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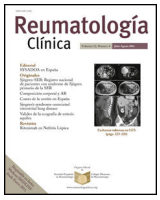

Special Article

Management, development and methodology of the Clinical Practice Guidelines and Recommendations of the Spanish Society of Rheumatology

Petra Díaz del Campo Fontecha,[a] Noe Brito-García,[a] Mercedes Guerra-Rodríguez,[a] Silvia Herrera-López,[a] Federico Díaz-González[b,c,*]

[a] *Unidad de Investigación. Sociedad Española de Reumatología, Madrid, Spain*
[b] *Servicio de Reumatología. Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain*
[c] *Departamento de Medicina Interna, Dermatología y Psiquiatría. Universidad de La Laguna, Santa Cruz de Tenerife, Spain*

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ABSTRACT

The Spanish Society of Rheumatology (SER) brings together the majority of Spain's rheumatologists and, among the many services it offers its members, has a Research Unit (RU). This unit provides methodological support to SER members in clinical and epidemiological research, coordinates and carries out research projects, designs and maintains large patient databases, develops qualitative research projects and produces evidence-based medicine (EBM) documents. Through this last activity, the RU of the SER produces clinical practice guidelines and recommendation documents on topics relevant to rheumatology that meet the most demanding methodological standards. The aim of this article is to describe the management process and methodology followed by the UI of the SER to identify the topics of its EBM documents and how it executes and develops its guidelines and recommendations.

Gestión, desarrollo y metodología de las Guías de Práctica Clínica y Recomendaciones de la Sociedad Española de Reumatología

Palabras clave:
Medicina basada en la evidencia
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RESUMEN

La Sociedad Española de Reumatología (SER) reúne a la mayoría de los especialistas en reumatología de España y entre los muchos servicios que ofrece a sus socios, cuenta con una Unidad de Investigación (UI). Esta unidad da apoyo metodológico en investigación clínica y epidemiológica a los socios de la SER, coordina y ejecuta proyectos de investigación, diseña y mantiene grandes bases de datos de pacientes, desarrolla proyectos de investigación cualitativa y realiza documentos de medicina basada en la evidencia (MBE). Mediante esta última actividad, la UI de la SER realiza guías de práctica clínica y documentos de recomendaciones sobre temas relevantes para la reumatología, que cumplen con los estándares metodológicos más exigentes. El objetivo de este artículo es describir el proceso de gestión y la metodología seguidos por la UI de la SER para identificar los temas de sus documentos de MBE y como ejecuta y desarrolla sus Guías y Recomendaciones.

* Corresponding author.
E-mail address: jfdiazg@ull.edu.es (F. Díaz-González).

Introduction

The Research Unit (RU) of the Spanish Society of Rheumatology (SER) was established in 2003 in order to provide methodological and research support to its members with a structure, level of professionalism and activity unencountered in any other scientific medical society in Spain. One of the most active and in demand areas of research covered by the RU-SER[1] is evidence-based medicine (EBM), where the RU develops clinical practice guidelines (CPG), recommendation documents, guides for patient and, to a lesser extent, other documents such as expert opinion documents (Table 1).

The objective of the EBM documents produced in the RU-SER is to assist healthcare professionals, patients and other agents involved in making clinical decisions in daily clinical practice. To do this, information is collected, synthesized and evaluated through systematic searches, using the most used and internationally validated methodology,[2] the Grading of Recommendations Assessment, Development, and Evaluation (GRADE), to identify the best available evidence for rheumatic disease management, reducing variability in clinical practice. The SER's EBM documents place the patient at the centre, encouraging their active and informed participation in decisions that affect their health.

Among the most important EBM documents is the CPG. A CPG is defined as a set of recommendations aimed at optimising patient care, which are based on the systematic review of evidence and the assessment of the benefits and risks of different therapeutic alternatives.[3]

CPGs also seek to reduce uncertainty and variability in the decision-making of the different people involved in patient management (patients, clinical professionals and other people such as managers or decision-makers). The development of a CPG is justified in clinical practice areas or issues where there is controversy or variability; when there is a significant health problem that must be addressed; when new treatments or procedures arise, or if there is perceived room for improvement in a specific area of action.

The SER also prepares recommendation documents. With a structure similar to CPGs, these documents have more limited scope and objectives than CPGs and are intended to inform healthcare professionals about specific issues emerging from a specific pathology or set of treatments.

This article describes the management process and methodology followed by the RU-SER to identify the topics of its MBE documents and how it coordinates and develops its Guidelines and Recommendations.

