AMERICAN COLLEGE OF RHEUMATOLOGY
Policy and Procedure Manual for Clinical Practice Guidelines

(February 2023)

Purpose of this Manual

This manual is intended to assist guideline project development groups* with information on American College of Rheumatology (ACR) processes, policies, and methodology to help them in their work of developing guidelines that will improve the care of patients with rheumatic diseases.

ACR Resources

The ACR seeks to partner with Principal Investigators (PIs)* and guideline project development groups* to produce high-quality guidelines that meet expectations regarding methodology, timeline, budget and deliverables agreed upon by the ACR and PIs before projects begin. To facilitate this outcome, the ACR provides project support in the following areas, at levels agreed between PIs and the ACR before the start of each project:

- Project funding
- Content, methodology and process expertise, as needed
- Literature searching, study identification and reference management
- Assistance with the evidence review, voting/decision making process, and manuscript preparation and revision, as resources permit
- Administrative assistance with logistical details of projects (e.g., meeting planning, conference call/webinar scheduling, communication assistance, and handling direct payments related to meetings, calls and panel stipends or travel expenses)
- Assistance with disclosure and conflict of interest requirements

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* **Guideline Project Development Group**: includes anyone intellectually involved in the development of ACR guidelines. Includes, but is not limited to, guideline voting panel members.
Guideline Voting Panel Members: individuals in a guideline project development group who are usually responsible for analyzing available evidence and voting on the final recommendations.
Principal Investigator or PI: the individual who leads an ACR guideline development project.

Guideline Development, Phase 1: Preparation

Priority Setting

Rheumatoid arthritis, osteoarthritis, and osteoporosis are guideline topics for which the ACR plans to maintain an ongoing commitment. Other guidelines are developed, as necessary, based on known gaps in care and developments in the field, as resources for such development are available. The ACR may partner with other organizations, as appropriate, in setting priorities in areas of common interest, and possibly working jointly on systematic literature reviews and guidelines.

Recommendation of Topics / Project and Funding Approval

The ACR Guideline Subcommittee recommends possible new topics and/or guidelines in need of revision to the ACR Committee on Quality of Care (QOC), based on needs expressed by the ACR membership, the broader rheumatology community, and/or ACR leadership, and length of time since a current guideline was updated. Possible new topics and/or revision projects are considered at the fall Guideline Subcommittee meeting, and decisions are made about which topics to recommend to QOC for inclusion in the next year's budget. Expressed needs are considered in the context of Guideline Subcommittee members' knowledge and investigation of discussed topics, as well as known topics of concern in rheumatologic care.

Each January, the QOC considers the Guideline Subcommittee's proposed topics as part of its normal budgetary process and makes a decision about recommending proposed topics to the ACR Board of Directors for funding approval. If the QOC desires possible involvement of another organization in either the guideline development or approval process, the QOC requests Board approval of that relationship at the time of project approval so the relationship can be initiated and its parameters established before the project begins. If the partner's process, timeline and/or forms are different from ACR's, the ACR may decide to adopt the partner's processes to accommodate the partner's preferences or requirements.

Call for Letters of Interest

Once a guideline topic has been approved and funded by the ACR Board of Directors, the Guideline Subcommittee develops a Call for Letters of Interest (LOI). The LOI, project timeline, ACR disclosure requirements and a link to the ACR Guideline Manual are posted together on the ACR website and distributed electronically to the ACR membership. The Call for LOI will include the guideline purpose, scope, audience, and timeline, an explanation of the research methods to be used for guideline development, and a list of "affected companies." (See below for explanation of affected companies.)

If the ACR plans to partner with an outside group to perform the systematic review, which is the foundation for recommendations, this information may be included in the Call for LOI.

Rarely, if warranted by issues of importance, timing, or other extenuating circumstances, the ACR may decide to proceed with a guideline development project without distributing a Call for LOI.

Eligible Applicants

Letters of interest may be submitted by teams or individuals from domestic for-profit and nonprofit organizations, public or private, including but not limited to universities, colleges, hospitals, laboratories, and private practices. Collaborations that include individuals from multiple types of institutions/organizations are particularly encouraged. The ACR requires that private practitioners as well as academicians must be included in guideline development groups, to better reflect the intended audience for the final guideline. The ACR aims to make the guideline development team as diverse as possible and encourages applications from those who are from traditionally underrepresented populations, have disabilities, and who otherwise would contribute diverse viewpoints. Individuals whose primary employment is with the pharmaceutical, biotechnology or insurance industries are not eligible to apply and should not be included in proposed guideline project development groups; "primary employment" is defined as 50 percent or more of an individual's working time.

As noted above, letters of interest will be accepted from teams as well as from individuals who are not proposed as part of a team. Well-formed teams may be given preference over individuals, but the ACR often decides to invite interested and qualified individuals to become part of the ACR project team, even

if they are not part of a proposed team. Proposed teams should expect that their composition will be altered by the ACR to accommodate other individuals who express interest in a project. The main focus of the letter of interest should be on the people who are proposed to partner with the ACR on this project, their qualifications for this work, and the particular roles for which they would be best suited.

