, H.B., GILDERMAN, A.M. and SIMPSON, G.M. (1985) Family management in the prevention of morbidity of schizophrenia. Clinical outcome of a two year longitudinal study. Archives of General Psychiatry, 42, 887-896.

FAVRE, S., GONZALES, C., LENDAIS, G., de SAUSSURE, N., SZIGETHY, L., BARRELET, L. and FERRERO, F. (1989) Expressed emotion of schizophrenic relatives. Poster at VIII World Congress of Psychiatry, Athens.

FEIGHNER, J.P., RUBINS, E., GUZE, S., WOODRUF, R.A., WINOKUR, G. and MUNOZ, R. (1972) Diagnostic criteria for use in psychiatric research. Archives of General Psychiatry, 26, 57-62.

FLEMINGER, J.J., DALTON, R. and STANDAGE, K.F. (1977) Handedness in psychiatric patients. British Journal of Psychiatry, 131, 448-452.

FRIIS, T., CHRISTENSEN, T.R. and GERLACH, J. (1983) Sodium valproate and biperiden in neuroleptic induced akathisia, parkinsonism and hyperkinesia. Acta Psychiatrica Scandinavica, 67, 178-187.

GARDOS, G., COLE, J.O., HASKELL, D., MARBY, D., PAINE, S.S. and MOORE, P. (1988) The natural history of tardive dyskinesia. Journal of Clinical Psychopharmacology, 8, Suppl.4, 31s-37s.

GARDOS, G., COLE, J.O. and LA BRIE, R. (1977) The assessment of tardive dyskinesia. Archives of General Psychiatry, 34, 1206-1212.

GENERAL REGISTRAR OFFICE, SCOTLAND (1971) Census 1971, Scotland. Edinburgh: HMSO.

GENERAL REGISTRAR OFFICE, SCOTLAND (1981) Census 1981, Scotland: Preliminary Report. Edinburgh: HMSO.

GIBB, W.R.G. and LEES, A.J. (1986) The clinical phenomenon of akathisia. Journal of Neurology, Neurosurgery and Psychiatry, 49, 861-866.

GILLBERG, C., WAALSTROM, J., FORSMAN, A., HELLGREN, L. and GILLBERG, I.C. (1986) Teenage psychoses - epidemiology, classification and reduced optimality in the pre-, peri- and neonatal periods. Journal of Child Psychology and Psychiatry, 27, 87-98.

GLAZER, W.M., AARONSON, H.S., PRUSOFF, B.A. and WILLIAMS, D.H. (1980) Assessment of social adjustment in chronic ambulatory schizophrenics. Journal of Nervous and Mental Disease, 168, 493-497.

GOLDBERG, E.M. and Warburton, R.W. (1979) Ends and Means in Social Work. The Development and Outcome of a Case Review System for Social Workers. London: George Allen and Unwin.

GRAM, L.F., FREDRICSON-OVERO, K. and KIRK, L. (1973) Tricyclic antidepressants and benzodiazepines; a drug combination without pharmacokinetic interaction in man. Nordisk Psychiatrisk Tidsskrift 27, 434-438.

GUR, R.E. (1977) Motoric laterality imbalance in schizophrenia. Archives of General Psychiatry, 34, 33-37.

HANSEN, L.B., LARSEN, N.E. and GULMANN, N. (1982) Dose-response relationships of perphenazine in the treatment of acute psychoses. Psychopharmacology, 78, 112-115.

HIRSCH, S.R., GAIND, R., ROHDE, P.D., STEVENS, B.C. and WING, J.K. (1973) Outpatient maintenance of chronic schizophrenic patients with long-acting fluphenazine: double-blind placebo trial. British Medical Journal, i, 633-637.

HODKINSON, H.M. (1972) Evaluation of a mental test score for assessment of mental impairment in the elderly. Age and Ageing, 1, 233-238.

HOGARTY, G.E., ANDERSON, C.M., REISS, D.J., KORNBLITH, S.J., GREENWALD, D.P., JAVNA, C.D. and MADONIA, M.J. (1986) Family psychoeducation, social skills training and maintenance chemotherapy in the aftercare treatment of schizophrenia. Archives of General Psychiatry, 43, 633-642.

