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REVIEW

The journey of rheumatoid arthritis patients: a review of reported lag times from the onset of symptoms

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Background: Even after achieving tremendous advances in diagnosis and treatment of rheumatoid arthritis (RA), many of the patients undergo delays in diagnosis and initiation of treatment, which leads to worsening of the condition and poor prognosis.

Objective: The objective of this study was to perform a literature review to quantify the lag times in diagnosis and treatment of RA and study the reported factors associated with it.

Methods: The authors searched literature published until September 2016 in electronic full-text and abstract databases and hand-searched the suitable articles.

Results: The weighted average of median lag time from symptom onset to therapy was 11.79 months (12 studies, 5,512 patients, range 3.6–24.0 months). Lag1 was 3.14 months (onset of symptoms to first physician consultant; 12 studies, 6,055 patients, range 0–5.7 months); lag2 was 2.13 months (physician visit to RA specialist referral; 13 studies, 34,767 patients, range 0.5–6.6 months); lag3 was 2.91 months (consultation with rheumatologist to diagnosis; 3 studies, 563 patients, range 0–5 months), lag4 was 2.14 months (diagnosis to initiation of disease-modifying antirheumatic drug therapy; 5 studies, 30,685 patients, range 0–2.2 months). Numerous patient- and physician-related factors like gender, ethnicity, primary care physician knowledge of the condition, availability of diagnostics, and so on were responsible for the delays.

Conclusion: This review estimated the delay times and identified the main factors for delay in RA patients in diagnosis and initiation of treatment. A most plausible solution to this is coordinated effort by the rheumatology and primary care physicians.

Keywords: arthritis, rheumatoid, rheumatologists, lag time, delay, diagnosis, disease management

Introduction

Rheumatoid arthritis (RA) follows a chronic course and invariably involves significant long-term disability and morbidity.[1,2] A diverse group of agents called disease-modifying antirheumatic drugs (DMARDs) and potent anti-inflammatory antibodies that block tumor necrosis factor are widely accepted, respectively, for slowing the progression of RA and alleviating the painful symptoms.[3,4] Though clinically effective, these drugs become less effective in halting the long-term progression of RA if initiation of therapy is delayed.[5,6] After onset of the symptoms, the disease progresses quickly leading to irreversible cartilage damage in <2 months.[7] This damage can only be prevented by the initiation of therapy within 2 months from the onset of symptoms.[7] Initial studies reported no such benefit;[8] however, carefully designed subsequent studies have established that patients in the earliest stages respond better to treatment compared to patients with long-established disease.[8,9]

With empirical evidence supporting early initiation of therapy in RA patients, it becomes necessary to minimize the lag time between the initiation of symptoms and

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therapy.[10] Unfortunately, the early stages of RA are characterized by nonspecific clinical signs that have been a frequent hurdle in timely initiation of the therapy.[11] A large study of 488 patients during 1950–1974 had shown that there was a median lag of 6 months between the onset of symptoms and diagnosis.[12] This has not improved even during the 1990s as 5 months lag between the onset of symptoms and diagnosis was very common.[13] Furthermore, some of the patients remain untreated for up to 10 years after the symptoms appear.[13]

A recent study performed in Saudi Arabia found that patients consulted an average of 4 physicians between their first symptom of RA and final diagnosis, with a mean time from the first physician visit to final RA diagnosis of ~30 months.[14] Although patients consulted with physicians at a mean of 7 months after the onset of RA symptoms, very few subjects initially sought a consultation with rheumatologists, who were ultimately responsible for diagnosing most RA patients.

Like any other disease, the RA patient's journey involves 3 distinct stages: onset of symptoms to consultation (lag1), consultation to rheumatology referral or definite RA diagnosis (lag2), and diagnosis to proper treatment (lag3). These lag times have been of interest to rheumatologists and have been reported by numerous studies[15,16] with some studies focusing specifically on the factors that contribute to these delays and measures undertaken to overcome these.

In this review, we examined the literature to study the lag times in RA patients with an aim to summarize the findings for future reference. Further analysis of factors was also undertaken to understand the reasons for these lags.