Composition of the ACR Guideline Project Development Group

Membership of each group should be broadly based. It must include:

- Rheumatologists, other physicians, specialists, and health professionals who care for patients with the target disease
- Private practitioners as well as academicians
- At least one clinician or clinical epidemiologist with significant GRADE methodology expertise and experience
- At least one person with expertise in biostatistics
- Patients who are part of the target population for the guideline (parents/caregivers of these patients may be included for pediatric guidelines)

A **Core Leadership Team** of approximately 5-6 people will be confirmed to lead the work of the project with ACR staff. At minimum, this team will include 1) a project PI, who will be primarily accountable with ACR staff for the completion of the work according to the agreed upon project plan and timeline; 2) a literature review leader; 3) a voting panel leader, who will lead the decision process regarding the recommendations; and 4) a GRADE expert. The project PI may also serve as the voting panel leader. However, because of the PI's prominent role in the development of the final guideline and the need for some separation between the systematic review and the guideline recommendation development processes, the project PI may not also lead the systematic review. The GRADE expert does not have to be a separate person, if one of the other Core Leadership Team members has significant GRADE expertise and experience and plans to advise the group on GRADE methodology and hold them accountable throughout the project.

A **Literature Review Team** of approximately 10-12 people (or more if required) will conduct the review of available evidence that will serve as the basis of the recommendations made in the guideline.

A **Voting Panel** of approximately 10-12 people will lead the decision process regarding the recommendations.

A **Patient Panel** of approximately 10-12 people who are part of the target population for the guideline (including parents/caregivers, for pediatric guidelines) will meet just before the voting panel meets to decide the recommendations. At least 2 patient panel members will serve as full voting panel members and will represent the patient panel's viewpoints during the voting panel deliberations about the final recommendations.

Other experts will be added to the guideline development group, as needed.

Disclosure of Relationships / Conflict of Interest

ACR Requires Full Disclosure of All Relationships, not just Potential Conflicts of Interest

Applicants must fully disclose their relationships at the time of application, using the ACR disclosure form. A completed ACR disclosure form must be included for anyone who will be intellectually involved in the guideline development project. Each form should list all relationships, including recent (i.e., within 1 year before Call for LOI deadline), existing, and planned (i.e., known at the time the form is completed but not yet begun).

When developing a Call for LOI, the ACR proactively identifies companies and organizations that may be affected by the work. This "affected companies" list includes but is not limited to pharmaceutical, biotechnology, or other companies that manufacture or market products or therapies that might be affected by the ACR's work, or competitors of these companies. Affected companies are ones that are reasonably likely to be positively or negatively affected by care delivered in accordance with the

guideline. The list of affected companies is included in the Call for Letters of Interest, with a requirement that disclosures related to these entities must be explicitly included in the disclosures submitted as part of the letter of interest. Note that the affected companies list provided by the ACR is not meant to be all-inclusive, but rather, to provide guidance for individual disclosure; applicants who have relationships with other affected companies, as defined above, must also explicitly disclose that information and indicate to the ACR that the relationship would likely be considered COI by the ACR's definition of an affected company. Individuals whose primary employment is with an affected company are not permitted to participate in guideline development teams.

Managing Conflict of Interest

PIs of guideline development projects are expected to be free of conflicts of interest (COI) relevant to the subject matter of the project for at least one year prior to LOI deadline, throughout the project until publication, and they are expected to remain free of such conflict of interest for at least one year after publication. If multiple co-PIs are named to lead a project, this expectation applies to both/all of them. The literature review leader is held to these same expectations.

The majority (at least 51 percent) of the guideline project development group must be free of conflicts of interest relevant to the subject matter of the project for at least one year prior to the LOI deadline and throughout the project until publication. Similarly, at least 51% of the Literature Review Team and at least 51% of the Voting Panel must have no conflicts of interest related to the subject of the guideline. NOTE: The 51% unconflicted threshold is a *minimum*; the ACR's goal will be to have significantly more than 51% unconflicted participants overall and on each smaller subgroup to allow for unanticipated mid-project personnel shifts (e.g., a participant drops out due to illness or schedule changes).

The conflict of interest thresholds will be based on an evaluation of relationships, primarily with affected companies. Unless their relationship completely excludes them from participation (e.g., industry employment), a person who has any relationship with an affected company is counted as conflicted (toward the allowed threshold) regardless of the type or subject of the relationship. Finally, although intellectual conflicts of interest are important and should be disclosed, they are ubiquitous and,

therefore, the ACR does not count someone with intellectual COI as conflicted (toward the allowed threshold) based on the intellectual conflict alone.

Guideline development group members are required to provide disclosure at the start of the project and update their disclosures during the project whenever relationships change. They are proactively asked to review and update their initially provided disclosures *at least* 1) immediately before the voting panel meeting(s) where final recommendations are decided; and 2) just before the final guideline manuscript is submitted to the journal. Disclosures are shared with the public in a project plan that is posted online as the project begins and also in the final publication. Disclosures are shared verbally by members of the Core Team at their first meeting, and at intervals determined by the PI, but not less than every 6 months. In addition, disclosures are shared in writing and verbally with voting panel members just before and during the voting panel meeting(s), for the purpose of full transparency in the discussions.

If the project's allowable COI thresholds are in jeopardy at any time during the project (e.g., due to unconflicted participants dropping out because of illness or schedule conflicts, or becoming employed by industry), immediate efforts are made to rebalance the overall group and relevant sub-team(s), often by inviting additional unconflicted individuals to participate. Individuals who drop off the project before completion are identified as such in the final publication, either on the author list (if the project is near completion and their involvement already warrants authorship) or in the acknowledgements section. Individuals who become employed by industry midway through the project are immediately ineligible for further participation in the guideline effort. Their names are listed in the final publication acknowledgements section with a footnote that their project involvement occurred only before their industry employment. Unless the guideline is already final and in queue for publication, they cannot remain as authors because, as industry employees, they would not be allowed to review and sign off on the final paper.

