Rheumatology Advance Access published November 23, 2009
RHEUMATOLOGY

Original article

doi:10.1093/rheumatology/kep340

Early referral to the rheumatologist for early arthritis patients: evidence for suboptimal care. Results from the ESPOIR cohort

Bruno Fautrel[1,2], Mathilde Benhamou[1,2], Violaine Foltz[1,2], Nathalie Rincheval[3], Anne-Christine Rat[4,5], Bernard Combe[6], Francis Berenbaum[7,8], Pierre Bourgeois[1,2] and Francis Guillemin[4,5]

CLINICAL SCIENCE

Abstract

Objective. To assess the time to access a rheumatologist (TTAR) by early arthritis (EA) patients participating in a nationwide incidental cohort (ESPOIR) and compare it with European League Against Rheumatism (EULAR) recommendations, which recommends rapid referral, ideally within 6 weeks, to a rheumatologist for patients presenting with EA.

Methods. Eight hundred and thirteen patients with EA were included in the cohort between 2002 and 2005. The inclusion criteria were 18–70 years old, two or more swollen joints, symptom duration from 6 weeks to 6 months and possible RA diagnosis. TTAR was defined as the time between the first synovitis and first visit to a rheumatologist. TTAR and satisfaction of the EULAR guidelines were investigated by multiple linear and logistic regressions.

Results. Mean TTAR was 76 days; only 46.2% of patients were seen by a rheumatologist within the EULAR-recommended time frame. Patients' patterns of accessing medical care substantially affected access to specialized care: mean TTAR was 58 days for patients who directly scheduled an appointment with the rheumatologist and 78 days for those referred by their general practitioner ($P < 0.0007$). Only 57.2 and 44.5%, respectively, were able to consult a rheumatologist within 6 weeks. Multivariate analysis confirmed the significant impact of indirect access on TTAR, after adjustment for EA characteristics and medical density in the region.

Conclusions. Significant disparities were identified in the care of EA patients in terms of early access to a rheumatologist. More effort is needed to optimize the physicians' knowledge about EA and to improve the efficiency of medical networks.

Key words: Rheumatoid arthritis, Disease management, Health service research, Clinical practice guidelines, Managed care.

Introduction

In the mid-1990s, a crucial question was formulated: 'Is rheumatoid arthritis (RA) a medical emergency?' [1]. At that time, physicians' knowledge about RA was mainly that the disease was the most frequent chronic inflammatory rheumatism, whose severity was mainly dependent on pain and functional limitations induced by synovial inflammation, progressive disability related to structural damage leading to joint dislocation and, eventually, increased mortality [2–7]. A couple of years later, scientific data revealed the rapid onset of joint damage [8] and the association with cardiovascular morbidity and mortality,

[1]APHP, Groupe Hospitalier Pitié-Salpêtrière, Service de Rhumatologie, [2]Université Pierre et Marie Curie – Paris VI, UFR de médecine, Paris, [3]Université Montpellier 1, UFR de Médecine, Institut Universitaire de Recherche Clinique, Montpellier, [4]Nancy Université, EA 4360 APEMAC, Ecole de Santé Publique, Faculté de Médecine de Nancy, [5]INSERM, CHU de Nancy, CIC-EC Centre D'épidémiologie Clinique, Nancy, [6]Centre Hospitalo-Universitaire du Montpellier, Hôpital Lapeyronie, Service de Rhumatologie, Montpellier, [7]APHP, Hôpital Saint Antoine, Service de Rhumatologie and [8]Université Pierre et Marie Curie – Paris VI, UFR de médecine, Paris, France.

Submitted 22 May 2009; revised version accepted 22 September 2009.

Correspondence to: Bruno Fautrel, Department of Rheumatology, Pitié-Salpétrière Hospital, 83 Boulevard de l'Hôpital, 75651 Paris Cedex 13, France. E-mail: bruno.fautrel@psl.aphp.fr

directly related to chronic systemic inflammation and thus modifiable by DMARDs [9–18]. Thus, as in diabetes or hypertension, early treatment for RA to prevent long-term disease consequences was important [19].

Modern therapies, either conventional DMARDs such as MTX or equivalent agents or new biologics, have been effective in blocking inflammation, preventing structural damage and reducing inflammation-induced cardiovascular morbidity and mortality [17, 18, 20, 21]. Their use in early RA stages, during a 'window of opportunity' [22, 23], has been associated with better outcomes than in late RA in terms of efficacy, remission and structural damage [24–26]. Also, the use of new DMARDs has been optimized by the concept of 'tight control', which combines (i) regular evaluation (every 1 or 3 months) of RA inflammatory activity [i.e. both swollen and tender joints, overall assessment of the disease by the patient on a visual analogue scale (VAS) and measurement of biological inflammation parameters, which enables the quantification of disease activity through composite indexes] [27–32]; and (ii) the definition of remission, or at least minimal disease activity, as a therapeutic goal [33–37].