Methods

The primary objective of this study was to review the reported delay in the duration (lag time) between symptom onset and initial physician visit, an initial visit to rheumatology referral, referral to diagnosis and diagnosis to proper treatment.

Secondary objectives are to review the significance of reported factors that may have contributed to delayed RA diagnosis, and the possible measures that could be taken to accelerate RA diagnosis and early initiation of treatment.

A systematic search of OVID and PubMed databases was conducted in March 2016 to identify all the data related to the journey of RA patients. In addition, Annals of Rheumatic Diseases, American College of Rheumatology Conference Index, and European League Against Rheumatism Conference Index were searched for relevant abstracts that are not published elsewhere.

The following keywords were used in the search for literature: [time lag, delay, duration] between [onset of symptoms of rheumatoid arthritis] and [presentation to/encounter/consult] of [a physician/rheumatologist]. In addition, we searched: [time lag, delay, duration] between [onset of symptoms of rheumatoid arthritis] and [initiation antirheumatic drugs]. All the search terms were "exploded" in conjunction with using a keyword search. The search was conducted on March 31, 2016, and was limited to English language papers.

Included databases were distributed among authors and were searched independently using the above keywords. In each database, all the search results were reviewed and papers were checked for their relevance to our primary and secondary objectives based on their title, abstract, and manuscript. Papers that were not related to our objectives were excluded primarily. After the first round of work, databases were switched among authors to ensure accuracy of literature search and selection. Disagreements were settled through discussion between the authors. The studies were subjected to 3-phase selection. Titles were screened in the first round, abstracts in the second round, and full-texts in the third round. The most recent study was considered in the case of duplicate or overlapping population studies.

Studies were eligible for inclusion if they contained original data on number of patients, lag between the onset of symptoms and first physician visit or lag between initial visit and rheumatology referral, or lag from referral to diagnosis and/or lag from diagnosis to the initiation of DMARDs. Papers analyzing the significance of factors contributing to these lags in RA patients were selected toward the secondary objective of this review. Studies satisfying the above criteria were eligible for inclusion, irrespective of demographic, geographic, or design variations.

Lag times were not reported uniformly among papers. For example, some considered lag1 as the time from onset to first medical encounter while others considered it as the time from first medical encounter until referral to rheumatologist, and so on. Many studies reported a single time lag (eg, from onset to diagnosis) and provided no further details. Some studies reported lag time in weeks and others in months. Some articles compared the results of 2 or more studies that were performed under similar settings but in 2 different time periods followed by comparison of lag times. Descriptive presentation also varied as some studies reported lag time as averages while others reported the median values. Except for the mean and median issue, we resolved other issues by setting our own definitions of lag times, namely lag1 as the time from onset of symptoms to seeking first medical consul-

tation; lag2 as time from seeking medical consultation until referral to rheumatologist; lag3 as the time from referral to definite RA diagnosis, and lag4 as the time from diagnosis to the initiation of DMARDs.

If detailed lag times were not reported in any study, but only a single lag time with a specific start and end points, cells in the corresponding row on the table were merged according to the start and end points specified in that study. We used months as time unit uniformly. Whenever the lag times were reported in weeks and days, we converted them into months. In the case of comparative studies, we only reported data from the latest studies.

For the mean and median issue, when calculating the total lag time, we included only studies that had reported the delay in mean and SD value in the calculation of the total lag times.

Results and discussion

The initial literature search returned 363 titles. After screening of titles for eliminating duplicates and irrelevant studies, we were left with 150 studies. Ninety-five studies were eliminated in the next stage after abstract and full-text screening (Figure 1). Out of these, 37 studies were relevant to 1 or multiple variables of our primary objective, and 18 studies were relevant to our secondary objective. Data from these papers were extracted and reviewed.