HOGARTY, G.E. and ULRICH, R.F. (1977) Temporal effects of drug and placebo in delaying relapse in schizophrenic outpatients. Archives of General Psychiatry, 34, 297-301.

- ITAL, T.M., REISBERG, B., HUQUE, M. and MEHTA, D. (1981) Clinical profiles of tardive dyskinesia. Comprehensive Psychiatry, 22, 282-288.
- JACOBSEN, B. and KINNEY, D.K. (1980) Perinatal complications in adopted and non-adopted schizophrenics and their controls. Acta Psychiatrica Scandinavica, 62, Suppl. 285, 337-346.
- JESTE, D.V., ROSENBLATT, J.E., WAGNER, R.L. and WYATT, R.J. (1979) High serum neuroleptic levels in tardive dyskinesia? New England Journal of Medicine, 301, 1184.
- JESTE, D.V., DeLISI, L.E., ZALCMAN, S., WISE, C.D., PHELPS, B.H., ROSENBLATT, J.E., POTKIN, S.G., BRIDGE, T.P. and WYATT, R.J. (1981) A biochemical study of tardive dyskinesia in young male patients. Psychiatry Research, 4, 327-331.
- JESTE, D.V., LINNOILA, M., WAGNER, R.L. and WYATT, R.J. (1982) Serum neuroleptic concentrations and tardive dyskinesia. Psychopharmacology, 76, 377-380.
- JESTE, D.V. and WYATT, R.J. (1981) Changing epidemiology of tardive dyskinesia: An overview. American Journal of Psychiatry, 138, 297-309.
- JOHNSON, D.A.W. (1978) Prevalence and treatment of drug-induced extrapyramidal symptoms. British Journal of Psychiatry, 132, 27-30.
- JOHNSON, D.A.W. (1979) Further observations on the duration of depot neuroleptic maintenance therapy in schizophrenia. British Journal of Psychiatry, 135, 524-530.
- KANE, J.M. and SMITH, J.M. (1982) Tardive dyskinesia: prevalence and risk factors. Archives of General Psychiatry, 39, 473-481.
- KANE, J.M., WOERNER, M. and LIEBERMAN, J. (1988) Tardive dyskinesia: prevalence, incidence and risk factors. Journal of Clinical Psychopharmacology, 8, Suppl. 4, 52s-56s.
- KENNEDY, P.F., HERSHON, H.I. and McGUIRE, R.J. (1971) Extrapyramidal disorders after prolonged phenothiazine therapy. British Journal of Psychiatry, 118, 509-518.
- KOLAKOWSKA, T., WILES, D.H., GELDER, M.G. and McNEILLY, A.S. (1976) Clinical significance of plasma chlorpromazine levels. Psychopharmacology, 49, 101-107.
- KRAWIECKA, M., GOLDBERG, D. and VAUGHAN, M. (1977) A standardised psychiatric assessment scale for rating chronic psychotic patients. Acta Psychiatrica Scandinavica, 55, 299-308.
- KRSKA, J., SAMPATH, B., SHAH, A. and SONI, S.D. (1986) Radioreceptor assay of serum neuroleptic levels in psychiatric patients. British Journal of Psychiatry, 148, 187-193.

KREISMAN, D.E., SIMMENS, S.J. and JOY, J.D. (1979) Rejecting the patient: preliminary validation of a self-report scale. Schizophrenia Bulletin, 5, 220-222.

KUIPERS, L. and BEBBINGTON, P. (1985) Relatives as a resource in the management of functional illness. British Journal of Psychiatry, 147, 465-470.

KUIPERS, L. and BEBBINGTON, P. (1988) Expressed emotion research in schizophrenia: theoretical and clinical implications. Psychological Medicine, 18, 893-909.

LANE, E.A. and ALBEE, G.W. (1966) Comparative birth weights of schizophrenics and their siblings. Journal of Psychology, 64, 227-231.

