

EULAR Standardized Operating Procedures for the Elaboration, Evaluation, Dissemination and Implementation of Recommendations endorsed by EULAR Standing Committee

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I. Background

It is the objective of the EULAR executive committee to promote actions and/or projects permitting to improve the knowledge and/or the recognition of musculoskeletal disorders.

The final aim is to contribute to improvement of outcome of patients with rheumatic disorders. Apart from the projects devoted to education, and research, projects permitting to either facilitate the conduct of clinical studies or to improve the management of musculoskeletal disorders are welcome. Such studies can be categorized in 4 sections:

- Studies dedicated to propose classification and/or diagnostic criteria.
- Recommendations for designing and/or conducting clinical trials in specific musculoskeletal disorders.
- Recommendations for monitoring and/or management and/or treatment of specific musculoskeletal disorders.
- Standardization of (laboratory and other) procedures

II. Rationale of Standardized Operating Procedures

It is the objective of the EULAR executive committee to maintain and to homogenize a high level of intrinsic quality and comparability of such studies.

In order to reach such objective, it appeared that the definition and publication of standardized procedures for the elaboration, evaluation, dissemination and implementation of recommendations might be a relevant and useful starting point.

Obviously these Standardized Operating Procedures should not be a barrier to acceptance of a project if not all points are satisfied but might be important to consider prior of a project.

III. Methodological and practical aspects

Introduction

At each step of such projects (application, elaboration, dissemination, ...), the individual items summarized in table 1 should be discussed. The reader is invited to visit the EULAR website in order to check the most recent updated version of these procedures.

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A. Which wording?

Three proposals: "points to consider", "recommendations", "guidelines".

It is the opinion of the EULAR executive committee members that on one hand "guidelines" might appear too constraining and that, at variance, "points to consider" be considered as too open. Recommendations can be considered as advices for performing the task/action, when applicable, as a marker of quality.

The choice of the wording should be decided based on the content of each project. For example, one can anticipate that if an evidence based approach fully answers the question, "guidelines" can be proposed, at variance if such approach fails to reach any conclusion "points to consider" can be preferred.

B. Which category?

As previously mentioned, it is anticipated that these procedures could be applied for studies proposing:

- Recommendations for conducting clinical studies and/or clinical trials
- Recommendations for management, monitoring or treatment in daily practice
- Recommendations for standardization of other procedures

C. Objectives

The objectives of the project should be made clear from the beginning.

The definition of the target population (the population interested in such project) will facilitate the different steps of the project from its design to its implementation.

For example, a target population can be defined as:

- Rheumatologists
- General practitioners
- Health professionals
- National and/or international drug agencies
- Drug companies

- Others

In practice, one single project can have several target populations. However, the presentation, dissemination, evaluation and implementation can be different for each sub-category of the target population.

D. *Steering group members*

Four categories of persons will have to be included in each project.

1. The convenor of the project

This person (single), preferably not a member of the EULAR executive committee, will be the link between the project group and the EULAR organization.

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It is anticipated that such convenor will be also the chairperson of the project because he/she has a high level of experience in the field of interest of the project.

2. The experts

Such persons should be representatives of the European rheumatological community.

They should come from at least 3 different European countries. However, top leaders in the field including non-rheumatologists, should be invited even if they come from outside the European community.

It is anticipated that these experts have an academic position, but they can also have other positions and invited as experts because of their high level of expertise in this field (for example national agencies and/or drug company representatives).

3. A clinical epidemiologist

In order to promote high level of quality and homogeneity of methodological issues in all projects, each study steering group should include an expert in clinical epidemiology (preferably not a member of the EULAR executive committee). If needed, the chairman of the EULAR Standing Committee on Epidemiology or the chairman of the ECSICIT will help in identifying such experts.

The clinical epidemiologist will attend at least the first meeting of the steering committee members and will be in charge to follow the project during its different steps.

4. The person in charge of the literature research

It is anticipated that for most of the projects a systematic literature research will be mandatory.

This research can be performed by a person outside of the steering group under the supervision of the convenor and/or a designed member of the steering committee.

E. *Evidence Based Approach*

1. Literature search strategy

If applicable such strategy includes 2 parts which have to be decided prior to performing the literature search.

a) Selection of specific modalities

For a specific project (*e.g.* management of knee osteoarthritis), it has to be decided whether the literature search will be focused on specific domains (*e.g.* intra-articular injections of steroids for knee osteoarthritis) or will be completely open.