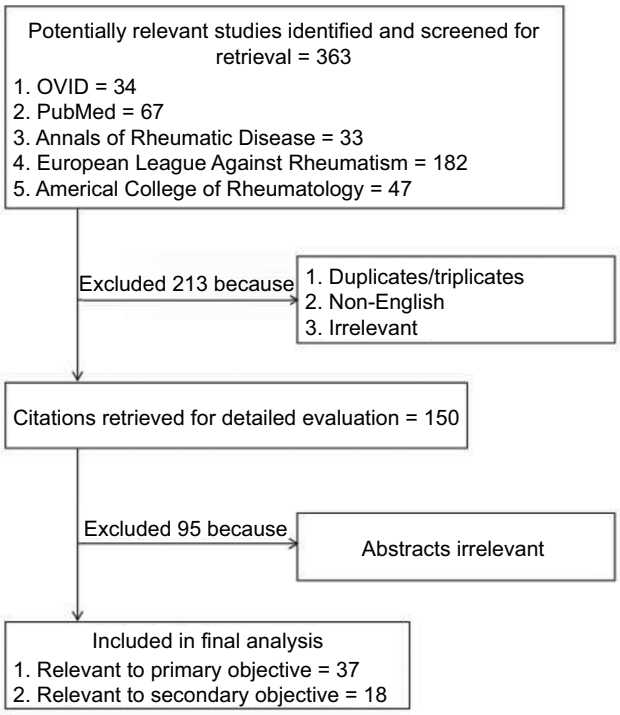

Figure 1 Flow diagram of study selection.

The full-text papers from the first and second category were reviewed. Studies that were only available as informative abstracts were included if complete data on the number of subjects and lag time were provided, even if published in non-English languages.

Table 1 outlines the main data from the eligible studies. Twelve studies reported the total lag time from the onset of symptoms to the initiation of DMARD therapy. The weighted average of median lag time of 5,512 patients from the onset of symptoms to therapy was 11.79 months with a range of 3.6–24.0 months (Figure 2).[16–26]

Lag1 data were also available from 12 studies on a total of 6,055 RA patients. The weighted average of median lag time from the onset of symptoms to the first physician consultation was 3.41 months with a range of 0–5.7 months.[17,20,22,26–34]

Lag2 data were available from 13 studies on a total of 34,767 RA patients. The weighted average of median lag time for RA specialist referral after consulting a physician was 2.13 months with a range of 0.5–6.6 months.[17,20,22,25,26,29–31,33–37]

Lag3 data were available from 3 studies on a total of 563 RA patients. The weighted average of median lag time for the diagnosis of RA after consulting a rheumatologist was 2.91 months with a range of 0–5 months.[16,17,21]

Lag4 data were available from 5 studies on a total of 30,685 RA patients. The weighted average of median lag time for initiation of DMARD therapy after definite diagnosis of RA was 2.14 months with a range of 0–2.2 months.[16,17,20,24,37]

Early RA diagnosis and gaps in care

The understanding of "early" RA is heterogeneous. Two of 3 rheumatologists use the term "early" for symptoms shorter than 3 months. The vast majority of the rheumatologists surveyed regard symptom duration of <3 months as early.[38]

Evidence is accumulating that very early RA (within the first 12 weeks) may be an immunopathologically distinct phase of disease**.** Thus, a "window of opportunity" may exist during which introducing DMARDs may have different effects than treatment at a later date, including prevention of erosions and possibly complete switching off of the disease.[39]

It was found that the strongest predictor of improvements in disease activity (according to the American College of Rheumatology definition) was shorter disease duration at the start of treatment.[39]

Gaps in care begin with the person's recognition of the symptoms and the action of visiting a family physician (FP). If RA is suspected, the FP refers the person to a rheumatologist who provides diagnosis and prescribes appropriate

