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Delays between the onset of symptoms and first rheumatology consultation in patients with rheumatoid arthritis in the UK

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Keywords

Rheumatoid arthritis; patient delay; Primary care delay; help-seeking; access to care;

Strengths of this study.

This study surveyed a large sample of patients with new onset rheumatoid arthritis in the UK to identified delays access to care.

This study identified that approximately 20% of patients saw a rheumatologist within 12 weeks of symptom onset, and factors associated with slower self-referral and slower GP referral were identified.

Limitations of this study.

Data was collected at the point of diagnosis from multiple sources including medical records and patient recall, future research should examine those at risk and follow their journey to diagnosis to avoid the limitations of retrospective data collection.

This research has identified factors associated with delays, however, further research is needed to identify factors which would speed up self-referral, GP referral and hospital waiting times for those experiencing early symptoms.

Abstract

Objective: To investigate delays to rheumatology assessment for patients with a new onset of rheumatoid arthritis (RA)

Methods: Newly presenting adults with either RA or unclassified arthritis were recruited from rheumatology clinics. Data on the length of time between symptom onset and first seeing a GP (patient delay), between first seeing a GP and being referred to a rheumatologist (primary care delay) and being seen by a rheumatologist following referral (secondary care delay) were captured.

Results: 822 patients participated (563 female, mean age 55 years). The median time between symptom onset and seeing a rheumatologist was 27.2 weeks (IQR 14.1–66 weeks); only 20% of patients were seen within the first 3 months following symptom onset. The median patient delay was 5.4 weeks (IQR 1.4-26.3 weeks). Patients who purchased over the counter medications or used ice/heat packs took longer to seek help. In addition, those with a palindromic or an insidious symptom onset delayed for longer. The median primary care delay was 6.9 weeks (IQR 2.3–20.3 weeks). Patients made a mean of 4 GP visits before being referred. The median secondary care delay was 4.7 weeks (IQR 2.9–7.5 weeks).

Conclusion: This study identified delays at all levels in the pathway towards assessment by a Rheumatologist. However, delays in primary care were particularly long. Patient delay was driven by the nature of symptom onset. Complex multi-faceted interventions to promote rapid help seeking and to facilitate prompt onward referral from primary care should be developed.

Introduction:

Rheumatoid arthritis (RA) is a chronic inflammatory disease affecting approximately 1% of the population.[1;2] Rheumatoid arthritis is associated with significant morbidity and reduced life expectancy, in large part as a consequence of extra-articular co-morbidities associated with systemic inflammation. In the UK it has been estimated that RA costs the NHS around £560 million per year and that additional costs to the economy of sick leave and work-related disability total £1.8 billion per year.[3] The first three months following the onset of RA symptoms represents an important therapeutic window.[4] Treatment during this phase improves long-term clinical outcomes, increasing the proportion of patients whose disease enters remission, reducing RA related joint damage and reducing the eventual need for joint replacement surgery.[5-10] Therefore, it is vital that patients are seen by Rheumatologists rapidly following the onset of RA symptoms. However, despite increased recognition of the benefits of early treatment there remains considerable delay between symptom onset and the initiation of therapy.[11-13] Indeed a report by the UK's National Audit Office (NAO) in 2009 estimated that only 10% of patients with RA were treated within three months of symptom onset. The NAO's modelling suggested significant financial benefits for the broader economy and quality of life benefits for the individual if the proportion of patients treated earlier was increased.[3]

The patient's pathway to care can be delayed for a number of reasons, including delays on the part of the patient in recognising the significance of the early symptoms of RA.[14-16] Recent research has linked patients' perceptions of RA and coping styles to the length of

time taken to seek help.[17] Before seeking medical help from a physician, patients may seek help from a range of services including complementary therapists, pharmacists and telephone and on-line services. However, the use of these services at the onset of inflammatory arthritis has not been fully explored. Primary healthcare professionals often find the early symptoms of RA difficult to distinguish from those of other rheumatic diseases, making timely and appropriate referrals to rheumatologists challenging.[18;19] There may thus be delays in healthcare professionals making a referral to a Rheumatologist and also in assessment at the secondary care level, contributing further to the delay in making a diagnosis and commencing appropriate therapy.

Several studies conducted across a range of countries have shown long delays between the onset of symptoms and a patient's first consultation with a rheumatologist.[20-23] However, data related to lengths of time between the onset of inflammatory musculoskeletal symptoms and first seeing a GP, between first seeing a GP and being referred to a rheumatologist and being seen by a rheumatologist following referral are not yet available across multiple NHS Trusts in multiple regions of the UK.

Aim

The aim of this study was to investigate the extent of delay in assessment of patients with RA in England and Scotland. Specifically the study assessed lengths of delay at pre-primary care, primary care and secondary care levels, exploring the relationships between lengths of delay and demographic variables and capturing data relating to sources of information, help and advice utilized by patients prior to GP consultation.

Methods

A questionnaire based survey of consecutively presenting patients with a new onset of RA or unclassified inflammatory arthritis was undertaken in England and Scotland. Networks such as the Early Rheumatoid Arthritis Network and Clinical Research Network were used identify Rheumatology centres to participate in this study. RJS also promoted the study during abstract presentations at British Society for Rheumatology meetings.

Data were collected from Rheumatology departments in 34 NHS Trusts. Rheumatology departments were secondary care based, although one rheumatology department operated clinics in both hospital and community settings. Eligible patients were recruited on their first or second visit to the rheumatology department following a primary care referral. Rheumatogists were asked to approach consecutively presenting patients who met the eligibility criteria. Eligible patients were newly referred adults (aged ≥ 18 years) with clinically apparent synovial swelling of one or more joints who had either a new onset of RA (according to 2010 ACR / EULAR criteria [24]) or unclassified arthritis (UA; defined as a failure to fulfil classification criteria for another inflammatory rheumatic disease). Patients with UA were recruited, as in many cases patients with UA at initial secondary care assessment progress to RA over time.[25]

Data were collected using two questionnaires. First, following consent, the recruiting healthcare professional completed a brief questionnaire that captured data on extents of delays between [1] symptom onset and seeing a healthcare professional (from herein referred to as 'patient delay', these data was gathered from the patient's account by the recruiting healthcare professional), [2] seeing a healthcare professional and being referred

to a rheumatologist (from herein referred to as 'primary care delay', these data was gathered from the patient's account by the recruiting healthcare professional), and [3] being referred to a rheumatologist and seeing a rheumatologist (from herein referred to as 'secondary care delay', these data were gathered from referral letters and hospital notes). Data were also collected on demographic variables including the patient's age, gender, education, employment status and postcode; deprivation ranks were calculated from postcode data using Geoconvert 2010 which produced an Index of Multiple Deprivation (IMD) score.[26] Data were gathered on the mode and rapidity of symptom onset (palindromic (defined as intermittent symptoms) vs. non-palindromic and acute vs. insidious). In addition, clinical data relating to duration of morning stiffness, swollen and tender joint counts, Disease Activity Score 28 (DAS28) and fulfilment of 2010 ACR/EULAR criteria for classification of RA[24] were collected at the time of assessment in secondary care. Questionnaires were returned to a named researcher (RJS) at the University of Birmingham for data entry and analysis using SPSS.[27]

Patients were asked to provide data on actions taken in relation to their symptoms prior to seeking help in primary care as part of a separate patient completed questionnaire. The questions included in that questionnaire were informed by previous qualitative research, including patient interviews and interviews with healthcare professionals. In addition, we had input from Patient Research Partners and the questions asked were validated and assessed for reliability[28].

Analysis

To ensure that the data met parametric assumptions, the distribution and levels of multicollinearity between variables were checked. Data on patient, primary care and secondary care delays were not normally distributed, therefore, log values of these delay data were created to generate normally distributed variables.

An Analysis of Variance assessed the main effects and two-way interactions for patient delay, primary care delay and secondary care delay between the following variables: gender, ethnicity, IMD score, age, education, employment status, palindromic onset, acute onset, patient reported family history of RA, and RA vs. UA. Two-way interactions which were not significant were removed in a backwards stepwise fashion, with the pairings with the highest p values being removed first, but all main effects were retained, so that the final model included all ten explanatory variables and any significant two-way interactions ($p<0.01$).

Results

1. Participant characteristics

Data were collected from 856 patients between 2011 and 2014. Patients were withdrawn from the study due to incomplete data (21 cases) and ineligibility (13 cases in whom there was no clinical synovitis reported at recruitment). Data were thus analysed from 822 patients of whom 68.5% were female with a mean age of 55 years. Characteristics of patients are presented in table 1.

Table 1: *Demographic and disease related characteristics of patients . Data are presented as either percentage (number) or median (IQR) as appropriate. Tender joint count is out of 42 joints (10 PIP, 10 MCP, 2 wrist, 2 elbow, 2 shoulder, 2 hip, 2 knee, 2 ankle, 10 MTP). Swollen joint count is out of 40 joints (10 PIP, 10 MCP, 2 wrist, 2 elbow, 2 shoulder, 2 knee, 2 ankle, 10 MTP).*

Female		68.5% (563)
Age, years		57 (45-67)
Diagnosis of RA		43% (368)
Ethnicity:	Black British	6.0% (49)
	South Asian	7.7% (63)
	White British	84.9% (698)
	Other	1.5% (12)
Self-reported family history of RA		34.9% (287)
Palindromic onset		42.8% (352)
Acute onset		35.9% (295)
Duration of morning stiffness, minutes		60 (10-120)
DAS28		4.88 (3.98 -5.80)

HAQ	1.13 (0.50-1.73)
Tender joint count	9 (4-18)
Swollen joint count	5 (2-10)

2. *Intervals between symptom onset and first rheumatology consultation*

Overall the median time between symptom onset and seeing a rheumatologist was 27.2 weeks (IQR 14.1 – 66 weeks); only 20% of patients were seen within the first 3 months following symptom onset. The median patient delay was 5.4 weeks (IQR 1.4-26.3 weeks). The median primary care delay was 6.9 weeks (IQR 2.3–20.3 weeks) with patients making a mean of 4 GP visits before being referred. The median secondary care delay was 4.7 weeks (IQR 2.9–7.5 weeks). Data are shown in Figure 1.

Patients with a palindromic symptom onset had a significantly longer patient delay than those with a non-palindromic onset (9.3 weeks (IQR 2-43 weeks) vs 4.3 weeks (IQR 1-17 weeks); $p<0.001$, t-test). Furthermore, those with an acute symptom onset had significantly shorter patient delays than those with an insidious symptoms onset (2.4 weeks (IQR 1 - 6.6 weeks) vs 11.1 weeks (IQR 4-44 weeks; $p<0.001$, t-test).

Resources used before seeking help from primary care

Patients reported taking a range of actions in relation to their symptoms before seeking help from their GP and in some cases these actions were associated with longer delays in GP consultation (see table 2). Most often patients reported purchasing tablets from 'the chemist', although only a small proportion actually reported speaking to a pharmacist. Other actions reported by patients included applying heat or cold packs to joints or buying joint supports.

Table 2. *Actions taken by patients with inflammatory arthritis before seeking help from their GP with comparison made for patient delay between those who did and did not undertake this action using independent t-tests; * P value for comparison of those who did and did not undertake this action.*

Actions taken before seeking help from GP	**% (number) of participants undertaking this action**	**Median (IQR) patient delay in weeks for those undertaking this action**	**Median (IQR) patient delay in weeks for those not undertaking this action**	**P value**
Bought tablets from the chemist	51.1% (273 out of 534)	6.9 (2-30.7)	4.7 (1.4-23)	p=0.036
Used an ice or heat pack on joint	47.8% (254 out of 531)	7.6 (2-30.3)	4.9 (2-26.1)	p=0.045
Took baths	47.4% (251 out of 529)	6.3 (2-30.4)	5.6 (2-26.1)	p=0.473
Bought joint supports	37.4%	4.4 (2.1-18.6)	5.1 (2-26.9)	p=0.362

(splints, tubi-grips etc)	(198 out of 529)			
Used alternative therapies	25.2% (134 out of 531)	8.3 (2-42.1)	5.3 (2-26.3)	p=0.020
Bought products from a health shop	19.0% (101 out of 532)	5.9 (2-36.3)	5.9 (2-26)	p=0.182
Modified diet	14.4% (76 out of 529)	6 (2.1-35.3)	6.1(2-26.3)	p= 0.183
Used prayer or sought spiritual guidance	8.4% (45 out of 534)	4.4 (2.1-18.6)	6.3 (2-26.9)	p=0.941
Spoke to a pharmacist	7.9% (41 out of 521)	5.9 (2-38.1)	5.9 (2-26.3)	p=0.544

Thirty-seven percent of patients reported looking on the internet (for example visiting the NHS direct website, BUPA website, Arthritis Research UK website and searching for information using search engines such as Google). Patients also reported seeking support via a telephone helpline; 5.7% described calling the NHS direct helpline or another telephone health advice service. Whilst, in the vast majority of cases, the GP was the first healthcare professional consulted by the patient, 3.7% sought help in the workplace (e.g. from an occupational nurse), 2% of patients went directly to A&E and 1% attended an NHS walk-in centre.