Improved treatment, strategies and disease management were the basis for the development of clinical practice guidelines aimed at facilitating wide diffusion of these notions. The European League Against Rheumatism (EULAR) developed guidelines for clinical practice that precisely mentioned the need for any patient with early arthritis (EA) to be 'referred and seen' by a rheumatologist within 6 weeks after symptom onset, which represents a short time interval [38]. The ESPOIR cohort (Evaluation et Suivi de POlyarthrites Indifférenciées Récentes), a French national EA cohort, offered the opportunity to measure the potential gap between the EULAR recommendation, which could be viewed as optimal care, and daily practice in a country where all the population is covered by publicly funded universal health insurance. The study aimed to (i) assess the time needed by patients with EA (first occurrence of stable swollen joint) to access a rheumatologist; (ii) estimate the proportion of patients able to consult a rheumatologist within the international guidelines-recommended time frame in a country with universal health insurance coverage; and (iii) identify determinants associated with the time to access a rheumatologist (TTAR), with special attention to the impact of direct or indirect [i.e. after referral by a general practitioner (GP)] access to the specialist.

Materials and methods

ESPOIR cohort

The ESPOIR cohort is a nationwide study sample of the French Society of Rheumatology that included 813 patients with EA from 14 rheumatology centres all over the country between 1 November 2002 and 30 April 2005. The inclusion criteria comprised patients aged 18–70 years and two or more swollen joints for >6 weeks and <6 months but not treated with any DMARD or steroids for >2 weeks [39]. Patients with a definite diagnosis different from RA were excluded. Thus, all included patients had inflammatory rheumatism for which RA diagnosis was considered or already confirmed. To facilitate recruitment, several national and regional general media, medical newspapers and continuing medical education journals advertised information about the cohort. Thus, GP and private practice rheumatologists were aware of the existence of the ESPOIR cohort project and had information about the local inclusion centre.

The ESPOIR research programme was approved by the ethics committee of Montpellier in July 2002, and all the patients who participated in the study gave written informed consent before entering the cohort.

Data available

ESPOIR cohort visits were scheduled every 6 months for 2 years, then annually. The present study used only data collected at inclusion. Data were available on patients' social and demographic characteristics, medical history, symptom onset and main clinical and biological findings at inclusion. Information about patient care was recorded, especially the time in days between onset of first symptoms attributable to joint disease and the first visit to the GP, if any, or to a rheumatologist.

TTAR was defined as the time in days between the occurrence of the first swollen joint(s)—as reported by the patient—and the first visit to the rheumatologist, either in private practice or at a hospital. TTAR was compared with the optimal 6-week time interval recommended by EULAR [38]. Satisfaction with the EULAR recommendation was defined as TTAR $\leqslant$45 days.

The potential determinants of TTAR investigated were age, sex, ethnicity, education, living arrangement, occupation, demographical characteristics of the area of residence, smoking status, alcohol consumption, main comorbidities such as history of cardiovascular or neoplastic disease, familial history of inflammatory joint disease, joint symptom duration, clinical presentation and arthritis activity at disease onset, overall disease activity based on the disease activity score for 28 joints (DAS28), disability assessed by the HAQ, patient pattern of accessing a rheumatologist (directly or indirectly through a GP), and density of physicians (GPs or specialists) in the region of residence based on the national health insurance records (Caisse Nationale d'Assurance Maladie des Travailleurs Salariés).

Statistical analysis

All statistical analyses involved Stata 9 (Stata Press Publications, College Station, TX, USA) and SAS 8.2 (SAS Institute, Cary, NC, USA). Statistical significance was tested by chi-square test for categorical variables and Mann–Whitney non-parametric test or one-way analysis of variance (ANOVA) for continuous variables. When needed, 95% CIs were estimated by bootstrap techniques with 500 replications.

The determinants of TTAR, expressed in days as a continuous variable, were studied by multivariate linear regression with a mixed model. Inclusion centres were introduced as an additional random-effect term to take into account clusters. Since TTAR was not normally distributed, the multivariate analysis involved TTAR log transformation. The determinants associated with satisfaction of the EULAR-recommended time interval were explored by multivariate logistic regression with generalized estimating equations to take into account correlation between patients belonging to the same centre (marginal model). In both models, backward stepwise procedure included all the variables significantly associated with the response, with $P \leqslant 0.2$ in the univariate analyses, and statistical significance was set at 0.05. Data are presented as regression estimates or odds ratios with 95% CIs.

Results

During the inclusion period, 813 patients with EA were included (Table 1). Their main characteristics have been presented elsewhere [40]. Briefly, the mean age of patients was 48.1 (12.5) years and the female:male ratio was 3.3:1. Only a minority of the patients [129 (15.1%)] had a family history of RA. Patients had 7.2/28 swollen joints and 8/28 tender joints, on average; mean ESR was 29.4 (24.5) mm at the first hour; and CRP level was 22.3 (34) mg/dl. Overall, mean disease activity as assessed by DAS28 was 5.2 (1.5). Serum IgM RF and anti-cyclic citrullinated peptide (anti-CCP) antibodies were present in 45.8 and 38.8% of patients, respectively. Only a few patients showed erosive disease as determined by clinicians in charge of inclusions. Finally, a substantial proportion of patients (74%) satisfied the 1987 classification criteria of the ACR.

Mean time to access specialized care

Complete information was available for 812 patients (Table 2). The time to visit a GP was 26.3 (41) days on average (median 15 days) for the 704 patients who consulted one; the subsequent delay to access the rheumatologist was 53.0 (70.8) days on average (median 30 days). For the entire population, mean TTAR was 75.5 (77) (median 60) days. Therefore, only 46.2% of these EA patients satisfied the EULAR recommendations to visit a rheumatologist within 6 weeks.