LEFF, J. (1973) The influence of selection of patients on results of clinical trials. British Medical Journal, iv, 156-158.

LEFF, J. (1986) Recent research on relatives' expressed emotion. In Contemporary Issues in Schizophrenia (eds. A. Kerr and P. Snaith). London: Gaskell.

LEFF, J., BERKOWITZ, R., SHAVIT, N., STRACHAN, A., GLASS, I. and VAUGHN, C. (1989) A trial of family therapy v a relatives group for schizophrenia. British Journal of Psychiatry, 154, 58-66.

LEFF, J., HIRSCH, S.R., GAIND, R., ROHDE, P.D. and STEVENS, B.C. (1973) Life events and maintenance therapy in schizophrenic relapse. British Journal of Psychiatry, 123, 659-660.

LEFF, J., KUIPERS, L., BERKOWITZ, R., EBERLEIN-VRIES, R. and STURGEON, D. (1982) A controlled trial of social intervention in the families of schizophrenic patients. British Journal of Psychiatry, 141, 121-134.

LEFF, J., KUIPERS, L., BERKOWITZ, R., and STURGEON, D. (1985) A controlled trial of social intervention in the families of schizophrenic patients: two year follow-up. British Journal of Psychiatry, 146, 594-600.

LEFF, J. and VAUGHN, C. (1972) Psychiatric patients in contact and out of contact with services: A clinical and social assessment. In Evaluating a Community Psychiatric Service, (eds. J.K. Wing and A.M. Hailey). London: Oxford University Press.

LEFF, J. and VAUGHN, C. (1980) The interactions of life events and relatives expressed emotion in schizophrenic and depressive neurosis. British Journal of Psychiatry, 136, 146-153.

LEFF, J., WIG, N.N., BEDI, H., MENON, D.K., KUIPERS, L., KORTEN, A., ERNBERG, G., DAY, R., SARTORIUS, N. and JABLENSKY, A. (1990) Relatives expressed emotion and the course of schizophrenia in Chandigarh. A two-year follow-up of a first-contact sample. British Journal of Psychiatry, 156, 351-356.



LEWIS, S.W. (1989) Congenital risk factors for schizophrenia. Psychological Medicine, 19, 5-13.

LEWIS, S.W. and MURRAY, R.M. (1987) Obstetric complications, neurodevelopmental deviance and schizophrenia. Journal of Psychiatric Research, 21, 413-421.

LEWIS, S.W., OWEN, M.J. and MURRAY, R.M. (1989) Obstetric complications and schizophrenia: methodology and mechanisms. In Schizophrenia: Scientific Progress (eds S.C. Schulz and C.A. Tamminga) New York: Oxford University Press.

LISHMAN, W.A. and McMEEKAN, E.R.L. (1976) Hand preference in psychiatric patients. British Journal of Psychiatry, 129, 158-166.

LOGAN, S., CURRY, S. and LADER, M. (1975) Interactions of orphenadrine and phenobarbitone with chlorpromazine: plasma concentrations and effects in man. British Journal of Clinical Pharmacology, 2, 197-208.

McCREADIE, R.G. (1982a) The Nithsdale Schizophrenia Survey: I, Psychiatric and social handicaps. British Journal of Psychiatry, 140, 582-6.

McCREADIE, R.G. (1982b) Schizophrenia. In: Rehabilitation in Psychiatric Practice (ed. R.G. McCreadie). London: Pitman.

McCREADIE, R.G., BARRON, E.T. and WINSLOW, G.S. (1982a) The Nithsdale Schizophrenia Survey II. Abnormal movements. British Journal of Psychiatry, 140, 587-599.

McCREADIE, R.G., CRORIE, J., BARRON, E.T. and WINSLOW, G.S. (1982b) The Nithsdale Schizophrenia Survey: III. Handedness and tardive dyskinesia. British Journal of Psychiatry, 140, 591-594.

McCREADIE, R.G. and PHILLIPS, K. (1988) The Nithsdale Schizophrenia Survey VII. Does relatives' high expressed emotion predict relapse? British Journal of Psychiatry, 152, 477-481.

