Symptoms associated with inflammatory arthritis are common and persistent in the primary care population

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Symptoms associated with inflammatory arthritis are common and persistent in the primary care population: results from the Joint Symptoms Survey.

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Abstract

Objectives: To describe the prevalence of self-reported inflammatory joint symptoms, such as joint pain, stiffness and swelling in UK primary care patients consulting for both musculoskeletal (MSK) and non-musculoskeletal (non-MSK) complaints.

Methods: A Joint Symptoms questionnaire survey was sent to 10,161 individuals, of whom 5,050 had consulted for MSK problems. These were matched by age, gender and general practice to non-MSK consulters. Participants provided data on relevant symptoms such as joint pain, stiffness and swelling. The prevalence of these symptoms, their severity and impact was compared between MSK and non-MSK consulters.

Results: 4,549 adults responded to the survey (adjusted response 45.8%) of whom 52.3% consulted for a musculoskeletal problem. The mean (SD) age was 61.6 (14.8) years and 58.9% were female. Persistent (on at least half of the days in the last month) inflammatory symptoms were common even in non-MSK consulters, with 42% reporting joint pain, 36% reporting joint stiffness and 18% reporting joint swelling. This is in comparison to 62% reporting joint pain, 50% stiffness and 24% swelling amongst MSK consulters.

Conclusions: Although symptoms such as persistent joint pain, swelling, and stiffness are predictive of inflammatory arthritis, large numbers of people consulting primary care for non-musculoskeletal reasons report these symptoms when asked by questionnaire. This compounds the challenges of diagnosing inflammatory arthritis in a non-specialist setting where new approaches are needed to ensure accurate, early diagnosis, facilitating a treat-to-target approach.

Keywords: inflammatory arthritis, joint pain, joint swelling, primary care

Key messages:

- Primary care consulters commonly report inflammatory symptoms such as persistent joint pain, stiffness and swelling.
- This makes accurate recognition of inflammatory arthritis challenging for primary care.

- Studies are needed to identify those at highest risk to facilitate early referral and diagnosis.

Introduction

The early treatment of inflammatory arthritis is key to improving clinical outcomes with evidence that prompt DMARD use is both clinically [1] and cost effective [2] and is emphasised in international guidelines for early arthritis [3]. Primary care practitioners are vital for the early identification and rapid referral of patients with suspected inflammatory arthritis. Thus the UK National Institute for Health and Care Excellence (NICE) guidelines recommend patients with persistent synovitis are referred within 3 working days [4]. Despite this, data from the Healthcare Quality Improvement Partnership Early Inflammatory Arthritis audit shows referral delays are common with only 20% patients referred within the target. [5]

Reasons for delay are multifactorial. First, GPs lack confidence in identifying synovitis [6]. Second, accurate case ascertainment is challenging. Musculoskeletal (MSK) disorders are very common in primary care (up to one in seven UK consultation)[7]. New diagnoses of RA are rare, with a whole time GP likely to see only one new case of RA a year [8]. Thus recognising RA is challenging for primary care physicians [9]. Studies of primary care records highlight the importance of joint swelling, stiffness and loss of function as symptoms frequently recorded within the primary care record prior to a later diagnosis of inflammatory arthritis [10, 11], although these symptoms such as pain and stiffness are common in conditions such as osteoarthritis and soft-tissue disorders, which are much more likely to be reasons for primary care consultation [7].

Following qualitative work with patients [12] supported as part of the EULAR taskforce, a symptom checklist questionnaire (Symptoms in Persons at Risk of Rheumatoid Arthritis, SPARRA) was derived to assess the presence, severity and impact of common symptoms (such as joint pain, stiffness and swelling) in patients at risk of developing RA [13]. However, to date little is known about how prevalent these symptoms are in the general primary care population. The aim of this study was to describe the prevalence of self-reported joint symptoms, shown to be associated with the development of RA, in primary care patients consulting for both MSK and non-MSK problems.