Impact of patient's medical trajectory on TTAR

A substantial difference was noted depending on the patient's pattern of accessing medical care for the EA. Most patients [704 (86%)] were referred to the specialist by a GP. For this specific subset of patients, the mean TTAR was 78.2 (median 60) days (95% CI 72.3, 84). For those who directly consulted a rheumatologist [108 (14%)], mean TTAR was 58.3 (median 40) days (95% CI 48.3, 68.3) (Mann–Whitney U-test, $P = 0.0007$). Patients who directly accessed the rheumatologist were significantly more likely to consult a rheumatologist within the

Table 1 Baseline characteristics of patients included in the ESPOIR cohort

Characteristics	$n = 813$
Age, mean (S.D.) (median), years	48.1 (12.5) (50)
Female, *n* (%)	624 (76.8)
Family history of inflammatory rheumatism, *n* (%)	129 (15.9)[a]
Swollen joint count, mean (S.D.) (median)	7.2 (5.4) (6)
Tender joint count, mean (S.D.) (median)	8.4 (7.0) (6)
ESR, mean (S.D.) (median)	29.4 (24.5) (22)
CRP, mean (S.D.) (median), mg/l	22.3 (34.0) (9)
DAS28, mean (S.D.) (median)	5.2 (1.5) (5.1)
IgM RF positivity, *n* (%)	372 (45.8)
Anti-CCP antibody positivity, *n* (%)	315 (38.8)
Typical damage seen on radiography[b] (centre reading), *n* (%)	110 (13.6)
Satisfaction of ACR RA classification criteria, *n* (%)	600 (73.8)

[a]RA in 89% of the cases. [b]Typical damage seen on radiography was defined as in the 1987 ACR criteria, i.e. radiographic changes typical of RA on postero-anterior hand and wrist radiographs, which must include erosions or unequivocal bony decalcification localized in or most marked adjacent to the involved joints (OA changes alone do not qualify).

Table 2 Time to consult a physician

Time between first symptom of RA and first visit to a physician	Number of days		Satisfaction of EULAR guidelines[a], *n* (%)
	Mean (S.D.) (median)	95% CI	
General practitioner, $n = 704$	26.3 (41) (15)	23.3, 29.4	NA
Rheumatologist, $n = 812$	75.5 (77) (60)	70.4, 80.6	375 (46.2)
Patients who directly accessed the rheumatologist, $n = 108$	58.3 (55) (40)	48.3, 68.3	62 (57.4)[b]
Patients who indirectly accessed the rheumatologist through the GP, $n = 704$	78.2 (79) (60)	72.3, 84.0	313 (44.5)[b]

[a]EULAR guidelines recommend EA patients to be seen by a rheumatologist within 6 weeks of symptom onset. [b]$P = 0.01$ (chi-square test). NA: non available.

first 6 weeks of the disease than patients who first consulted a GP and were then referred to the specialist (57.2 *vs* 44.5%; $\chi^2 = 6.32$; $P < 0.01$).

Other determinants associated with time to access specialized care

On univariate analysis it was found that age, ethnicity, education, living arrangement and socio-professional status were not significantly associated with TTAR or EULAR-recommended TTAR (Table 3). However, rapid disease onset (acute or subacute), persistent joint swelling (contrary to transient or intermittent joint swelling) and fever were associated with reduced TTAR. Also, reduced TTAR was associated, although not significantly, with the deterioration of general health at arthritis onset, increased functional impairment (HAQ > 2) and high disease activity (DAS28 $\geqslant$ 5.1). In addition, increased TTAR was associated, although not significantly, with residence in regions with lowest medical density (i.e. <150 GPs/100 000 inhabitants or <15 rheumatologists/100 000 inhabitants).

Multivariate analyses

The factors significantly associated with reduced TTAR were acute or subacute onset, persistent joint involvement, fever and direct access to the rheumatologist without any former visit to the GP (Table 4). Consistent with the above findings, the determinants significantly associated with the satisfaction of the EULAR-recommended TTAR were acute or subacute onset, persistent joint involvement, fever and increased functional impairment (Table 5). In addition, direct access to the rheumatologist and living in a region with GP density >150/100 000 inhabitants were also associated with the satisfaction of EULAR recommendations. No interaction was found between the different determinants of TTAR or EULAR-recommended TTAR.

Discussion

Our comparison of physicians' current practice for EA and recently issued EULAR guidelines using the ESPOIR cohort highlights the problems in adequately managing EA, which is difficult to diagnose, in terms of adequate and efficient referral of such patients to a rheumatologist for early treatment. Less than half the cohort (46.2%) visited a rheumatologist within the EULAR-recommended time frame of 6 weeks after symptom onset. Multivariate analysis confirmed the impact of indirect access on reduced TTAR, and the importance of clinical expression of EA and density of medical practitioners in the area of residence. Our findings have implications for meeting the recommendations of EULAR for early treatment of EA to avoid later morbidity and mortality consequences.

