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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

Mathilde Benhamou[1], **Nathalie Rincheval**[2], **Carine Roy**[3], **Violaine Foltz**[1], **Sylvie Rozenberg**[1], **Jean Sibilia**[4], **Thierry Schaeverbeke**[5], **Pierre Bourgeois**[1], **Philippe Ravaud**[3], and **Bruno Fautrel**[1,*]

[1]Service de Rhumatologie AP-HP, Hôpital Pitié-Salpêtrière, Université Pierre et Marie Curie - Paris VI, 47-83, boulevard de l'Hôpital 75651 PARIS Cedex 13,FR.

[2]Centre de coordination CHRU Montpellier, Hôpital Lapeyronie, Montpellier,FR.

[3]Département d'épidémiologie, biostatistique et recherche clinique AP-HP, Hôpital Bichat - Claude Bernard, 46 rue Henri Huchard 75018 Paris,FR.

[4]Physiopathologie et antibiologie microbiennes Université Louis Pasteur - Strasbourg I : EA3432, FR.

[5]Service de rhumatologie CHU Bordeaux, FR.

Abstract

Introduction—To compare rheumatologists' prescription for first disease-modifying anti-rheumatic drug (DMARD) in early rheumatoid arthritis (RA) in real-life settings with two clinical practice guidelines (CPG), STPR [1] and EULAR [2] and thus assess the gap between practices and guidelines.

Methods—ESPOIR is a French multicentre cohort study that included 813 early arthritis patients between 2002 and 2005. 'Definite' and 'probable' RA were defined according to ACR criteria and the level of diagnostic certainty. The objectives were to: 1/assess conformity between the observed first-line DMARD prescribed for those patients and the guidelines' recommended DMARD; and 2/ conduct a mail survey of patients' usual rheumatologists to explore the reasons for their non-conformity with guidelines.

Results—627 patients with definite or probable RA were identified. Conformity rates were 58% for STPR guidelines and 54% for EULAR guidelines. At 6 months, 83 (34%) patients with early RA did not receive any DMARD. Main determinants associated with conformity to guidelines were: disease activity and presence of severity predictive factors. The main reason leading to a discrepancy between guidelines and daily practice appeared to be diagnostic uncertainty, i.e., the difficulty to reliably assess RA diagnosis as soon as the first visits to the rheumatologist.

Conclusion—There is a substantial gap between CPG and rheumatologists' daily practice concerning the first DMARD to prescribe in early RA. It is explained mainly by diagnostic uncertainty. More attention should be paid in future guidelines to the diagnostic difficulties of early RA.

* Correspondence should be adressed to: Bruno Fautrel bruno.fautrel@psl.aphp.fr.

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Keywords

Adolescent; Adult; Aged; Antirheumatic Agents; therapeutic use; Arthritis, Rheumatoid; diagnosis; drug therapy; Early Diagnosis; Female; France; Humans; Male; Middle Aged; Physician's Practice Patterns; standards; statistics & numerical data; Practice Guidelines as Topic; Prospective Studies; Rheumatology; methods; standards; Time Factors; Uncertainty; Young Adult

Keywords

rheumatoid arthritis; earlyarthritis; first-line DMARD; clinical practice guideline; guideline adherence; disease management

INTRODUCTION

Promulgation of clinical practice guidelines (CPG) is intended to synthesise available medical information and improve quality of care.[3–9] Barriers to their application, however, often limit their implementation in daily practice.[10,11] Actual application depends on a variety of indicators, including confidence in the guideline developer [12,13], accessibility of the guidelines, their ease of use [14], and applicability to specific patients, as well as the strategies used to promote implementation.[15,16]

Rheumatoid arthritis (RA) is interesting to consider from this point of view because treatment for it has changed substantially in recent years. Key aspects of these changes include early start of treatment, use of drugs that can prevent joint destruction (that is, proven to prevent or delay structural damage) and disease flares, importance of regular monitoring of disease activity and structural changes to ensure tight control of the disease.[17–22] For this reason, several expert groups and professional societies have issued guidelines on this topic in recent years.[1,2,23, 24]

Two different groups produced two sets of guidelines about prescription of first-line disease-modifying antirheumatic drugs (DMARD) in early RA: the French Society of Rheumatologists' STPR working group [1] (French acronym for "Therapeutic strategies in RA") and a EULAR expert group [2] (European League Against Rheumatism). The STPR guidelines present a decision tree for choosing the first DMARD to be used in early RA (less than 6 months duration).[1] The EULAR guidelines put methotrexate as the anchor drug that should be used first in patients at risk of developing persistent disease.[2]

