

## Medically unexplained symptoms: how often and why are they missed?

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### Summary

We assessed risk factors affecting the provisional diagnosis of medically unexplained symptoms made by physicians in new patients, in 526 clinical encounters. Comparisons were made between the doctor's initial assessments regarding the nature of symptoms, and the final diagnosis. Physicians were more likely to err on the side of diagnosing the symptoms as medically explained rather than unexplained. When

physicians perceived the interaction with the patient to be positive, they were more likely to make a provisional diagnosis that the symptoms were explained. Conversely, a negative perception of the interaction was associated with an increased likelihood of viewing symptoms as medically unexplained. Physicians should be aware of the effect of their own perceptions on their diagnostic behaviour.

### Introduction

Patients with common psychiatric disorders such as anxiety and depression frequently present to their doctor with medically unexplained physical symptoms. Previous studies have focused on risk factors for doctors failing to recognize such presentations of anxiety and depression<sup>1–3</sup> which have been labelled as 'somatization'. However, many patients with medically unexplained physical symptoms do not have psychiatric disorders: they may instead be the result of minor pathological change, physiological perceptions, and other factors including previous experience of illness.<sup>4</sup> We wanted to know what factors influence a doctor's initial belief that a patient's symptoms are unexplained, and how accurately doctors make this judgement at the first consultation.

The degree to which organic conditions are misdiagnosed as medically unexplained symptoms or syndromes has not been studied systematically. Many

case reports suggest that this can happen: for example the misdiagnosis of lead poisoning, hypopituitarism, coeliac disease, haemochromatosis, and dermatomyositis for chronic fatigue syndrome,<sup>5–9</sup> or misdiagnosis of ankylosing spondylitis for fibromyalgia.<sup>10</sup> We were interested in determining the characteristics of patients with defined organic disease in whom doctors made an initial diagnosis that the symptoms were unexplained.

This study therefore aimed to determine the accuracy of physicians' provisional diagnoses of medically unexplained symptoms at their first encounter with the patient. This initial assessment was compared with a detailed case-note review of subsequent investigations (which will be referred to as the 'gold standard diagnosis'). Risk factors for the doctor making the wrong provisional diagnosis (that the patient had an organic disorders when they had

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medically unexplained symptoms or vice versa) were then assessed.

## Methods

This study was a part of the epidemiological study of medically unexplained somatic symptoms in the general hospital, described in detail elsewhere.<sup>11</sup>

## Patients

We recruited consecutive new patients resident in South-East London referred by their general practitioners to out-patient clinics at King's College Hospital and Dulwich Hospital, between 1995 and 1997. The clinics were Gastroenterology, Gynaecology, Neurology, Rheumatology, Chest, Cardiology, and Dentistry. Subjects were eligible for inclusion if they were aged between 16 and 65 years and were attending the above clinics. Subjects who could not read or speak English, and those diagnosed as having psychotic or organic brain syndromes, were excluded. Thirty-six physicians took part in this study. Of these, 12 were consultants, 20 were registrars, and four were senior house officers.

## Data collection

Patients attending the above clinics were given a questionnaire with a return stamped addressed envelope. At the end of clinical encounters, physicians completed a single page form recording the patients' complaint(s), the physicians' view of the relative contribution of 'organic' and 'psychological' factors, and their impressions of the doctor-patient relationship. Case notes were reviewed to determine the final diagnosis approximately 3 months after the initial visit.

## Questionnaires

### Outcome variables

Physicians were asked to state whether they thought the patients' symptoms were medically explained or medically unexplained. Subsequently case notes were examined to determine whether investigations or later examinations revealed an explained cause of patients' symptoms.

The final (gold standard) diagnosis of medically unexplained symptoms was operationally defined according to the following: (a) the patient presented with physical symptoms; (b) they received investigations for this; and (c) the investigations and clinical

examinations revealed no abnormality, or abnormalities which were thought to be trivial or incidental. This method has been used elsewhere<sup>12</sup> and recent work suggests it can be applied by liaison psychiatrists and physicians with good inter-rater reliability (kappa 0.76–0.88).<sup>13</sup>

We then generated four outcome variables for the purposes of this study: (i) provisional diagnosis of medically *unexplained* symptoms subsequently confirmed; (ii) provisional diagnosis of medically *explained* symptoms subsequently confirmed; (iii) symptoms which the physician initially thought were explained, but were later found to be unexplained; and (iv) symptoms which were initially thought to be unexplained, but were later found to be explained. Outcome (iii) is referred to as 'missed unexplained', outcome (iv) as 'missed explained'.