Table 1 Characteristics of the studies providing data relevant to our analysis

Study	Country	No. of patients	Symptoms to first physician visit (Lag1; months)	Initial visit to rheumatology referral (Lag2; months)	Referral to diagnosis (Lag3; months)	Diagnosis to DMARD initiation (Lag4; months)
Cho et al[27]	Korea	98	2			
			5.75			
			42			
Irvine et al[28]	UK	74	4			
Sokka and Pincus[47]	USA	232	5.1			
Ayas and Nur[36]	UK	269	6			
				3		
Lacaille et al[37]	Canada	27,710		2.2 (IQR 0.7–6.4)		30% prior to or at the time of diagnosis and 70% within 2.2 months after diagnosis (IQR 0.76–6.6)
Clemente et al[19]	Spain	865	14			
Feldman et al[48]	Canada	13,237	2.6 (IQR 0.9–7.6)			
Kumar et al[29]	UK	169	3.25 in RF-positive patients compared to 1 in RF-negative patients	0.5 (IQR 0.25–2.5)		
			5.75 (IQR 3–13.5)			
Badsha et al[49]	United Arab Emirates	100	14.4 (average)			
			19.2 (average)			
Ankjær-Jensen[50]	Denmark	NA			5.6	
Kiely et al[26]	UK and Ireland	808	4 (IQR 2–9)	1 (IQR 1–2)	1 (IQR 0–2)	
			5 (IQR 3–12)			
			8 (IQR 4–13)			
Koh et al[51]	Singapore	386	8.4±9.0			
Fathi et al[52]	Egypt	196	24.1±44.2			
			31.5±50.0			
van der Linden et al[30]	The Netherlands	598	0.6	2		
			3.4			
Robinson and Taylor[46]	New Zealand	128	1.7 (IQR 0.93–3.17) in urgent patients; 3.8 (IQR 1.5–11) in semi-urgent patients			
			4.1 (IQR 2.7–8.1) in urgent patients; 6.9 (IQR 4.6–18.8) in semi-urgent patients			
			4 (IQR 3–7.23) in urgent patients; 7.3 (IQR 4.4–18) in semi-urgent patients			
Blanco et al[53]	Spain	915	6.3±11.3			2.3±10.2
					4.0±13.5	
Rodríguez-Polanco et al[16]	Venezuela	272	13			1
			5.5		5	
			24			
Jamal et al[17]	Canada	204	3.03 (IQR 1.02–8.04)	2.01 (IQR 1.02–4.01)	0.0	0.0 (IQR 0.00–0.99)
			6.35 (IQR 3.29–12.01)			
Raza et al[54]	Pan Europe	482	6 (IQR 3.3–16.55)			
Verschueren et al[55]	Belgium	182	5.5 (IQR 3.08–9.75)			
Zafar et al[56]	United Arab Emirates	100	7.8			
			12.5			
Nanji et al[34]	Canada	151	4	0.8		
			5			
Kimura et al[31]	Japan	296	2.2 (IQR 0.11–1)	1.25 (IQR 0.1–0.67)		
			6.72 (IQR 0.36–2.313)			

(*Continued*)

Table 1 (*Continued*)

Study	Country	No. of patients	Symptom to first physician visit (Lag1; months)	Initial visit to rheumatology referral (Lag2; months)	Referral to diagnosis (Lag3; months)	Diagnosis to DMARD initiation (Lag4; months)
Gómez Caballero et al[57]	Spain	183	11.3±13.2			
			10.2±12.7			
			11.1±12.8			
Natalia et al[32]	Argentina	316	1 (IQR 0.3–2)		0.8 (IQR 0.2–12.17)	
			3 (IQR 1.2–7)			
			5.5 (IQR 1–12.17)			
Doornum et al[25]	Australia	135	5.4 (IQR 2.9–10.8)			
				1.1 (IQR 0.3–1.8)		
				0		
			3.26 (same research, but no IQR)			
Fautrel et al[33]	France	813	0.5	1		
De Cock et al*[58]	Belgium	69				0.25 (IQR 1)
			6.75 (IQR 29.5)			
Zonana Nacach et al[22]	Mexico	98	2.9	6.6		
			9.9			
Gibson et al[59]	Australia	177	44.4			
Widdifield et al[35]	Canada	1,086		2		
De Cock et al[23]	Belgium	156	2.5 (IQR)	1.75 (IQR)		0.25 (IQR)
			5.75 (IQR)			
Sørensen and Hetland[60]	Denmark	13,721	4			
Benaglio et al[61]	Italy	513	3.5			
Ješe et al[21]	Slovenia	87	2.47 (IQR 1.1–6.3)	3.17 (IQR 1.5–6.5)		
			3.6 (IQR 1.9–6.9)			
Widdifield et al[20]	Canada	2,430	5.7	2.2		1.8
			10.9			
			>13.3			
Hussain et al[14]	Saudi Arabia	250	6.2±5.5	30.2±16.0		

Notes: Lag times are median values in month. Values are also presented as mean ± SD wherever available. *The article had provided enough data to calculate IQR values.
Abbreviation: IQR, interquartile range; DMARD, disease-modifying antirheumatic drug; RF, rheumatoid factor; NA, not available.