To compare these CPG with the usual care provided by rheumatologists, we used the data of a French nationwide cohort, ESPOIR (acronym for "Study and Follow-up of Undifferentiated Early Arthritis"), which included patients between 2002 and 2005.[25] It is important to note the chronology: the ESPOIR inclusion period overlapped with the production and diffusion of both CPG. The STPR results were presented at the ACR annual scientific meeting in November 2004 and published in January 2006, while the EULAR results were presented at the EULAR annual scientific meeting in June 2005 and published in January 2007. Our aim therefore was not to assess adherence to guidelines. Instead we sought to explore the potential gap between daily rheumatologic practice and guidelines for the first DMARD prescription in early RA, before their dissemination, for such gaps are likely to be barriers to implementation.

PATIENTS AND METHODS

Study design

Our primary objective was to assess the conformity between the first DMARD prescribed to patients in the ESPOIR cohort and the DMARD recommended by each of the two sets of guidelines. At the same time we assessed the determinants of this conformity, the influence of the patient's inclusion date, and the extent of the gap with the STPR guidelines. Our secondary objective was to explore the reasons for any discrepancies we observed between the rheumatologists' decisions and CPG. Accordingly, in cases where the treatment did not match the STPR guidelines, we sent a questionnaire (described in Appendices) to the patients' attending rheumatologists.

Patients

The ESPOIR cohort—ESPOIR was a nationwide prospective cohort study of adults (18 to 70 years old) sponsored by the French Society of Rheumatology.[25,26] Inclusion criteria were: inflammatory arthritis for at least 6 weeks but not longer than 6 months, involvement of more than two joints, clinical diagnosis of RA as certain or probable or clinical diagnosis of undifferentiated arthritis potentially becoming RA, and no DMARD or steroid treatment since the onset of symptoms. Patients with other definite inflammatory rheumatic diseases or with too much uncertainty of developing RA were excluded.

Recruitment in 14 university hospital rheumatology departments was conducted through several media inviting patients and physicians to participate in each regional area. Each centre acted as an observational centre and did not interfere with patient treatment, except in charge of a patient. The patients were routinely treated and followed by private rheumatologists of the geographical area.

In all, 813 patients were recruited from November 2002 to April 2005 and have been longitudinally followed since then, seen every 6 months in the 14 hospital centres participating in the project. Baseline data is updated at the 6-month follow-up.

RA diagnosis—A selection of patients most at risk to be RA patients was conducted in ESPOIR database, to allow a study of conformity with guidelines in case of the less diagnostic uncertainty of RA. Therefore fulfilment of ACR criteria [27] and the attending rheumatologist's diagnostic certainty at baseline (0 to 100 visual analogue scale – VAS) were used.

'Definite RA' was defined if patients met at least 4 (of 7) ACR criteria and diagnostic certainty was rated at ≥75 (threshold determined by ESPOIR steering committee). 'Probable RA' was defined as meeting at least 3 ACR criteria, even with a diagnostic certainty <75.

Guidelines

STPR guidelines:[1]—The STPR decision tree determines the DMARD to prescribe according to 3 items: level of disease activity based on the Disease Activity Score for 28 joints (DAS28) (low: 3.2; moderate: ≤3.2–5.1; high: ≥5.1), the presence of structural damage, and rheumatoid factor (RF) status. The decision tree leads to four possible therapeutic options of increasing severity. Each calls for the choice of one of two DMARDs: A/hydroxychloroquine or sulfasalazine, B/sulfasalazine or methotrexate, C/methotrexate or leflunomide, D/methotrexate or TNF-blocker agents. (Appendix 1)

EULAR guidelines:[2]—These guidelines recommend methotrexate as a first treatment for early arthritis at risk to be persistent, since it acts on structural damage, prevents flares and may thus be viewed as an anchor drug for additional DMARDs in case of inadequate response.

Conformity with guidelines: We then assessed conformity with the STPR and the EULAR guidelines. To evaluate STPR conformity we needed data about the 3 items of the STPR algorithm whereas to evaluate EULAR conformity we were able to compare therapeutic decision with the recommended treatment everytime.

