

# Controlled comparison of the characteristics of patients with panic disorder

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## SUMMARY

**Background.** Increased general practice attendance rates have been associated with the diagnosis of mental illness but panic disorder has not been specifically investigated in this respect. In addition, studies have failed adequately to assess type and frequency of secondary care referral and patterns of psychotropic prescription in patients with panic disorder in relation to matched controls.

**Aim.** This study set out to compare subjects with panic disorder with age and sex matched controls on measures of general practice consultation rate; psychotropic and non-psychotropic drug use; referral to secondary care, laboratory and radiological tests and hospital admissions; history of illness and complaints; and psychiatric comorbidity.

**Method.** The study was carried out in nine practices in the Forth Valley area. One hundred patients with panic disorder, previously diagnosed using DSM III-R criteria, were identified and matched by age and sex with controls. Data were collected by review of general practice case notes.

**Results.** Subjects with panic disorder had significantly higher rates of general practice consultation over the 10 year period prior to DSM III-R diagnosis of panic disorder than controls. Subjects with panic disorder had also been prescribed a significantly greater number of psychotropic and non-psychotropic medications over this period, had had more secondary care investigations and had higher rates of mainly minor illness and related complaints than controls. High comorbidity of panic disorder with depression which had been diagnosed over the 10 year period prior to DSM III-R diagnosis of panic disorder was found.

**Conclusion.** The results of this study describe a population of subjects with panic disorder who are long-term heavy users of primary care services. The results also suggest an association between panic disorder and both minor illness and psychiatric comorbidity over the 10 year period prior to DSM III-R diagnosis of panic disorder.

**Keywords:** panic; consultation rates; drug therapy; referral to hospital for consultation; morbidity.

## Introduction

PANIC disorder is an incapacitating anxiety disorder which is relatively common (prevalence estimated at between 0.4%

and 6%).<sup>1</sup> The essential features of this disorder are severe panic attacks often accompanied by restrictive avoidance behaviour. Recurrent panic attacks represent a severe problem, and sufferers make heavy demands on health care services.<sup>2,3</sup>

Most research on panic disorder has focused on treatment techniques and there is still much to learn about the general characteristics of the disorder. While diagnoses of mental illness have been associated with increased medical attendance rates,<sup>2,3</sup> there do not appear to have been any studies that have looked specifically at panic disorder in relation to this, nor has the referral rate of patients with panic disorder to secondary care been investigated. While studies have alluded to patients with panic disorder having multiple medical investigations for their symptoms or being referred for extensive physical assessments by specialists,<sup>2-5</sup> age and sex matched controls have seldom been used in such studies.

The association of panic disorder with a range of somatic symptoms and hence a tendency for patients with the disorder to somatize their psychological disturbance and for it to remain undiagnosed is one reason put forward to explain high utilization of medical services.<sup>6</sup> In both the United States of America and the United Kingdom, most patients who are considered psychiatrically ill by their family doctors initially present with a physical complaint.<sup>7</sup> Patients with panic disorder may selectively focus on one or two specific frightening physical symptoms such as chest pains or palpitations; other common complaints are headaches, upset stomach or nausea, and muscle pain.<sup>8,9</sup> The lack of age and sex matched comparison groups, however, makes it difficult to determine whether such somatic complaints are specific to panic disorder.

Another explanation for the high rate of general practice attendance in patients with panic disorder is the suggested high concurrence of physical illness with psychiatric disorder.<sup>10,11</sup> The studies which have investigated this are, however, often based on patient self report and are therefore subject to response biases. The use of medical case notes for the collection of data on physical illness would be one way of making this process more objective.

It has been argued that patients with panic disorder may be heavy users of psychotropic medication.<sup>12</sup> There is controversy regarding the most appropriate form of pharmacological intervention for panic disorder.<sup>13,14</sup> No published studies to date have made a controlled comparison of psychotropic and non-psychotropic medication use by patients with panic disorder in primary care.