Multivariate analysis: Patient delay

The interaction model showed main effects for mode of onset (palindromic vs. non-palindromic; F=26.65, P<0.01) and rapidity of onset (acute vs. insidious; F= 65.36, P<0.01). An interaction was found between mode of onset and gender (F=45.658, P<0.01); men with a palindromic onset waited for longer before seeking help (Figure 2).

Multivariate analysis: GP delay

A main effect was found for ethnicity (F=6.26, P<0.01). Significant differences in primary care delay were found between White British and South Asian patients (6.2 weeks (IQR 2-18.6) vs 22 weeks (IQR 6.5-39.8); P<0.001) and between White British and Black British patients (6.2 weeks (IQR 2-18.6) vs 11.1 weeks (IQR 4.3-21.7); P<0.001). No significant difference was found between South Asian and Black British patients (P=1.000).

A main effect was also found for family history (F=5.89, P<0.01); the median primary care delay for those with a self-reported family history of RA was 9 weeks (IQR 2.4-25.7), while primary care delay for those with no family history was 6.3 weeks (IQR 2.3-19). Interactions at a statistically significant level (<0.01) were not found.

Multivariate analysis: Secondary care delay

The original model included main effects and two-way interactions for the following explanatory variables: gender, ethnicity, IMD score, age, education, employment status, mode of onset, rapidity of onset, family onset and RA vs. UA. None of the main effects or interactions (when removed backwards) were significant in predicting the delay between referral and being seen in secondary care.

Discussion

International guidelines recommend that the treatment of RA should begin as soon as possible after the onset of symptoms, ideally aiming to capture patients within the first 3 months following symptom onset. However, this large UK study of delays in access to care for RA patients found that the median patient delay in seeking help at the onset of symptoms was 5.4 weeks, while the median delay between seeing a healthcare professional and being referred was 6.9 weeks. Our study highlights that only 20% of patients were seen within the first 3 months of symptom onset. This appears to be much lower than the rate reported in other European countries for example a recent study in Austria reported at 38% of patients were seen within the first 3 months[29]. The present study also found an average delay of 4.7 weeks from referral until the patient was seen by a rheumatologist, similar to figures reported in the NOA report[3]. Unlike other some previous studies conducted in the UK,[3;12] we found that GP delay was the largest contributor to overall delay.

This research highlights that delays in primary care are long, and a major contributor to overall delays between symptom onset and the first rheumatology visit. General practitioners are faced with a number of barriers to identifying patients with newly presenting RA including the often non-specific nature of symptoms at the earliest stages of RA.[18] Research is underway to define symptom complexes most predictive of RA development in patients with newly presenting musculoskeletal symptoms and it is likely that a combination of education, and evidence based referral algorithms, will be needed to ensure that suspected cases are referred early. For example, in Fife, Scotland GPs do not have access to rheumatoid factor testing, and use guidelines with pictorial representations

to help identify early synovitis (personal communication Dr Helen Harris). Fife was a participating centre in this study, and was found to have the lowest GP referral time of all centres surveyed. Furthermore, facilitating access to secondary care, for example through the establishment of rapid assessment clinics whose main aim is to identify whether the patient does or does not have synovitis have been shown to significantly reduce delays in the assessment of patients.[30] A limitation of our research is that the study was not able to assess regional differences across NHS Trust in England and Scotland. A study comparing delays and referral patterns between NHS Trusts with local policies and practices which may influence the time between onset and first consultation would be welcome.

A number of factors were found to influence GP delay, including ethnicity and deprivation. Studies in the field of oncology have also found that people from ethnic minority backgrounds face longer GP delays,[31;32] and that GPs working in more deprived communities take longer to make referrals.[33] In the context of RA it is possible that the early symptomatology of patients from ethnic minority backgrounds is different from, and less typical of RA than that of, patients of white British background, thus making recognition more challenging for GPs. Data certainly exist that the clinical phenotype of established RA differs in patients of South Asian origin compared with patients of White British origin,[34] though data relating the clinical presentations of RA in these groups are lacking. Furthermore, it is unclear why a self-reported family history of RA would be associated with longer delays although it is important to recognise that GPs may not have elicited this information from the patient.[35]

Previous qualitative studies and a meta-synthesis have identified barriers to help seeking at the onset of RA.[36-39] The present study identifies that before seeking formal medical attention, people experiencing the early symptoms of RA seek information and help from a number of alternative sources and often self-medicate. We identified that buying tablets from a pharmacy, and using heat or ice on joints was significantly associated with longer patient delays. This finding highlights that some self-management behaviours, particularly those linked to accessing pharmacy services can negatively impact on the time it takes to seek help; this needs further exploration. Factors previously suggested to be associated with delays in GP consultation included an insidious onset of mild symptoms and a lack of knowledge about RA, personal susceptibility to RA and the availability of treatments to slow disease progression. In our national sample 64.1%% of people describe an insidious onset of RA, and 42.8% describe a palindromic onset of RA. Therefore, the majority of patients surveyed experienced a slow and / or intermittent onset of their RA symptoms. Our quantitative data are thus consistent with results from qualitative studies, demonstrating that the mode and rapidity of onset of symptoms is significantly associated with patient delays.

Whilst delays in primary care are the largest contributor to overall delay, patient delay and secondary care delay represent important components. This study found that the nature of symptoms onset influenced how quickly patients with RA sought help, suggesting that those with an acute onset of persistent symptoms seek help faster than those with insidious and palindromic onsets. Interventions to encourage rapid help seeking should consider highlighting the frequently insidious onset of RA to members of the public stressing that help should be sought even when symptoms are mild.

Interventions at multiple levels, including at the levels of the public, the services which the public consult after the onset of symptoms (e.g. pharmacies), primary care and secondary care will be needed to reduce overall delays in access to appropriate specialists.

Limitations

This study has a number of limitations. Firstly, the interval between first consultation with a Rheumatologist and initiation of disease modifying anti-rheumatic drug (DMARD) treatment was not measured. Any additional delay in in commencing DMARD treatment will negatively impact the patient and variables associated with delays at this level should be assessed in future studies.

During the course of this study a number of guidelines were published which may have influenced practice, and patterns of referral. However, the rate of recruitment over time was not controlled e.g. at the start of the study recruitment was slow, and then increased later as more centres participated. Future investigation should assess the impact of policy changes on patterns of help-seeking, referral and assessment.

The rheumatology centres participating in this study were self-selecting, therefore, there may be biases in the characteristics of the rheumatology centres which participated in this study. For example, the participating rheumatology units may have had a particular interest in early arthritis. Only a study which recruited consecutive patients from all rheumatology units across the UK would be able to provide a truly national picture.

Data relating to the onset of symptoms and initial GP consultation were gathered from patients' histories, and therefore relied on patient recollection. However, a previous study addressing delay in patients with RA, has highlighted the accuracy of patient recollection by comparing patient accounts of their journey to first rheumatology consultation against medical records[40].

Competing interests

No competing Interest:

Contributorship

All authors made substantial contributions to the conception or design of the work. The acquisition of data was undertaken by RJS, KR, PK and CD. The analysis and interpretation of data were undertaken by RJS, PN and KR. All authors were involved in drafting the work and revising it critically for important intellectual content. All authors gave final approval of the version published. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Data sharing statement

Data are available upon request from the corresponding author.

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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Yes
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Yes
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	Yes
Objectives	3	State specific objectives, including any prespecified hypotheses	Yes
Methods			
Study design	4	Present key elements of study design early in the paper	Yes
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	Yes
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	Cross-sectional study - Yes
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	Yes
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*Yes*
Bias	9	Describe any efforts to address potential sources of bias	Yes
Study size	10	Explain how the study size was arrived at	N/A
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	Yes
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	Yes
		(*b*) Describe any methods used to examine subgroups and interactions	Yes

	(*c*) Explain how missing data were addressed
	(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy
	(*e*) Describe any sensitivity analyses

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Yes
		(b) Give reasons for non-participation at each stage	Yes
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Yes
		(b) Indicate number of participants with missing data for each variable of interest	Yes
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	*Yes*
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	N/A
		(*b*) Report category boundaries when continuous variables were categorized	Yes
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	Yes
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Yes
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Yes
Generalisability	21	Discuss the generalisability (external validity) of the study results	Yes
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Yes

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Delays between the onset of symptoms and first rheumatology consultation in patients with rheumatoid arthritis in the UK: an observational study

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Title: Delays between the onset of symptoms and first rheumatology consultation in patients with rheumatoid arthritis in the UK: an observational study

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Keywords

Rheumatoid arthritis; patient delay; Primary care delay; help-seeking; access to care;

Strengths of this study.

This study surveyed a large sample of patients with new onset rheumatoid arthritis in the UK to identified delays in access to care.

This study identified that approximately 20% of patients saw a rheumatologist within 12 weeks of symptom onset, and factors associated with slower self-referral and slower GP referral were identified.

Limitations of this study.

Data were collected at the point of diagnosis and information regarding key dates (in particular the onset of symptoms and presentation to primary care) were reliant on patient recall.

This research has identified factors associated with delays, however, further research is needed to identify factors which would accelerate self-referral, GP referral and hospital waiting times for those experiencing early symptoms.

Abstract

Objective: To investigate delays from symptom onset to rheumatology assessment for patients with a new onset of rheumatoid arthritis (RA) or unclassified arthritis.

Methods: Newly presenting adults with either RA or unclassified arthritis were recruited from rheumatology clinics. Data on the length of time between symptom onset and first seeing a GP (patient delay), between first seeing a GP and being referred to a rheumatologist (general practitioner delay) and being seen by a rheumatologist following referral (hospital delay) were captured.

Results: 822 patients participated (563 female, mean age 55 years). The median time between symptom onset and seeing a rheumatologist was 27.2 weeks (IQR 14.1–66 weeks); only 20% of patients were seen within the first 3 months following symptom onset. The median patient delay was 5.4 weeks (IQR 1.4-26.3 weeks). Patients who purchased over the counter medications or used ice/heat packs took longer to seek help than those who did not. In addition, those with a palindromic or an insidious symptom onset delayed for longer than those with a non-palindromic or acute onset. The median general practitioner delay was 6.9 weeks (IQR 2.3–20.3 weeks). Patients made a mean of 4 GP visits before being referred. The median hospital delay was 4.7 weeks (IQR 2.9–7.5 weeks).

Conclusion: This study identified delays at all levels in the pathway towards assessment by a Rheumatologist. However, delays in primary care were particularly long. Patient delay was driven by the nature of symptom onset. Complex multi-faceted interventions to promote rapid help seeking and to facilitate prompt onward referral from primary care should be developed.

Introduction:

Rheumatoid arthritis (RA) is a chronic inflammatory disease affecting approximately 1% of the population.[1;2] Rheumatoid arthritis is associated with significant morbidity in large part as a consequence of extra-articular co-morbidities associated with systemic inflammation. In the UK it has been estimated that RA costs the NHS around £560 million per year and that additional costs to the economy of sick leave and work-related disability total £1.8 billion per year.[3] The first three months following the onset of RA symptoms represents an important therapeutic window.[4] Treatment during this phase improves long-term clinical outcomes, increasing the proportion of patients whose disease enters remission, reducing RA related joint damage and reducing the eventual need for joint replacement surgery.[5-10] Therefore, it is vital that patients are seen by Rheumatologists rapidly following the onset of RA symptoms to allow the rapid introduction of disease modifying anti-rheumatic drug treatment. However, despite increased recognition of the benefits of early treatment there remains considerable delay between symptom onset and the initiation of therapy.[11-13] Indeed a report by the UK's National Audit Office (NAO) in 2009 estimated that only 10% of patients with RA were treated within three months of symptom onset. The NAO's modelling suggested significant financial benefits for the broader economy and quality of life benefits for the individual if the proportion of patients treated earlier was increased.[3]

The patient's pathway to care can be delayed for a number of reasons, including delays on the part of the patient in recognising the significance of the early symptoms of RA.[14-16]

Recent research has linked patients' perceptions of RA and coping styles to the length of time taken to seek help.[17] Before seeking medical help from a physician, patients may seek help from a range of services including complementary therapists, pharmacists and telephone and on-line services. However, the use of these services at the onset of inflammatory arthritis has not been fully explored. Primary healthcare professionals often find the early symptoms of RA difficult to distinguish from those of other rheumatic diseases, making timely and appropriate referrals to rheumatologists challenging.[18;19] There may thus be delays in healthcare professionals making a referral to a Rheumatologist and also in assessment at the secondary care level, contributing further to the delay in making a diagnosis and commencing appropriate therapy.