Only few data are available in the literature on this topic. In the late 1990s, work conducted in Scotland revealed substantial reduction in the time interval between the occurrence of the first arthritis symptoms and the first assessment in the rheumatology clinic in a sample of 198 RA patients. The time decreased from >20 months before 1989 to 7 months between 1990 and 1993, and to 4 months between 1994 and 1997 [41]. Of course, such a marked decrease was associated with quicker initiation of DMARDs, from >70 months before 1989 to 8 months in the mid-90s, which is the ultimate goal of EA management. However, these data were from a single centre, which might limit the extrapolation of the results. Another study from the UK, in the Birmingham area, also reported a suboptimal time of 23 weeks (161 days) to access a rheumatologist [42]. The authors proposed patient-dependent factors to explain the delayed access to the rheumatologist, the median time to access the GP being 12 weeks (84 days). More recently, a multicentre Canadian study reported a median time interval of 214.5 days (5.36 months) from symptom onset to the first visit to the rheumatologist, which resulted in a mean time of 8.4 months to start therapy with DMARDs [43]. Thus, the time intervals we observed in the ESPOIR cohort seem to indicate a more rapid access to specialized care for patients with EA in France, which might reflect differences in health care systems as well as geographical differences, Canada having more remote areas with more difficult access to medical care than France. Discrepancies in results might also be explained by some selection biases. The inclusion or non-inclusion criteria required swollen joints to be present for >6 weeks but <6 months, which could have led to the exclusion of patients seen late after arthritis onset. Moreover, patients exposed to steroids for >2 weeks were not suitable for inclusion. Such patients were estimated to be <30 across the inclusion centres which seems small enough to avoid any significant selection bias. Another source of discrepancy between the studies might come from the definition of symptom onset, which often relies on self-reported information since patients often visit their doctor a couple of days or weeks after symptom onset. This might effectively introduce some inaccuracy in the reported symptom duration; however, if memory recall bias cannot be completely ruled out, the 6-month time frame explored during patient interview is sufficiently short to make it probably insignificant.

The large sample size of our cohort allowed us to investigate the determinants of rapid or delayed access to specialized care (the rheumatologist). As expected, the symptom intensity at arthritis onset (i.e. acute onset, presence of extra-articular symptoms such as fever) was associated with reduced TTAR and therefore a high proportion of patients consulting a rheumatologist within the EULAR-recommended time frame. In other words, the more symptomatic the disease, the more quickly the patient consulted a physician and the lower the TTAR. As observed in other painful rheumatic conditions, such as FM, patient-perceived symptom intensity is an important driver of seeking care and health resource use. This may be problematic to some extent, since such patients could obstruct access to the rheumatologist for patients less symptomatic but with clear negative prognosis factors. Besides, assessment of coping

TABLE 3 Determinants of the time between symptom onset and access to specialized care (i.e. first visit to the rheumatologist)

Time between first symptom of RA and the first visit to the rheumatologist	Number of days			Time ⩽45 days (EULAR)	
	Mean (S.D.)	95% CI	*P*-value	Per cent	*P*-value
Patient characteristics					
Sex					
Female, $n=624$	76.2 (81)	69.9, 82.5	0.5	47.0	0.4
Male, $n=188$	73.4 (58)	65.1, 81.6		43.6	
Age, years					
18–39, $n=216$	74.4 (85)	63.3, 85.6	0.2	48.6	0.7
40–54, $n=318$	80.9 (83)	71.7, 90.2		45.0	
55–75, $n=271$	69.9 (60)	62.5, 77.3		46.1	
Ethnicity					
Caucasian, $n=748$	75.8 (77)	54.1, 91.1	0.3	45.9	0.5
Non-Caucasian, $n=64$	72.6 (74)	70.3, 80.8		50.0	
Education					
Primary, $n=371$	75.6 (66)	69.0, 82.2	0.8	43.9	0.4
High school, $n=186$	79.7 (88)	67.2, 92.2		45.7	
Some postgraduate education, $n=129$	72.9 (89)	57.2, 88.6		47.3	
University, $n=126$	71.8 (74)	58.9, 84.6		52.4	
Living arrangement					
Single, $n=218$	81.5 (87)	70.1, 92.9	0.6	45.0	0.7
Couple, $n=594$	73.4 (72)	67.2, 79.6		46.6	
Occupation					
Agricultural occupation, $n=27$	68.3 (42)	51.8, 84.8	0.6	33.3	0.1
Craft or sale workers, $n=51$	91.1 (91)	66.7, 115.5		33.3	
Administrative workers, $n=384$	71.1 (74)	63.9, 78.3		49.2	
Production/transportation, $n=82$	80.0 (51)	69.0, 91.0		37.8	
Intermediate occupation, $n=129$	78.0 (82)	64.0, 92.1		45.7	
Management, business, $n=106$	76.7 (92)	59.5, 93.9		51.9	
Unemployed or at home, $n=33$	84.2 (77)	57.9, 110.6		45.5	
RA characteristics					
Family history of inflammatory arthritis					
Absence, $n=683$	74.6 (70)	69.3, 79.9	0.6	45.5	0.4
Presence, $n=129$	80.5 (103)	62.6, 98.5		49.6	
RA onset					
Insidious or intermittent, $n=403$	91.4 (91)	82.4, 100.5	<0.001	38.0	<0.001
Acute or subacute, $n=409$	59.9 (54)	54.7, 65.0		54.3	
Initial joint symptom					
Single joint involvement, $n=145$	91.0 (120)	72.6, 109.5	0.5	43.5	0.5
Oligo or polyarthritis, $n=667$	72.2 (63)	67.2, 77.2		46.8	
Arthritis evolution					
Migrating, $n=238$	88.5 (97)	77.1, 99.9	0.005	38.2	0.003
Persistent, $n=574$	70.1 (66)	64.7, 75.6		49.5	
Fever at RA onset					
Absent, $n=732$	76.9 (74)	71.7, 82.2	0.0001	43.9	<0.001
Present, $n=80$	62.8 (97)	41.1, 84.6		67.5	
Health status deterioration					
Absent, $n=651$	78.2 (81)	71.6, 84.7	0.1	44.9	0.1
Present, $n=161$	65.0 (52)	56.8, 73.1		51.6	
DAS28 at inclusion					
Low disease activity ($\leqslant 3.2$), $n=62$	86.6 (93)	62.6, 110.5	0.5	46.8	0.09
Moderate disease activity (>3.2 to <5.1), $n=344$	76.6 (73)	68.8, 84.3		41.9	
High disease activity ($\geqslant 5.1$), $n=407$	73.0 (77)	65.0, 81.0		49.8	
HAQ at inclusion					
Mild limitation (0–1), $n=411$	78.9 (76)	71.9, 86.0	0.08	43.6	0.9
Moderate limitation (>1–2), $n=310$	75.8 (83)	66.4, 85.1		47.1	
Important limitation (>2–3), $n=89$	58.9 (48)	49.1, 68.8		56.2	