Intent of ACR disclosure/COI policies

The intent of ACR disclosure/COI policies is not to exclude all investigators with potential conflicts from participating in the project, but to manage such conflicts in a prospective, structured, and reasonable manner to minimize the likelihood of inappropriate influence of such conflicts on guideline

development. Specifically, the ACR's disclosure and COI policies and procedures are meant to deal with individuals' conflicts that may potentially bias how evidence is chosen, assembled, assessed, and synthesized, or bias the recommendations based on such evidence. The description of strategies for managing conflicts related to the specific agents and approaches used to treat the target disease will be explicitly laid out in the final manuscript. This process and information will be considered in the review process. (See disclosure/COI section below).

Funding

In general, the ACR funds its guideline development efforts without outside financial support. However, if topic priorities and development methodologies are similar, the ACR will consider partnering with another medical professional or patient advocacy organization or other guideline developer, in which case funding from this other organization may be acceptable. In this situation, the other organization's funding contribution must not come from industry or any other funding source the ACR would not use for its own guideline efforts. In kind support is accepted only from these partner organizations or other groups with which the ACR agrees to collaborate to conduct systematic reviews (e.g., AHRQ).

The amount of funding ACR will provide for each project is approved before the project begins. The ACR covers all project expenses directly. The project budget may include some salary support or honoraria for the project PI, the literature review leader, other Core Team members, and possibly others who are contracted to help support the literature review. Salary support and indirect costs of up to 25% may be provided to organizations of lit review team members if a significant percentage of their time is spent on this project for a dedicated period of time (e.g., 6 months at nearly 100% effort). This support and the entire project budget are discussed with the PI and literature review leader at the time they are being confirmed. Additional funding will be separately provided for any future guideline updates.

If the ACR is working with an outside group to conduct the systematic review, the funding timeline will be altered, as needed, to accommodate both the ACR's and the outside group's needs. In either case, however, the funding timeline and related deliverables will be set and agreed upon by all parties before the guideline development process begins.

Project Timeline

The overall timeline for the development of ACR guidelines through this process is approximately 15-18 months from the beginning of Phase 2 – Development (i.e., convening of the systematic review team – see below for more details) until ACR approval of the final guideline manuscript. This is a tight timeline and requires vigilant oversight on the part of the project PI, the systematic review leader, the guideline panel leader (if not the project PI), and the ACR. Team members involved in all processes are expected to adhere to deadlines.

The major timeline milestones are 1) confirmation of the PI and guideline development team; 2) development and finalization of the protocol/project plan; 3) completion of the systematic review; 4) development of evidence summaries and vote on recommendations; 5) development of guideline drafts; and 6) joint publication of the guideline in *Arthritis Care & Research, Arthritis & Rheumatology,* and on the ACR website.

For guidelines that are developed based on a systematic review produced by a group with which the ACR is partnering, timelines may differ.

Letters of Interest / Application Deadlines

Letters of interest (LOI) are usually due no more than 8-12 weeks after the Call for LOI is posted. Letters must include all required elements listed in the Call for LOI, and applicants must complete disclosures for everyone who will be intellectually involved in the guideline development. Incomplete or late letters of interest may not be reviewed.

Letter of Interest Procedure

Standardized forms for the submission of LOIs to the ACR are not provided. Letters over 10 pages will not be considered for evaluation. This page count should include but may not be limited to a complete list of investigators and personnel who are proposed to work on the project (or just one person, if not a group LOI), a specification of the capacity in which each person might best work (e.g., literature review team, voting panel), and a description of their relevant expertise and experience.

Two appendices are required outside of the 10-page limitation, for either group or individual LOIs: 1) a curriculum vitae (CV) or NIH biosketch for each of the listed participants; and 2) completed ACR disclosure for each project development group member (i.e., anyone intellectually involved in the entire guideline development process). This is an essential part of the application; **applications that do not include a CV/biosketch and completed disclosure for all intellectually involved persons will not be considered**.

Proposal Review

ACR staff initially reviews all letters to ensure they are complete and in compliance with basic ACR policies (e.g., all CVs and disclosure forms are included/completed, a suggested PI has no COI, etc.).

LOIs that pass this initial staff review are then submitted for consideration by the Guideline Subcommittee as they determine the final guideline development team. The subcommittee's decision making includes evaluation of proposed guideline development group members' training and experience, diversity, capacity, and anticipated group dynamics. The subcommittee may combine interested participants in different ways than were proposed in the letters of interest, including combining members of proposed teams and adding individuals who expressed interest. The subcommittee may also include people whose names were not received in response to the Call for LOI.

Once the ACR Guideline Subcommittee has confirmed the team, final decisions are conveyed to all who submitted letters of interest.

Confirmation of PI / Literature Review Leader/ Guideline Project Development Group and Initial Funding

Once the project PI and literature review leader have been confirmed, ACR staff discusses financial / logistical details with them and confirms an ACR Board liaison for the project. ACR staff also confirms with the PI and lit review leader the other members of the project's Core Oversight Team. Once verbal agreements have been made on these issues, ACR staff sends all Core Team members, including the PI and lit review leader, a written letter of agreement, a list of agreed upon deliverables and

responsibilities, and a detailed timeline, for individual and, if necessary, institutional approval and signature.

Guideline Development, Phase 2: Development

Accountability

ACR staff, committees, PI, and other members of the guideline project development group (including the systematic review team and voting panel) have specific responsibilities for which each is held accountable over the course of the project. Among other responsibilities, PIs are expected to work with the ACR to confirm project timelines, milestones, deliverables, and related funding details in writing before the project begins.