Methods

Study Design

A cross-sectional Joint Symptoms questionnaire was mailed to adults (age >18 years) registered with one of 56 general practices (GP) within the NIHR Clinical Research Network: West Midlands (CRN: WM), UK. Participating general practices sent a questionnaire to all adults who had consulted in the previous month with an MSK condition and whose records showed they did not have an existing diagnosis of inflammatory arthritis (n=5,050). The same Joint Symptoms questionnaire was also mailed to 5,111 adults matched on age, gender and general practice to the MSK consulters who had consulted and received a Read code for a non-MSK condition in their GP medical record in the same period and whose records also showed they did not have an existing diagnosis of inflammatory arthritis. Those not responding to the initial questionnaire were sent a reminder postcard after 2 weeks and those not responding at 4 weeks were sent a further Joint Symptoms questionnaire.

Questionnaire Data collection

The SPARRA questionnaire collected data on the presence of 13 symptoms including joint pain, joint stiffness and swelling and other early symptoms identified by patients as important, such as fatigue and emotional distress [13]. For each symptom, data were collected on presence of the symptom and number of days over the past month with each symptom (0, 1-5, 6-15 or 16-30). For those reporting one day or greater of a symptom, the severity (none, mild, moderate or severe) and the impact (no impact, small, moderate or large impact) of each symptom on ability to carry out daily activities was assessed.

Participants were also asked to complete an 11-item Early Inflammatory Arthritis (EIA) Detection tool [14,15], which is a binary checklist including joint pain, hand and wrist pain, hand and wrist swelling, early morning stiffness, difficulty making a fist and impact of symptoms. Demographic data, smoking status, and self-reported body mass index (BMI) were also collected in the questionnaire. Ethical approval for the study was obtained from the West Midlands - Edgbaston Research Ethics Committee (15/WM/0034) and all participants provided written informed consent.

Statistical analysis

Responders were compared to non-responders and those excluded (e.g. incorrect address information, dementia) according to age, gender and whether their index consultation was for an MSK condition. The sample of responders was summarised using frequencies and percentages, and means and standard deviations as appropriate. T-tests and chi-square tests were used to compare continuous and categorical responses, respectively between those whose index consultation was for an MSK or non-MSK condition. Persistent symptoms were defined as symptoms occurring for 16-30 days. The severity (none/mild versus moderate/severe) and impact (none/small versus moderate/large) of each symptom was reported only in those people who reported the presence of the symptom on one or more days. The proportion of people with the persistent symptom triad of joint pain, stiffness and swelling (often considered to be the hallmark of inflammatory arthritis) was calculated in those completing all three items.

The EIA detection tool was first scored as the number of "yes" responses, and second using the weighted scoring algorithm described by Tavares et al [15]. This weighted score was developed to optimally detect inflammatory arthritis within a rheumatology triage setting and includes age, gender, difficulty making a fist, early morning stiffness and patients reporting being told they have RA or psoriasis. A higher score on the EIA, under either scoring mechanism suggests a higher likelihood of inflammatory arthritis. Specifically, for the weighted score, a positive score predicts inflammatory arthritis, whereas a negative score predicts non-inflammatory arthritis [15].

Results

Response Rates and Demographics

4,549 adults responded to the questionnaire (adjusted response, (exclusions removed from denominator) 45.8%) of whom 52.3% (n=2,738) were in the MSK consultation group. Responders were older (mean (SD) (age 61.6 (14.8) years) than non-responders (50.4 (17.0) years) $p<0.0001$) and more likely to have been from the MSK consultation group (responders MSK consultation 2,378 (52.3%) vs non-MSK consultation group 2,564 (47.6%),

p<0.0001) (Table 1). Other than self-reported BMI (where those with an MSK consultation reported a higher BMI), demographic characteristics were similar between MSK and non-MSK consulters. Baseline demographic data are summarised in Table 2.