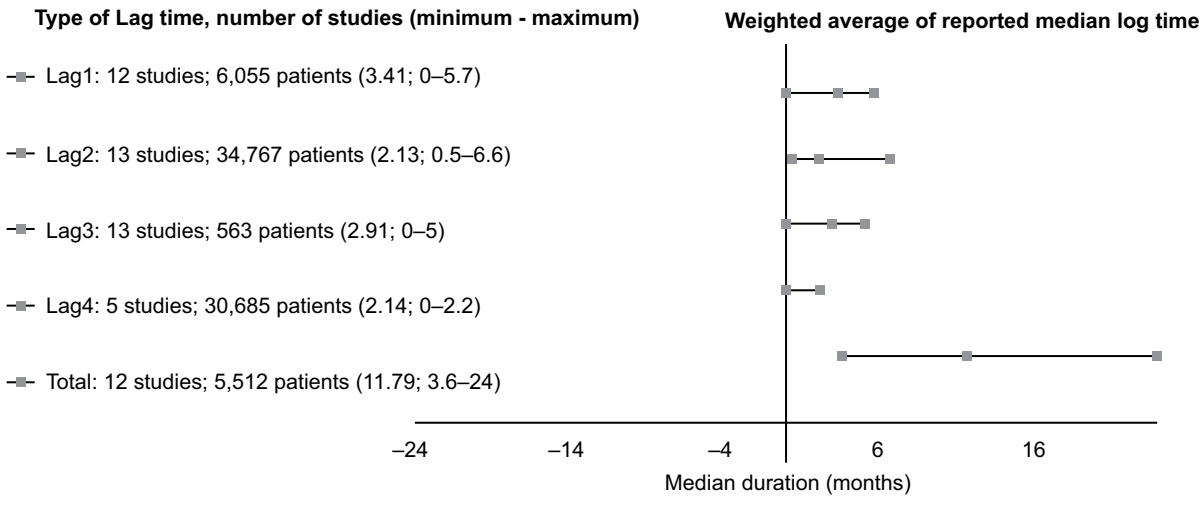

Figure 2 Reported lag times in rheumatoid arthritis patients.

medications. Next, the person will be periodically assessed by a rheumatologist.

Studies performed in the past 2 decades which evaluate the onset of DMARDs treatment in patients with early RA, performed in the USA, Spain, Canada, the UK, the Middle East, and in European countries, show that the mean time since the onset of disease and the onset of disease-modifying antirheumatic treatment ranges from 6 to 18 months.[22] This indicates that the diagnosis of RA after the onset of symptoms is delayed, and therefore, the objective of starting treatment early is not achieved in most of the cases.

Causes of delay

Delay is probably due to a combination of patient-related and physician-related factors. We reviewed 17 papers and analyzed factors contributing to the delay in care for RA patients (Table 2).

The results of a recent study published in 2014 evaluating the time since the beginning of disease and the visit to the FP, the time since this and the referral to the rheumatologist, and the time to onset of DMARD treatment,[22] showed that only in 19% of patients, DMARDs were started in the first 3 months after disease onset and that the delay in the prescription of DMARDs was mainly due to the delay in referral from family medicine to the rheumatologist.