## Explanatory variables

These included: (i) demographic data—age, gender, marital status, educational level (recorded as number of years of full-time education), ethnicity, work status, and occupation; (ii) functional impairment (brief disability questionnaire), use of alternative treatments, and receipt of state benefits; (iii) psychiatric morbidity (Hospital Anxiety and Depression Scale, HADS);<sup>14</sup> (iv) doctor-patient relationship (physician-rated), a questionnaire which included the physicians' subjective judgement of the patient's co-operation, reliability as an historian, and the quality of the interaction. The reliability coefficient alpha for these three items together was 0.88. These three items were then summed to produce a physician satisfaction score, a high score indicating a positive relationship. We then converted this to a dichotomous variable using the first quartile (lowest score/physician satisfaction) as the exposure and tested associations against the outcome variables.

## Statistical analysis

Congruence between the final diagnosis (the gold standard) and the physicians' provisional diagnosis of medically unexplained symptoms was assessed using 2 × 2 tables. The data were then divided into two sets according to the final diagnosis: a group of medically unexplained symptoms and a group of medically explained symptoms. Analyses were then performed to determine the predictors of incorrect provisional diagnoses.

Odds ratios were used as the main measurement for associations. The outcome variable was measured as dichotomous, and all explanatory variables were also coded or transformed into categorical variables. The explanatory variables were categorized into three groups, namely: demographic variables; symp-

toms and psychiatric morbidity; and consequences of illness. Univariate analysis was used to examine the association of the outcome variable with each variable of interest in turn.  $\chi^2$  statistics were reported. Logistic regression modelling which adjusted for the effect of many variables simultaneously was then used for multivariate analysis. The regression modelling was systematically conducted in steps beginning with demographic variables, adjusting for other variables within the same group. The symptoms and psychiatric morbidity variables were then modelled adjusted for demographic variables, and further adjusting for variables within their own group in the next step. Only variables which were statistically associated with the outcomes and those which were clinically relevant despite being statistically non-significant were included in the model in each step. All logistic regression modelling was performed using the STATA software package.<sup>15</sup> All  $\chi^2$  values reported were based on likelihood ratio statistics.

## Results

We identified 890 patients, of whom 582 (65%) completed and returned the questionnaires. There was a significant association between clinics and response rate ( $\kappa=16.77$ ,  $df=6$ ,  $p=0.01$ ). The dental clinic had the highest response rate (75%) while gastroenterology had the lowest (55%). Non-responders did not differ from responders in terms of ethnicity and doctor satisfaction at the clinical encounter. However, responders were more likely to be female (62% responders vs. 53% non-responders,  $\kappa=5.55$ ,  $df=1$ ,  $p=0.02$ ) and slightly older (mean  $\pm$  SD  $43.2 \pm 12.6$  years for responders versus  $39.5 \pm 11.8$  non-responders,  $t=4.26$ ,  $df=887$ ,  $p<0.01$ ).

Of all eligible patients, 32 sets of case notes were missing, leaving 550 patients in the analysis. Characteristics of samples from different clinics differed in many aspects, including demography (age, sex, work status, education level, ethnicity), and details of the clinical encounter including physicians' views on the quality of doctor-patient interaction (details reported elsewhere).<sup>11</sup>

Table 1 compares the physicians' provisional dia-

gnosis to the 'gold standard' final diagnosis. From 526 clinical encounters where data from both physicians' diagnosis at first encounter and the final diagnosis were available, 51% were finally diagnosed as being medically unexplained by the gold standard. Of those with 'gold standard' unexplained symptoms, 44% were initially rated as unexplained, but 56% were provisionally diagnosed as explained. For those with a final diagnosis of medically explained symptoms, physicians provisionally diagnosed medically unexplained symptoms in 17%. The sensitivity of the provisional diagnosis of medically unexplained symptoms was 43.7% (95%CI 37.9–49.7) and the specificity was 83.2% (95%CI 78.3–87.4). The provisional diagnosis of medically unexplained symptoms was approximately three times as likely to be made in a patient with, as opposed to a patient without, medically unexplained symptoms measured by the gold standard (likelihood ratio for the positive result = 2.6, 95%CI 1.9–3.5).