The rates of comorbidity of panic disorder with other psychiatric disorders, particularly depression and other anxiety disorders have varied across studies, depending upon the diagnostic assessment procedure used.<sup>15-17</sup> A number of studies have reported that depression occurs most frequently secondary to the development of anxiety disorder, especially panic disorder and agoraphobia.<sup>16,18</sup> Others have, however, argued that depression can equally occur prior to panic disorder.<sup>19,20</sup> Unfortunately such studies are often compromised by small sample sizes.<sup>19,20</sup>

The present study attempts to rectify some of the methodological problems and gaps in the literature mentioned above. In this study, the mental and physical health characteristics of a large group of patients with panic disorder are reported, and compared with those of age and sex matched controls.

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## Method

This study was conducted with the consent of general practitioners involved in the Forth Valley General Practitioners Research Group, from nine different practices in the Forth Valley area between February and May 1992. The nine practices served a population with a wide socioeconomic range.

## Patients

A consecutive series of 100 patients with panic disorder referred for an ongoing study coordinated by the Forth Valley General Practitioners Research Group were identified. The study was investigating the treatment efficacy of fluvoxamine, cognitive behaviour therapy, placebo, fluvoxamine plus cognitive behaviour therapy, and placebo plus cognitive behaviour therapy in primary care. Panic disorder was diagnosed using DSM III-R criteria by a clinical psychologist (D S). In order to maintain the homogeneity of the classification of panic disorder in the treatment study patients were excluded if currently suffering from other psychiatric disorder for example, psychoses, major depression or obsessive-compulsive disorder. Patients were also excluded if suffering from medical conditions which contraindicated the study treatments. Pre-determined criteria were established for conditions such as impairment of renal or hepatic function, unstable epilepsy or heart disease of significant clinical importance. Exclusions were determined by the patient's general practitioner following medical examination and review of the case notes prior to referral to the study.

One hundred control patients from the same practices as the patients with panic disorder were randomly selected and matched by age and sex with the patients with panic disorder. Patients were selected by proceeding alphabetically through the patient card index from the place where the index patient with panic disorder was located until the first patient matched for sex and age was reached. Possible controls were excluded if their general practice case notes recorded that they had ever been diagnosed as having panic disorder by a clinical psychologist or psychiatrist.

Index and control patients accepted into the study had been registered with their respective general practices for at least 10 years prior to 1992.

## Data collection

The general practice case notes of the index and control patients were reviewed. The method used was similar to that used in a controlled comparison of long-term benzodiazepine users in general practice.<sup>21</sup> Data were collected for the 10 year period prior to the DSM III-R diagnosis for the subjects with panic disorder and prior to the matching procedure for the control subjects. The characteristics noted for both patient groups included age and sex, history of psychotropic and non-psychotropic medication and the frequency of general practice consultations. Information was also collected on the number of referrals to secondary care and mental health specialists, the number of laboratory and radiological tests ordered and the number of self-referrals to accident and emergency departments. Hospital admissions in the 10 year period were also noted.

An analysis of illnesses and complaints, by body system, was carried out for both groups. All diagnoses and reported complaints recorded over the 10 year period in the medical summary sheets, in hospital letters to or from general practitioners, or in continuation sheets were listed. Complaints were distinguished from illnesses on the basis of being somatic or emotional, reported by the patient, recorded in the continuation sheets or in referral letters from the general practitioner and not constituting a definite illness diagnosis by the general practitioner (for example, abdominal pain, headache or sore throat). The classification of

illnesses and complaints, by body system, was checked by an experienced principal in general practice (R S) in order to ascertain that groupings were correct. The general practitioner was blind to the study groups.

R S divided the illnesses into major and minor episodes. Allocation to major or minor illness was based on the need for hospital referral, inpatient treatment, investigation or long-term medication, permanent disability and the effect of the illness on the life of the patient. The system of categorization into major or minor illness employed was identical to that used in a previous investigation.<sup>21</sup> R S also classified all complaints as to whether or not they involved the reporting of pain. An analysis of complaints involving pain by body system, was also made. Finally, all types of mental health diagnoses made by general practitioners over the 10 year period were recorded for each patient.

## Analysis

Statistical analysis involved the use of paired and unpaired two-tailed *t*-tests to calculate differences between patients with panic disorder and controls for the characteristics investigated. For non-parametric comparisons the chi square test was used.