Possible determinants of conformity studied were: social and demographic patient characteristics (sex, age, ethnic origin, educational level, comorbidities), disease characteristics (number of tender joints, number of swollen joints, symptoms duration, DAS28 score, HAQ score), prognostic factors (presence of rheumatoid factor (RF) or Anti-CCP antibodies (CCP-Abs), presence of radiographic erosions, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels), category of diagnostic certainty (definite versus probable RA) and finally the geographical area of inclusion.

In view of the length of the ESPOIR inclusion period, we also assessed the influence of the inclusion period, subdivided into four quartiles (November 2002 through May 2003, June 2003 through December 2003, January 2004 through June 2004, and July 2004 through April 2005).

When treatment was not the same as the STPR guidelines, the discrepancy could be either important or slight. We therefore pooled the different treatment decisions in 3 broad categories: no DMARD prescription, prescription of DMARD that only prevents flares (hydroxychloroquine, gold salts, tiopronin), and prescription of at least one DMARD that prevents flares and has been proven to inhibit structural damage (methotrexate, leflunomide, sulfasalazine and TNF-blocker agents). We then assessed the observed and expected (according to STPR guidelines) DMARD prescriptions according to these three categories.

Mail survey

In May 2007, a survey was mailed to the initial attending rheumatologists of all patients whose treatment differed from STPR guidelines. The questionnaire was carefully phrased to not seem judgmental, especially since no aspect of either CPG was mandatory. All therapeutic options were presented at the same level, without any labeling as good or bad, optimal or suboptimal. The questionnaire asked about the reasons for the decision and then about awareness of the STPR and EULAR guidelines. Rheumatologists were also asked about their perception of the guidelines' pertinence and the decision they would make for a similar patient visiting in 2007.

Statistical analysis

Statistical analysis used SAS software, version 9-1 (SAS Institute Inc., Cary, NC, USA). Conformity was scored 1 if the treatment and guidelines matched and 0 if not. Conformity was expressed as a percentage. Categorical variables were compared with Pearson's $\chi 2$-test or Fisher's exact test, as appropriate. The statistical significance level was set at α=0.05 in two-tailed tests.

Univariate analyses determined the factors associated with conformity. Multivariate logistic regression with generalized estimating equations (mixed model) was used to account for the clusters (14 hospital centres). Variables with a p-value less than 20% were kept in the final model. The likelihood of dependent variables is presented as odds ratios with their 95% confidence intervals. The responses to the mail survey are expressed as percentages.

Ethics Committee

The ESPOIR study was approved by the central ethics committee of Montpellier, and written informed consent was obtained from each participant in the cohort. Both the scientific and steering committee of the ESPOIR cohort approved this study.

RESULTS

Of the 813 cohort members, 627 had definite or probable RA and were included in the further analysis. (Figure 1)

Baseline patient characteristics

Table 1 summarises the main baseline characteristics of the 627 patients. They were predominantly female (76.6%), and their mean age was 48.7 years. Almost 30% had at least one comorbid disease at inclusion. They presented with active, very recent-onset disease: mean tender joint count was 9.4 +/− 7.1, mean swollen joint count 8.2 +/− 5.3, mean DAS28 5.4 +/− 1.2, and mean symptom duration (from onset of the first persistently swollen joint) less than 15 weeks.

In all, 505 patients (80.5% of 627 patients) began DMARD treatment within a mean of 17.6 +/− 9.1 weeks (median 16.4) from the onset of the first persistently swollen joint. The DMARD prescribed most frequently was methotrexate — in 340 patients (54.2% of 627). Combination therapies were noted in 41 patients (6.5%). (Table 2)

Conformity with guidelines

Conformity with the STPR guidelines could be determined for 581 patients (92.7%) (Figure 1) and ranged between centres from 35 to 79%. Overall, 337 DMARD prescriptions (58.0%) matched the STPR guidelines (66% in the group “definite RA” and 47% in the group “probable RA”).

Conformity with the EULAR guidelines could be determined for all 627 patients and ranged between centres from 22 to 75.4%. In all, 340 DMARD choices (54.2%) matched the EULAR guidelines (61% in the group “definite RA” and 45% in the group “probable RA”).