Management and selection of issues for the evidence-based documents of the Spanish Society of Rheumatology

The SER's MBE documents are managed by the SER's Guidelines and Recommendations Commission, made up of members of the Board of Directors and rheumatologists who are experts in the preparation of this type of documents.

Recommendation topics are suggested by its members, depending on their interests and are scheduled annually by the Guidelines and Recommendations Commission according to criteria of overall interest and feasibility.

Regarding the CPGs, the SER currently prepares three: the Clinical Practice Guideline for the Management of Patients with Rheumatoid Arthritis (GUIPCAR), the Clinical Practice Guideline for the Treatment of Axial Spondyloarthritis and Psoriatic Arthritis (ESPOGUÍA) and the Clinical Practice Guideline for the Management of Patients with Gout (GuipClinGot). The CPGs are generally renewed every five years.

Preparation process of a Clinical Practice Guideline or document of recommendations of the Spanish Society of Rheumatology

The process of preparing CPGs and SER Recommendation documents takes into account the quality criteria established by national and international organisations that set the methodology and assess the methodological rigour and transparency with which a guide is prepared.[4,5] The preparation process phases are contained in Fig. 1.

Creation of the development group (DG). Using the usual means of SER communication (website and newsletters), the initial evidence-based document is publicised among rheumatologists. Interested parties send a declaration of interests and their CV, focused on the document topic and the SER's Guidelines and Recommendations Commission, using meritocratic criteria, selects the members of the DG from among the applicant rheumatologists. The DG will comprise a clinical leader, a panel of experts with a variable number of between 4–5 for the Recommendations and 10–12 for the CPGs, and the RU'smethodological coordinators.

Professionals from other specialties related to the topic will also be invited to participate, either individually or if the document is a coordinated action between the SER and another scientific society, as representatives of their corresponding scientific societies. Patients (and other people such as informal caregivers, if necessary) are also incorporated into the DG. Patients participate in the SER EBM documents by contributing their vision of the disease and through qualitative techniques (see patient perspective section below), unmet needs in the clinical management of their disease are identified. The methodological experts of the RU coordinate the process in the different stages of the development of the Evidence-Based Document (EBD).

Determination of scope and objectives. The DG determines the scope and content of the document, establishing:

- *General objective:* establish systematically developed and scientific evidence-based recommendations to help professionals and patients in decision-making when confronting the health condition or problem addressed by the guideline.
- *Specific objectives:* reduce the variability of clinical practice.
- *Healthcare aspects:* prevention and/or screening and/or diagnosis and/or treatment, etc.
- Target population at which the recommendations are intended to be applied.
- End users at whom the guideline is aimed.
- Clinical questions at which a response is aimed.

Formulation of clinical research questions. PICO questions. The EG decides which questions could have the greatest impact. Next, it is determined which of them need to be answered by asking the question Patient, Intervention, Comparison, Outcome (PICO). The number of clinical questions will depend on the type of document, its dimension, scope and objectives. Generally, in recommendation documents there are between two and four questions, and in CPG between 10 and 12 questions.

Systematic bibliographic search and selection of evidence. EBD SER recommendations are essentially based on systematic reviews (SR) of the evidence to answer the clinical questions raised. The bibliographic search for the evidence is carried out by an expert documentarian, generally in the PubMed (MEDLINE), EMBASE (Elsevier) and Cochrane Library (Wiley Online) databases. The process is completed with a manual search in the references of the identified studies, as well as the examination of other references that the reviewers and experts provide.

Evaluation and synthesis of scientific evidence. Evidence quality assessment is carried out in keeping with the methodology of the

Table 1
Finished or currently programmed evidence-based documents in the RU.