## Results

The group with panic disorder comprised 73 women and 27 men with a mean age of 41 years (standard deviation 11 years, range 20–71 years). The mean age of the men was 40 years (SD 11 years, range 20–55 years). The mean age of the women was 41 years (SD 11 years, range 23–71 years).

## Consultation rates

For each of the 10 years of the study period, patients with panic disorder consulted their general practitioner significantly more often than the control group (Table 1). In addition, a steady rise over the years and a marked increase in consultation rate from year 4 to year 1 in the index patients was not shown to the same extent in the controls.

## Psychotropic and non-psychotropic medication

Over the 10 year period patients with panic disorder had been prescribed significantly more pharmacologically distinct psychotropic drugs on at least one occasion than controls (Table 2). Of the patients with panic disorder 89% had been prescribed at

**Table 1.** Mean annual number of consultations for group with panic disorder and control group for each year of 10 year study period.

Year of study period <sup>a</sup>	Mean annual number of consultations (SD)	
	Index group (n = 100)	Control group (n = 100)
Year 10	3.8 (3.8)	2.4 (3.3) *
Year 9	4.2 (4.0)	2.7 (3.5) **
Year 8	4.4 (4.1)	2.9 (3.2) **
Year 7	4.7 (4.1)	2.8 (3.0) ***
Year 6	5.8 (5.3)	3.0 (3.1) ***
Year 5	5.0 (4.7)	3.0 (3.5) **
Year 4	5.9 (6.2)	3.3 (3.5) ***
Year 3	7.0 (5.9)	3.3 (3.7) ***
Year 2	9.0 (6.6)	3.4 (3.8) ***
Year 1	8.9 (6.7)	4.1 (4.1) ***
Year 1–10	5.9 (3.4)	3.1 (2.4) ***

SD = standard deviation. *n* = number of patients in group. <sup>a</sup>Year 1 is year immediately prior to DSM III-R diagnosis. Paired *t*-tests with 99 degrees of freedom: \**P*<0.05, \*\**P*<0.01, \*\*\**P*<0.001.

**Table 2.** Mean number of pharmacologically distinct drugs prescribed for group with panic disorder and control group.

Drug	Mean number of drugs prescribed (SD)	
	Index group (n = 100)	Control group (n = 100)
Benzodiazepine	0.93 (1.00)	0.20 (0.60) ***
Antidepressant	1.06 (1.20)	0.25 (0.70) ***
Other psychotropic	1.08 (1.00)	0.24 (0.60) ***
All psychotropic	3.06 (2.46)	0.60 (1.20) ***
Non-psychotropic	16.74 (10.50)	10.22 (7.90) ***

SD = standard deviation. n = number of patients in group. Paired t-tests with 99 degrees of freedom: \*\*\* P<0.001.

least one psychotropic drug compared with 34% of the control group, and 50% had been prescribed three or more different psychotropic drugs compared with 8% of controls. Patients with panic disorder had also been prescribed significantly greater numbers of benzodiazepines, antidepressants and other psychotropic drugs than controls (Table 2). The other psychotropic drugs were primarily beta-blockers and non-benzodiazepine anxiolytics. There were no recorded prescriptions for major tranquilizers in either group.

The number of pharmacologically distinct non-psychotropic drugs prescribed on at least one occasion was significantly greater for the group with panic disorder than for the controls. Of the group with panic disorder 36% had 20 or more different non-psychotropic drugs prescribed over the 10 year period compared with 11% of the controls.

#### Referral to secondary care, laboratory and radiological tests and hospital admission

Patients with panic disorder had significantly more referrals to secondary care (including mental health specialists) over the 10 year period than the control patients — mean 1.7 (SD 1.5) versus 1.2 (SD 1.2);  $t = 3.1$ , 99 degrees of freedom,  $P < 0.01$ . However, there was no difference between index and control patients in referral to different medical and paramedical specialists. Significantly more patients with panic disorder than controls had a history of self-referral to an accident and emergency department — 34 versus 19;  $\chi^2 = 5.8$ , 1 df,  $P < 0.05$ . Significant differences were also apparent on comparing the mean number of la-

boratory tests (panic disorder group 7.8 (SD 7.7) versus 4.5 (SD 5.1) for controls;  $t = 3.8$ , 99 df,  $P < 0.01$ ), radiological tests (1.0 (SD 1.3) versus 0.5 (SD 0.8);  $t = 3.1$ , 99 df,  $P < 0.01$ ) and hospital admissions (0.7 (SD 1.5) versus 0.3 (SD 0.6);  $t = 2.5$ , 99 df,  $P < 0.05$ ).