Analysis of determinants associated with conformity

STPR guidelines: Results of the univariate analysis are presented in Table 3. The final multivariate analysis adjusted for inclusion centre, found three variables to be significantly associated with conformity: presence of RF or CCP-Abs and a ‘definite’ diagnosis of RA were associated with better conformity (odds ratios >1), while poorer conformity was found for women patients (odds ratios <1). (Table 4)

EULAR guidelines: The data from the univariate analysis are not shown. The multivariate analysis, adjusted for inclusion centre, found the following significant determinants associated with better conformity: moderate and high DAS28 scores, radiographic bone erosions, and the presence of RF or CCP-Abs (odds ratios >1). (Table 4)

Influence of inclusion period—We observed a trend towards better conformity with the STPR guidelines over time during the ESPOIR inclusion period. During the last period (July 2004 through April 2005), conformity with STPR reached 67.4%, compared with 56.5% for the previous periods. This difference was not, however, statistically significant ($\chi 2=6.9$, DF=3, p=0.07).

Importance of the divergence in cases of non-conformity with the STPR guidelines Overall, 433 (69.1%) received at least one DMARD proven to inhibit structural damage, 72 (11.5%) a DMARD that did not, and 122 (19.5%) did not receive any DMARD until the 6-month follow-up visit.

We then focused on the 244 patients treated differently than the STPR guidelines recommend (Table 5): 116 (47.5%) had mild to moderate disease (no structural damage and low or moderate DAS28 scores). In this group, 62 patients (25.4%) had no DMARD prescribed, 31 (12.7%) only a flare-preventing DMARD, and 23 (9.4%) at least one flare-preventing DMARD also proven to inhibit structural damage. Of the 128 (52.5%) with severe disease (either structural damage or high DAS28 score), 21 (8.6%) had no DMARD prescribed, 39 (16.0%) only a flare-preventing DMARD, and 68 (27.9%), at least one DMARD that inhibited structural damage and prevented flares.

Mail survey

The mail questionnaire was sent out in May 2007 and the analysis was performed in August 2007: 204 separate surveys were sent to 124 rheumatologists. We received 113 answers (55.4% of 204) from 73 rheumatologists (58.9% of 124). (Figure 1)

They responded that their treatment decision was based, in decreasing order, on: diagnostic uncertainty (36.1%), presumed best benefit/risk ratio (25.0%), hospital decision (13.9%), usual practice (7.4%), patient decision (5.6%), “don’t remember” (4.6%), inclusion in a clinical trial (3.7%), and patient comorbidities (3.7%). The percentages reported by respondents who decided not to use any DMARD differed slightly, with diagnostic uncertainty accounting for 47.4% of the reasons; the order thereafter did not differ. At the time of the survey, 56 rheumatologists (76.7%) were aware of the STPR guidelines and 59 (80.8%) of the EULAR guidelines.

In 66 cases (58.4% of 113), the rheumatologist reported they would choose a different treatment now, and 57 (50.4%) would choose the treatment recommended by STPR. The main reason for continued disagreement with STPR guidelines remained diagnostic uncertainty.

DISCUSSION

Our study demonstrates a rather substantial discrepancy between the recently published guidelines for the first-line DMARD to be prescribed for patients with early RA, and daily French practice between 2002 and 2005.

We have not found similar data in the literature with which we can compare our results. Although some studies that retrospectively assessed the application of CPG for therapeutic decisions report conformity rates ranging from 40 to 60%, study designs and methods vary greatly.[8,28–30] For example, in the field of rheumatology, Denoeud et al. showed that the French general practitioners treating osteoarthritis of the knee conform with the EULAR guidelines in 54% of the cases.[28] The conformity rates in our study, even before implementation of the CPG, are rather encouraging and suggest rheumatologists will find them acceptable.

The conformity with guidelines improved during the study period with a rate of 67% for the STPR guidelines during the last period of ESPOIR inclusions. There were connections between the members of the STPR group and the ESPOIR steering committee as a few people participated in both groups (AC, BC, BF, RMF, XLL, OM, AS). This could have led to better dissemination of STPR guidelines in the ESPOIR inclusion centres, even if patients were followed by their usual rheumatologist. Moreover some discrepancies have been observed in

the different centres which might be due to local prescription habits or impact of local opinion leaders. Some of the ESPOIR centres are also important recruitment centres for clinical trials which lead to DMARD prescriptions different from guidelines. However, treatment decisions were made by usual practising rheumatologist and not directly by the people involved in the recruitment and follow-ups of the ESPOIR patients.

