Patients repeatedly referred to secondary care with symptoms unexplained by organic disease: prevalence, characteristics and referral pattern

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Background. Patients with medically unexplained symptoms (MUS) are commonly referred to specialist clinics. Repeated referrals suggest unmet patient need and inefficient use of resources.

Objectives. How often does this happen, who are the patients and how are they referred?

Methods. The design of the study is a case-control survey. The setting of the study is five general practices in Scotland, UK. The cases were 193 adults with three or more referrals over 5 years, at least two of which resulted in a diagnosis of MUS. The controls were (i) patients referred only once over 5 years and (ii) patients with three or more referrals with symptoms always diagnosed as medically explained. The measures of the study are SF-12 physical and mental component summaries; symptom count; and number of referrals, number of different GPs who had referred and number of specialist follow-up appointments.

Results. A total of 1.1% [95% confidence interval (CI) 1.0–1.2%] of patients had repeated (median 3, range 2–6) referrals with MUS. Compared to infrequently referred controls, they were older and more likely to be female, living alone and unemployed. Compared to controls with medically explained symptoms, their health status was comparable or worse: odds ratio for SF-12 physical component summary <40, 1.2 (95% CI 0.72–2.0); SF-12 mental component summary <40, 1.8 (95% CI 1.1–3.0); reporting eight or more physical symptoms, 2.2 (95% CI 1.2–3.8). They were referred by more GPs and received less specialist follow-up.

Conclusions. A small proportion of primary care patients are repeatedly referred to specialist clinics where they receive multiple diagnoses of MUS. The needs of these patients and how they are managed merits greater attention.

Keywords. Clinical diagnosis, family medicine, medically unexplained symptoms, mental health, somatisation.

Introduction

Many patients referred from primary care to secondary care are considered by the specialist to have symptoms, which cannot be adequately explained by organic disease: so-called medically unexplained symptoms (MUS).1,2 This is the diagnosis made in as many as a third of new referrals.3–6 Furthermore, clinical experience suggests that some patients are referred again and again to secondary care even after having received multiple specialist opinions that their symptoms were medically unexplained. We believe that this phenomenon is worthy of greater attention because (i) these patients are unlikely to benefit from repeated referral to specialist medical services that are designed to find or exclude disease rather than to manage symptoms; (ii) the repeated referrals consume limited diagnostic resources to little benefit and (iii) these patients are likely to have treatable problems such as anxiety and depression that would be amenable to alternative approaches to management.7

We therefore set out to find out more about these patients and their referral patterns. Using record linkage between primary and secondary care data, we identified patients who had received repeated referrals to specialist services for the assessment of symptoms, which were subsequently regarded as MUS by the assessing specialist.

In this study, we aimed to (i) determine the prevalence of patients in primary care who met operational criteria for repeated referrals with MUS (RRMUS
Methods

Design
The study used a case–control design: the cases were patients who had been repeatedly referred to hospital specialist outpatient clinics where they had received multiple specialist opinions that their symptoms were not associated with organic disease, i.e. MUS. We refer to these patients as ‘repeatedly referred with MUS’ (RRMUS). We chose two control groups: The first was of patients who had been infrequently referred to hospital for symptoms (IRS). This control group was chosen to enable us to determine how RRMUS patients differ from a primary care population. The second was of patients who had been repeatedly referred for symptoms that specialists considered to be medically explained (RRMES). This control group was intended to allow us to determine which characteristics were specific to RRMUS and which were a result of being symptomatic and experiencing repeated referral to hospital.

The criteria used for categorization were as follows: RRMUS patients were those who had three or more referrals in the 5-year study period, at least two of which resulted in a diagnosis of MUS; IRS patients were those who had been referred only once for symptoms in the 5 years, regardless of whether those symptoms were considered medically explained or not; RRMES patients were those with three or more referrals for symptoms, all of which had resulted in a specialist diagnosis of medically explained symptoms (MES).

Sample
The initial study sample was all patients registered with five primary care practices, representing 30 GPs in Edinburgh, UK, and serving practice populations totalling 39,562 patients. The practices were chosen to represent a range of socio-economic areas. Data were collected by case note review and questionnaire between June 2003 and March 2005.