McCREADIE, R.G., PHILLIPS, K., HARVEY, J.A., WALDRON, G., STEWART, M. and BAIRD, D. (1991) The Nithsdale schizophrenia surveys. VIII Do relatives want family intervention - and does it help? British Journal of Psychiatry, 158, 110-113.

McCREADIE, R.G., ROBERTSON, L.J. and WILES, D.H. (1992) The Nithsdale Schizophrenia Surveys IX Akathisia, parkinsonism, tardive dyskinesia and plasma neuroleptic levels. British Journal of Psychiatry, 161, 793-799.

McCREADIE, R.G. and ROBINSON, A.D.T. (1987) The Nithsdale Schizophrenia Survey: VI. Relatives' expressed emotion: prevalence, patterns and clinical assessment. British Journal of Psychiatry, 150, 640-644.

McGUFFIN, P., FARMER, A. and GOTTESMAN, I. (1987) Is there really a split in schizophrenia: the genetic evidence. British Journal of Psychiatry, 150, 581-592.

McNEIL, T.F. and KAIJ, L. (1978) Obstetric factors in the development of schizophrenia. In The Nature of Schizophrenia (eds L.C. Wynne, R.L. Cromwell and S. Matthysen) New York: John Wiley.

MARSDEN, C.D. and JENNER, P. (1980) The pathophysiology of extra-pyramidal side-effects of neuroleptic drugs. Psychological Medicine, 10, 55-72.

MINDHAM, R.H.S., GAIND, R., ANSTEE, B.H. and RIMMER, L. (1972) Comparison of amantadine, orphenadrine and placebo in the control of phenothiazine-induced parkinsonism. Psychological Medicine, 2, 406-13.

MURRAY, R.M., LEWIS, S.W. and REVELEY, A.M. (1985) Towards an aetiological classification of schizophrenia. Lancet, i, 1023-1026.

NASRALLAH, H.A., KEELOR, K., VAN SCHROEDER, C.V. and WHITTERS, M.M. (1981) Motoric lateralization in schizophrenic males. American Journal of Psychiatry, 138, 1114-15.

NIMGAONKAR, V.L., WESSELY, S. and MURRAY, R.M. (1988) Prevalence of familiarity, obstetric complications and structural brain damage in schizophrenic patients. British Journal of Psychiatry, 153, 191-197.

NIMH PSYCHOPHARMACOLOGY SERVICE CENTRE COLLABORATIVE STUDY GROUP (1964) Phenothiazine treatment in acute schizophrenia. Archives of General Psychiatry, 10, 246-261.

O'CALLAGHAN, E.O., LARKIN, C., KINSELLA, A. and WADDINGTON, J.L. (1990) Obstetric complications, the putative familial - sporadic distinction, and tardive dyskinesia in schizophrenia. British Journal of Psychiatry, 157, 578-584.

O'CALLAGHAN, E.O. and WADDINGTON, J.L. (1990) Obstetric complications in schizophrenia and the validity of maternal recall. Psychological Medicine, 20, 89-94.

OVERALL, J.E. and HOLLISTER, L.E. (1979) Comparative evaluation of research diagnostic criteria for schizophrenia. Archives of General Psychiatry, 36, 1198-1205.

OWEN, M. and McGUFFIN, P. (1990) Obstetric complications and schizophrenia. Lancet, 336, 122.

OWENS, D.G.C. and JOHNSTONE, E.C. (1980) The disabilities of chronic schizophrenia - their nature and the factors contributing to their development. British Journal of Psychiatry, 136, 384-396.

PARNAS, J ., SCHULSINGER, F., TEASDALE, T.W., SCHULSINGER, H., FELDMAN, P.M. and MEDNICK, S.A. (1982) Perinatal complications and clinical outcome within the schizophrenia spectrum. British Journal of Psychiatry, 140, 416-420.