The ACR staff will provide oversight of the project in partnership with the PI and Core Team. Staff will also provide administrative assistance with logistical details of the project (e.g., meeting planning, conference call scheduling, communication assistance, and/or handling direct payments related to meetings, calls/webinars and panel stipends or travel expenses); provide assistance with disclosure and COI requirements; and potentially assist with literature searching and associated functions, as required by the project and as ACR resources permit. The ACR staff and committee volunteers will also provide process and methodology expertise, and content expertise, as needed.

An organizational conference call between the PI, Core Team, ACR Board liaison, and ACR staff will be scheduled by ACR staff at the outset of the project to ensure that everyone understands their roles and responsibilities.

Use of GRADE to Evaluate the Evidence and Develop Recommendations

The ACR uses the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology for all guideline development projects, including systematic reviews of evidence and guideline recommendations. Information about GRADE may be found online at

http://www.gradeworkinggroup.org. In addition, several useful articles are included in the reference list.[1-14]

GRADE provides a transparent, systematic, and explicit approach to the development of recommendations, which are characterized as either strong or conditional and are based on evidence, the quality of which is assessed as high, moderate, low, or very low. GRADE makes a clear distinction between quality of evidence and strength of recommendations.[2] Other factors, such as patient and clinician preferences and values, are also taken into consideration and are explicitly stated in the guideline recommendations.[1] The GRADE system helps guideline development groups make decisions about quality of evidence and strength of recommendations in a systematic and transparent manner, but it does not eliminate the need for judgments. [12]

Initial Project Planning: Protocol/Project Plan Development and Approval

A systematic literature review is used as the basis for development of the recommendations within all ACR guidelines. The systematic review is based on a project protocol (i.e., project plan) that is developed by the project PI, systematic review team leader, and the rest of the Core Team, as well as selected project participants (including the systematic review team, the voting panel, and the leader of the voting panel, if the project PI is not also serving in this role), in conjunction with the ACR. In addition to serving as the basis for the literature review, the protocol guides project leaders and participants as they work to accomplish the goals and objectives of the project. The protocol is essential to minimize bias[15] and to ensure that the end product(s) delivered meet the needs of the ACR membership and the original intent of the project. The protocol will address broad specifications for the project, as well as the detailed information related to the systematic review. (See below for more details of what will be included in the project protocol.)

Development of Clinical Research Questions / PICO Questions

Specific clinical questions need to be answered in the systematic review, and the literature search strategy is based on these questions. The "PICO" format informs the key questions/clinical questions being asked. The acronym PICO stands for **P**opulation (condition(s), patient, or problem being

addressed); **I**nterventions (e.g., treatment), **C**omparator (alternative intervention for comparison), and **O**utcomes (clinical outcomes of interest).[11] Important and critical outcomes should be the focus[11], i.e., as defined by patient or clinician, rather than those driven by available evidence. In addition to PICO, pre-specified types of studies are included as part of the criteria for the systematic review development. Sometimes the setting is also an important aspect of the question. The project PI and Core Team develop PICO questions for each guideline project with input from the rest of the guideline development team. Once the clinical questions have been developed, they are included in the project protocol for public comment via the online feedback mechanism described below.

An example of a question framed according to PICO format is: "In patients with symptomatic knee OA, are balance exercises effective in reducing pain and improving function compared to strengthening exercises?" The population is patients with symptomatic knee OA, the intervention is balance exercises, the comparator is strengthening exercises, and the outcomes are pain reduction and improved function.

Other Details included in the Protocol

The protocol will also include how studies will be identified (and possibly include an electronic strategy for Medline/PubMed search with a notation that the search will be modified for other named databases, and how and if gray literature will be identified), inclusion and exclusion criteria for studies, information about quality assessment, and *a priori* specification, for example, about how to deal with such methodological issues as heterogeneity.

Final Approval of the Protocol / Public Comments

The project protocol will be posted on the ACR web site for public comment. The ACR Guideline Subcommittee will review and formally vote re: approval of the protocol simultaneous to the public comment period, providing feedback to the guideline development team, if needed. Feedback received via the public comment mechanism and/or the ACR Guideline Subcommittee will be considered as the systematic review begins. If warranted, the PI/Core Team may decide to modify the protocol as a result of this evaluation (especially if required by the ACR Guideline Subcommittee). Responses received during the public comment period will usually be posted online with the final guideline manuscript, including each respondent's name, professional affiliation, city/state, and disclosure. NOTE: To facilitate

meeting major project milestones, the early stages of the literature review (i.e., searching) may occur simultaneous to the public comment period, with modifications made to the searches, if needed, in response to the review comments.

Use of Existing, Current Systematic Reviews

As a general rule, ACR guidelines will be based on systematic reviews that are performed as part of the ACR guideline development process. However, in order to reduce duplication of effort, in rare cases, it may be determined that existing, current systematic reviews or meta-analyses that address the questions of interest to the ACR/guideline developers can be used in the ACR guideline project. These exceptions must be approved in advance by the ACR, and these systematic reviews will be quality-assessed, for instance with the use of the AMSTAR tool.[16] The PI/Core Team reviews the systematic review team's recommendations for use of certain systematic reviews in the project, along with the quality assessment of each systematic review, before conveying its final approval to use them.

Output of Systematic Review / Drafting Recommendations

The systematic review team compiles output from the systematic review to help inform the drafting of recommendations. This information takes the form of evidence summaries that provide simple, transparent summaries of the quality of evaluated studies and their findings relevant to the outcomes being examined in the guideline. The Summary of Findings information includes a qualification of the quality of evidence as very low, low, moderate, or high, based on several factors explicitly outlined in the GRADE methodology.