(continued)

Table 3 Continued

Time between first symptom of RA and the first visit to the rheumatologist	Number of days			Time ⩽45 days (EULAR)	
	Mean (s.d.)	95% CI	*P*-value	Per cent	*P*-value
Medical demography (national health insurance)					
GP regional density					
<150/10^5, $n=223$	89.1 (96)	77.3, 100.9	0.004	39.5	0.02
150–169/10^5, $n=245$	73.3 (67)	64.8, 81.6		46.9	
170–189/10^5, $n=156$	60.7 (54)	52.6, 68.9		55.8	
⩾190/10^5, $n=187$	74.3 (76)	63.6, 84.9		45.5	
Rheumatologist regional density					
<15/10^5, $n=37$	120.9 (137)	80.0, 161.8	0.002	35.1	0.17
15–24/10^5, $n=209$	77.6 (68)	66.8, 88.4		44.5	
25–34/10^5, $n=262$	69.2 (68)	61.2, 77.2		51.2	
⩾35/10^5, $n=303$	73.8 (67)	66.4, 81.2		44.6	

Table 4 Multivariate analysis of determinants influencing the time between first symptom of RA and first consultation with the rheumatologist (multiple linear regression with generalized estimating equations to take into account a potential centre effect)

Determinants	β-Estimates	*P*-value
Acute or subacute onset (*vs* insidious or intermittent)	−0.15	<0.0001
Persistent arthritis (*vs* migrating)	−0.09	0.007
Fever	−0.16	0.0002
Direct access to the rheumatologist	−0.14	0.0007
Intercept	1.70	<0.0001

The variables included in the model were direct *vs* indirect access to the specialist; regional density of GPs (<150/10 000 *vs* ⩾150/10 000 inhabitants, based on univariate analysis); regional density of rheumatologists (<15/10 000 *vs* ⩾15/10 000 inhabitants, based on univariate analysis); number of involved joints at onset (1 *vs* ⩾2); rapidity of arthritis onset (acute or subacute *vs* insidious or intermittent); symptom stability (migrating or fixed arthritis); fever at arthritis onset; general health status deterioration at arthritis onset; functional impairment (HAQ ⩽2 *vs* >2, based on univariate analysis); and disease activity (DAS28 < 5.1 *vs* ⩾5.1 inhabitants, based on univariate analysis).

Table 5 Multivariate analysis of determinants associated with the satisfaction of EULAR-recommended TTAR (multiple logistic regression with generalized estimating equations to take into account a potential centre effect)

Determinants	Odds ratio (95% CI)	*P*-value
Acute or subacute onset (*vs* insidious or intermittent)	1.82 (1.37, 2.41)	<0.0001
Persistent arthritis (*vs* migrating)	1.39 (1.02, 1.90)	0.04
Fever at disease onset	2.66 (1.65, 4.28)	<0.0001
HAQ ⩾2	1.33 (1.02, 1.75)	0.04
Regional GP density ⩾150/100 000 inhabitants	1.33 (1.09, 1.61)	0.004
Direct access to the rheumatologist	1.64 (1.15, 2.33)	0.006

The variables included in the model were direct *vs* indirect access to the specialist; regional density of GPs (<150/10 000 *vs* ⩾150/10 000 inhabitants, based on univariate analysis); regional density of rheumatologists (<15/10 000 *vs* ⩾15/10 000 inhabitants, based on univariate analysis); number of involved joints at onset (1 *vs* ⩾2); rapidity of arthritis onset (acute or subacute *vs* insidious or intermittent); symptom stability (migrating or fixed arthritis); fever at arthritis onset; general health status deterioration at arthritis onset; functional impairment (HAQ ⩽2 *vs* >2, based on univariate analysis); and disease activity (DAS28 < 5.1 *vs* ⩾ 5.1 inhabitants, based on univariate analysis).

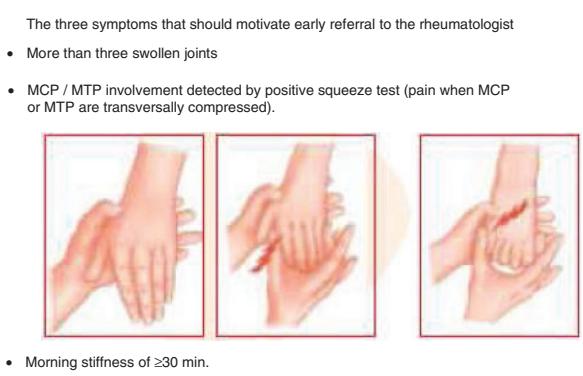
strategies was not available in ESPOIR data and previous studies have shown that it could be an important determinant of patient behaviour [44].