Document name	Objectives	Disease studied	Methodology	Databases consulted	Type of review	Number of questions	Final report/article
SER recommendations on treatment of uveitis	Develop recommendations for the management of patients with non-infectious, non-neoplastic and non-demyelinating uveitis.	Non-infectious, non-neoplastic and non-demyelinating uveitis	GRADE	PubMed, Embase and Cochrane Library	Systematic	3	DOI 10.1016/j.reumae.2023.07.003
SER recommendations on the treatment of refractory Behçet's disease	Develop recommendations for the management of patients with Behçet's Disease refractory or recurrent to conventional treatment.	Behçet's disease	GRADE	PubMed, Embase and Cochrane Library	Systematic	4	DOI 10.1016/j.reuma.2023.12.001
SER recommendations on risk management of treatment with targeted biological and synthetic DMARDs in patients with rheumatoid arthritis.	Develop recommendations to minimise the risk of using targeted therapy in patients with rheumatoid arthritis.	Rheumatoid arthritis	GRADE	PubMed, Embase and Cochrane Library	Systematic	6	DOI 10.1016/j.reuma.2023.07.001 https://www.ser.es/wp-content/uploads/2023/06/Recomendaciones-SER-gesti%C3%B3n-de-riesgo_AR.pdf
Update of the SER Recommendations on the use of biological therapies in SLE	Update of recommendations for the management of SLE with biological treatments.	Systemic lupus erythematosus	GRADE	PubMed, Embase and Cochrane Library	Systematic	3	Under development
SER recommendations on management of periodontitis in patients with rheumatoid arthritis	Develop recommendations for the management of periodontitis in patients with rheumatoid arthritis.	Rheumatoid arthritis	GRADE	PubMed, Embase and Cochrane Library	Systematic	3	Under development
SER special article on the use of platelet-rich plasma (PRP) applied to rheumatic pathologies	Description and classification of the technology used to obtain PRP and its indications in patients with knee osteoarthritis, shoulder tendinosis, enthesitis and fasciitis.	Knee osteoarthritis, shoulder tendinosis, enthesitis and fasciitis	Article based on expert opinion	PubMed	Narrative	3	Under development
	Description and characterisation of the technique and its indications in patients with scleroderma and related pathologies. Interpretation and parameters through a standardised form that allows the homogenisation of criteria.	Scleroderma, dermatomyositis and MCTD	Article based on expert opinion	PubMed	Narrative	3	Under development
SER consensus document on the use of targeted biological and synthetic therapies in rheumatoid arthritis.	Update the SER consensus on the use of biological therapies and targeted synthetic drugs in patients with rheumatoid arthritis	Rheumatoid arthritis	Article based on expert opinion	PubMed	Narrative	15	Pending publication
ESPOGUÍA 2024. Update of the Clinical Practice Guideline for the treatment of axial spondyloarthritis and psoriatic arthritis	Update on the safety and effectiveness of therapy in the management of patients with axial spondyloarthritis and psoriatic arthritis.	Axial spondyloarthritis and psoriatic arthritis	GRADE	PubMed, Embase and Cochrane Library	Systematic/ restrictive bibliographic search	7 Systematics 8 narratives	Under development
GUIPCAR 2025. Update of the Clinical Practice Guideline for the Management of Patients with Rheumatoid Arthritis	Update on the safety and effectiveness of therapy in the management of patients with rheumatoid arthritis	Rheumatoid arthritis	GRADE	PubMed, Embase and Cochrane Library	Systematic/ restrictive bibliographic search	5 Systematics 16 narratives	Under development

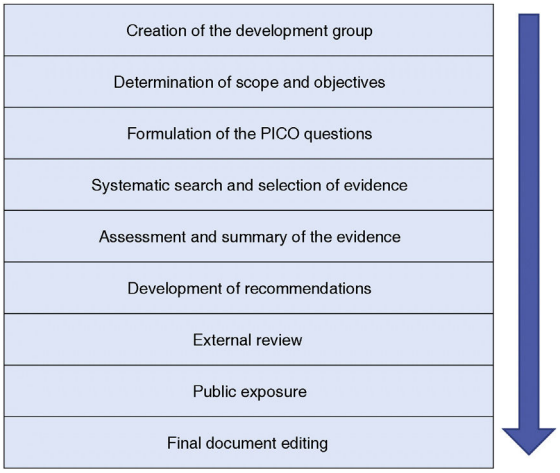

Fig. 1. Preparation phases of a CPG or recommendation document.

international GRADE[2] working group, by a group of rheumatologists who are experts in this methodology (SER evidence-based rheumatology [EBR]) work group, assisted by RU staff and by external specialists. To determine the quality or certainty of the evidence, in addition to the design and methodological quality of individual studies, the GRADE system involves the evaluation of other factors that influence confidence in study estimates. The following are analysed: the consistency of outcomes between the studies; the direct/indirect nature of the evidence (indirect comparison of the interventions of interest and/or differences in the population, the intervention, the comparator and/or the outcomes of interest with respect to the objectives of this report); the precision of the estimates, and the publication bias (Table 2 with the classification of the quality of the evidence using the GRADE system). According to the combination of all the factors described, the quality of the evidence is classified as high (it is very unlikely that new studies will change the estimate), moderate (it is likely that new studies will change the confidence we have in the outcome), low (it is highly likely that new studies will have an impact on the confidence we have in the outcome and could modify it) or very low (any estimated outcome is highly doubtful).