PEREL, J.M., O'BRIEN, L., BLACK, N.B., BELLUARD, G.D. and DAYTON, P.G. (1974) Imipramine and chlorpromazine in hepatic microsomal systems. In: The Phenothiazines and Structurally Related Drugs (eds I.S. Forrest, W. Carr and E. Usdin) New York: Raven Press.

POLLACK, M. and GREENBERG, I.M. (1966) Paranatal complications in hospitalized schizophrenics and non-schizophrenic patients. Journal of the Hillside Hospital, 15, 191-204.

RIVERA-CALIMLIN, L., CASTENADA, L. and LASAGNA, L. (1973) Effects of mode of management on plasma chlorpromazine in psychiatric patients. Clinical Pharmacology and Therapeutics, 14, 978-986.

ROBERTS, G.W. (1991) Schizophrenia: a neuropathological perspective. British Journal of Psychiatry, 158, 8-17.

ROBINSON, A.D.T. and McCREADIE, R.G. (1986) The Nithsdale Schizophrenia Survey V. Follow-up of tardive dyskinesia at 3½ years. British Journal of Psychiatry, 149, 621-623.

SATZ, P., ACHENBACK, K. and FENNELL, E. (1967) Correlations between assessed manual laterality and predicted speech laterality in a normal population. Neuropsychologia, 5, 295-310.

SEEMAN, M.V. (1981) Tardive dyskinesia: two year recovery. Comprehensive Psychiatry, 22, 189-192.

SCHOOLER, N.R. and KANE, J.M. (1982) Research diagnoses for tardive dyskinesia. Archives of General Psychiatry, 39, 486-487.

SCOTTISH HEALTH STATISTICS 1991 (1991) Edinburgh: Information and Statistics Division, Common Services Agency for the Scottish Health Service.

SCOTTISH SCHIZOPHRENIA RESEARCH GROUP (1992) The Scottish first episode schizophrenia study VIII Five year follow-up: clinical and psychosocial findings. British Journal of Psychiatry. In Press.

SEEMAN, M.V. (1981) Tardive dyskinesia: two year recovery. Comprehensive Psychiatry, 22, 189-192.

SIMPSON, G.M. and ANGUS, J.W.S. (1970) A rating scale for extrapyramidal side effects. Acta Psychiatrica Scandinavica, Suppl.212, 11-19.

SIMPSON, G.M., COOPER, T.B., BARK, N., SUD I. and LEE, J.H. (1980) Effect of antiparkinsonian medication on plasma levels of chlorpromazine. Archives of General Psychiatry, 37, 205-208.

SMITH, J.M. and BALDESSARINI, R.J. (1980) Changes in prevalence, severity and recovery in tardive dyskinesia with age. Archives of General Psychiatry, 37, 1368-1373.

SMITH, J.M., KUCHARSKI, L.T., EBLEN, C., KNUTSEN, E. and LINN, C. (1979) An assessment of tardive dyskinesia in schizophrenic out-patients. Psychopharmacology, 64, 99-104.

STECK, H. (1954) Le syndrome extrapyramidal et diencephalique au cours des traitements au largactil et au serpasil. Annales Medico-Psychologiques (Paris) 112, 734-744.

TARRIER, N., BARROWCLOUGH, C., VAUGHN, C., BAMRAH, J.S., PORCEDDU, K., WATTS, S. and FREEMAN, H. (1988) The community management of schizophrenia. A controlled trial of a behavioural intervention with families to reduce relapse. British Journal of Psychiatry, 153, 532-542.

TARRIER, N., BARROWCLOUGH, C., VAUGHN, C., BAMRAH, J.S., PORCEDDU, K., WATTS, S. and FREEMAN, H. (1989) Community management of schizophrenia. A two-year follow-up of a behavioural intervention with families. British Journal of Psychiatry, 154, 625-628.

TAYLOR, P.J., DALTON, R. and FLEMINGER, J.J. (1980) Handedness in schizophrenia. British Journal of Psychiatry, 136, 375-383.

TURNER, S.W., TOONE, B.K. and BRETT-JONES, J.R. (1986) Computerised tomographic scan changes in early schizophrenia - preliminary findings. Psychological Medicine, 16, 219-225.