Procedure
Identifying patients with repeated and infrequent referrals. Patient identification was achieved using National Health Service (NHS) Scotland information systems. These record all outpatient activity and all GP registrations using a common patient identifier, which enables data linkage at the individual patient level with high levels of accuracy and completeness.8 Patients registered with the practices and who had been referred to hospital outpatient clinics within the previous 5 years were identified through the hospital outpatient activity database (SMR00) of the Information Services Division (ISD) of the NHS in Scotland (www.isdscotland.org). Referrals to the following clinical specialties were included in the search strategy: Cardiology, Dermatology, Ear, Nose and Throat, Endocrinology/Metabolic, Gastroenterology, General Medicine, General Surgery, Gynaecology, Neurology/Neurosurgery, Ophthalmology, Orthopaedics, Respiratory Medicine, Rheumatology and Urology.

Identifying from patients with repeated referrals those that resulted in an opinion of MUS or MES. A research nurse (KM) reviewed the GP records, both paper and electronic, of (i) all patients who had been referred three or more times and (ii) patients in the once-referred group whose referral had been within the last year. Referral records were checked to validate the SMR00 data and, if appropriate, patient’s status was corrected—for instance, if a patient referred through the NHS had also been referred to a private specialist, the number of referrals was amended. Data were extracted on referrals to secondary care and are reported here.

For the repeatedly referred patients, the correspondence between the practice and specialists over the 5-year period was reviewed to identify those referral episodes, which were for symptoms and to record the final specialist diagnosis in each case. An episode was defined as the initial and subsequent outpatient attendances resulting from a single referral for assessment of physical symptoms until the patient was discharged, referred to another speciality or died. For each included referral episode, the specialist’s final diagnosis was classified using pre-specified criteria (Appendix 1) as one consistent with either MES or MUS. The allocation to these categories was made by the researcher based on the explicit criteria; where there was uncertainty, the case was reviewed by two other raters (MS and DW) and categorized as MUS only if agreement was unanimous.

Prior to commencing this study, we had carried out a pilot study in a sixth practice to test the methods of patient identification and case note review.9

Questionnaire survey
All patients in the RRMUS, IRS and RRMES groups were sent a pack by post that included an invitation from the patient’s own GP, a consent form, the study questionnaire and a voucher to the value of £5 to promote completion.
and 5 points is regarded as clinically important. We poorer health status and a difference of between 3 expected mean of 50 and SD 10; lower scores indicate summaries, the results of which are norm-based, with an reported as the physical and mental component summary category using a cut-off of 4/5. SF-12 results were descriptively. We condensed deprivation scores to a bivariate measure. Physical symptoms were recorded using the Personal Health Questionnaire (PHQ-15) scale; this measure has been validated as a measure of symptom experience and as a screening measure for ‘somatization’ (as this study involved men and women, we omitted the item concerning menstrual symptoms from the analysis).

Analysis
SMR00, case note review and questionnaire data were manually entered into a database and analysed in SPSS 14.0. We compared the data linkage (SMR00) and case note review methods of identifying referrals descriptively. We condensed deprivation scores to a binary category using a cut-off of 4/5. SF-12 results were reported as the physical and mental component summaries, the results of which are norm-based, with an expected mean of 50 and SD 10; lower scores indicate poorer health status and a difference of between 3 and 5 points is regarded as clinically important. We converted continuous variables into categories, either based on a priori constructs (SF-12) or after inspection of the data (PHQ-15, referrals).

Our analysis strategy was as follows: first, we compared respondents and non-responders to the questionnaire in terms of age, sex, deprivation and years registered with the practice. Second, we compared demographic and social data using logistic regression with referral group as the dependent variable; we made separate comparisons of RRMUS versus IRS and RRMUS versus RRMES referral groups. Third, we compared health status (SF12 component summaries) and symptom count (PHQ-15) between referral groups using logistic regression before and after adjustment for the effects of age, sex and deprivation; once again, we carried out separate analyses of RRMUS versus IRS and RRMUS versus RRMES groups. Finally, we compared referral and follow-up patterns (number of referrals, number of review appointment per first appointment and number of different GPs referring the patient) between RRMUS and RRMES groups using logistic regression before and after adjustment for age, sex, deprivation and, for the number of referring GPs, the total number of referrals. All logistic regression results were expressed as odds ratios (ORs) with 95% confidence intervals (CIs). Sample size was based on feasibility and informed by the findings of the pilot study. The study received ethical approval from the local health service Research Ethics Committee.