This decision will permit to clearly define the KEY WORDS which will be the starting point of the literature research.

b) Techniques of the literature search

Each project should clearly describe the different LIBRARY BASES explored in the literature search (*e.g.* MEDLINE, PUBMED, ...). It is strongly recommended to include the COCHRANE LIBRARY in every search regarding treatments.

2. Quality scoring of the manuscripts

The methodology used for scoring the different evaluated manuscripts (quantity, quality) has to be precisely described.

The following practical decision can be anticipated:

- To describe only the number of evaluated manuscripts
- To categorize each evaluated manuscript (*e.g.* placebo randomised controlled trial, randomised controlled trial, prospective *versus* retrospective, ...).
- To score each evaluated manuscript. For this purpose, several scoring systems have been proposed in particular for the evaluation of the report of therapeutic trials. The choice of the scoring system should take into account the nature of the project (in particular pharmacological *versus* non pharmacological treatment modalities). A reference for a specific scoring system is given in Annex I.

3. Estimation of the relevance of the evaluated item

We can anticipate four situations:

a) Evaluation of treatment modalities

In order to get an objective evaluation of different treatment modalities one could consider of interest to quantify treatment effects.

For example, in knee osteoarthritis, the decision has been taken to focus on a single variable (pain) and thereafter to present the results as either effect size (for the continuous variables) or Number Needed to Treat (for the dichotomous variables). If the dichotomous variable is chosen (*e.g.* responder yes/no, success yes/no) and if the domain (*e.g.* pain) has been evaluated by using a continuous variable (*e.g.* change in a 0-100 mm VAS) a cut-off has to be decided a priori (*e.g.* improvement of at least 30% in pain will be defined a success).

b) Evaluation of outcome variables

In a project aimed at proposing recommendations on the design and the conduct of clinical trials in a specific musculoskeletal disease, one could consider it interesting to evaluate the performances of different proposed outcome measures (*e.g.* face validity, reliability, sensitivity to change and discriminant capacity, ...).

c) Evaluation of a proposed criterion

In a project aimed at proposing classification criteria (for example, the definition of the disease at entry in a clinical trial), one could consider important to evaluate also the performances of such set of criteria (*e.g.* sensitivity, specificity, pre and post test probability).

d) Recommendations

It is strongly suggested that recommendation should only be made on the basis of homogenous and quantifiable information.

4. Categorising evidence

Categorizing evidence has been clearly defined regarding the treatment modalities. These categories are summarized in the following table:

Categories of evidence

Category	Evidence
1A	Evidence from meta-analysis of randomised controlled trials
1B	Evidence from at least one randomised controlled trial
2A	Evidence from at least one controlled study without randomisation
2B	Evidence from at least one of the type of quasi experimental study
3	Evidence from descriptive studies, such as comparative studies, correlation studies or case-control studies
4	Evidence from expert committee reports or opinions and/or clinical experience of respected authorities

This categorization has to be given for each recommendation regarding treatment modality

5. Strength of recommendations

Strength of recommendations is clearly defined in what concerns treatment modalities. These categories are summarized in the following table:

Strength of recommendations

A	Directly based on category I evidence
B	Directly based on category II evidence or extrapolated recommendations from category I evidence
C	Directly based on category III evidence or extrapolated recommendation from category I or II evidence
D	Directly based on category IV evidence or extrapolated recommendation from category II or III evidence

The main difference between “categories of evidence” and ‘strength of recommendations” is that the category of evidence is only based on a systematic literature research and that the “strength of recommendations” takes also into account the knowledge of the experts. The strategy permitting to provide the “strength of recommendations” should be clearly described in the project (e.g. vote of the experts after getting the results of the literature research).

F. Expert Opinion Approach

It is admitted that the publication of the Evidence Based Approach alone may be too complicated to be fully used by the target population.

For example, the interpretation of the effect-size of a treatment modality and/or the Kappa coefficient for the reliability of an outcome measure requires a specific knowledge.

In order to make clear, the recommendations may include summary statements from the experts based on the reported evidence or personal experience.

Such expert opinion should appear only after or in parallel to an Evidence Based approach but never alone.

Contents derived from expert opinion should be clearly identified, together with the reasons for that approach.

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G. Presentation of recommendations

1. Example of recommendations for management/monitoring/treatment specific disorders

Two main categories have been proposed:

- To present the results using an algorithm (tree decision).
- To present the results using different short sentences (bullets, take home messages).

Whatever the decision, the dissemination of the recommendations will be highly facilitated if the presentation is as simple as possible.