Once this work has been completed by the systematic review team, each voting panel member is asked to consider the quality of available evidence, judge the balance between desirable and undesirable effects, consider patient / clinician values and preferences as well as resource allocation (i.e., cost), and determine what type and strength of recommendations should be made. The strength of the recommendations is categorized as either "strong" or "conditional."[9] Typically, if voting panel members are very certain that benefits do, or do not, outweigh risks and burdens, they will make a strong recommendation. If voting panel members decide that benefits and risks/burdens are balanced, and/or considerable uncertainty exists about the magnitude of benefits and risks, they may make a

conditional recommendation.[7] In addition, when voting panel members believe that fully informed patients are likely to make different choices based on their own values and preferences despite strong evidence, they will likely offer a conditional recommendation.[7]

Voting Panel Decision-Making

The voting panel members will then vote on guideline recommendations. Sometimes there may be little published high-quality evidence on outcomes of interest. When there is no high-quality evidence and expert opinion is more heavily required when formulating a recommendation, this will be transparently presented both in the guideline development process and the final guideline paper. This is an opportunity to help influence the research agenda for work on the outcome in question.

Finalizing the Guideline Recommendations

Detailed recommendation tables will be developed and will include for each recommendation statement: 1) the overall quality of the evidence related to that recommendation; and 2) the strength of the recommendation (i.e., strong or conditional). Underlying values and preferences of members of the guideline panel should be included in the guideline, if possible, as well as other clinical notes and context to assist with the interpretation and application of the recommendation, as appropriate. Recommendations will be synthesized into a final guideline document for publication in *Arthritis Care & Research* and *Arthritis & Rheumatology* (see below).

Guideline Development, Phase 3: Approval, Publication, and Dissemination

Authorship

Assuming the guideline development team was assembled by the ACR, using an objective process to ensure adequate balance and expertise, authorship is individual, and the project PI will be the first author. Although it is ACR policy that the PI will be first author, the ACR expects the PI to do the requisite work to justify the first authorship position (e.g., lead the project and draft the final guideline paper).

The PI is ultimately responsible for making other authorship decisions (i.e., who is an author and what is the appropriate author order), in consultation with the Core Team and the ACR, and using the guidance of the International Committee of Medical Journal Editors.[17] However, most often the Core Team is listed after the PI/first author, followed by the voting panel in alphabetical order, followed by the systematic review team in alphabetical order, followed by the lead ACR staff person, followed by a last/senior author decided at the start of the project, e.g., a co-PI, Core Team member, or the literature review leader, if not a paid contractor. All individuals are expected to do the requisite work to justify their authorship positions, which can be changed if this requisite work is not being done.

On the rare occasions an objective process is *not* used to determine who will participate on the guideline development team, authorship must be corporate unless an exception is approved by both the ACR and *Arthritis Care & Research* and *Arthritis & Rheumatology*.

Guideline Content and Design Formatting

To make ACR guidelines consistently of high quality, easy to use and more easily identifiable to users, a standardized template is used for ACR guideline papers. The template includes certain sections and language that must be included in every ACR guideline.

ACR staff assist PIs with the initial draft of each guideline, using the ACR template. Core Teams then provide input/revisions, followed by the voting panel and then the rest of the guideline development team, as guideline authors. A guideline summary is also developed.

ACR Approval, Copyright, Journal Approval and Publication

ACR funding or participation does not imply or guarantee ACR approval of the final publication or product of the project. To obtain ACR approval, guidelines must be formally reviewed by the ACR and approved by the ACR Board of Directors. Similarly, ACR approval does not imply journal approval, which involves a separate review process.

The ACR reviews guidelines for approval using standardized processes and templates, against pre-determined review criteria. Manuscripts or other submitted documents are subjected to multiple levels

of review by subject area and methodological experts. The ACR and the journals make independent review and approval decisions, although at certain points the administrative processes overlap for purposes of efficiency. The ACR reassesses its review process, as needed, to promote high quality publications, editorial independence, and timely publication.

Predetermined guideline manuscript standards and limits have been agreed upon between the ACR and journal editors and are included in the ACR guideline template, with exceptions granted only at the discretion of the journal editors. Supporting information is also submitted (e.g., evidence reports, tables, search strategies, detailed recommendations). Supplemental appendices are not peer reviewed in the same way as the manuscript but will be posted online alongside the published guideline paper, on both the ACR and journal sites.

The ACR and journal review process is conducted as follows, and takes approximately 6 months, depending on extent and timeliness of necessary revisions and the timing of ACR committee/Board meetings:

ACR REVIEW: Once the authors approve the initial draft, the guideline and summary are submitted to the ACR for formal review. The paper is reviewed simultaneously by the ACR Guideline Subcommittee and Quality of Care Committee, followed by any necessary author revisions. If recommended for ACR approval, the ACR Board then considers the guideline and summary for final ACR approval.

GUIDELINE SUMMARY POSTING AND JOURNAL PEER REVIEW OF MANUSCRIPT: Once ACR approval is given, the guideline summary is posted on the ACR web site, and the manuscript is submitted for journal review. *Arthritis Care & Research* and *Arthritis and Rheumatology* have the right of first refusal for all ACR guidelines. ACR guidelines are jointly published in *AC&R* and *A&R*, with the journal reviews being overseen by one or the other journal on an alternating basis. ACR staff submit the paper to either *AC&R* or *A&R*, on behalf of the authors, with a notation in the cover letter that the paper is the product of an ACR project and, therefore, journal approval and publication are desired.