Results
Identification of patients and prevalence
A total of 14,034 patients (53% of the practices’ population aged between 18 and 64 years) were identified in the hospital activity database as having had at least one referral over the 5-year study period. Figure 1 shows the numbers at each stage of recruitment.

The number of referrals identified on case note review matched that in the database in 536 (69%) of cases; it was slightly higher in 231 (30%) patients but this made little difference in allocation to study categories. Thirty-five (4.5%) patients were reclassified after the case note review; 30 initially identified as single referrals were found to have been referred three or more times (when referrals from the GP practice to relevant non-NHS clinics were included) and five had been counted three times for one referral, owing to defaulted or rearranged appointments. Of the 779 patients identified, 48 had died or changed address and 13 (1.6%) were deemed unsuitable to participate by their GP because of other health or social problems.

The remaining 718 patients were invited to take part, of whom 507 (70.6%) completed and returned the questionnaire. Table 1 shows that responders were more likely to be older, female and to be living in a less-deprived area than non-responders (see Table 1). The response rate was, however, similar for all three patient groups: RRMUS 72.2%, IRS 68.8% and RRMES 70.4%. The final sample comprised 193 patients with RRMUS, 152 with IRS and 162 with RRMES.

The prevalence of RRMUS was 1.1% (95% CI 1.0–1.2%) of the population of these aged 18–64 years registered with the study practices.

Demographic characteristics
Table 2 shows the age, sex and social deprivation category of the three patient groups. RRMUS patients were slightly older than IRS patients and similar in age to RRMES patients. RRMUS patients were more likely to be female and to be living in a deprived area than either of the other groups. The rate of unemployment and receipt of disability-related benefits was greater in RRMUS patients than in IRS patients and similar to those in RRMES patients.

Ill health characteristics
The median physical and mental component scores of the SF-12 for RRMUS patients were 42.3 and 47.2,
respectively. The mean (95% CI) differences between RRMUS and IRS patients were as follows: physical component summary –10.8 (95% CI –12.9 to –8.7) and mental component summary –4.4 (95% CI –6.9 to –2.0).

Mean differences between RRMUS and RRMES patients were physical component summary –1 (95% CI –2.6 to 1.6) and mental component summary –3.7 (95% CI –6.1 to –1.2), respectively. The PHQ-15 symptom count was also higher in the RRMUS patients than in either the IRS or the RRMES patients: mean difference 2.5 (95% CI 1.9–3.1) and 1.1 (95% CI 0.5–1.8), respectively.

The adjusted ORs obtained by logistic regression for comparisons of RRMUS with both IRS and RRMES patients for the SF-12 component scores and PHQ-15 symptom counts are reported in Table 3. These confirm that differences persisted even after adjusting for age, sex and deprivation.

Referral patterns
Patients in the RRMUS group had received a median of 3 (range 2–6) referrals that had resulted in a diagnosis of MUS. Table 4 shows the referral patterns of both RRMUS and RRMES patients. RRMUS patients were more likely to have been referred by multiple
GPs within the practice and this effect was still present after adjusting for the total number of referrals. The finding that RRMUS patients received fewer follow-up appointments per new referral than RRMES, mean (95% CI) = 1.4 (1.2–1.6) and 1.8 (1.5–2.2), respectively, was an interesting but unexpected finding.

**Discussion**

This is the first study of primary care patients who have been repeatedly referred with symptoms unexplained by organic disease. They also reported more symptoms than both control groups. Our initial hypotheses that RRMUS patients would have worse health status were therefore largely confirmed. Our other hypothesis that when compared to RRMES patients they would had received more referrals and to have been referred by multiple GPs within their practice was also supported. An incidental finding was that they had also received less planned specialist follow-up.

**Strengths and limitations of the study**

This study used a representative sample of primary care practices with data obtained at individual patient level. There was a high rate of ascertainment of referrals and patients were allocated to the study categories using the gold standard of a specialist’s diagnosis rather than that of the GP: the assessment...
of conditions as unexplained by GPs is sometimes wrong, and the subsequent discovery of explanatory pathology is much less likely in patients who have been assessed in specialist medical clinics. To allow for the generic effects of ill health, we used two control groups: one (IRS) was of patients who had some experience of specialist referral for symptoms but were relatively healthy and the other (RRMES) had a high level of referrals and poor health status.