Several studies conducted across a range of countries have shown long delays between the onset of symptoms and a patient's first consultation with a rheumatologist.[20-23] However, data related to lengths of time between the onset of inflammatory musculoskeletal symptoms and first seeing a GP, between first seeing a GP and being referred to a rheumatologist and being seen by a rheumatologist following referral were not available across multiple NHS Trusts in multiple regions of the UK at the time of this study.

Aim

The aim of this study was to investigate the extents of delay in assessment of patients with RA and unclassified arthritis. Specifically the study assessed extents of delay at the level of the patient in seeking help from the general practitioner, the general practitioner in referring to a Rheumatologist and the Rheumatologist in assessing the patient following referral. The relationships between extents of delay and clinical and demographic variables

were explored and data captured relating to sources of information, help and advice utilized by patients prior to GP consultation.

Methods

A questionnaire based survey of consecutively presenting patients with a new onset of RA or unclassified inflammatory arthritis was undertaken in England and Scotland. Networks such as the Early Rheumatoid Arthritis Network[24] and the National Institute for Health Research Clinical Research Network[25] were used identify Rheumatology centres to participate in this study. RJS also promoted the study during abstract presentations at British Society for Rheumatology meetings.

Data were collected from Rheumatology departments in 34 NHS Trusts. Rheumatology departments were secondary care based, although one rheumatology department (Sandwell and West Birmingham Hospitals) operated clinics in both hospital and community settings. Eligible patients were recruited on their first or second visit to the rheumatology department following a primary care referral (data were not collected on the numbers of patients whose data were collected at their first visit or at their second visit). Rheumatogists were asked to approach consecutively presenting patients who met the eligibility criteria. Eligible patients were newly referred adults (aged ≥ 18 years) with clinically apparent synovial swelling of one or more joints who had either a new onset of RA (according to 2010 ACR / EULAR criteria [26]) or unclassified arthritis (UA; defined as a failure to fulfil classification criteria for another inflammatory rheumatic disease). Patients with UA were recruited, as in many cases patients with UA at initial secondary care assessment progress to RA over time.[27]

Data were collected using two questionnaires (available from the corresponding author on request). First, following consent, the recruiting healthcare professional, with the patient present, completed a questionnaire that captured data on extents of delays between [1] symptom onset and seeing a healthcare professional (from herein referred to as 'patient delay', these data was gathered from the patient's account by the recruiting healthcare professional), [2] seeing a general practitioner and being referred to a rheumatologist (from herein referred to as 'general practitioner e delay', these data was gathered from the patient's account by the recruiting healthcare professional), and [3] being referred to a rheumatologist and seeing a rheumatologist (from herein referred to as 'hospital delay', these data were gathered from referral letters and hospital notes). Data were also gathered on [1] demographic variables including the patient's age, gender, education, employment status and postcode; deprivation ranks were calculated from postcode data using Geoconvert 2010 which produced an Index of Multiple Deprivation (IMD) score,[28] [2] clinical variables including the mode of symptom onset (palindromic (defined as intermittent symptoms) vs. non-palindromic (defined as persistent symptoms)), rapidity of symptom onset (acute vs. insidious; an acute onset was typically viewed as an onset of symptoms which came on rapidly over 24-48 hours), duration of morning stiffness, swollen and tender joint counts, Disease Activity Score 28 (DAS28) and fulfilment of 2010 ACR/EULAR criteria for classification of RA[26].

In addition, via a separate questionnaire that patients completed by themselves, patients provided data on actions taken in relation to their symptoms prior to seeking help from primary care . The variables captured were informed by previous qualitative research,

including patient interviews and interviews with healthcare professionals. In addition, we had input from Patient Research Partners and the questions asked were validated and assessed for reliability[29].

Patient and Public Involvement

Patient and public involvement was an important element of this study. Patient representatives from Sandwell and West Birmingham Hospitals NHS Trust were involved in the study design, advised on the content of patient facing materials including participant information sheets and consent forms and the content of questionnaires including questions related to actions taken by patients prior to consulting their GPs. Patients were members of the Project Management Group reviewing study recruitment and supporting the Group in developing approaches to ensure that recruitment proceeded to time and target

Analysis

To ensure that the data met parametric assumptions, the distribution and levels of multicollinearity between variables were checked. Data on patient delays, general practitioner delays and hospital delays were not normally distributed, therefore, log values of these delay data were created to generate normally distributed variables.

For each of the outcomes patient delay, general practitioner delay and hospital delay a general linear model was used with main effects and two-way interactions for the following explanatory variables: gender, ethnicity, IMD score, age, education, employment status, mode of onset, rapidity of onset, patient reported family history of RA and RA vs. UA. For

each outcome any two-way interactions which were not significant were removed in a backwards stepwise fashion, with the pairings with the highest p values being removed first. All main effects were retained, so that the final model for each outcome included all ten explanatory variables and any significant two-way interactions ($p<0.01$). All significant main effects and interactions are reported in the Results section.

Results

1. Participant characteristics

Data were collected from 856 patients between 2011 and 2014. Patients were withdrawn from the study due to incomplete data (21 cases) and ineligibility (13 cases in whom there was no clinical synovitis reported at recruitment). Data were thus analysed from 822 patients of whom 68.5% were female with a mean age of 55 years. Characteristics of patients are presented in table 1.

Table 1: *Demographic and disease related characteristics of patients. Data are presented as either percentage (number) or median (IQR) as appropriate. Tender joint count is out of 42 joints (10 PIP, 10 MCP, 2 wrist, 2 elbow, 2 shoulder, 2 hip, 2 knee, 2 ankle, 10 MTP). Swollen joint count is out of 40 joints (10 PIP, 10 MCP, 2 wrist, 2 elbow, 2 shoulder, 2 knee, 2 ankle, 10 MTP).*

Female	68.5% (563)
Age, years	57 (45-67)
Diagnosis of RA	73% (603)
Ethnicity: Black British	6.0% (49)

South Asian White British Other	7.7% (63) 84.9% (698) 1.5% (12)
Self-reported family history of RA	34.9% (287)
Palindromic onset	42.8% (352)
Acute onset	35.9% (295)
Duration of morning stiffness, minutes	60 (10-120)
DAS28	4.88 (3.98 -5.80)
HAQ	1.13 (0.50-1.73)
Tender joint count	9 (4-18)
Swollen joint count	5 (2-10)

2. *Intervals between symptom onset and first rheumatology consultation*

Overall the median time between symptom onset and seeing a rheumatologist was 27.2 weeks (IQR 14.1 – 66 weeks); only 20% of patients were seen within the first 3 months following symptom onset. The median patient delay was 5.4 weeks (IQR 1.4-26.3 weeks). The median general practitioner delay was 6.9 weeks (IQR 2.3–20.3 weeks) with patients making a mean of 4 GP visits before being referred. The median hospital delay was 4.7 weeks (IQR 2.9–7.5 weeks).

Patients with a palindromic symptom onset had a significantly longer patient delay than those with a non-palindromic onset (9.3 weeks (IQR 2-43 weeks) vs 4.3 weeks (IQR 1-17 weeks); p<0.001, t-test). Furthermore, those with an acute symptom onset had significantly shorter patient delays than those with an insidious symptoms onset (2.4 weeks (IQR 1 - 6.6 weeks) vs 11.1 weeks (IQR 4-44 weeks; p<0.001, t-test).

Resources used before seeking help from primary care

Patients reported taking a range of actions in relation to their symptoms before seeking help from their GP and in some cases these actions were associated with longer delays in GP consultation (see table 2). Most often patients reported purchasing tablets from 'the chemist', although only a small proportion actually reported speaking to a pharmacist. Other actions reported by patients included applying heat or cold packs to joints or buying joint supports.

Table 2. *Actions taken by patients with inflammatory arthritis before seeking help from their GP with comparison made for patient delay between those who did and did not undertake this action using independent t-tests; * P value for comparison of those who did and did not undertake this action.*

Actions taken before seeking help from GP	% (number) of participants undertaking this action	Median (IQR) patient delay in weeks for those undertaking	Median (IQR) patient delay in weeks for those not undertaking	P value

		this action	this action	
Bought tablets from the chemist	51.1% (273 out of 534)	6.9 (2-30.7)	4.7 (1.4-23)	p=0.036
Used an ice or heat pack on joint	47.8% (254 out of 531)	7.6 (2-30.3)	4.9 (2-26.1)	p=0.045
Took baths	47.4% (251 out of 529)	6.3 (2-30.4)	5.6 (2-26.1)	p=0.473
Bought joint supports (splints, tubi-grips etc)	37.4% (198 out of 529)	4.4 (2.1-18.6)	5.1 (2-26.9)	p=0.362
Used alternative therapies	25.2% (134 out of 531)	8.3 (2-42.1)	5.3 (2-26.3)	p=0.020
Bought products from a health shop	19.0% (101 out of 532)	5.9 (2-36.3)	5.9 (2-26)	p=0.182
Modified diet	14.4% (76 out of 529)	6 (2.1-35.3)	6.1(2-26.3)	p= 0.183
Used prayer or sought spiritual guidance	8.4% (45 out of 534)	4.4 (2.1-18.6)	6.3 (2-26.9)	p=0.941
Spoke to a pharmacist	7.9% (41 out of 521)	5.9 (2-38.1)	5.9 (2-26.3)	p=0.544

Thirty-seven percent of patients reported looking on the internet (for example visiting the NHS direct website, BUPA website, Arthritis Research UK website and searching for information using search engines such as Google). Patients also reported seeking support via a telephone helpline; 5.7% described calling the NHS direct helpline or another telephone health advice service. 3.7% sought help in the workplace (e.g. from an occupational nurse), 2% of patients went directly to the Accident and Emergency Department and 1% attended an NHS walk-in centre.

Multivariate analysis: Patient delay

The interaction model showed main effects for mode of onset (palindromic vs. non-palindromic; $F=26.65$, $P<0.01$) and rapidity of onset (acute vs. insidious; $F= 65.36$, $P<0.01$). An interaction was found between palindromic onset and gender ($F=45.658$, $P<0.01$); men with a palindromic onset waited significantly longer before seeking help.

Multivariate analysis: General practitioner delay

A main effect was found for ethnicity (F=6.26, P<0.01). Significant differences in general practitioner delay were found between White British and South Asian patients (6.2 weeks (IQR 2-18.6) vs 22 weeks (IQR 6.5-39.8); P<0.001) and between White British and Black British patients (6.2 weeks (IQR 2-18.6) vs 11.1 weeks (IQR 4.3-21.7); P<0.001). No significant difference was found between South Asian and Black British patients (P=1.000).

A main effect was also found for family history (F=5.89, P<0.01); the median general practitioner delay for those with a self-reported family history of RA was 9 weeks (IQR 2.4-25.7), while general practitioner delay for those with no family history was 6.3 weeks (IQR 2.3-19). Interactions at a statistically significant level (<0.01) were not found.

Multivariate analysis: Hospital delay

The original model included main effects and two-way interactions for the following explanatory variables: gender, ethnicity, IMD score, age, education, employment status, mode of onset, rapidity of onset, family onset and RA vs. UA. None of the main effects or interactions (when removed backwards) were significant in predicting the delay between referral and being seen in secondary care.