Standard journal peer review processes are followed, including probable requests for manuscript revisions before final journal approval. Authors are expected to respond in a timely manner to these requests so the journal review and approval process can be completed as soon as possible. Authors are also expected to complete journal disclosure and author contribution attestations, when requested.

The manuscript is usually published about 4 months after final approval is given by *both* ACR and the journals, although online e-publication of the final, edited manuscript may be achieved sooner and will be the ACR's goal, if possible.

Copyright and Title

ACR guidelines will be copyrighted by the ACR. Upon final approval by the ACR, the recommendations will be known as the ACR *[name of guideline].* ACR guidelines, including any interim updates, will also be published on the ACR website. The review and publication process for an interim update will be similar to that of the original guideline. The interim update may also be published in *AC&R* and *A&R* according to the same process described above, at the discretion of the ACR and its journals.

Dissemination

After a guideline has been approved by ACR and the journals and a final copyedited draft has been produced, a pocket guide and app version may be developed by the PI and/or other guideline team members in conjunction with ACR staff. These tools are posted on the ACR web site alongside the new guideline as soon as it is published or soon thereafter. Their purpose is to provide easy to use references for busy clinicians to remember the key points in the guideline. They are not meant as stand-alone documents that could be used in lieu of the full guideline. Other means of disseminating the guidelines are evaluated and may be pursued by the ACR, as resources and opportunities are available.

Guideline Development, Phase 4: Ongoing Review, Revision and Updating of Published Guidelines

Guidelines can become outdated for a number of reasons, including new studies that report on major or invalidating new evidence, and changes in practice. The ACR's goal is to inform clinicians of changes in research, which will sometimes require the development of completely new guidelines or changes to some recommendations within already published guidelines. ACR funds are allocated and approved for this work, as needed. The decision to update a guideline will be based on sound evaluation and empirical research in order to minimize unnecessary use of resources and time.

Updated Literature Searches

The ACR will update literature searches periodically and evaluate whether a guideline update is needed, and if so, which form the update will take.

*Signals for Updating Clinical Practice Guidelines**

The ACR will review the information resulting from the updated literature searches, to decide if there is a need to update either the entire guideline or some recommendations within the guideline. The ACR looks for major or potentially invalidating changes in evidence, especially for the target population specified in the guideline/PICO(s). Examples include:

a. At least one new high-quality, randomized controlled trial (RCT) with a population at least twice or three times the size of the largest RCT cited in the guideline
b. At least one new meta-analysis with one new trial not considered in the existing guideline
c. At least one new RCT, where before recommendations were based on non-randomized studies
d. RCTs using patient important outcomes (such as quality of life or mortality), where before recommendations were based on surrogates (such as lung function)

If any of the following applies, it is likely that a recommendation update would be warranted:

1. Potentially invalidating changes in evidence
    a. Opposing Findings: New evidence suggests conclusions opposite to those underlying current recommendations

   b. Substantial Harm: New evidence suggests that the intervention would no longer be recommended due to substantial harm
   c. Superior New Treatment: New evidence suggests that another intervention is significantly superior, based on efficacy or harm, such that it would be preferred in most settings

2. Major change in evidence: Recommendation is still essentially valid, but new evidence clearly has the potential to affect clinical decision making
   a. Important changes in effectiveness, but not opposing findings: new evidence suggests that the benefit is greater or less than reflected in the current recommendations
   b. Expansion of treatment
   c. Important Caveat: New evidence suggests an important caveat about the patient population who may benefit, way in which treatment has to be delivered, sustainability of benefit, or increases in harm not sufficient to undermine use altogether but that would affect the decision to recommend the intervention for at least some patient populations.

Options for ACR action following evaluation of the evidence^

NO NEW EVIDENCE, NO CHANGES TO GUIDELINE/RECOMMENDATIONS**:** Publish an update on the ACR website, with a notice in *Arthritis Care & Research* and *Arthritis and Rheumatology.* In addition, insert a notation within the most recent version of the guideline paper published online, referring to the update that is now available on the ACR website. In the update on the ACR website, report the search strategy for the updated literature search and the ACR review process, including dates and number of abstracts / studies reviewed, and indicate that no new evidence has been identified and thus no changes were made to the recommendations. This update will be developed by the Guideline Subcommittee and ACR staff, possibly in conjunction with the guideline PI and/or other experts. The Board of Directors does not need to approve the update.

NEW EVIDENCE, BUT NO CHANGE TO RECOMMENDATIONS**:** Same e-update approach as above, with summary of updated search and review, plus identification of references for new evidence within the update posted on the ACR web site. The Board of Directors does not need to approve the update. Same approval process as above.

The QOC will provide an annual verbal report to the ACR Board of Directors on updates for the above 2 options.

NEW EVIDENCE, AND RECOMMENDATIONS CHANGE**:** The regular ACR guideline development, review and approval processes are used, and the updated guideline is published in *Arthritis Care & Research* and *Arthritis and Rheumatology* and posted on the ACR website.

For drugs or other therapies that have been withdrawn (e.g., due to harm), a notice is appended to the guideline on the ACR website, a notice is printed in *Arthritis Care & Research* and *Arthritis and Rheumatology,* and if possible, this notice is linked to the guideline published online at *Arthritis Care & Research* and *Arthritis and Rheumatology.*

In these cases, the Board of Directors will formally review the changes based on the new evidence and approval by the Board of Directors will be required.