Joint Pain

Joint pain symptoms were common in both MSK and non-MSK consulters (Table 3), with 81.5% (1,827) of MSK consulters and 65% (1,316) of non-MSK consulters reporting current joint pain. In terms of persistent symptoms, 921 (42%) of non-MSK consulters reported joint pain on more than half of the days in the last month, compared with 62% (1,483) of those consulting for a MSK indication (p<0.001). However, those consulting for an MSK indication were more likely to describe their symptoms as moderate or severe (75% (1,593 patients) vs 62% (1,021 patients)) and more likely to report significant impact on activities of daily living (62% (1,324) vs 44% (728))) than non-MSK consulters.

Joint Swelling

Joint swelling symptoms were reported less frequently, but were still common even in non-MSK consulters with persistent joint swelling (half of days in last month) being reported in 385 (18%) of the non-MSK consulters compared with a quarter of MSK consulters (580, 24%). However, symptoms were more often reported to be moderate or severe and have greater impact in those consulting for an MSK indication. Similar results were seen for joint stiffness, again with greater symptom severity and impact in MSK consulters (Table 3).

Other symptoms such as fatigue and sleep problems were reported more frequently in the MSK consulters than those consulting for non-MSK indications (Table 3). Looking at the symptom triad of joint pain, stiffness and swelling, 266 (14%) of non MSK consulters reported persistent pain, stiffness and swelling compared with 448 (21%) of MSK consulters.

There was significant missing data, especially for some of the less specific symptoms such as numbness and colour change. Whilst in part this may reflect questionnaire fatigue, or people not responding to items they did not consider relevant (which may have occurred especially in those consulting for non-MSK disorders) to account for this we conducted a best-worst/worst-best analysis (as recommended by Jakobsen et al [16]), (Supplementary

Table 1). This highlights that in either scenario there remains a significant symptom burden even in those consulting for non-MSK disorders.

Early Inflammatory Arthritis (EIA) Detection Tool

Using the EIA detection tool, 70.4% (1,460) of non-MSK consulters reported joint pain and 44.7% (929) reported hand and wrist pain. However, the numbers reporting either joint pain (1,920, 83.8%) or hand and wrist pain (1,124, 48.9%) were significantly higher in those consulting for an MSK indication. Even early morning stiffness of over 60 minutes, was reported in almost one quarter of non-MSK consulters, although it was more prevalent in those consulting for an MSK indication (MSK 802 (34.7%) vs. 511 (24.5%) non-MSK). Furthermore, using a weighted score for the EIA detection tool, designed to detect inflammatory arthritis in the triage setting, 1,619 (74%) of the non-MSK consulters had a positive score. However, the majority of symptoms were reported more frequently in those consulting for an MSK indication (Table 4). Both the mean total score and the proportion of people with a positive weighted overall EIA detection score were higher in those consulting for an MSK indication (mean total score 4.13 vs 3.39).

Discussion

Early diagnosis of RA is key to improving outcomes. However, identifying inflammatory arthritis can be challenging for general practitioners given that MSK symptoms are common (even in those not consulting for these problems), whilst new diagnoses of inflammatory arthritis are infrequent. This study highlights that primary care patients, whether consulting for an MSK indication or not, commonly self-report (by questionnaire) symptoms which may be suggestive of inflammatory arthritis. These can include joint pain, stiffness and swelling, with up to 18% of non-MSK consulters reporting persistent joint swelling on half of the days of the last month and 14% reporting persistent pain, stiffness and swelling.

Our results suggest a similar prevalence of symptoms in the MSK consulters (the majority of whom would not be expected to have an inflammatory condition) to patients with clinically suspect arthralgia (ie considered to be at high risk of developing inflammatory arthritis), recruited as part of the original SPARRA study [13], In part, this may reflect differences using

the instrument in a postal questionnaire compared with questionnaire responses obtained within a clinic setting.