In addition to the assumption of incompetency and poor knowledge, a qualitative research among osteoarthritis (OA) and RA patients in Germany, France, Spain, UK, and Italy revealed that for the majority of interviewed patients, their general practitioner visit is rated as disappointing due to poor communication and a focus merely on pain control. The journey that a patient undergoes before seeking medical advice is frequently long and emotionally exhausting.[40]

Delay in the diagnosis and management of RA may stem from slow diagnosis by physicians rather than postponed medical consultation by patients. This may be because patients with RA often do not seek the advice of rheumatologists at the onset of their symptoms and non-rheumatologists fail to refer RA patients to rheumatologists soon enough. In Saudi Arabia, although patients consulted with physicians at a mean of 7 months after the onset of RA symptoms, very few subjects initially sought a consultation with rheumatologists, who were ultimately responsible for diagnosing most RA patients.[14] It is thus believed that delayed specialist

Table 2 Factors associated with delays in the diagnosis and treatment of rheumatoid arthritis

Reference	Location; patients (research time)	Factor studied	Findings	Author recommendation
Lard et al[62]	N/A; 142 F + 82 M (1993–1999)	1. Gender	1. More delay in women as compared to men (median of 93 vs 58 days)	GPs should be made aware that early detection and early referral of patients with RA are crucial for early treatment
Xibillé-Friedmann et al[63]	México; 530 (2002)	1. PCP	1. Only 20% of the PCP referrals are confirmed as RA 2. PCPs do not utilize the laboratory and X-ray technologies effectively, leading to a delay in accurate diagnosis 3. Even diagnosed cases were referred with a huge delay of 3 years	A vigorous effort in educating PCP is needed to achieve early diagnosis and referral of RA cases
Neill et al[64]	Ireland; N/A (2011)	1. PCP	1. PCPs lack knowledge on diagnosis and importance of timely treatment of RA 2. Diagnostic uncertainty and shortage of rheumatologists lead to delay in referral from PCPs	Diagnostics facility and training of PCPs
Widdifield et al[65]	Canada; 27,127 (1997–2008)	1. Age 2. SES 3. Having a male PCP 4. Measures of poor access	1. Increasing age, lower SES, and having a male PCP limits timely access to rheumatologists 2. Measures of poor access (poor continuity of primary care, density, and proximity to rheumatologists) negatively impacted rates of encounters with a rheumatologist	Proactive, tailored approaches are needed to provide rheumatology care to such populations
Panchal[66]	UK; 189 (2012)	1. Ethnicity	1. Black minorities experienced more delay as compared to Caucasians	There may be a range of ethnically specific culturally centered reasons for such delay

(*Continued*)

Table 2 (*Continued*)

Reference	Location; patients (research time)	Factor studied	Findings	Author recommendation
Zafar et al[56]	United Arab Emirates; N/A (2006)	1. Public awareness	1. A positive and statistically significant reduction in the lag time to both diagnosis and the initiation of DMARD therapy was achieved in 5 years of launching a public awareness campaign	This difference in lag time may in part be attributed to the inception of the patient support groups, coupled with the general drive toward increasing public awareness about RA
Delaurier et al[67]	Canada; N/A (2009–2010)	1. Rheumatologist appointment	1. Most patients with RA are still not receiving an appointment to a rheumatologist in a timely manner	Effective triage tools to decrease these delays should be instituted
Grygielska[68]	Poland; 1,000 (2009–2010)	1. Geographical factor 2. Gender 3. Age	1. Inhabitants of rural area are diagnosed earlier than inhabitants of big cities 2. Men were diagnosed earlier than women 3. Respondents with first symptoms in younger age were diagnosed later than older patients	
Molina et al[69]	USA; 1,209 (2014)	1. SES	1. Lower SES leads to significant delay in DMARD treatment (8.5 vs 6.1 years for middle and upper SES patients), both of which were independently associated with worse clinical outcomes	
Barnabe et al[70]	Canada; 1,142 (2012)	1. Severity of disease activity 2. Serology results (anti-CCP antibody-positive patients) 3. Lower income levels 4. Ethnicity 5. Underlying comorbidities	1. Higher number of swollen joints, elevated acute-phase reactants, and worse patient global scores decrease time to diagnosis 2. Positive serology results are associated with delays in time to diagnosis in multivariate analysis. The reasons for this unanticipated finding are unclear. One potential reason is that some triage units may delay assigning a priority to the patient for an appointment until the serology results are available, which will delay the time to diagnosis. In addition, availability of anti-CCP testing is restricted in some regions of Canada, despite its utility in diagnosis and prognosis of RA. 3. Patients with lower income levels are at risk of delays in diagnosis 4. Did not find any evidence of discrimination in time to diagnosis based on ethnicity or underlying health comorbidities	
Sung et al[71]	Korea; 714 (2014)	1. Age 2. Education 3. Income 4. Disease activity	1. Older onset age, higher education level and higher income lead to early diagnosis 2. DAS28 remained similar but hand joints were more eroded in delayed diagnosis	
Widdifield et al[72]	Canada; 2,430 (2015)	1. PCP	1. Approximately 1 in 3 PCP referrals to rheumatologists were referred for a systemic inflammatory rheumatic disease	Understanding the referral patterns of PCPs can identify opportunities to improve PCP management of patients prior to rheumatology referral