Discussion

International guidelines recommend that the treatment of RA should begin as soon as possible after the onset of symptoms, ideally aiming to capture patients within the first 3 months following symptom onset. However, this large UK study of delays in access to care for RA patients found that the median patient delay in seeking help at the onset of symptoms was 5.4 weeks, while the median delay between seeing a healthcare professional and being referred was 6.9 weeks. Our study highlights that only 20% of patients were seen within the first 3 months of symptom onset. This appears to be lower than the rate reported in other European countries for example a recent study in Austria reported at 38% of patients were seen within the first 3 months[30]. The present study also found an average delay of 4.7 weeks from referral until the patient was seen by a rheumatologist, similar to figures reported in the NAO report[3]. Unlike our previous study conducted at a single centre in the UK where patient delay accounted for the largest element of delay,[13] we found that GP delay was the largest contributor to overall delay; patient delay was less than we had previously reported in our single centre study.

This research highlights that delays in primary care are long, and a major contributor to overall delays between symptom onset and the first rheumatology visit. General practitioners are faced with a number of barriers to identifying patients with newly presenting RA including the often non-specific nature of symptoms at the earliest stages of RA.[18] Research is underway to define symptom complexes most predictive of RA development in patients with newly presenting musculoskeletal symptoms. For example, a questionnaire has been developed and validated to capture such symptoms in patients

presenting with joint symptoms which by history are suggestive of an underlying inflammatory cause[31] and data are currently being collected from such patients in secondary care based longitudinal observational cohort studies to identify symptoms that may predict RA development. Furthermore an assessment of primary care databases has identified a range of symptoms including hand related joint symptoms, morning stiffness and carpal tunnel syndrome type symptoms as being ones with which patients frequently present to the GP prior to the point at which the GP refers the patient to a Rheumatologist or records a diagnosis of RA [32] It is likely that a combination of education, and evidence based referral algorithms, will be needed to ensure that suspected cases are referred early. For example, in Fife, Scotland GPs did not have access to rheumatoid factor testing during the course of our study, and used guidelines with pictorial representations to help identify early synovitis (personal communication Dr Helen Harris). Fife was a participating centre in this study, and was found to have the lowest GP referral time of all centres surveyed. Furthermore, facilitating access to secondary care, for example through the establishment of rapid assessment clinics whose main aim is to identify whether the patient does or does not have synovitis have been shown to significantly reduce delays in the assessment of patients.[33] A limitation of our research is that the study was not able to assess regional differences across NHS Trusts. A study comparing delays and referral patterns between hospitals with local policies and practices which may influence the time between onset and first consultation would be useful and an international study would be particularly helpful.

A number of factors were found to influence GP delay including ethnicity. Studies in the field of oncology have also found that people from ethnic minority backgrounds face longer GP delays,[34;35] In the context of RA it is possible that the early symptomatology of patients from

ethnic minority backgrounds is different from, and less typical of RA than that of, patients of white British background, thus making recognition more challenging for GPs. Data certainly exist that the clinical phenotype of established RA differs in patients of South Asian origin compared with patients of White British origin,[36] though data relating the clinical presentations of RA in these groups are lacking. Furthermore, it is unclear why a self-reported family history of RA would be associated with longer delays although it is important to recognise that GPs may not have elicited this information from the patient.[37] Qualitative approaches may be helpful to address some of these issues in the future.

Previous qualitative studies and a meta-synthesis have identified barriers to help seeking at the onset of RA.[37-43] The present study identifies that before seeking formal medical attention, people experiencing the early symptoms of RA seek information and help from a number of alternative sources and often self-medicate. We identified that buying tablets from a pharmacy, and using heat or ice on joints was significantly associated with longer patient delays. This finding highlights that some self-management behaviours, particularly those linked to accessing pharmacy services can negatively impact on the time it takes to seek help; this needs further exploration. Factors previously suggested to be associated with delays in GP consultation included an insidious onset of mild symptoms and a lack of knowledge about RA, personal susceptibility to RA and the availability of treatments to slow disease progression. In our national sample 64.1% of people describe an insidious onset of RA, and 42.8% describe a palindromic onset of RA. Therefore, majority large proportion of patients surveyed experienced a slow and / or intermittent onset of their inflammatory joint symptoms. Our quantitative data are thus consistent with results from qualitative studies,

demonstrating that the mode and rapidity of onset of symptoms is significantly associated with patient delays.

This study has a number of limitations. Firstly, the interval between first consultation with a Rheumatologist and initiation of disease modifying anti-rheumatic drug (DMARD) treatment was not measured. Any additional delay in commencing DMARD treatment will negatively impact the patient and variables associated with delays at this level should be assessed in future studies. Secondly, during the course of this study a number of guidelines related to RA management were published which may have influenced practice, and patterns of referral. We were not able to explore the relationships between the availability / local adoption of guidelines and delays in the assessment of patients. Future investigation should assess the impact of policy changes on patterns of help-seeking, referral and assessment. Thirdly, the rheumatology centres participating in this study were self-selecting, therefore, there may be biases in the characteristics of the rheumatology centres which participated in this study. For example, the participating rheumatology units may have had a particular interest in early arthritis. Only a study which recruited consecutive patients from all rheumatology units across the UK would be able to provide a truly national picture. Fourthly, whilst we were able to document the length of delay at a primary care level there were important variables which may have influenced this delay which we did not record and so were unable to explore. For example it would have been helpful have access to results tests performed in primary care to assess whether levels of inflammatory markers or RA related autoantibodies measured in primary care influenced the rapidity of referral from primary care. Indeed a recent quantitative survey of GPs' anticipated actions in primary care when dealing with patients with suspected RA suggest that results of these tests may influence GP behaviours[44]. Future research should address this. Similarly, a number of

secondary care related variables may have influenced the extent of secondary care delay including the number of rheumatologists at each Trust, whether a dedicated early arthritis clinic was in place and approaches taken to the triage of referrals. Data relating to these variables were not collected though future work addressing issues of delay should address these important issues. Fifthly, data relating to the dates of onset of symptoms and initial GP consultation were gathered from patients' histories, and therefore relied on patient recollection with a possible associated error. However, a previous study addressing delays in the assessment of patients with RA, compared patient accounts of their journeys to first rheumatology consultation against medical records and highlighted the accuracy of patient recollection in relation to dates found to be documented in primary care records[45]. This, to some extent, validates our approach of using patient memory to define the dates of symptom onset and initial GP presentation. An alternative approach would be a longitudinal observational study in the general population to track the development of symptoms and the relationship between that and GP consultation, GP referral and secondary care assessment. A challenge with this approach is the low incidence of RA and thus the requirement for a very large sample size. One could potentially enrich the population for RA risk by, for example, following individuals who are at increased risk of RA (e.g. the first degree relatives of patients with RA). However, one of the challenges with this strategy is that simply being involved in such a study may influence subsequent patient and GP behaviour.

Whilst delays in primary care are the largest contributor to overall delay, patient delay and hospital delay represent important components. This study found that the nature of symptoms onset influenced how quickly patients with RA sought help, suggesting that those

with an acute onset of persistent symptoms seek help faster than those with insidious and palindromic onsets. Interventions to encourage rapid help seeking should consider highlighting the frequently insidious onset of RA to members of the public stressing that help should be sought even when symptoms are mild. However, even those with a rapid onset of persistent symptoms often delayed for prolonged periods before seeking help. We have previously shown that members of the public view musculoskeletal symptoms, even those with clear inflammatory features, as less worrisome and less requiring rapid assessment as compared with symptoms of other common diseases such as ischaemic type chest pain or bowel disturbance with associated rectal blood loss[46]. Enhanced public education to highlight the significance of inflammatory type musculoskeletal symptoms is thus likely to be needed. Interventions at multiple levels, including at the levels of the public, the services which members of the public consult after the onset of symptoms (e.g. pharmacies), primary care and secondary care will be needed to reduce overall delays in access to appropriate specialists.

Competing interests

No competing Interest:

Contributorship

RJS, CJ, SHM, CDM, KS, RH, CD, PK and KR made substantial contributions to the conception or design of the work. The acquisition of data was undertaken by RJS, KR, PK and CD. RJS, CJ and SHM facilitated patient and public involvement in the design, delivery and interpretation of this study. The analysis and interpretation of data were undertaken by RJS, PN and KR. RJS, PN CJ, SHM, CDM, KS, RH, CD, PK and KR were involved in drafting the work and revising it critically for important intellectual content. RJS, CJ, SHM, CDM, KS, RH, CD, PK and KR gave final approval of the version published. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Ethical approval information Ethical approval was obtained from South Birmingham Research Ethics Committee (reference no. 10/H1207/98) and all participants gave written informed consent.

Data sharing statement

Data are available upon request from the corresponding author.

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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation		
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Yes	(Page 1)
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Yes	(page 4)
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported		Yes (pages 5-7)
Objectives	3	State specific objectives, including any prespecified hypotheses		Yes (pages 6-7)
Methods				
Study design	4	Present key elements of study design early in the paper		Yes (page 1, and page 7)
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection		Yes (page 7- 9)
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants		Cross-sectional study – Yes (Page 7)
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case		
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable		Yes (page 7-8)
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group		*Yes (page 7-8, also see table 1)*
Bias	9	Describe any efforts to address potential sources of bias		Yes (Pages 17-22)
Study size	10	Explain how the study size was arrived at		N/A
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why		Yes (page 10)
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding		Yes (page 10)

(*b*) Describe any methods used to examine subgroups and interactions	Yes
(*c*) Explain how missing data were addressed	
(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	N/A
€ Describe any sensitivity analyses	

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Yes (pages 17-18)
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Yes (pages 17-18)
		(b) Indicate number of participants with missing data for each variable of interest	Yes (table 1)
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	*N/A*
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	*N/A*
		Cross-sectional study—Report numbers of outcome events or summary measures	*Yes*
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	N/A
		(*b*) Report category boundaries when continuous variables were categorized	Yes (pages 17-18)
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	Yes (Page 22)
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Yes (page 20)
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Yes (page 20-22)
Generalisability	21	Discuss the generalisability (external validity) of the study results	Yes (page 22)
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Yes (page 25)

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely

available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Delays between the onset of symptoms and first rheumatology consultation in patients with rheumatoid arthritis in the UK: an observational study

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Title: Delays between the onset of symptoms and first rheumatology consultation in patients with rheumatoid arthritis in the UK: an observational study

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Strengths and limitations of this study.

A key strength of this study is that it surveyed a large sample of patients with new onset rheumatoid arthritis in the UK to identified delays in access to care.

Limitations include the fact that data were collected at the point of diagnosis and information regarding key dates (in particular the onset of symptoms and presentation to primary care) were reliant on patient recall.

Abstract

Objective: To investigate delays from symptom onset to rheumatology assessment for patients with a new onset of rheumatoid arthritis (RA) or unclassified arthritis.

Methods: Newly presenting adults with either RA or unclassified arthritis were recruited from rheumatology clinics. Data on the length of time between symptom onset and first seeing a GP (patient delay), between first seeing a GP and being referred to a rheumatologist (general practitioner delay) and being seen by a rheumatologist following referral (hospital delay) were captured.

Results: 822 patients participated (563 female, mean age 55 years). The median time between symptom onset and seeing a rheumatologist was 27.2 weeks (IQR 14.1–66 weeks); only 20% of patients were seen within the first 3 months following symptom onset. The median patient delay was 5.4 weeks (IQR 1.4-26.3 weeks). Patients who purchased over the counter medications or used ice/heat packs took longer to seek help than those who did not. In addition, those with a palindromic or an insidious symptom onset delayed for longer than those with a non-palindromic or acute onset. The median general practitioner delay was 6.9 weeks (IQR 2.3–20.3 weeks). Patients made a mean of 4 GP visits before being referred. The median hospital delay was 4.7 weeks (IQR 2.9–7.5 weeks).

Conclusion: This study identified delays at all levels in the pathway towards assessment by a Rheumatologist. However, delays in primary care were particularly long. Patient delay was driven by the nature of symptom onset. Complex multi-faceted interventions to promote rapid help seeking and to facilitate prompt onward referral from primary care should be developed.