#### History of illness and complaints

Patients with panic disorder had significantly more reported episodes of major illness than controls: 25 versus 16 had one episode, four versus two had two episodes, four versus two had three, one versus none had four and one versus none had five ( $t = 2.7$ , 99 df,  $P < 0.01$ ). Patients with panic disorder also had significantly more reported episodes of minor illness than controls: 26 versus 47 had 1–5 episodes, 24 versus 27 had 6–10, 19 versus 12 had 11–15, 12 versus eight had 16–20, eight versus two had 21–25 and six versus none had 26–35 ( $t = 4.7$ , 99 df,  $P < 0.001$ ). The frequencies of major illness were low compared with minor illness. In addition, patients with panic disorder had significantly more systems of the body affected by major and minor illness than controls (mean 4.4 (SD 1.8) versus 3.6 (SD 1.9);  $t = 3.5$ , 99 df,  $P < 0.01$ ). Patients with panic disorder also had significantly more complaints than controls (mean 8.3 (SD 4.8) versus 4.2 (SD 3.8);  $t = 4.8$ , 99 df,  $P < 0.001$ ). Of the control patients, 24% reported no complaints compared with 6% of patients with panic disorder.

The distribution of previous episodes of major and minor illness and complaints in specific systems of the body among patients with panic disorder and controls is shown in Table 3. Patients with panic disorder exhibited significantly more episodes of minor gastrointestinal illness, minor genitourinary illness, minor respiratory illness and minor miscellaneous illnesses than controls. Patients with panic disorder also exhibited significantly more major genitourinary illness than controls but this was the only system in the body where there was a significant difference in major illness. When complaints were examined, patients with panic disorder exhibited significantly more types of cardiovascular, gastrointestinal, central nervous system, locomotor system and miscellaneous complaints (for example, headache) than controls.

Patients with panic disorder had reported significantly more complaints involving pain than the controls (mean 3.9 (SD 2.4) versus 2.5 (SD 2.3);  $t = 4.5$ , 99 df,  $P < 0.001$ ) and significantly more body systems were involved (mean 3.6 (SD 1.5) versus 2.5

**Table 3.** Previous episodes of major and minor illness and complaints among 100 patients with panic disorder and 100 control patients.

Body system	Number of episodes					
	Major illness		Minor illness		Complaints	
	Index group	Control group	Index group	Control group	Index group	Control group
Cardiovascular	4	7	19	20	18	8*
Central nervous	2	0	6	4	13	3*
Ear/nose/throat	1	1	186	131	68	50
Endocrine	5	6	9	8	3	0
Gastrointestinal	13	5	108	59*	158	73***
Genitourinary	12	0**	206	92***	23	15
Haematology	2	1	6	2	0	0
Locomotor	7	4	40	28	173	128*
Ophthalmic	0	1	26	34	26	9
Respiratory	5	3	229	107***	28	17
Skin	0	0	164	122	7	3
Miscellaneous <sup>a</sup>	3	2	121	73*	323	110***
Total	54	30	1120	680	840	416

<sup>a</sup>For example influenza, headache. Paired t-tests with 99 degrees of freedom: \*P<0.05, \*\*P<0.01, \*\*\*P<0.001.

(SD 2.0);  $t = 4.8$ , 99 df,  $P < 0.001$ ) with significantly more gastrointestinal pain (mean 0.7 (SD 0.6) versus 0.3 (SD 0.8);  $t = 3.3$ , 99 df,  $P < 0.001$ ) and miscellaneous complaints involving pain (for example multiple aches and pains) (mean 0.9 (SD 1.1) versus 0.5 (SD 0.8);  $t = 3.8$ , 99 df,  $P < 0.001$ ).