Formulation of recommendations. After completing evidence assessment and synthesis, relevant information on the different aspects of the recommendations is available for each of the questions. In the process of integrating these aspects, the frameworks proposed by GRADE (evidence to decision frameworks) are used, specifically created to guide the making of the necessary judgments.[6] These frameworks assess:

- The quality or certainty of the scientific evidence identified.
- Patient values and preferences.
- The balance between desirable and undesirable effects of interventions.
- Aspects related to costs.
- Aspects such as equity, acceptability and feasibility of implementation.
- Other considerations.

All the collected information is used to formulate the recommendations, their classification into categories of strength such as strong or weak/conditional and opinion (for or against), and the drafting of the justification for them by the DG. The different implications for the different users are contained in Table 3.

Furthermore, there are occasions when the DG may consider aspects require emphasis and for which there is no quality scientific evidence to support them. In general, these cases are related to an aspect of the treatment considered good clinical practice (GCP) and that no one would normally question. These aspects are valued as GCP points or recommendations.

External review. To increase document validity and ensure recommendation accuracy, the final draft of the EBDs undergoes an external review process. For this task, several professionals are

Table 2
Classification of scientific evidence quality in the GRADE[2] system.

Quality	Study design	Lower if*	Raise if**
High ⊕⊕⊕⊕	RCT	• Quality limitation (design):	Association:
Moderate ⊕⊕⊕⊖	–	Important (-1)	• Scientific evidence of a strong association (RR > 2 or < .5 based on observational studies without confounding factors) (+1)
		Very important (-2)	• Scientific evidence of a very strong association (RR > 5 or < .2 based on studies with no possibility of bias) (+2)
Low ⊕⊕⊖⊖	Observational studies	• Inconsistency:	• Dose-response gradient (+1)
		important (-1) Very important (-2)	
		• Direct evidence:	
		Important (-1) Very important (-2)	• Possible factors of confusion could have lowered the observed effect (+1)
		• Imprecision:	
		Important (-1) Very important (-2)	
Veyr low ⊕⊖⊖⊖	Other types of design	• High probability of publication bias: (-1)	

RCT: randomised clinical trial; RR: relative risk.
* In the case of RCTs, the rating of the quality of the scientific evidence can be lowered.
** In the case of observational studies, the quality rating of the scientific evidence can be raised.

Table 3
Implications of the strength of recommendation in the GRADE[2] system.

Recommendation	Patients	Clinicians	Managers/planners
Strong	Most people would agree with the recommended action and only a small proportion of them would not.	Most patiens should receive the recommended intervention.	The recommendation may be adopted as a healthcare policy in most situations.
Weak or conditional	Most people would agree with the recommended action but a large number of them would not.	It recognises that different opinions would be appropriate for different patients and that the doctor has to help each patient to make the decision most in keeping with the patient's values and preferences.	There is a need for serious debate and participation from stakeholders.

selected (between 2 and 3) for their knowledge of the pathology addressed and the methodology in preparing the EBD. They comment on the document content and robustness.

Public exposure. The EBM documents are submitted to a public exposure process by SER members and different stakeholders, such as other scientific societies, the pharmaceutical sector, patient associations, etc., who have not participated in the previous stages of drafting and external review. The objective is to collect their appraisal and scientific commentary on the methodology and recommendations made. The CPG or the recommendations document, in draft phase, is available for a period of two to three weeks on the SER website, along with a form for formulating affirmations. The affirmations are assessed within approximately four weeks by the DG who will ultimately decide whether or not to take them on board and whether to do so partially or totally. All affirmations, together with the arguments behind them and the DG's responses are contained on the SER website.

Final draft and dissemination of the SER EBM documents. The drafting of the documents is the DG's responsibility, in accordance with a previously established index and format. The RU coordinates its final edition, prepares the section related to the methodology and also ensures document coherence and style. When considered appropriate, additional materials will be included such as: summarised version, information version or chapter for patients, therapeutic and/or diagnostic algorithms, brochures and charts or diagrams.

EBM documents are published in various formats. CPGs are published as complete or summartised versions on the SER website, as well as in paper format. They are also published as a special article in Clinical Rheumatology, the SER's communication channel. For recommendation documents, the full report is disseminated on the SER website and the article version in Clinical Rheumatology.