Introduction:

Rheumatoid arthritis (RA) is a chronic inflammatory disease affecting approximately 1% of the population.[1;2] Rheumatoid arthritis is associated with significant morbidity in large part as a consequence of extra-articular co-morbidities associated with systemic inflammation. In the UK it has been estimated that RA costs the NHS around £560 million per year and that additional costs to the economy of sick leave and work-related disability total £1.8 billion per year.[3] The first three months following the onset of RA symptoms represents an important therapeutic window.[4] Treatment during this phase improves long-term clinical outcomes, increasing the proportion of patients whose disease enters remission, reducing RA related joint damage and reducing the eventual need for joint replacement surgery.[5-10] Therefore, it is vital that patients are seen by Rheumatologists rapidly following the onset of RA symptoms to allow the rapid introduction of disease modifying anti-rheumatic drug treatment. However, despite increased recognition of the benefits of early treatment there remains considerable delay between symptom onset and the initiation of therapy.[11-13] Indeed a report by the UK's National Audit Office (NAO) in 2009 estimated that only 10% of patients with RA were treated within three months of symptom onset. The NAO's modelling suggested significant financial benefits for the broader economy and quality of life benefits for the individual if the proportion of patients treated earlier was increased.[3]

The patient's pathway to care can be delayed for a number of reasons, including delays on the part of the patient in recognising the significance of the early symptoms of RA.[14-16] Recent

research has linked patients' perceptions of RA and coping styles to the length of time taken to seek help.[17] Before seeking medical help from a physician, patients may seek help from a range of services including complementary therapists, pharmacists and telephone and on-line services. However, the use of these services at the onset of inflammatory arthritis has not been fully explored. Primary healthcare professionals often find the early symptoms of RA difficult to distinguish from those of other rheumatic diseases, making timely and appropriate referrals to rheumatologists challenging.[18;19] There may thus be delays in healthcare professionals making a referral to a Rheumatologist and also in assessment at the secondary care level, contributing further to the delay in making a diagnosis and commencing appropriate therapy.

Several studies conducted across a range of countries have shown long delays between the onset of symptoms and a patient's first consultation with a rheumatologist.[20-23] However, data related to lengths of time between the onset of inflammatory musculoskeletal symptoms and first seeing a GP, between first seeing a GP and being referred to a rheumatologist and being seen by a rheumatologist following referral were not available across multiple NHS Trusts in multiple regions of the UK at the time of this study.

Aim

The aim of this study was to investigate the extents of delay in assessment of patients with RA and unclassified arthritis. Specifically the study assessed extents of delay at the level of the patient in seeking help from the general practitioner, the general practitioner in referring to a Rheumatologist and the Rheumatologist in assessing the patient following referral. The relationships between extents of delay and clinical and demographic variables

were explored and data captured relating to sources of information, help and advice utilized by patients prior to GP consultation.

Methods

A questionnaire based survey of consecutively presenting patients with a new onset of RA or unclassified inflammatory arthritis was undertaken in England and Scotland. Networks such as the Early Rheumatoid Arthritis Network[24] and the National Institute for Health Research Clinical Research Network[25] were used identify Rheumatology centres to participate in this study. RJS also promoted the study during abstract presentations at British Society for Rheumatology meetings.

Data were collected from Rheumatology departments in 34 NHS Trusts. Rheumatology departments were secondary care based, although one rheumatology department (Sandwell and West Birmingham Hospitals) operated clinics in both hospital and community settings. Eligible patients were recruited on their first or second visit to the rheumatology department following a primary care referral (data were not collected on the numbers of patients whose data were collected at their first visit or at their second visit). Rheumatogists were asked to approach consecutively presenting patients who met the eligibility criteria. Eligible patients were newly referred adults (aged ≥ 18 years) with clinically apparent synovial swelling of one or more joints who had either a new onset of RA (according to 2010 ACR / EULAR criteria [26]) or unclassified arthritis (UA; defined as a failure to fulfil classification criteria for another inflammatory rheumatic disease). Patients with UA were recruited, as in many cases patients with UA at initial secondary care assessment progress to RA over time.[27]

Data were collected using two questionnaires (available from the corresponding author on request). First, following consent, the recruiting healthcare professional, with the patient present, completed a questionnaire that captured data on extents of delays between [1] symptom onset and seeing a healthcare professional (from herein referred to as 'patient delay', these data was gathered from the patient's account by the recruiting healthcare professional), [2] seeing a general practitioner and being referred to a rheumatologist (from herein referred to as 'general practitioner e delay', these data was gathered from the patient's account by the recruiting healthcare professional), and [3] being referred to a rheumatologist and seeing a rheumatologist (from herein referred to as 'hospital delay', these data were gathered from referral letters and hospital notes). Data were also gathered on [1] demographic variables including the patient's age, gender, education, employment status and postcode; deprivation ranks were calculated from postcode data using Geoconvert 2010 which produced an Index of Multiple Deprivation (IMD) score,[28] [2] clinical variables including the mode of symptom onset (palindromic (defined as intermittent symptoms) vs. non-palindromic (defined as persistent symptoms)), rapidity of symptom onset (acute vs. insidious; an acute onset was typically viewed as an onset of symptoms which came on rapidly over 24-48 hours), duration of morning stiffness, swollen and tender joint counts, Disease Activity Score 28 (DAS28) and fulfilment of 2010 ACR/EULAR criteria for classification of RA[26].

In addition, via a separate questionnaire that patients completed by themselves, patients provided data on actions taken in relation to their symptoms prior to seeking help from primary care . The variables captured were informed by previous qualitative research,

including patient interviews and interviews with healthcare professionals. In addition, we had input from Patient Research Partners and the questions asked were validated and assessed for reliability[29].

Patient and Public Involvement

Patient and public involvement was an important element of this study. Patient representatives from Sandwell and West Birmingham Hospitals NHS Trust were involved in the study design, advised on the content of patient facing materials including participant information sheets and consent forms and the content of questionnaires including questions related to actions taken by patients prior to consulting their GPs. Patients were members of the Project Management Group reviewing study recruitment and supporting the Group in developing approaches to ensure that recruitment proceeded to time and target

Analysis

To ensure that the data met parametric assumptions, the distribution and levels of multicollinearity between variables were checked. Data on patient delays, general practitioner delays and hospital delays were not normally distributed, therefore, log values of these delay data were created to generate normally distributed variables.

For each of the outcomes patient delay, general practitioner delay and hospital delay a general linear model was used with main effects and two-way interactions for the following explanatory variables: gender, ethnicity, IMD score, age, education, employment status, mode of onset, rapidity of onset, patient reported family history of RA and RA vs. UA. For

each outcome any two-way interactions which were not significant were removed in a backwards stepwise fashion, with the pairings with the highest p values being removed first. All main effects were retained, so that the final model for each outcome included all ten explanatory variables and any significant two-way interactions ($p<0.01$). All significant main effects and interactions are reported in the Results section.

Results

1. Participant characteristics

Data were collected from 856 patients between 2011 and 2014. Patients were withdrawn from the study due to incomplete data (21 cases) and ineligibility (13 cases in whom there was no clinical synovitis reported at recruitment). Data were thus analysed from 822 patients of whom 68.5% were female with a mean age of 55 years. Characteristics of patients are presented in table 1.

Table 1: *Demographic and disease related characteristics of patients. Data are presented as either percentage (number) or median (IQR) as appropriate. Tender joint count is out of 42 joints (10 PIP, 10 MCP, 2 wrist, 2 elbow, 2 shoulder, 2 hip, 2 knee, 2 ankle, 10 MTP). Swollen joint count is out of 40 joints (10 PIP, 10 MCP, 2 wrist, 2 elbow, 2 shoulder, 2 knee, 2 ankle, 10 MTP).*

Female	68.5% (563)
Age, years	57 (45-67)
Diagnosis of RA	73% (603)
Ethnicity: Black British	6.0% (49)

South Asian White British Other	7.7% (63) 84.9% (698) 1.5% (12)
Self-reported family history of RA	34.9% (287)
Palindromic onset	42.8% (352)
Acute onset	35.9% (295)
Duration of morning stiffness, minutes	60 (10-120)
DAS28	4.88 (3.98 -5.80)
HAQ	1.13 (0.50-1.73)
Tender joint count	9 (4-18)
Swollen joint count	5 (2-10)

2. *Intervals between symptom onset and first rheumatology consultation*

Overall the median time between symptom onset and seeing a rheumatologist was 27.2 weeks (IQR 14.1 – 66 weeks); only 20% of patients were seen within the first 3 months following symptom onset. The median patient delay was 5.4 weeks (IQR 1.4-26.3 weeks). The median general practitioner delay was 6.9 weeks (IQR 2.3–20.3 weeks) with patients making a mean of 4 GP visits before being referred. The median hospital delay was 4.7 weeks (IQR 2.9–7.5 weeks).

Palindromic onset is defined as intermittent symptoms, while non-palindromic is defined as persistent symptoms. Acute onset defined as symptoms which came on rapidly over 24-48 hours, while insidious onset is defined as symptoms which developed slowly over an extended period of time. Patients with a palindromic symptom onset had a significantly longer patient delay than those with a non-palindromic onset (9.3 weeks (IQR 2-43 weeks) vs 4.3 weeks (IQR 1-17 weeks); p<0.001, t-test). Furthermore, those with an acute symptom onset had significantly shorter patient delays than those with an insidious symptoms onset (2.4 weeks (IQR 1 - 6.6 weeks) vs 11.1 weeks (IQR 4-44 weeks; p<0.001, t-test).

Resources used before seeking help from primary care

Patients reported taking a range of actions in relation to their symptoms before seeking help from their GP and in some cases these actions were associated with longer delays in GP consultation (see table 2). Most often patients reported purchasing tablets from 'the chemist', although only a small proportion actually reported speaking to a pharmacist. Other actions reported by patients included applying heat or cold packs to joints or buying joint supports.

Table 2. *Actions taken by patients with inflammatory arthritis before seeking help from their GP with comparison made for patient delay between those who did and did not undertake this action using independent t-tests; * P value for comparison of those who did and did not undertake this action.*

Actions taken before seeking help from GP	% (number) of participants undertaking this action	Median (IQR) patient delay in weeks for those undertaking this action	Median (IQR) patient delay in weeks for those not undertaking this action	P value
Bought tablets from the chemist	51.1% (273 out of 534)	6.9 (2-30.7)	4.7 (1.4-23)	p=0.036
Used an ice or heat pack on joint	47.8% (254 out of 531)	7.6 (2-30.3)	4.9 (2-26.1)	p=0.045
Took baths	47.4% (251 out of 529)	6.3 (2-30.4)	5.6 (2-26.1)	p=0.473
Bought joint supports (splints, tubi-grips etc)	37.4% (198 out of 529)	4.4 (2.1-18.6)	5.1 (2-26.9)	p=0.362
Used alternative therapies	25.2% (134 out of 531)	8.3 (2-42.1)	5.3 (2-26.3)	p=0.020
Bought products from a health shop	19.0% (101 out of 532)	5.9 (2-36.3)	5.9 (2-26)	p=0.182
Modified diet	14.4% (76 out of 529)	6 (2.1-35.3)	6.1(2-26.3)	p= 0.183

Used prayer or sought spiritual guidance	8.4% (45 out of 534)	4.4 (2.1-18.6)	6.3 (2-26.9)	p=0.941
Spoke to a pharmacist	7.9% (41 out of 521)	5.9 (2-38.1)	5.9 (2-26.3)	p=0.544

Thirty-seven percent of patients reported looking on the internet (for example visiting the NHS direct website, BUPA website, Arthritis Research UK website and searching for information using search engines such as Google). Patients also reported seeking support via a telephone helpline; 5.7% described calling the NHS direct helpline or another telephone health advice service. 3.7% sought help in the workplace (e.g. from an occupational nurse), 2% of patients went directly to the Accident and Emergency Department and 1% attended an NHS walk-in centre.

Multivariate analysis: Patient delay

The interaction model showed main effects for mode of onset (palindromic vs. non-palindromic; $F=26.65$, $P<0.01$) and rapidity of onset (acute vs. insidious; $F= 65.36$, $P<0.01$). An interaction was found between palindromic onset and gender ($F=45.658$, $P<0.01$); men with a palindromic onset waited significantly longer before seeking help.

Multivariate analysis: General practitioner delay

A main effect was found for ethnicity (F=6.26, P<0.01). Significant differences in general practitioner delay were found between White British and South Asian patients (6.2 weeks (IQR 2-18.6) vs 22 weeks (IQR 6.5-39.8); P<0.001) and between White British and Black British patients (6.2 weeks (IQR 2-18.6) vs 11.1 weeks (IQR 4.3-21.7); P<0.001). No significant difference was found between South Asian and Black British patients (P=1.000).

A main effect was also found for family history (F=5.89, P<0.01); the median general practitioner delay for those with a self-reported family history of RA was 9 weeks (IQR 2.4-25.7), while general practitioner delay for those with no family history was 6.3 weeks (IQR 2.3-19). Interactions at a statistically significant level (<0.01) were not found.