The burden of symptoms reported by participants in this study highlight the challenges of successfully implementing public health campaigns designed to raise awareness of early symptoms of RA. Such campaigns aim to encourage people to consult more readily in primary care, but given that (self-reported) inflammatory symptoms are so common and that new cases of RA so infrequent, accurate case ascertainment is difficult. Current UK guidelines [4], which suggest referring any person with suspected persistent synovitis, especially of small joints, urgently to rheumatology and the EULAR early arthritis guidelines which suggest patients with arthritis (any joint swelling, associated with pain or stiffness) should also be referred to, and seen by, a rheumatologist, within six weeks of the onset of symptoms [3] .Thus for primary care, determining which patients are likely to have persistent symptoms (requiring referral), without overwhelming secondary care early arthritis services is challenging, requiring primary care expertise especially in the assessment of synovitis. Previous work with GPs, using a questionnaire survey (n=1338) suggested that the majority (>80% of GPs) agreed that "the earliest phases of RA are difficult to diagnose", and rated themselves as only moderately confident (on a numeric rating scale) at diagnosing RA, with the majority preferring to order additional tests prior to referral [6], in contrast to guideline recommendations [3,4]. This raises further challenges for secondary care to prioritise the right patients for early review. Continuing education for GPs (especially around assessment of synovitis) and audit (and feedback) of referrals to and from secondary care may help address this challenge.

In addition, studies are needed to compare the self-reported and clinical assessment findings especially of joint swelling, within primary care consulters. Given the frequency of inflammatory type MSK symptoms observed in this study, but the small risk of RA, risk prediction models need to be developed for use specifically within primary care populations, as at present data derived from these populations are lacking. Current studies and risk prediction tools focus on people who are anti-CCP antibody positive [17, 18] or involve ultrasound assessment for synovitis [19]. The cost-utility of implementing widespread autoantibody testing in patients with joint symptoms has yet to be established.

There are a number of strengths and limitations which need to be considered when interpreting the results of this study. This is a large unselected cohort of primary care consulters and as such the results are likely to be widely generalizable. Furthermore, joint symptoms were assessed using validated questionnaires including the SPARRA questionnaire [13] and inflammatory arthritis triage tools [14, 15]. However, as expected for a postal questionnaire study there was significant missing data. Whilst the original SPARRA study imputed missing data using pre-agreed definitions [13], the levels of missing data were lower in the original study since the questionnaire was completed within a clinic setting rather than by post. . Also, as expected, levels of missing data were higher in those consulting for non-MSK conditions, as some patients may have felt some of the items were not relevant to them. To account for this we undertook a best/worst case analysis as recommended by Jakobsen [16] and in either case scenario there remains a significant symptom burden.

Furthermore, the GP practices participating in the study were located within the northern region of the CRN:WM, hence the majority of participants resided in North Staffordshire or South Cheshire and reported themselves to be of white ethnicity, limiting the generalisability to populations of other ethnicities. As expected for GP consulters, the population was older and responders were more likely to be female, although this was similar across both MSK and non-MSK consulters.

In conclusion, possible inflammatory arthritis symptoms such as persistent joint pain and swelling are commonly reported within primary care consulters, even those consulting for non-MSK reasons. Further studies are required to determine which patients with symptoms are at highest risk to ensure effective early referral and treatment of patients with RA.

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Table 1: Comparison of responders and non-responders

	Responders (n=4549)	Non-responders/Refusals (n=5390)	Exclusions (n=222)*
Mean age (SD)	61.56 (14.83)	50.42 (17.02)	57.14 (20.38)
Female gender	2678 (58.9)	2936 (54.5)	123 (55.4)
MSK consulter	2378 (52.3)	2564 (47.6)	108 (48.7)

*Exclusions indicates those with incorrect address information or dementia.

Table 2: Baseline demographic and health characteristics in responders with and without an MSK consultation

	MSK Consulters (n=2378)	Non-MSK consulters (n=2171)
Mean age (SD)	61.4 (14.8)	61.7 (14.8)
Female gender	1407 (59.2)	1271 (58.5)
Lives alone	462 (19.8)	433 (20.4)
Marital status		
Married/cohabiting	1685 (72.1)	1520 (71.4)
Divorced/separated	213 (9.1)	201 (9.5)
Widowed	265 (11.3)	246 (11.6)
Single	175 (7.5)	161 (7.6)
Ethnicity		
White British	2275 (97.2)	2073 (97.6)
Other	66 (2.8)	52 (2.5)
Employment status		
Employed	874 (37.6)	789 (37.5)
Retired	1112 (47.8)	1054 (50.1)
Other*	340 (14.6)	261 (12.4)
Smoking status		
Never	1184 (50.4)	1111 (50.1)
Previously	913 (38.9)	834 (39.1)