Inclusion of the patient's perspective in the evidence-based documents of the Spanish Society of Rheumatology

Obtaining information about how patients perceive their health status can help professionals involved in their care understand other factors that influence the disease process.[7]

The SER EBM documents contain the patient's viewpoint using several different procedures:

1) Direct participation of one or two patient representatives in the DG.
2) Undertaking a systematic review of existing scientific studies on the experience of patients and their family members and/or carers.
3) Undertaking a primary qualitative study with patients who voluntarily wish to recount their experiences and concerns regarding the disease.

The information and outcomes obtained using these procedures are subsequently reflected in the CPG or recommendation documents.

1 *Patient representatives in the DG.* Patient representatives in the DG are either participants in primary qualitative research or are patient representatives recruited through patient associations. Although no formal qualification is required for recruitment, some of the following criteria are taken into account: disease experience; degree of knowledge; understanding; availability; skills in expressing opinion, and the ability to work as a team. Patients work at the same level and in the same phases as professionals and receive specific training for the methodological comprehension of the process.
2 *Systematic review of qualitative evidence.* A systematic review of scientific studies on patient experience of the disease is performed to collect their concerns and needs and those of their families and caregivers.

Study inclusion and exclusion criteria: The clinical questions are drafted using the Setting, Perspective, Intervention, Comparison, Evaluation (SPICE)[8] format.

Only qualitative studies are considered for inclusion, and descriptive studies (questionnaires, surveys) are excluded.

Search for and selection of studies: The bibliographic search is carried out in the databases used for quantitative studies including PubMed (MEDLINE), EMBASE (Elsevier), Cochrane Library (Wiley Online) and other more specific qualitative research databases such as Cinahl and PsycInfo. The search strategies specify key and free text terms related to the pathology and include methodological filters to identify qualitative evidence.

Appraisal of qualitative evidence quality, analysis, and synthesis:

- To assess the methodological limitations of each selected study, an instrument agreed upon by the Health Technology Assessment Agencies/Units (Quality Plan for the SNS of the MSSSI)[9] is used, selecting the five key questions in which an affirmative answer provides significant value to the study quality.
- To analyse the studies, the Confidence in the Evidence from Reviews of Qualitative research (GRADE-CERQual) approach is used, evaluating the confidence in the outcomes from primary studies and reviews of qualitative evidence synthesis (Table 4).[10] The CERQual approach, developed by the Cochrane group, is based on the principles of the GRADE method used for reviews of quantitative studies. Confidence assessment is based on four

Table 4
Component of the study confidence appraisal.[10]

1. *Methodological limitations of the included studies:* the degree of concern regarding the quality of the design or conduct of the primary studies included as evidence for each of the conclusions of the review.
2. *Consistency of review results*: an assessment of how clear and convincing the relationship is between the data from the primary studies and a review conclusion that synthesizes that data. By "convincing," we mean well supported.
3. *Adequacy of data contributing to a review conclusion:* the overall determination of the degree of richness and quantity of data supporting a review conclusion.
4. *Relevance of included studies to the review question:* The extent to which the body of evidence from primary studies supporting a conclusion of the review is applicable to the context (population or perspective, phenomenon of interest, setting) specified in the review question.

components[10,11] (Table 4). Confidence is judged as high, moderate, low or very low.

• Finally, in the evidence synthesis process, the main themes must be identified. Each theme contains different findings and these are evidenced by the preparation of a thematic map.

3 *Primary qualitative study*. Qualitative research allows us to investigate the experiences that patients have with the disease, within our cultural context. For this, focus group and in-depth interview techniques are used. The information obtained is transcribed and classified to interpret outcomes. The most relevant patient issues may therefore be identified and analysed. All of this is used to complete the information obtained with the systematic review of the literature.

Information development for patients

With a guideline based on the recommendations of the CPG or the recommendations document and based on the information obtained by the systematic review of qualitative studies, a model version for patients is prepared. This information is prepared in a language and style format adapted to the recipients at whom it is directed and includes aspects of the disease that may be most useful to them (SER website).[1]

The developers of this information come from a specific work subgroup which includes some of the clinicians and patients who participate in the DG.

Conclusions

The SER has been preparing MBE documents for over 20 years. These documents, in which clinical experts and SER evidence reviewers participate, are coordinated from the RU by a group of professionals with extensive experience in the systematic collection of information and its evaluation using GRADE. With this methodology, the SER produces solid documents that have the necessary prestige to be considered useful by the community of rheumatologists in Spain. This demonstrates SER's commitment to continually improving patient care and promoting excellence in rheumatology.

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Conflict of interests

The authors have no conflict of interest to declare in relation to this methodology document.

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