Multivariate analysis: Hospital delay

The original model included main effects and two-way interactions for the following explanatory variables: gender, ethnicity, IMD score, age, education, employment status, mode of onset, rapidity of onset, family onset and RA vs. UA. None of the main effects or interactions (when removed backwards) were significant in predicting the delay between referral and being seen in secondary care.

Discussion

International guidelines recommend that the treatment of RA should begin as soon as possible after the onset of symptoms, ideally aiming to capture patients within the first 3 months following symptom onset. However, this large UK study of delays in access to care for RA patients found that the median patient delay in seeking help at the onset of symptoms was 5.4 weeks, while the median delay between seeing a healthcare professional and being referred was 6.9 weeks. Our study highlights that only 20% of patients were seen within the first 3 months of symptom onset. This appears to be lower than the rate reported in other European countries for example a recent study in Austria reported at 38% of patients were seen within the first 3 months[30]. The present study also found an average delay of 4.7 weeks from referral until the patient was seen by a rheumatologist, similar to figures reported in the NAO report[3]. Unlike our previous study conducted at a single centre in the UK where patient delay accounted for the largest element of delay,[13] we found that GP delay was the largest contributor to overall delay; patient delay was less than we had previously reported in our single centre study.

This research highlights that delays in primary care are long, and a major contributor to overall delays between symptom onset and the first rheumatology visit. General practitioners are faced with a number of barriers to identifying patients with newly presenting RA including the often non-specific nature of symptoms at the earliest stages of RA.[18] Research is underway to define symptom complexes most predictive of RA development in patients with newly presenting musculoskeletal symptoms. For example, a questionnaire has been developed and validated to capture such symptoms in patients

presenting with joint symptoms which by history are suggestive of an underlying inflammatory cause[31] and data are currently being collected from such patients in secondary care based longitudinal observational cohort studies to identify symptoms that may predict RA development. Furthermore an assessment of primary care databases has identified a range of symptoms including hand related joint symptoms, morning stiffness and carpal tunnel syndrome type symptoms as being ones with which patients frequently present to the GP prior to the point at which the GP refers the patient to a Rheumatologist or records a diagnosis of RA [32] It is likely that a combination of education, and evidence based referral algorithms, will be needed to ensure that suspected cases are referred early. For example, in Fife, Scotland GPs did not have access to rheumatoid factor testing during the course of our study, and used guidelines with pictorial representations to help identify early synovitis (personal communication Dr Helen Harris). Fife was a participating centre in this study, and was found to have the lowest GP referral time of all centres surveyed. Furthermore, facilitating access to secondary care, for example through the establishment of rapid assessment clinics whose main aim is to identify whether the patient does or does not have synovitis have been shown to significantly reduce delays in the assessment of patients.[33] A limitation of our research is that the study was not able to assess regional differences across NHS Trusts. A study comparing delays and referral patterns between hospitals with local policies and practices which may influence the time between onset and first consultation would be useful and an international study would be particularly helpful. In addition, this study did not examine the distances between patients' homes and their local GP surgeries, and hospital and so we were unable to assess whether physical distance between the patient's home and the GP surgery or hospital influenced delay.

A number of factors were found to influence GP delay including ethnicity. Studies in the field of oncology have also found that people from ethnic minority backgrounds face longer GP delays.[34;35] In the context of RA it is possible that the early symptomatology of patients from ethnic minority backgrounds is different from, and less typical of RA than that of, patients of white British background, thus making recognition more challenging for GPs. Data certainly exist that the clinical phenotype of established RA differs in patients of South Asian origin compared with patients of White British origin,[36] though data relating the clinical presentations of RA in these groups are lacking. Furthermore, it is unclear why a self-reported family history of RA would be associated with longer delays although it is important to recognise that GPs may not have elicited this information from the patient.[37] Qualitative approaches may be helpful to address some of these issues in the future.

Previous qualitative studies and a meta-synthesis have identified barriers to help seeking at the onset of RA.[37-43] The present study identifies that before seeking formal medical attention, people experiencing the early symptoms of RA seek information and help from a number of alternative sources and often self-medicate. We identified that buying tablets from a pharmacy, and using heat or ice on joints was significantly associated with longer patient delays. This finding highlights that some self-management behaviours, particularly those linked to accessing pharmacy services can negatively impact on the time it takes to seek help; this needs further exploration. Factors previously suggested to be associated with delays in GP consultation included an insidious onset of mild symptoms and a lack of knowledge about RA, personal susceptibility to RA and the availability of treatments to slow disease progression. In our national sample 64.1% of people describe an insidious onset of RA, and 42.8% describe a palindromic onset of RA. Therefore, majority large proportion of

patients surveyed experienced a slow and / or intermittent onset of their inflammatory joint symptoms. Our quantitative data are thus consistent with results from qualitative studies, demonstrating that the mode and rapidity of onset of symptoms is significantly associated with patient delays.

This study has a number of limitations. Firstly, the interval between first consultation with a Rheumatologist and initiation of disease modifying anti-rheumatic drug (DMARD) treatment was not measured. Any additional delay in commencing DMARD treatment will negatively impact the patient and variables associated with delays at this level should be assessed in future studies. Secondly, during the course of this study a number of guidelines related to RA management were published which may have influenced practice, and patterns of referral. We were not able to explore the relationships between the availability / local adoption of guidelines and delays in the assessment of patients. Future investigation should assess the impact of policy changes on patterns of help-seeking, referral and assessment. Thirdly, the rheumatology centres participating in this study were self-selecting, therefore, there may be biases in the characteristics of the rheumatology centres which participated in this study. For example, the participating rheumatology units may have had a particular interest in early arthritis. Only a study which recruited consecutive patients from all rheumatology units across the UK would be able to provide a truly national picture. Fourthly, whilst we were able to document the length of delay at a primary care level there were important variables which may have influenced this delay which we did not record and so were unable to explore. For example it would have been helpful have access to results tests performed in primary care to assess whether levels of inflammatory markers or RA related autoantibodies measured in primary care influenced the rapidity of referral from primary care. Indeed a recent quantitative survey of GPs' anticipated actions in primary care

when dealing with patients with suspected RA suggest that results of these tests may influence GP behaviours[44]. Future research should address this. Similarly, a number of secondary care related variables may have influenced the extent of secondary care delay including the number of rheumatologists at each Trust, whether a dedicated early arthritis clinic was in place and approaches taken to the triage of referrals. Data relating to these variables were not collected though future work addressing issues of delay should address these important issues. Fifthly, data relating to the dates of onset of symptoms and initial GP consultation were gathered from patients' histories, and therefore relied on patient recollection with a possible associated error. However, a previous study addressing delays in the assessment of patients with RA, compared patient accounts of their journeys to first rheumatology consultation against medical records and highlighted the accuracy of patient recollection in relation to dates found to be documented in primary care records[45]. This, to some extent, validates our approach of using patient memory to define the dates of symptom onset and initial GP presentation. An alternative approach would be a longitudinal observational study in the general population to track the development of symptoms and the relationship between that and GP consultation, GP referral and secondary care assessment. A challenge with this approach is the low incidence of RA and thus the requirement for a very large sample size. One could potentially enrich the population for RA risk by, for example, following individuals who are at increased risk of RA (e.g. the first degree relatives of patients with RA). However, one of the challenges with this strategy is that simply being involved in such a study may influence subsequent patient and GP behaviour.

Whilst delays in primary care are the largest contributor to overall delay, patient delay and hospital delay represent important components. This study found that the nature of symptoms onset influenced how quickly patients with RA sought help, suggesting that those with an acute onset of persistent symptoms seek help faster than those with insidious and palindromic onsets. Interventions to encourage rapid help seeking should consider highlighting the frequently insidious onset of RA to members of the public stressing that help should be sought even when symptoms are mild. However, even those with a rapid onset of persistent symptoms often delayed for prolonged periods before seeking help. We have previously shown that members of the public view musculoskeletal symptoms, even those with clear inflammatory features, as less worrisome and less requiring rapid assessment as compared with symptoms of other common diseases such as ischaemic type chest pain or bowel disturbance with associated rectal blood loss[46]. Enhanced public education to highlight the significance of inflammatory type musculoskeletal symptoms is thus likely to be needed. Interventions at multiple levels, including at the levels of the public, the services which members of the public consult after the onset of symptoms (e.g. pharmacies), primary care and secondary care will be needed to reduce overall delays in access to appropriate specialists.

Competing interests

No competing Interest:

Contributorship

RJS, CJ, SHM, CDM, KS, RH, CD, PK and KR made substantial contributions to the conception or design of the work. The acquisition of data was undertaken by RJS, KR, PK and CD. RJS, CJ and SHM facilitated patient and public involvement in the design, delivery and interpretation of this study. The analysis and interpretation of data were undertaken by RJS, PN and KR. RJS, PN CJ, SHM, CDM, KS, RH, CD, PK and KR were involved in drafting the work and revising it critically for important intellectual content. RJS, CJ, SHM, CDM, KS, RH, CD, PK and KR gave final approval of the version published. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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informed consent. Data was stored in a secure location and protected by multiple security systems.

Data sharing statement

Data are available upon request from the corresponding author.

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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation		
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Yes	(Page 1)
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Yes	(page 4)
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported		Yes (pages 5-7)
Objectives	3	State specific objectives, including any prespecified hypotheses		Yes (pages 6-7)
Methods				
Study design	4	Present key elements of study design early in the paper		Yes (page 1, and page 7)
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection		Yes (page 7- 9)
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants		Cross-sectional study – Yes (Page 7)
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case		
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable		Yes (page 7-8)
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group		*Yes (page 7-8, also see table 1)*
Bias	9	Describe any efforts to address potential sources of bias		Yes (Pages 17-22)
Study size	10	Explain how the study size was arrived at		N/A
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why		Yes (page 10)
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding		Yes (page 10)

(*b*) Describe any methods used to examine subgroups and interactions	Yes
(*c*) Explain how missing data were addressed	
(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	N/A
€ Describe any sensitivity analyses	

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Yes (pages 17-18)
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Yes (pages 17-18)
		(b) Indicate number of participants with missing data for each variable of interest	Yes (table 1)
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	*N/A*
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	*N/A*
		Cross-sectional study—Report numbers of outcome events or summary measures	*Yes*
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	N/A
		(*b*) Report category boundaries when continuous variables were categorized	Yes (pages 17-18)
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	Yes (Page 22)
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Yes (page 20)
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Yes (page 20-22)
Generalisability	21	Discuss the generalisability (external validity) of the study results	Yes (page 22)
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Yes (page 25)

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely

available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Delays between the onset of symptoms and first rheumatology consultation in patients with rheumatoid arthritis in the UK: an observational study

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Keywords:	RHEUMATOLOGY, access to care, help seeking, health service research, rheumatoid arthritis

Title: Delays between the onset of symptoms and first rheumatology consultation in patients with rheumatoid arthritis in the UK: an observational study

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Keywords

Rheumatoid arthritis; patient delay; Primary care delay; help-seeking; access to care;

Strengths and limitations of this study.

A key strength of this study is that it surveyed a large sample of patients with new onset rheumatoid arthritis.

Participants were recruited from multiple NHS Trusts in the UK to identified delays in access to care.

Data on delay timepoints, demographic characteristics and consultation behaviour were gathered from multiple sources including patient self-report, healthcare professionals assessment and referral letters.

Limitations include the fact that data were collected at the point of diagnosis and information regarding key dates (in particular the onset of symptoms and presentation to primary care) were reliant on patient recall.

An additional limitation was that the interval between first consultation with a Rheumatologist and initiation of treatment was not measured.

Abstract

Objective: To investigate delays from symptom onset to rheumatology assessment for patients with a new onset of rheumatoid arthritis (RA) or unclassified arthritis.

Methods: Newly presenting adults with either RA or unclassified arthritis were recruited from rheumatology clinics. Data on the length of time between symptom onset and first seeing a GP (patient delay), between first seeing a GP and being referred to a rheumatologist (general practitioner delay) and being seen by a rheumatologist following referral (hospital delay) were captured.