The associations of physicians wrongly predicting symptoms to be medically unexplained are shown in Table 2. Physicians were more likely to fail to recognize medically unexplained symptoms in older patients and those in work. Psychiatric morbidity and receiving alternative therapy increased the likelihood of recognizing medically unexplained symptoms, but not statistically significantly. Different clinics had different rates of correctly detecting medically unexplained symptoms. The clinic variable was thus a potential confounder for the association between other explanatory variables and the misdiagnosis of medically unexplained symptoms.

Physicians who perceived the interaction with the patient in a positive light were less likely to make a provisional diagnosis of medically unexplained symptoms in patients who had them. In other words they were more likely to make organic/physical diagnoses, which were subsequently revised.

The associations of physicians wrongly predicting symptoms to be medically unexplained after controlling for potential confounders using logistic regression analysis are shown in Table 3. After controlling for confounders, increasing age, being employed, and in receipt of alternative therapy were associated with an increased likelihood of the physician missing

**Table 1** Proportion of misdiagnosis (the final diagnosis from case notes is the gold standard)

Physicians' provisional diagnosis	Final diagnosis ('gold standard')	
	Medically unexplained	Medically explained
Medically unexplained	118 (43.7%)	43 (16.8%)
Medically explained	152 (56.3%)	213 (83.2%)
Total	270 (100%)	256 (100%)

**Table 2** Risk factors for the physician making an incorrect provisional diagnosis of medically *explained* symptoms ( $n=270$ )

Explanatory variables	No. of patients* (% case)	OR (95% CI)
<i>Demographic variables</i>		
Age		
16–25	31 (35.5)	Reference
26–35	75 (54.7)	2.2 (0.9, 5.2)
36–45	62 (54.8)	2.2 (0.9, 5.4)
46–55	65 (66.1)	3.6 (1.4, 8.7)
56–65	37 (62.2)	3.0 (1.1, 8.0)
Gender**		
Male	67 (44.8)	
Female	152 (55.9)	1.6 (0.9, 2.8)
Marital status		
Married	133 (56.4)	
Non-married	134 (56.0)	1.0 (0.6, 1.6)
Ethnicity		
Non-white	82 (56.1)	
White	185 (55.7)	1.0 (0.6, 1.7)
Work status		
Without work	62 (46.8)	
With work	201 (59.7)	1.7 (1.0, 3.0)
Age of leaving full-time education		
≤ 16 years	108 (56.5)	
> 16 years	140 (55.7)	1.0 (0.6, 1.6)
Social class		
Partly skilled/unskilled	29 (48.3)	Reference
Skilled	94 (64.9)	2.0 (0.8, 4.6)
Professional	97 (49.5)	1.0 (0.5, 2.4)
Clinics		
Gastroenterology	28 (32.1)	Reference
Cardiology	42 (50.0)	2.1 (0.8, 5.7)
Dental	25 (56.0)	2.7 (0.9, 8.2)
Rheumatology	41 (70.7)	5.1 (1.8, 14.4)
Neurology	60 (43.3)	1.6 (0.6, 4.2)
Chest	23 (69.6)	4.8 (1.5, 15.9)
Gynaecology	51 (72.6)	5.6 (2.0, 15.2)
<i>Psychiatric morbidity</i>		
Anxiety (HAD-A)		
Non-case (<11)	186 (59.7)	
Case (≥)	75 (50.7)	0.7 (0.4, 1.2)
Depression (HAD-D)		
Non-case (<11)	235 (58.3)	
Case (≥11)	27 (48.2)	0.7 (0.3, 1.5)
<i>Consequences of the illness</i>		
Alternative treatment received		
Yes	114 (48.3)	
No	134 (59.0)	1.5 (0.9, 2.6)
Disability (BDQ score)		
None	113 (55.8)	Reference
Mild	28 (60.7)	1.2 (0.5, 2.8)
Moderate	59 (49.2)	0.8 (0.4, 1.4)
Severe	57 (59.7)	1.2 (0.6, 2.2)
Benefits received		
No	152 (59.2)	
Yes	91 (52.8)	0.8 (0.5, 1.3)
<i>Physician's perception of the clinical encounter</i>		
Negative	64 (35.9)	
Positive	206 (62.6)	3.0 (1.7, 5.4)

\* Total number of patients for each variable varies because of missing data. \*\* Excluding gynaecology.