	Currently	253 (10.8)	189 (8.9)
Frequency of alcohol consumption			
	Daily	221 (9.5)	205 (9.6)
	1-4 times a week	929 (39.8)	874 (41.1)
	1-3 times a month	343 (14.7)	281 (13.2)
	Less than once a month	841 (36.0)	769 (36.1)
BMI (kg/m^2)			
	<25	558 (30.3)	599 (36.3)
	25-29.9	722 (39.3)	645 (39.1)
	30-34.9	376 (20.5)	290 (17.6)
	≥35	183 (10.0)	117 (7.1)

n (%) unless otherwise stated. Other indicates unemployed or seeking work, homemaker or other

Table 3: Prevalence of possible early inflammatory arthritis symptoms in MSK and non-MSK consulters.

Symptom		Symptom duration, n (%)			Symptom severity, n (%)			Symptom impact, n (%)		
		0-15 days	16-30 days	Missing	None/mild	Moderate /severe	Missing	None /small	Moderate /severe	Missing
Joint pain	MSK	805 (33.9)	1483 (62.4)	90 (3.4)	419 (19.7)	1593 (74.8)	117 (505)	735 (34.5)	1324 (62.2)	70 (3.3)
	Non MSK	1117 (51.5)	921 (42.4)	133 (6.1)	540 (32.6)	1021 (61.5)	98 (5.9)	839 (50.6)	728 (43.9)	92 (5.6)
Joint swelling	MSK	1618 (68.0)	580 (24.4)	180 (7.6)	409 (32.7)	719 (57.5)	123 (9.8)	438 (35.0)	692 (55.3)	121 (9.7)
	Non MSK	1580 (72.8)	385 (17.7)	206 (9.5)	370 (39.4)	444 (47.3)	125 (13.3)	426 (45.4)	368 (39.2)	145 (15.4)
Joint stiffness	MSK	1098 (46.2)	1182 (49.7)	98 (4.1)	506 (27.0)	1273 (68.0)	94 (5.0)	744 (39.7)	1060 (56.6)	69 (3.7)
	Non MSK	1257 (57.9)	781 (36.0)	133 (6.1)	536 (37.1)	798 (55.3)	110 (7.6)	746 (51.7)	597 (41.3)	101 (7.0)
Burning in joints	MSK	1802 (75.8)	387 (16.3)	189 (8.0)	314 (30.3)	573 (55.3)	149 (14.4)	395 (38.1)	501 (13.5)	140 (13.5)
	Non MSK	1760 (81.1)	224 (10.3)	187 (8.6)	236 (33.4)	326 (46.1)	145 (20.5)	285 (40.3)	267 (37.8)	155 (21.9)
Tingling in joints	MSK	1876 (78.9)	352 (14.8)	150 (6.3)	477 (41.4)	545 (47.3)	130 (11.3)	620 (53.8)	400 (34.7)	132 (11.5)
	Non MSK	1763 (81.2)	231 (10.6)	177 (8.2)	432 (48.4)	340 (38.1)	121 (13.6)	513 (57.5)	239 (26.8)	141 (15.8)
Numbness in joints	MSK	1854 (78.0)	324 (13.6)	200 (8.4)	396 (39.4)	459 (45.7)	150 (14.9)	454 (45.2)	390 (38.8)	161 (16.0)
	Non MSK	1729 (79.6)	234 (10.8)	208 (9.6)	330 (42.8)	295 (38.3)	146 (18.9)	372 (48.3)	234 (30.4)	165 (21.4)
Skin colour changes	MSK	1992 (83.8)	168 (7.1)	218 (9.2)	242 (41.1)	178 (30.2)	169 (28.7)	320 (54.3)	80 (13.6)	189 (32.1)
	Non MSK	1833 (84.4)	136 (6.3)	202 (9.3)	180 (38.8)	133 (28.7)	151 (32.5)	236 (50.9)	50 (10.8)	178 (38.4)
Muscle cramps	MSK	1934 (81.3)	292 (12.3)	152 (6.4)	508 (36.2)	771 (55.0)	123 (8.8)	809 (57.7)	468 (33.4)	125 (8.9)
	Non MSK	1851 (74.3)	165 (7.6)	155 (7.1)	536 (45.0)	544 (45.6)	112 (9.4)	812 (68.1)	253 (21.2)	127 (10.7)
Weakness	MSK	1391 (58.5)	842 (35.4)	145 (6.1)	468 (29.7)	985 (62.4)	125 (7.9)	529 (33.5)	930 (58.9)	119 (7.5)
	Non MSK	1447 (66.7)	551 (25.4)	173 (8.0)	432 (37.3)	593 (51.2)	133 (11.5)	484 (41.8)	535 (46.2)	139 (12.0)