In addition, two determinants related to the overall health care system had a significant deleterious impact on the TTAR: indirect access to a rheumatologist through a GP instead of direct access and low regional density of GPs or specialists. Such information was not available for the studies from the UK or Canada, where access to specialists is usually constrained and limited to patients who first consult a GP. During the ESPOIR inclusion period, in France, direct access to a specialist was permitted by the national health insurance system, and patients were free to schedule an appointment with a rheumatologist of their choice without any referral from a GP (this option became unavailable in 2006 if patients wanted to be fully reimbursed by the national health insurance system). This situation enables the identification of substantial retardation in time to access specialized care for patients who first consult a GP. Therefore, high TTAR could have been due, at least in part, to difficulties in scheduling quick appointments with the GP or the

referred rheumatologist. This situation was found in regions with very low density of physicians—either GPs or specialists. In the multivariate analysis, both low density of physicians and indirect access to a specialist remained statistically significant. Other reasons for high TTAR might be GPs experiencing difficulties in identifying patients with early RA because the clinical presentation might be misleading or incomplete at disease onset. For many years, the diagnosis of EA was neglected because RA, as well as other chronic inflammatory rheumatisms, was thought to be latent and slowly progressive. At that time, medical students or even non-specialist physicians were taught only established rheumatic diseases. The identification of early damage within the first 2 years of RA [8] and of the impact of early DMARD initiation on both remission and structural damage [22, 25, 45, 46] substantially changed the management of early RA, which resulted in two main messages: 'RA is a medical emergency' like diabetes or hypertension [1] and 'treat now, not later' [47]. Thus, more attention was paid to the recognition of RA in the early stages. A group of European experts developed a set of three criteria in a consensus statement for GPs to identify the beginning of inflammatory rheumatic disease: three or more swollen joints, MCP/MTP involvement assessed by a squeeze test (Fig. 1) and morning stiffness longer than 30 min. Any of these three signs should lead GPs to rapidly refer a patient to a rheumatologist [48]. Although such an algorithm may lead to referral to the rheumatologist of many patients with conditions different from RA, the main message of this consensus statement has been integrated in several recommendations for daily clinical practice [38, 49]. The ESPOIR cohort revealed no temporal relation (data not shown) between TTAR and the establishment of either guideline. The need for better implementation of these guidelines in the medical community, specifically GPs, is now crucial since a recent reform of the French health care system has reduced the ability of patients to freely consult the physician of their choice. To be fully covered by the national health insurance, patients must officially state a preferred GP, who becomes the 'gate keeper', or the mandatory first step for any medical problem (with a few exceptions, none of them being in the musculoskeletal field). Although not completely forbidden, direct access to a rheumatologist now incurs financial penalties for the patient. In such standardized patient care, GPs must have adequate knowledge about EA and efficient medical networking for optimal care.

As mentioned before, the ultimate goal of rapid referral for patients with EA is the quick start of DMARD therapy for patients diagnosed with RA by the rheumatologist, and thus to better control the disease activity. A previous study of the ESPOIR cohort showed that 80.5% of such patients actually received a DMARD quickly after their inclusion in the cohort, with a mean time from symptom onset to initiation of DMARD of 123 (median 115) days [50]. In a first analysis, the time to enter the health care system did not directly affect the start of therapy with DMARDs [51]. Future longitudinal data collected for the ESPOIR cohort will allow us to fully explore the effect of 'on-time' *vs* 'delayed' access to specialized care on RA outcomes.

Fig. 1 Early referral guide for GP for patients with EA. Adapted from Emery *et al*. [48].



Rheumatology key messages

- The time to access specialized care for patients with early RA is often suboptimal.
- Additional efforts are needed to widely implement guidelines on EA within the GP community.

Acknowledgements

The authors wish to thank Nathalie Rincheval for expert monitoring and data management, and all the investigators who recruited and followed the patients (Dr M. Rousière, Saint Antoine Hospital, Paris; Pr M.-C. Boissier, Bobigny; Pr A. Cantagrel, Toulouse; Pr M. Dougados, Cochin Hospital, Paris; Pr P. Fardelone and Dr P. Boumier, Amiens; Pr R.-M. Flipo, Lille; Pr P. Goupille, Tours; Pr F. Lioté, Lariboisière Hospital, Paris; Pr X. Le Loët and O. Vittecoq, Rouen; Pr X. Mariette, Bicetre Hospital, Paris; Pr O. Meyer, Bichat Hospital, Paris; Pr A. Saraux, Brest; Pr T. Schaeverbeke, Bordeaux; Pr J. Sibilia, Strasbourg). We also thank Laura Heraty for copyediting.

The cohort was funded by an unrestricted grant from Merck Sharp and Dohme (MSD) allocated for the first 5 years. Two additional grants from INSERM were obtained to support part of the biological database. The French Society of Rheumatology, Abbott and Wyeth also supported the ESPOIR cohort study.

Funding: Institutional support.

Disclosure statement: The authors have declared no conflicts of interest.