Our study found quite similar rates of conformity for both sets of guidelines, which recommend methotrexate as the principal treatment in early RA. Of the 505 (67%) patients who received a DMARD in this study, 340 were prescribed methotrexate. These results are similar to those in other studies. Methotrexate is the leading DMARD prescribed for RA in Europe, the United States, and Australia; it accounts for 46 to 83% of all DMARDs prescribed, according to country.[31–36]

We also wondered if the results of conformity with EULAR guidelines would be different by assuming that using leflunomide as a first DMARD was equivalent to use methotrexate. The rate of conformity was then 59.2% instead of 54.2%.

A key point in the recent therapeutic advances in the management of RA is the need to start treatment early with a DMARD that reduces joint damage (radiographic progression).[18,20, 22] Delaying its initiation in patients with early RA is thus very clearly suboptimal treatment. The STPR and EULAR guidelines differ in that STPR grades the prescription according to disease activity and factors predictive of severity (structural damage, RF status). In particular, the STPR group does not recommend methotrexate for RA patients who have a low DAS28 and no structural damage and are negative for RF, that is, for mild or perhaps doubtful RA. The randomized controlled PROMPT study points in the same direction. It showed in a subgroup of patients with early arthritis who were negative for RF and CCP-Abs and thus might not develop RA that methotrexate did not improve patient outcomes at 3 years.[37] The STPR guidelines rely on this concept and introduce treatment that is graded according to the potential benefit/risk ratio of methotrexate, compared with other conventional DMARDs, such as hydroxychloroquine.

It was also interesting to determine whether the patients treated differently than the STPR guidelines recommend had received a DMARD that stops joint damage. Although only 23 of the 116 patients with mild or moderate disease (20%), had been treated with such a drug, negative consequences to this lack of treatment were least likely in this group.[37] On the other hand, 60 of the 128 patients with severe disease (47%) had still not received a DMARD effective against structural involvement 6 months after inclusion in the study, and their treatment can be considered suboptimal, as several authors have shown.[20,38,39]

An important reason for non-conformity with guidelines and, by extension, for suboptimal care is diagnostic uncertainty, which is a well-known difficulty in the management of early RA. Classification criteria and clinical standards for diagnosis are useful after 1 or 2 years of disease, but not necessarily at the first consultation. In practice, early arthritis is frequently undifferentiated.[40] An RA diagnosis is thus generally based upon the rheumatologist's opinion, perhaps after consideration of the ACR classification criteria[27], as here. These criteria do not, however, perform as well in early arthritis as they do in established RA.[41] Other criteria, such as those from the Leiden clinic [42], have been developed to address early RA diagnosis more specifically.

Some limitations in our study must be noted. Although the cohort was observational and intended for the study of routine practice, it is not certain that mere participation did not influence rheumatologists' treatment decisions and thereby introduce possible bias. Furthermore, compliance bias undoubtedly plays a role in physicians' answers to questions about their practices, because it is well known that the even experts' answers about their

prescription habits are sometimes rather far from their real practice, as Headrick et al showed. [43]

To conclude, we found a gap between recent guidelines for treatment of early RA and daily practice by specialists during the period the guidelines were under development. In some cases, especially when the RA diagnosis is uncertain or predictive factors of severity are absent, these differences are unlikely to be harmful. In other cases, however, care appeared to be suboptimal. Future efforts will concern the establishment of reliable criteria for diagnosis of early RA, necessary to improve the implementation of the treatment guidelines.

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APPENDICES

Appendix 1. Therapeutic options recommended by STPR for prescription of first DMARD in early RA, derived from the STPR guidelines [1]

Patients	No structural damage		With structural damage	
DAS28	RF negative	RF positive	RF negative	RF positive
Low: 0–3.2	A	B	C	C
Moderate: 3.2–5.1	B	B	C	C
High: >5.1	C	C	C	D

DAS 28: Disease Activity Score on 28 joints; RF: rheumatoid factor Four Therapeutic options recommended by STPR for prescription of first DMARD in early RA:

A: Hydroxychloroquine or sulfasalazine

B: Sulfasalazine or methotrexate

C: Methotrexate or leflunomide

D: Methotrexate or TNF-blocker agents

Appendix 2: Questionnaire mailed to patients' attending rheumatologists

Patient N°

Dear colleague,

You participated in the ESPOIR cohort between 2002 and 2005, by including a patient on the ../../…

Your patient, Mr (Mrs) xxx/xx, … years old, presented with :

- … tender joints, … swollen joints,
- Erythrocyte Sedimentation Rate was … mm at 1st hour, C-Reactive Protein was … mg/L, Rheumatoid Factor was positive/negative.
- DAS 28 was …,
- Radiography showed some (did not show any) structural damage typical of rheumatoid arthritis (RA).