Fatigue	MSK	1550 (65.2)	668 (28.1)	160 (6.7)	451 (30.4)	898 (60.5)	135 (9.1)	547 (36.9)	792 (53.4)	145 (9.8)
	Non MSK	1495 (68.9)	507 (23.4)	169 (7.8)	442 (34.8)	683 (53.8)	144 (11.4)	525 (41.4)	592 (46.7)	152 (12.0)
Emotional distress	MSK	1810 (76.1)	424 (17.8)	144 (6.1)	441 (34.0)	737 (56.8)	120 (9.2)	573 (44.1)	611 (47.1)	114 (8.8)
	Non MSK	1678 (77.3)	338 (15.6)	155 (7.1)	390 (35.9)	575 (52.9)	123 (11.3)	514 (47.2)	440 (40.4)	134 (12.3)
Concentration difficulties	MSK	1892 (79.6)	311 (13.1)	175 (7.4)	428 (40.3	503 (47.4)	130 (12.3)	454 (42.8)	472 (44.5)	135 (12.7)
	Non MSK	1757 (80.9)	223 (10.3)	191 (8.8)	407 (45.4)	356 (39.7)	133 (14.8)	411 (45.9)	324 (36.2)	161 (18.0)
Sleep problems	MSK	1508 (63.4)	765 (32.2)	105 (4.4)	448 (27.8)	1074 (66.6)	91 (5.6)	717 (44.5)	802 (49.7)	94 (5.8)
	Non MSK	1450 (66.8)	584 (26.9)	137 (6.3)	448 (33.3)	799 (59.4)	99 (7.4)	668 (49.6)	561 (41.7)	117 (8.7)

Reported symptoms in MSK and non MSK consulters. Note symptom severity and impact are only reported for participants reporting ≥ 1 day of a symptom.

Table 4: Frequency of possible EIA symptoms in MSK and non-MSK consulters from the Early Inflammatory Arthritis Detection Tool.

	MSK Consulters (n=2378)	Non-MSK consulters (n=2171)
Joint pain	1920 (83.8)	1460 (70.4)
Hand and wrist pain	1124 (48.9)	929 (44.7)
Hands/wrists swollen	429 (18.8)	345 (16.7)
Difficulty making a fist	398 (17.4)	293 (14.2)
Early morning stiffness	1550 (67.8)	1117 (53.9)
Early morning stiffness >60 minutes	802 (34.7)	511 (24.5)
Symmetrical joint involvement	948 (42.0)	756 (37.4)
Impact on self care/work/leisure	1301 (57.4)	762 (37.5)
Told have RA	281 (12.2)	210 (10.0)
Family history of RA	696 (31.0)	615 (29.9)
Diagnosed with psoriasis	207 (8.9)	187 (8.9)
Mean (sd) total score	4.13 (2.41)	3.39 (2.55)
Mean (sd) weighted score	1.13 (1.55)	0.86 (1.51)
Number with a positive weighted score	1859 (78.2)	1619 (74.6)

n (%) unless otherwise stated.