2. Example of recommendations for conducting clinical studies

It is recommended to follow the structure of a protocol and to discuss the following different points if relevant for the project.

a) Inclusion and exclusion criteria

- Definition the disease (which set of criteria?)
- Definition of the activity of the disease (which set of criteria?)
- Definition of the severity of the disease (which set of criteria?)
- Demographics (age, gender, ...)
- Concomitant therapies (allowed, prohibited, wash-out period before entry, ...)
- Concomitant disorders

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- b) Outcome measures
 - Recommended primary outcome measure
 - Detailed list of recommended outcome measures
 - Time to collection
- c) Sample size calculation
 - The known (or unknown) expected placebo (and/or conventional therapy) effect
 - The clinically relevant expected treatment effect (differences between the study treatment and the control treatment).

H. Relevance of the recommendations

- If applicable, this evaluation has to be planned from the beginning of the project.
- An “external” evaluation can be easily performed according to the AGREE instrument. A paper version of this instrument is available on demand for ongoing projects at the ECSICIT secretariat, such instrument is also available on the web (www.agreecollaboration.org).
- The evaluation can also be performed at the level of the target population. For example, one survey can be performed in order to check whether the proposed recommendations of a treatment are in accordance with the daily practice of the target population (e.g. general practitioners). Concerning the conduct of clinical studies, these recommendations can be presented and discussed at a meeting in which health agencies and drug company representatives are invited.
- The evaluation should also address the potential use of the proposed recommendations for teaching rheumatology (medical schools, post-graduate training, health professional schools, ...).
- Such evaluation could be developed as a specific project.

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I. Dissemination of the recommendations

Strategies for disseminating the proposed recommendation to the target population should be included in the project.

Whatever the project, the steering group is expected to:

- submit an abstract for presentation at the annual EULAR scientific meeting
- submit a manuscript for publication in the EULAR Journal.

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J. Implementation of the recommendations

It is the goal of recommendations to change practices and let them converge towards harmonization. Implementation is the process by which targeted users (researchers or clinicians) integrate the actions recommended into their practice. An efficient implementation

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conditions successful changes. However, the potential impact of the proposed recommendations in daily practice is worth being assessed, since it is dependent on the degree of implementation. On one hand, one could consider that any project aimed at either evaluating and/or disseminating the proposed recommendations will have an impact on the daily practice.

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On the other hand, some studies suggest that the dissemination of recommendations is not sufficient to get such impact.

Several other techniques have been proposed:

- Opinion leaders
- Outcome visits or academic detailing
- Audit feed back
- Continuing Medical Education
- Reminder (paper print reminders, electronic reminders, phone call reminders)

A detailed information concerning the efficacy (including references related to the above techniques) of the different techniques permitting to check the implementation of medical recommendations is available (in French but with the references in English) on the web at the following address: www.anaes.fr

Such evaluation could be developed as a specific project.

K. Update policy of the recommendations

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During the process of the elaboration of recommendations, it has to be anticipated to answer the following questions:

- Do proponents anticipate an update of the proposed recommendations?
- If yes, when? How? By whom?

L. Practical and financial aspects of the project

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1. Practical aspects

It is anticipated that each project will require the following:

- a) Meeting(s) of the steering group members

For each project, the following information will be required at the beginning:

- How many planned meetings?
- How many persons will attend such meeting(s)?
- Calendar of the planned meetings

As soon as the project is endorsed by EULAR (see below), the secretariat of EULAR will take care of the practical aspects of these meetings (hotel reservation, meeting room reservation, travel expenses).

- b) Fellowship for the literature research

If possible, this fellow has to be designated prior to the first meeting of the steering group. The amount (full *versus* partial time) and the duration of his/her work has to be anticipated.

2. Financial aspects

The budget of each project will include:

- The organization of the meetings of the steering group (hotel reservation, travel expenses)
- If necessary, a grant for the fellow in charge of the literature research
- If necessary, a grant for the statistical analysis
- If necessary, a grant for the secretariat of the steering committee

There will be no honorarium for the participation of the experts.

M. EULAR endorsement policy

Endorsement by EULAR should be sought according to the EULAR procedures (see the EULAR website). In summary, the first step is to get such endorsement after submission to the appropriate EULAR standing committee of an application taking into account the different points summarized in table 1.

This EULAR endorsement will permit to start the project but will be able to be cancelled in case of any deviation from the present procedure during the different steps of the project. For this purpose, the clinical epidemiologist in charge of the project will have to send to the chairman of the appropriate standing committee a report after each meeting of the steering committee. Moreover, the material (abstract, manuscript) planned to be published should get the approval of the chairman of the appropriate standing committee before any submission.