**Table 3** Risk factors for the physician making an incorrect provisional diagnosis of medically *explained* symptoms after controlling for confounders

Explanatory variables	Odds ratio (95% CI)	
Age*		
16–25	Reference	
26–35	1.6 (0.6, 4.2)	
36–45	1.7 (0.6, 4.4)	
46–55	4.2 (1.6, 11.3)	
56–65	4.3 (1.4, 12.9)	$\chi^2 = 13.47$ , $df = 4$ , $p = 0.009$
Work status*		
Without work		
With work	2.3 (1.2, 4.5)	$\chi^2 = 06.63$ , $p = 0.01$
Receipt of alternative treatment**		
Yes		
No	1.7 (1.0, 3.0)	$\chi^2 = 03.70$ , $p = 0.05$
Physician's perception of the clinical encounter***		
Negative		
Positive	3.4 (1.7, 7.0)	$\chi^2 = 11.95$ , $p < 0.001$

\* Variable included age, work status, and clinics ( $n = 263$ ). \*\* Adjusted for age, work status, and clinics ( $n = 243$ ).

\*\*\* Variables included age, work status, clinics, doctor-patient relationship, patient satisfaction, and alternative treatments ( $n = 243$ ).

medically unexplained symptoms. High physician satisfaction with the clinical encounter was the strongest predictor of missing medically unexplained symptoms.

The predictors of physicians making provisional diagnoses of medically unexplained symptoms for symptoms which were later revealed to be explained are shown in Table 4. Physicians were more likely to make incorrect provisional diagnoses of unexplained symptoms in unmarried patients, those with anxiety, and those who received benefits. Doctor dissatisfaction was strongly associated with making an incorrect provisional diagnosis of medically unexplained symptoms.

The associations of physicians wrongly predicting symptoms to be medically unexplained after controlling for potential confounders are shown in Table 5. Single marital status and being in receipt of benefits were associated with an increased likelihood of incorrectly making a provisional diagnosis of medically unexplained symptoms. However, doctor dissatisfaction with the clinical encounter was the strongest predictor.

## Discussion

Most studies in this area have concentrated the problems of missing organic diagnoses in patients with apparently unexplained symptoms. However, we have deliberately reversed this emphasis, since we believe it is time for doctors to become more concerned with the positive identification of unexplained symptoms.

Many will take issue with the stark dichotomy we present, dividing symptoms into medically explained and unexplained. In reality there are psychological contributions to the experience of symptoms in even the most 'organic' medical condition, whilst there are many physiological explanations for so called 'unexplained' symptoms.<sup>16</sup> We accept the arbitrary nature of this division, but point out that this is merely a reflection of the prevailing medical dualistic culture. This is how, rightly or wrongly, most doctors approach the problem of symptoms.

Our study is the first to estimate the degree to which physicians accurately make provisional diagnoses of medically unexplained symptoms at initial contact with a new patient. The under-diagnosis of medically unexplained symptoms is similar to the rate of unrecognized psychiatric disorders reported by others.<sup>1–3</sup> The results also show that physicians are more likely to under-diagnose than over-diagnose medically unexplained symptoms (56.3% vs. 16.8%). Physicians appear to worry more about errors of omission than errors of commission.<sup>17</sup> This may well relate to over-investigation in patients with medically unexplained symptoms.<sup>17</sup>

Our findings suggest that physicians are more likely to make provisional diagnoses of medically explained symptoms which are later reversed in older patients; those in employment; those not receiving alternative remedies, and those whom the clinical encounter is rated as positive. The opposite profile of younger, unmarried patients in receipt of benefits, and for whom doctor satisfaction is rated as poor, are more likely to be suspected of having medically

**Table 4.** Risk factors for the physician making an incorrect provisional diagnosis of medically *unexplained* symptoms ( $n=256$ )