The mean number of complaints among patients with panic disorder and controls who had no recorded illnesses in three of the body systems where significant differences in total complaints were found is shown in Table 4. Even when those patients with physical diagnoses were excluded, significant differences emerged in complaints in these body systems. For the gastrointestinal system 50 patients with panic disorder had no recorded illness but 110 complaints were reported while for the controls, 66 had no recorded illness but only 36 complaints were reported.

#### Mental health diagnosis and referral

Of the control group, 25 had at least one diagnosis of a mental health problem made by their general practitioner while 94 of the patients with panic disorder had at least one mental health diagnosis in the 10 year period prior to the diagnosis of panic disorder. The mean number of such diagnoses for the 25 control patients was 1.3 (SD 0.5, range 1–2) and for the 94 patients with panic disorder 2.0 (SD 0.9, range 1–5).

Of the 94 patients with panic disorder who had a general practitioner diagnosis of another previous mental health disorder, 66 (70%) had had at least one diagnosis of anxiety, 41 (44%) of depression and 57 (61%) of panic attacks in the 10 year period preceding diagnosis of panic disorder. For two patients with panic disorder there was a mention of alcohol abuse, for 11 agoraphobia and for four claustrophobia. Anorexia nervosa, globus hystericus and drug abuse were all mentioned for one patient each.

For the 75 patients with panic disorder who had two or more general practitioner diagnoses of a mental health disorder, the major patterns and order of diagnoses emerging were as follows: diagnosis of anxiety first and then panic at a later date for 24 of these patients; diagnoses of depression first and then anxiety/panic for 20; diagnosis of anxiety/panic and then depression for 23.

Of the 100 patients with panic disorder, 18 had been given a diagnosis by a psychiatrist at least once in the 10 years prior to the diagnosis of panic disorder and the total number of referrals by a general practitioner to a psychiatrist was 23. For the 18 patients, the diagnoses were as follows: depression (three patients), agoraphobia (five), mixed anxiety and depression (four), anxiety with panic (one), alcohol withdrawal (one), alcohol abuse (one), obsessional personality (one), personality disorder (one), and suicidal tendencies (one).

**Table 4.** Complaints in patients with panic disorder and controls with no recorded gastrointestinal, cardiovascular or central nervous system illness.

Body system	Mean number of complaints (SD)	
	Index group	Control group
Gastrointestinal ( $n = 50/66$ )	1.10 (0.16)	0.36 (0.76) ***
Cardiovascular ( $n = 81/80$ )	0.20 (0.40)	0.07 (0.27) *
Central nervous ( $n = 93/97$ )	0.12 (0.36)	0.03 (0.17) *

SD = standard deviation.  $n$  = number of patients with panic disorder/controls with no recorded illness. Unpaired  $t$ -tests: \* $P < 0.05$ , \*\*\* $P < 0.001$ .

#### Discussion

While previous research<sup>2-5</sup> has been hampered by lack of controls, this study employed an age and sex matched control group. In addition, information on physical illness, previously collected in other studies by self report<sup>10,11</sup> was obtained here using medical case notes. Research into physical illness has tended to concentrate on a limited number of body systems<sup>8,9</sup> but this study considered illnesses and complaints classified into 12 body systems.

The higher proportion of women than men with panic disorder found in this study is consistent with previous findings.<sup>6</sup> The significantly higher consultation rate found for patients with panic disorder in primary care compared with controls matches a previous finding for psychiatric illness in general medical services,<sup>10</sup> as did the finding of a marked increase in consultation rate prior to referral to a psychologist or psychiatrist.<sup>22</sup>

The significant differences between patients with panic disorder and controls in terms of the number of psychotropic drugs prescribed would suggest that many of these patients' symptoms of mental illness are being pharmacologically treated in primary care. Three drug groups — benzodiazepines, antidepressants and other psychotropics — were prescribed with approximately equal frequency suggesting that general practitioners are not prescribing benzodiazepines more often than other drug groups as has been previously suggested.<sup>2,23</sup> The variety of drug groups prescribed may also reflect the fact that many psychotropic drugs have antipanic effects and at present no one drug group shows obvious superiority in the treatment of panic disorder.<sup>14</sup>

The fact that 25% of the control group had at least one diagnosis of a mental health problem made by their general practitioner over the 10 year period is not surprising given the suggestion that a sixth or more of patients attending in general practice are suffering from a mental illness.<sup>15</sup> The relatively small number of referrals of the group with panic disorder to psychiatrists suggests that most patients with a mental illness are managed in primary care.<sup>24</sup> The finding that 94% of the patients with panic disorder had between one and five diagnoses of a mental health problem made by their general practitioner indicates marked psychological distress in this population prior to a diagnosis of panic disorder.