Results: 822 patients participated (563 female, mean age 55 years). The median time between symptom onset and seeing a rheumatologist was 27.2 weeks (IQR 14.1–66 weeks); only 20% of patients were seen within the first 3 months following symptom onset. The median patient delay was 5.4 weeks (IQR 1.4-26.3 weeks). Patients who purchased over the counter medications or used ice/heat packs took longer to seek help than those who did not. In addition, those with a palindromic or an insidious symptom onset delayed for longer than those with a non-palindromic or acute onset. The median general practitioner delay was 6.9 weeks (IQR 2.3–20.3 weeks). Patients made a mean of 4 GP visits before being referred. The median hospital delay was 4.7 weeks (IQR 2.9–7.5 weeks).

Conclusion: This study identified delays at all levels in the pathway towards assessment by a Rheumatologist. However, delays in primary care were particularly long. Patient delay was driven by the nature of symptom onset. Complex multi-faceted interventions to promote rapid help seeking and to facilitate prompt onward referral from primary care should be developed.

Introduction:

Rheumatoid arthritis (RA) is a chronic inflammatory disease affecting approximately 1% of the population.[1;2] Rheumatoid arthritis is associated with significant morbidity in large part as a consequence of extra-articular co-morbidities associated with systemic inflammation. In the UK it has been estimated that RA costs the NHS around £560 million per year and that additional costs to the economy of sick leave and work-related disability total £1.8 billion per year.[3] The first three months following the onset of RA symptoms represents an important therapeutic window.[4] Treatment during this phase improves long-term clinical outcomes, increasing the proportion of patients whose disease enters remission, reducing RA related joint damage and reducing the eventual need for joint replacement surgery.[5-10] Therefore, it is vital that patients are seen by Rheumatologists rapidly following the onset of RA symptoms to allow the rapid introduction of disease modifying anti-rheumatic drug treatment. However, despite increased recognition of the benefits of early treatment there remains considerable delay between symptom onset and the initiation of therapy.[11-13] Indeed a report by the UK's National Audit Office (NAO) in 2009 estimated that only 10% of patients with RA were treated within three months of symptom onset. The NAO's modelling suggested significant financial benefits for the broader economy and quality of life benefits for the individual if the proportion of patients treated earlier was increased.[3]

The patient's pathway to care can be delayed for a number of reasons, including delays on the part of the patient in recognising the significance of the early symptoms of RA.[14-16] Recent

research has linked patients' perceptions of RA and coping styles to the length of time taken to seek help.[17] Before seeking medical help from a physician, patients may seek help from a range of services including complementary therapists, pharmacists and telephone and on-line services. However, the use of these services at the onset of inflammatory arthritis has not been fully explored. Primary healthcare professionals often find the early symptoms of RA difficult to distinguish from those of other rheumatic diseases, making timely and appropriate referrals to rheumatologists challenging.[18;19] There may thus be delays in healthcare professionals making a referral to a Rheumatologist and also in assessment at the secondary care level, contributing further to the delay in making a diagnosis and commencing appropriate therapy.

Several studies conducted across a range of countries have shown long delays between the onset of symptoms and a patient's first consultation with a rheumatologist.[20-23] However, data related to lengths of time between the onset of inflammatory musculoskeletal symptoms and first seeing a GP, between first seeing a GP and being referred to a rheumatologist and being seen by a rheumatologist following referral were not available across multiple NHS Trusts in multiple regions of the UK at the time of this study.

Aim

The aim of this study was to investigate the extents of delay in assessment of patients with RA and unclassified arthritis. Specifically the study assessed extents of delay at the level of the patient in seeking help from the general practitioner, the general practitioner in referring to a Rheumatologist and the Rheumatologist in assessing the patient following referral. The relationships between extents of delay and clinical and demographic variables

were explored and data captured relating to sources of information, help and advice utilized by patients prior to GP consultation.

Methods

A questionnaire based survey of consecutively presenting patients with a new onset of RA or unclassified inflammatory arthritis was undertaken in England and Scotland. Networks such as the Early Rheumatoid Arthritis Network[24] and the National Institute for Health Research Clinical Research Network[25] were used identify Rheumatology centres to participate in this study. RJS also promoted the study during abstract presentations at British Society for Rheumatology meetings.

Data were collected from Rheumatology departments in 34 NHS Trusts. Rheumatology departments were secondary care based, although one rheumatology department (Sandwell and West Birmingham Hospitals) operated clinics in both hospital and community settings. Eligible patients were recruited on their first or second visit to the rheumatology department following a primary care referral (data were not collected on the numbers of patients whose data were collected at their first visit or at their second visit). Rheumatogists were asked to approach consecutively presenting patients who met the eligibility criteria. Eligible patients were newly referred adults (aged ≥ 18 years) with clinically apparent synovial swelling of one or more joints who had either a new onset of RA (according to 2010 ACR / EULAR criteria [26]) or unclassified arthritis (UA; defined as a failure to fulfil classification criteria for another inflammatory rheumatic disease). Patients with UA were recruited, as in many cases patients with UA at initial secondary care assessment progress to RA over time.[27]

Data were collected using two questionnaires (available from the corresponding author on request). First, following consent, the recruiting healthcare professional, with the patient present, completed a questionnaire that captured data on extents of delays between [1] symptom onset and seeing a healthcare professional (from herein referred to as 'patient delay', these data was gathered from the patient's account by the recruiting healthcare professional), [2] seeing a general practitioner and being referred to a rheumatologist (from herein referred to as 'general practitioner e delay', these data was gathered from the patient's account by the recruiting healthcare professional), and [3] being referred to a rheumatologist and seeing a rheumatologist (from herein referred to as 'hospital delay', these data were gathered from referral letters and hospital notes). Data were also gathered on [1] demographic variables including the patient's age, gender, education, employment status and postcode; deprivation ranks were calculated from postcode data using Geoconvert 2010 which produced an Index of Multiple Deprivation (IMD) score,[28] [2] clinical variables including the mode of symptom onset (palindromic (defined as intermittent symptoms) vs. non-palindromic (defined as persistent symptoms)), rapidity of symptom onset (acute vs. insidious; an acute onset was typically viewed as an onset of symptoms which came on rapidly over 24-48 hours), duration of morning stiffness, swollen and tender joint counts, Disease Activity Score 28 (DAS28) and fulfilment of 2010 ACR/EULAR criteria for classification of RA[26].

In addition, via a separate questionnaire that patients completed by themselves, patients provided data on actions taken in relation to their symptoms prior to seeking help from primary care . The variables captured were informed by previous qualitative research,

including patient interviews and interviews with healthcare professionals. In addition, we had input from Patient Research Partners and the questions asked were validated and assessed for reliability[29].

Patient and Public Involvement

Patient and public involvement was an important element of this study. Patient representatives from Sandwell and West Birmingham Hospitals NHS Trust were involved in the study design, advised on the content of patient facing materials including participant information sheets and consent forms and the content of questionnaires including questions related to actions taken by patients prior to consulting their GPs. Patients were members of the Project Management Group reviewing study recruitment and supporting the Group in developing approaches to ensure that recruitment proceeded to time and target

Analysis

To ensure that the data met parametric assumptions, the distribution and levels of multicollinearity between variables were checked. Data on patient delays, general practitioner delays and hospital delays were not normally distributed, therefore, log values of these delay data were created to generate normally distributed variables.

For each of the outcomes patient delay, general practitioner delay and hospital delay a general linear model was used with main effects and two-way interactions for the following explanatory variables: gender, ethnicity, IMD score, age, education, employment status, mode of onset, rapidity of onset, patient reported family history of RA and RA vs. UA. For

each outcome any two-way interactions which were not significant were removed in a backwards stepwise fashion, with the pairings with the highest p values being removed first. All main effects were retained, so that the final model for each outcome included all ten explanatory variables and any significant two-way interactions ($p<0.01$). All significant main effects and interactions are reported in the Results section.

Results

1. Participant characteristics

Data were collected from 856 patients between 2011 and 2014. Patients were withdrawn from the study due to incomplete data (21 cases) and ineligibility (13 cases in whom there was no clinical synovitis reported at recruitment). Data were thus analysed from 822 patients of whom 68.5% were female with a mean age of 55 years. Characteristics of patients are presented in table 1.

Table 1: *Demographic and disease related characteristics of patients. Data are presented as either percentage (number) or median (IQR) as appropriate. Tender joint count is out of 42 joints (10 PIP, 10 MCP, 2 wrist, 2 elbow, 2 shoulder, 2 hip, 2 knee, 2 ankle, 10 MTP). Swollen joint count is out of 40 joints (10 PIP, 10 MCP, 2 wrist, 2 elbow, 2 shoulder, 2 knee, 2 ankle, 10 MTP).*

Female	68.5% (563)
Age, years	57 (45-67)
Diagnosis of RA	73% (603)
Ethnicity: Black British	6.0% (49)

South Asian White British Other	7.7% (63) 84.9% (698) 1.5% (12)
Self-reported family history of RA	34.9% (287)
Palindromic onset	42.8% (352)
Acute onset	35.9% (295)
Duration of morning stiffness, minutes	60 (10-120)
DAS28	4.88 (3.98 -5.80)
HAQ	1.13 (0.50-1.73)
Tender joint count	9 (4-18)
Swollen joint count	5 (2-10)

2. *Intervals between symptom onset and first rheumatology consultation*

Overall the median time between symptom onset and seeing a rheumatologist was 27.2 weeks (IQR 14.1 – 66 weeks); only 20% of patients were seen within the first 3 months following symptom onset. The median patient delay was 5.4 weeks (IQR 1.4-26.3 weeks). The median general practitioner delay was 6.9 weeks (IQR 2.3–20.3 weeks) with patients making a mean of 4 GP visits before being referred. The median hospital delay was 4.7 weeks (IQR 2.9–7.5 weeks).

Palindromic onset is defined as intermittent symptoms, while non-palindromic is defined as persistent symptoms. Acute onset defined as symptoms which came on rapidly over 24-48 hours, while insidious onset is defined as symptoms which developed slowly over an extended period of time. Patients with a palindromic symptom onset had a significantly longer patient delay than those with a non-palindromic onset (9.3 weeks (IQR 2-43 weeks) vs 4.3 weeks (IQR 1-17 weeks); p<0.001, t-test). Furthermore, those with an acute symptom onset had significantly shorter patient delays than those with an insidious symptoms onset (2.4 weeks (IQR 1 - 6.6 weeks) vs 11.1 weeks (IQR 4-44 weeks; p<0.001, t-test).

Resources used before seeking help from primary care

Patients reported taking a range of actions in relation to their symptoms before seeking help from their GP and in some cases these actions were associated with longer delays in GP consultation (see table 2). Most often patients reported purchasing tablets from 'the chemist', although only a small proportion actually reported speaking to a pharmacist. Other actions reported by patients included applying heat or cold packs to joints or buying joint supports.

Table 2. *Actions taken by patients with inflammatory arthritis before seeking help from their GP with comparison made for patient delay between those who did and did not undertake this action using independent t-tests; * P value for comparison of those who did and did not undertake this action.*

Actions taken before seeking help from GP	% (number) of participants undertaking this action	Median (IQR) patient delay in weeks for those undertaking this action	Median (IQR) patient delay in weeks for those not undertaking this action	P value
Bought tablets from the chemist	51.1% (273 out of 534)	6.9 (2-30.7)	4.7 (1.4-23)	p=0.036
Used an ice or heat pack on joint	47.8% (254 out of 531)	7.6 (2-30.3)	4.9 (2-26.1)	p=0.045
Took baths	47.4% (251 out of 529)	6.3 (2-30.4)	5.6 (2-26.1)	p=0.473
Bought joint supports (splints, tubi-grips etc)	37.4% (198 out of 529)	4.4 (2.1-18.6)	5.1 (2-26.9)	p=0.362
Used alternative therapies	25.2% (134 out of 531)	8.3 (2-42.1)	5.3 (2-26.3)	p=0.020
Bought products from a health shop	19.0% (101 out of 532)	5.9 (2-36.3)	5.9 (2-26)	p=0.182
Modified diet	14.4% (76 out of 529)	6 (2.1-35.3)	6.1(2-26.3)	p= 0.183

Used prayer or sought spiritual guidance	8.4% (45 out of 534)	4.4 (2.1-18.6)	6.3 (2-26.9)	p=0.941
Spoke to a pharmacist	7.9% (41 out of 521)	5.9 (2-38.1)	5.9 (2-26.3)	p=0.544

Thirty-seven percent of patients reported looking on the internet (for example visiting the NHS direct website, BUPA website, Arthritis Research UK website and searching for information using search engines such as Google). Patients also reported seeking support via a telephone helpline; 5.7% described calling the NHS direct helpline or another telephone health advice service. 3.7% sought help in the workplace (e.g. from an occupational nurse), 2% of patients went directly to the Accident and Emergency Department and 1% attended an NHS walk-in centre.