References

1 Pincus T. Rheumatoid arthritis: a medical emergency? Scand J Rheumatol Suppl 1994;100:21–30.

2 Leigh JP, Fries JF. Predictors of disability in a longitudinal sample of patients with rheumatoid arthritis. Ann Rheum Dis 1992;51:581–7.

3 Panush RS, Kramer N, Rosenstein ED. Assessment and prognosis of rheumatoid arthritis. Curr Opin Rheumatol 1992;4:355–64.

4 Ward MM, Leigh JP, Fries JF. Progression of functional disability in patients with rheumatoid arthritis. Associations with rheumatology subspecialty care. Arch Intern Med 1993;153:2229–37.

5 Reilly PA, Cosh JA, Maddison PJ, Rasker JJ, Silman AJ. Mortality and survival in rheumatoid arthritis: a 25 year prospective study of 100 patients. Ann Rheum Dis 1990; 49:363–9.

6 Wolfe F, Cathey MA. The assessment and prediction of functional disability in rheumatoid arthritis. J Rheumatol 1991;18:1298–306.

7 Pincus T, Brooks RH, Callahan LF. Prediction of long-term mortality in patients with rheumatoid arthritis according to simple questionnaire and joint count measures. Ann Intern Med 1994;120:26–34.

8 van der Heijde DM. Joint erosions and patients with early rheumatoid arthritis. Br J Rheumatol 1995;34(Suppl. 2), 74–8.

9 Callahan LF, Pincus T. Mortality in the rheumatic diseases. Arthritis Care Res 1995;8:229–41.

10 Goodson NJ, Wiles NJ, Lunt M, Barrett EM, Silman AJ, Symmons DP. Mortality in early inflammatory polyarthritis: cardiovascular mortality is increased in seropositive patients. Arthritis Rheum 2002;46:2010–9.

11 Goodson N, Marks J, Lunt M, Symmons D. Cardiovascular admissions and mortality in an inception cohort of patients with rheumatoid arthritis with onset in the 1980s and 1990s. Ann Rheum Dis 2005;64:1595–601.

12 Kvalvik AG, Jones MA, Symmons DP. Mortality in a cohort of Norwegian patients with rheumatoid arthritis followed from 1977 to 1992. Scand J Rheumatol 2000;29: 29–37.

13 Navarro-Cano G, Del Rincon I, Pogosian S, Roldan JF, Escalante A. Association of mortality with disease severity in rheumatoid arthritis, independent of comorbidity. Arthritis Rheum 2003;48:2425–33.

14 Wolfe F, Michaud K, Gefeller O, Choi HK. Predicting mortality in patients with rheumatoid arthritis. Arthritis Rheum 2003;48:1530–42.

15 Krause D, Schleusser B, Herborn G, Rau R. Response to methotrexate treatment is associated with reduced mortality in patients with severe rheumatoid arthritis. Arthritis Rheum 2000;43:14–21.

16 Choi HK, Hernan MA, Seeger JD, Robins JM, Wolfe F. Methotrexate and mortality in patients with rheumatoid arthritis: a prospective study. Lancet 2002;359:1173–7.

17 Dixon WG, Symmons DP. What effects might anti-TNFalpha treatment be expected to have on cardiovascular morbidity and mortality in rheumatoid arthritis? A review of the role of TNFalpha in cardiovascular pathophysiology. Ann Rheum Dis 2007;66:1132–6.

18 Jacobsson LT, Turesson C, Nilsson JA *et al*. Treatment with TNF blockers and mortality risk in patients with rheumatoid arthritis. Ann Rheum Dis 2007;66:670–5.

19 Pincus T, Gibofsky A, Weinblatt ME. Urgent care and tight control of rheumatoid arthritis as in diabetes and hypertension: better treatments but a shortage of rheumatologists. Arthritis Rheum 2002;46:851–4.

20 Sokka T, Kautiainen H, Hakkinen A, Hannonen P. Radiographic progression is getting milder in patients with early rheumatoid arthritis. Results of 3 cohorts over 5 years. J Rheumatol 2004;31:1073–82.

21 Descalzo MA, Carmona L, Tobias A. Total joint replacement surgery of hip and knee in the biologics era. A time-trend analysis from 1997–2005. Arthritis Rheum 2007;56(Suppl), S351.

22 Finckh A, Liang MH, van Herckenrode CM, de Pablo P. Long-term impact of early treatment on radiographic progression in rheumatoid arthritis: a meta-analysis. Arthritis Rheum 2006;55:864–72.

23 Boers M. Understanding the window of opportunity concept in early rheumatoid arthritis. Arthritis Rheum 2003;48:1771–4.

24 Anderson JJ, Wells G, Verhoeven AC, Felson DT. Factors predicting response to treatment in rheumatoid arthritis: the importance of disease duration. Arthritis Rheum 2000; 43:22–9.

25 Lard LR, Visser H, Speyer I *et al*. Early versus delayed treatment in patients with recent-onset rheumatoid arthritis: comparison of two cohorts who received different treatment strategies. Am J Med 2001;111:446–51.

26 Makinen H, Kautiainen H, Hannonen P *et al*. Sustained remission and reduced radiographic progression with combination disease modifying antirheumatic drugs in early rheumatoid arthritis. J Rheumatol 2007;34:316–21.