The therapeutic decision was to: start … (not start) a DMARD.

I) Can you explain the reasons leading to this therapeutic decision, reviewing your file if necessary?

(Please circle the answer you prefer)

1. This was my usual practice
2. This option had the best benefit/risk ratio
3. This was the best option because of patient comorbidities
4. The RA diagnosis was uncertain
5. Therapeutic decision was due to hospital colleagues
6. The patient refused another proposal

7. The patient was included in a clinical trial
8. I don't remember

II) Various guidelines have been published for choosing the first DMARD for patients presenting with early RA. Are you aware of the following guidelines?

(Please fill in one circle per item)

1. STPR, in 2006 Le Loët X. et al., ARD 2006;65;45–50.
    - Yes
    - No
2. EULAR, in 2007 Combe B. et al., ARD2007;66;34–45.
    - Yes
    - No

III) Considering these guidelines and their impact in your practice, how would you treat a similar case today?

(Please circle the answer you prefer)

1. Would not start a DMARD.
2. Introduction of:
    - Hydroxychloroquine
    - Sulfasalazine
    - Gold salts
    - Methotrexate
    - Leflunomide
    - Combined therapy:
        - Hydroxychloroquine + sulfasalazine
        - Methotrexate + hydroxychloroquine
        - Methotrexate + sulfasalazine
        - Methotrexate + leflunomide
        - Methotrexate + gold salts
        - Methotrexate + hydroxychloroquine + gold salts
    - TNF-blocker agent alone or with another DMARD
    - Others:

IV) In a similar case, the STPR work group (Stratégies Thérapeutiques dans la Polyarthrite Rhumatoïde) would have recommended:

Either …, either …, as a single treatment.

Do you agree with this guideline in this patient's case?

(Please circle the answer you prefer)

1. Yes
2. No

- If you answered « No », please circle the reason why or describe why under “other”:

➢ This is not my usual practice

➢ This option does not have the best benefit/risk ratio

➢ This is not the best option because of patient comorbidities

➢ The diagnosis of RA is uncertain

➢ I think that a combination of DMARDs is needed, included one of the drugs recommended

➢ I think that a combination of DMARDs is needed, not including either of the two recommended drugs

➢ Other:

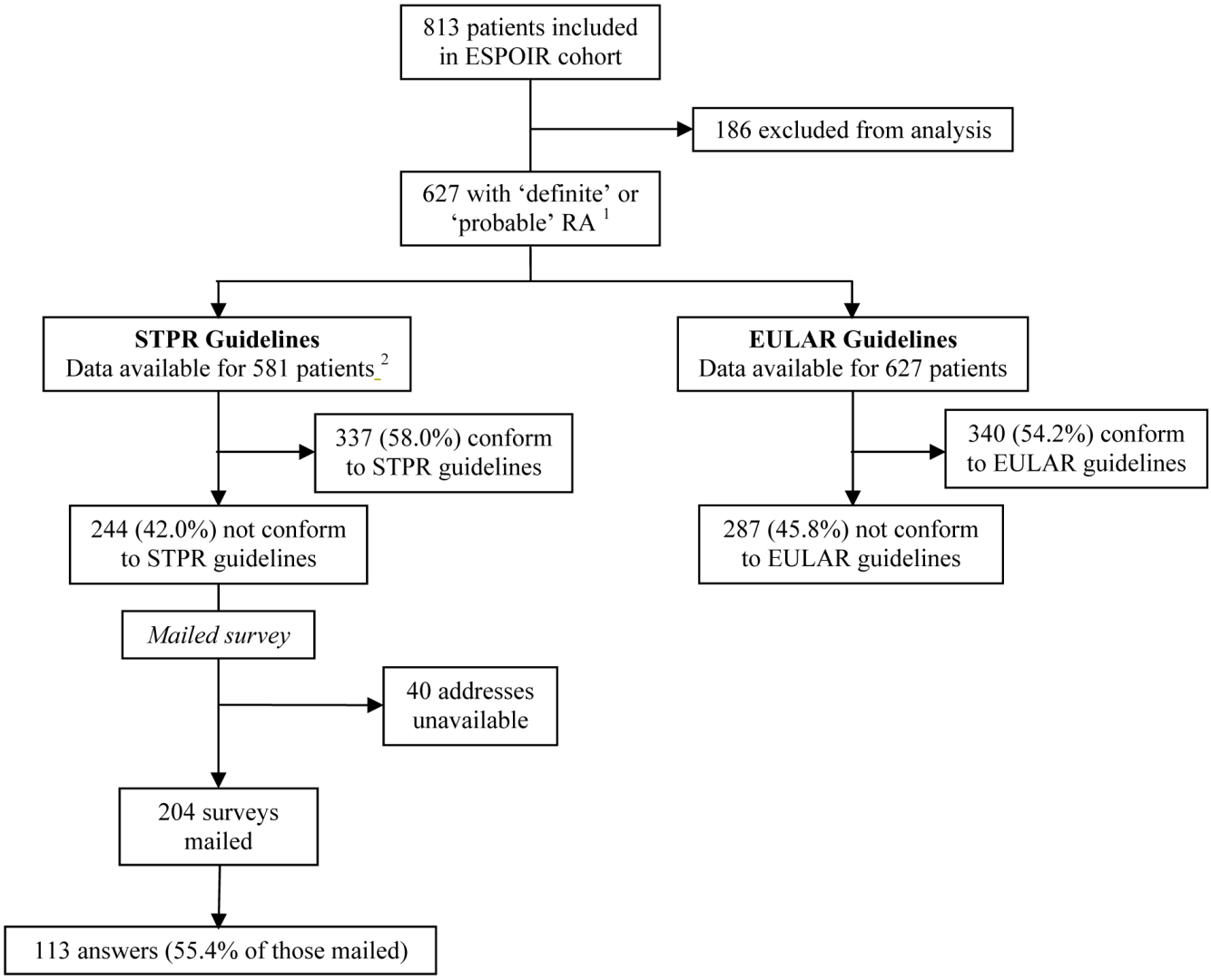

Figure 1. Study design

[1]RA: Rheumatoid arthritis

[2] 581 patients had complete sets of data (DAS 28 score, the structural damage status and RF status) (92.7%)

Table 1

Patient baseline characteristics

ESPOIR cohort patients	**'Definite' and 'Probable' RA n=627**
Social and demographic characteristics	
Women, *n (%)*	**480 (76.6)**
Age (years), *mean +/− SD (median)*	**48.7 +/− 12.4 (51.1)**
Caucasian, *n (%)*	**582 (92.8)**
Post-secondary level of education, *n (%)*	**96 (15.3)**
History/Comorbidities	
Personal or familial history of psoriasis, *n (%)*	**103 (16.4)**
At least one comorbid factor*, *n (%)*	**178 (28.7)**
BMI** (kg/m^2), *mean +/− SD (median)*	**25.2 +/− 4.6 (24.5)**
Disease characteristics	
Tender joints***, *mean +/− SD (median)*	**9.4 +/− 7.1 (8.0)**
Swollen joints***, *mean +/− SD (median)*	**8.2 +/− 5.3 (7.0)**
Symptom duration (weeks), *mean +/− SD (median)*	**14.7 +/− 7.5 (13.4)**
DAS28** value, *mean +/− SD (median)*	**5.4 +/− 1.2 (5.3)**
HAQ**, *mean +/− SD (median)*	**1.0 +/− 0.7 (1.0)**
Prognostic factors	
Positive for RF **, *n (%)*	**343 (54.7)**
Positive for CCP-Abs **, *n (%)*	**278 (44.8)**
Presence of bone erosion on x-ray, *n (%)*	**146 (26.0)**
ESR** (mm at 1 hour), *mean +/− SD (median)*	**30.4 +/− 24.4 (24.0)**
CRP** (mg/L), *mean +/− SD (median)*	**23.4 +/− 34.3 (10.0)**
RA diagnosis	
Fulfilled 4 ACR** criteria, *n (%)*	**539 (86.0)**
RA diagnostic certainty on 0–100 VAS, *mean +/− SD (median)*	**78 +/− 18 (80)**
Patients with,	
'Definite RA', *n (%)*	**359 (57.3)**
'Probable RA', *n (%)*	**268 (42.7)**

* Presence of at least 1 comorbid factor among following items: ischemic heart disease, diabetes mellitus, hypertension, renal disease (clearance <60 ml/min or proteinuria or hematuria), current cancer, or chronic viral infection (HIV, HBV, HCV)

** BMI: Body Mass Index; DAS28: Disease Activity Score on 28 joints; HAQ: Health Assessment Questionnaire; RF: Rheumatoid factor; CCP-Abs: Anti-CCP antibodies; ESR: Erythrocyte sedimentation rate; CRP: C-reactive protein; ACR: American College of Rheumatology