Differences in the physical and mental component summary scores of the order of 3–5 points are usually regarded as clinically relevant. For the physical component summary, the CIs demonstrate differences of such a magnitude for the RRMUS versus IRS comparison and exclude differences of such a magnitude for the RRMUS versus RRMES comparison. For the mental component summary scores, our results for both comparisons are consistent with differences of such a magnitude but are also consistent with more modest differences, of the order of 1–2 points.

Our data represent the activity of all 30 GPs in the five practices that took part. While the five GP practices were chosen to represent a population with a range of socio-demographic characteristics, we tested the possibility that characteristics of the practice might affect referral behaviour by adding the patient’s GP practice to the logistic regression models after adjusting for age, sex and deprivation. This produced minimal change in residual deviance suggesting that there was little difference between practices in referral behaviour. However, as this study was limited to practices willing to participate within one city, its generalizability may be limited.

The use of data from ISD has been previously validated and offers advantages of completeness, freedom from observer bias and low error rates. Although it was necessary to recode the data on a small number of patients following detailed case note review, overall there was good agreement between ISD data and case note data. Few patients were untraceable or excluded by their GP. While we were able to compare ISD and practice data on referrals to secondary care, we did not compare these with hospital records. The nature of UK general practice records, with copies of correspondence to and from the specialist, means that this is unlikely to have led to under-reporting of referrals. The recording of follow-up hospital appointments in the GP record may have been less complete but it is unlikely that there are systematic biases between groups in these data. Other elements of case note review may have been subject to bias as not all ratings were checked by a second researcher. It is also possible that recording of details in the notes by the GP could have differed between patient groups. In view of this limitation, we focused on objective items (such as demographics and number of referrals) rather than more subjective measures, such as the GPs diagnoses or attributions. The response rate to the questionnaire (70%), while less than ideal, was comparable to other studies both in magnitude and in characteristics of non-responders (younger age, male sex and greater deprivation).

Finally, we chose to administer self-report measures by questionnaire rather than by face-to-face interview in order to maximize the sample size. Although, in general, interviews may have yield data of greater validity, both of the self-report measures used here (SF-12 and PHQ-15) have been extensively used and validated.

### Comparison with other studies

Previous studies of patients with MUS have been hindered by the inherent uncertainty about the diagnosis. Some studies have used diagnostic codes recorded in practice or hospital databases or inference applied to the primary care record; we combined objective database searching with a specialist diagnosis indicating MUS. Previous hospital-based studies using specialist diagnoses have been limited by being of only one specialism or have used attendance rather than referral as the indicator or activity.

In keeping with our findings, previous studies of frequent users of primary and secondary care with MUS have reported impaired quality of life. None have however focused specifically on patients who have been repeatedly referred to hospital for MUS.

### Implications for clinicians and policymakers

Patients who are repeatedly referred for symptoms that specialists assess as unexplained by disease constitute a small but clinically important group who warrant more focused effort from health care providers. Far from being the worried well, their physical, mental and social disability is at least as severe as that of

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**Table 4: Comparison of referral patterns and follow-up between RRMUS and RRMES groups by logistic regression after adjustment for age, sex and deprivation**

<table>
<thead>
<tr>
<th>RRMUS</th>
<th>RRMES</th>
<th>OR (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sample size</td>
<td>193</td>
<td>162</td>
<td></td>
</tr>
<tr>
<td>Number of referrals to specialists</td>
<td>3–4 (%)</td>
<td>82 (42%)</td>
<td>94 (58)</td>
</tr>
<tr>
<td>5–6 (%)</td>
<td>79 (41)</td>
<td>51 (33)</td>
<td>1.86 (1.16 to 2.99)</td>
</tr>
<tr>
<td>7+ (%)</td>
<td>32 (17)</td>
<td>17 (10)</td>
<td>2.11 (1.06 to 4.18)</td>
</tr>
<tr>
<td>Review appointments per first appointment</td>
<td>&lt;1.0 (%)</td>
<td>87 (45)</td>
<td>53 (33)</td>
</tr>
<tr>
<td>1.0–1.9 (%)</td>
<td>58 (30)</td>
<td>55 (34)</td>
<td>0.59 (0.35 to 0.99)</td>
</tr>
<tr>
<td>2.0–2.9 (%)</td>
<td>30 (16)</td>
<td>27 (17)</td>
<td>0.62 (0.32 to 1.18)</td>
</tr>
<tr>
<td>≥3.0 (%)</td>
<td>18 (9)</td>
<td>27 (17)</td>
<td>0.38 (0.19 to 0.78)</td>
</tr>
<tr>
<td>Number of GPs referring the patient</td>
<td>1 (%)</td>
<td>37 (19)</td>
<td>41 (25)</td>
</tr>
<tr>
<td>2 (%)</td>
<td>73 (38)</td>
<td>79 (49)</td>
<td>0.95 (0.53 to 1.68)</td>
</tr>
<tr>
<td>3 or more</td>
<td>83 (43)</td>
<td>42 (26)</td>
<td>1.78 (0.97 to 3.26)</td>
</tr>
</tbody>
</table>