Explanatory variables	No. of patients* (% case)	OR (95% CI)
<i>Demographic variables</i>		
Age		
16–25	12 (33.3)	2.2 (0.6, 8.7)
26–35	58 (19.0)	1.0 (0.4, 2.6)
36–45	45 (20.0)	1.1 (0.4, 2.9)
46–55	75 (9.3)	0.5 (0.2, 1.3)
56–65	66 (18.2)	Reference
Gender**		
Male	96 (19.8)	
Female	132 (18.2)	0.9 (0.5, 1.8)
Marital status		
Married	136 (11.8)	
Non-married	117 (22.2)	2.1 (1.1, 4.2)
Ethnicity		
Non-white	79 (21.5)	
White	175 (14.9)	0.6 (0.3, 1.3)
Work status		
With work	154 (16.2)	
Without work	98 (17.4)	1.1 (0.6, 2.1)
Age of leaving full-time education		
≤16 years	128 (16.4)	
>16 years	109 (16.5)	1.0 (0.5, 2.0)
Social class		
Partly skilled/unskilled	36 (13.9)	Reference
Skilled	78 (15.4)	1.1 (0.4, 3.5)
Professional	76 (14.5)	1.0 (0.3, 3.3)
Clinics		
Dental	32 (25.0)	Reference
Cardiology	41 (31.7)	10.0 (2.1, 47.6)
Gastroenterology	22 (18.2)	4.8 (0.8, 28.4)
Rheumatology	50 (16.0)	4.1 (0.8, 28.4)
Neurology	38 (21.1)	5.7 (1.1, 28.9)
Chest	45 (4.4)	7.2 (1.4, 36.5)
Gynaecology	28 (0.0)	–
<i>Psychiatric morbidity</i>		
Anxiety (HAD-A)		
Non-case (<11)	188 (14.9)	
Case (≥11)	61 (24.6)	1.9 (0.9, 3.8)
Depression (HAD-D)		
Non-case (<11)	216 (16.7)	
Case (≥11)	32 (21.9)	1.4 (0.6, 3.5)
<i>Consequences of the illness</i>		
Alternative treatment received		
Yes	146 (17.8)	
No	93 (17.2)	1.0 (0.5, 1.9)
Disability (BDQ score)		
None	70 (12.9)	Reference
Mild	39 (20.5)	1.8 (0.6, 5.0)
Moderate	71 (16.9)	1.4 (0.5, 3.5)
Severe	64 (18.8)	1.6 (0.6, 4.0)
Benefits received		
No	129 (12.4)	
Yes	108 (22.2)	2.0 (1.0, 4.0)
<i>Physician's perception of the clinical encounter</i>		
Positive	193 (12.4)	
Negative	63 (30.2)	3.0 (1.5, 6.0)

\* Total number of patients for each variable varies because of missing data. \*\* Excluding gynaecology. \*\*\* Gynaecology clinic dropped and 37 observed not used due to zero cell.

**Table 5.** Risk factors for the physician making an incorrect provisional diagnosis of medically *unexplained* symptoms after controlling for confounders

Explanatory variables	Odds ratio (95% CI)	
Marital status*		
Married		
Non-married	2.2 (1.0, 4.6)	$\chi^2 = 4.46, p = 0.03$
HAD-A**		
Non-case		
Case	2.0 (0.9, 4.4)	$\chi^2 = 2.75, p = 0.10$
Receipt of benefits***		
No		
Yes	2.4 (1.0, 5.7)	$\chi^2 = 3.78, p = 0.05$
Physician's perception of the clinical encounter****		
Positive		
Negative\$	2.6 (1.1, 6.0)	$\chi^2 4.90, p = 0.03$

\* Variable included age, marital status, and clinics ( $n=226$ ). \*\* Adjusted for age, marital status, and clinics ( $n=221$ ). \*\*\* Adjusted for age, marital status, clinics, and HAD-A ( $n=207$ ). \*\*\*\* Adjusted for age, marital status, clinics, HAD-A, and benefits ( $n=207$ ).

unexplained symptoms. Patient characteristics clearly influence physicians' clinical impressions, and negative perceptions of the patient may influence the diagnosis of medically unexplained symptoms. Fixed patterns of perception can adversely affect the clinical observations we make.<sup>18</sup>

Unlike previous studies which were based in general practice, we conducted our study in general hospitals. This allow more precise diagnosis of medically unexplained symptoms as most patients were investigated. Our study, is therefore more objective but may be less generalizable due to the sample we recruited. Another limitation of our study was the lack of direct observation of the doctor-patient interaction. Studies that use video recording of medical behaviours during interview training<sup>19-21</sup> suggest that interview techniques affect the rate of detecting psychiatric disorders. We suspect that similar findings would have been found had we used direct observation in our study. However, it is difficult to conduct video-recordings in the real clinical setting, especially with such large numbers of encounters.

In summary, our study suggests two related concepts regarding clinical decision making. Firstly, doctors are more likely to estimate that a patient has an explained cause of symptoms than they are to class the symptoms as unexplained. This is probably related to the greater perceived danger of missing a biomedical explanation for the symptoms, and may explain the special reluctance to diagnose unexplained symptoms in older patients. Secondly, doctors' own perceptions of the medical encounter has a strong influence on the diagnosis made, and negative perceptions bias the doctor towards diagnosing medically unexplained symptoms.

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