^Options for ACR action following the evaluation of evidence: Adapted and reprinted with permission. (c) 2011. American Society of Clinical Oncology. All rights reserved.

Guideline Development: Disclosure and Conflicts of Interest

The intent of disclosure of relationships, including but not limited to any potential conflict of interest, is to ensure that ACR guidelines are balanced, independent, objective, and scientifically rigorous. The ACR requires each guideline project development group member and others who contribute intellectually to the guideline development effort to disclose all information regarding their relationships, including any possible conflict of interest, financial or otherwise.

Activities related to the Committee on Quality of Care and its subcommittees, including the Guideline Subcommittee, should be free from actual or perceived industry influence. Therefore, the ACR does not utilize external support from commercial entities and insurers/health plans for activities of the QOC or its subcommittees. In addition, the QOC does not review quality-related products for ACR approval if industry funding was used to support their development. On a case-by-case basis, support may be considered for dissemination materials or strategies.

Disclosure of relationships and management of potential or real conflicts of interest are important at every level of the QOC's work, from prioritizing topics and selecting projects, through development and ACR approval of final papers.

Committee on Quality of Care (QOC) / Subcommittee Disclosure and Management of COI

The QOC and its subcommittees, including the Guideline Subcommittee, are guided by two main principles related to disclosure and management of conflicts of interest. One relates to general discussions and decisions, and the other is more specific to particular projects.

- Members of QOC and its subcommittees should not influence policy decisions based on their relationships with outside organizations, and members should be aware of each other's relationships**.** Therefore:
    - QOC members provide written disclosures once each year and update these disclosures as needed during the year. They also verbally disclose at the start of every face-to-face meeting. The QOC chair receives copies of the written disclosures annually for review.
    - QOC subcommittees also disclose verbally at the start of every meeting.
    - Members recuse themselves from any discussions where a potential COI or the appearance of COI exists.

- Members of QOC and its subcommittees should not preferentially receive funding from the ACR through the QOC, and members' presence should not influence committee decisions about projects in which they are involved. Therefore:
    - No members are involved with developing a Call for Letters of Interest to which they plan to respond. Members who are interested in responding to Calls for LOI declare this conflict before the call is conceptualized and recuse themselves from all subsequent QOC / subcommittee discussions related to those calls.
    - Members who have been suggested as possible guideline development team members recuse themselves from any discussions related to confirming that project team (or competitors).
    - If members are involved in projects, they are recused from any future QOC or subcommittee discussions related to their projects that involve decision-making and/or problematic situations with the projects. They may participate in informative project update discussions, at the committee's discretion.

Project-related Disclosure and Management of COI

Disclosures of relationships are obtained from anyone contributing intellectually to an ACR guideline development project, using either the ACR or the journals' disclosure mechanisms, depending on the stage of the project/review. This disclosure happens at various points in the application, development, and approval process, both in writing and verbally. See Table 1 below for more detail about who is expected to disclose and when.

Letter of interest phase

People responding to an ACR Call for Letters of Interest must fully disclose their relationships immediately after they submit their LOI, using the ACR online mechanism. Completed ACR disclosure information must be included for anyone who is proposed to be intellectually involved in the guideline development project. Each form should list all relationships, including recent (i.e., within 1 year before LOI deadline), existing, and planned (i.e., known at the time the form is completed but not yet begun).

When developing a Call for Letters of Interest, the ACR proactively identifies companies and organizations that may be affected by the work. This "affected companies" list includes but is not limited to pharmaceutical, biotechnology, or other companies that manufacture or market products or therapies that might be affected by the ACR's work, or competitors of these companies. Affected companies are ones that are reasonably likely to be positively or negatively affected by care delivered in accordance with the guideline. The list of affected companies is included in the Call for LOI, with a requirement that disclosures related to these entities must be explicitly included in the written disclosures submitted as part of the Letter of Interest. Note that the affected companies list provided by the ACR is not meant to be all-inclusive, but rather, to provide guidance for individual disclosure; applicants who have relationships with other affected companies, as defined above, must also explicitly disclose that information and indicate to the ACR that the relationship would likely be considered COI per the ACR's definition of an affected company.

PIs (or multiple co-PIs, if applicable) of guideline development projects are expected to be free of conflicts of interest (COI) relevant to the subject matter of the project for at least one year prior to the

LOI deadline, throughout the project until publication, and they are expected to remain free of such conflict of interest for at least one year after publication. The literature review leader is held to these same expectations.

The majority (at least 51 percent) of the guideline project development group must be free of conflicts of interest relevant to the subject matter of the project for at least one year prior to the LOI deadline and throughout the project until publication. Similarly, at least 51% of the Literature Review Team and 51% of the Voting Panel must have no conflicts of interest related to the subject of the guideline. NOTE: The 51% unconflicted threshold is a *minimum*; the ACR's goal will be to have significantly more than 51% unconflicted participants overall and on each smaller subgroup to allow for unanticipated mid-project personnel shifts (e.g., a participant drops out due to illness or schedule changes).

The conflict of interest thresholds will be based on an evaluation of relationships, primarily with affected companies. Unless their relationship completely excludes them from participation (e.g., industry employment), a person who has any relationship with an affected company is counted as conflicted (toward the allowed threshold) regardless of the type or subject of the relationship. Finally, although intellectual conflicts of interest are important and should be disclosed, they are ubiquitous and, therefore, the ACR does not count someone with intellectual COI as conflicted (toward the allowed threshold) based on the intellectual conflict alone.