US DEPARTMENT OF HEALTH, EDUCATION AND WELFARE (1976) Abnormal Involuntary Movements Scale (AIMS). In ECDEU Assessment Manual, (ed. W.Guy), pp 534-7. Rockville, Maryland: US Department of Health, Education and Welfare.

VAN PUTTEN, T. (1974) Why do schizophrenic patients refuse to take their drugs? Archives of General Psychiatry, 31, 67-72.

VAN PUTTEN, T. (1975) The many faces of akathisia. Comprehensive Psychiatry, 16, 43-47.

VAN PUTTEN, T., MAY, P.R.A. and MARDER, S.R. (1984) Akathisia with haloperidol and thiothixene. Archives of General Psychiatry, 41, 1036-1039.

VAUGHN, C.E. and LEFF, J.P. (1976a) The influence of family and social factors on the course of psychiatric illness. A comparison of schizophrenic and depressed neurotic patients. British Journal of Psychiatry, 129, 125-137.

VAUGHN, C.E. and LEFF, J.P. (1976b) The measurement of expressed emotion in the families of psychiatric patients. British Journal of Social and Clinical Psychology, 15, 157-165.

WADDINGTON, J.L., YOUSSEF, H.A. and KINSELLA, A. (1990) Cognitive dysfunction in schizophrenia followed up over 5 years and its longitudinal relationship to the emergence of tardive dyskinesia. Psychological Medicine, 20, 835-842.

WEISSMAN, M.M. and BOTHWELL, S. (1976) Assessment of social adjustment by patient self-report. Archives of General Psychiatry, 33, 1111-1115.

WEISSMAN, M.M. and PAYKEL, E.S. (1974) The Depressed Woman: A Study of Social Relationships. Chicago: University of Chicago Press.

WEISSMAN, M.M., PRUSOFF, B.A., THOMPSON, W.D., HARDING, P.S. and MYERS, J.K. (1978) Social adjustment by self-report in a community sample and in psychiatric out-patients. Journal of Nervous and Mental Disease, 166, 317-326.

WIDERLOV, E., HAGGSTROM, J.E., KILTS, C.D., ANDERSSON, U., BREESE, G.R. and MAILMAN, R.B. (1982) Serum concentrations of thioridazine, its major metabolites and serum neuroleptic-like activities in schizophrenics with and without tardive dyskinesia. Acta Psychiatrica Scandinavica, 66, 294-305.

WING, J.K. (1961) A simple and reliable sub-classification of schizophrenia. Journal of Mental Science, 107, 862-875.

WING, J.K., and FRYERS, T. (1976) Psychiatric Services in Camberwell and Salford. London: MRC Social Psychiatry Unit, University of London.

WING, J.K., COOPER, J.E. and SARTORIUS N. (1974) The Measurement and Classification of Psychiatric Symptoms. Cambridge: Cambridge University Press.

WOERNER, M.G., POLLACK, M. and KLEIN, D.F. (1973) Pregnancy and birth complications in psychiatric patients: a comparison of schizophrenia and personality disorder patients with their siblings. Acta Psychiatrica Scandinavica, 49, 712-721.

WOJCIK, J.D., GELENBERG, A.J., LA BRIE, R.A. and MIESKE, M. (1980) Prevalence of tardive dyskinesia in an outpatient population. Comprehensive Psychiatry, 21, 370-379.

WORLD HEALTH ORGANISATION (1974) Glossary of Mental Disorders and Guide to their Classification for Use in Conjunction with the International Classification of Diseases. Eighth Revision. Geneva: WHO.

YASSA, R. and NAIR, V. (1989) Mild tardive dyskinesia: an 8-year follow-up study. Acta Psychiatrica Scandinavica, 81, 139-140.

YESAVAGE, J.A., TANKE, E.D. and SHEIKH, J.I. (1987) Tardive dyskinesia and steady-state serum levels of thiothixene. Archives of General Psychiatry, 44, 913-915.