27 van der Heijde DM, van't Hof M, van Riel PL, van de Putte LB. Development of a disease activity score based on judgment in clinical practice by rheumatologists. J Rheumatol 1993;20:579–81.

28 van der Heijde DM, van't Hof M, van Riel PL, van de Putte LB. Validity of single variables and indices to measure disease activity in rheumatoid arthritis. J Rheumatol 1993;20:538–41.

29 Smolen JS, Breedveld FC, Schiff MH *et al*. A simplified disease activity index for rheumatoid arthritis for use in clinical practice. Rheumatology 2003;42:244–57.

30 van Riel P. DAS and EULAR response criteria using CRP instead of ESR. Ann Rheum Dis 2004;63(Suppl. 1), 17.

31 Leeb BF, Andel I, Sautner J *et al*. Disease activity measurement of rheumatoid arthritis: comparison of the simplified disease activity index (SDAI) and the disease activity score including 28 joints (DAS28) in daily routine. Arthritis Rheum 2005;53:56–60.

32 Aletaha D, Ward MM, Machold KP, Nell VP, Stamm T, Smolen JS. Remission and active disease in rheumatoid arthritis: defining criteria for disease activity states. Arthritis Rheum 2005;52:2625–36.

33 Svensson B, Schaufelberger C, Teleman A, Theander J for the BARFOT study group. Remission and response to early treatment of RA assessed by the disease activity score. Rheumatology 2000;39:1031–6.

34 Grigor C, Capell H, Stirling A *et al*. Effect of a treatment strategy of tight control for rheumatoid arthritis (the TICORA study): a single-blind randomised controlled trial. Lancet 2004;364:263–9.

35 Fransen J, Moens HB, Speyer I, van Riel PL. Effectiveness of systematic monitoring of rheumatoid arthritis disease activity in daily practice: a multicentre,

cluster randomised controlled trial. Ann Rheum Dis 2005; 64:1294–8.

36 van der Kooij SM, Allaart CF, Goekoop-Ruiterman YPM *et al*. Chances of continued low disease activity in patients with rheumatoid arthritis treated by DAS guided protocol: results from the BeSt study. Arthritis Rheum 2006;54:S704.

37 Allaart CF, Goekoop-Ruiterman YP, de Vries-Bouwstra JK, Breedveld FC, Dijkmans BA. Aiming at low disease activity in rheumatoid arthritis with initial combination therapy or initial monotherapy strategies: the BeSt study. Clin Exp Rheumatol 2006;24:S77–82.

38 Combe B, Landewe R, Lukas C *et al*. EULAR recommendations for the management of early arthritis: report of a task force of the European Standing Committee for International Clinical Studies Including Therapeutics (ESCISIT). Ann Rheum Dis 2007;66:34–45.

39 Combe B, Benessiano J, Berenbaum F *et al*. The ESPOIR cohort: a ten-year follow-up of early arthritis in France: methodology and baseline characteristics of the 813 included patients. Joint Bone Spine 2007;74:440–5.

40 Combe B. Early rheumatoid arthritis: strategies for prevention and management. Best Pract Res Clin Rheumatol 2007;21:27–42.

41 Irvine S, Munro R, Porter D. Early referral, diagnosis, and treatment of rheumatoid arthritis: evidence for changing medical practice. Ann Rheum Dis 1999;58:510–3.

42 Kumar K, Daley E, Carruthers DM *et al*. Delay in presentation to primary care physicians is the main reason why patients with rheumatoid arthritis are seen late by rheumatologists. Rheumatology 2007;46:1438–40.

43 Tavares R, Tomlinson G, Boire G, Laupacis A, Bombardier C. Time to disease modifying anti-rheumatic drug treatment in a national, multi-centre, historical inception cohort of randomly selected, early rheumatoid arthritis. Arthritis Rheum 2007;56:S84.

44 Esselens GH, De Brabander A, Ovaere L, De Brabanter G, Moons P, Westhovens R. Personal attributes as determinants of timely care in rheumatoid arthritis. Ann Rheum Dis 2006;65:967–8.

45 Emery P. Evidence supporting the benefit of early intervention in rheumatoid arthritis. J Rheumatol 2002; 66(Suppl), 3–8.

46 Nell VP, Machold KP, Eberl G, Stamm TA, Uffmann M, Smolen JS. Benefit of very early referral and very early therapy with disease-modifying anti-rheumatic drugs in patients with early rheumatoid arthritis. Rheumatology 2004;43:906–14.

47 Weinblatt ME. Rheumatoid arthritis: treat now, not later! Ann Intern Med 1996;124:773–4.

48 Emery P, Breedveld FC, Dougados M, Kalden JR, Schiff MH, Smolen JS. Early referral recommendation for newly diagnosed rheumatoid arthritis: evidence based development of a clinical guide. Ann Rheum Dis 2002;61: 290–7.

49 Hyrich KL. Patients with suspected rheumatoid arthritis should be referred early to rheumatology. Br Med J 2008; 336:215–6.

50 Benhamou M, Rincheval N, Roy C *et al*. The gap between practice and guidelines in the choice of first-line disease modifying antirheumatic drug in early rheumatoid arthritis: results from the ESPOIR cohort. J Rheumatol 2009;36: 934–42.

51 Lukas C, Guillemin F, Landewe R *et al*. Factors determining a DMARD initiation in early inflammatory arthritis patients. The ESPOIR cohort study. Clin Exp Rheumatol 2009;27:84–91.