The high comorbidity of panic disorder with diagnoses of anxiety and depression is consistent with previous research.<sup>25</sup> Of the patients who had a general practitioner diagnosis of another previous mental health disorder prior to the diagnosis of panic disorder, 44% had at least one diagnosis of depression suggesting that depressive illness may occur concurrently or months or years prior to panic disorder<sup>19</sup> and is not always a secondary problem. However, such general practitioner diagnoses must be viewed with caution, as it cannot be assumed that these constitute mental illness classifications. In addition, the index sample was a clinical sample rather than an epidemiological sample possibly exaggerating the level of comorbidity.<sup>25</sup>

The frequencies of major illness were low across both groups. However, patients with panic disorder presented significantly more episodes of minor illness than control patients and there were significant differences for illnesses of the gastrointestinal, genitourinary and respiratory systems. There are two possible explanations for the higher physical illness among the population with panic disorder. First, specific systems of the body may exhibit vulnerability and weakness to panic and anxiety. The significant difference in gastrointestinal illness between the two groups would support the previous finding of an association between the gastrointestinal system and anxiety disorders.<sup>26,27</sup> The significant differences in respiratory and genitourinary illness between the two groups suggests that infectious disease may be implicated. An immune dysfunction has been suggested in

panic disorder.<sup>28</sup> Secondly, individuals with panic disorder may present with minor ailments more frequently than controls and they may also become more vigilant about their physical health in general. In addition, the symptoms of panic may exacerbate physical illness leading to lower tolerance of minor ailments. Low frequencies of hospital admissions and secondary care referrals would seem to reflect the fact that most illnesses were minor ailments.

The significant differences between patients with panic disorder and control patients for referrals and investigations may reflect the tendency of some doctors to refer on to specialists those patients presenting consistently with somatic symptoms for which no definite diagnosis can be found. Of interest was the fact that more patients with panic disorder had referred themselves to accident and emergency departments than controls. It is possible that patients with panic disorder are attending such departments with acute symptoms of anxiety or panic. Reasons for self-referral were not, however, routinely recorded in the general practice case notes.

Patients with panic disorder reported a significantly higher number of somatic complaints than controls particularly those of the gastrointestinal, cardiovascular, central nervous and locomotor systems and also in the category of miscellaneous complaints. This difference persisted for three body systems — gastrointestinal, cardiovascular and central nervous system — even after controlling for the presence of definite physical illness in these body systems. Hence, the reporting of ill-defined miscellaneous complaints relating to the subjective experience of panic may be a factor in the higher attendance rates of the patients with panic disorder.

The results of this study describe a population of people who are heavy users of primary care facilities. They also suggest an association between panic disorder and minor illness, in addition to a pattern of somatization of the psychological distress of panic. These findings justify more detailed investigation of the consulting patterns of patients with panic disorder and more detailed recording of each general practice attendance. This would allow a closer examination and more thorough understanding of the developmental course of panic disorder, the pattern of somatization and its relation to physical disease over time. The results of this study also highlight the continuing need to develop and research tolerable and effective treatments for this disorder which is associated with such heavy use of the medical system, high comorbidity with other mental health diagnoses and evident physical and mental suffering for the patients afflicted.

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### NUTRITION: MAKING A DIFFERENCE

Joint RCGP/HEA Study Day

9 November 1994

This Study Day, organised jointly with the Health Education Authority, is aimed at GPs and all members of the primary health care team. It will combine a knowledge update on aspects of nutrition, with description of skills and approaches to helping people change what they eat. There will also be chance, within a safe environment - to have a practice! The whole day will be designed to consider and address the realities of life within general practice.

Section 63 and PGEA approval being sought.

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