(*Continued*)

Table 2 (*Continued*)

Reference	Location; patients (research time)	Factor studied	Findings	Author recommendation
Simons et al[73]	UK; 32 F + 6 M (2015)	1. Perceived causes of symptoms 2. Presentation, location, and experience of symptoms 3. Perceived impact of symptoms on daily life 4. Self-management of symptoms 5. GP-related drivers and barriers	1. Factors prompting GP consultation included: – a sudden and severe symptom onset – symptoms resistant to self-management strategies – symptoms not easing – symptoms disrupting daily activities – the perception that symptoms were unusual and could not be explained 2. Numbers of patients were trying to identify external causative factors, or felt that joint pain and stiffness were simply part of getting older and as a result they would delay or avoid seeking medical attention. Others mentioned "knocks" and other injuries as a possible cause, specifically when experiencing symptoms in a single joint. They would delay help-seeking if they suspected injury as a causal factor 3. RA patients interviewed within a year of diagnosis, described using over-the-counter medications prior to, or instead of, seeking medical advice or while awaiting a formal diagnosis	
Molina[74]	USA; 1,209 (1996–2009)	1. Potential health barriers 2. Distance to the rheumatologist 3. SES	1. All the 3 factors were independently associated with disease activity, joint damage, and physical disability 2. Distance was not significantly correlated with DMARD lag and was inversely associated with these clinical measures, suggesting that patients who live closer to the rheumatologist have more severe RA. This result was unexpected 3. On average, patients with lower SES waited 8.5 years after the onset of RA symptoms to begin DMARD treatment, compared to those in the middle and upper SES tertiles who waited ~6.16 years	
Peerboom et al[75]	Belgium; 94 (2015)	1. Pain 2. PCP	1. Pain is the foremost related symptom at the onset and the most important reason to visit the GP, accelerating diagnosis 2. 25% of patients needed >5 visits before ERA was detected	
Mølbæk et al[76]	Denmark; 11 (2014)	1. Nature and severity of symptoms	1. When symptoms were obvious to patients, there was a shorter delay between symptom onset and contacting their GP. In cases where symptoms gradually worsened or were difficult to interpret, there was a longer delay 2. Participants with a high degree of body awareness appeared to be good at detecting when something was not normal, and they responded quickly to their symptoms	

(*Continued*)

Table 2 (*Continued*)

Reference	Location; patients (research time)	Factor studied	Findings	Author recommendation
			3. For those who regarded the doctor as a resource to which they were entitled and who were not worried about getting a diagnosis, there was a shorter delay 4. Diffuse symptoms seemed to confuse GPs and can contribute to physician delay in the investigation process 5. The presence of other diseases can result in a prolonged period before referral to a rheumatologist 6. The results showed that the greater the awareness of the patient's body, the better the disease recognition, the fewer barriers to contacting the GP and the shorter the delay in doing so	
Pratt et al[77]	UK; 173 (2011–2014)	1. Serology results (anti-CCP antibody-positive patients)	1. Retrospective analysis to determine whether time to treatment following symptom onset differs between RA patients according to autoantibody status 2. ACPA+/RF+ patients experienced significantly longer symptom duration before DMARD initiation 3. This accounted for delays in their presentation to primary care following symptom onset 4. In contrast, ACPA–/RF– patients were significantly more likely to experience delays in DMARD initiation after presenting to secondary care 5. Causes of treatment delays in early RA differ according to patients' autoantibody status	
Hussain et al[14]	Saudi Arabia; 250 (2016)	1. Early referral to rheumatology 2. Presence of early symptoms (hand/wrist involvement, fatigue) 3. Geographic distribution	1. Nonrheumatologists offered diagnoses in 24.4% of cases, while rheumatologists diagnosed 75.6% 2. The absence of early hand/wrist involvement and fatigue were associated with delayed RA diagnosis (long lag2; $p<0.01$). Moreover, geographic distribution influenced RA diagnosis, with rural patients experiencing a greater delay than urban patients ($p<0.0001$)	RA diagnosis can be accelerated by encouraging early referral to rheumatologists