The intent of ACR disclosure/COI policies is not to exclude all investigators with potential conflicts from participating in the project, but to manage such conflicts in a prospective, structured, and reasonable manner to minimize the likelihood of inappropriate influence of such conflicts on guideline development. Specifically, the ACR's disclosure and COI policies and procedures are meant to deal with individuals' conflicts that may potentially bias how evidence is chosen, assembled, assessed, and synthesized, or bias the recommendations based on such evidence. The description of strategies for managing conflicts related to the specific agents and approaches used to treat the target disease will be explicitly laid out in the final manuscript. This process and information will be considered in the review process.

If the Guideline Subcommittee seeks input from topic area experts when making decisions about the guideline development group, these experts must disclose their relationships before they are confirmed, and they may not include any individuals employed by or engaged to represent an affected company.

Development phase

Once a group has been named by the ACR to do the development work, the PI and ACR staff share responsibility for ensuring that any changes in the composition of the guideline development group do not adversely affect the balance originally established in the group. If a person drops out of the group mid-project, an evaluation of the effect on overall group balance is done, and an additional participant may be sought, if needed. If a person needs to be added to the group mid-project, the person will be asked to complete an ACR disclosure form, which must be considered and the person's involvement approved *before* officially inviting the person to participate. If approved to participate, the new person's disclosure information is then shared with the rest of the group.

Similarly, the ACR staff and PI share responsibility for monitoring how any mid-project changes to a group members' disclosure/COI might affect the required majority (51%) of development group participants without COI.

Guideline development group members are required to provide disclosure at the start of the project and update their disclosures during the project whenever relationships change. They are proactively asked to review and update their initially provided disclosures *at least* 1) immediately before the voting panel meeting(s) where final recommendations are decided; and 2) just before the final guideline manuscript is submitted to the journal. Disclosures are shared with the public in a project plan that is posted online as the project begins and also in the final publication. Disclosures are shared verbally by members of the Core Team at their first meeting, and at intervals determined by the PI, but not less than every 6 months. In addition, disclosures are shared in writing and verbally with voting panel members just before and during the voting panel meeting(s), for the purpose of full transparency in the discussions.

If the project's allowable COI thresholds are in jeopardy at any time during the project (e.g., due to unconflicted participants dropping out because of illness or schedule conflicts, or becoming employed by industry), immediate efforts are made to rebalance the overall group and relevant sub-team(s), often by inviting additional unconflicted individuals to participate.

Guideline project development group members or ACR representatives may not discuss a guideline's development with employees or representatives of affected companies. In addition, they may not accept unpublished data from affected companies, nor permit affected companies to review guidelines in draft form.

Post-development / Final publication phase

All ACR-approved guidelines must include in the final publication full (not just relevant) disclosures of relationships from authors and anyone who contributed intellectually to the work, plus members of the ACR Guideline Subcommittee, who were responsible for reviewing the paper. Papers must also reference 1) disclosures of the members of the ACR QOC and Board of Directors (at the time the paper was reviewed and approved), which are made publicly available online, in perpetuity; and 2) any abstentions from voting during guideline development processes.

Individuals who drop off the project before completion are identified as such in the final publication, either on the author list (if the project is near completion and their involvement already warrants authorship) or in the acknowledgements section. Individuals who become employed by industry midway through the project are immediately ineligible for further participation in the guideline effort. Their names are listed in the final publication acknowledgements section with a footnote that their project involvement occurred only before their industry employment. Unless the guideline is already final and in queue for publication, they cannot remain as authors because, as industry employees, they would not be allowed to review and sign off on the final paper.

All members of guideline development teams are expected to decline offers from affected companies to speak about the guideline on behalf of a company, in any setting, for a period of one year after publication of a guideline. PIs (or co-PIs, if applicable) of guideline development projects are expected to

remain free of COI for at least one year after publication; the ACR has the same expectation of lit review leaders.

If there are any ACR manuscript reviewers who are not members of the ACR Guideline Subcommittee, the QOC, or the ACR Board, they must submit written disclosures as part of the reviewer selection process before they are sent the guideline for review. Because non-committee manuscript reviewers are confidential, neither their names nor their disclosures are made publicly available.

Table 1: Disclosure Requirements for Guideline Development Projects

	In writing	**Verbally**
PI applicant, and all members of the guideline project development group, including systematic review team and voting panel members	Initially via ACR disclosure mechanism provided immediately after receipt of LOI or via separate communication from ACR (if the person's name was not included in an LOI), then update every 6 months	At start of mtgs/calls, including immediately before panel deliberations/voting begins
Experts/consultants who provide guidance on any aspect of application review, development or final review/approval process	At the point of involvement, then every 6 months, if longer term involvement; via ACR disclosure mechanism	At start of mtgs/calls

	In writing	Verbally
Voting Panel Members	See above (i.e., initially via ACR mechanism provided immediately after receipt of LOI or via separate communication if the person's name was not included in an LOI), then update every 6 months)	At start of mtgs/calls, including immediately before panel deliberations/voting begins
Manuscript authors	At time of manuscript submission to journal, via journal form	
Non-committee manuscript reviewers (ACR) (if any)	As part of ACR reviewer selection process, via ACR mechanism, before they are confirmed and sent the manuscript for review	
Manuscript reviewers (journal)	Journal manuscript reviewers are required to disclose relationships and provide an explanation of any COI, then journal editors decide whether they will serve as reviewers	
Staff (methodological/content contributors, not admin. staff)	Initially via ACR mechanism, then update every 6 months	At start of mtgs/calls, including immediately before panel deliberations/voting begins

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