Multivariate analysis: Patient delay

The interaction model showed main effects for mode of onset (palindromic vs. non-palindromic; $F=26.65$, $P<0.01$) and rapidity of onset (acute vs. insidious; $F= 65.36$, $P<0.01$). An interaction was found between palindromic onset and gender ($F=45.658$, $P<0.01$); men with a palindromic onset waited significantly longer before seeking help.

Multivariate analysis: General practitioner delay

A main effect was found for ethnicity (F=6.26, P<0.01). Significant differences in general practitioner delay were found between White British and South Asian patients (6.2 weeks (IQR 2-18.6) vs 22 weeks (IQR 6.5-39.8); P<0.001) and between White British and Black British patients (6.2 weeks (IQR 2-18.6) vs 11.1 weeks (IQR 4.3-21.7); P<0.001). No significant difference was found between South Asian and Black British patients (P=1.000).

A main effect was also found for family history (F=5.89, P<0.01); the median general practitioner delay for those with a self-reported family history of RA was 9 weeks (IQR 2.4-25.7), while general practitioner delay for those with no family history was 6.3 weeks (IQR 2.3-19). Interactions at a statistically significant level (<0.01) were not found.

Multivariate analysis: Hospital delay

The original model included main effects and two-way interactions for the following explanatory variables: gender, ethnicity, IMD score, age, education, employment status, mode of onset, rapidity of onset, family onset and RA vs. UA. None of the main effects or interactions (when removed backwards) were significant in predicting the delay between referral and being seen in secondary care.

Discussion

International guidelines recommend that the treatment of RA should begin as soon as possible after the onset of symptoms, ideally aiming to capture patients within the first 3 months following symptom onset. However, this large UK study of delays in access to care for RA patients found that the median patient delay in seeking help at the onset of symptoms was 5.4 weeks, while the median delay between seeing a healthcare professional and being referred was 6.9 weeks. Our study highlights that only 20% of patients were seen within the first 3 months of symptom onset. This appears to be lower than the rate reported in other European countries for example a recent study in Austria reported at 38% of patients were seen within the first 3 months[30]. The present study also found an average delay of 4.7 weeks from referral until the patient was seen by a rheumatologist, similar to figures reported in the NAO report[3]. Unlike our previous study conducted at a single centre in the UK where patient delay accounted for the largest element of delay,[13] we found that GP delay was the largest contributor to overall delay; patient delay was less than we had previously reported in our single centre study.

This research highlights that delays in primary care are long, and a major contributor to overall delays between symptom onset and the first rheumatology visit. General practitioners are faced with a number of barriers to identifying patients with newly presenting RA including the often non-specific nature of symptoms at the earliest stages of RA.[18] Research is underway to define symptom complexes most predictive of RA development in patients with newly presenting musculoskeletal symptoms. For example, a questionnaire has been developed and validated to capture such symptoms in patients

presenting with joint symptoms which by history are suggestive of an underlying inflammatory cause[31] and data are currently being collected from such patients in secondary care based longitudinal observational cohort studies to identify symptoms that may predict RA development. Furthermore an assessment of primary care databases has identified a range of symptoms including hand related joint symptoms, morning stiffness and carpal tunnel syndrome type symptoms as being ones with which patients frequently present to the GP prior to the point at which the GP refers the patient to a Rheumatologist or records a diagnosis of RA [32] It is likely that a combination of education, and evidence based referral algorithms, will be needed to ensure that suspected cases are referred early. For example, in Fife, Scotland GPs did not have access to rheumatoid factor testing during the course of our study, and used guidelines with pictorial representations to help identify early synovitis (personal communication Dr Helen Harris). Fife was a participating centre in this study, and was found to have the lowest GP referral time of all centres surveyed. Furthermore, facilitating access to secondary care, for example through the establishment of rapid assessment clinics whose main aim is to identify whether the patient does or does not have synovitis have been shown to significantly reduce delays in the assessment of patients.[33] A limitation of our research is that the study was not able to assess regional differences across NHS Trusts. A study comparing delays and referral patterns between hospitals with local policies and practices which may influence the time between onset and first consultation would be useful and an international study would be particularly helpful. In addition, this study did not examine the distances between patients' homes and their local GP surgeries, and hospital and so we were unable to assess whether physical distance between the patient's home and the GP surgery or hospital influenced delay.

A number of factors were found to influence GP delay including ethnicity. Studies in the field of oncology have also found that people from ethnic minority backgrounds face longer GP delays.[34;35] In the context of RA it is possible that the early symptomatology of patients from ethnic minority backgrounds is different from, and less typical of RA than that of, patients of white British background, thus making recognition more challenging for GPs. Data certainly exist that the clinical phenotype of established RA differs in patients of South Asian origin compared with patients of White British origin,[36] though data relating the clinical presentations of RA in these groups are lacking. Furthermore, it is unclear why a self-reported family history of RA would be associated with longer delays although it is important to recognise that GPs may not have elicited this information from the patient.[37] Qualitative approaches may be helpful to address some of these issues in the future.

Previous qualitative studies and a meta-synthesis have identified barriers to help seeking at the onset of RA.[37-43] The present study identifies that before seeking formal medical attention, people experiencing the early symptoms of RA seek information and help from a number of alternative sources and often self-medicate. We identified that buying tablets from a pharmacy, and using heat or ice on joints was significantly associated with longer patient delays. This finding highlights that some self-management behaviours, particularly those linked to accessing pharmacy services can negatively impact on the time it takes to seek help; this needs further exploration. Factors previously suggested to be associated with delays in GP consultation included an insidious onset of mild symptoms and a lack of knowledge about RA, personal susceptibility to RA and the availability of treatments to slow disease progression. In our national sample 64.1% of people describe an insidious onset of RA, and 42.8% describe a palindromic onset of RA. Therefore, majority large proportion of

patients surveyed experienced a slow and / or intermittent onset of their inflammatory joint symptoms. Our quantitative data are thus consistent with results from qualitative studies, demonstrating that the mode and rapidity of onset of symptoms is significantly associated with patient delays.

This study has a number of limitations. Firstly, the interval between first consultation with a Rheumatologist and initiation of disease modifying anti-rheumatic drug (DMARD) treatment was not measured. Any additional delay in commencing DMARD treatment will negatively impact the patient and variables associated with delays at this level should be assessed in future studies. Secondly, during the course of this study a number of guidelines related to RA management were published which may have influenced practice, and patterns of referral. We were not able to explore the relationships between the availability / local adoption of guidelines and delays in the assessment of patients. Future investigation should assess the impact of policy changes on patterns of help-seeking, referral and assessment. Thirdly, the rheumatology centres participating in this study were self-selecting, therefore, there may be biases in the characteristics of the rheumatology centres which participated in this study. For example, the participating rheumatology units may have had a particular interest in early arthritis. Only a study which recruited consecutive patients from all rheumatology units across the UK would be able to provide a truly national picture. Fourthly, whilst we were able to document the length of delay at a primary care level there were important variables which may have influenced this delay which we did not record and so were unable to explore. For example it would have been helpful have access to results tests performed in primary care to assess whether levels of inflammatory markers or RA related autoantibodies measured in primary care influenced the rapidity of referral from primary care. Indeed a recent quantitative survey of GPs' anticipated actions in primary care

when dealing with patients with suspected RA suggest that results of these tests may influence GP behaviours[44]. Future research should address this. Similarly, a number of secondary care related variables may have influenced the extent of secondary care delay including the number of rheumatologists at each Trust, whether a dedicated early arthritis clinic was in place and approaches taken to the triage of referrals. Data relating to these variables were not collected though future work addressing issues of delay should address these important issues. Fifthly, data relating to the dates of onset of symptoms and initial GP consultation were gathered from patients' histories, and therefore relied on patient recollection with a possible associated error. However, a previous study addressing delays in the assessment of patients with RA, compared patient accounts of their journeys to first rheumatology consultation against medical records and highlighted the accuracy of patient recollection in relation to dates found to be documented in primary care records[45]. This, to some extent, validates our approach of using patient memory to define the dates of symptom onset and initial GP presentation. An alternative approach would be a longitudinal observational study in the general population to track the development of symptoms and the relationship between that and GP consultation, GP referral and secondary care assessment. A challenge with this approach is the low incidence of RA and thus the requirement for a very large sample size. One could potentially enrich the population for RA risk by, for example, following individuals who are at increased risk of RA (e.g. the first degree relatives of patients with RA). However, one of the challenges with this strategy is that simply being involved in such a study may influence subsequent patient and GP behaviour.

Whilst delays in primary care are the largest contributor to overall delay, patient delay and hospital delay represent important components. This study found that the nature of symptoms onset influenced how quickly patients with RA sought help, suggesting that those with an acute onset of persistent symptoms seek help faster than those with insidious and palindromic onsets. Interventions to encourage rapid help seeking should consider highlighting the frequently insidious onset of RA to members of the public stressing that help should be sought even when symptoms are mild. However, even those with a rapid onset of persistent symptoms often delayed for prolonged periods before seeking help. We have previously shown that members of the public view musculoskeletal symptoms, even those with clear inflammatory features, as less worrisome and less requiring rapid assessment as compared with symptoms of other common diseases such as ischaemic type chest pain or bowel disturbance with associated rectal blood loss[46]. Enhanced public education to highlight the significance of inflammatory type musculoskeletal symptoms is thus likely to be needed. Interventions at multiple levels, including at the levels of the public, the services which members of the public consult after the onset of symptoms (e.g. pharmacies), primary care and secondary care will be needed to reduce overall delays in access to appropriate specialists.

Competing interests

No competing Interest:

Contributorship

RJS, CJ, SHM, CDM, KS, RH, CD, PK and KR made substantial contributions to the conception or design of the work. The acquisition of data was undertaken by RJS, KR, PK and CD. RJS, CJ and SHM facilitated patient and public involvement in the design, delivery and interpretation of this study. The analysis and interpretation of data were undertaken by RJS, PN and KR. RJS, PN CJ, SHM, CDM, KS, RH, CD, PK and KR were involved in drafting the work and revising it critically for important intellectual content. RJS, CJ, SHM, CDM, KS, RH, CD, PK and KR gave final approval of the version published. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Ethical approval information Ethical approval was obtained from South Birmingham Research Ethics Committee (reference no. 10/H1207/98) and all participants gave written

informed consent. Data was stored in a secure location and protected by multiple security systems.

Data sharing statement

Data are available upon request from the corresponding author.

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STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation		
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	Yes	(Page 1)
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	Yes	(page 4)
Introduction				
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported		Yes (pages 5-7)
Objectives	3	State specific objectives, including any prespecified hypotheses		Yes (pages 6-7)
Methods				
Study design	4	Present key elements of study design early in the paper		Yes (page 1, and page 7)
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection		Yes (page 7- 9)
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants		Cross-sectional study – Yes (Page 7)
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case		
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable		Yes (page 7-8)
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group		*Yes (page 7-8, also see table 1)*
Bias	9	Describe any efforts to address potential sources of bias		Yes (Pages 17-22)
Study size	10	Explain how the study size was arrived at		N/A
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why		Yes (page 10)
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding		Yes (page 10)

(*b*) Describe any methods used to examine subgroups and interactions	Yes
(*c*) Explain how missing data were addressed	
(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	N/A
€ Describe any sensitivity analyses	

Continued on next page

Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Yes (pages 17-18)
		(b) Give reasons for non-participation at each stage	N/A
		(c) Consider use of a flow diagram	N/A
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Yes (pages 17-18)
		(b) Indicate number of participants with missing data for each variable of interest	Yes (table 1)
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	*N/A*
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	*N/A*
		Cross-sectional study—Report numbers of outcome events or summary measures	*Yes*
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	N/A
		(*b*) Report category boundaries when continuous variables were categorized	Yes (pages 17-18)
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	N/A
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	N/A
Discussion			
Key results	18	Summarise key results with reference to study objectives	Yes (Page 22)
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	Yes (page 20)
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	Yes (page 20-22)
Generalisability	21	Discuss the generalisability (external validity) of the study results	Yes (page 22)
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	Yes (page 25)

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely

available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.