Abbreviations: M, male; F, female; N/A, not available; GP, general practitioner; RA, rheumatoid arthritis; PCP, primary care physician; SES, socioeconomic status; DMARD, disease-modifying antirheumatic drug; CCP, cyclic citrullinated peptide; DAS28, disease activity score; ERA, early rheumatoid arthritis; ACPA, anti-citrullinated protein antibody; RF, rheumatoid factor.

referrals constitute a principal reason for late diagnosis and subsequent treatment.

Possible interventions

It is necessary to implement measures that act on early diagnosis and treatment of RA, through the diffusion of knowledge relating to the disease in the general population, advertising campaigns as well as an increase in the level of knowledge regarding RA in primary care physicians.

Successful intervention is largely dependent on the availability of local programs and the coordination among the rheumatologist, the FP, and other health professionals. Moving from one level of care to the next involves a potential wait period.[41]

A 2013 systematic literature review addressed and identified 3 main areas of delay to care for patients with inflammatory arthritis (IA) and potential solutions.[42] From the onset of symptoms to primary care, several websites provided informa-

tion but were of varying quality and insufficient to aid early referral. At a primary care level, many guidelines emphasized the need for early referral with providing specific referral criteria.[39,43] Once referred, early arthritis clinics provided a point of early access to rheumatology assessment. Triage systems, including triage clinics, helped prioritizing clinic appointments for patients with IA. Use of referral forms standardized the information required, further optimizing the triage process.

Guidelines for early referral are needed.[38] Clinical criteria would facilitate early referral of the patient with suspected RA to a rheumatologist for definitive diagnosis and initiation of DMARD treatment. In a recently published study by Almoallim et al,[44] we have validated the variables that may aid in the design of referral criteria. These are based on musculoskeletal examination techniques to assess the presence of arthritis by primary care physicians in "target" joints; wrists, second and third metacarpophalangeals, and third proximal interphalangeal joints.[45] This is in addition to positive rheumatoid factor and anti-citrullinated protein antibody (anti-cyclic citrullinated peptide).

Key points of the referral criteria were formed based on literature review. Clinical evidence strongly supports the observations that rapid referral to a rheumatologist is advised when RA is suspected, which may be supported by the presence of any of the following: persistent joint swelling in more than 1 joint, early morning stiffness ≥30 minutes, or involvement of metacarpophalangeal or metatarsophalangeal joints.[39,43] These criteria were mainly based on experts' opinion not on validated measures as in our unpublished work. Urgent referral (ideally within 6 weeks of symptom onset) to rheumatology should then be made with a clear indication that IA (or RA) is suspected. This should be done without waiting for the results of tests such as rheumatoid factor and plain radiographs, which are often normal in the early phase of disease.[39,43]

All rheumatologists should make it a priority to see patients with suspected IA on an urgent basis. Triage is important to facilitate early treatment; however, rheumatologists in this service are not currently triaging suspected RA referrals with reference to known poor prognostic indicators.[46] However, several interventions could improve both informative referrals and triaging of referrals to decrease time to diagnosis and treatment including public education, general practitioner education sessions with associated distribution of referral guidelines, and reminding triaging rheumatology clinicians about the available prognostic factors often present in general practitioner referrals that assist with correct triage.[46]

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Disclosure

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