aORs adjusted for age, sex and deprivation.

bAlso adjusted for number of referral.

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Reference:

[13] No author given. (2018). Family Practice—an international journal. 484. Some studies have used diagnostic codes recorded in practice or hospital databases or inference applied to the primary care record; we combined objective database searching with a specialist diagnosis indicating MUS. Previous hospital-based studies using specialist diagnoses have been limited by being of only one specialism or have used attendance rather than referral as the indicator or activity.

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Patients repeatedly referred to secondary care with symptoms unexplained by organic disease

patients whose symptoms are wholly attributable to disease.

The practice of repeatedly referring these patients to hospital clinics is unlikely to be the best way to address their needs for three reasons: first, in many cases, it is not what the patient actually wants; second, the process is designed to reach a disease diagnosis rather than deal with symptoms, which often have complex aetiologies; third, these patients are quickly discharged back to the referring general practice without structured follow-up. Our finding that they are referred to specialists by a greater number of different GPs than those with disease, suggests that they also have less continuity, or consistency, of care within their general practice.

While we have described and characterized this group of patients, it is currently unclear what would be the most effective interventions to improve patient care and reduce referrals, which is an important question for future research. However, the findings presented already suggest that the criteria proposed (two referrals for symptoms judged by the specialist to have no organic cause over 5 years) identify a group of patients who are likely to benefit from being identified, comprehensively assessed and consistently and actively managed in primary care.

Conclusions

The simple criterion of a history of at least three referrals in a 5-year period that have led to two or more specialist diagnoses of MUS identifies a potentially important group of patients. They report more physical symptoms, poorer health status and greater socioeconomic deprivation than infrequently referred patients and a health status is comparable to patients requiring repeated referral with proven organic disease. Their patterns of referral and specialist care suggest inconsistent management in primary care and rapid discharge from specialist follow-up. This criterion could be used in routine care to identify patients who required more comprehensive assessment before re-referral.

In an era where services are seeking to improve quality while simultaneously reducing costs, research is needed to identify better and more cost-effective management strategies to address real health needs of these patients.

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Contributors: The study was planned and supervised by MS and DW and conducted by KM. GM carried out the analysis and CB drafted the paper. All contributors were involved in revisions to the paper. MS acts as guarantor.

Declaration

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Ethical approval: local health service Research Ethics Committee.

Conflict of interest: none.

References

Appendix 1. Operationalized criteria for MUS

Referrals for complaints fall into several categories and only referrals for symptoms are included.

The core of the operationalized criteria:

1. The patient is referred with a symptom the cause of which is not known.
2. How explained the symptom is, based on the specialist’s opinion.

Determining MUS from case notes

The following criteria will be applied to each consultation episode:

1. The patient presents with subjective physical symptoms.
2. A history is taken by a specialist and/or clinical examination(s) and/or investigations are done.
3. The specialist completes all planned investigations and sends a letter to the GP.

MUS is the diagnosis when there is an absence of evidence that a defined organic disease caused the symptom. This is possible when:

1. The final diagnosis suggests doubt surrounding the cause of symptom.
2. The final diagnosis is a recognized medically unexplained (functional) syndrome.
3. The investigations performed were normal or, if abnormal, was felt by the specialist to be an incidental finding or unlikely to account for the severity of the presenting symptom.

In all cases, the underlying opinion of the specialist should be interpreted from the case notes and we should not attempt to second guess this opinion.