Deleted: Concerning the financial support, several possibilities can be anticipated: project completely supported by EULAR, partially supported or not at all financially supported by EULAR.¶
In case of an "external" financial support and in particular in case of a grant provided by one or several drug companies, the representatives of such external support do not interfere with both the choice of the members of the steering committee and the design of the project.¶
Such representatives (no more than 2) can physically attend the meetings but do not participate at the different discussions and/or decisions taken by the steering group.¶

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Table 1: Points to consider for the application of a study focused on recommendations in order to get an EULAR endorsement.

- A. Which wording?** (points to consider *versus* recommendations *versus* guidelines)
- B. Which category?** (management *versus* treatment *versus* conducting studies)
- C. Objectives?** (which target population: GP *versus* rheumatologists *versus* health professionals...)
- D. Steering group committee members** (Who is participating at such project?)
- E. Evidence Based Review**
 - Literature research strategy
 - Quality scoring of the manuscripts
 - Estimating of a “treatment/criterion” effect size
 - Categorising evidence
 - Strength of recommendations
- F. Evidence Based *versus* Expert Opinion Approach**
- G. The presentation of the recommendations** (algorithm *versus* bullet *versus* ...)
- H. The relevance of the recommendations:**
 - Which anticipated study(ies)?
 - Which methodology?
- I. The dissemination of the recommendations**
 - Presentation at different meetings
 - Publication of a manuscript in a peer review journal *e.g.* EULAR journal
 - ...
- J. The implementation of the recommendations**
 - How such recommendations can impact the daily practice?
 - Which anticipated study(ies)?
 - Which methodology?
- K. The update policy of the recommendations**
 - When such recommendations will be updated?
- L. The practical aspects**
 - a) Organization (meetings, research, .time lag)
 - b) Financial support

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Annex I

Example of a scoring system of a manuscript summarizing the results of a therapeutical trial.
 Reference: The feasibility of creating a checklist for the assessment of the methodological quality both of randomised and non-randomised studies of health care interventions

J Epidemiol Community Health 1998;52:377-88

Score range: 0 = worst to 28 = best

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Items: .

Items	Score		Total
	Yes	No	
1. Is the Hypothesis/Aims/Objectives described?	1	0	
2. Are outcomes described in introduction or methods?	1	0	
3. Patient inclusion/exclusion criteria outlined?	1	0	
4. Intervention described?	1	0	
5. Age/Weight/Sex/Disease characteristics?	2 (1)*	0	
6. Main findings in simple outcome data?	1	0	
7. Estimates of random variability?	1	0	
8. Measurement of adverse events?	1	0	
9. Characteristics of subjects lost to follow-up described?	1	0	
10. Have actual probability values been reported?	1	0	
11. Is the source of the subject recruitment recorded?	1	0	
12. Is the proportion of subjects willing to participate recorded?	1	0	
13. Were the staff, places and facilities representative?	1	0	
14. Are the study subjects blinded?	1	0	
15. Are those measuring the main outcomes blinded?	1	0	
16. Are all the outcomes described in the results referenced in the introduction/methods?	1	0	
17. Are there adjustments for different lengths of follow-up?	1	0	
18. Are the statistical tests appropriate?	1	0	
19. Is compliance with the intervention monitored?	1	0	
20. Were the outcome measures used clearly described?	1	0	
21. Are the patient characteristics similar between groups?	1	0	
22. Were the subjects recruited over the same time period?	1	0	
23. Were the study subjects randomised to intervention groups?	1	0	
24. Was the randomisation assignment concealed from subjects and staff?	1	0	
25. Was there an attempt to adjust for significant differences in subjects Age/Weight/Sex/Main disease characteristics between intervention groups?	1	0	
26. Were losses of subject to follow-up taken into account?	1	0	
27. Did the study calculate the number of subjects required to provide sufficient power?	1	0	

*1 = partial information

Scoring System

- A) Paper number NE
- B) Reference _____
- C) Specific intervent
- D) Scoring system

1. Is the Hypothesis/
2. Are outcomes c
methods?
3. Patient inclusion /
4. Interventions descr
5. Age/Weight / Sex /
6. Main findings in si
7. Estimates of rando
8. Measurement of ac
9. Characteristics of
described?
10. Have actual probab
11. Is the source of the
12. Is the proportion c
recorded?
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representative?
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16. Are all the outcc
referenced in the in
17. Are there adjustn
follow up?
18. Are the statistical t
19. Is compliance with
20. Were the outcc
described?
21. Are the patient c
groups?
22. Were the subjects
period?
23. Were the study sub
groups?
24. Was the randomisa
subjects and staff?
25. Was there an att
differences in subj
of OA between inte
26. Were losses of su
account?
27. Did the study cal
required to provide

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