*** Number of tender and swollen joints on a 28-joint count

Table 2

Details of therapeutic decisions

Type of DMARD prescribed	**'Definite' and 'Probable' RA n=627**
No DMARD prescribed	122/627 (19.5%)
One DMARD prescribed	464/627 (74.0%)
Methotrexate	*300/464 (64.7%)*
Sulfasalazine	*59/464 (12.7%)*
Hydroxychloroquine	*58/464 (12.5%)*
Leflunomide	*31/464 (6.7%)*
others	*14/464 (3.0%)*
TNF-blocker agents (Etanercept, Adalimumab)	*2/464 (0.4%)*
Two DMARDs prescribed	32/627 (5.1%)
Methotrexate + hydroxychloroquine	*18/32 (56%)*
Methotrexate + TNF-blocker agents (Etanercept, Adalimumab)	*8/32 (25%)*
Methotrexate + *others*	*3/32 (10%)*
Methotrexate + sulfasalazine	*2/32 (6%)*
Hydroxychloroquine + sulfasalazine	*1/32 (3%)*
Three DMARDs prescribed	9/627 (1.4%)
Methotrexate + hydroxychloroquine + gold salts	*9/9 (100%)*

Table 3

Conformity with STPR guidelines and univariate analysis of determinants

Determinants	N=581	% of Conformity	*p*
Sex			
Male	141	65.3	0.04
Female	440	55.7	
Post-secondary level of education			
No	493	60.0	0.02
Yes	88	46.6	
Personal or familial history of psoriasis			
No	484	60.3	0.01
Yes	97	46.4	
Number of swollen joints (28 joint count)			
0–3	105	49.5	0.04
4–8	238	55.9	
9–28	238	63.9	
DAS28 value*			
0–3.2	29	37.9	0.03
3.2–5.1	232	56.0	
>5.1	318	61.6	
Elevated level of ESR*			
No	305	53.8	0.02
Yes	274	63.1	
Positive for RF* and/or CCP-Abs*			
No	237	45.6	<0.001
Yes	344	66.6	
‘Definite’ RA			
No	249	47.0	<0.001
Yes	332	66.3	
Fulfilled 4 ACR criteria for diagnosis of RA*			
No	80	42.5	0.003
Yes	501	60.5	
Observational centre (14 centres)	19 to 62	Range: 35.0 to 79.0	-

*DAS28: Disease Activity Score on 28 joints; ESR: Erythrocyte sedimentation rate; RF: Rheumatoid factor; CCP-Abs: Anti-CCP antibodies; ACR: American College of Rheumatology

Table 4

Multivariate Analysis of determinants of conformity with guidelines

Variables	Odds Ratio	95% Confidence Interval	*p*
Conformity with STPR guidelines			
Women	0.70	0.50 – 0.98	0.04
Positive for RF* and/or CCP-Abs*	1.96	1.34 – 2.87	<0.001
'Definite' RA	1.77	1.29 – 2.44	<0.001
Conformity with EULAR guidelines			
DAS28 value*			
3.2–5.1 *vs* 0–3.2	3.03	1.28 – 7.18	0.01
>5.1 *vs* 0–3.2	4.18	1.57 – 11.1	0.004
Positive for RF* and/or CCP-Abs*	2.28	1.71 – 3.02	<0.001
Bone erosion on x-ray	1.45	1.01 – 2.08	<0.05

* DAS28: Disease Activity Score on 28 joints; RF: Rheumatoid factor; CCP-Abs: Anti-CCP antibodies

Table 5

Comparison of the observed prescribed DMARDs classified in 3 categories with STPR-recommended therapeutic options in the 244 patients treated differently from STPR guidelines.

		STPR-recommended Therapeutic Options				
		A N=35	**B** N=81	**C** N=120	**D** N=8	**Total** N=244
Observed prescribed DMARD	**No DMARD prescribed**	32	30	20	1	83 (34.0%)
	Only flare-preventing DMARD	0	31	38	1	70 (28.7)
	At least one DMARD with proven structural effect	3	20	62	6	91 (37.3%)

Four Therapeutic Options recommended by STPR for prescription of first DMARD in early RA (appendix 1):

A: Hydroxychloroquine or sulfasalazine

B: Sulfasalazine or methotrexate

C: Methotrexate or leflunomide

D: Methotrexate or TNF-blocker agents